GEORGIS' PARASITOLOGY FOR VETERINARIANS

NINTH EDITION

Dwight D. Bowman

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Preface

In the ninth edition of *Georgis' Parasitology for Veterinarians,* the text begun by Jay and Marion Georgi, I have worked to change most of the images to a color format. Fortunately, many of the images that were originally captured by the Georgis in black and white were also photographed in color, making it possible to have many of the same images appear in this edition as they were originally viewed. At the same time, not every single image was available in color, and some would not benefit much by a color presentation. The various images that were captured using differential interference contrast, especially the unstained nematodes, appear basically gray under the microscope and remain just as crisp in a black and white format as they would in color. Also, some of the black and white images have been retained because they are historical and represent prior work that was done at a time when black and white art was the major form of presenting illustrations in publications, as in the images originally collected by Dr. John H. Whitlock and images that were published elsewhere in black and white. In some cases, color images were not available for every single parasite in a plate, and in those cases the black and white plates were maintained, giving us something to strive for in the next edition.

The American Association of Veterinary Parasitologists (AAVP) has worked hard, through the donated time of Drs. Anne M. Zajac of Virginia Tech and Gary A. Conboy of the University of Prince Edward Island, to generate a color edition of *Veterinary Clinical Parasitology*. This is a great book, and I consider it an excellent ancillary text for anyone routinely working on parasite diagnosis. The funds generated by their text support the continued efforts of the AAVP, and I strongly support use of the text.

I have had a good deal of help in preparing this edition. Dr. Hanni Lee, now in a residency in Comparative Medicine, University of Missouri-Columbia, helped with preparing many of the color images of arthropods, protozoa, and platyhelminths for the text, and her help is greatly appreciated. Dr. Danielle Armato, now practicing veterinary medicine in Manhattan, assisted with a rewrite of the section regarding annotated parasite lists in the chapter on diagnostics to make them more informative. Dr. Araceli Lucio-Forster, with me here at Cornell, through her work in diagnostic instruction of third- and fourth-year veterinary students helped find many of the additional parasites, eggs, and cysts that have been added new in color format. Overall, this has been labor intensive, but great fun. Drs. Lee, Armato, and Lucio-Forster have worked hard to help give the new edition its new look.

I have tried to update the text while also keeping basically the same structure of the older editions. Because of the current interest in vector-transmitted disease, I asked Dr. Susan E. Little, who holds

the endowed Krull-Ewing Chair in Veterinary Parasitology at Oklahoma State University, to add a chapter on these diseases for this edition. We parasitologists never could figure out the best way to fit into a text the various microbes that do not usually fall under the umbrella of animal parasitology but yet are pathogens that we believe need to be discussed. I think readers will find the chapter very helpful.

In his chapter and throughout the text, Dr. Randy C. Lynn, of IDEXX Pharmaceuticals, worked to update information on all the antiparasitics currently in use. We have also worked to upgrade the tables of antiparasitics in the major hosts; however, it is almost impossible to keep the list up to date—an indication of how great an effort is expended by our industrial colleagues to continuously supply better products for parasite control and treatment. To Dr. Lynn's chapter on antiparasitics has also been added a table by Dr. Marshall W. Lightowlers, associate professor in the Faculty of Veterinary Science of the University of Melbourne, on vaccines against parasites. Not all of these vaccines may be available in the United States, but they are out there, have been used in some regions for years, and still show great promise in some areas for parasite control. It seemed time to try and summarize them for practitioners.

Dr. Mark L. Eberhard, of the Division of Parasitic Diseases, Centers for Disease Control and Prevention, has reworked the chapter on parasites in tissue sections. This chapter could be a book

in its own right, but as it is serves as a very good introduction to how to identify the parasites that pathologists see. It is hoped that the color images help in presentation of this material.

Dr. Hanna M. Roisman, of the Classics Department of Colby College, has helped me again with the various derivations of many of the parasitology terms that appear on the front and back inside covers of the text. She also provided assistance as I worked through the terminology that appears in Chapter 1 in which I attempt to define zoonosis as it relates to disease transmission among animals. Veterinarians need to remain highly active in this field, because many diseases found in wildlife are highly devastating to domestic animals and also because of animal diseases that can be transmitted to humans. I really think that words are useful although they may not enter common usage. It has also been great fun to periodically delve into matters outside the world of parasitology, such as the relationship of Odysseus to *The Usual Suspects* and Greek predestination within the *Terminator*.

I thank my colleagues within Cornell, especially Drs. Barr, Simpson, Hornbuckle, Smith, Nydam, Ducharme, Miller, Scott, and McDonough, who keep me refocused on matters veterinary; all the colleagues in AAVP and industry who are always there to help when needed; and, of course, all my students, past, present, and future, who make the whole thing worthwhile.

Finally, I thank Don O'Connor for his help with the new color drawings for the text. I really also want to thank the staff at

Elsevier—Jolynn Gower, managing editor, Anne Altepeter, senior project manager, and Amy Buxton, design manager—for helping me work through this edition, which underwent significant reorganization and to which many new images were added. They have given much time to making the book look great and to seeing to it that the text was carefully edited throughout. The effort was considerable, and they made what could have been a highly strenuous and taxing project something that was fun and productive. I hope that you the reader will find the new edition a marked improvement over the eighth edition and a useful resource in your study of veterinary parasitology.

On a final note, for years now I have been using the term "xenodochology" for the study of the host in opposition to the word "parasitology" for the study of the parasite. I have read about the word and the various hostels, or "xenodochoi," that sprang up in Europe for travelers in the Middle Ages. I even garnered at one point while working in immunoparasitology in Wisconsin within the laboratory of Dr. Robert Grieve (where I spent three wonderful years working with Marsha Mika-Grieve, David Abraham, Jim Parsons, Glen Frank, and Meisen Mok) a T-shirt inscribed with the word "Xenodochologist." Thus it was

to my great enjoyment when out looking into a system that can produce hydroponic lettuce without white fly contaminants that I drove down a country road past a barn (see figure) emblazoned with the words “Xenodocha Stock Farm.” The owner did not know from whence the name derived, but had kept the name on the barn. So, there was a hostel for bovine hosts for many of the parasites that have been of such critical importance in the development of veterinary parasitology. You can often stumble upon great and simple pleasures in places where you least expect them.

Dwight D. Bowman

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CHAPTER 1

Introduction

COMMON TERMS IN PARASITOLOGY

A **parasite** is a smaller organism that lives on or in and at the expense of a larger organism called the **host**. A louse is a parasite and so is a virus. The host's expenses in supporting its parasites may be trivial, or they may be substantial or even unbearable. This depends on the number of parasites, the kind and degree of injury they inflict, and the vigor and nourishment of the host. A series of terms (e.g., *mutualism, commensalism*, and *parasitism*) have been defined to express the degree of unilateral or mutual injury or benefit that is characteristic of particular symbiotic relationships. As a matter of convention, however, if the smaller organism is found in association with humans or with animals or plants that humans esteem, it is called a *parasite*, whether its presence is detrimental, indifferent, or beneficial. This convention is adopted in this book and is harmless enough provided we remember that parasites vary in pathogenicity.

A **species** of animal is an interbreeding natural population that is reproductively isolated from other such populations. For example, there are two species of rather distantly related ascarid parasites of dogs, *Toxocara canis* and *Toxascaris leonina*. These two species are sufficiently similar in size and appearance to present some difficulty in their differentiation, but although they may share the small

intestine of the same dog, they never interbreed. The consequent distinctness of their genetic material is expressed in modest differences in structure and in very substantial differences in life history. *T. canis* and *T. leonina,* however, share enough similarities to make their kinship obvious. We assume that these similarities stem from the evolution of both species from common ancestral stock (divergent evolution) because the number and nature of the similarities induce us to reject the alternative explanation—i.e., that they represent the adaptations of unrelated forms to the same selection pressures (convergent evolution). We recognize kinship of *T. canis* and *T. leonina* by considering them both to be members of the same zoologic order (Ascaridida); each is a leaf, if you will, on the same evolutionary branch.

CONVENTIONS OF TAXONOMIC CLASSIFICATION

Classification is an inductive process. Unfortunately, for those who seek perfection in the correspondence of the classification scheme to the true history of evolution, there is very little objective evidence of the kinship of parasites. The progenitors of the horse *(Equus caballus)* left a clear fossil record of equine evolution, but the ancestors of our parasites merely rotted and withered away, leaving only an occasional trace. The entire hierarchy of taxonomic categories above that of species (genus, subfamily, family, superfamily, suborder, order, class, and phylum) is built of subjective inductions based on degrees of similarity and dissimilarity among the various groups of organisms. Fortunately, the result is nonetheless useful to us in organizing our information about parasites in an orderly and logical way. In short, any

particular zoologic classification scheme is no more than an opinion about how the relationships among various groups of organisms may best be expressed.

It is helpful to be acquainted with a few nomenclatural conventions. The full zoologic name of an animal is a **binomen** consisting of the genus name followed by the species name. The genus name is capitalized and both genus and species names are italicized in print or underlined in manuscript, e.g., *Filaroides milksi*. In taxonomic publications and in other scientific and professional journals, the zoologic name is followed by the name of the person(s) who described the species in question and the date that the description was first published, e.g., *Filaroides milksi* Whitlock, 1956. If, at a later date, another taxonomist decides for one reason or another that this particular species really ought to belong to a different genus, the original describer's name is now placed in parentheses and the name of the taxonomist that moved the species may follow outside the parentheses, e.g., *Andersonstrongylus milksi* (Whitlock, 1956) Webster, 1981. We are not forced to accept Webster's opinion and may continue to call this species by its original name, *Filaroides milksi*, if we believe that we have good enough reason to do so. The species *milksi* is objective in that it is based on real and tangible specimens that Whitlock studied and described in 1956. Assigning *milksi* to any particular genus is, however, largely subjective and based on taxonomic judgment. That is why we frequently come across the same species relegated to two or even more genera.

Certain categories have characteristic suffixes that help to identify them. For example, the genus *Strongylus* belongs to the following

hierarchy of higher taxa: subfamily Strongylinae, family Strongylidae, superfamily Strongyloidea, order Strongylida. In this text the suffixes *-inae*, *-idae*, *-oidea*, and *-ida* are applied to all subfamily, family, superfamily, and order names.

The principal objectives of zoologic nomenclature are to promote stability and universality of zoologic names and to ensure that each name is unique and distinct. Not every taxonomist is hard at work changing the names to confuse others, as students are prone to suspect.

IDENTIFICATION AND DIAGNOSIS

Identification is determining which taxonomic groups a species belongs to, whereas diagnosis is determining the cause and nature of a case of disease. Both are deductive processes. The diagnosis of parasitism per se requires only that some life stage of the particular species of parasite be identified. Diagnosis of parasitic disease requires much more. In fact, interpretation of the significance of the information regarding the parasite or parasites identified in a particular case of disease frequently taxes our knowledge and interpretive skill to the utmost. In a very few cases, we have a direct cause-and-effect relationship to make it easy. For example, *Haemonchus contortus*, a nematode parasite of sheep, causes disease when the mass of worms present in the abomasum sucks more blood than the sheep can replace, and the disease haemonchosis, manifested as clinical anemia, results. If too few *H. contortus* worms are present to overtax the hematopoietic capacity of the sheep or if a particular sheep manages to make restitution for blood loss that might lay another low, the case is one of subclinical *H. contortus*

infection. Simply put: no anemia, no haemonchosis. One makes the diagnosis of haemonchosis by examining the visible mucous membranes or a sample of blood for evidence of anemia.

Diagnosing haemonchosis is easy. It is very much more difficult to evaluate the clinical significance of most other parasitic infections. For example, when the veterinarian is confronted with a case of chronic diarrhea, finding a few coccidian oocysts in the animal's stool may mislead the veterinarian to neglect other possible causes and jump to the conclusion that the animal has the disease coccidiosis when in fact the coccidian infection is incidental. The specific identity of the cysts in the feces supplies the diagnostician with a concrete fact that may, in the midst of uncertainty, prove nearly irresistible. A difficult situation indeed, and there are many more like it. In this book we have tried to present information helpful in deciding when parasites are responsible for clinical disease and when they are not. In truth, there is much still to be learned.

Identification of the common parasites of domestic cats, dogs, cattle, sheep, goats, horses, and pigs is a relatively simple matter. It requires only one semester of study to get fairly good at it. By restricting the scope of the problem to particular host species, it is possible to simplify identification criteria, accommodate reasonably complete sets of illustrations in the available space, and make helpful lists of the kinds of parasites likely to be encountered in particular organs. Chapter 7 is devoted to such criteria, illustrations, and lists. However, when the scope of interest is broadened to include exotic pets and captive and wild mammals and birds, such a detailed approach would inevitably lead to a shelf full of books.

Fortunately, many shelves full of books are already to be found in the better academic and municipal libraries, and that is where we must go to get the necessary information. The first step is to determine the scientific name of the host species; if we don't already know it, *Webster's International Dictionary* is the best readily available general source of this information.

Finally, it should be remembered that when we find worms or various diagnostic stages of parasites, our goal is typically to determine the species group to which the individual specimens belong. However, we do not "speciate" parasites, we simply identify them. *Speciation* refers to something done by a creature as it evolves from one species type to another. Therefore the only thing that can speciate is the creature itself. The term *speciation* should be restricted in its usage to discussions that deal with how species originated, such as discussions about new species and beak shapes on the various finches of the Galapagos.

RELATIONSHIP BETWEEN PARASITES AND HOSTS

A number of terms are useful relative to the study of parasitology in general. Animals that live in close association with each other are called **symbionts** living together in the process of **symbiosis**. This has been further characterized for certain specific types of relationships. In the case of **mutualism**, one of the hosts benefits while the other just exists; this is what occurs with the various ciliates and bacteria that live within the rumen of a ruminant. When the two organisms just live together and neither "loses" or "wins," the condition is called **commensalism**, and the organisms living in this way are called **commensals**. An example might be the various

amoeba that live within the cecum and colon of cattle and sheep for which no disease has ever been recorded. In the case of **phoresis**, one organism serves to carry the other organism from place to place. This is what takes place in the live history of the fly *Dermatobia hominis*, which uses other flies to carry the larvated eggs to the vertebrate host that becomes infected. Finally, in the case of **parasitism** (quoting Dr. James Law) "one of the two draws its subsistence from the other to the appreciable injury of the latter." The parasite, by definition, has negative effects on its host.

There are some terms relative to parasites in specific that are used in certain ways by convention. Thus, **endoparasites**, parasites within the bodies of hosts, are considered to produce **infections**, whereas **ectoparasites**, those that live on the external surface of a host or in the skin, are said to cause **infestations**. Some parasites are considered to be **obligate parasites:** they always require a host. Other organisms are parasites only if given the opportunity, and they are termed **facultative parasites** (e.g., *Balamuthia mandrillaris* and *Halicephalobus gingivalis*). Hosts that live only on or in a single host are considered to be **host-specific**, with classic examples being the various lice of birds and mammals. The host in which the adult or sexually reproductive processes of the parasite occur is called a **definitive host**. A host in which there is required development of intermediate or larval stages is called an **intermediate host**. In the case of a **paratenic host**, the host is infected with a parasite that does not undergo any required development, although the parasite sometimes can grow very large in the chain of paratenic hosts that are used (as in the piscine hosts of the larvae of *Diphyllobothrium latum*). Organisms that transmit parasites from host to host are

termed **vectors. Mechanical vectors** are basically living contaminated syringes, i.e., they are not essential in the normal life cycle of the organism being moved from host to host. In the case of a **biologic vector**, the vector is required in the life cycle of the parasite.

Parasites may cycle in different animals than those we consider the host of interest, and these hosts are considered **reservoir hosts**. When parasites are present at some stable rate in a population, they are said to be **endemic** (although for animals the more appropriate term is really **enzootic**). If the disease is present at a very high level in a population, it is said to be **hyperendemic. Endemicity** is often measured in terms of **prevalence**, the percentage of infected individuals in an area at any given time. **Incidence** refers to the rate at which new infections are occurring within a population, e.g., new cases of heartworm in California in the past 6 months. When there is a sharp increase in incidence with a concomitant rise in the prevalence, the term that is used is **epidemic**. There are similar terms that are used specifically for animals—**enzootic, hyperenzootic, epizootic**—but these are unfamiliar to many, so often the human-related terms are used instead.

The term **zoonosis** means literally a disease of animals, but the word has come to mean a disease of animals transmitted to people. Hoare (1962) cited four terms to describe pathogen transmission between humans and animals.

1. **Anthropozoonosis** (etymologically, simply a disease of humans and animals) defines a disease of humans acquired from animals, e.g., rabies, plague, brucellosis, leptospirosis, Rhodesian sleeping

sickness, tick-borne encephalitis or relapsing fever, babesiosis, ehrlichiosis, Chagas' disease, and trichinosis.

2. **Zooanthroponosis**, considered by some as "reverse zoonosis," defines a disease of animals acquired from people—e.g., transmission of *Entamoeba histolytica* to cats, *Giardia lamblia* to dogs, tuberculosis to cattle, or *Schistosoma mansoni* to baboons.

3. **Amphixenosis** (etymologically, disease of both hosts) defines an infection interchangeable between people and other vertebrates, e.g., Chagas' disease, *Schistosoma japonicum*, or *Staphylococcus* species.

4. **Anthroponoses** (etymologically, disease of humans) defines infections restricted to humans that evolved from infections of lower animals—e.g., malaria, typhus, and relapsing fever.

Other terms presented included *euzoonosis* for infections common to humans and reservoir hosts (probably the same as amphixenosis), e.g., *S. japonicum* in humans and various mammals, and *parazoonosis*, in which humans are infected with a zoonotic agent only rarely, e.g., canine heartworm.

The biology of agents has also been defined relative to zoonosis. **Cyclozoonosis** describes zoonotic agents restricted to vertebrates, e.g., *Taenia solium*. M**etazoonosis** describes agents that cycle between vertebrates and invertebrates, e.g., malaria. **Saprozoonosis** is for agents cycling between a vertebrates and nonanimal hosts, e.g., *Fasciola hepatica* with metacercariae on vegetation.

No words are apparently in existence to address the transmission of agents from wild to domestic animals and the opposite, the

transmission of pathogens from domestic animals to domestic or wild animals. Infections of animals with agents for which they are atypical hosts are herein divided into three groups (ignoring the infections shared between different wild animals): (1) infection of domestic animals with pathogens from wildlife, (2) infection of domestic animals with pathogens of domestic animals, and (3) infection of wild animals with pathogens of domestic animals. I have worked with Dr. Hanna Roisman, the Francis F. Bartlett and Ruth K. Bartlett Professor of Classics, Classics Department of Colby College, Waterville, Maine, to develop terms that aid in defining these conditions.

Zootherionosis (*zoon*, animal + *therion*, wild animal + *o* + *nosos*, disease) is used to define diseases of domestic animals infected with pathogens of wildlife. The classic example is the infection of imported domestic animals with African wildlife trypanosomes. Other examples include infections with *Leishmania*, plague, Lyme disease, and rickettsiae from rodent reservoirs; the viruses of foot and mouth disease and avian influenza, and Hendra and Nipah viruses; larval infections with *Alaria* species, spargana, tetrathyridia, larval *Baylisascaris procyonis* and *Armillifer armillata*, and bots of *Cuterebra;* and horses and cats, which serve as hosts of the asexual stages of the equine protozoal myeloencephalitis agent, *Sarcocystis neurona*. Cats are lethally infected with *Cytauxzoon felis* of the bobcat. Infections with sexually mature pathogens include the trematodes *Paragonimus kellicotti* in dogs and cats, *Fascioloides magna* in cattle and sheep, *Alaria marchianae* and *Platynosomum fastosum* in cats, and *Heterobilharzia americanum* in dogs; the cestodes *Spirometra mansonoides* in dogs and cats and *Thysanosoma* and *Wyominia* in

domestic ruminants; and the nematodes *Parelaphostrongylus tenuis* in ruminants, *B. procyonis*, *Dracunculus insignis*, *Onchocerca*, and *Dioctophyme renale* in dogs and *Lagochilascaris minor* in cats.

Zootithasonosis (*zoon*, animal + *tithas*, tamed + *o* + *nosos*, disease) is used for those cases in which a pathogen from one type of domestic animal infects other domestic animals. Feline panleukopenia virus adapted to dogs, causing a global outbreak of canine morbidity and mortality. Bovine diarrhea virus infects sheep and goats, causing border disease. Cats infect dogs with ringworm, *Microsporum canis*. Cats and ferrets are parasitized with adult canine heartworms, *Dirofilaria immitis*. *Trichostrongylus axei* of ruminants infects the domestic horse. Cats and rabbits develop visceral larval migrans from infections with the dog roundworm, *T. canis*. The cat roundworm, *Toxocara cati*, causes white spot disease in the livers of pigs. Ruminants are infected with taeniid tapeworms of dogs and large cats. The cat can be a host of the coenurus of *Taenia serialis*, which uses dogs as final hosts.

Theriotithasonosis* is used for those cases in which wild animals can be infected with pathogens from domestic animals. Lions in the Serengeti and in captivity have succumbed to a variant of the distemper virus from dogs. Wolves, coyotes, and African wild dogs have been infected with canine parvovirus from domestic dogs. Macropodid marsupials sometimes are infected with ovine Johne's disease bacteria (*Mycobacterium avium* subspecies *paratuberculosis*). Domestic goats infect wild goats with infectious keratoconjunctivitis *(Mycoplasma conjunctivae)*. Domestic cattle with contagious bovine pleuropneumonia (*Mycoplasma mycoides* subspecies *mycoides* [small colony type]) have infected African water buffaloes and zebu cattle.

T. canis routinely infects rodents and birds and can infect tortoises. *Toxoplasma gondii* causes infections in numerous wild animals and has now been reported to cause disease in aquatic mammals. Adult heartworms cause disease in sea lions, and *Dicrocoelium dendriticum* causes infections in deer, rabbits, and woodchucks.

REFERENCE

Hoare CA. Reservoir hosts and natural foci of human protozoal infections. *Acta Tropica*. 1962;19:281.

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* Because there is no one word in Greek for domesticated animals (unlike *therio* for wild animals), the full words should have been *tithasozootherionosis, tithasozootithasozoonosis,* and *theriotithasozoonosis;* however, we opted for simplicity and sonority. The term for infection of wild animals with agents from other wild animals would be *theriotherionosis,* abbreviated to *therionosis,* simply, a disease of wild animals.

TABLE 2-2 Some Details on the Times Required for the Life Cycle Stages of Various Diptera, Fleas, and Lice*

Group	Egg (persistence and time to hatching)	Larva	Pupa	Adult Life Span	
				Male	Female
NEMATOCERA					
Mosquito	Days to years	7 days	2-3 days	1 wk	4-5 mo; can hibernate
Blackfly	3-7 days diapause	7-12 days	2-6 days	2-10 wk	Weeks to months
BRACHYCERA					
Tabanid	5-7 days 1 generation/year in temperate climates	1 yr 6 mo-3 yr	1-3 wk	Few days	Months
CYCLORRHAPHA					
Musca	8-12 hr 10-12 generations/summer	5 days	4-5 days	<Females	2-10 wk; can hibernate
Stomoxys	1-3 days	9-60 days	4-9 days	Weeks	
Haematobia	1 day	4-8 days	6-8 days (overwintering stage)	Weeks	
Calliphorid	6-48 hr	3-9 days	5-10 days		35 days
Cochliomyia	11-21 hr	3.5-4.5 days	7 days		Weeks
Sarcophagid	Often skipped	14 days			Weeks
Melophagus	Skipped	Hours (10-12/female)	3 wk		4 mo (1 mo to mature)
Gasterophilus	5 days	9-11 mo	3-5 wk		Weeks (early spring)
Hypoderma	5-7 days	8-11 mo	4-5 wk		Weeks
Oestrus	Skipped	25-35 days or 8-10 mo	Hibernation or 3-6 wk		4 wk
FLEAS: SIPHONAPTERA					
Ctenocephalides	2-21 days	9-15 days	7 days-1 yr		Weeks (can be kept alive a long time in laboratory)

LICE: PHTHIRAPTERA (SIMPLE METAMORPHOSIS)

Group	Egg	Nymph (no larvae or pupae)	Adult
Pediculus	7-9 days	9-11 days	30 days
Haematopinus	11 days	11-22 days	14 days
Felicola	10-20 days	14-21 days	14-21 days
Trichodectes	7-14 days	14 days	20 days

*These represent generalities.

CHAPTER 2

Arthropods

Arthropods are a group of organisms composed of the familiar insects, spiders, crustaceans (e.g., shrimp), and a few other types of organisms. The body of a typical arthropod is composed of a series of segments, some of which bear jointed legs. Not all arthropods display these characteristics. Body segmentation has all but disappeared with the evolution of the mites and ticks, and many insect larvae have no legs. Adaptation to parasitism has led to extreme deviation in body form in certain cases. For example, mites of the genus *Demodex* have evolved into tiny cigar-shaped organisms that fit comfortably into the hair follicles and sebaceous glands of the skin. An even more extreme example is provided by *Sacculina*, a relative of barnacles that grows like a plant's root system in the body of its crab host. However, most parasitic arthropods resemble their free-living relatives morphologically but differ from them in quite remarkable physiologic and behavioral adaptations to the parasitic mode of life. For example, the bloodsucking stable fly, horn fly, and tsetse strongly resemble their scavenging cousin the common housefly, and there is no obvious morphologic difference among the many species of maggots that thrive in decaying plant and animal matter and the "screwworm" that completes its larval development in living flesh. The resemblance of certain parasites to their free-living relatives creates a diagnostic pitfall. Even their presence at the scene of the crime is not sufficient proof of guilt. Fly maggots and coprophilic beetles are frequently found in fecal specimens. In almost every such case, these insects have invaded the fecal mass after defecation and never were parasites at all.

Unfortunately, even when we restrict our consideration to unambiguously parasitic arthropods, we still have too big a chore on

our hands. Medical entomology is a formidable subject, and the selection of appropriate information is not always an easy task because certain topics that at first appear to bear directly on current problems of veterinary practice actually lie within the responsibilities of very few veterinarians. For example, information on mosquitoes may occupy half of a textbook of medical entomology, and mosquitoes serve as vectors of such important diseases as equine encephalomyelitis and canine heartworm infection. However, few veterinarians invest the time and effort necessary to acquire a detailed knowledge of mosquitoes because control of these pests is usually the responsibility of the medical entomologist. Of more direct interest to veterinarians are the kinds of parasitic arthropods that live in more prolonged and intimate association with domestic animals. In this book, considerably more attention is therefore devoted to lice, fleas, ticks, and mites than to mosquitoes.

The arthropods of veterinary importance belong to the classes Insecta, Arachnida, Crustacea, and Diplopoda. Insects and arachnids compose the bulk of this chapter. The Crustacea class contains many taxa that serve as intermediate hosts of helminth parasites (copepods, crabs, crayfish, and sow bugs), but only the copepods are discussed because they tend to be a little less familiar to the average person. One group of crustaceans, the Pentastomida or tongue worms, are parasites in their own right of the respiratory system of terrestrial vertebrates, reptiles, birds, and mammals and are considered briefly in their own section. The class Diplopoda (millipedes), which contains at least one genus, *Narceus*, that serves as the intermediate host of *Macracanthorhynchus ingens*, a very large

acanthocephalan parasite of the raccoon and domestic dog, is mentioned only in passing in this book.

CLASS INSECTA

Structure

The body of adult insects consists of the head, thorax, and abdomen. The head consists of a variable number of fused segments and bears two eyes, two antennae, and a complex set of mouthparts. The thorax consists of three segments, the prothorax, mesothorax, and metathorax, and bears six jointed legs and four, two, or no wings, depending on the zoologic order to which the insect in question belongs. Thus roaches (Dictyoptera), caddisflies (Trichoptera), beetles (Coleoptera), and certain bugs (Hemiptera) have four wings, most flies (Diptera) have two, and the lice (Mallophaga and Anoplura) and fleas (Siphonaptera) are wingless. When four wings are present, one pair arises from the mesothorax and the second pair from the metathorax. The functional wings of Diptera arise from the mesothorax. The abdomen consists of 11 or fewer segments, of which the terminal ones are modified for copulation or egg laying. As typical arthropods, insects have a chitinous cuticle secreted by the hypodermis, a single layer of columnar epithelial cells of ectodermal origin, which is cast off or molted at intervals to permit growth and metamorphosis. The chitinous cuticle serves as an exoskeleton, thus as both a body covering and a place for attachment of muscles. Heavily chitinized areas or plates of cuticle are connected by thinner, lightly chitinized areas, thus permitting movement and some degree of expansion as, for example, when the abdomen of a feeding female mosquito fills with blood. Insect

muscles are striated and often capable of extraordinarily rapid contraction. The cuticle is overlain by a thin lipoidal surface layer, the epicuticle, which is impermeable to water but freely permeable to lipids and lipid-soluble substances.

When a developing insect has grown too large for its cuticle, the hypodermis lays down a new, thin, elastic cuticle under the old one. The old cuticle then splits, and the insect emerges from it. This process, termed **molting** or **ecdysis,** divides the life of the individual insect into a series of **stages**, or **instars.** All instars of cockroaches, bugs, and lice resemble their parents except for being smaller, whereas a newly hatched fly, beetle, or flea looks more like a worm than an insect. The former situation is called **simple metamorphosis (hemimetabolous metamorphosis)** and the series of juvenile instars are called **nymphs,** whereas the latter situation is called **complex metamorphosis (holometabolous metamorphosis)** and the juvenile wormlike stages are called **larvae.** In complex metamorphosis, the complete restructuring necessary for the transformation of the wormlike larva into the adult insect takes place during the **pupal** stage, and all related events are referred to as **pupation.** The exiting of an adult insect from its pupal case is termed **eclosion** for the purpose of distinguishing adult emergence from the pupal case from the hatching of a larva from an egg.

Order Trichoptera, Caddisflies

Trichoptera is a very large group of flies (some 7000+ species) that is better known to fly fishermen than to medical entomologists. These flies have four wings and short mouth parts that are used for

consuming water and nectar (Figure 2-1). In species that occur in temperate climates, the adult population is often limited to one generation per year, and they may occur in large blooms. The larvae are aquatic in fresh water and feed on microorganisms or as predators on other insects. The larvae will often construct a portable case in which they live, with only their legs and head protruding. Ultimately the larva will form a cocoon from which the adult emerges. The males swarm over bodies of water, and females fly into the swarms to be fertilized. The females lay their eggs near water so the larvae that hatch can make their way into this environment. A good guide to the species of caddisflies has been produced for the fly-fishing enthusiast (Pobst and Richards, 1999).

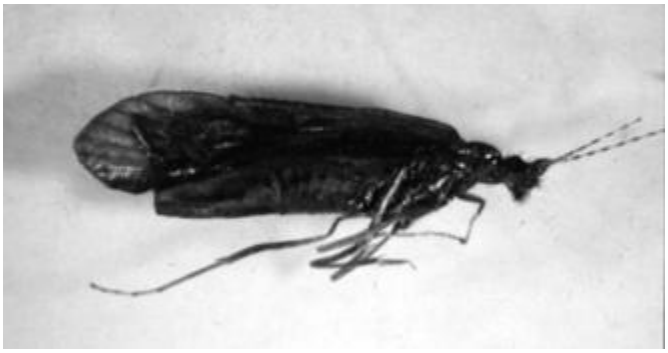

FIGURE 2-1 Caddisfly adult. The larvae of these flies become infected with the metacercariae of trematodes harboring the causative agent of Potomac horse fever.

Courtesy Dr. John E. Madigan, School of Veterinary Medicine, University of California, Davis, California.

Caddisflies became important in veterinary medicine only recently. Work by Madigan and others at the University of California–Davis has shown that they serve as vectors of Potomac horse fever's causative agent, *Neorickettsia risticii*. It seems that the caddisflies are intermediate hosts of the metacercarial stage of trematode parasites of bats (trematodes of the family

Lecithodendriidae) or trout, *Deropegus* species, *Crepidostomum* species, and *Creptotrema* species (Pusterla et al, 2000). Unfortunately, these trematodes are often, as in the case of the rickettsial disease of salmon poisoning in dogs, infected with a rickettsia, *N. risticii*. Horses fed mature caddisflies *(Dicosmoecus gilvipes)* developed the clinical and hematologic disease of Potomac horse fever (Madigan et al, 2000). Thus when the horse digests the caddisfly containing the trematode metacercaria, the action releases the *N. risticii* that causes the disease in the horse. The finding is important because control can be as simple as providing horses with waterers that are covered in some fashion to prevent the bodies of these flies from contaminating the horse's drinking water.

Order Diptera, Flies

Adult dipteran flies, except certain specialized groups such as the parasites of the family Hippoboscidae, have one pair of functional mesothoracic wings. The metathoracic pair are represented by club-shaped balancing organs called **halteres** (Figure 2-2), which are present even in the wingless hippoboscids. Metamorphosis is complex. Although most flies produce eggs or are **oviparous,** a few deposit larvae that have already hatched, and the females producing larvae in this manner are said to be **ovoviviparous.** Hippoboscids and tsetses retain their larvae within their abdomens through the third larval instar, and these larvae pupate almost immediately on being born.

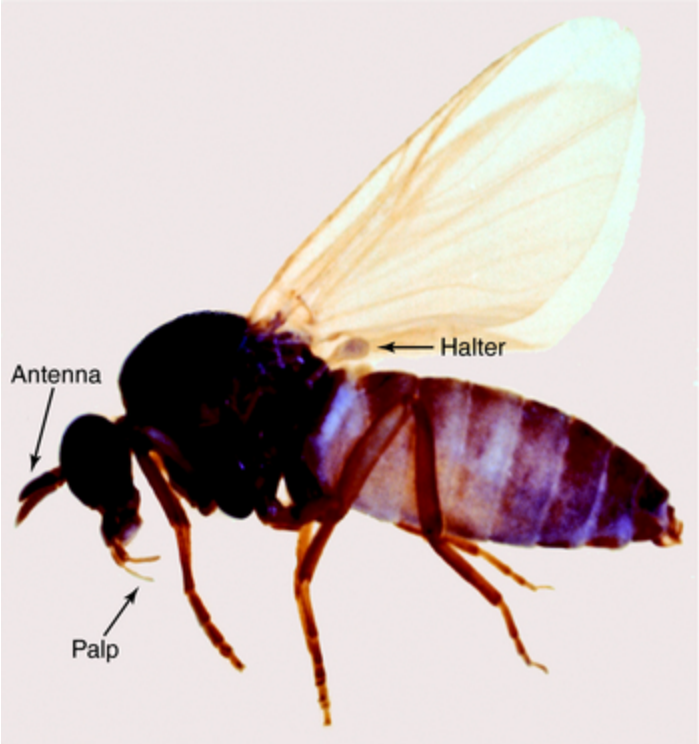

FIGURE 2-2 *Simulium* (Nematocera: Simuliidae), a blackfly. The halteres (singular, haltere) are balancing organs that have evolved in Diptera in place of the metathoracic wings. The maxillary palpi are sensory structures associated with the mouthparts. The antennae of blackflies consist of 11 similar segments.

There are three main groups of flies: the gnats and mosquitoes of the Nematocera, the horseflies and deerflies of the Brachycera, and the houseflies, flesh flies and blowflies, botflies, tsetse flies, and keds of the Cyclorrhapha (Table 2-1). All three major groups contain bloodsucking species, many of which serve as disease vectors. In the Nematocera and Brachycera, only the females take blood meals, and, usually, larval development occurs in aquatic environments. Larvae of muscid, sarcophagid, calliphorid, and oestrid cyclorrhaphans can invade living tissues to produce a pathologic condition called **myiasis.** The developmental times of various flies, along with those of some fleas and lice, are presented in Table 2-2.

TABLE 2-1 Classification of the Diptera

Nematocera	Brachycera	Cyclorrhapha
Culicidae, mosquitoes	Horseflies and deerflies	Muscidae, houseflies
Simuliidae, blackflies		Hippoboscidae, keds
Ceratopogonidae, midges		Sarcophagidae, flesh flies
Psychodidae, sandflies		Calliphoridae, blowflies
		Oestridae and other botflies

Nematocera

Nematocerans are typically small and relatively delicate. The antennae are long and many-segmented, and the individual segments resemble one another like beads on a string. Nematocerans generally breed in aquatic or semiaquatic habitats, and their larvae are suitably endowed with appendages for swimming, breathing, and gathering food in water. Only female nematocerans suck blood; the males never do and subsist instead on nectar.

Family Culicidae, mosquitoes

Identification

Mosquitoes have long, 14- or 15-segmented antennae, an elongated proboscis consisting of a bundle of stylets loosely encased in a sheath formed by the labium, and fringes of scales on the wings (Figure 2-3). These anatomic details are sufficient taxonomic

characteristics to reliably distinguish the taxon that we recognize as mosquitoes from other insects with which they might be confused.

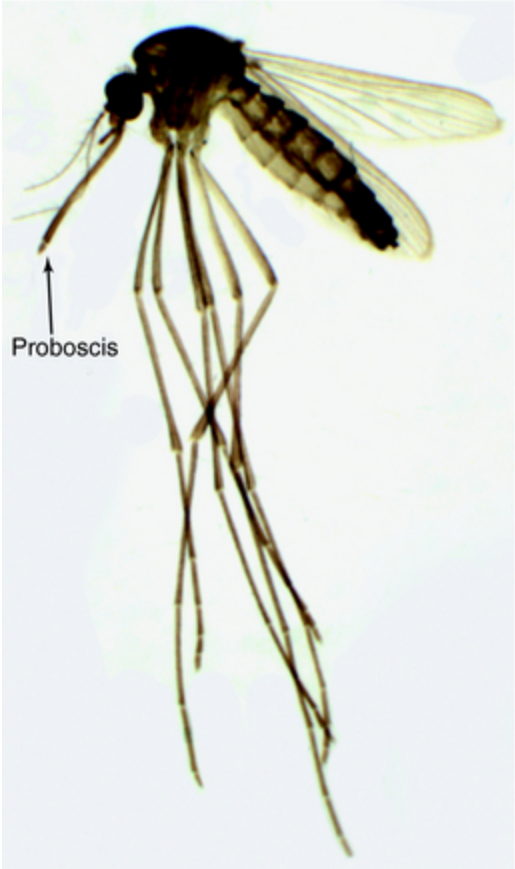

FIGURE 2-3 A mosquito (Nematocera: Culicidae). Note the long antennae and long mouthparts (proboscis).

Life history

Mosquitoes lay their eggs on water or in dry places that tend to flood seasonally. Eggs laid on water hatch in less than a week. Larvae (Figure 2-4) are air breathers and die within hours if their air supply is shut off by an oil film on the water's surface. The larvae molt four times, usually within the space of 2 weeks, and then pupate. As is characteristic of all nematocerans and brachycerans, the adult emerges through a T-shaped hole in the back of the last

larval skin. Culicid pupae are elaborate, free-swimming organisms with a large cephalothorax. As development proceeds, the structures of the adult mosquito become apparent (Figure 2-5). The pupal stage ordinarily lasts from 2 days to a week, but a few hours suffice for certain dry climate species. The adult mosquito emerges through a T-shaped hole in the back of the pupal case as it floats at the water's surface. After about 24 hours, the wings have expanded and hardened, and the mosquito is able to fly. Only female mosquitoes suck blood, the protein of which is necessary for the maturation of the ovaries. The female mosquito will very typically feed every few days, with each blood meal being used to nourish the next batch of eggs to be produced and laid; after the eggs are laid, the female will then seek out another host. It is the repeated feeding of female mosquitoes on different hosts that makes them such efficient vectors of disease. Males and nonreproductive females get by on nectar and plant juices. The females of some species that normally feed on blood are sometimes capable of ovarian maturation without a blood meal (i.e., the females are **autogenous**). Other species of mosquitoes feed only on plants, and therefore these species are of little interest as pests or disease vectors. Mammals and birds are preferred hosts (or victims), both of blood-feeding mosquitoes and of the various disease organisms that they transmit.

FIGURE 2-4 Mosquito larva.

FIGURE 2-5 Mosquito pupa. The "trumpets" on the cephalothorax are pupal respiratory structures. The eyes, legs, thorax, and abdomen of the developing adult mosquito can be seen through the pupal cuticle.

Injury

Under ordinary circumstances the amount of blood lost to mosquito attack is entirely trivial. Sometimes, however, circumstances favor the simultaneous emergence of enormous swarms of mosquitoes that by their concerted attacks can actually bleed cattle to death. For example, 7 days after Hurricane Allen (August 10, 1980) brought a prolonged drought to an abrupt end and flooded 5000 acres of a Texas ranch, cattle were observed to be visibly distressed by swarms of *Aedes sollicitans* mosquitoes. The next morning, 15 cattle were found dead of exsanguination manifested by extreme pallor of the

mucous membranes and postmortal evidence of severe anemia. The interval of 7 days between flooding of the pastures and the sudden death of the cattle corresponded exactly to the time required for *A. sollicitans* to develop from egg to biting adult once its dormancy had been ended by high water. The flood led to the synchronous development of vast numbers of eggs that had accumulated during the prolonged drought, thus producing the enormous swarms of mosquitoes capable of exsanguinating mature cattle overnight. Abbitt and Abbitt, who obtained and thoughtfully analyzed the evidence in this outbreak, estimated that 3.8 million mosquito bites (5300 bites per minute for 12 hours) would be required to remove half of the total blood volume from a 366-kg cow, assuming that a mosquito removes 0.0039 mL per blood meal (Abbitt and Abbitt, 1981). Cats will sometimes develop allergies to mosquito bites that will manifest as large pruritic and erythemic lesions on the nose or other parts of the face (Clare and Medleau, 1997).

Disease transmission

A **vector** is an animal, often an arthropod, that transmits an infective organism from one host to another. (An inanimate object that serves to transmit infections, such as a doorknob or dirty tissue, is called a **fomite.**) A vector that transmits infective organisms directly (and, necessarily, promptly) to a recipient host without development or multiplication of the organisms having occurred is called a **mechanical vector.** A **biologic vector,** by contrast, is one in which the infective organisms either undergo development or multiply or do both before being transmitted to the recipient host. Thus a biologic vector is a true host of the disease organism. In the case of sexually reproducing disease organisms such as protozoans

and helminths, vectors that host developing or asexually reproducing stages of the organism are termed **intermediate** hosts, whereas vectors that host sexually mature stages are termed **definitive** hosts. Mosquitoes are vectors of many pathogens (Table 2-3). *Culex*, *Aedes*, *Anopheles*, and other genera of mosquitos serve as biologic vectors (intermediate hosts) of filariid worms such as *Dirofilaria immitis*, the canine heartworm, and *Wuchereria bancrofti*, the cause of human lymphatic filariasis. Mosquitoes of the genus *Anopheles* serve as biologic vectors (definitive hosts) of the blood-inhabiting protozoon genus *Plasmodium*, which causes malaria in birds, rodents, and primates. Mosquitoes also serve as biologic vectors of viral encephalitides (e.g., equine encephalomyelitis), West Nile virus, and the viruses of rabbit myxomatosis, fowl pox, and yellow, dengue, and Rift Valley fevers. In the case of viruses, bacteria, and the like, the terms *intermediate* and *definitive* are redundant inasmuch as sexual reproduction does not occur in these groups.

TABLE 2-3 Some Pathogens Vectored by Nematoceran Flies

Vector	Some Transmitted Pathogens
Culicidae (mosquitos)	Filariids
	Setaria: horses, cattle, deer
	Heartworm: dogs and cats
	Wuchereria and *Brugia:* humans and cats
	Protozoa
	Malaria *(Plasmodium):* birds and primates

	Viruses
	Equine encephalitis
	West Nile virus
	Rift Valley fever
Simuliidae (blackflies)	Filariids
	Onchocerca: horses, cattle, sheep, humans
	Protozoa
	Malaria *(Leucocytozoon):* birds
Ceratopogonidae (biting midges)	Filariids
	Onchocerca: horses
	Dipetalonema: primates
	Protozoa
	Malaria *(Leucocytozoon):* birds
	Viruses
	Blue tongue
	African horse sickness
Psychodidae (sandflies)	Protozoa
	Leishmania species
	Rickettsia
	Bartonella
	Viruses
	3-day fever virus

Family Simuliidae, blackflies

Identification

Blackflies (see Figure 2-2) are small, stout-bodied, black, gray, or yellowish-brown flies with relatively short antennae consisting of nine to 12 (usually 11) similar segments, and short mouthparts with prominent maxillary palps (Figure 2-6).

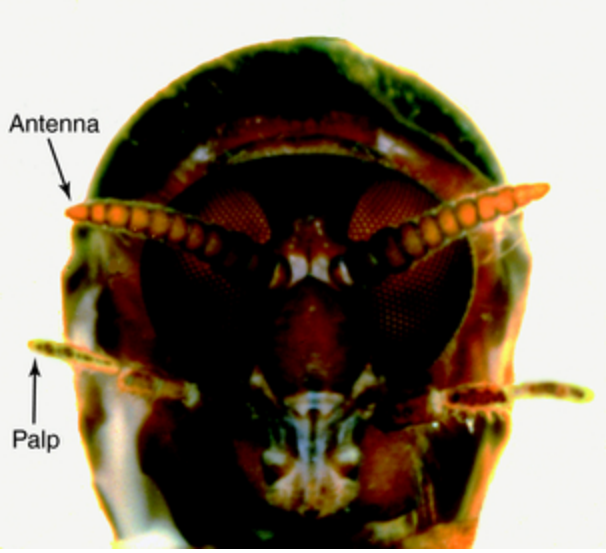

FIGURE 2-6 Head of a blackfly (Nematocera: Simuliidae).

Life history

Blackflies breed only in running water. Although mountain torrents and temporary upland streams are favored breeding sites of many species, some particularly important species breed in large rivers. Eggs are deposited on the water's surface or on partly submerged stones, twigs, or vegetation. In species that produce several broods per year (**multivoltine** species), larvae hatch from these eggs a few days later, but in species that produce only one brood per year (**univoltine** species), the eggs remain in a protracted state of metabolic quiescence, or **diapause,** and do not hatch until the following year. Blackfly larvae manage to cling to the surfaces of

stones in rapidly moving, turbulent streams partly by means of little hooks on their posteriors and on a short **proleg** near the anterior end of their bodies (Figure 2-7). By flexing their bodies, the larvae are able to move from place to place like inchworms. Blackfly larvae also spin silken strands to help anchor themselves and later to form cocoons, by means of which the pupae continue to cling to the rocks. Adults emerge from these pupae and are carried to the surface in a bubble of air.

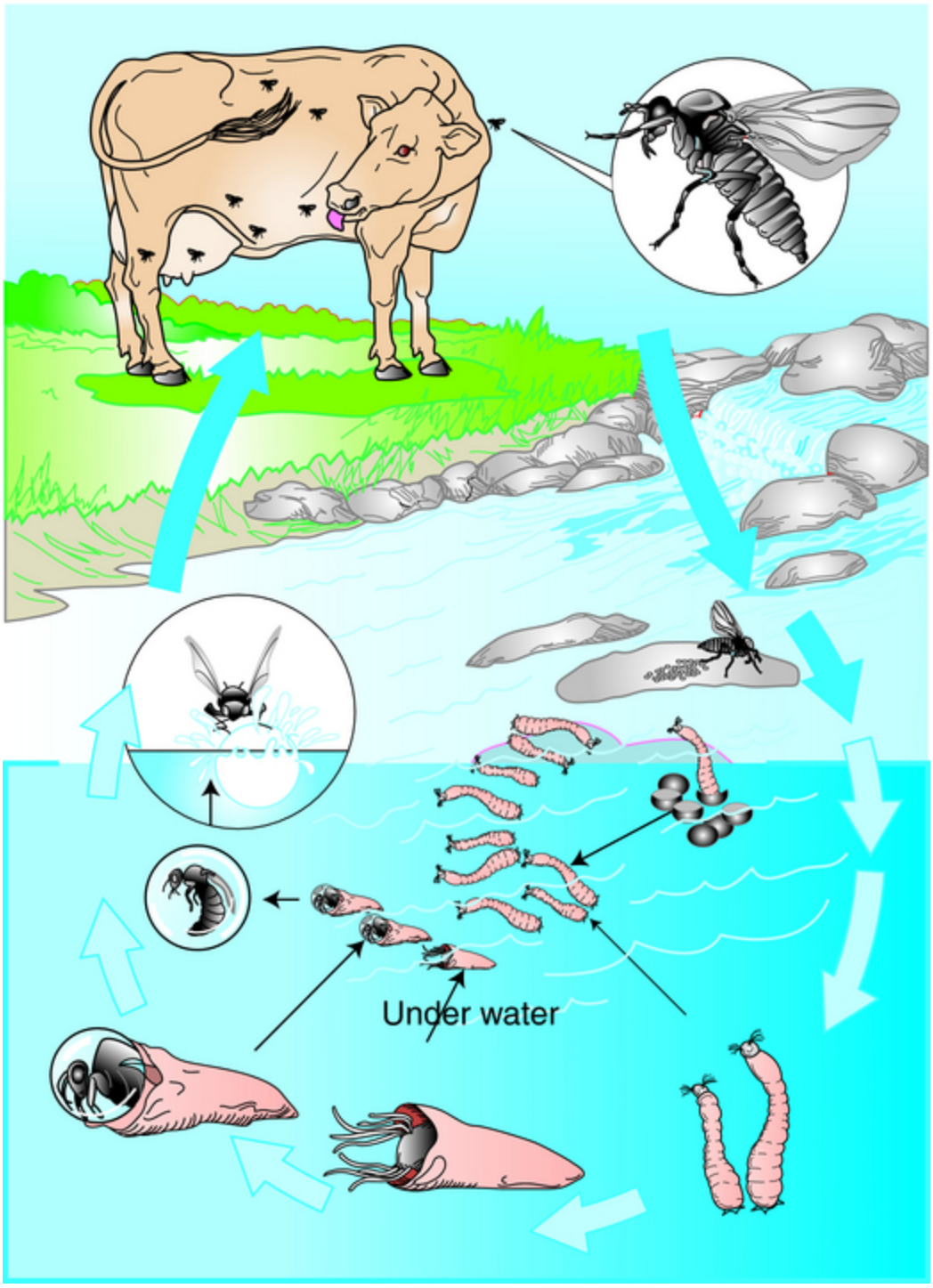

FIGURE 2-7 Life history of a blackfly (family Simuliidae). The female blackfly deposits her eggs on partly submerged objects in rapidly flowing streams. The larvae that hatch from these eggs cling to the stones and feed on organic matter carried by the current. When ready to pupate, the larvae spin silken cocoons that secure them to the

substrate. Adults that emerge from these pupal cases are carried to the surface in a bubble of air and fly off in search of a blood meal.

Injury

The female blackfly is a vicious biter. Her mouthparts consist of a bundle of flattened, serrated, bladelike stylets loosely ensheathed by the labium, which itself terminates in a pair of labella. Instead of piercing a blood vessel and feeding from the lumen as a mosquito, bedbug, or sucking louse does, the female blackfly lacerates tissues until a pool of blood forms, and then she imbibes the blood from the pool.

Susceptibility to and severity of host reaction to the bites of many arthropods vary remarkably among individuals. With continued exposure to bites, initially susceptible individuals may become relatively immune so that they are less frequently bitten or suffer less reaction to the bites. Or, less fortunately, they may become hypersensitive so that continued attack excites a more severe and sometimes even fatal reaction. Sensitivity to the bites of blackflies is a common phenomenon, and the reactive wheal may continue to itch for many days and tends to be aggravated by scratching. In a hypersensitive person a single bite may evoke sufficient edematous reaction to force the eyelids shut. Burghardt, Whitlock, and McEnerney (1951) described a dermatitis in cattle due to *Simulium*. The lesions consisted of blisters, welts, and scabs affecting the head, thorax, and ears, and acute exudative lesions along the midabdominal line. Heavy swarms of blackflies have been known to kill grazing livestock by the thousands. However, the exact cause of death, whether it be anemia, hypersensitivity reactions, or toxin

absorbed from fly saliva injected into the bite, remains problematic. During blackfly season, dogs and cats can manifest small pruritic bloody spots on the ears, face, or body. Prevention of such bites is best accomplished using repellents.

Disease transmission

Blackflies transmit a number of pathogens (see Table 2-3). Blackflies (e.g., *Simulium aureum*, *Simulium jenningsi*, *Simulium vittatum*, and *Simulium pictipes*) transmit leucocytozoonosis, a disease of poultry and wild birds caused by several species of the haemosporidian protozoan genus *Leucocytozoon*. Blackflies also serve as obligate intermediate hosts of the filariid nematode *Onchocerca gutturosa*, an apparently innocuous parasite of cattle. In the blackfly the worm develops from the skin-dwelling microfilarial stage ingested by the fly to the third-stage larval nematode that is infective to the next host. Blackflies (e.g., *Simulium damnosum* and *Simulium ochraceum*) also serve as vectors of the related nematode parasite *Onchocerca volvulus*, which causes human onchocerciasis, manifested by the formation of dermal nodules and which leads, predominantly in the African form of the disease, to blindness. Because some of these vectors are riverine breeders, the disease tends to be concentrated along valleys, and the ensuing blindness is therefore called “river blindness.”

Control

Blackflies attack in swarms during daylight hours and when the air is relatively still. Smoke repels them, and, although chemical repellents afford a degree of protection, campers, gardeners, and livestock usually find their surest relief in the lee of a smudge pot.

Livestock should be stabled until sundown during seasons of particularly heavy blackfly attack. Blackflies can be discouraged from attacking horses' ears by applying petroleum jelly to the inner surface of the pinna.

Family Ceratopogonidae (Heleidae), biting midges, "no-see-ums"

Identification

Ceratopogonids are tiny (less than 2 mm), relatively glabrous flies. Their antennae are long and slender, and their mouthparts are relatively short (Figure 2-8).

FIGURE 2-8 *Culicoides* (Nematocera: Heleidae), a "no-see-um." *Culicoides* differs from Culicidae mosquitoes in being smaller and having a shorter proboscis.

Life history

Life histories of various species differ in detail; some species require freshwater and others saltwater habitats. Some breed in water-filled

holes in trees, others in decaying vegetation, sandy and silt soils, and the like. Adults are crepuscular and nocturnal. Only females suck blood, and, although they are fairly strong flyers, they tend to remain close to their breeding grounds. A few, however, may venture forth as far as a half mile when the air is still. Most important species belong to the genera *Culicoides* and *Leptoconops*.

Injury

The bites of *Culicoides* inflict pain far out of proportion to the size of the fly. In fact, people victimized by these tiny terrors frequently do not realize that they are being tormented by insects, sometimes mistaking them for a bit of cigarette ash because of their small size. *Culicoides* easily pass through standard window screening and make themselves obnoxious to sleepers. In sensitized individuals the reaction to the bites lasts longer and is more painful than that to mosquito bites.

"Queensland itch," demonstrated by Riek (1953b) as representing allergic dermatitis caused by the development of hypersensitivity to the bites of *Culicoides robertsi*, affect only certain horses. Other horses pastured with the affected ones never show any signs of disease. Initial lesions are discrete papules confined to the dorsal surfaces. Later, the hair mats and crusts form and eventually fall off, leaving hairless areas that in severe cases become confluent. Pruritus is intense, and horses may injure themselves by scratching and rolling to relieve the itching. Antihistamine therapy accelerates regression of the lesions (Riek, 1953a).

Disease transmission

Culicoides species transmit the viruses of bluetongue and African horse sickness (see Table 2-3). *Onchocerca cervicalis* of horses, *Onchocerca gibsoni* of cattle, and three relatively innocuous filariid parasites of humans *(Dipetalonema perstans*, *Dipetalonema streptocerca*, and *Mansonella ozzardi)* all develop from microfilaria to infective third-stage larva in the bodies of *Culicoides* organisms. Protozoans transmitted by *Culicoides* include *Hepatocystis* of Old World monkeys and *Haemoproteus* and *Leucocytozoon* of wild and domestic birds.

Family Psychodidae, sandflies

Identification

Psychodids are small, dull-colored, slender flies with long antennae. The wing veins radiate in nearly straight lines from the base to the tip of the wing (Figure 2-9).

FIGURE 2-9 *Phlebotomus* (Nematocera: Psychodidae). The wing veins radiate in nearly straight lines from the base to the tip of the wing.

Life history

Psychodids lay their eggs in cracks, crevices, or burrows in which moderate temperatures, darkness, and nearly 100% humidity prevail. They spend at least 2 months as egg, larvae, and pupae but are short-lived as adults. Adult psychodids are weak flyers and nocturnal in habit. Important species belong to the genera *Phlebotomus* and *Lutzomyia*. *Phlebotomus* occurs in the Old World and *Lutzomyia* in the New World; all species are tropical or relatively subtropical in distribution. Species of *Lutzomyia* are found in the

United States, including *Lutzomyia vexator*, *Lutzomyia apache*, *Lutzomyia shannoni*, and others, but it is not clear how many of these species serve as successful vectors of *Leishmania* species in the wild.

Disease transmission

Psychodids transmit *Leishmania* species, hemoflagellate parasites of dogs, rodents, and primates, including humans (see Table 2-3). It appears that molecules in the salivary gland secretions of the phlebotomine vector modulate to some extent the course of *Leishmania* development in the host that is bitten (Warburg et al, 1994). Also transmitted by phlebotomines are the 3-day fever virus and *Bartonella bacilliformis* infection of humans.

Control

Sandflies can be prevented from biting dogs by the use of deltamethrin-impregnated collars and a combination of permethrin and imidacloprid in a spot-on formulation. The collar can provide up to 6 months of protection. Deltamethrin-impregnated collars for the control of canine leishmaniasis (Manzillo et al, 2006) and the spot-on formulation provide excellent protection between monthly applications (Mencke et al, 2003).

Brachycera

Family Tabanidae, horseflies and deerflies

Identification

Tabanids are stout-bodied flies varying from about the size of a housefly to as large as a hummingbird. The short, stout, anteriorly projecting antennae consist of three markedly different segments

(Figures 2-10 and 2-11). The first segment is small, the second may be expanded, and the third is marked by annulations that make tabanid antennae appear to have many more than three units.

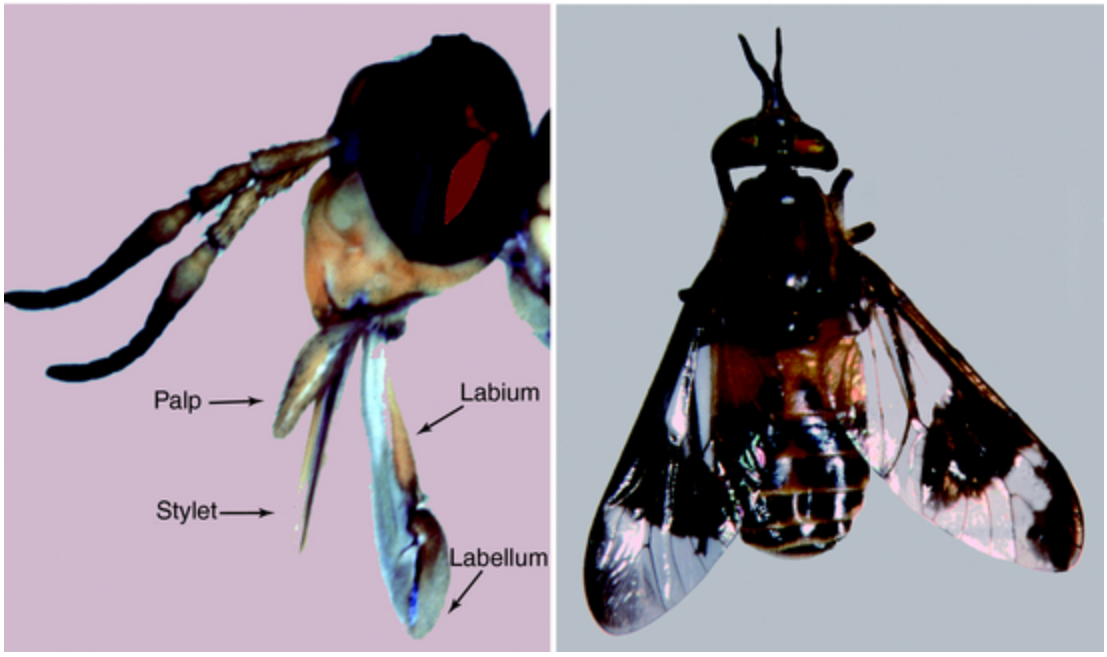

FIGURE 2-10 *Chrysops* (Brachycera: Tabanidae), a deerfly. Because the distal segment of the tabanid antenna is annulated, it gives the impression that the antenna consists of many segments; however, there are only three. The wings often have dark markings.

FIGURE 2-11 *Tabanus* (Brachycera: Tabanidae), a horsefly. The wings are typically without markings.

Life history

Female tabanids require a blood meal for maturation of their eggs and obtain it from mammals, reptiles, and occasionally, birds. Male tabanids are not blood feeders but subsist on nectar, sap, and aphid feces; the females also require these sources of carbohydrate in addition to blood (Mally and Kutzer, 1984). Except for a few xerophilic species, tabanids tend to be concentrated along watercourses. Eggs are neatly glued in masses of 400 to 1000 to foliage overhanging water. Larvae hatch in a week or so, depending on temperature and relative humidity, and drop into the water. First- and second-stage larvae do not feed, but the third and later stages are aggressively carnivorous or saprophagic and feed on insect larvae, crustaceans, snails, earthworms, young frogs, plant tissues, and dead organic matter, depending on the species of

tabanid and the availability of food (Mally and Kutzer, 1984). In temperate regions, larvae overwinter by burying themselves in soil or dead vegetation and pupate the following spring. Thus usually only one generation is produced each year. Adult tabanids are strong flyers and very difficult to discourage. In Michigan, *Hybomitra* species were found to reach maximum abundance in early summer (May to June), whereas *Chrysops* and *Tabanus* species were most abundant in late summer (early to late July; Strickler and Walker, 1993). In the salt marshes of Cape Cod, Massachusetts, the greenhead flies *Tabanus nigrovittatus* and *Tabanus conterminus* were found to be most active in the afternoon (Hayes et al, 1993). In Florida, peak *Chrysops* activity occurred in the morning and evening, with a correlation to relative humidity rather than to temperature and light intensity (Cilek and Schreiber, 1996). Konstantinov (1993) showed that masking the visibility of a cow by placing it in a wooded area did not reduce the number of *Hybomitra* flies that found the cow when they were released 150 meters from the host animal.

Injury

All arthropod attacks cause some annoyance to the host and exact some expenditure of energy in efforts to avoid or relieve their effects. When flies are particularly numerous, pastured livestock may be driven frantic by incessant attacks and can spend so much time and energy combating the onslaught that they cannot rest or graze adequately. The resultant exhaustion always interferes with production and sometimes proves fatal. Certain insects are particularly feared by livestock. Some horseflies are as large as hummingbirds and inflict an excruciating bite. When one of these

monsters attacks, horses are likely to bolt, and it behooves the rider or driver to come promptly to their aid. In biting, the mandibles and maxillae of tabanids lacerate the blood vessels and the labella lap up the blood that flows freely from the wound. Repeated attacks in the skinfolds about a cow's udder and in the groove between the udder halves lead to extensive weeping eczematous lesions that may become secondarily infected with bacteria. After a tabanid has finished feeding, the bite wound tends to bleed for many minutes, thus attracting opportunists such as *Musca*. In fact, *Musca* and other flies can often be seen clustered about a feeding tabanid, exploiting the bounty afforded by its sloppy manner of taking a meal. Vicious daylight bloodsuckers, tabanids do not usually attack indoors, but if already feeding when the host enters a building, they will continue to feed until replete. The most efficient solution to tabanid attack is to stable the animals during the hours of peak fly activity.

Disease transmission

The pain that a tabanid inflicts when it bites tends to increase its efficiency as a mechanical vector of disease organisms. The fly, driven away by its victim's defenses before it has had time to feed to repletion, soon alights on a second host to finish its meal and perhaps to contaminate the wound with fresh, mechanically borne bacteria (e.g., anthrax), viruses (e.g., equine infectious anemia), and the like. The large volume of blood imbibed by each tabanid (up to four times the weight of the fly; Krinsky, 1976) also contributes to its efficiency as a mechanical vector by helping to compensate for the low concentration of microorganisms usually found in blood, and for their failure to multiply in the body of the intermediate host.

Tabanids have been incriminated in the mechanical transmission of anaplasmosis (*Anaplasma* species), anthrax *(Bacillus anthracis)*, tularemia ("deerfly fever," *Francisella tularensis*), and equine infectious anemia virus. Mechanical transmission of equine infectious anemia virus from acutely infected ponies to susceptible ponies occurred after as few as 10 bites by contaminated *Tabanus fuscicostatus*, but all attempts at transmission from a chronically infected pony failed (Hawkins et al, 1973). Mammalian trypanosomes (hemoflagellate protozoans) may be transmitted mechanically or biologically by tabanids, depending on the species involved. Surra *(Trypanosoma evansi)*, a fatal disease of horses, camels, elephants, and dogs in Asia, is transmitted mechanically, and the flies lose their ability to transmit the infection a few hours after feeding on an animal infected with surra (Table 2-4). *Trypanosoma theileri*, on the other hand, must multiply in the body of the tabanid because it is so scarce in the blood of cattle that one must usually resort to culture techniques to demonstrate its presence there. Otherwise, *T. theileri* would not be distributed throughout the world as a parasite of cattle and their near relatives. A vector in which such parasitic organisms multiply is sometimes referred to as a **cyclopropagative host** to distinguish it from a **cyclodevelopmental host,** in which the parasite actually undergoes ontogenetic development. An example of the latter is *Elaeophora schneideri*, the arterial worm of deer, elk, and domestic sheep in the southwestern United States, which develops from the microfilarial stage in the blood to the infective third stage within the body of the tabanid (Hibler and Adcock, 1971). More details concerning disease

transmission by tabanids are to be found in the review by Krinsky (1976).

TABLE 2-4 Some Pathogens Vectored by Brachyceran Flies

Mechanically Vectored	Biologically Vectored
Anthrax Tularemia	Filariids: *Elaeophora*—elk, sheep
Protozoa: *Trypanosoma evansi*	Protozoa: *Trypanosoma theileri*—cattle

Control

Horseflies and deerflies are very difficult to kill or repel; often the best solution is to stable livestock during the hours of peak fly activity. These flies can use blood from wild animals as food and have larval habitats independent of domestic livestock. Thus unlike flies more directly dependent on their hosts, such as *Stomoxys* and *Haematobia*, these flies can be controlled chemically by repellents alone (Foil and Hogsette, 1994). Konstantinov (1992) showed that only 3% of flies attacking a cow are killed by the cows during their attacks. McMahon and Gaugler (1993) suggested that the draining of salt marsh areas to decrease mosquito populations may inadvertently have actually increased habitats preferred by larval tabanids and hence increased the numbers of these biting flies.

Cyclorrhapha

The Cyclorrhapha group represents the apex of dipteran evolution, and the common housefly, *Musca domestica*, is a typical example.

Instead of the aquatic habitats favored by nematocerans and brachycerans, cyclorrhaphans tend to breed in decaying plant and animal tissues, manure, carrion, and the like. The three larval instars are more or less conical animals with a mouth, usually armed with hooks, at the apex and a pair of prominent respiratory openings called **spiracles** or **stigmata** at the base. Slender larvae of the families Muscidae, Sarcophagidae, and Calliphoridae are usually referred to as **maggots** (Figure 2-12), whereas the rather stout larvae of the family Oestridae and its relatives are called **bots** or **grubs** (compare with Figure 2-25). When the third instar larva enters the pupal stage, its integument hardens to form a puparium, or pupal case. Pupae of most cyclorrhaphan flies are found in decaying organic material or soil. A few species have specialized pupation sites. For example, pupae of the sheep ked *Melophagus ovinus* are found attached to the wool of their host. The adult fly emerges (ecloses) through a circular hole in the anterior end of the puparium. Cyclorrhaphan antennae consist of three dissimilar segments, the third and largest of which bears a frondlike structure called an arista near its proximal end. The antennae are directed ventrally, but the aristae project anteriorly (Figure 2-13). Parasitic specialization has proceeded in two directions in the Cyclorrhapha. In the families Muscidae and Hippoboscidae there has been specialization from a type adapted to lapping up liquids (e.g., *Musca*) (see Figure 2-13) toward a bayonet-like proboscis for piercing the skin and sucking blood (e.g., *Stomoxys*) and thus toward parasitism in the adult stage. In the families Calliphoridae and Sarcophagidae and certain members of the family Muscidae, the adult flies have retained their lapping mouthparts and remained

scavengers; instead, it is in the larval stages that parasitism has evolved. The botflies (e.g., *Hypoderma* and *Gasterophilus*) have proceeded even further in this direction. Their larvae have become highly specialized host- and site-specific parasites, whereas the mouthparts of the adult flies have become vestigial and nonfunctional. Parasitism by fly larvae is termed *myiasis* and is of worldwide economic importance.

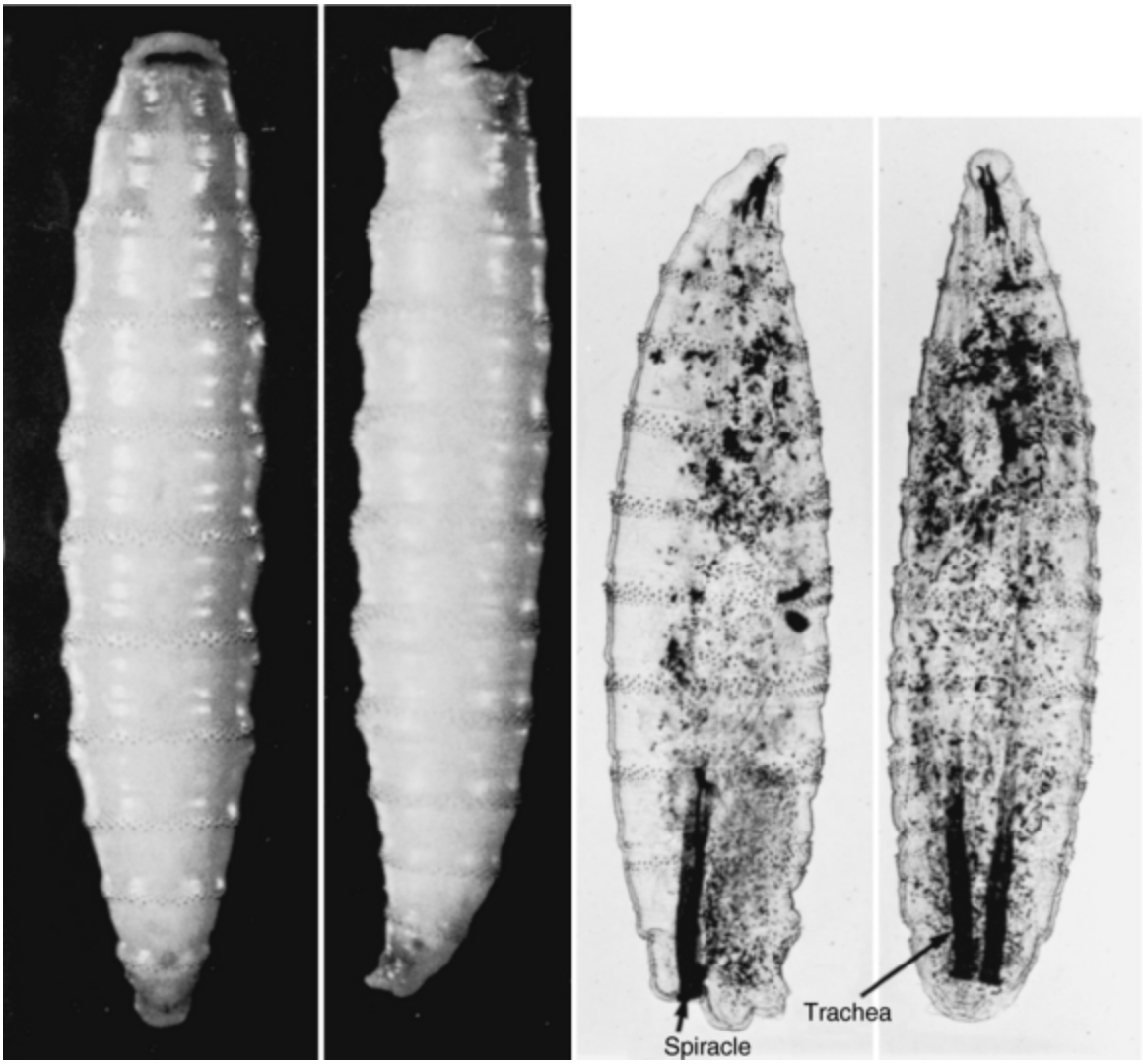

FIGURE 2-12 Muscoid third-stage larva or maggot of the family Calliphoridae. Note the pigmented tracheal trunks leading from the posterior spiracles. Pigmented tracheae are a specific character of *Cochliomyia hominivorax*, the American screwworm.

Specimens courtesy R.J. Gagné.

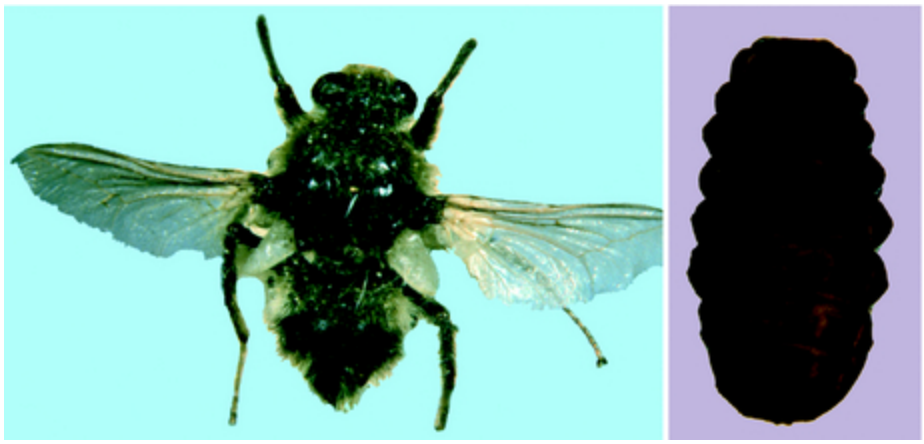

FIGURE 2-25 *Hypoderma bovis*. *Left*, Adult fly. *Right*, Mature bot removed from a warble.

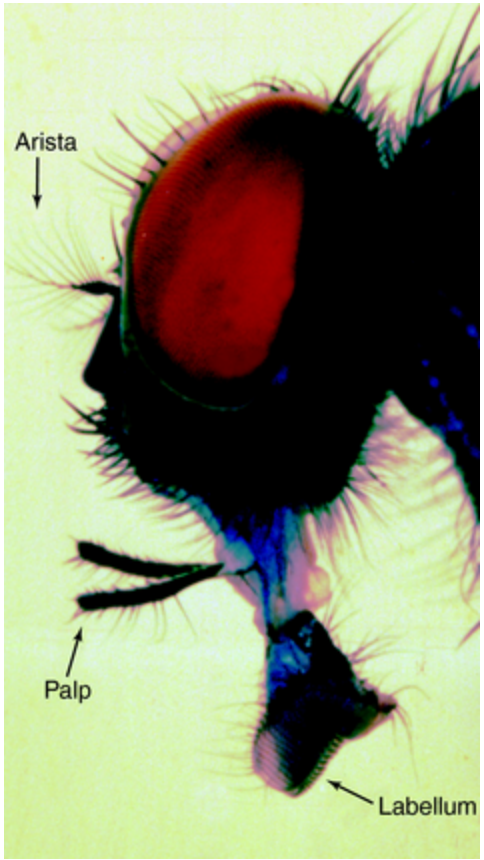

FIGURE 2-13 Head of *Musca domestica* (Cyclorrhapha: Muscidae), the common housefly. The proboscis is retractable into the head.

Family Muscidae

Musca

Identification

The genus *Musca* contains 26 species of which three, *M. domestica*, the common housefly, *Musca autumnalis*, the face fly, and *Musca vetustissima*, the Australian bush fly, may serve as examples. These three species resemble one another closely enough to require an expert to distinguish specimens on morphologic grounds but differ sufficiently in behavior to make their identities obvious to anyone familiar with their habits. The mouthparts of these all too familiar flies consist of a fleshy, retractable proboscis terminating in a pair of corrugated spongy organs, the labella (see Figure 2-13).

Life history and disease transmission

M. domestica lays its eggs on animal manure or almost any kind of decaying organic material. A female *M. domestica* may deposit 2000 eggs in an average lifetime of 6 to 8 weeks. A tiny, white, first-stage larva (maggot) hatches from the egg in a day or less at summer temperatures. This larva grows, molts twice, and in a few days becomes a fully developed third-stage larva. When ready to pupate, the third-stage larva migrates into a drier medium, shortens, thickens, and becomes darker in color as a result of hardening and tanning of the third-stage cuticle in forming the puparium. The adult fly emerges in 2 or 3 weeks by forcing off the end of the puparium with its **ptilinum,** a bladderlike structure inflated with hemolymph. The ptilinum projects from the **frontal suture** and is withdrawn into the head after the fly has emerged from the

puparium. Like the umbilicus of mammals, it is of no further service to the animal. The adult fly then makes its way to the surface of the medium in which the pupa lies buried, expands its wings by pumping hemolymph into the wing veins, and flies away in search of food. The housefly feeds on feces, syrup, milk, decaying fruit, and other dissolved and soluble materials. Houseflies will feed on secretions around the eyes, nostrils, and mouth and on blood that continues to ooze from wounds made by tabanids. *Musca* species annoy horses and cattle to distraction on warm, sunny days. Bacteria, protozoan cysts, helminth eggs, and other disease organisms may be transported from filth to food, body openings, and wounds by way of the feces, vomit spots, sticky feet, and body hairs of houseflies. The housefly also serves as a biologic vector of *Draschia megastoma* and *Habronema muscae*, nematode parasites of the stomach of the horse (Table 2-5).

TABLE 2-5 Some Pathogens Vectored by Flies of the Family Muscidae

Fly	Mechanically Vectored	Biologically Vectored
Musca domestica	Suspected of transmitting many agents but seldom shown conclusively	Spirurid nematodes
		Draschia megastoma: horses
		Habronema muscae: horses
Musca autumnalis	Keratoconjunctivitis	Spirurid nematodes
		Thelazia species: cattle

Fannia	Unknown	Spirurid nematode
		Thelazia species: dogs
Stomoxys	Suspected	Spirurid nematodes
		Habronema microstoma: horses
Haematobia	Suspected	Filariid nematodes
		Stephanofilaria: cattle

M. autumnalis (the face fly) was introduced into North America from Europe, Asia, or Africa in the early 1950s. These flies crawl about the faces of horses and cattle, feeding on the ocular and nasal discharges induced by their presence, and are extremely annoying to pastured animals. Eggs are deposited in fresh cattle dung, and the larvae pupate in the dried dung or nearby soil. The adult flies overwinter in buildings. These hibernating adults, like those of the cluster fly, *Pollenia rudis* (a calliphorid fly that as a maggot parasitizes earthworms and whose adults cluster together inside dwellings in winter to hibernate), cause considerable annoyance to the human occupants when, aroused by a spell of warmish weather, they go buzzing and blundering about the house, falling into drinks and making themselves generally disagreeable. Curiously, the active adult face fly of summer appears loath to enter buildings and may be observed to swarm off dairy cows as they enter the stable to be milked. They wait outside during milking and swarm back on the cows as they emerge from the stable. This, of course, contrasts with the behavior of *M. domestica*, so appropriately called the housefly.

Grazing cattle afflicted with face fly infestations have been shown to increase their herbage dry matter intake as they graze deeper in the sward by taking heavier bites as they try to dislodge the flies from their muzzles (Dougherty et al, 1993). Face flies serve as biologic vectors of *Thelazia* species (eyeworm), a genus of nematode worms that infect the conjunctival sacs of horses and cattle (Chitwood and Stoffolano, 1971). *M. autumnalis* also serves as mechanical vector of infectious bovine keratoconjunctivitis organisms *(Moraxella bovis)*, which can survive for up to 3 days on the legs of the fly (Steve and Lilly, 1965). Cattle protected from face flies had less keratoconjunctivitis and yielded fewer isolates of hemolytic *M. bovis* than did unprotected cattle. “Infection first began to spread from herd to herd after face fly populations exceeded 10/animal for 1 month” (Gerhardt et al, 1981).

M. vetustissima, the Australian bush fly, resembles *M. autumnalis* in preferring to remain outdoors, by breeding in livestock manures, and in crawling about on the faces of livestock. However, *M. vetustissima* differs in displaying an exasperating affinity for the faces of human beings as well as livestock, by involvement of its larvae in wound myiasis, and by an inability to hibernate. Instead of hibernating, *M. vetustissima* reinvades southeastern Australia each spring from the more tropical regions to the north.

In South Africa, *Musca lusoria*, *Musca fasciata*, and *Musca nevilli* have been identified as vectors of a filariid worm, *Parafilaria bovicola*, that lives in the subcutis, bores a hole to the surface, and discharges its eggs in the bloody fluid that weeps from the lesion (Nevill, 1975, 1985; Kleynhans, 1987).

Fannia canicularis (the lesser or little housefly) breeds in ground contaminated with septage drainage and is commonly found associated with large concentrations of chicken manure. These flies can reach impressive numbers as pests and can require pest management. Species of *Fannia* in California are capable of the transmission of the canine eye worm, *Thelazia californiensis*.

Control of filth flies

Selection and manner of applying insecticide must conform to regulations that are subject to change. Read the label carefully before applying any insecticide to premises or to domestic animals. Regular spraying of animal sheds, stables, and kennels with residual insecticides should provide good control of flies and other flying insects if reasonable effort is expended to minimize the extent of breeding sites available to these insects. Space sprays, insecticidal baits, and insecticidal resin strips offer additional control. Diazinon, tetrachlorvinphos, and dichlorvos have excellent residual activity against houseflies, face flies, horn flies, stable flies, and mosquitoes for 1 to 4 weeks after application. Spraying resting and breeding areas is often effective. Dichlorvos, pyrethrins, and pyrethroids are used as space sprays for feedlots and sheds. These insecticides may be misted over the backs of animals every 3 to 7 days. Fly baits containing dichlorvos may be sprayed or sprinkled on fly-roosting areas. The sugar fly bait New Improved Golden Malrin contains methomyl and muscalure, a fly-attracting pheromone. The bait is sprinkled around barns. Muscalure attracts and keeps the flies around the bait, thus achieving an increased kill by the insecticide.

Fly control in dairy barns and milk rooms may be achieved with dichlorvos baits, foggers, and sprays. Tetrachlorvinphos and coumaphos are used as sprays or in dust bags and may be applied after milking.

The application of insecticides to lactating cows producing milk for human consumption demands extreme caution because there must not be any pesticide in the milk. *Read the label before using any pesticide*. It is against the law to use a pesticide in any manner not specified on the label, and violations with respect to dairy cows are particularly serious.

The control of face flies and houseflies on beef cattle and dry dairy cattle may be achieved by regular application of insecticides to animals and fly-breeding sites. Dichlorvos in mineral oil may be smeared daily on the faces of cattle for face fly control. Coumaphos or tetrachlorvinphos may be applied to cattle as a free-flowing dust two or three times a week or self-applied by means of self-treatment dust bags. Pyrethrin or pyrethroid sprays may also be used. Pyrethroid-containing ear tags and similar devices that can be attached to animals allow a continuous, controlled release of insecticides to aid in the control of flies attacking cattle. Tetrachlorvinphos, a larvicidal organophosphate, prevents the growth of larvae of coprophilic flies in the manure of cattle fed this compound and may be given to lactating dairy cows.

Face fly control on horses may be attempted by application of coumaphos, pyrethrins, or pyrethroids to the entire horse, and elimination or insecticidal treatment of breeding sites (i.e., cow manure) when feasible. Face flies do not pursue their victims

indoors, so stabling horses during hours of peak fly activity often proves to be the best solution.

Biologic control methods using parasitoid wasps have been developed and commercialized for the control of *Musca* species. The larvae of the wasps develop in the maggots of these flies, causing their death. It is possible to purchase parasitized fly pupae from which the adult wasps will emerge, and these can be used to release the wasps on farms. The use of these wasps has proved to be of some benefit when incorporated into integrated fly management programs (Geden et al, 1992).

Stomoxys

Identification

The stable fly, *Stomoxys calcitrans*, resembles *Musca* species but has a long, pointed proboscis with which it inflicts painful bites instead of the vacuum cleaner affair with which *Musca* sucks up liquids from little puddles. The palpi of *Stomoxys* are shorter than the proboscis (Figure 2-14; compare with *Haematobia*, Figure 2-15). The third-stage larvae resemble those of *Musca* and have posterior spiracles with sinuous slits, but the spiracles are set farther apart than those of *Musca* (see Figure 2-19).

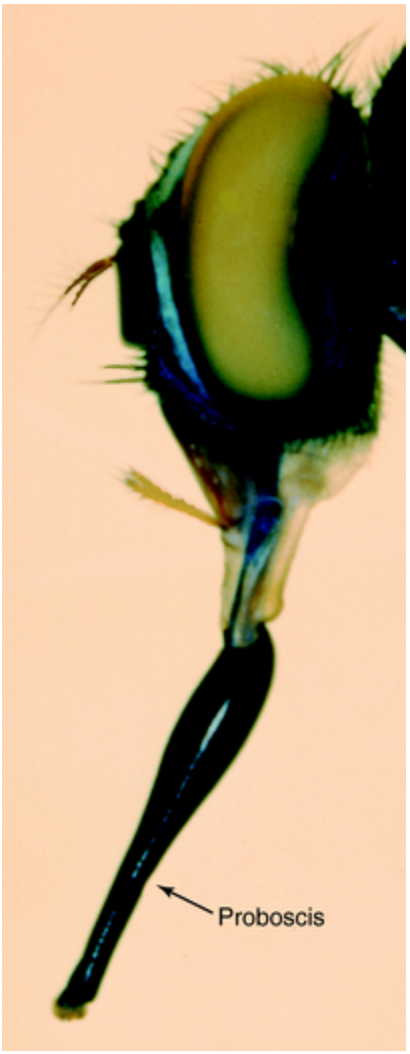

FIGURE 2-14 Head of *Stomoxys calcitrans* (Cyclorrhapha: Muscidae), the stable fly. In feeding, the entire proboscis is thrust into the skin of the host.

FIGURE 2-15 Head of *Haematobia irritans* (Cyclorrhapha: Muscidae), the horn fly. *Haematobia* somewhat resembles *Stomoxys* but is only half as large and has palps almost as long as its proboscis (compare with Figure 2-14).

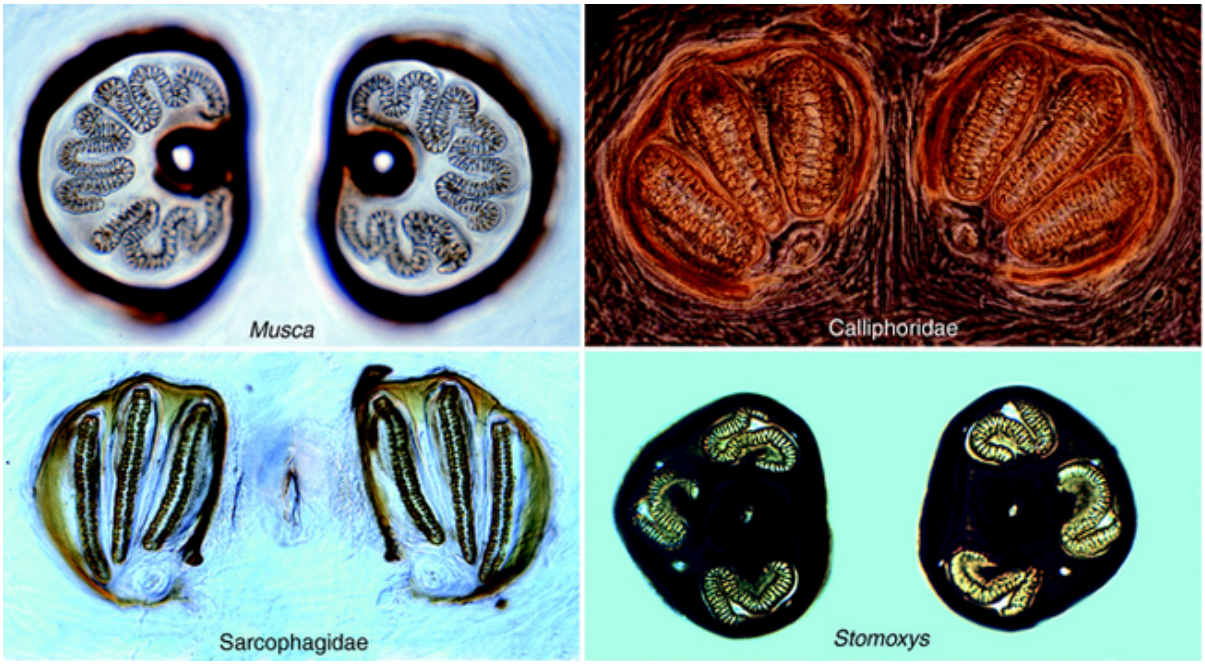

FIGURE 2-19 Muscoid spiracles.

Life history

Stable flies have a life history similar to that of face flies but differ in preferring decaying organic materials, such as piles of lawn

clippings, damp hay, grain, or animal manure for egg laying. Stable flies of both sexes feed on blood once or twice a day, depending on the ambient temperature, and suspend operations entirely during cold spells.

Injury and disease transmission

The presence of *Stomoxys* on grazing cattle will cause increased head and ear movement, skin twitches, and tail swishes. It is interesting to note that the annoyed cattle will increase their herbage dry matter intake and bite masses (Dougherty et al, 1994). The bite of the stable fly is painful and results in the interrupted feeding patterns observed with tabanids. The stable fly serves as biologic vector of *Habronema microstoma*, a nematode parasite of the stomach of the horse (see Table 2-5).

Control of stable flies

Stable flies attack cattle, horses, most other domestic animals, and humans on warm days throughout the summer. Regular application of pyrethrins, synergized pyrethrins, pyrethroids, coumaphos, or dichlorvos is indicated. Efforts to control *S. calcitrans* should include elimination of breeding sites (e.g., lawn clippings, green chop, damp bedding) and application of insecticides to areas where they habitually rest. Repellents in the form of sprays or smears may afford relief for several hours. These flies, with their piercing mouthparts, can theoretically be controlled with systemic and topical insecticides. Chlorpyrifos, coumaphos, phosmet, or tetrachlorvinphos is applied either by spray or with self-treatment dust bags or backrubbers. The biologic control of *S. calcitrans* by the release of parasitoid wasps seems to require further refinement

before routine success occurs in the field (Andress and Campbell, 1994).

Haematobia

Identification

The horn fly, *Haematobia irritans*, found on the backs of cattle and to a lesser extent on horses, is about half the size of *Stomoxys* and has a relatively shorter proboscis. The palps are nearly long enough to reach the tip of the proboscis, in contrast to those of *Stomoxys* (compare Figures 2-14 and 2-15). Horn flies were first reported in the United States in the fall of 1887 when they were found in Camden, New Jersey. They spread rapidly throughout the United States, appeared in Hawaii in 1897, and have spread though Mexico, Central America, and northern South America (e.g., Guyana) (Craig, 1976). The horn fly was also discovered in Argentina, and it has rapidly spread throughout that country (Anziani et al, 1993).

Life history

Horn flies remain on cattle during the warmer seasons of the year, periodically biting their hosts and sucking blood. They are most obvious on the backs of their hosts but take refuge on the ventral abdomen during rain or on particularly hot, sunny days. When a cow defecates, a number of her horn flies swarm to the dropping to lay their eggs and then return to the cow. Larvae hatch in less than a day and crawl into the dropping to feed. Pupation occurs in 4 days, and emergence of the adult follows in 6 more days. In ideal warm, humid weather, the entire cycle from egg to egg requires 2

weeks or less but may require a month or longer in dryer, cooler weather. In temperate climates, the horn fly overwinters in the pupal stage, with diapause occurring principally during September (Thomas, Hall, and Berry, 1987).

Injury and disease transmission

When sufficiently numerous, horn flies can impair milk production and weight gains. Cattle protected from horn fly attack by ear tags impregnated with fenvalerate achieved 18% greater live weight gains than did untreated controls (Foil, DeRoven, and Morrison, 1996; Haufe, 1982). *H. irritans* serves as a biologic vector of *Stephanofilaria stilesi*, a filarioid nematode parasite of North American cattle and etiologic agent of stephanofilariasis, a dermatitis usually confined to the midventral region of the abdomen.

Control of horn flies

Because they remain on the host most of their lives, adult horn flies are vulnerable to effective insecticides applied to cattle by means of sprays, dusts, backrubbers, stock oilers, and insecticide-impregnated plastic ear tags. In fact, horn fly control has depended almost exclusively on insecticides, with the unfortunate development of resistance on the part of the fly to many of them (e.g., DDT, methoxychlor, toxaphene, fenchlorphos, stirofos, permethrin, and fenvalerate) (Marchionado, 1987). The insecticide tetrachlorvinphos or the synthetic juvenile hormone methoprene may be fed to cattle to render the manure unfit for development and pupation, thus interrupting the life history of *H. irritans*. Treatment of cattle with eprinomectin produced efficacy against horn flies for at least 2

weeks with good efficacy for longer periods, whereas ivermectin in a pour-on form is effective for at least 4 weeks (Arrioja-Dechert, 1997; Shoop et al, 1996).

The Bruce walk-through horn fly trap affords 50% reduction in horn fly numbers mechanically. Cattle walking through the 10-foot trap contact strips of canvas or carpeting, which dislodge the horn flies on their backs and sides. The host leaves some of its flies behind in the trap, and, provided the process is repeated often enough, the population of horn flies in the herd is significantly reduced (Hall, Doisy, and Teasley, 1987).

Glossina

Identification

Tsetses (*Glossina* species) are localized to Africa and are of significant importance to human and animal health, to the preservation of African wildlife, and to the economy of Africa and the world at large. Each antenna of *Glossina* has a long arista that is "feathered" along one edge. The palps and long slender proboscis are equal in length, the palps forming a sheath for the proboscis at rest (Figure 2-16).

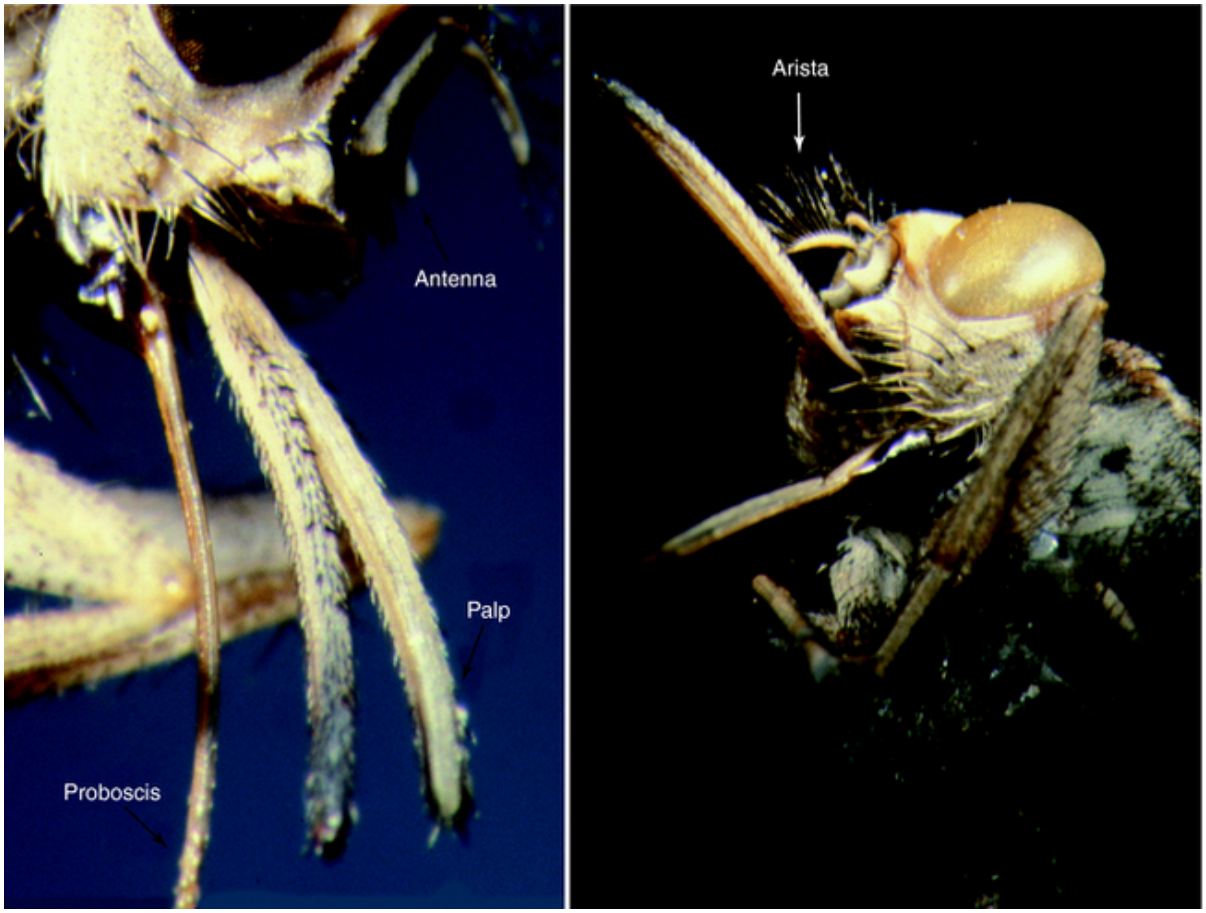

FIGURE 2-16 Head of *Glossina* (Cyclorrhapha: Muscidae), the tsetse that transmits many important species of African trypanosomes.

Life history

The female tsetse bears only one larva at a time. Larval development is completed in the abdomen of the mother, with all three stages feeding on fluids from special uterine glands. It is interesting that milk secretion has evolved independently among both the highest vertebrates and the highest invertebrates. Several blood meals at regular intervals are required to support the larva during its developmental period of roughly 1 to 4 weeks. When extruded by the female tsetse, the fully developed third-stage larva almost immediately burrows into the soil and prepares to enter the pupal

stage. A fourth larval stage occurs within the puparium before metamorphosis to the adult stage at last takes place.

Disease transmission

The great importance of the tsetse is its role as biologic vector of various trypanosomiases of humans and their domestic animals. African sleeping sickness of humans and "nagana" and related diseases of domestic animals are considered in Chapter 3.

Eradication

The tsetse has been eradicated from Zanzibar, the island next to the African continent (Vreysen et al, 2000). Thought has now been given to a major sterile release campaign program as was used in the control of *Cochliomyia hominivorax* (discussed later) throughout the rest of the African continent (Kabayo, 2002). Some think the entire plan too mammoth and unworkable (Rogers and Randolph, 2002). The International Atomic Energy Agency continues to support the plan, and the first releases of sterile males occurred in Ethiopia in June of 2007. There is concern that the complete removal of these great protectors of African wildlife (trypanosomes and their tsetse vectors have protected the game of Africa through the prevention of successful colonization by nonindigenous species) may have colossal long-term impacts on the environment of the African continent if imported species can be allowed to compete for the same geographic regions as the long-protected indigenous wildlife. This potential eradication of the tsetse can be viewed as a major ethical dilemma for veterinarians weighing the advantages of disease eradication, wildlife protection, improved nutrition for the African continent, and ecologic protection.

Family Hippoboscidae, keds

Identification

Hippoboscids are dorsoventrally flattened, sometimes wingless flies with piercing mouthparts. The antennae are embedded in pits in the sides of the head. *M. ovinus*, the sheep ked; *Hippobosca equina*, the horse louse fly; and *Lipoptena cervi*, the deer ked, are examples (Figure 2-17). *Melophagus* is wingless; the wings of *Hippobosca* remain well developed and functional throughout life; and *Lipoptena* have wings when they emerge from the pupal case. However, the wings of *Lipoptena* break off near the base (see Figure 2-17) once the fly has alighted on a host. *Lipoptena* may attack horses and other domestic animals in addition to deer, and casual observation suggests that their attacks are particularly obnoxious to horses.

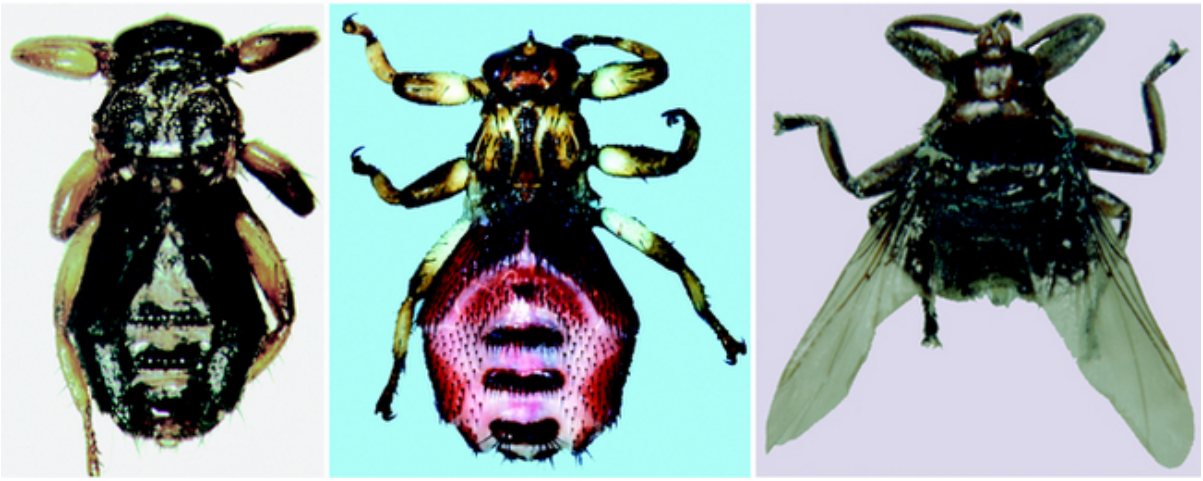

FIGURE 2-17 Examples of family Hippoboscidae. *Left*, *Melophagus ovinus*, the sheep ked; *center*, *Lipoptena cervi*, the deer ked recovered from a horse; *right*, a *Pseudolynchia* from a bird.

Life history

Like tsetses, hippoboscids retain their larvae in their abdomens until they are ready to pupate, nourishing them during development with uterine gland secretions. In the case of *M. ovinus*, larval development requires about a week, and the extruded larva pupates within a few hours. The chestnut-brown pupal cases remain glued to the wool of the host sheep throughout metamorphosis of the adult fly, which emerges in 3 to 6 weeks, depending on the ambient temperature. The entire life of the sheep ked is thus spent on the host. Shearing and organophosphorus insecticides make life very uncertain for these parasites.

Dealate *L. cervi* males and females remain on their normal North American hosts, white-tailed deer *(Odocoileus virginianus)* and wapiti *(Cervus canadensis)*, through most of the year. In spring, larvae are deposited in the haircoat, where they pupate and fall to the ground. Adult *L. cervi* flies emerge from the puparia from September to early December and fly off in search of a host. As soon as the ked alights on a deer, its wings break off and the ked begins to feed. The bite of *L. cervi* is relatively painless to humans but may be followed in several days by a pruriginous welt that may remain intensely pruritic for 2 to 3 weeks (Bequaert, 1942).

Disease transmission

M. ovinus is host to *Trypanosoma melophagium*, which it transmits to sheep. If all keds are removed, the trypanosomes rapidly disappear from the sheep's blood, so it is the ked and not the sheep that represents the true reservoir of infection. Like *T. theileri* of cattle, *T. melophagium* appears to be totally nonpathogenic to its vertebrate host.

Control of hippoboscids

Coumaphos and diazinon as dips or sprays provide excellent control of *M. ovinus* when applied after shearing. In small flocks, diazinon can be applied most conveniently with a garden sprinkling can. Groups of about 20 sheep should be crowded in a small pen so there is just room enough left for one person to move among them. Waterproof overalls and boots should be worn while sprinkling the insecticide over the backs of the sheep. Ivermectin at 200 mg/kg given subcutaneously in sheep controls *M. ovinus* (Molina and Euzeby, 1982). *L. cervi* has been controlled also in red deer and roe deer by the administration of ivermectin (Kutzer, 1988).

What to do about attacks of *L. cervi* on horses short of keeping them indoors until the alate hippoboscids find their proper hosts is problematic.

Family Sarcophagidae, flesh flies

An adult sarcophagid is about twice as large as a housefly. The thorax is gray with dark, longitudinal stripes, and the abdomen is checkered gray and black (Figure 2-18). Third-stage sarcophagid larvae resemble housefly maggots but are larger. The posterior spiracles are deeply sunken in a rounded concavity; the inner slit of each spiracle is directed down and away from the median line (Figure 2-19). Differentiation of *Sarcophaga* and *Wohlfahrtia* larvae requires that adult flies be reared from them. Place the larvae in question and a piece of liver on 3 to 5 cm of sand or loamy soil in a canning jar. When, after a day or so, the larvae have entered the substrate to pupate, remove the liver to avoid obnoxious odors and cover the mouth of the jar with a layer of cheesecloth secured with

a rubber band to provide air yet prevent the escape of flies after they have emerged from the pupal cases. The arista of *Wohlfahrtia* bears only very short hairs, whereas the arista of *Sarcophaga* is covered nearly to its tip with long hairs. These rearing instructions serve equally well for calliphorids, but best results are obtained with larvae that are almost ready to pupate, especially when obligate parasitic species are involved.

FIGURE 2-18 *Sarcophaga* (Cyclorrhapha: Sarcophagidae), a flesh fly. About twice as large as a housefly, *Sarcophaga* is gray, with longitudinal dark stripes on the thorax and a checkered gray and black abdomen.

Family Calliphoridae, blowflies

Identification

Adult calliphorids (Gr. *kallos*, beauty + *phoros*, bearing) are usually intermediate in size between *Musca* and *Sarcophaga* and typically display brilliant metallic blue, green, copper, or black hues (Figure

2-20). The common names “bluebottle” and “greenbottle” fly refer to the coloration of these flies, which are also called “blowflies” because they “blow” (i.e., deposit) their eggs or larvae in meat. Particular species differ in their preferences regarding the freshness of the meat, from living flesh to carrion in an advanced state of decomposition. Most calliphorids are scavengers or facultative parasites, but a few (e.g., *C. hominivorax*, the American screwworm) are obligate parasites. Third-stage larvae of Calliphoridae are muscoid maggots that differ from those of Sarcophagidae in having posterior spiracles that lie flush with the posterior face of the larva (or, less commonly, are sunken in a shallow, slitlike concavity); the inner slits of the spiracles are directed obliquely downward and toward the median line (see Figure 2-19). Larvae of the very important species *C. hominivorax* may be identified by the dark pigmentation of their tracheal trunks through the last three or four segments (see Figure 2-12).

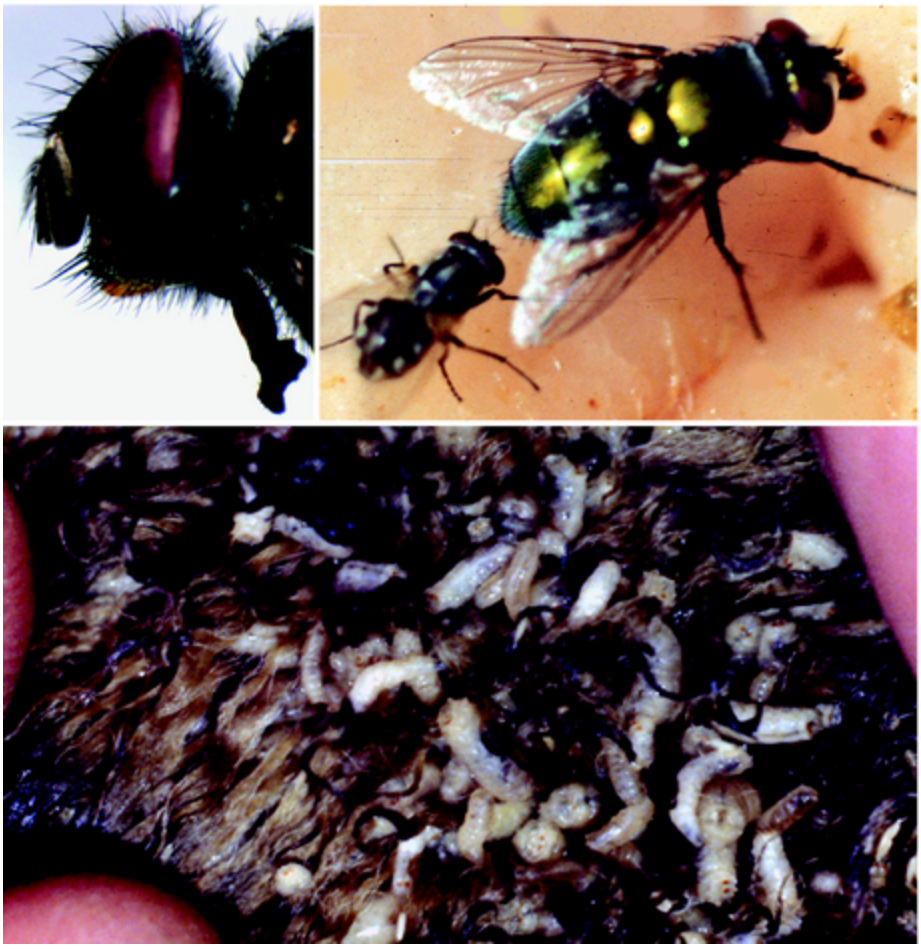

FIGURE 2-20 Calliphorid flies. *Top left*, The mouthparts and head, similar to *Musca*. *Top right*, A large shiny calliphorid, *Lucilia cuprina*, with another fly that is about the size of the housefly. *Bottom*, Maggots of *Lucilia cuprina* in the fleece of a sheep with wool strike.

Life history and injury (myiasis)

Myiasis can be defined and described in different ways. Relative to the biology of the flies, **primary myiasis** typically refers to myiasis in cases in which the insect requires a living host for the larvae to feed on. **Secondary myiasis** is then said to represent cases due to flies that usually feed on dead and decaying flesh sometimes developing in weak, debilitated, wounded, soiled, or immobilized

animals. Myiasis can also be described by the site of the lesion, e.g., aural myiasis, nasal myiasis, and so on.

Facultatively parasitic calliphorids are drawn to such attractions as suppurating wounds; skin soiled with urine, vomitus, or feces; and bacterial decomposition products that tend to accumulate in the fleece of a wet sheep. Once established in exudate or necrotic tissue, some kinds of these facultative parasites may later invade living tissue, whereas others do not. For example, the "surgical maggots" of *Phaenicia sericata* and *Phormia regina* are still used occasionally in the treatment of osteomyelitis and other refractory suppurative lesions to clear away necrotic debris and promote healing. Ideally the surgical maggots do not invade healthy tissue, but strains vary and some of them do not know where to stop. A brave and resourceful gentleman of Dr. Georgi's acquaintance applied this technique in treating his own wounds when a prisoner of war in Vietnam. Once the maggots had done their work to his satisfaction, he flushed them away with his urine.

Wool strike is a common and serious problem in many sheep-raising regions of the world (Figure 2-21). Adult calliphorids are attracted to areas of fleece that have become soiled by feces or urine or were kept damp long enough for bacterial growth to occur and generate odors that lure flies to feed and lay their eggs. The areas involved in wool strike thus include the perineum, prepuce, and, during periods of considerable rainfall, water-soaked wool of the flanks, withers, and ventral neck region. Fleece rot, caused by *Pseudomonas aeruginosa*, and dermatophilosis, caused by *Dermatophilus congolense*, predispose sheep to wool strike by *Lucilia cuprina*, and a significantly greater incidence of body strikes was

observed in lambs infected with both of these bacteria than with either bacterium alone (Gherardi et al, 1983). Several genera of calliphorid flies are commonly involved, and each geographic region has its particular scourge among the general assemblage of facultative parasites and scavengers. In Australia, one species, *L. cuprina*, stands out as a specialist in wool strike. This fly, although still a facultative parasite in that it is able to develop in carrion, has become so adept at locating suitable sheep on which to deposit its eggs that it has become the culprit responsible for initiating most cases of wool strike in Australia. The maggots feed on scales and exudate at the surface of the skin, occasionally penetrating the underlying tissues. When ready to pupate, the larvae of *L. cuprina* wait until night to leave the carcass (Smith et al, 1981). In this way the pupae and emerging adults of this highly specialized parasite tend to become concentrated around the preferred resting sites, or camps, of their host species. Once *L. cuprina* has initiated a strike, other species of flies are attracted to feed and lay their eggs in the developing lesions. As the morbid process advances, these less-specialized newcomers tend to replace *L. cuprina*. Toxins absorbed from the myiasis lesion rapidly incapacitate the sheep and lead to its death in a matter of days. Eventually, scavenger species take over the carcass and reduce it to hair and bone. Financial loss caused by wool strike is reckoned in terms of outright death losses, loss of wool, decreased quality of wool, loss of weight, and costs of treatment and preventive measures.

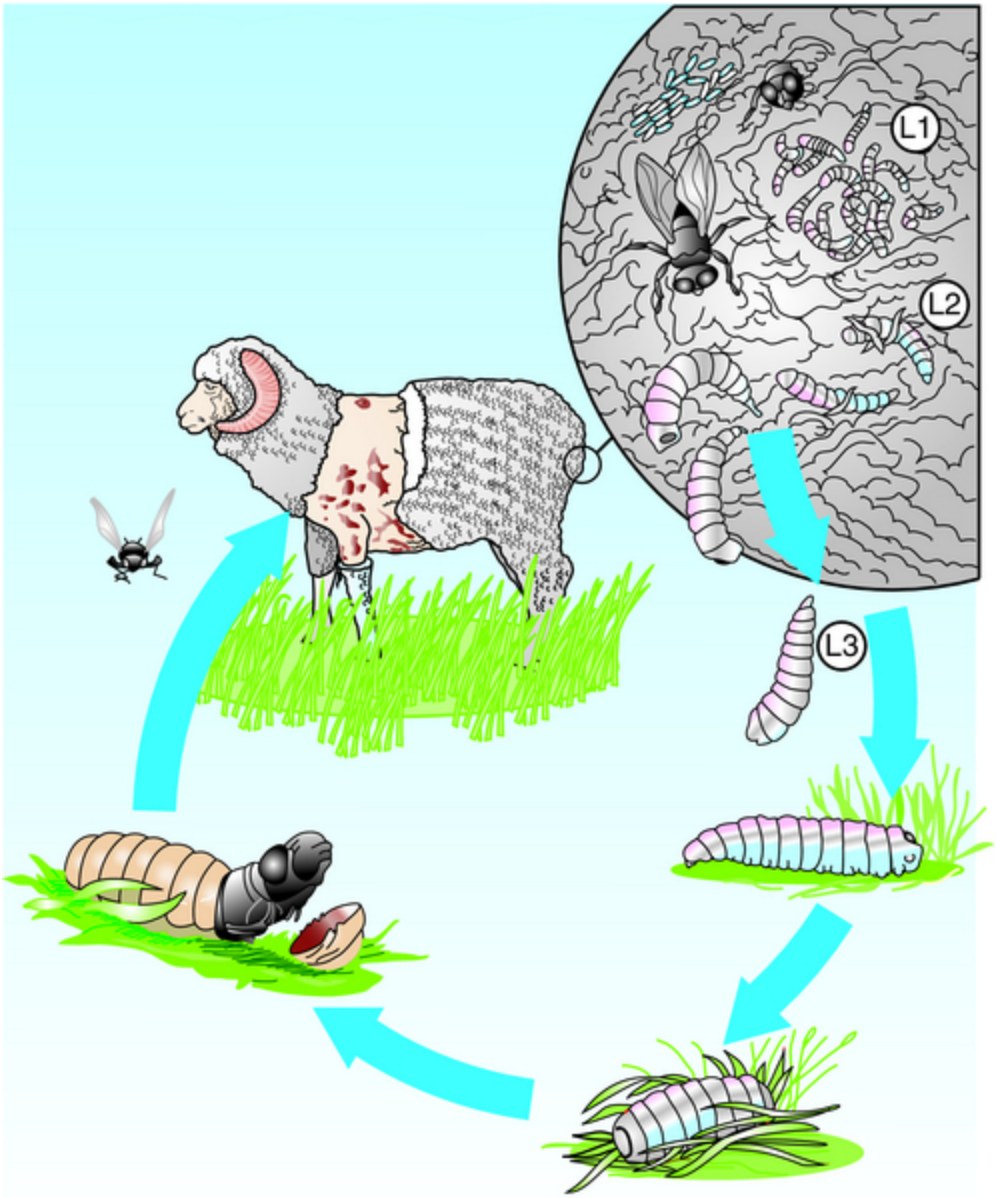

FIGURE 2-21 Life history of the wool strike fly, *Lucilia cuprina*. Adult female *L. cuprina* flies deposit their eggs in moist and soiled wool. Larvae hatch from these eggs, feed on scales and exudate at the surface of the skin, and undergo two molts before falling to the ground to pupate. The adult fly pushes off the end of the puparium by inflating its baglike ptilinum with hemolymph. Having emerged from the puparium, the fly inflates its wings by pumping hemolymph into the wing veins, retracts its ptilinum into the head once and for all, and flies off in search of suitably smelly sheep. The Australian Merino wether in the picture has suffered fly-strike in three stages. The flies first attacked a spot between his shoulders that had collected rainwater and supported

bacterial growth. The exudate from this lesion flowed over the wether's shoulders and brisket and greatly extended the area susceptible to fly attack. The shepherd has clipped all of the wool from both shoulders and brisket and treated the lesions with an insecticide, but now the flies are attracted to the breech area, which is soiled with feces, so this area too must be clipped and medicated or the wether will likely die of "crutch strike."

Old, weakened, or paretic dogs with urine-soaked haircoats sometimes develop a form of myiasis analogous to wool strike. As such an unfortunate animal lies in the "healing rays of the sun," the blowflies are busy laying eggs in its haircoat, and in a few days maggots will be skinning it alive. Frequently owners who present long-haired dogs with advanced cases of cutaneous myiasis are totally unaware of the mayhem taking place underneath the haircoat. The condition of the patient can be evaluated accurately and effective treatment undertaken only after the hair has been clipped away and all affected areas bathed. Most of the maggots will be removed in the process; any remaining may be routed by judicious local application of an insecticidal solution such as a pyrethroid or an organophosphate. A really vigorous application of insecticide might easily kill the debilitated and denuded host.

Weakened or defective calves born at pasture are also fair game for members of the family Calliphoridae. It is amazing how quickly the shiny flies appear seemingly out of nowhere and how rapidly their egg masses accumulate about the umbilicus of a newborn calf with cerebellar hypoplasia or muscle contracture. The possibility of myiasis must always be considered in the case of animals incapacitated during warm weather, especially if they are forced to remain outdoors.

Rabbits, wild animals, and birds may suffer serious losses to myiasis. Domestic rabbits are often victims of myiasis. Flies attracted to lay their eggs on rabbits can cause horrible lesions in rabbits that are housed outdoors even in relatively good conditions for short periods of time. The lesions are horrible and can be fatal to the rabbit, along with causing severe distress to the owners. This is unfortunately not an uncommon event, and rabbits need to be protected from such infestations (Anderson and Huitson, 2004). Larvae of the sarcophagid fly *Neobellieria citellivora* cause lethal myiasis in ground squirrels *(Spermophilus columbianus)* in Canada (Michener, 1993). Arendt (1985) estimated that infection with larvae of *Philornis deceptivus* (family Muscidae) were responsible for 97% of the mortality observed among pearly-eyed thrasher nestlings *(Margarops fuscatus)* in Puerto Rico. In North America, major causes of avian myiasis are bloodsucking maggots of the genus *Protocalliphora* (Sabrosky, Bennett, and Whitworth, 1989). Larvae of sarcophagid flies, genus *Cistudinomyia*, are capable of causing lethal myiasis in geckos (DeMarmels, 1994).

The American screwworm fly, *C. hominivorax*, is an example of a primary myiasis producing fly. Females lay their eggs on fresh, uninfected wounds of all kinds. About 200 eggs are deposited in tidy rows. The eggs hatch within a day, and the obligate parasitic maggots commence feeding on living flesh and in so doing produce a foul-smelling, brownish-red discharge. The larvae leave the host in 5 to 7 days and enter the soil to pupate. Adult flies emerge from the pupal cases one to several weeks later. Wherever it occurs, *C. hominivorax* is a serious menace to man and beast alike. Unconscious victims of accidents or alcohol intoxication lying

helplessly exposed have been fatally infected or have had their facial bones completely eaten away by screwworm maggots. Docking and castrating wounds, wire cuts, the navels of newborn animals, tick-bite wounds, shear cuts, needle grass wounds, and even fresh brands may attract the attentions of *C. hominivorax*. A nationwide control program based on treating wounds of all infected animals with insecticidal smears and releasing billions of sterilized flies has succeeded in eliminating screwworm myiasis from the United States. The adult flies are sterilized by gamma radiation, which induces dominant lethal mutations in the sperm. Because the female screwworm mates only once and because the wild population of the fly is relatively small, adding hordes of sexually competent but sterile males reduces the probability of successful fertilization to nil. By the use of sterile males produced in Mexico, the American screwworm was eradicated from Libya where it had been accidentally introduced, probably on imported livestock, in 1988 (Linquist, Abusowa, and Hall, 1992).

Treatment of myiasis

Coumaphos is widely employed in the treatment of cutaneous myiasis. This agent may be applied to the cattle by dipping, but most commonly it is sprayed or smeared directly on the maggot-infested lesions. Ivermectin and doramectin administered subcutaneously to cattle can serve as a prophylactic against infestation by larvae of *C. hominivorax* and appear to be useful aids in the prevention of umbilical myiasis and fly-strike associated with castration (Anziani and Loreficce, 1993; Muniz et al, 1995).

For treatment of wool strike in sheep, coumaphos and diazinon are recommended as sprays, dips, or local applications to affected areas. All wool soiled or underrun by maggots should first be clipped away. Ivermectin when applied as a jetting fluid appears to aid against blowfly-strike of sheep in Australia (Eagleson et al, 1993). Subcutaneous injections of infested sheep in Hungary with either ivermectin or moxidectin failed to cause rapid-acting treatment of the infested sheep, and 7 days after treatment the majority of treated sheep were still severely infested (Farkas et al, 1996). Also used in Australia with good success is a jetting fluid with cyromazine, an insect growth regulator, that can be mixed with diazinon (Levot and Sales, 1998).

The extent of measures taken to prevent fly-strike in sheep should be proportional to the degree of risk. Clipping the wool of the breech and area around the prepuce greatly reduces the amount of moisture and filth that can be retained in those regions of the fleece. Amputating the tails of lambs represents about the minimum of effort that ought to be expended on fly-strike control, but in some parts of the world lambs manage to grow up with their tails intact. In the **Mules' operation,** widely practiced in Australia, with perhaps up to 30 million lambs treated each year, redundant folds of skin from the posterior aspects of the thighs and the tail head are removed with a pair of sharp dagging shears. When the resultant wounds heal, the skin of the breech is drawn taut, thus extending the relatively hairless area immediately surrounding the anus and vulva and thereby reducing the moisture- and filth-carrying capacity of the breech. This operation, carried out in a minute or so without surgical preparation, anesthesia, or aftercare, seems brutal until one

has had an opportunity to compare its effects on the patient with those inflicted by *L. cuprina*.

Families Oestridae, Hypodermatidae, Gasterophilidae, and Cuterebridae; the botflies

The botflies are highly host-specific and site-specific parasites in the larval (i.e., bot) stage and total slaves to reproduction in the adult stage. The adults have vestigial mouthparts and must carry on their courtship rituals and egg laying on energy stored away when they were larvae. Fully developed bots are larger and stouter than are muscid, sarcophagid, and calliphorid maggots, from which they can readily be distinguished by their posterior spiracles (Figure 2-22; see also Figure 2-19). In fact, when found in their accustomed locations in their normal hosts, bots present very little in the way of a diagnostic challenge; a bot in a sheep's nasal passages is an *Oestrus;* a bot in a cow's dorsal subcutis is a *Hypoderma;* a bot in a horse's stomach is a *Gasterophilus;* and there is hardly any sense in making more an exercise of it than that. However, the earlier stages of bots are more difficult to distinguish from maggots and, if found migrating in other than its normal host, will require the services of an expert entomologist for identification. First-stage *Hypoderma* larvae have been found migrating aberrantly through the brain of horses, and *Cuterebra* larvae, normally parasites of rodents and lagomorphs, have been found in the brains of cats and dogs and much more commonly in their subcutaneous tissues. *Hypoderma* and *Cuterebra* also occasionally invade humans and migrate subcutaneously. *Oestrus ovis* may larviposit in the eyes of shepherds and thus cause a temporary but painful ocular myiasis.

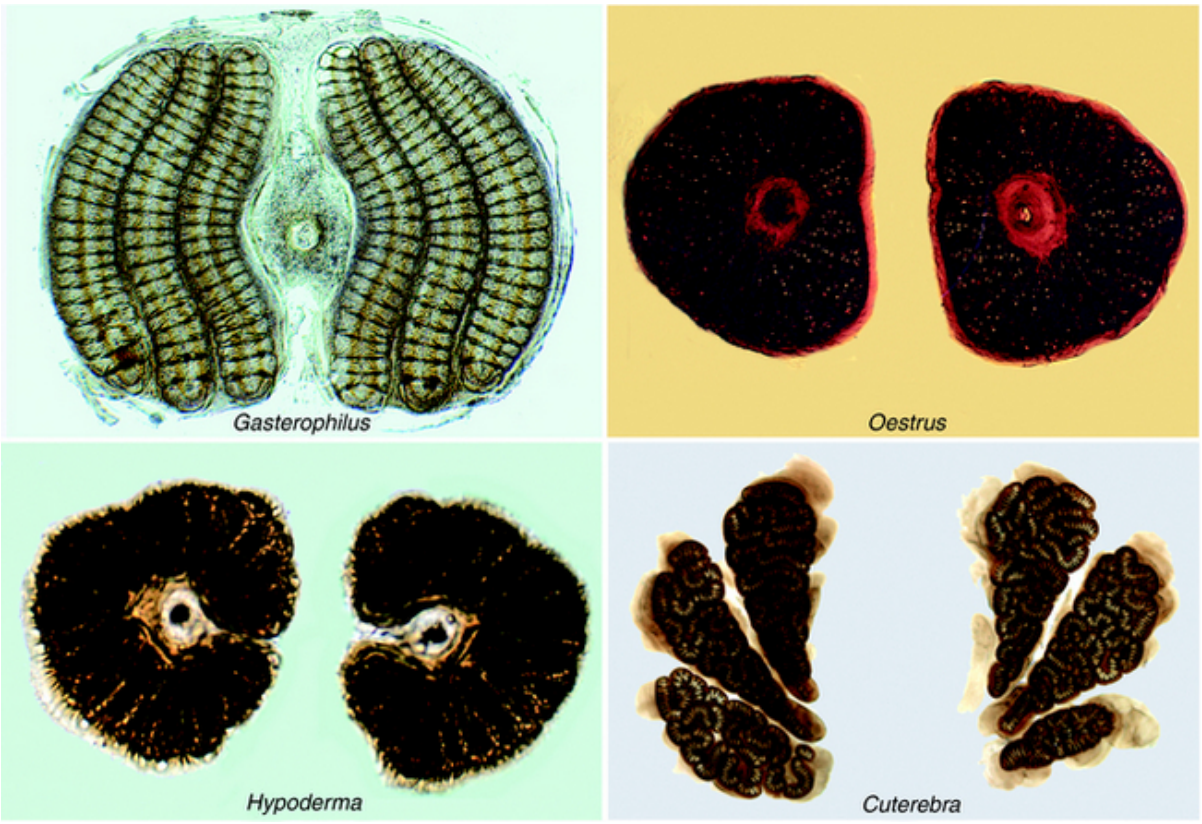

FIGURE 2-22 Bot spiracles (*Gasterophilus* and *Oestrus* ×27; *Hypoderma* ×55; *Cuterebra* ×65).

Oestrus ovis

O. ovis, the sheep nasal botfly, somewhat resembles a honeybee (Figure 2-23). It is a stout, grayish-brown fly, about 1 cm long and covered with short hairs; the mouthparts are vestigial. The flies are most active during the warmer hours of the day, especially during intervals of bright sunshine. In early morning and late afternoon, they are more likely to be found resting on buildings, tree trunks, water tanks, and the like. It is interesting to watch a mob of Australian Merino sheep on a warm, sunny day with a few scattered clouds. While in the shadow of a cloud, the sheep tend to distribute themselves more or less at random over the paddock, but as the sun

emerges from behind the cloud, the sheep immediately huddle together and continue to graze with their heads toward the center of the huddle, only to disperse again with the arrival of the next cloud. This behavior may represent a defensive adaptation to the attack of the larvipositing female *O. ovis*; it seems plausible, at least. While *O. ovis* females are actively depositing their larvae in sheep's nostrils, the sheep hold their noses close to the ground or in each other's fleeces, stamp their feet as if annoyed, and occasionally bolt away. The tiny first-stage larvae may be demonstrated postmortem by sawing the skull in half longitudinally, rinsing the nasoturbinates and nasal sinuses with water, and examining the collected rinsings with a hand lens or stereoscopic microscope. The fully developed third-stage bots can hardly escape notice in the frontal sinuses.

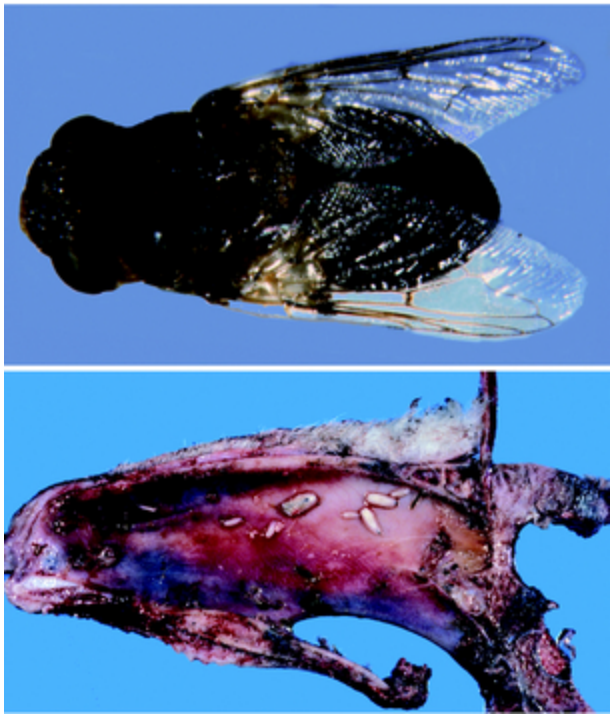

FIGURE 2-23 *Oestrus ovis*. *Top*, The adult female fly. *Bottom*, Bots in the nasal sinuses of sheep at necropsy.

Life history

On being deposited in the nostril of a sheep, the larva crawls onto the mucous membrane of the nasal passage, where it will remain for at least 2 weeks anchored to the mucous membrane by its mouth hooks. Larvae arriving late in the season remain arrested in the first stage throughout the winter, and development proceeds only with the return of warm weather. After a sojourn in the nasal cavity, the larvae proceed to the frontal sinuses, where development to the third stage is completed (see Figure 2-23). On reaching full development, the third-stage larvae crawl down into the nasal passages, are expelled by the sheep's sneezing, and enter the soil to pupate. Adults may emerge in about 4 weeks in summer but require considerably longer in cool weather. When pupation occurs in autumn, adult flies do not emerge until the following spring. Thus *O. ovis* overwinters both as arrested first-stage larvae in the nasal cavities of sheep and as pupae in soil.

Pathologic significance

Although moderate numbers of *O. ovis* larvae in the nasal and paranasal sinuses do no apparent harm, heavy infections cause sneezing, nasal discharge, and partial blockage of the nasal passages.

Treatment of nasal bots

The larva of *O. ovis* is very susceptible to ivermectin at the standard dosage rate of 0.2 mg/kg (Roncalli, 1984). Nasal bots in sheep have been treated with eprinomectin at both 0.5 mg/kg and 1 mg/kg body weight with efficacies ranging from 83.5% to 100% (Habela et

al, 2006; Hoste et al, 2004). Dichlorvos may be sprayed directly into the nostrils for the control of nasal bots.

Other nasal bots

Rhinoestrus purpureus infects horses in parts of Europe, Asia, and Africa; *Cephalopsis titillator* infects camels and dromedaries in Africa; and *Cephenomyia* species infect deer, elk, caribou, and other cervids in the Northern Hemisphere. Their life histories generally resemble that of *O. ovis*. However, the third-stage larvae of *R. purpureus* and *C. titillator* are found in the nasal and paranasal sinuses, pharynx, and even larynx, and those of *Cephenomyia* species are found in the pharyngeal pouches (Figure 2-24).

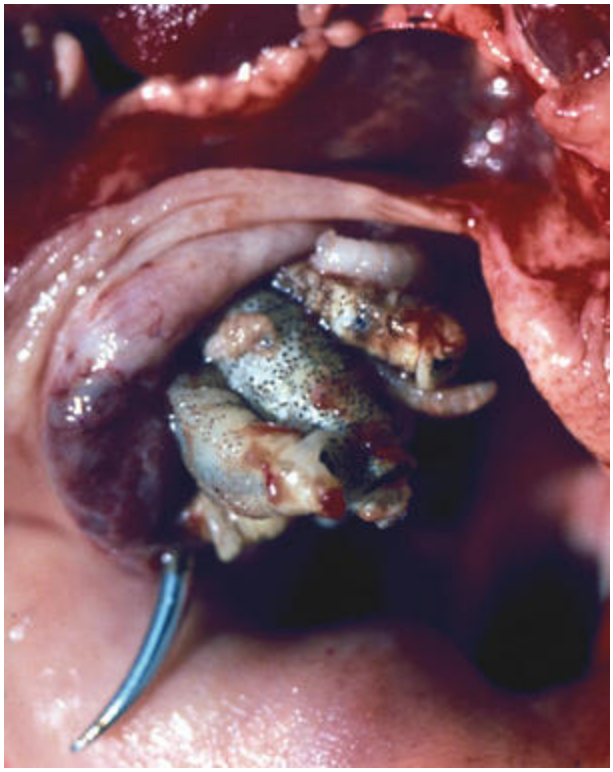

FIGURE 2-24 *Cephenemyia* bots in the retropharyngeal pouch of a deer.

Hypoderma

Identification

Hypoderma bovis and *Hypoderma lineatum*, the heel flies or gadflies, occur in cattle-raising areas of the Northern Hemisphere between 25° and 60° North latitude. The adult fly is about 15 mm long and looks rather like a bumblebee (Figure 2-25). Although these flies have no functional mouthparts for biting, and the process of oviposition on the hairs is presumably painless, cattle tend to become apprehensive and excited at their approach and gallop off aimlessly with their tails held high over their backs. Such behavior, termed "gadding about," tends to involve the whole herd simultaneously in needless, hysterical exertion and distracts it from the more profitable business of grazing. (Agricultural research administrators, practiced in the art of extracting financial support for their institutions from legislative bodies, can tell you exactly how much this form of bovine entomophobia costs the American stockman each year.) The fully developed third-stage *Hypoderma* larva or "cattle grub" is found in walnut-sized lumps, or warbles, on the backs of cattle in spring. Each warble has a small hole at its summit to which the posterior spiracles of the larva are pressed to obtain air. When it emerges or is extracted from the warble, the larva (sometimes also called a warble) is about 25 mm long and whitish to light brown.

Life history and pathogenesis

H. lineatum and *H. bovis* females glue their eggs to the hairs on the legs of cattle. *H. lineatum* appears with the advent of warm weather and remains active for about 2 months. Then *H. bovis* takes over and persists into summer. The eggs hatch spontaneously in less than a

week, and the larvae burrow through the skin and set off on prolonged migrations through the connective tissues of their host. Larvae of *H. lineatum* accumulate in the tissues of the esophagus 5 months later and remain there for about 3 months. Finally, they migrate to the subcutaneous tissues of the back, cut breathing holes in the skin to which they appose their spiracles, and, molting twice, grow larger. The larvae spend about 2 months in warbles in the backs of the infested cows (Pruett and Kunz, 1996). When fully developed (see Figure 2-25) the larvae enlarge their breathing holes, emerge through them, and fall to the ground to pupate. Adult flies emerge from pupal cases about 1 month later and immediately set about their reproductive duties. *H. bovis* larvae tend to accumulate in the spinal canal instead of the esophagus and appear in the subcutaneous tissues of the back about 2 months later than those of *H. lineatum*.

Hypoderma larvae occasionally invade horses and render them useless for equitation by warble formation in the saddle area or even cause fatal neurologic disease by migrating into the brain (Olander, 1967). In humans, *Hypoderma* larvae tend to produce bouts of creeping subcutaneous myiasis (“migrating lumps”) as the confused larvae try to find the top of the cow in which they “think” they are migrating. Local paralysis may result from invasion of the spinal cord, and blindness may result from invasion of the eye. These fortunately are rare accidents.

Treatment and control of *Hypoderma*

Hypoderma infection is treated most commonly these days with systemic macrocyclic lactones ivermectin, doramectin,

eprinomectin, or moxidectin. Eprinomectin and moxidectin pour-on can be used for treating both beef and dairy cattle. The “safe periods” for applying these insecticides vary for different localities because of differences in fly activity. The insecticides must be applied immediately after adult *Hypoderma* activity ceases for the season. Host-parasite reactions manifested clinically by bloat, salivation, ataxia, and posterior paralysis may occur when cattle are treated with larvicidal insecticides while *H. lineatum* larvae are in the esophagus or while *H. bovis* larvae are in the spinal canal. The host-parasite reaction was once thought to be an anaphylactoid reaction caused by antibodies produced by cattle in response to *Hypoderma* larval antigens. However, experimental evidence indicates that this reaction is caused by a toxin liberated from the dead *Hypoderma* larvae. Injection of phenylbutazone at a dosage rate of 20 mg/kg body weight 20 minutes before injection of larval toxin protected calves against both systemic shock and local inflammatory reactions (Eyre, Boulard, and Deline, 1981). The host-parasite reaction is best treated with sympathomimetic drugs (e.g., adrenaline) and steroids to alleviate local inflammatory reactions. Atropine, the antidote for cholinesterase-inhibiting agents, is contraindicated; host-parasite reaction is not a manifestation of organophosphate toxicity even though it may be precipitated by organophosphate medication.

In cases in which preventive treatment has been neglected, late second-stage and third-stage *Hypoderma* larvae can be safely and quickly removed from the backs of cattle by slowly injecting 1 mL of 3% hydrogen peroxide solution into the breathing hole using a blunt canula or needle shank of the syringe and taking care not to pierce

the grub. Most grubs will emerge within 15 seconds after the foaming action of the hydrogen peroxide begins and leaves behind a cleansed cavity (Scholl and Barrett, 1986).

National eradication efforts directed against *Hypoderma* species have met with success in Denmark, the Federal Republic of Germany, the Netherlands, and the Republic of Ireland, and the incidence in Great Britain has been reduced from 38% in 1978 to 0.01% in 1985 (Wilson, 1986). Surveillance against reintroduction of *Hypoderma* species in imported cattle is critical as evidenced by 19% of tested cattle entering Great Britain in 1993 being seropositive for *Hypoderma* (Sinclair, 1995). In parts of Great Britain where the ox warble has persisted or reappeared, all cattle over 12 weeks old are required to undergo treatment within specific dates, and cattle are routinely inspected at livestock sales and on farms.

Related species

Hypoderma diana occurs in deer and occasionally in man in Europe. Other species of *Hypoderma* and genera of warble flies parasitize sheep, goats, and deer in Mediterranean countries and India. *Oedemagena tarandi* is a serious enough pest of reindeer, musk oxen, and caribou in the subarctic regions to require prophylactic medication of these wild or semiwild hosts. In one study 70% of untreated reindeer harbored more than 100 *O. tarandi* larvae (Washburn et al, 1980). Both ivermectin and doramectin have proven highly effective in the treatment of infections with this parasite.

Gasterophilus

Identification

The adult fly superficially resembles a honeybee, with a long, curved ovipositor carried beneath the abdomen (Figure 2-26). The females may be observed on warm, sunny days hovering near horses and darting very rapidly to attach an egg to a hair.

FIGURE 2-26 Adult female *Gasterophilus intestinalis;* the ovipositor is curved around and under the body.

Eggs are deposited by *Gasterophilus nasalis* females on the hairs of the intermandibular space, by *Gasterophilus hemorrhoidalis* on the short hairs that adjoin the lips, and by *Gasterophilus intestinalis* on the hairs of the forelegs and shoulders (Figure 2-27). An illustrated key for identifying the eggs of the eight species of *Gasterophilus* that occur around the world has been prepared by Cogley (1991).

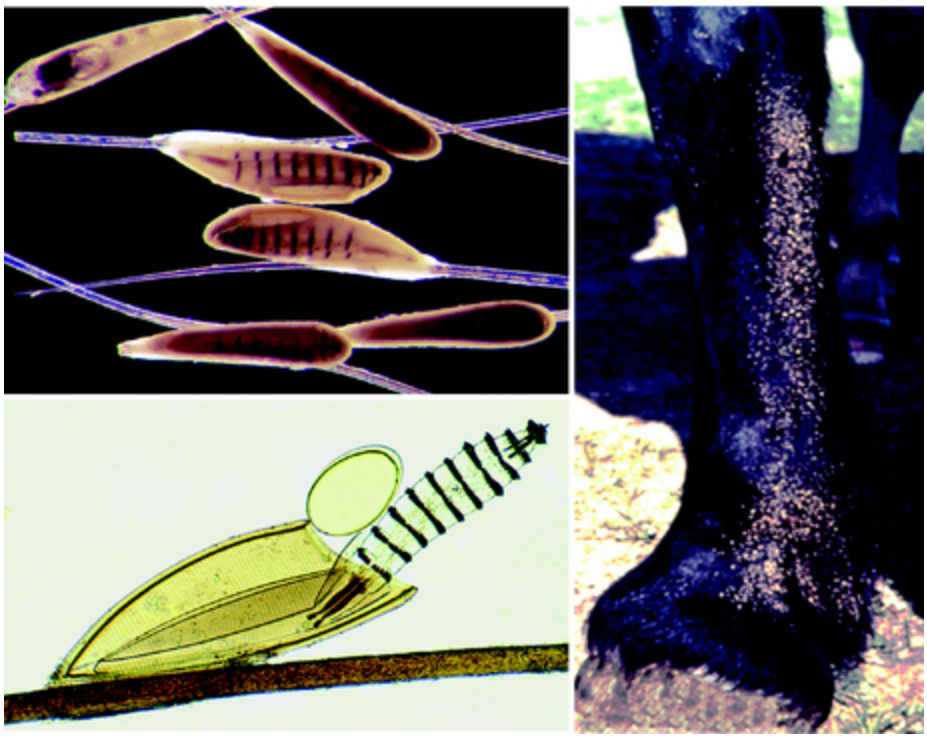

FIGURE 2-27 *Gasterophilus intestinalis*. *Left*, Eggs of *G. intestinalis* (Cyclorrhapha: Gasterophilidae) on horse hairs; on the bottom images the operculum has become dislodged and the maggot is partially out of the shell. R*ight*, Eggs attached to the hairs on the leg of a horse.

First-stage larvae of *G. intestinalis* can be found in tunnels in the epithelium covering the dorsal surface of the rostral two thirds of the tongue and in pockets between the molar teeth. Second-stage larvae are found in interdental pockets, attached to the root of the tongue, and attached to the wall of the stomach (Cogley, Anderson, and Cogley, 1982). Less is known regarding the initial migrations of other species of *Gasterophilus*. First- and second-stage larvae of *G. nasalis* are usually completely hidden well below the gum line in interdental pus pockets extending into the root sockets of molar teeth (Schroeder, 1940).

The third-stage larva of *G. nasalis* is yellowish and has one row of spines on each segment (see Figure 2-23); it is usually found in the first ampulla of the duodenum. The following three species of *Gasterophilus* have two rows of spines per segment. The *G. intestinalis* third-stage larva is red, has coarse spines that are blunted at their tips, and attaches in clusters in the nonglandular part of the stomach either near the margo plicatus or in the saccus cecus. The following species have small spines that taper to a fine point: *G. hemorrhoidalis*, which is reddish and found in the duodenum and rectum of horses in the North-Central United States and Canada, and *Gasterophilus inermis*, which is light yellow and found in the rectum of European horses. Individual larvae of all species may occasionally be found in atypical locations in the alimentary tract.

Life history

G. nasalis females deposit their eggs on the hairs of the intermandibular space. These eggs hatch spontaneously in 5 or 6 days, and the larvae crawl downward toward the chin until they arrive at a point opposite the commissures of the lips, whereupon they proceed directly toward the mouth and pass between the lips. The black eggs of *G. hemorrhoidalis* on the hairs adjoining the lips hatch after 2 to 4 days on contact with moisture, penetrate the epidermis of the lips, and burrow toward the mucous membrane of the mouth (Wells and Knipling, 1938).

The eggs of *G. intestinalis* on the hairs of the front legs are far removed from their destination and depend on direct assistance from the horse to find their way into the mouth (Figures 2-28 and 2-29). Five days after being laid, these eggs contain first-stage larvae

that are prepared to hatch rapidly in response to the sudden rise in ambient temperature that occurs when the horse brings its warm muzzle and breath in contact with them; they do not respond to gradual warming (Knipling and Wells, 1935). The larvae then enter the horse's mouth and burrow into the stratified squamous epithelium on the dorsal surface of the tongue. The first- and second-stage larvae of *G. intestinalis* spend about 1 month in the oral cavity. The white first-stage larvae drill burrows up to 13 cm long in the mucosa of the tongue, with "air holes" at an average interval of 4.2 mm to which they apply their caudal spiracles to breathe (Cogley, Anderson, and Cogley, 1982). The burrows typically extend in a rostral to caudal direction, but all terminate several centimeters rostral to the vallate papillae. Having approximately doubled in size during their sojourn in the tongue, the first-stage larvae now enter pockets in the interdental spaces predominantly of the upper molar teeth, where they molt from first to second stage. The second-stage larvae develop a red color as a result of synthesis of the insect's own hemoglobin, an adaptation to the low oxygen tension environment they will presently encounter in the stomach. At last, the second-stage larvae leave the interdental spaces, attach briefly to the root of the tongue, and then proceed to the stomach where they molt to the third larval stage, or full-grown bot (Cogley, Anderson, and Cogley, 1982). The oral migrations of other species of *Gasterophilus* have not yet been elucidated in such detail as they have been for *G. intestinalis*. However, migration within tissues affords protection from the host's teeth and a source of nourishment and is probably a key feature of the oral migrations of other *Gasterophilus* species as well.

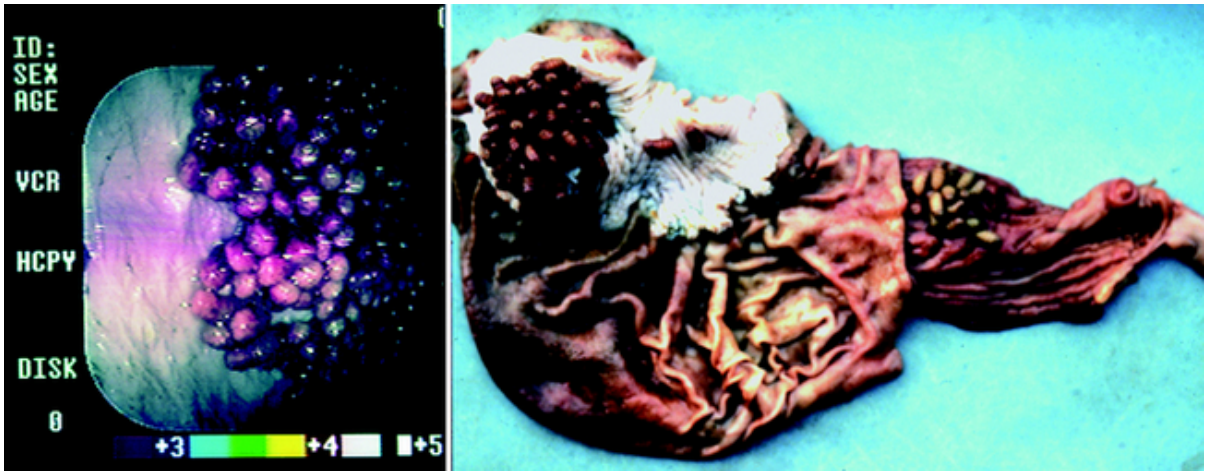

FIGURE 2-28 *Gasterophilus* bots. *Left,* Endoscopy of the bots of *Gasterophilus intestinalis; right,* stomach of a horse with the bots of *G. intestinalis* in its typical predilection site near the margo plicatus and with the bots of *Gasterophilus nasalis* in the first ampulla of the duodenum.

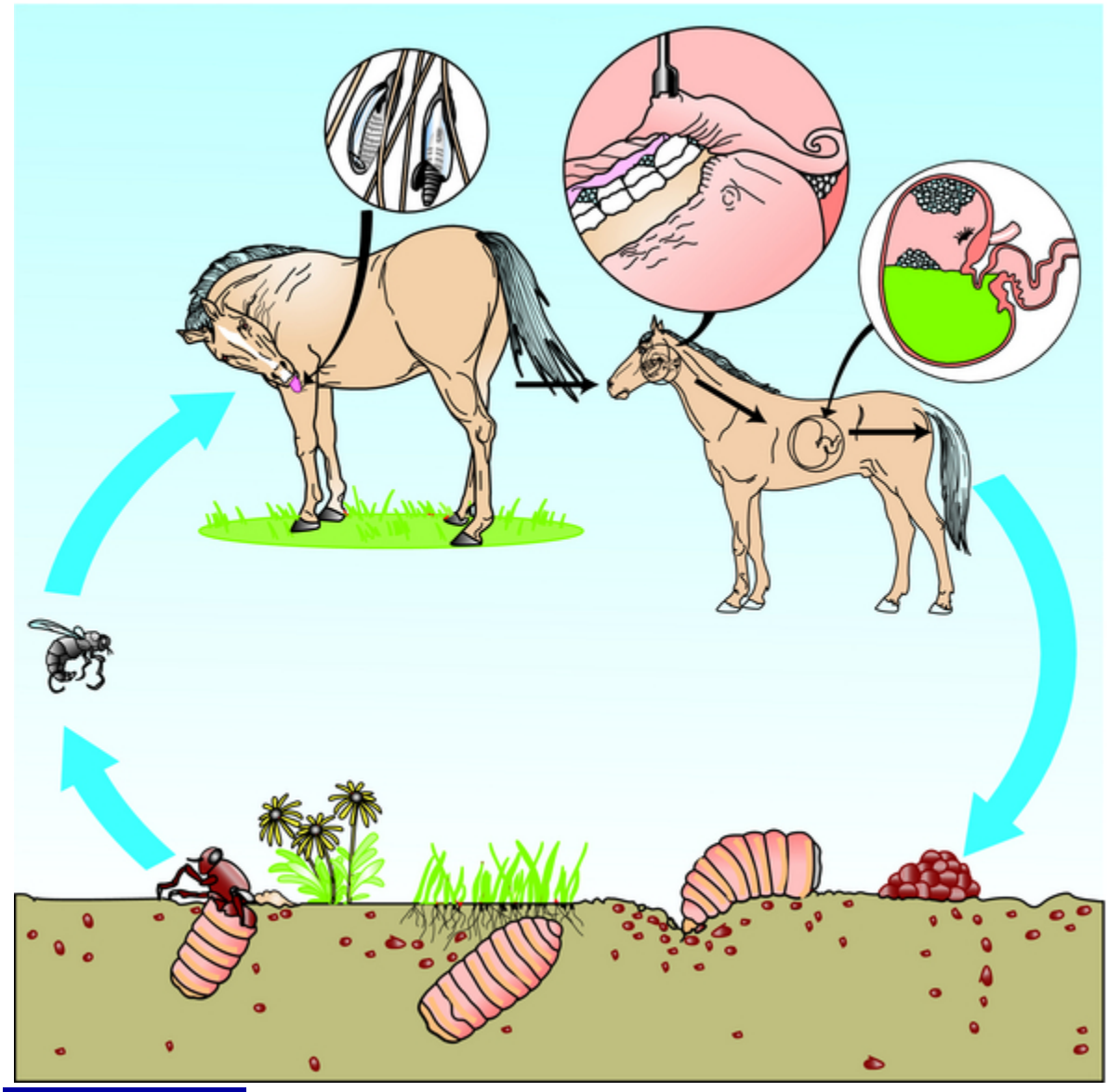

FIGURE 2-29 Life history of the equine stomach bot *Gasterophilus intestinalis*. The female botfly attaches fertilized eggs on the hair shafts of the forelegs and shoulders of horses. First-stage larvae develop in 5 days and stand ready to literally pop out of their shells in response to the warm breath of the horse. Having landed on the horse's face and entered its mouth, the larvae first tunnel quite extensively in the mucous epithelium of the dorsum and sides of the tongue, then enter pockets between the upper molar teeth, where they molt to the second stage. One month after infection, the larvae emerge from the interdental spaces, attach temporarily to the wall of the pharynx, then pass to the stomach, where they molt to the third stage. The third-stage larvae remain attached in the saccus cecus or along the margo plicatus for almost a year. From late spring onward,

they let go, pass out in the feces, and pupate in the soil. Adult *G. intestinalis* flies emerge from their pupal cases 3 to 9 weeks later and fly off in search of a horse.

The third-stage larvae remain attached by their mouth hooks to the wall of the stomach *(G. intestinalis)* or duodenum *(G. nasalis)* for up to 12 months (farthest from the intestine—*intestinalis;* farthest from the nose—*nasalis*). The predilection sites of both species are located above the fluid level in the alimentary tract. In these locations the bots are surrounded by gas pockets that apparently supply these air-breathing animals with sufficient oxygen (Figure 2-30; Price and Stromberg, 1987). From late spring onward, the larvae release their grip on the mucosa and pass out with the feces to pupate in the soil. Adult botflies emerge from the pupal cases in 3 to 9 weeks, depending on the ambient temperature. Botfly activity continues through summer and fall but ceases completely when cold weather sets in.

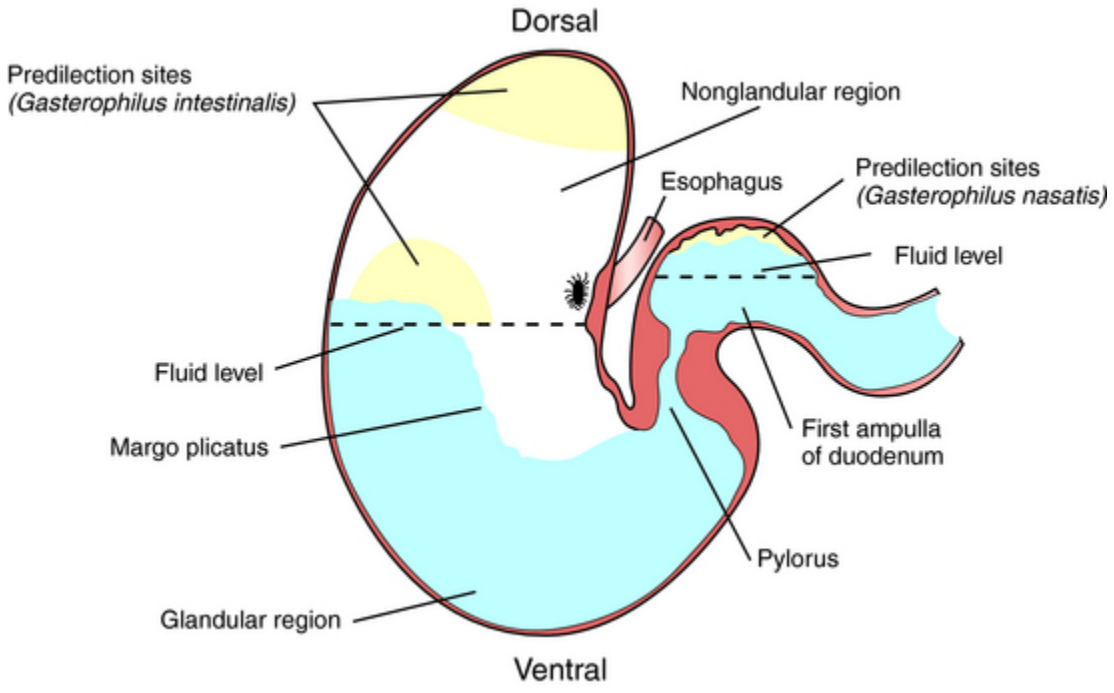

FIGURE 2-30 Predilection sites of *Gasterophilus intestinalis* and *Gasterophilus nasalis* in the stomach and duodenum of the horse.

From Price RE, Stromberg PC: American Journal of Veterinary Research 48:1225, 1987, American Veterinary Medical Association.

Importance

Despite the rather impressive oral lesions produced by first- and second-stage larvae and the chronic lesions in gastric and intestinal mucosae caused by attachment of the second and third stages, there is remarkably little pathologic or experimental evidence associating *Gasterophilus* infection with clinical illness. In fact, many horses support substantial populations of these parasites without apparent ill effect. However, disease is not a simple subject, and *Gasterophilus* infection has been held to etiologic account in cases of stomach rupture, subserosal abscess, splenic abscess, ulceration, and peritonitis (Rainey, 1948; Rooney, 1964; Underwood and Dikmans, 1943; Waddell, 1972). Principato (1988) described, classified, and superbly illustrated the main macroscopic lesions produced by larvae of *G. intestinalis*, *G. nasalis*, *G. hemorrhoidalis*, *G. inermis*, and *Gasterophilus pecorum* in freely ranging horses in Italy.

Treatment of *Gasterophilus* infection

The common treatment is now a macrocyclic lactone. In the southern United States, botflies are active most of the year (Craig, 1984), and in the case of *G. intestinalis*, the eggs glued to the hairs of the forelegs remain infective long after adult fly activity has ceased. The eggs may be removed from the haircoat with a special fine-tooth comb available from saddlery shops, but the process is rather slow and laborious. If more than a very few horses are involved, the

larvae can be lured out of their egg cases by copious sponging with water at 40° to 48° C (104° to 118° F) (Knipling and Wells, 1935); the addition of 0.06% coumaphos ensures rapid destruction of these larvae as they emerge. The eggs of *G. nasalis* and *G. hemorrhoidalis* hatch spontaneously when development of the larva is complete.

Cuterebra

Identification

The rarely seen (or noticed) adult fly somewhat resembles a bumblebee and has vestigial mouthparts (Figure 2-31). The fully developed third-stage larva is large (up to 45 mm) and dark-brown to black, the color being due to the stout black spines that cover the body (Figure 2-32). The posterior spiracles consist of groups of elegantly curved openings (see Figure 2-22). Earlier stages are much paler or even white and the posterior spiracles are quite different from those of the third stage, but the dark spines covering the body furnish evidence of the larva's identity as *Cuterebra*. At the present state of knowledge, it is impossible to differentiate species of even fully developed third-stage larvae of *Cuterebra*, except in the few cases in which their life histories have been worked out in detail.

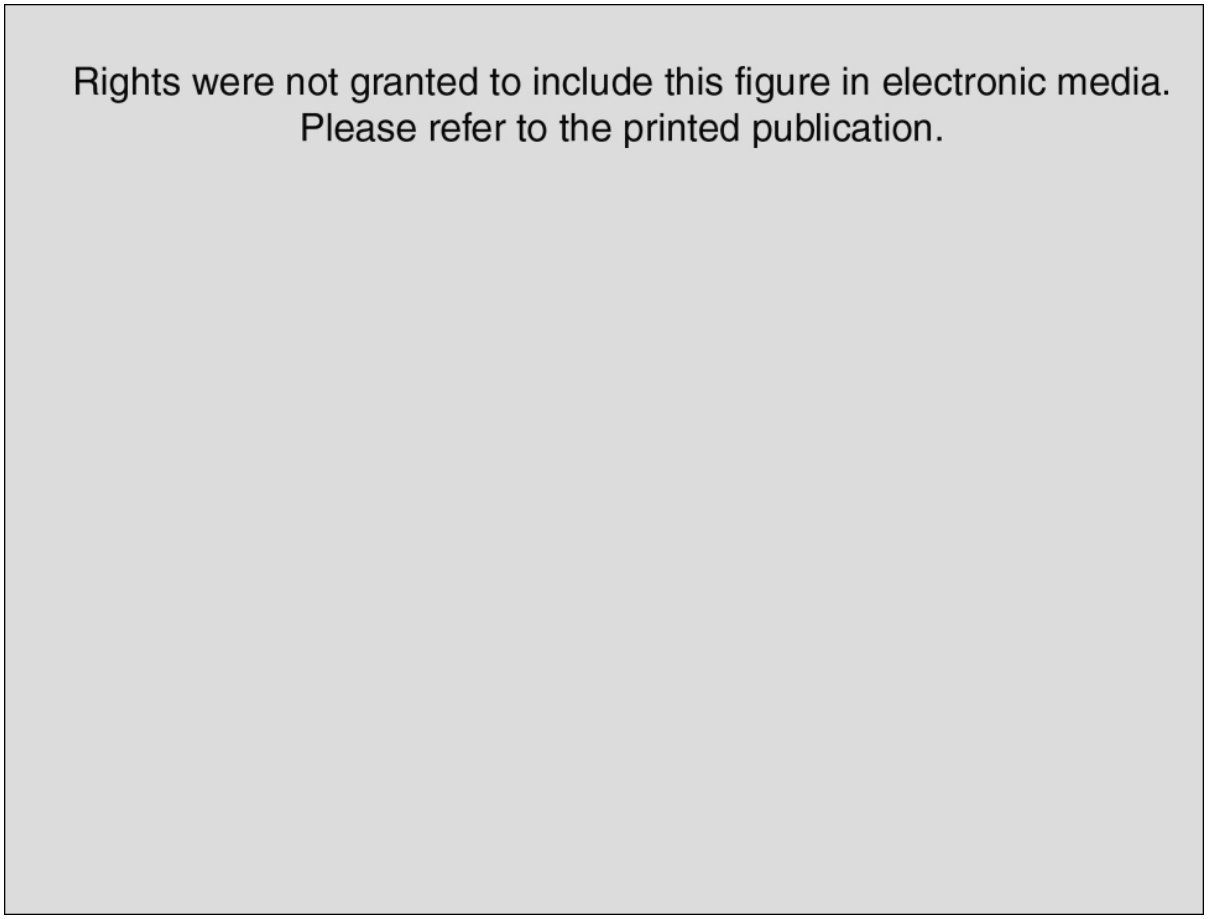

FIGURE 2-31 *Cuterebra jellisoni* (Cyclorrhapha: Cuterebridae), a botfly. The mouthparts of botflies are vestigial.

From Baird CR: J Med Entomol 8:615, 1971.

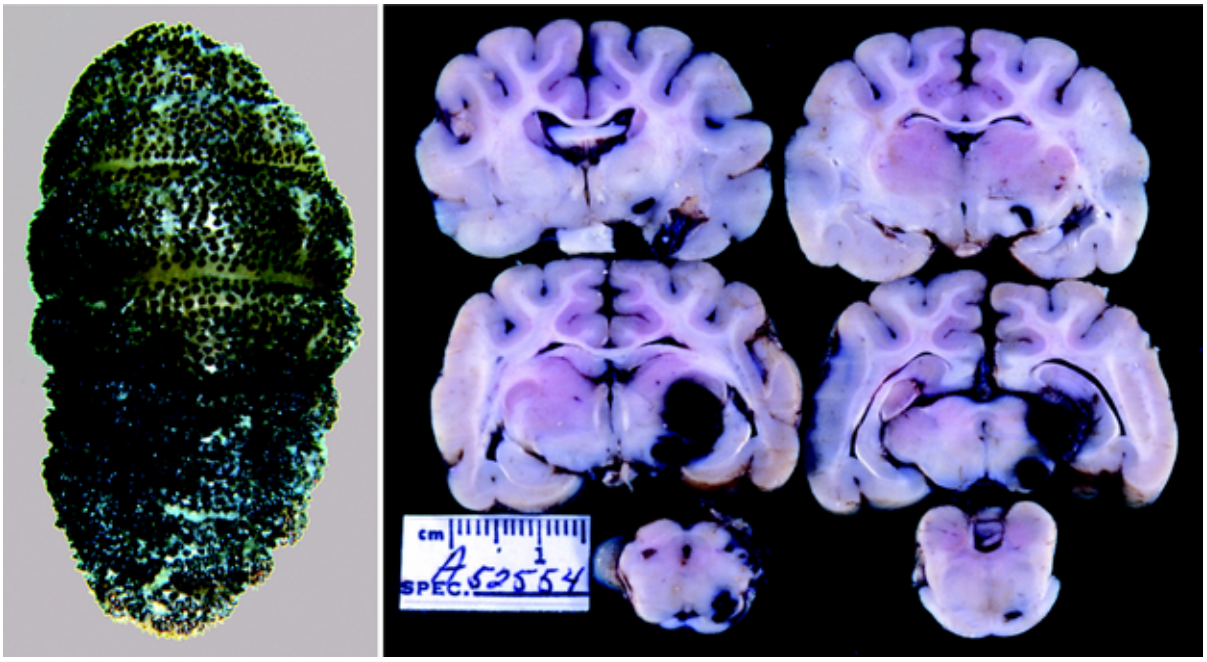

FIGURE 2-32 Cuterebridae. *Left*, A mature bot as it would appear when it is ready to leave the warble and drop to the ground to pupate. *Right*, The brain of a cat that died from the migration of a misguided *Cuterebra* larva.

Life history and pathogenesis

Cuterebra species infect rabbits, squirrels, chipmunks, mice, cats, dogs, and occasionally humans (Baird, Podgore, and Sabrosky, 1982). Female *Cuterebra* flies lay their eggs along rabbit runs and near rodent burrows. As the host brushes past, the first-stage larvae hatch instantaneously and crawl immediately into the host's fur. These larvae enter the host through its natural body openings (Baird, 1971, 1972; Timm and Lee, 1981). *Cuterebra* larvae are usually found in the cervical subcutaneous connective tissue of cats and dogs during August, September, and October. *Cuterebra* larvae may also locate in the nasal and oral regions and sometimes migrate through the brains of cats and dogs, with fatal results. The migration of the larva in the brain of cats is believed to cause

infarction and be responsible for feline ischemic encephalopathy (Williams, Summers, and de Lahunta, 1998).

Treatment of cuterebriasis

A *Cuterebra* larva that has made its way into a warble can be removed by enlarging its breathing hole in the skin sufficiently to allow it to be extracted with forceps, with care being taken not to crush the larva in the process. Tranquilization or sedation facilitates restraint but is rarely necessary. The wound heals rather slowly and sometimes suppurates or even sloughs; this may be a result of secondary bacterial infection or leakage of *Cuterebra* antigens into the surrounding tissues during extraction. When the worms are in ectopic sites, they may be removed.

The topically applied flea and tick products, imidacloprid and fipronil, may kill the young maggots on the haircoats of cats. Also, although no data are available, cats on avermectin heartworm preventatives, such as ivermectin, milbemycin, or selamectin, might be protected from *Cuterebra* infection through the killing of larvae during the initial phases of their migration in the cat. None of these products are, however, approved for preventing cuterebriasis.

Dermatobia

Identification

The adult of *Dermatobia hominis*, another member of the family Cuterebridae, somewhat resembles a brilliant blue calliphorid fly but, like all botflies, has vestigial mouthparts (Figure 2-33). The fully developed third-stage larva is pear-shaped and has posterior

spiracles with straight slits deeply sunken in a concavity (see Figure 2-33).

FIGURE 2-33 *Dermatobia hominis*. *Top*, The adult female fly. *Bottom*, The maggot that crawled out of the arm of an infected human.

Life history and pathogenesis

The *D. hominis* female uses a slave to carry her eggs to a prospective host. She captures another fly, usually a bloodsucker such as a mosquito or a stable fly, and glues her eggs to its abdomen. The eggs develop in a week or two, and the larvae inside them stand ready to disembark when the slave fly alights on the skin of a warm-blooded animal to feed. Each *D. hominis* larva that succeeds in penetrating the skin develops at or near the site of penetration in a separate warble. The larva emerges through the breathing hole to pupate about 6 weeks later. The *D. hominis* larva is a serious pest of humans, cattle, sheep, dogs, and other mammals in Central and

South America. The adult flies tend to concentrate at the edges of large forests.

Expert identification of myiasis larvae

The major taxa of fully developed myiasis larvae can be identified by means of the criteria set forth earlier. More detailed information can be found in James (1948). However, identification of all three larval stages of even the more common species is a chore for a taxonomic specialist. If preliminary findings are inconclusive, intriguing, or of great practical importance, larvae can be cleaned by shaking them vigorously in water, fixing them in 70% ethyl alcohol or 10% formalin, and submitting these specimens for expert identification. Precise identification in certain cases requires rearing the adult fly; instructions are provided under Sarcophagidae in an earlier section. Living larvae also may be submitted for expert identification in addition to but not in lieu of fixed specimens; include these in a separate jar loosely packed in moist cotton.

Order Phthiraptera, Lice

There are two main kinds of lice, represented by the suborders Anoplura, or bloodsucking lice, and three suborders, the Ischnocera, Amblycera, and Rhychophthirina that are for simplicity grouped here under the heading Mallophaga, or chewing lice (Table 2-6). Anoplurans have piercing mouthparts consisting of three stylets that, in fixed specimens, are usually concealed within the relatively narrow head (Figure 2-34). Anoplurans are parasites of placental animals only. Mallophagans have stout mandibles on the ventral side of their relatively broad heads (Figure 2-35), and these lice feed on epidermal scales, feathers, and sebaceous secretions of birds and

mammals. Both anoplurans and mallophagans spend their entire lives among the hairs or feathers of their hosts and display a high order of host specificity. Even the eggs are securely attached to the hairs or feathers of the host (see Figure 2-37). The lice that hatch from these eggs are tiny replicas of the adults; they molt several times but undergo only minor changes in appearance (i.e., **simple metamorphosis**). The cycle from egg to egg requires several weeks, and only one or two eggs may be found developing within the abdomen of a female louse at any one time, but enormous populations may develop notwithstanding. The hatching process itself is of passing interest. The young louse swallows air and ejects it through its anus to form a cushion of compressed air that forces the animal against the operculum (i.e., lid) of the eggshell until it pops open. Thus it may be said (with due application of etymology and low humor) that "every louse is hoisted by its own petard."

TABLE 2-6 Lice Found on Domestic Animals and Humans

Host	Anoplura	Mallophaga
Dog	*Linognathus setosus*	*Trichodectes canis*
		Heterodoxus spiniger
Cat	None	*Felicola subrostratus*
Cow	*Haematopinus eurysternus*	*Damalinia bovis*
	Haematopinus quadripertusus	
	Haematopinus tuberculatus	
	Linognathus vituli	
	Solenopotes capillatus	

Horse	*Haematopinus asini*	*Damalinia equi*
Pig	*Haematopinus suis*	None
Sheep	*Linognathus ovillus*	*Damalinia ovis*
	Linognathus pedalis	
	Linognathus africanus	
Goat	*Linognathus africanus*	*Damalinia caprae*
	Linognathus stenopsis	*Damalinia crassipes*
		Damalinia limbata
Rat	*Polyplax spinulosa*	None
Mouse	*Polyplax serrata*	None
Guinea pig	None	*Gliricola porcelli*
		Gyropus ovalis
		Trimenopon hisidum
Human	*Pediculus humanus capitus*	None
	Pediculus humanus humanus	
	Pthirus pubis	

FIGURE 2-34 Head and thorax of an anopluran louse. The bloodsucking stylets occupy the median plane of the head; mouth at arrow.

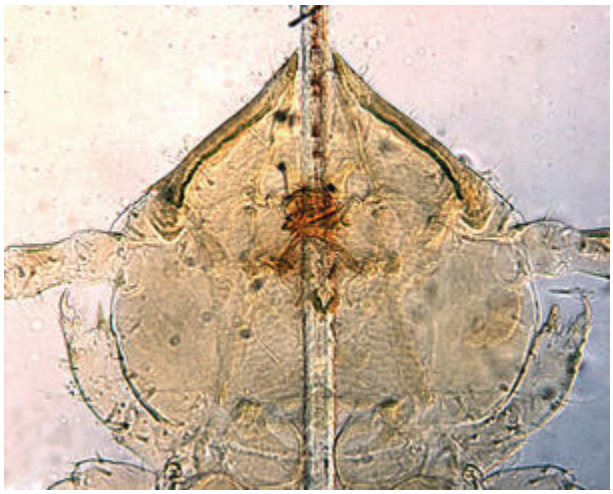

FIGURE 2-35 Mandibles of a mallophagan louse, *Felicola subrostratus*, grasping a cat hair.

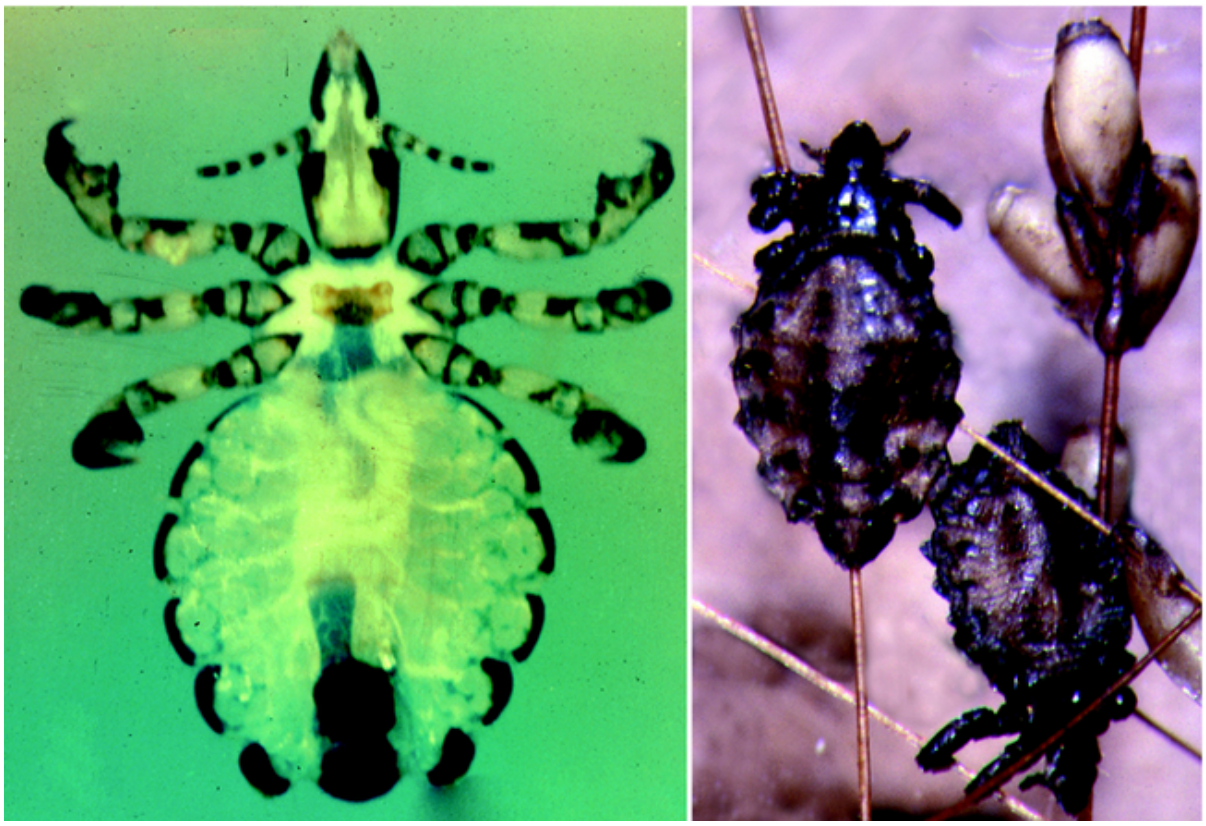

FIGURE 2-37 *Left*, *Haematopinus suis* (Anoplura) of swine. *Right*, Two *Haematopinus asini* clinging to horse hairs, and several operculate eggs glued to the hair of the equine host.

Because of the sedentary habits of lice, one searches for them by carefully examining the haircoat or plumage of the host. The one exception to this generalization, the human body louse *Pediculus humanus humanus*, clings to the fibers of the clothing instead of body hairs while it feeds on its host. With a little practice, bloodsucking lice and chewing lice can be distinguished by inspection. This plus high host specificity simplifies identification, especially for hosts that have only one species of louse (e.g., *Haematopinus suis* on *Sus scrofa* and *Felicola subrostratus* on *Felis catus*). The next simplest case involves one anopluran and one mallophagan species per host species (e.g., *Haematopinus asini* plus *Damalinia equi* on *Equus*

caballus and *Linognathus setosus* plus *Trichodectes canis* on *Canis familiaris*). Cattle *(Bos taurus)* present a more complex case; they are infested by three anoplurans and one mallophagan, and attention to generic morphologic characteristics is required for their differentiation. Occasionally a few lice are collected from sources other than their normal host. For example, *Pthirus pubis*, the human crab louse, has been reported now and again on dogs. In such cases it is necessary to note the obvious morphologic differences displayed by *L. setosus*, the anopluran normally found on dogs, and *P. pubis*, denizen of the human pubic hairs, to avoid misdiagnosis.

Lice are well-adapted parasites and are usually more a nuisance than a threat to their hosts. The role of the human body louse in the spread of *Rickettsia prowazekii*, the causative agent of epidemic typhus, is an outstanding exception, and a few other examples of lice serving in the role of vectors and intermediate hosts can be cited. However, it takes a large population of lice to drain the vitality of their host directly, and usually contributory conditions such as stress of inclement weather, crowding, poor nutrition, and individual diathesis can be demonstrated in cases of clinical illness related to louse infestation. If a very large number of lice is found on cattle, on a puppy, or on a stock of laboratory rats, there is something wrong in the way the animals are kept, and merely spraying insecticide to kill the lice falls far short of full clinical management of the case.

Suborder Anoplura

Anoplurans, about 400 some species, have pincerlike tarsal claws for clinging to the hairs of their hosts. The size of these claws is related

to the diameter of the hair shaft and is probably an important factor in establishing host specificity and site specificity. Without hair, these lice are helpless; they pass from host to host most efficiently when a "bridge" of hair exists between host individuals. This is why *P. pubis* is frequently transmitted during sexual intercourse. According to Chandler and Read (1961), the French call this parasite "papillon d'amour."

Haematopinus

All tarsal claws are of equal size, and the lateral margins of the abdomen are heavily sclerotized (Figure 2-36). The two other anopluran genera found on cattle, *Linognathus* and *Solenopotes*, differ in having smaller claws on their first pair of legs. Species of *Haematopinus* that infest domestic animals include *H. asini* of horses, *H. suis* of swine (Figure 2-37), and *Haematopinus eurysternus*, *Haematopinus quadripertusus*, and *Haematopinus tuberculatus* of cattle. *H. eurysternus* is a common parasite of domestic cattle *(B. taurus)* in North America and tends to concentrate on the neck, poll, brisket, and tail, but in heavy infestation it may be generally distributed over the body. *H. quadripertusus*, normally a tropical and subtropical parasite of *Bos indicus* and *B. indicus–B. taurus* hybrids, lays its eggs in the tail switch but may be found around the eyes and long hairs of the ears (Roberts, 1952). *H. tuberculatus* is an Old World parasite of water buffalo (*Bubalus bubalus*) and of domestic cattle associated with them (Meleney and Kim, 1974).

FIGURE 2-36 *Haematopinus eurysternus* (Anoplura) of cattle. All tarsal claws are of equal size.

Heavy infestations of *H. eurysternus* are capable of causing severe anemia in adult range cattle (Peterson et al, 1953). Certain individuals are predisposed to the growth of large populations of lice, whereas other members of the same herd support only light infestations. These "louse breeders," as they are called, are likely to perish during winter storms, weakened as they are by their louse burdens. Such animals may be saved by insecticide applications. The rate of increase in hematocrit is, however, considerably slower than one would expect in a simple blood loss anemia.

Linognathus

Unlike *Haematopinus*, the first pair of tarsal claws of *Linognathus* is smaller than the second and third pairs, and the lateral margins of

the abdomen are not heavily sclerotized (Figure 2-38). *Linognathus* differs from *Solenopotes* in having more than one row of setae per abdominal segment and in lacking a sternal plate and protuberant abdominal spiracles. Species of *Linognathus* infesting domestic animals include *Linognathus vituli* of cattle; *Linognathus ovillus*, *Linognathus pedalis*, and *Linognathus africanus* of sheep; *Linognathus stenopsis* and *L. africanus* of goats; and *L. setosus* of dogs and foxes (Figure 2-39).

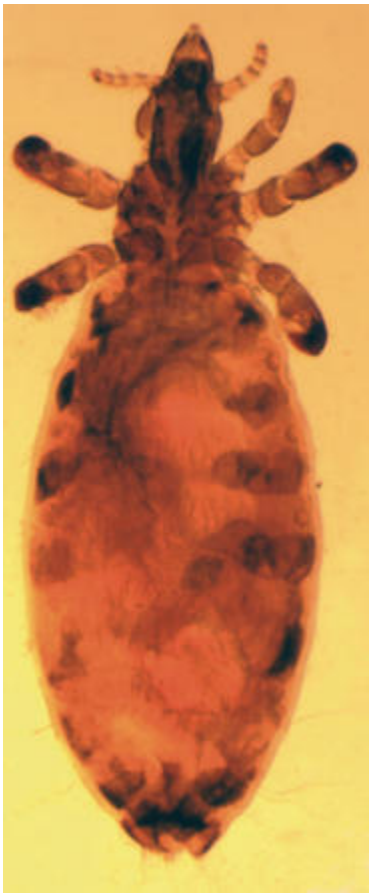

FIGURE 2-38 *Linognathus vituli* (Anoplura) of cattle. The first pair of tarsal claws is smaller than the second and third pairs. Spiracles are flush with the surface of the abdomen, and there is more than one row of setae per abdominal segment.

FIGURE 2-39 *Linognathus setosus* (Anoplura) of dogs and foxes.

Solenopotes

Solenopotes capillatus, the "little blue louse" of cattle, is distinguished from *Linognathus* in having only one row of setae per abdominal segment, a sternal plate at least half as wide as it is long, and protuberant abdominal spiracles (Figure 2-40).

FIGURE 2-40 *Solenopotes capillatus* (Anoplura) of cattle. The first pair of tarsal claws is smaller than the second and third pairs. Spiracles protrude above the surface of the abdomen, and there is only one row of setae per abdominal segment.

Polyplax

Polyplax spinulosa is a parasite of the rat, and *Polyplax serrata* is a parasite of the mouse (Figure 2-41). Both of these anoplurans may develop into serious nuisances in laboratory animal colonies and, when sufficiently abundant, may even bleed animals to death (Figure 2-42). Treatment of infested rats has been performed with the topical spray application of fipronil (Diaz, 2005).

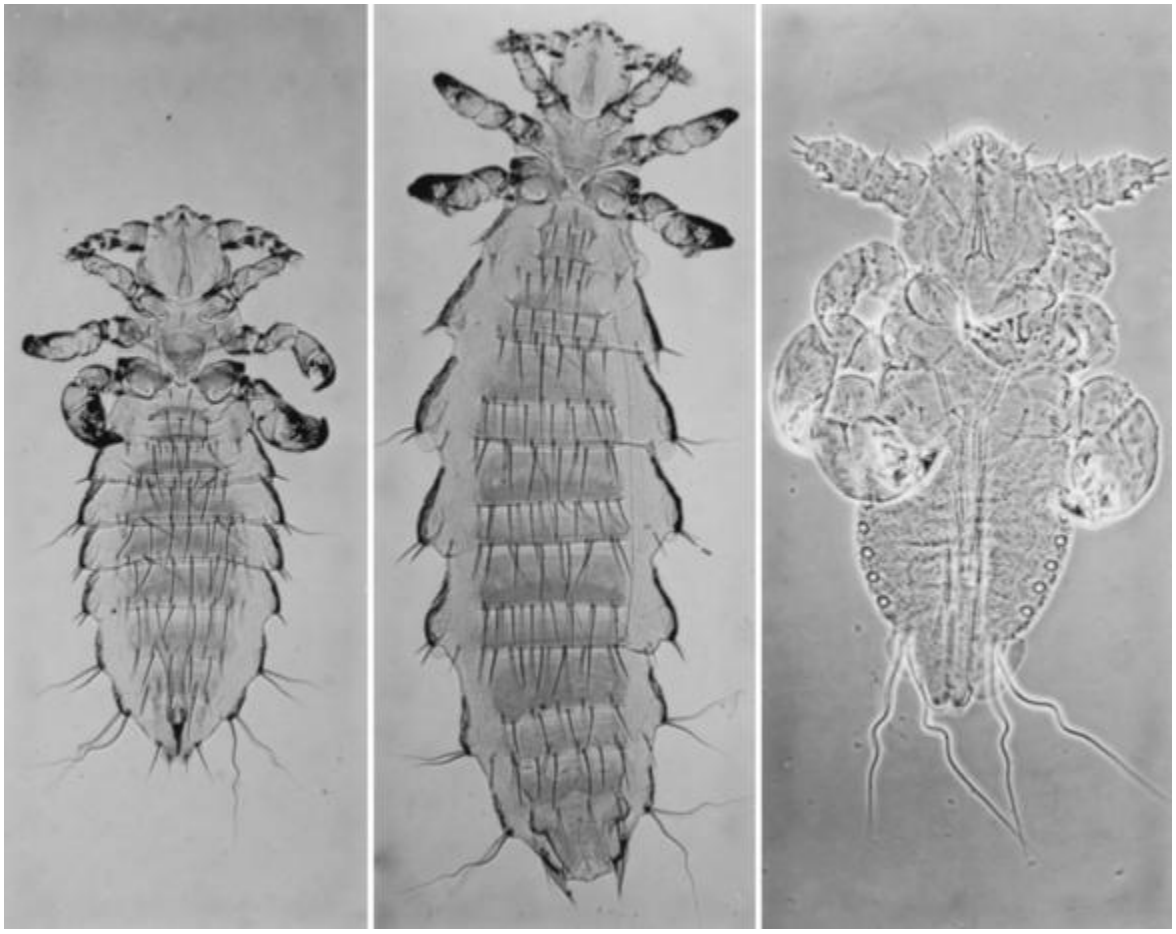

FIGURE 2-41 *Polyplax serrata* (Anoplura) of the mouse. *Left*, Male. C*enter*, Female. *Right*, Nymph.

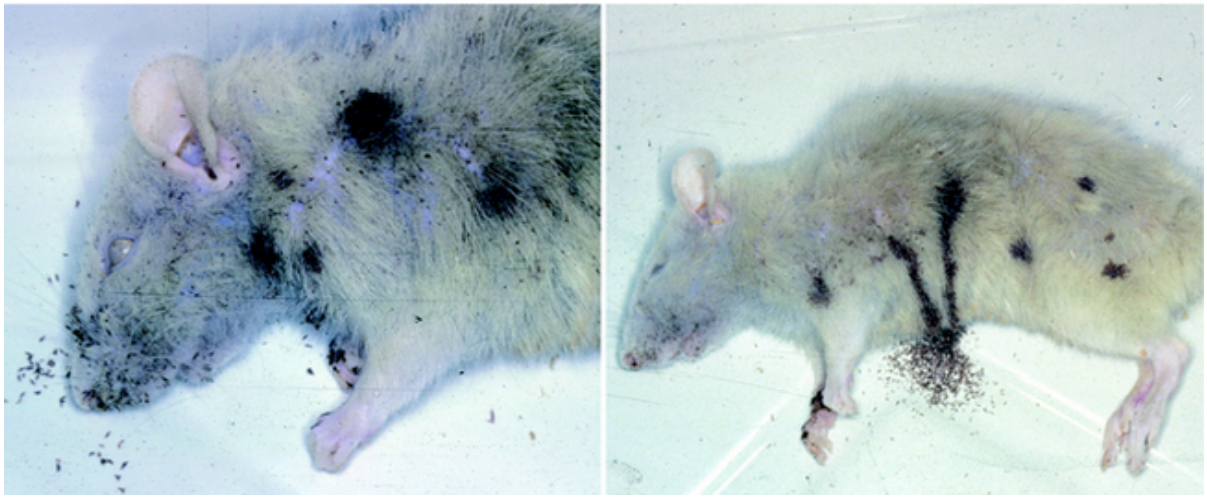

FIGURE 2-42 *Polyplax spinulosa* leaving a rat that died of the effects of its louse population. Urged on by the heat of an incandescent bulb, these lice are emulating their

host's legendary tendency to flee from unpromising situations. This is a general phenomenon among the more mobile ectoparasites and can be exploited to advantage in diagnosis. However, if it is necessary to euthanize the host, do not use chloroform, ether, or other agents that will surely kill the parasites as well as their hosts.

Pthirus

The large tarsal claws of *P. pubis* (Figure 2-43) are adapted to the coarse hairs of the pubic and perianal regions, armpits, mustache, beard, and, particularly in young children, the eyebrows and eyelashes, these latter two furnishing the nearest approximation to a pubic hair that a child has to offer. Pruritus is intense, and a papular dermatitis with discoloration of the skin develops. Once feeding, these lice display a marked disinclination to move and tend to remain fixed at one point for days while their feces accumulate about them. The life cycle requires about 1 month from egg to egg, so that considerable time may elapse between acquisition and awareness of infestation. Although sexual contact is the principal means of transmission between individuals, towels, clothing, and bedding used by an infested person are to be avoided. Entire families, children and family dog included, may become infested through fomites such as these. During crises of this sort, the dog may be presented to the veterinarian for euthanasia in the mistaken belief that the dog is the culprit and reservoir of pestilence. Dealing with a family outbreak of crab lice and falsely incriminated dog requires considerable tact.

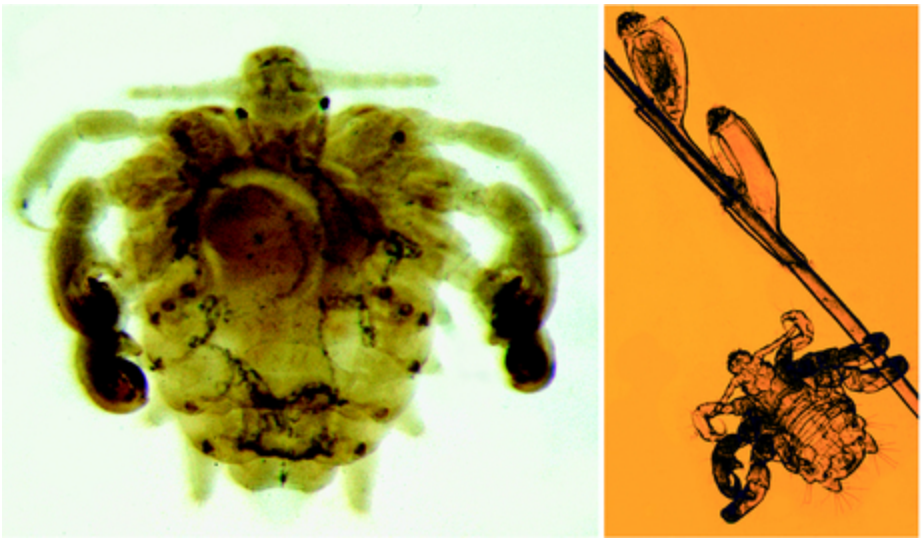

FIGURE 2-43 *Pthirus pubis* (Anoplura). *Left*, An adult female human crab louse. *Right*, A louse and two eggs on a pubic hair. Dogs occasionally acquire *P. pubis* by contact with infested humans or their clothing.

Pediculus

The human head louse, *Pediculus humanus capitis*, stays mainly on the human head, especially around the ears and nape of the neck (Figure 2-44). Dogs are rarely infested. Eggs are attached firmly to the hairs and hatch within a week. Infestation spreads rapidly because of the ease with which hairs are shed and wafted about. Outbreaks of head lice may occur under the best conditions of sanitation and personal deportment. The human body louse, *Pediculus humanus humanus*, does not cling to hair. Instead, this louse clings to the fibers and deposits its eggs in the seams of clothing. Except in very heavy infestations, all people need do to be rid of body lice is to remove their clothing. When people are unable to bathe and change clothing for extended periods, as, for example, during wars and natural disasters, body louse populations are likely to expand rapidly. Under such circumstances, epidemic typhus *(R.*

prowazekii), which is transmitted by the body louse, is likely to break out, and it is not for mere comfort's sake that vigorous delousing measures must be adopted.

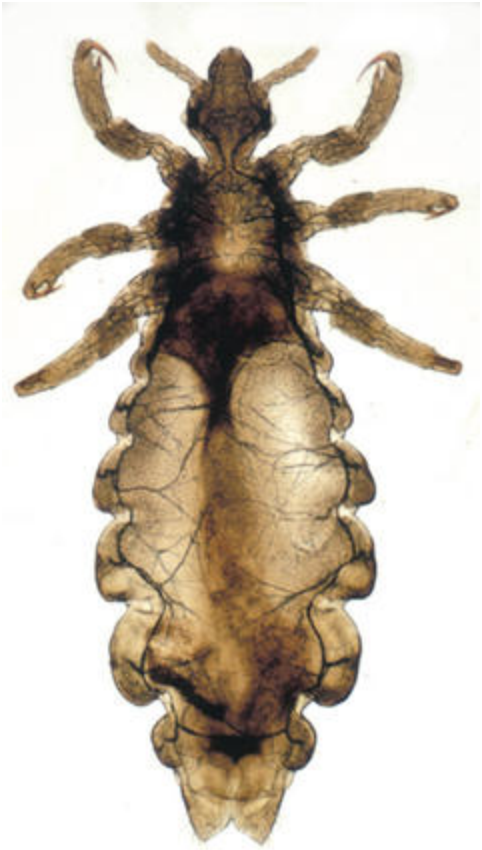

FIGURE 2-44 *Pediculus humanus capitis* (Anoplura), the human head louse collected from a child attending public school in Ithaca, New York.

Humans and gorillas share species of pubic lice (*P. pubis* on people and *Pthirus gorillae* on gorillas), but there are none found on chimpanzees (Reed et al, 2007). At the same time, chimpanzees are host to *Pediculus schaeffi*, humans are host to *P. humanus*, and gorillas are not parasitized by species in this genus.

The Mallophaga

Some 4000 species of mallophagans, or chewing lice, are parasites of birds and mammals. All bird lice are biting lice, and there are many species of them. Mallophagans ingest a variety of epidermal materials. Some readily ingest feather keratin and can be cultured on this substance in vitro. A few, such as *Heterodoxus spiniger* of the dog and related amblyceran parasites of birds, are blood feeders (Agarwal, Chandra, and Saxena, 1982).

Because their hosts are insectivorous and very fastidious, bird lice are in constant danger of being eaten by their host instead of vice versa. However, they tend to be far less sluggish than their relatives that parasitize mammals; many have long legs to help them keep "one step ahead," and they frequently develop enormous populations. Mallophagans may cause their hosts considerable irritation when present in large numbers, especially in situations in which it is difficult for the animals to groom themselves, as in the case of stanchioned cattle. There are three suborders of chewing lice: Ischnocera, Amblycera, and Rhynchophthirina.

Suborder Ischnocera

Ischnocerans have salient antennae that are three-jointed in species infesting mammals (Figure 2-45) and five-jointed in species infesting birds; all lack maxillary palps (Figure 2-46).

FIGURE 2-45 *Damalinia (Holokartikos) crassipes* (Mallophaga: Ischnocera) of the goat. Typical of ischnocerans parasitizing mammals, *D. crassipes* has three-segmented antennae.

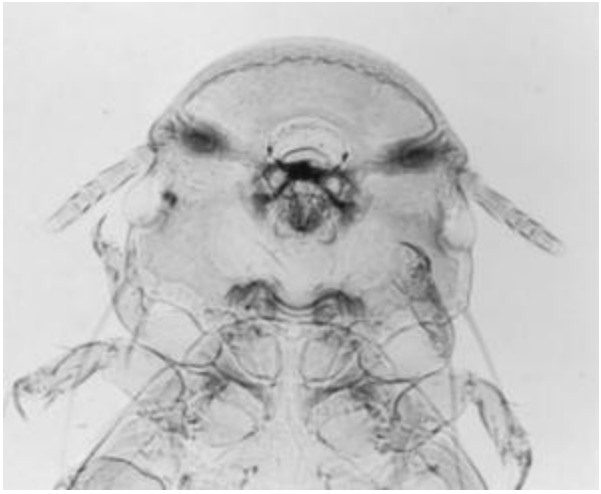

FIGURE 2-46 *Goniocotes* sp. (Mallophaga: Ischnocera) of the chicken. Typical of ischnocerans parasitizing birds, *Goniocotes* has five-segmented antennae.

Damalinia (Bovicola)

Species infesting domestic mammals include *Damalinia bovis* on cattle, *Damalinia equi* (also goes by the name *Werneckiella equi*) on horses (see Figure 2-45), *Damalinia ovis* on sheep, and *Damalinia caprae*, *Damalinia limbata*, and *Damalinia (Holokartikos) crassipes* on goats.

Trichodectes

T. canis, the canine chewing louse (Figure 2-47), may serve as intermediate host (cyclodevelopmental vector) of the tapeworm *Dipylidium caninum*, although fleas of the genus *Ctenocephalides* are far more important in this respect. *T. canis* must be differentiated from the anopluran *L. setosus* and from the warm-climate amblyceran, *H. spiniger*.

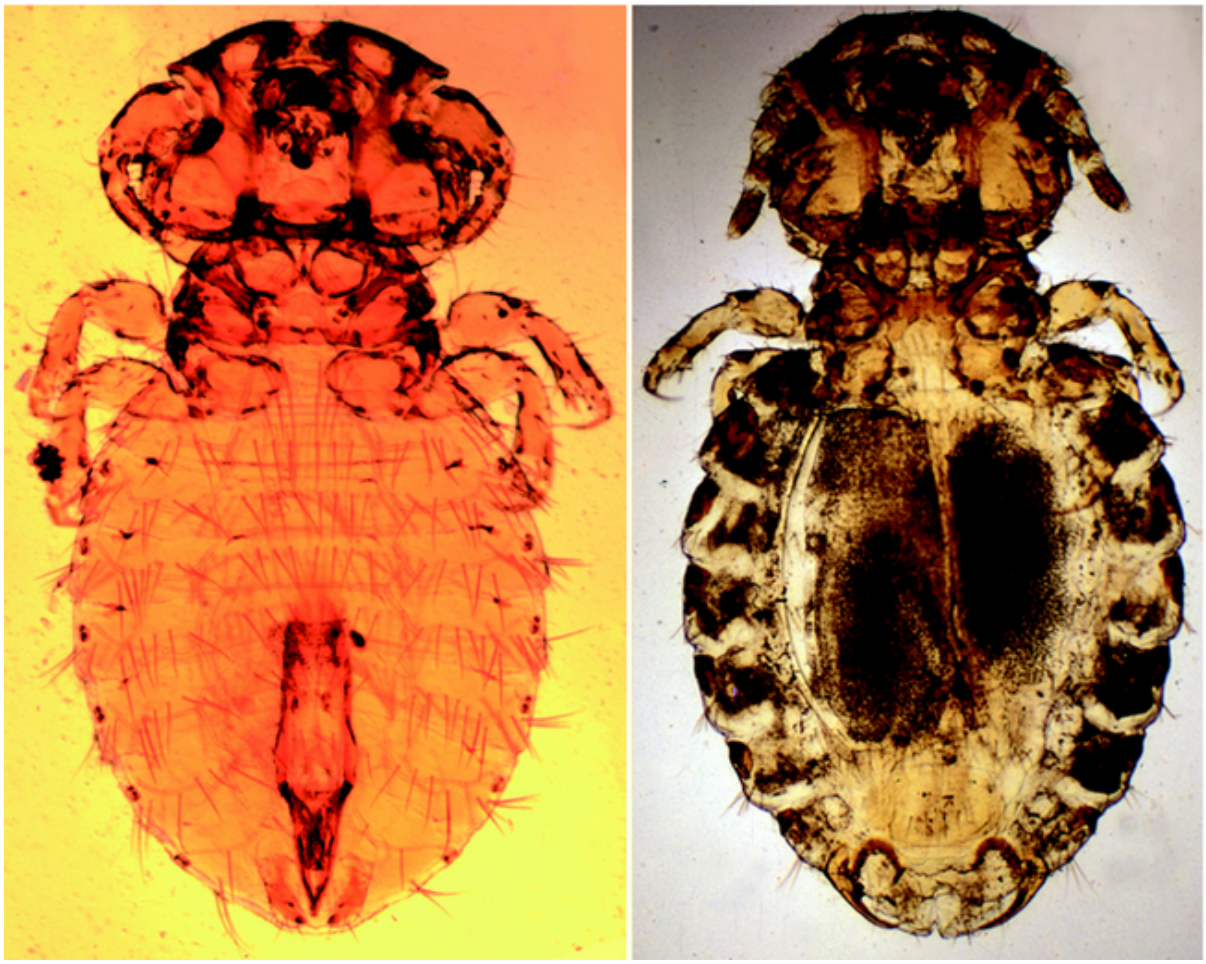

FIGURE 2-47 *Trichodectes canis* (Mallophaga: Ischnocera) of the dog: male on left, female on right.

Felicola

F. subrostratus is the only louse found on cats (Figure 2-48). This louse is characterized by the triangular shape of the anterior portion of the head.

FIGURE 2-48 *Felicola subrostratus* (Mallophaga: Ischnocera) of the cat.

Suborder Amblycera

Amblycerans have club-shaped antennae that lie in grooves in the head and four-segmented maxillary palpi (Figure 2-49). Many amblycerans are parasites of birds, but one species, *H. spiniger*, is a parasite of dogs in warm climates, and three species, *Gliricola porcelli*, *Gyropus ovalis*, and *Trimenopon hispidum*, are parasites of the guinea pig (Figure 2-50 and see Figure 7-103).

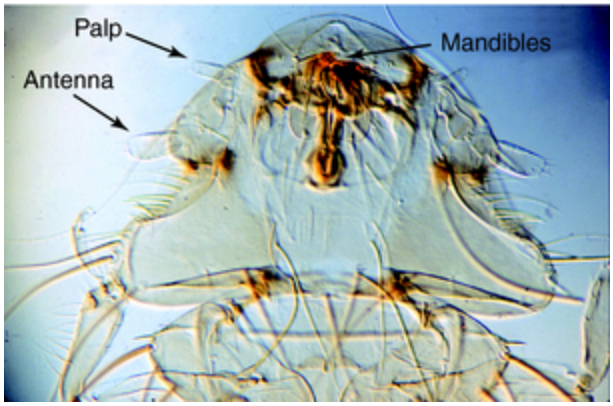

FIGURE 2-49 *Menopon* sp. (Mallophaga: Amblycera) of the chicken.

FIGURE 2-50 *Gliricola porcelli* (Mallophaga: Amblycera) of the guinea pig.

Suborder Rhynchophthirina

Haematomyzus species are parasites of both Asian and African elephants and of wart hogs (Figure 2-51). The preferred location on

elephants is the posterior aspect of the ears and adjacent areas of the head and neck.

FIGURE 2-51 *Haematomyzus elephantis* (Mallophaga: Rhynchophthirina) of the elephant.

Treatment of Louse Infestations

Dogs and Cats

Topical monthly application products have been found to be very efficacious in treating mallophagan infestations in dogs and cats. Selamectin has been shown to have high efficacy in the treatment of lice on dogs and cats (Shanks et al, 2003). *T. canis* has been shown to be treated with both fipronil and imidacloprid (Hanssen et al, 1999; Pollmeier et al, 2002). Fipronil has also been shown to be highly efficacious against *F. subrostratus* (Pollmeier et al, 2004). Lice are readily controlled with carbaryl-containing shampoo, spray, or dip. Usually two treatments are adequate when applied at an interval of 1 week.

In the case of dogs, the anopluran *Linognathus setosus* has been very successfully treated with both imidacloprid and selamectin (Gunnarsson, Christensson, and Palmer, 2005; Hanssen et al, 1999).

Beef and Nonlactating Dairy Cattle

Most cases of louse infestation in cattle are mild and manifested only by occasional scratching and restlessness on the part of the animals. However, as populations increase through the winter and early spring, the degree of irritation to the animals (and to any sympathetic observer) verges on the unbearable, and treatment must be carried out. Coumaphos, chlorpyrifos, and tetrachlorvinphos as sprays, dips, or pour-ons provide excellent control of lice. The macrocyclic lactones administered subcutaneously are highly

effective against anopluran infestations in cattle. The pour-on formulations of the macrocyclic lactones also provide good efficacy against *D. bovis*. It has been shown in New York State that calves housed in outdoor hutches have markedly lower louse infestation rates than calves held in collective stalls or pens in barns (Geden, Rutz, and Bishop, 1990).

Dairy Cattle

Tetrachlorvinphos, synergized pyrethrins, and coumaphos are applied to lactating dairy cows as sprays, in dust bags, in backrubbers, and as sprinkle-on dusts. Two applications should provide good control. Eprinomectin is efficacious against louse infestations of lactating cows.

Swine

Coumaphos and tetrachlorvinphos provide good control of lice when applied as sprays or poured on the topline from shoulders to hips. It is good practice when treating swine to apply insecticide also to the bedding of the holding pens. Usually two applications are adequate. Ivermectin, doramectin, and moxidectin all have excellent efficacy against *H. suis*.

Horses

Lice are found on horses principally during winter and spring. Two spray applications of coumaphos 2 weeks apart should provide adequate control. In cold weather, dusting horses with a mixture of rotenone and synergized pyrethrins is a less stressful procedure.

Elephants

Treatment of *Haematomyzus elephantis* infestations with oral administration of ivermectin at doses in the range 0.059 to 0.087 mg/kg body weight was found to be highly effective (Karesh and Robinson, 1985).

Humans

The treatment for lousy people is to be done under the supervision of a human physician. However, the veterinarian has a role in protecting pets from the all too common implication that they are the source of the human infestation. People get their lice from other people. Treatments for people containing various insecticides are typically in the form of creams, lotions, or shampoos; and in the United States, these products can usually be procured as over-the-counter products. Usually one application suffices, but treatment may need to be repeated in heavy infestations. Lice and their eggs are killed by exposure to a temperature of 50° C for 30 minutes, so sufficiently rigorous laundering can be an effective adjunct in control (Kraus and Glassman, 1976). If a home has an infestation of some of the family members, toys, brushes, combs, and so on can be placed in a clothes drier in a pillowcase and dried to destroy any lice or eggs that might be present on these items.

Order Siphonaptera, Fleas

Adult fleas are wingless, laterally flattened insects that have long legs for jumping and a large abdomen (Figure 2-52). Fleas feed on the blood of such animals as dogs, cats, pigs, humans, rodents, and

birds. Metamorphosis is complex, with three caterpillar-like larval stages and an enduring pupal stage enclosed in a silken cocoon. Certain hosts develop hypersensitive reactions to flea bites characterized by intense pruritus. A hypersensitive dog or human suffers intolerably from the bites of a small number of fleas that a normal individual would scarcely notice. Various species of fleas transmit plague *(Yersinia pestis)*, murine typhus *(Rickettsia typhi)*, rabbit myxomatosis virus, and feline parvovirus (Torres, 1941) and serve as intermediate hosts of the tapeworm *D. caninum* and the filariid nematode *Dipetalonema reconditum*.

FIGURE 2-52 Adult male *Pulex irritans* (Siphonaptera), lateral view, showing the six long legs, the head, three thoracic segments, and the abdomen.

Ctenocephalides

Identification

The ubiquitous *Ctenocephalides felis* and the relatively rare *Ctenocephalides canis* are parasites of a very wide range of domestic and wild mammals, including cats, dogs, cattle, and humans. *Ctenocephalides* have both genal and pronotal combs (Figure 2-53), which easily distinguishes them from *Echidnophaga* (Figure 2-54), *Xenopsylla* (Figure 2-55), and *Pulex* (Figure 2-56; see also Figure 2-52), which have neither genal nor pronotal combs, and from certain rodent fleas that have only pronotal combs. *Cediopsylla* (Figure 2-57), a rabbit flea, resembles *Ctenocephalides* in having both genal and pronotal combs but can be distinguished as follows. If a line drawn along the bases of the genal teeth runs parallel to the long axis of the head, the specimen is *Ctenocephalides*, whereas if it runs at an appreciable angle, it is *Cediopsylla*. Do not fail to recognize the eggs and larvae of fleas as such (Figures 2-58 and 2-59). *Ctenocephalides* lay their eggs on the host. Especially in the case of dogs with thick and soiled haircoats, many of these 0.5-mm-long, glistening, white eggs may remain on the host long enough to hatch; so sometimes, not only adults but eggs and larvae of *Ctenocephalides* are found in the haircoat of infested dogs and cats.

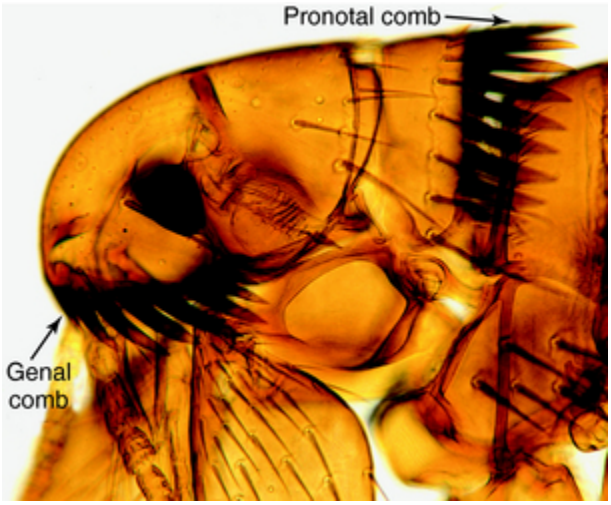

FIGURE 2-53 *Ctenocephalides* (Siphonaptera) of the cat and dog. The bases of the genal teeth of *Ctenocephalides* lie on a line running parallel to the long axis of the head, thus serving to distinguish this genus from certain rodent and leporid fleas that have both genal and pronotal combs.

FIGURE 2-54 *Echidnophaga* (Siphonaptera). *Echidnophaga gallinacea*, the poultry sticktight flea, may be found firmly attached in clusters on chickens' heads and on the eyelids or in the ear canals of dogs, cats, and other animals.

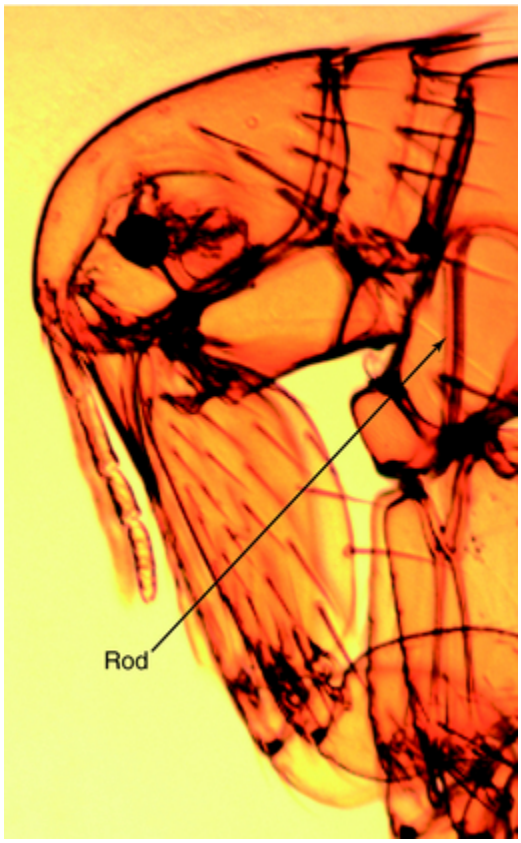

FIGURE 2-55 *Xenopsylla* (Siphonaptera), a rat flea and biologic vector of plague *(Yersinia pestis)* and endemic typhus *(Rickettsia typhi)*. The vertical rod on the mesothorax distinguishes this genus from *Pulex*.

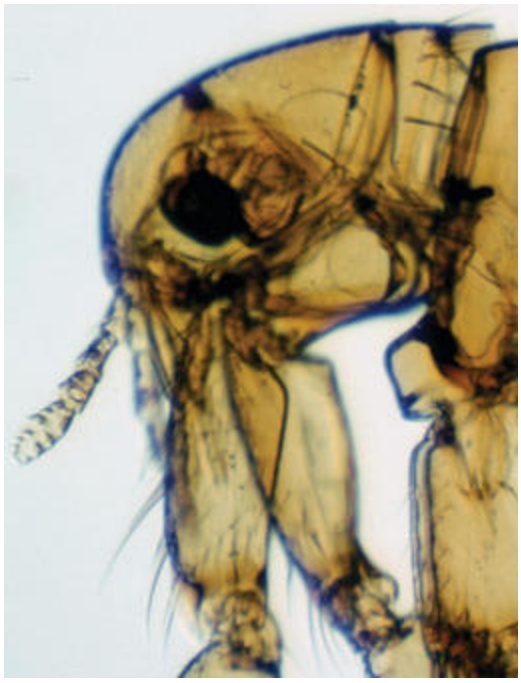

FIGURE 2-56 *Pulex* (Siphonaptera). *Pulex irritans*, the human flea, attacks a wide range of hosts.

FIGURE 2-57 *Cediopsylla* (Siphonaptera) of the rabbit. The bases of the genal teeth lie on a line running at an angle to the long axis of the head, thus serving to distinguish this genus from *Ctenocephalides*.

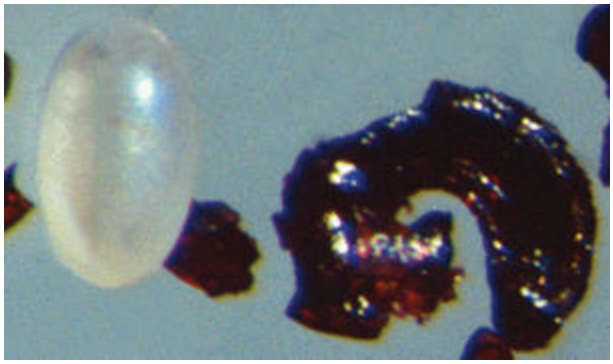

FIGURE 2-58 Egg of *Ctenocephalides* and two masses of flea feces. Flea feces consists essentially of dried host's blood and serves as food for the flea larvae, which have chewing mouthparts.

FIGURE 2-59 Larva of *Ctenocephalides*. Flea larvae are frequently overlooked or misidentified.

Diagnosis of dog and cat flea infestation is sometimes difficult because only a few fleas are required to cause great misery, especially in a sensitized individual. Flea feces are essentially tiny particles of dried blood. The larval fleas eat their parents' feces, as well as other organic debris. Flea feces may be detected in the haircoat of a dog or cat by a sort of paper chromatography. Suspect detritus may be placed on filter paper or other absorbent material that has been dampened with dilute soap or detergent solution.

Hemoglobin will diffuse out of flea feces in a few minutes and form a red halo around the speck of debris, or a similarly dampened pledget of absorbent cotton may be rubbed over the haircoat and skin to pick up particles of flea feces; little red spots appear on the cotton.

Life history

Metamorphosis of fleas is complex, with life stages consisting of egg, larval stages one, two, and three, pupa, and adult (Figure 2-60). The adult *Ctenocephalides* displays little tendency to leave its dog or cat host unless the population approaches about 200. Then a few fleas may get off occasionally, especially when their host comes in contact with another, possibly less parasitized individual. A common misconception exists that *Ctenocephalides* fleas constantly jump on and off their hosts and find new hosts in this manner. In fact, most of the fleas a dog or cat acquires are brand new ones straight out of their pupal cases, and it is most important to remember this fact in connection with control efforts (Figure 2-61). For every flea on the host, there are many eggs, larvae, pupae, and newly emerged adults in the environment, and these tend to be concentrated wherever the host habitually rests. The longer the host stays in one place, the more eggs and adult flea feces will be deposited there. Flea feces serve as the principal food of the three larval stages. Development of *C. felis* from egg to adult occurs within the ranges 13° to 32° C and 50% to 92% relative humidity and requires from 14 to 140 days at the extremes of temperature.

Temperatures above 35° C are lethal to larvae and pupae. Unfed adults may survive for many weeks under cool, humid conditions but probably cannot long withstand the low relative humidities associated with subfreezing conditions (Silverman, Rust, and Reierson, 1981). Unfed *Ctenocephalides* adults can survive for about 2 months waiting for a host to happen by. People returning home after an absence of several weeks may be greeted by hordes of bloodthirsty fleas that, although preferring to feed on dogs, are quite willing to make do with humans when no dog is available. One of Dr. Georgi's mentors used to deal with this situation as follows. On arriving back in town, he would go directly to the kennel where his dog had been housed during his absence and take the dog home to collect the hungry fleas that were sure to be lying in wait there. After a brief tour of the house, the dog was immediately taken back to the kennel for a flea bath while the rest of the family retook possession of the house.

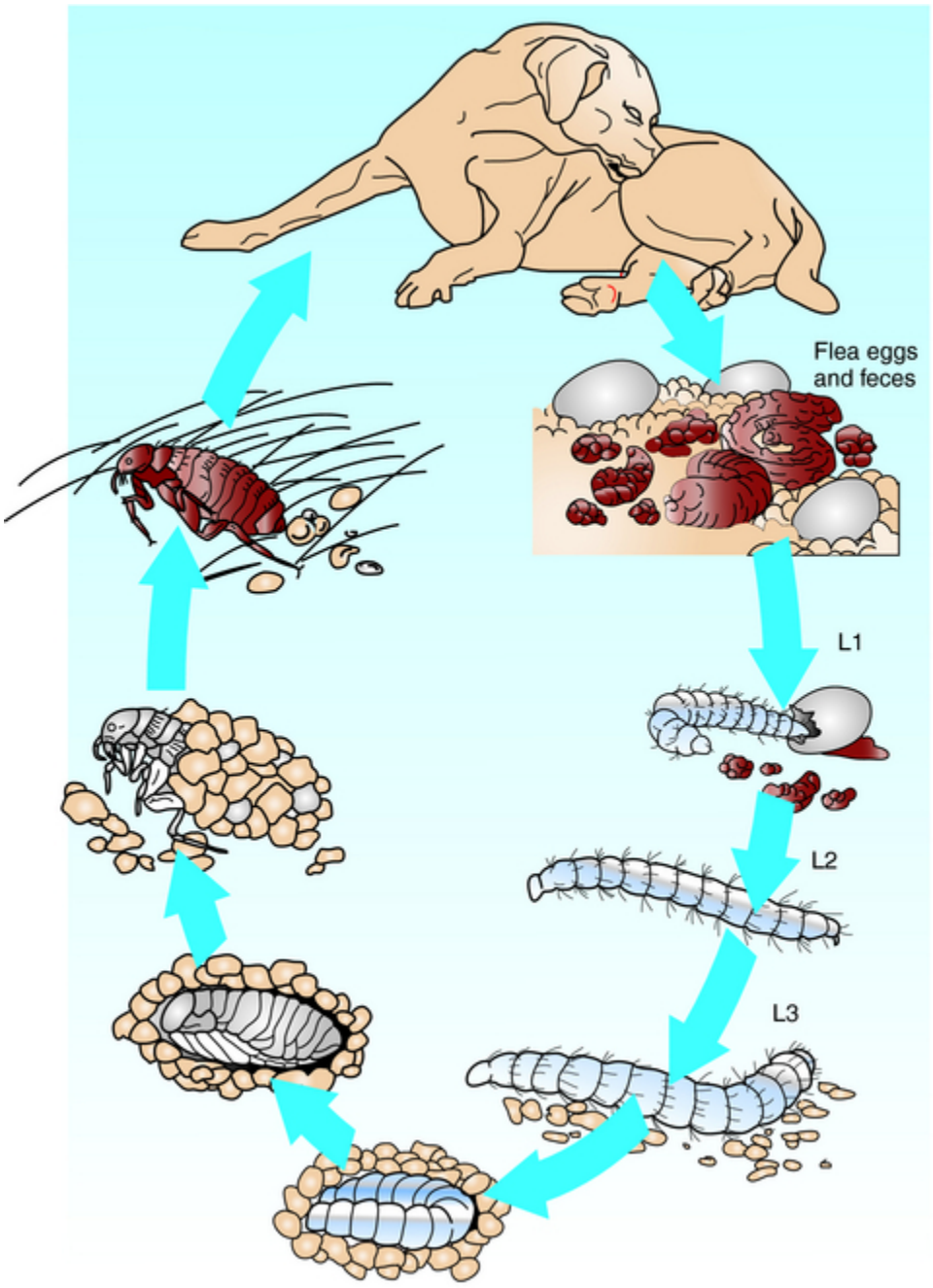

FIGURE 2-60 Life history of *Ctenocephalides felis*. Eggs appear 2 days after male and female fleas arrive on a cat or dog. Most eggs fall out of the pelage and tend to accumulate where the host habitually rests, and first-stage larvae (L1) begin to hatch out of them on day 4. Larvae feed on adult flea feces, which, like the eggs, continuously rain down from the coat of an infested dog or cat, and pass through two molts. In about 2 weeks of warm, moist conditions, the third-stage larvae begin to spin cocoons and metamorphose into adult fleas (i.e., pupate). The cocoons are sticky so that fine debris, such as the sand grains in the picture, tends to accumulate on their surfaces. Adults begin

to emerge from cocoons at 3 to 4 weeks, females preceding males by several days. Having found a dog or cat, the adult *C. felis* remains aboard, feeding repeatedly and reproducing until it is exhausted and dies or is nipped and swallowed by the host. *C. felis* rarely leaves a suitable host of its own accord.

FIGURE 2-61 Cocoons of *Ctenocephalides felis*. *Left*, The cocoon has been opened to reveal the larva within. *Bottom right*, The cocoon shows a flea that has almost completed metamorphosis.

Disease transmission

C. canis and *C. felis* are true intermediate hosts (biologic vectors) of the tapeworm *D. caninum* and the filariid nematode *D. reconditum*. Fleas acquire *D. caninum* infection as larvae, because these are the stages with chewing mouthparts suitable for ingesting solid material such as the eggs of this tapeworm. The cysticercoid that develops from the egg is passed along through metamorphosis to the adult flea and infects the dog or cat that chances to ingest that particular flea. Microfilariae of *D. reconditum* are ingested by the blood-feeding adult flea and develop into third-stage larvae capable of infecting a dog. Feline parvovirus, the causative agent of feline panleukopenia,

can be transmitted from infected to susceptible cats by *C. felis* (Torres, 1941).

Treatment of infestations with *Ctenocephalides*

Flea control has changed dramatically over the past few years because of the introduction of several products designed to be administered monthly to dogs and cats. The impact of these products has been so dramatic that pest control operatives in the United States are seeing a decline in their flea-control contracts. It has been recommended that for fiscal reasons they should enter into local agreements with veterinarians over the sale of flea-control products (Fehrenbach, 1996). Pets, clients, and veterinarians have gained remarkably in their ability to control flea infestations with the new products that have come on the market in the last 10 years.

Environmental control is still a major means of controlling fleas, and it does not necessarily require chemicals. The vacuum cleaner is virtually indispensable in reducing the number of eggs, larvae, pupae, and unfed adult fleas in the environment. Remove, close, and dispose of the bag after vacuuming to prevent fleas from escaping back into the cleaned areas. Efforts to control fleas should be concentrated on the places where the dog or cat habitually rests, because here is where eggs and flea feces, the provender of larvae, are most likely to be deposited, and the development of adults fleas is likely to follow. One simple measure that affords 100% control of fleas is to keep the dogs or cats in wire-bottom cages elevated at least 13 inches (33 cm) above the ground or floor. In a commercial

beagle-breeding establishment housing several thousand dogs and employing no chemical flea control, there were no fleas at all because the dogs in the colony were beyond the range of the staunchest jump that *C. felis*, champion jumper of the universe, can put forth (i.e., 33 cm) (Rothschild et al, 1973). Application of this latter environmental control method is clearly limited to strictly confined animals.

There are still numerous products designed for topical application to both animals and premises that will continue to be useful in flea control. Products that contain pyrethrins, carbaryl, phosmet, tetrachlorvinphos, and methoprene are usually effective and suitable for application to both animals and their surroundings. Resistance to carbaryl and some organophosphates is on the rise, however, and this possibility must be taken into account in cases of apparent insecticide failure. Clients may treat pets with several different preparations and the premises with additional preparations, but if the labels are examined, it might be discovered that all preparations contain the same active ingredient. On the market are various dog and cat flea collars impregnated with various insecticidal compounds: chlorpyrifos, tetrachlorvinphos, diazinon, amitraz. Some also are impregnated with the insect growth regulator, methoprene. These products do produce a certain level of control, and when combined with careful premise management can produce rather successful treatment programs.

There are other available methods for the control of fleas that differ widely in their apparent effect on flea populations under

various conditions. There are several traps commercially available for the capture of adult fleas. Some of these traps will collect more than 85% of released fleas, whereas others collect only slightly more than 10% (Dryden and Bruce, 1993). Brewer's yeast failed as a repellent to fleas on dogs when fed as a dietary supplement at the rate of 14 g/day (Baker and Farver, 1983). Ultrasonic flea collars also do not repel fleas from dogs, at least under certain laboratory conditions (Dryden, Long, and Gaafar, 1989).

Fipronil, both the spray and the spot-on formulations, has been found to cause severe toxic reactions in rabbits treated for flea control. Thus the nonapproved use of fipronil on rabbits should be suspended for the time being.

It is important to remember that all insecticides are toxicants, not only to the insects but to the animal on which they are applied and to the person who applies them. Frequently the chore of treating dogs and cats falls on one or two members of a veterinary hospital staff, and by the nature of their work such persons repeatedly come into contact with these insecticides. It is the responsibility of veterinarians in charge to enforce procedures designed to minimize exposure of their employees to toxic chemicals.

Echidnophaga

Echidnophaga gallinacea, the sticktight flea of poultry, attacks all kinds of domestic birds, as well as dogs, cats, rabbits, horses, and humans, in subtropical America. Dr. Georgi once found several

embedded in the eyelids of a cat recently arrived in New York from Alabama. On birds, *E. gallinacea* embeds itself in the skin around the eyes and cloaca and on the combs, wattles, and other glabrous areas. These are small fleas with angular heads devoid of genal and pronotal combs; the thoracic tergites (dorsal sclerites of the thorax) are very narrow (see Figure 2-54).

Tunga

Tunga penetrans, the "jigger" or "chigoe," is a small (1 mm) flea of tropical America and Africa that somewhat resembles *Echidnophaga* in having an angular head and narrow thoracic segments and in lacking combs. The impregnated *Tunga* female embeds in the skin of the ankles, instep, and between the toes, with only the last few abdominal segments protruding (Figure 2-62). Eggs are retained in the abdomen, and the flea swells to the size of a pea. Lesions caused by this flea are painful and subject to secondary infection and are supposedly the inspiration for the sailor's oath, "I'll be jiggered" (Chandler and Read, 1961).

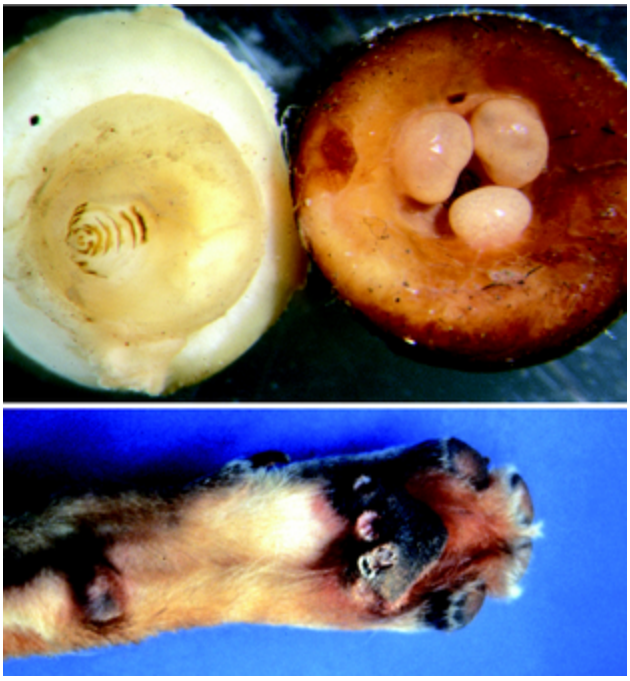

FIGURE 2-62 *Tunga penetrans*. *Top, Tunga* specimens from a goat and a pig in Ecuador. *Left*, The posterior end of the goat specimen shows normal terminal segments. *Right*, The anterior of the pig specimen has three large sacculations with the head within enclosed in the space between them. *Bottom*, The paw of a dog with several of these fleas embedded in the skin.

Xenopsylla

Xenopsylla is a widely distributed genus of rat fleas that also attack humans and are an important vector of plague *(Y. pestis)* and murine (endemic) typhus *(R. typhi)*. Combs are absent, and the head is smoothly rounded, thus distinguishing *Xenopsylla* from the foregoing genera; it differs from *Pulex* in having a vertical rod on the mesothorax (see Figure 2-55).

Disease transmission

Plague is normally a disease of rodents caused by the bacterium *Y. pestis* and transmitted by various fleas, of which *Xenopsylla cheopis*

stands out, especially in relation to human infection. The great plague pandemics that decimated civilization during the Middle Ages may have been precipitated by large-scale plague mortality among humans' rodent cohabitants, resulting in the vector turning to humans for its blood meals and communicating *Y. pestis* to them in the process.

Pulex

Pulex irritans, the human flea, is widely distributed and attacks a wide range of hosts, including humans, swine, and dogs. *Pulex* resembles *Xenopsylla* but lacks the mesothoracic rod (see Figures 2-52 and 2-56).

Order Hemiptera, Bugs

Hemipterans have two pairs of wings (which may be vestigial), a triangular shield between the wing bases, four-segmented antennae, and a three-segmented beak that is directed caudally beneath the head when not in use (Figures 2-63 and 2-64).

FIGURE 2-63 Triatomin bug (Hemiptera: Reduviidae), an assassin bug. Vector of *Trypanosoma cruzi* in North America. *Right*, The proboscis of the bug that is partially inserted into the host when the bug feeds.

FIGURE 2-64 *Cimex lectularius* (Hemiptera: Cimicidae), the bedbug.

Development is by means of **simple metamorphosis.** Some hemipterans feed on plants; some kill insects and suck their juices; and some are bloodsuckers and pests of rodents and humans, occasionally attacking other animals. Predacious reduviids (assassin bugs) inflict painful bites, and many such species have been reported to attack humans, but the bites of the more specialized parasitic reduviids (cone-nose bugs) and cimicids (bedbugs) are painless.

Family Reduviidae, Assassin Bugs, and Kissing or Cone-Nose Bugs

The reduviids (see Figure 2-63) have wings and a characteristic three-segmented beak. The parasitic species of the subfamily Triatominae, which feed exclusively on the blood of vertebrates, have a more slender beak than the predatory species and are able to feed painlessly enough so as not to awaken a sleeping host. They hide in crevices by day and attack their sleeping hosts by night in the manner of bedbugs, argasid ticks, and some species of mesostigmatid mites. Triatominae of the genera *Triatoma*, *Rhodnius*, and *Panstrongylus* transmit American trypanosomiasis or Chagas' disease *(Trypanosoma cruzi)*. The transmission of *T. cruzi* is in the feces of the bug, and therefore this is defined as transmission via the **posterior station.** This is for the purposes of distinguishing this type of transmission from the **anterior station** transmission (via mouthparts and bite) of trypanosomes by tsetses and a few trypanosomes, such as *Trypanosoma rangeli*, that are transmitted by the bites of triatomin bugs. The bug *Triatoma sanguisuga* may play a minor role in the transmission of equine encephalomyelitis.

Family Cimicidae, Bedbugs

Bedbugs (see Figure 2-64) have oval, dorsoventrally flattened bodies, vestigial wings, three-segmented beaks, and a disagreeable odor. They are nocturnal and secretive bloodsucking parasites of humans, chickens, bats, and nesting birds. Like triatomids, bedbugs hide in crevices by day and attack their sleeping host at night. They

lay their eggs in their hiding places and molt five times at approximately weekly intervals, taking one blood meal between each molt and another before egg laying. Bedbugs can endure starvation for several months. Although such a blood-feeding pattern as this would seem ideally suited to the transmission of disease organisms, bedbugs, though frequently indicted, have yet to be convicted on any such counts.

Order Blattaria, Cockroaches

Cockroaches are important as intermediate hosts of certain parasitic worms such as the spirurid nematodes *Spirura*, *Oxyspirura*, and *Gongylonema;* the acanthocephalans *Moniliformis*, *Prosthenorchis*, and *Homorhynchus;* and the pentastomid *Raillietiella*. They also serve as mechanical vectors of filth-borne diseases of humans. Inspection of premises where food is prepared is often a veterinary function. Presence or absence of cockroaches is an important criterion of the adequacy of food sanitation (Figure 2-65).

FIGURE 2-65 A cockroach, *Periplaneta americana* (Blattaria).

Order Coleoptera, Beetles

Beetles have hard, shell-like outer wing covers called **elytra** that lack venation (Figure 2-66). Development is via **complete metamorphosis;** the larvae are grubs.

FIGURE 2-66 A beetle, *Aleochara bimaculata* (Coleoptera; Staphylinidae). This beetle is an ectoparasite on horn fly and face fly pupae as a larva and feeds on fly eggs as an adult. The elytra of this beetle cover only the anterior portion of the abdomen.

Beetles, like cockroaches, are important as intermediate hosts of parasitic worms that infect domestic animals and humans. The spirurid nematodes *Gongylonema* and *Physocephalus*, the acanthocephalans *Macracanthorhynchus* and *Moniliformis*, and the cestodes *Hymenolepis* and *Raillietina* (not to be confused with the pentastomid *Raillietiella* or, for that matter, with the mesostigmatid

Raillietia), all develop in beetles to the stage infective for the vertebrate host.

Some species of beetles are also extremely toxic. For example, **blister beetles** (*Epicauta* species) (Figure 2-67) release an irritant and vesicant chemical **(cantharidin)** when crushed during single-operation mowing and crimping of alfalfa hay. Hay containing these crushed beetles is lethal for horses and may remain so even after years of storage. Clinical signs of cantharidin toxicosis include abdominal pain, fever, depression, frequent urination, shock, and, occasionally, synchronous diaphragmatic flutter, and mortality may exceed 70% of affected individuals. Hematologic findings included hemoconcentration, neutrophilic leukocytosis, and hypocalcemia. As in all clinical poisonings, locating the source of the toxic agent is essential both to reaching a definitive diagnosis and to preventing further losses; the beetles should be sought in hay fed to the affected horses (Schoeb and Panciera, 1978, 1979). The lethal dose of cantharidin for the horse is probably less than 1 mg/kg body weight (Beasley et al, 1983).

FIGURE 2-67 *Epicauta* sp. striped blister beetles. Consumption of alfalfa hay containing dead striped blister beetles causes acute cantharidin toxicosis in horses.

Courtesy Dr. R.J. Panciera.

Dung beetles (some 14,000 species of the family Scarabaeidae) are very important in the grazing ecology because they break up, remove, and bury manure (Figure 2-68). Without their services, ruminant and horse dung tends to accumulate on the pasture, where it breeds flies, physically interferes with the growth of grass, and discourages grazing in the immediate vicinity. Besides simply clearing the surface of pastures, dung beetles enhance fertility and filth by burrowing in the soil and carrying their little balls of dung down into the burrows, where it is attacked by bacteria and fungi and the nutrients therein are made available to plants. Australia has

gone so far as to import dung beetles from Africa in a successful effort to reduce accumulations of cattle dung on pasture and the fly populations that breed therein. Administration of ivermectin to grazing cattle suppressed not only target organisms but dung beetle populations as well. This unforeseen effect of anthelmintic medication may have potentially disastrous effects on dung removal and soil nutrient cycling, at least under some environmental conditions and dosage regimens (Coe, 1987; Wall and Strong, 1987).

FIGURE 2-68 Dung beetle from Canton, Ohio, rolling a ball of dung to burial.

The small **hive beetle**, *Aethina tumida*, was introduced into the United States sometime around 1998 (Elzen et al, 1999). The beetle is now known to be in Florida, Georgia, South Carolina, Pennsylvania, Ohio, Minnesota, and Michigan. The beetles enter the hives of the European honeybee *(Apis mellifera)*, and the beetle larvae feed on honey in the combs and cause the bees to flee the hive. This is one of several recently introduced arthropod pathogens

of honeybees that have caused severe damage to these important pollinators throughout the United States.

CLASS ARACHNIDA

Although the class Arachnida includes spiders, scorpions, whip scorpions, and other forms that are of occasional interest to veterinarians, the following exposition is restricted to the ticks and mites. Larval stages of both ticks and mites normally have three pairs of legs, and the nymphs and adults have four pairs. The head, thorax, and abdomen are fused; antennae and mandibles are absent. The mouthparts (palps, chelicerae, and hypostome) together with the basis capituli, form a capitulum, or gnathosome (Figure 2-69).

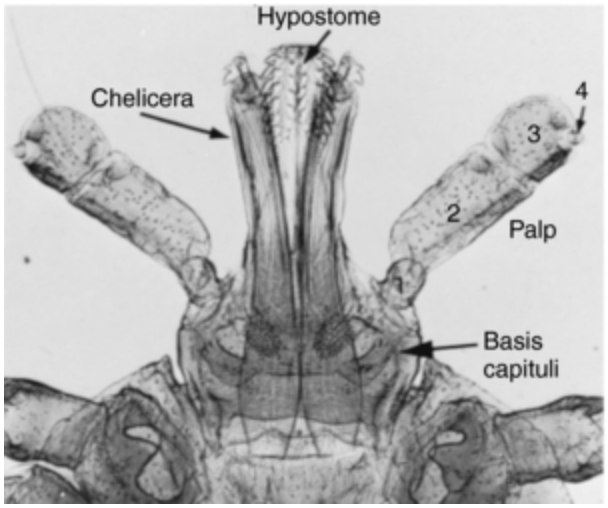

FIGURE 2-69 Capitulum of *Amblyomma*.

Suborder Metastigmata, Ticks

All ticks are bloodsucking parasites. The hypostome is armed with backward-projecting teeth, and the chelicerae are armed with

movable denticles (see Figure 2-69). The lateral stigmata are caudodorsal to the fourth coxae (Figure 2-70) and lack the sinuous peritremes characteristic of the somewhat similar suborder Mesostigmata.

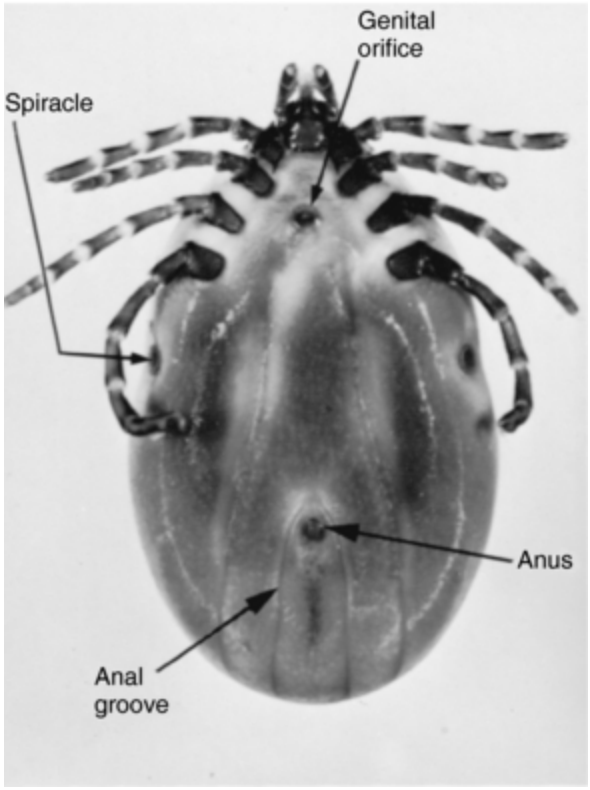

FIGURE 2-70 Ventral aspect of *Ixodes*. The anal groove of *Ixodes* curves anteriorly around the anus.

The greatest importance of ticks attaches to the large number and variety of microbial diseases that they transmit among domestic animals. These diseases are listed later in the discussion on the particular genera involved as vectors. Other injuries inflicted by ticks include toxicosis, the bite wound, worry, and blood loss. There are two major families of ticks, the Argasidae, or **soft ticks,** and the

Ixodidae, or **hard ticks.** (There is a third family of ticks, the Nuttalliellidae, represented by a single species in the genus *Nuttalliella*, which are of real importance only to arachnidologists.) Besides markedly different morphology, soft and hard ticks vary greatly in their behavior. The Argasidae family tends to be composed of species that live in nests or burrows from where they surreptitiously feed quickly on unsuspecting hosts. Ixodid ticks tend to spend most of their lives in fields or scrub areas where they await passing hosts. These ixodid ticks then attach and remain attached to their hosts for up to several days before they release and drop to the ground.

Family Argasidae

The family Argasidae, or soft ticks, is small, consisting of 140 species belonging to four genera, *Argas*, *Ornithodoros*, *Otobius*, and *Carios*. *Carios* species are limited to bats and will not be considered further here. Argasids live in nests, burrows, buildings, and sleeping places of their host animals and are distributed mostly in arid regions or in drier habitats in moist regions. The life stages consist of the egg (laid in several batches of hundreds), larva, two or more nymphal stages, and adult male and female. Unlike ixodid nymphs and adults, which require several days to complete engorgement and feed only once during each stage, argasid nymphs and adults feed to repletion on their sleeping hosts in minutes or hours and feed repeatedly. Female argasids lay a clutch of eggs after each blood meal. Argasid larvae, on the other hand, feed for several days,

and *Otobius* nymphs may remain in the external ear canal of cattle for several weeks.

Argas

Identification

Argas species are 5- to 10-mm, flattened, ovoid, and yellow to reddish-brown ticks with leathery, mammillated, and wrinkled dorsal and ventral surfaces meeting at a sharp lateral margin. The mouthparts are on the ventral surface and thus hidden when the tick is viewed from above (Figure 2-71). *Argas* is rarely found on the host; to find these ticks, search cracks and crannies in the hen house for this parasite. In the United States, *Argas* is restricted to areas along the Gulf of Mexico and the Mexican border.

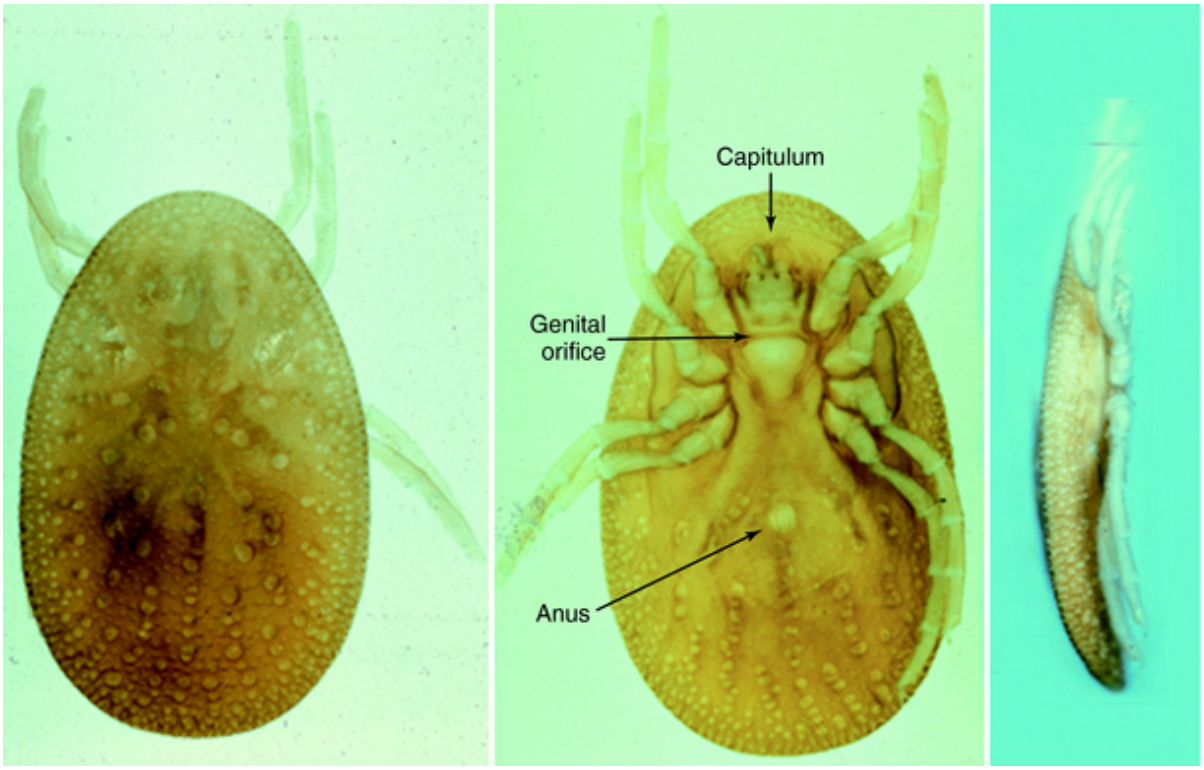

FIGURE 2-71 *Argas*. *Left*, Dorsal aspect. *Center*, Ventral aspect. *Right*, Lateral aspect.

Life history

Female *Argas* ticks deposit their eggs in clutches of 25 to 100 in the crevices that serve as hiding places during the day. Several clutches are laid, each preceded by a blood meal lasting 45 minutes or less. The six-legged larva hatches in 1 to 4 weeks, attaches to a host, and feeds for about 5 days; the larva is thus active day and night. When replete, the larva leaves the host and finds a hiding place in which to spend a week or so molting into a nymph. The eight-legged nymph feeds at night and undergoes a second molt to a second nymphal stage, which again feeds and undergoes a third molt into an adult male or female. Although development from egg to adult may be completed in as few as 30 days, lack of suitable hosts may prolong the process. Larvae and nymphs may survive for months and adults for more than 2 years without a blood meal. Trying to starve them out does not pay.

Disease transmission

In South America, *Argas* species transmit fowl or avian spirochetosis *(Borrelia anserina)*, via tick fecal contamination, to domestic poultry, grouse, canaries, guinea fowl, and pigeons. Ticks may remain infective for 6 months or more and transmit the spirochetes to their offspring via the ovaries (transovarial transmission). *Argas* species also transmit a rickettsial agent, *Aegyptianella pullorum*, to chickens and geese in the tropics and subtropics of the Old World.

Tick paralysis

Infestation with larvae of *Argas persicus* can result in fatal flaccid paralysis of young chickens (Rosenstein, 1976).

Ornithodoros

Identification

Ornithodoros differs from *Argas* in being more globular, in lacking a sharp lateral margin, and in not appearing distinctly ovoid when viewed from above. The body is flattened in unfed specimens but strongly convex dorsally when distended with blood. These ticks (Figure 2-72) are found in cracks and crannies of avian roosts and nests, rodent burrows, and the resting places of large mammals.

FIGURE 2-72 *Ornithodoros*.

Life history

Species of *Ornithodoros* differ with respect to whether the larvae feed, to the number of nymphal instars (three to five), and to host and lair preferences. *Ornithodoros hermsi* is a rodent parasite in the Rocky Mountain and Pacific Coast states, breeding in rodent burrows and rodent-infested buildings, whereas *Ornithodoros coriaceus* of California and Oregon attacks deer and cattle from the soil of their bedding areas. As typical argasids, *Ornithodoros* can survive unfed for months or even years.

Disease transmission

Ornithodoros are most important as vectors and reservoirs of relapsing fever spirochetes *(Borrelia recurrentis)* of humans. Infection may be maintained in tick populations for many years by transovarial transmission of the spirochetes from female ticks to their offspring and tends to remain endemic in wild rodent populations. Tick-borne relapsing fever typically involves an individual or small group of campers who have slept in a tick-infested cabin out in the wilderness. Because the *Ornithodoros* ticks involved in transmission are nocturnal and surreptitious, relapsing fever victims are frequently unaware of recent tick exposure.

Otobius

Identification

Larvae and two nymphal stages of *Otobius megnini*, the spinose ear tick, parasitize the ear canals of cattle, remaining in a particular

host for as long as 4 months. Other domestic animals and humans also sometimes serve as hosts. One of Dr. Georgi's former students reported that he had suffered several painful attacks by *Otobius*. As implied by the common name, the cuticle of *Otobius* is covered by spines. The second nymphal stage is particularly distinctive (Figure 2-73).

FIGURE 2-73 *Otobius megnini*. *Left*, First nymph. *Right*, Second nymph.

Life history

Larvae feed in the ear canal and molt into the first nymphal stage, which in turn feeds in the same host's ear canal and molts into the second nymphal stage, which again feeds but leaves the ear canal and drops to the ground to molt to the adult stage. Adult *Otobius* have vestigial hypostomes and do not feed; they copulate within a day or two after emergence, and the females oviposit in the soil. Larvae survive unfed for as long as 2 months. Thus, *Otobius* differs

from *Argas* and *Ornithodorus* in being a one-host tick and in laying only one clutch of eggs.

Family Ixodidae

Members of the family Ixodidae, or **hard ticks,** have a shield, or **scutum,** that covers the entire dorsal surface of the male but only part of the dorsal surface of the female (Figure 2-74). The size of the scutum remains constant during engorgement of a female and consequently covers a progressively smaller proportion of her dorsum. A tick's eye, if present, is a mere roundish lucent area at the margin of the scutum about opposite the second coxa. The scutum and the posterior edge of the body may bear a series of indentations or folds along the margin; these are called **festoons.** Also, the scutum may have colored patterns on the surface (an **ornate scutum**) or it may be without coloration (an **inornate scutum**). The large **stigmata** (respiratory openings attached to the tracheal system) are behind the last pair of legs on the sides of the body. The anterior end of the tick houses the feeding apparatus, which consists of a **basis capituli** that is adjacent ot the body. On the anterior portion of the basis capituli are the **palps,** one on each side of the paired **chelicerae** and the central **hypostome.** The palps consist of four segments, with the distal fourth pretty well buried in the third. Each chelicera has large cutting blades on the distal end, and the hypostome has numerous small teeth or denticles.

FIGURE 2-74 *Amblyomma maculatum*. The male *(left)* has an ornamented scutum that covers the entire body. In the case of the female *(right)*, the scutum is also ornate but covers only a portion of the dorsal surface of the tick. As the female engorges, the scutum remains constant in size and, at last, covers only a small proportion of the fully engorged female.

Eggs are laid in a single clutch of thousands. Ixodid larvae, nymphs, and adults each feed only once, and several days are usually required for complete engorgement. Ixodids usually live outdoors and attach to passing host animals. There are two molts: the first from larva to nymph and the second from nymph to adult. Species that complete both molts without leaving the host are called **one-host ticks;** species whose engorged nymphs drop off to molt are called **two-host ticks;** and those whose nymphs and larvae drop off to molt are called **three-host ticks.** *Dermacentor variabilis* is a three-host tick whose larvae and nymphs engorge on small

mammals and whose adults engorge on dogs. *Rhipicephalus sanguineus* is a three-host tick whose larvae, nymphs, and adults all engorge on dogs. The individual or species identity of the host has no bearing on the use of these terms. What is important relative to these terms is that a one-host tick or a three-host tick that feeds on only one host is often easier to control through the management of the single host than a three-host tick that has different hosts throughout the environment. For example, if cattle are hosts to a one-host tick, dipping and other applications of chemotherapeutic agents or vaccination of the cattle will have effects on all life stages of the tick. If three hosts were involved, the first host might be a rodent, the second a rabbit or bird, and the third cattle. Thus it would be more difficult to manage these two- or three-host systems because it would be difficult to manage or treat all three hosts involved. That three-host ticks may feed on several different hosts during their lives, from small rodents to large mammals, make them perfect vectors for the transmission of zoonotic agents to humans, e.g., the larva feeds on a rodent, and the nymph or adult will feed on humans; thus transmission from rodents to humans becomes a real possibility. This is exactly what occurs in the case of Lyme borreliosis.

Two- and three-host ticks can transmit disease organisms via **interstadial transmission;** that is, infection acquired by a larval tick is carried through the molt to the nymphal stage and then conveyed to the host on which the nymph feeds, or infection acquired by a nymph is carried through the molt and conveyed to

the host on which the adult tick feeds. Thus three-host ticks can transmit disease organisms interstadially through both larva to nymph and nymph to adult transitions, whereas two-host ticks are limited to the latter. In **transovarial transmission,** the disease organisms are passed from the adult female tick to her larvae through infection of her ovaries. *Babesia bigemina* is transmitted from the adult female *Rhipicephalus* (fomerly *Boophilus,* this genus has now been subsumed within the genus *Rhipicephalus*) tick to her progeny by way of her ovaries. Transovarial transmission of disease organisms is the only mechanism that allows one-host ticks, such as *Rhipicephalus annulatus*, to serve as vectors.

Ixodid ticks found attached to domestic animals may be removed individually by cautious traction with thumb forceps. The long hypostomes of *Ixodes, Amblyomma*, and *Hyalomma* are effective anchors. *Dermacentor*, *Rhipicephalus,* and *Haemaphysalis* compensate for their shorter hypostomes by secreting a cement in which the mouthparts are embedded and that attaches them securely to the skin (Moorhouse, 1973; Moorhouse and Tatchell, 1966). Therefore unless reasonable care is exercised, the capitulum may be torn away and remain embedded as a foreign body in the skin of the host. Outdoor areas suspected as sources of ixodid tick infestation may be surveyed with a drag made by attaching one edge of a square yard of flannel to a stick and drawing it slowly over the vegetation. Hungry ticks will climb aboard the passing drag and can then be removed at intervals and placed in specimen bottles.

Veterinarians should carefully examine the ticks they encounter in practice. If a specimen is found that looks different from normal ticks, it should be sent to a diagnostic laboratory for expert identification. However, many practical problems can be solved by generic identification of adult ixodid ticks, and criteria for accomplishing that goal are presented here. No attempt is made here to identify larvae and nymphs beyond the family level; larvae have six legs (Figure 2-75) and nymphs have eight legs and a scutum of the female type, but the genital aperture is absent (Figure 2-76). A key to the nymphs of ixodid ticks that may be helpful to veterinarians has been presented elsewhere (Bowman and Giovengo, 1991).

FIGURE 2-75 Six-legged *Ixodes* larva.

FIGURE 2-76 Eight-legged *Ixodes* nymph. Although difficult to discern in this figure, an anterior anal groove can be found in the nymphal and larval stages of ticks of the genus *Ixodes*.

In the following outline of genera of ixodid ticks, the **character in bold type** is either sufficient or nearly sufficient to represent the genus alone, provided, of course, that the corresponding morphologic feature of the specimen is seen and correctly interpreted. Any ixodid tick must have one or another of these characters, and they serve as convenient starting points for identifying specimens; however, to be on the safe side, check each subsidiary character as well. Further details may be found in *Ticks of Veterinary Importance*, Animal and Plant Health Inspection Service (APHIS), United States Department of Agriculture (USDA), Agriculture Handbook No. 485.

Approximately 700 species of hard ticks are included in a total of 12 genera. The currently recognized genera are *Amblyomma*,

Anomalohimalaya, Bothriocroton, Cosmiomma, Dermacentor, Haemaphysalis, Hyalomma, Ixodes, Margaropus, Nosomma, Rhipicentor, and *Rhipicephalus,* with the genus *Boophilus* becoming a subgenus of the genus *Rhipicephalus* (Horak, Camicas, and Keirans, 2002). The five genera that are found in North America include *Ixodes, Haemaphysalis, Rhipicephalus, Dermacentor,* and *Amblyomma*. The other genera from outside North America are sometimes found here on imported animals.

Genera Found in North America

Ixodes

Identification

The anal groove forms an arch anterior to the anus; this can be seen with oblique illumination of uncleared specimens (Figure 2-77). Other genera have a groove posterior to the anus or no groove at all. *Ixodes* species have no eyes, festoons, or scutal ornamentation; their palpi are broadest at the junction of segments two and three (Figure 2-78).

FIGURE 2-77 The anus and the anterior anal groove present on the posterior ventral surface of all stages of ticks in the genus *Ixodes*.

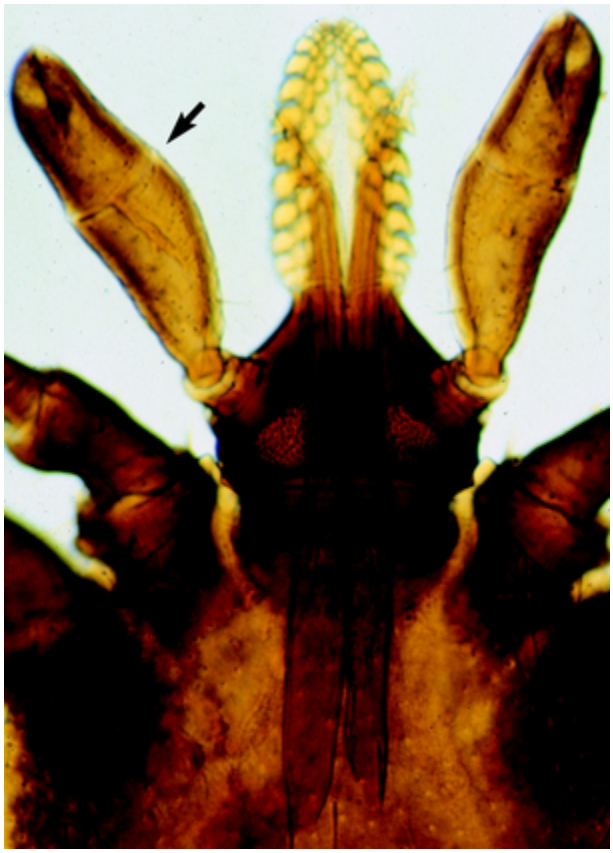

FIGURE 2-78 Capitulum of *Ixodes*. The palps of *Ixodes* are broadest at the junction of the second and third segments *(arrow)*.

Life history and disease transmission

In Europe, species of *Ixodes* are vectors of bovine piroplasmosis and various viral diseases, including louping ill. *Ixodes holocyclus* of Australia is the most virulent tick paralysis producer known. *Ixodes pacificus* is known to cause tick paralysis in North America. Species of *Ixodes* are the major vectors of Lyme disease in North America and Europe.

Nymphs of *Ixodes scapularis*, a three-host tick that normally feeds on mice and voles as larva and nymph and on deer as adult, transmits microtine piroplasmosis *(Babesia microti)*, Lyme disease

(Borrelia burgdorferi), and human granulocytic ehrlichiosis to humans (Burgdorfer et al, 1982; Spielman, 1976), dogs (Hinrichsen et al, 2001; Lissman et al, 1984), and other animals. In the northeastern United States, the white-footed mouse, *Peromyscus leucopus*, is the principle reservoir host for *B. burgdorferi* and serves as host for larvae and nymphs of *I. scapularis*, and the white-tailed deer, *O. virginianus*, serves as host to the adult tick, transmitting the spirochete both transovarially and transstadially (Lane and Burgdorfer, 1987). *Amblyomma americanum* may also occasionally transmit Lyme disease to humans (Matushka and Spielman, 1986). *I. pacificus* is a major vector of Lyme disease and human granulocytic ehrlichiosis in the western United States (Piesman, 1991). The incidence of human Lyme disease in May and June coincides with the activity of nymphs that were infected as larvae the previous summer. Thus nymphs feed in each transmission season before the larvae do. The white-tailed deer plays a dominant role as principal host of the adult *I. scapularis* ticks, which feed on this host from late fall through winter (Matushka and Spielman, 1986).

Haemaphysalis

Identification

The palpi have laterally flared second segments (Figure 2-79). Avoid confusing these structures with the hexagonal basis capituli of *Rhipicephalus*. Like *Ixodes*, these ticks have neither eyes nor scutal ornamentation, but they differ in having festoons and a posterior anal groove.

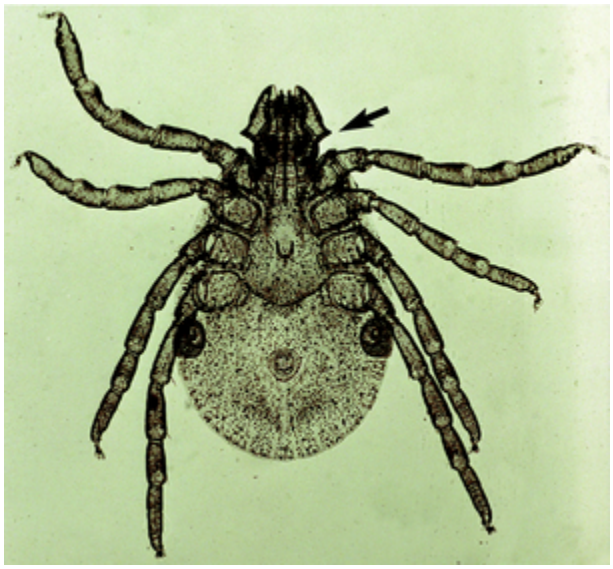

FIGURE 2-79 *Haemaphysalis*. The second palpal segment *(arrow)* is flared laterally.

Life history

Larvae and nymphs of *Haemaphysalis leporispalustris*, the rabbit tick, feed on ground-nesting birds and small mammals, and the adults attach to rabbits, especially to the ears and around the eyes. Occasional specimens are collected from cats.

Rhipicephalus

Identification

The basis capituli is hexagonal (Figure 2-80); eyes and festoons are present, but the scutum is unornamented (Figure 2-81); males have salient adanal and accessory shields (Figure 2-82).

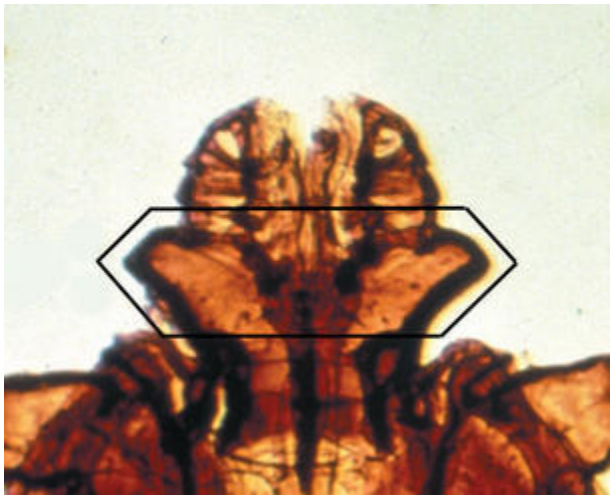

FIGURE 2-80 Capitulum of *Rhipicephalus*. The basis capituli is hexagonal.

FIGURE 2-81 *Rhipicephalus sanguineus* male *(left)* and female *(right)*. The posterior of the scutum on the male bears indentations, festoons, along the posterior margin *(arrow)*. The eyes are the relatively lighter areas on the sides of the scutum of the male and the female that are at about the level of where the second pair of legs extend from the ventral surface.

FIGURE 2-82 Ventral aspects of a male *Rhipicephalus (left)* and a male *Dermacentor (right)*. Coxae of male *Dermacentor* progress in size from the first to fourth coxa *(1 to 4)*. On the posterior of the male *Rhipicephalus* can be seen the large and pronounced adanal shields on each side of the anus.

Life history and disease transmission

Larvae, nymphs, and adults of *R. sanguineus*, the brown dog tick, all feed on dogs and sometimes on humans (Figure 2-83). Originally a tropical species, *R. sanguineus* has taken advantage of central heating to spread into the temperate zones, where it often generates enormous populations in homes, kennels, and veterinary hospitals; it cannot survive the winter outdoors in the North. Dogs living in temperate regions frequently acquire their *R. sanguineus* ticks in such infested premises, but during summer, infestation may occur outdoors. Therefore if enduring results are to be achieved, elimination of these ticks must include acaricidal treatment of both

the dog and the home or kennel. The latter procedure is a job for a professional exterminator. Development from egg to egg may be completed in slightly more than 2 months under favorable conditions; unfed adults may survive for well over a year. A household, including two dogs and the client's wife and mother-in-law who never left England, apparently acquired infestations with *R. sanguineus* through the introduction of the ticks into the client's car when he gave rides to a neighbor's dogs while at his summer home in France (Jagger, Banks, and Walker, 1996). He brought the ticks home to England from France in his car, thus indicating just how mobile are the ticks of this species. *R. sanguineus* transmits canine piroplasmosis *(Babesia canis)* transovarially and canine monocytic ehrlichiosis *(Ehrlichia canis)* interstadially.

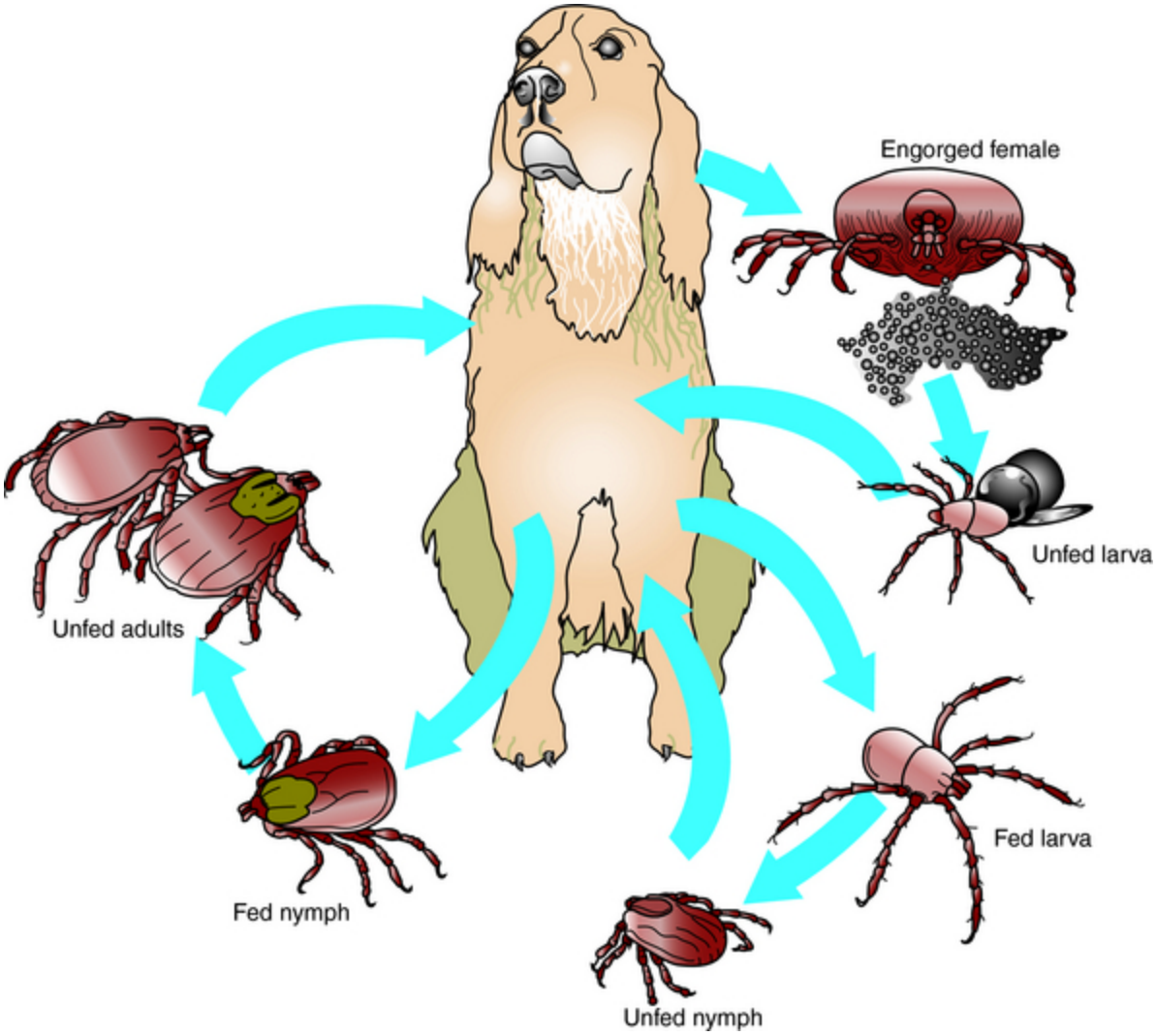

FIGURE 2-83 Life history of the brown dog tick, *Rhipicephalus sanguineus*. Six-legged larvae feed on the dog for a few days, drop off, and molt to the eight-legged nymphal stage. Nymphs feed on the dog for about a week, drop off, and molt into male and female adults. Females are fertilized on the dog, feed for 1 to 3 weeks, and become greatly engorged with blood before dropping to the floor to lay their clutches of 2000 to 4000 eggs several weeks later. Eggs emerge from the genital opening one at a time and accumulate in front of the female tick over a period of several more weeks. The complete cycle requires 2 to 3 months, which is fast compared with that of most tick species.

Rhipicephalus* (formerly *Boophilus*) *annulatus, the transovarial vector of bovine piroplasmosis, was brought to the Americas on cattle from Africa or the Mediterranean coast of Europe. This species

and a few others were placed until recently in their own genus, *Boophilus*, but this is now considered a synonym of *Rhipicephalus* (Barker and Murrell, 2004). Other African species of *Rhipicephalus* serve as vectors of the devastating East Coast fever *(Theileria parva)* and other forms of bovine theileriosis, bovine piroplasmosis *(B. bigemina)*, and the virus of Nairobi sheep disease. *R. annulatus* (Figure 2-84) is similar to *R. sanguineus* in that the adults have a hexagonal basis capituli, eyes, and an unornamented scutum, and the males have adanal and accessory shields. However, *R. annulatus* differs from *R. sanguineus* in that it has palpi that are ridged dorsally and laterally, and the adults of *R. annulatus* lack festoons.

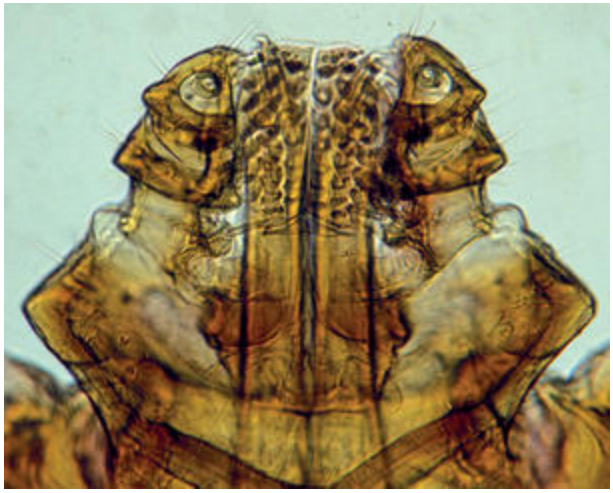

FIGURE 2-84 Capitulum of *Rhipicephalus* (*Boophilus*) *annulatus*. The basis capituli is hexagonal, and the palpi are ridged dorsally and laterally *(arrows)*.

R. annulatus was eradicated from the United States through 40 long years of dipping cattle that began in 1906. Losses from piroplasmosis were estimated then at 40 to 100 million dollars per year at a time when cattle were selling at 2 to 4 cents a pound.

Eradication was favored by the affinity of this tick species for cattle and by its one-host life history, which made it possible to destroy a substantial proportion of the tick population each time the cattle were dipped (Figure 2-85). Comparable efforts to eradicate any species with broader host preferences, especially those feeding on wildlife, would have been much more difficult. *Rhipicephalus microplus*, also a piroplasmosis vector, has a broader host range that includes horses, goats, sheep, and deer. *Rhipicephalus* specimens encountered in the field in North America should be immediately reported to state or federal authorities because of the one-host (cattle) nature of *R. annulatus* and its great vector potential for transmitting bovine piroplasmosis.

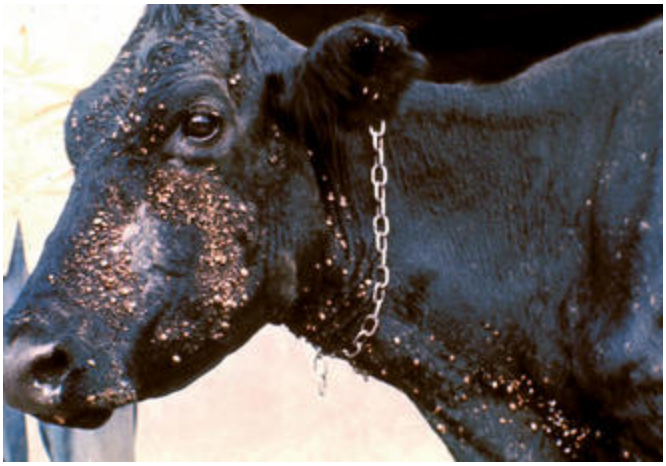

FIGURE 2-85 Cow with a fairly large number of attached *Rhipicephalus* (*Boophilus*) *annulatus* ticks.

Dermacentor

Identification

The basis capituli is rectangular as viewed from above (Figure 2-86). Coxae of males progress in size from the first to the fourth (see Figure 2-82). *Dermacentor* resembles *Rhipicephalus* in having eyes and 11 festoons, but the basis capituli is rectangular, the scutum is ornamented (Figure 2-87), and the males lack adanal shields. *Dermacentor* (*Anocentor*) *nitens*, the tropical horse tick, has only seven festoons.

FIGURE 2-86 Capitulum of *Dermacentor*. The basis capituli is rectangular.

FIGURE 2-87 *Dermacentor* male. Notice the ornamented scutum.

Life history and disease transmission

D. variabilis, the American dog tick, is widely but discontinuously distributed over the eastern half and West Coast of the United States and parts of Canada and Mexico. Larvae and nymphs engorge on small rodents; adults engorge on humans, dogs, horses, cattle, and wildlife. *D. variabilis* transmits Rocky Mountain spotted fever *(Rickettsia rickettsii)* and tularemia *(F. tularensis)* and causes tick paralysis. Adult females feed to repletion over several days, becoming larger each day (Figure 2-88).

FIGURE 2-88 *Dermacentor* female ticks that have engorged for different numbers of days from 1 to 5.

Dermacentor andersoni, the Rocky Mountain wood tick, requires 1 to 3 years to complete its life history, depending on the latitude, altitude, and abundance of small mammals on which it feeds as larva and as nymph. *D. andersoni* transmits Rocky Mountain spotted fever, tularemia, Colorado tick fever, and Q fever and causes tick paralysis.

D. nitens, the tropical horse tick, is limited, in the United States, to the southern portions of Florida and Texas. Preferring the external ear canals of horses but also found on other sites and other hosts such as cattle, sheep, goats, and deer, *D. nitens* is the vector of equine piroplasmosis *(Babesia caballi)*. Other North American species of *Dermacentor* include *Dermacentor albipictus*, the winter tick that causes heavy losses among deer, elk, and moose; *Dermacentor nigrolineatus*, the brown winter tick; and *Dermacentor occidentalis*, the Pacific Coast tick.

In moose *Alces alces*, infestation with *D. albipictus* causes hair loss, which progresses rapidly from February to April and may amount to as much as 44% of the haircoat. McLaughlin and Addison (1986) estimated that loss of 30% of its hair in a winter environment of −20° C would double the daily energy requirements of an otherwise normal 230-kg yearling moose. The increased catabolic rate imposed by hair loss then leads to reduction in body fat stores and to lowered resistance to disease and predation.

Amblyomma

Identification

The mouthparts are much longer than the basis capituli; the second palpal segment is at least twice as long as the third (see Figure 2-69). Eyes and festoons are present, scutum is ornamented, and adanal shields are absent. *Aponomma elaphensis* resembles *Amblyomma* but is smaller and lacks eyes; it is a parasite of a rat snake in Texas.

Disease transmission

In the United States, species of *Amblyomma* that attack humans, livestock, dogs, and cats (e.g., *A. americanum* [Figure 2-89], *Amblyomma maculatum* [see Figure 2-74], *Amblyomma cajennense*, and *Amblyomma imitator*) are distributed mainly in the southeastern coastal states, Missouri, Oklahoma, and Texas, but specimens may occasionally be found as far north as Ithaca, New York. These species have been incriminated in the transmission of Rocky Mountain spotted fever, *Ehrlichia chaffeensis*, *Ehrlichia ewingi*, and tularemia and in the causation of tick paralysis. African species of *Amblyomma* transmit heartwater *(Ehrlichia ruminantium)* of cattle, sheep, and goats, as well as the virus of Nairobi sheep disease. *Amblyomma dissimile*, the iguana tick, and *Amblyomma tuberculatum*, the gopher tortoise tick, are parasites of reptiles and amphibians; the latter is the largest ixodid tick found in North America, with engorged females reaching a length of 25 mm (Figure 2-90). The

largest tick, *Amblyomma varium*, is a parasite of sloths in South America.

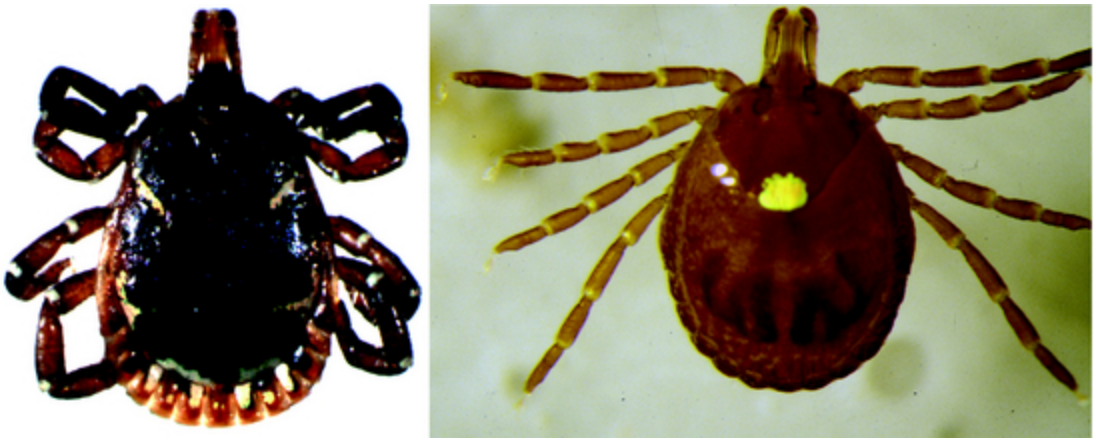

FIGURE 2-89 *Amblyomma americanum*. The male has an ornamented scutum with festoons. The scutum of the female bears a single large light-colored dot, hence the name *lone-star tick*. The mouthparts of *Amblyomma* are relatively proportionately longer than those of other ticks commonly found in the United States.

FIGURE 2-90 An engorged *Amblyomma* female next to a U.S. quarter for size comparison purposes.

Genera Not Found in North America

Hyalomma

Hyalomma resembles *Amblyomma* in having mouthparts much larger than the basis capituli but differs in that the second and third palpal segments are approximately the same length (Figure 2-91). Eyes are

present, festoons are irregularly coalesced; the male has adanal and accessory shields.

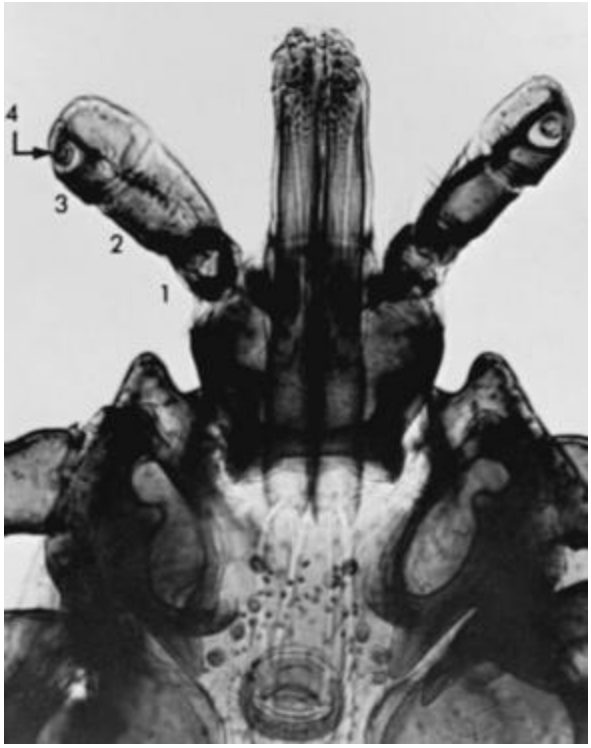

FIGURE 2-91 Capitulum of *Hyalomma*. Palpal segments two and three of *Hyalomma* are approximately the same length, whereas the second palpal segment of *Amblyomma* is about twice as long as the third.

Margaropus

Margaropus resembles *Rhipicephalus*, but the palps are not ridged and the legs of the male progress in size from the first to the fourth.

Rhipicentor

Rhipicentor resembles *Rhipicephalus* dorsally and *Dermacentor* ventrally; eyes and festoons are present, adanal and accessory shields are absent, and fourth coxae are greatly enlarged.

Direct Effects of Ixodid Ticks on the Host

Tick toxicosis

In North America the species most frequently involved in tick paralysis are *D. andersoni*, *D. variabilis*, *A. americanum*, and *A. maculatum*. Tick paralysis is an ascending paralysis caused by absorption of toxins from the saliva of engorging female ticks. The tick injects a considerable volume of saliva into the wound partly as an aid to digestion and partly as a means of disposing of surplus water extracted from the blood meal. A single female tick can produce paralysis in humans, dogs, or cats, especially if the site of attachment is near or on the head, but paralysis does not invariably occur even if many ticks of a suitable species are present. Usually, heavy infestations are required to produce tick paralysis in cattle. The first clinical sign is incoordination of the hindquarters that rapidly proceeds to complete paralysis and spreads to the forequarters, the neck, and finally the respiratory muscles, with fatal consequences. Removal of engorging ticks usually leads to gratifyingly rapid recovery. In Australia, *I. holocyclus*, a parasite of the bandicoot and other marsupials, causes a particularly severe form of tick paralysis in domestic animals. Of 577 Australian dogs affected and seen by veterinarians in 1998, 5% of the dogs died from the disease (Atwell, Campbell, and Evans, 2001). Effective treatment of paralysis caused by *I. holocyclus* requires administration of specific antitoxin and general supportive treatment as well as removal of all ticks from the victim. Even larvae and nymphs of *I.*

holocyclus are potentially capable of inducing paralysis when present in sufficient numbers. However, as is the case with other tick paralysis species, the engorging female of *I. holocyclus* is usually responsible. The surest prevention of tick paralysis lies in careful daily examination of exposed animals and removal of ticks. Because clinical signs of paralysis do not begin to appear until the ticks have been feeding for at least 4 days, they should be large enough to be found relatively easily before clinical signs develop. In areas of heavy exposure, weekly acaricidal dipping is necessary. It is sometimes difficult to know if a dog has an attached tick; a case of tick toxicosis due to an *I. holocyclus* occurred in the United Kingdom in a dog very recently brought from Australia that appeared to have been infected while with the transport agency. In this case the owner noticed the signs of ataxia and found the tick attached to the pinna of the ear, and the dog made a full recovery (Adamantos, Boag, and Church, 2005).

The bite wound

Ixodes, *Amblyomma*, and other genera with long mouthparts produce deep, painful bite wounds that tend to become inflamed, secondarily infected with bacteria, and flyblown. In Great Britain, secondary infection of *Ixodes ricinus* bites with *Staphylococcus* results in both local and metastatic abscessation (tick pyemia) in lambs. In the Gulf Coast states, *A. maculatum*, which prefers to attach to the ears of larger mammals, causes such pain and swelling that cattle are unable or at least reluctant to flick their ears and thus ward off flies.

Before screwworm control, such ears were prone to invasion by larvae of *C. hominivorax*, frequently with the loss of the external ear or death.

Blood loss and worry

Sir Arnold Theiler once collected half of the *Rhipicephalus decoloratus* ticks from a horse that had died of acute anemia. His collection weighed 14 lb (Theiler, 1911). That horse's tick burden must have contained about 13 L of blood. This example may appear extreme to those of us who dwell in temperate zones and experience only an occasional mosquito or blackfly bite, but there are places in the tropics where light-colored cattle are so totally covered by the dark bodies of engorging ticks that they appear from a distance to be black. Loss of blood, pain from and swelling of bite wounds, secondary infection, myiasis, and absorption of toxins, in moderate and varying proportions, result in a form of ill thrift referred to as "tick worry." Because tick worry is the most common practical consequence of tick infestation, it may be even more important than the more dramatic ones.

Treatment and Control of Tick Infestations

Dogs and cats

Ticks on dogs and cats are now most easily treated by prevention with the topical application of fipronil. The application of this pesticide has been found to be an excellent means of preventing tick infestations of dogs and cats. Other topical products include

pyrethrin and permethrin (permethrin should not be used on cats). One such product that has received widespread use is a combination of imidacloprid and permethrin for use on dogs. Another approach is to use collars containing amitraz, chlorpyrifos, diazinon, or tetrachlorvinphos. Amitraz has now been formulated for the prevention and treatment of ticks in dogs in a topical application format where it is applied with metaflumizone, which provides flea control. Control of *R. sanguineus* in buildings may be achieved by spraying with diazinon and could require the use of professional exterminators.

Lactating dairy cattle

For lactating dairy cattle, coumaphos and dichlorvos are applied as sprays or in backrubbers for the control of ticks. There are no restrictions when used as recommended.

Beef and nonlactating dairy cattle

For beef cattle and nonlactating dairy cattle, coumaphos and dichlorvos may be used as dips and sprays in the control of ticks. *O. megnini* ear ticks are treated with insecticidal dusts or emulsion concentrates instilled into the ear canal from squeeze bottles or an oil can. Ivermectin, doramectin, and moxidectin all provide some level of protection against ticks, but none of these products is currently labeled for tick control.

Horses

In horses particularly, tick-attachment sites may become markedly irritated and lead to an itch-scratch cycle marked by serious self-mutilation. Coumaphos is effective as a spray or dust when applied to the horse's entire body. Always wear rubber gloves and wash skin thoroughly after handling organophosphate and carbamate insecticides.

Environment

There are attempts, mainly driven by the fear people have of becoming infected with Lyme disease by tick bite, to develop means of controlling ticks within the environment. One means used is removal of an essential host. This has been tried for *I. scapularis* by eliminating all deer in an area (Wilson et al, 1988). Such a drastic method may produce significant tick reductions, although alternative hosts may be found that allow the ticks to persist in the environment at lower numbers. Methods also have been examined for reducing the numbers of ticks on deer by the use of ivermectin-treated feed bait (Pound et al, 1996); this method also shows some potential for control. Another approach has been to attack the larvae of ticks by using acaricidal-impregnated baits or nesting material containing ectoparasiticides, which mice and rats carry to their nesting areas (Mather, Ribiero, and Spielman, 1987); again, this method can be quite successful in controlling ticks in isolated areas. Work is also underway to produce vaccines against ticks causing the host to produce antibodies that the tick ingests while feeding and that damage the gut of the feeding tick (Willadsen et al,

1995); such vaccines are likely to be used more and more widely as they become available for use in cattle, dogs, and cats.

Suborder Mesostigmata, Mesostigmatid Mites

Mesostigmatids, as the name implies, have their **stigmata** (respiratory pores) in the middle of their bodies. A stigma lies between the third and fourth coxae on each side of the body and is connected to a sinuous **peritreme.** The coxae are evenly spaced and crowded into the anterior half of the body; the tarsi are generally armed with claws; and the ventrum is armored with sclerotized plates (Figure 2-92).

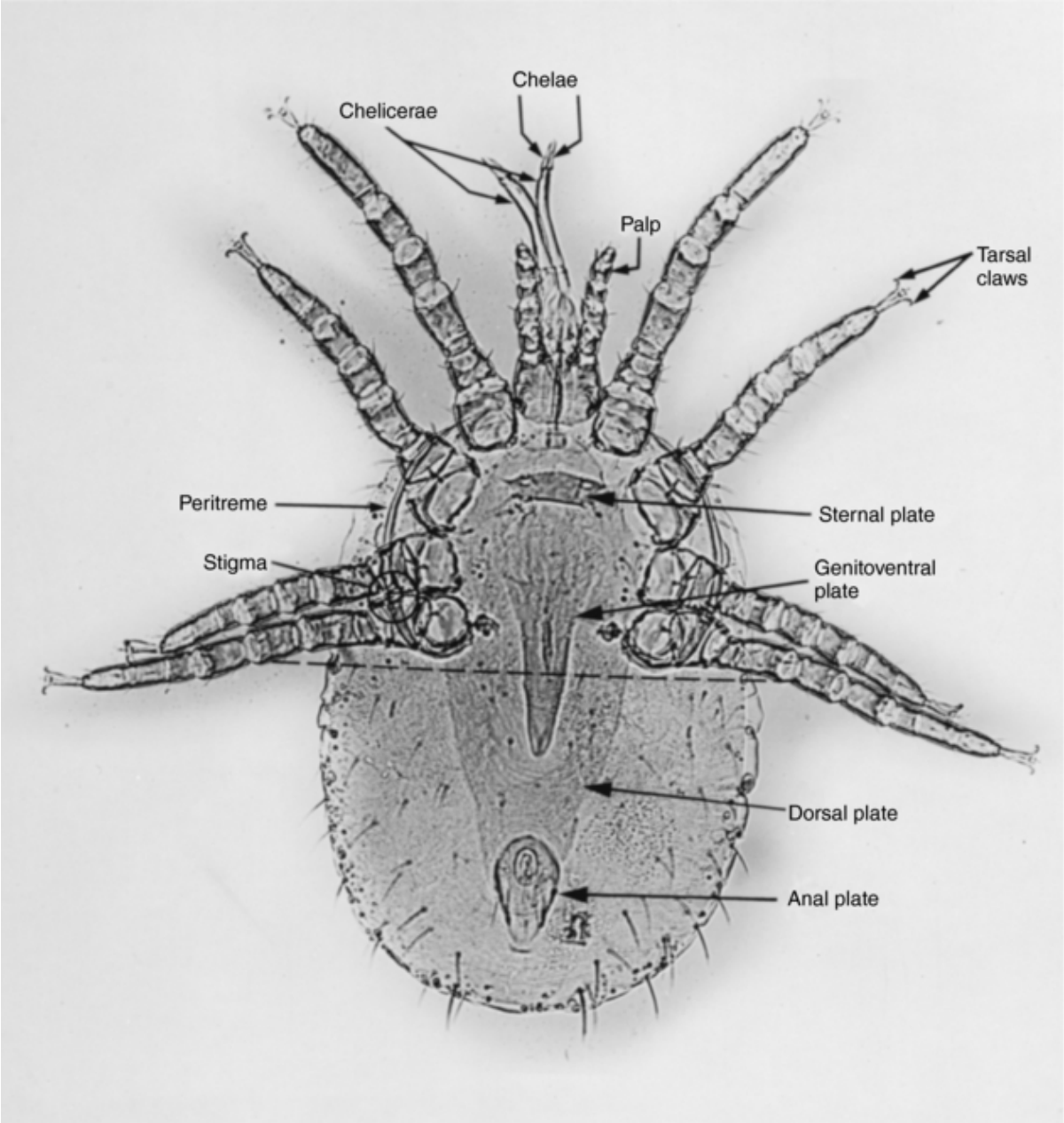

FIGURE 2-92 *Ornithonyssus sylviarum*, a bloodsucking mesostigmatid mite. The legs are confined to the anterior half of the body of mesostigmatid mites; the stigma is located between the third and fourth coxae and has a peritreme. The chelae of *Ornithonyssus* are much larger than those of *Dermanyssus*.

Families Dermanyssidae and Macronyssidae

Bloodsucking mesostigmatid mites that parasitize birds (e.g., *Dermanyssus gallinae*, *Ornithonyssus sylviarum*) and rodents (e.g., *Ornithonyssus bacoti*, *Liponyssoides sanguineus*) frequently turn on the human inhabitants of a building when deprived of their normal hosts, as may occur when fledglings leave their nests or after rodents have been exterminated. Generic or even familial identification of these mites is sufficient to establish the general nature of the epidemiologic situation, but specific identification sometimes provides a very helpful lead in the search for nests. For example, a hospital administrator submitted a specimen of a mite that was causing great consternation by its abundance in the hospital's linens. Dr. Georgi identified the specimen as a dermanyssid mite and advised the gentleman to hunt for bird or rodent nests. A few days later, he reported no success in finding nests of either kind. However, by that time the specimen had been shown to an expert acarologist who identified it as *Dermanyssus hirundinis*, a relatively host-specific parasite of swallows. Thus advised, the hospital administrator knew just where to look, and the problem was quickly solved.

Dermanyssids and macronyssids all look very much alike on casual inspection, but because they vary significantly in habits and host preferences, accurate identification is a prerequisite to effective control. The **chelicerae** (piercing mouthparts), **chelae** (scissorlike structures on the end of the chelicerae), and form and septation of

various sclerotized plates provide the main taxonomic characters used in differentiating these mites.

Dermanyssus (Dermanyssidae)

The chelicerae are long and slender and the chelae minute (Figure 2-93). There is a single dorsal plate; the sternal plate has two pairs of setae; and the anus is in the posterior half of the anal plate. *Dermanyssus* mites are infrequently found on the bird because these mites hide in nests, roosts, and the like during the day and attack the sleeping bird at night. Life stages include the egg, which is deposited in the diurnal hiding places of the mites; the six-legged, nonfeeding larva; and the blood-feeding protonymph, deutonymph, and adult male or female. A generation can be completed in as little as a week, and large populations may build up in chicken houses or birds' nests. The adults can survive starvation for months. *Dermanyssus* mites remove enough blood to kill nestlings and reduce egg production. Ramsay and Mason (1975) reported a case in a dog that was so severe that the mites crawling through the hair resembled the "walking dandruff" usually associated with *Cheyletiella* infestations. Their importance as disease vectors is unclear.

FIGURE 2-93 Gnathosome of *Dermanyssus gallinae*. The chelicerae of *Dermanyssus* are slender and whiplike, and the chelae are very small.

Liponyssoides (Dermanyssidae)

The chelicerae are long and slender and the chelae minute. There are two dorsal plates, the anterior plate 10 times as large as the posterior; the sternal plate has three pairs of setae. *Liponyssoides (Allodermanyssus) sanguineus*, a parasite of the house mouse, *Mus musculus*, and other small rodents, is the vector of rickettsial pox *(Rickettsia akari)* of humans.

Ornithonyssus (Macronyssidae)

The chelicerae are much stouter than those of *Dermanyssus*, and the chelae are easily visible under ordinary magnification. There is a single dorsal plate, and the anus is in the anterior half of the anal plate (see Figure 2-92). When the mite is alive, the gut often appears black or dark red (Figure 2-94). Common species include *O. sylviarum*, the northern fowl mite; *Ornithonyssus bursa*, the tropical fowl mite; and *O. bacoti*, the tropical rat mite. *Ornithonyssus* species. remain on the host much of the time and cause considerable loss of blood. Persons handling eggs from laying flocks heavily infested with *O. sylviarum* may experience annoyance and serious discomfort from the bites of these mites. *O. bacoti* is an important pest in laboratory rodent stocks and serves as intermediate host for *Litomosoides carinii*, a filariid parasite of the cotton rat, *Sigmodon hispidus*. *L. carinii* is a favorite laboratory model for testing antifilarial drugs.

FIGURE 2-94 Living *Ornithonyssus sylviarum* crawling on a chicken feather collected from litter. Note the dark X-shaped gut.

Ophionyssus (Macronyssidae)

Ophionyssus natricis, the snake mite, is a formidable bloodsucking pest that tends to thrive on captive snakes (Figure 2-95). Treatment of snakes has been performed using injectable ivermectin (Stanchi and Grisolia, 1986).

FIGURE 2-95 Gnathosome of *Ophionyssus*.

Family Raillietidae

Raillietia

Raillietia auris (Figure 2-96), long considered a harmless parasite of the ears of cattle, has been shown to cause ulceration and blockage of the auditory canals by pus with resultant loss of hearing (Heffner

and Heffner, 1983). Jubb, Vasallo, and Wroth (1993) reported that infestations with this mite were associated with calves circling, ataxia, and unilateral facial paralysis. In their work, calves were cleared of their infestations with the application of flumethrin to the ear canal, whereas the topical application of flumethrin or subcutaneous ivermectin was unsuccessful.

FIGURE 2-96 *Raillietia auris*, a mesostigmatid parasite of the ear canal of cattle. In this reflected light photomacrograph, the specimen appears as it would under a stereoscopic microscope or powerful hand lens.

Family Halarachnidae

Pneumonyssus

Groups of *Pneumonyssus simicola* mites may be found in the lung parenchyma of most if not all *Macaca mulatta* monkeys. The lesions are pinhead or larger, whitish or yellow foci (Figure 2-97) that have soft or empty centers and contain mites and a black pigment. These lesions are scattered throughout the lungs and may be mistaken for

those of tuberculosis. It is difficult to correlate clinical signs of pulmonary acariasis with the degree of pathologic change in the lungs, and antemortem diagnosis is difficult. Monkeys can be reared free of *Pneumonyssus* infection if they are separated from their mothers at birth and reared in isolation from adult monkeys. The histopathologic diagnosis of *P. simicola* infection is discussed in Chapter 8.

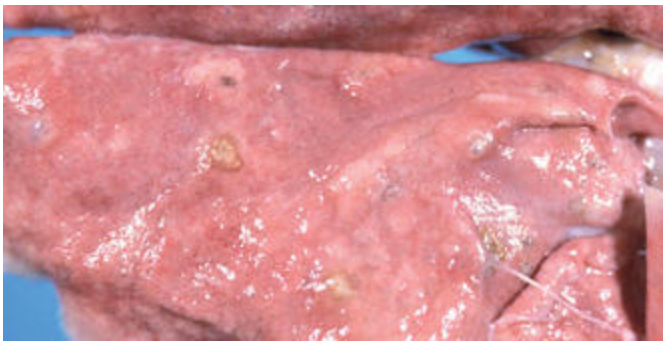

FIGURE 2-97 *Pneumonyssus simicola* lesions in the lungs of a macaque.

Pneumonyssoides

A parasite of the nasal and paranasal sinuses of dogs (Figure 2-98), *Pneumonyssoides caninum* sometimes causes chronic sneezing and epistaxis. Occasionally, nasal discharge has been reported in dogs with this infestation (King, 1988). Rhinoscopy and nasal swabbing are aids to diagnosis. Treatment of *P. caninum* is easily induced by the subcutaneous administration of ivermectin (Mundell and Ihrke, 1990).

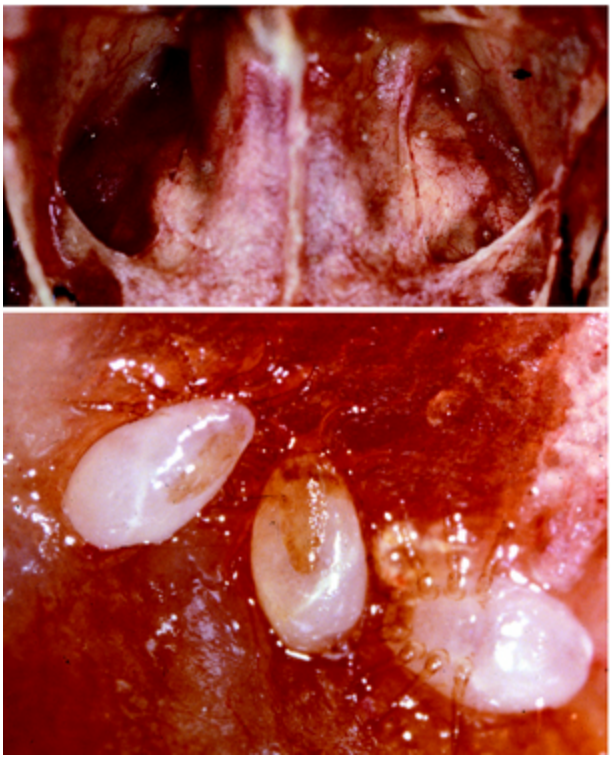

FIGURE 2-98 *Pneumonyssoides caninum*. *Top*, A view into the nasal sinuses of a dog at necropsy showing the mites in situ. *Bottom*, A closer view of three adult mites.

Family Rhinonyssidae

Sternostoma

Sternostoma tracheacolum is a bloodsucking mite of the respiratory passages, including the abdominal air sacs, of canaries, finches, and a wide range of other wild and domestic birds (Figure 2-99; see also Figure 7-48). *S. tracheacolum* infection may not be apparent clinically or may cause chronic respiratory illness manifested by loss of voice, shaking of the head, and sneezing. Diagnosis in the living bird is facilitated by moistening and parting the feathers in the neck region and transilluminating the trachea with a strong light; the mites appear as shadowy spots in the trachea. On necropsy

examination, these mites appear to the unaided eye as black spots in the posterior nares, trachea, air sacs, lung tissues, and abdominal cavity (Kummerfeld and Hinz, 1982).

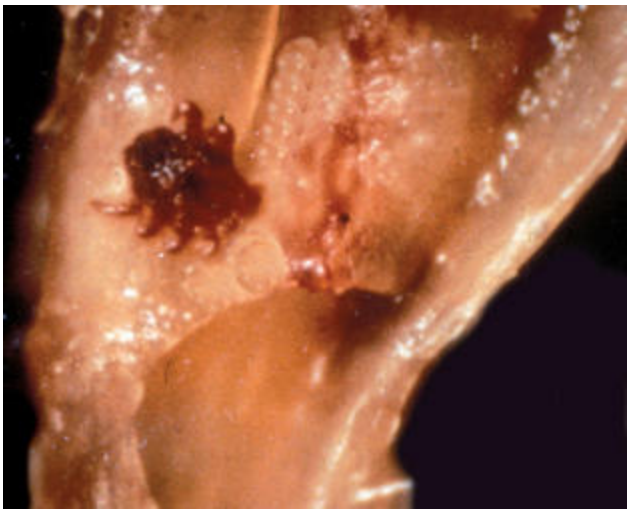

FIGURE 2-99 *Sternostoma* mite in the trachea of a bird.

Family Varroidae

Varroa

Varroa destructor (formerly known as *Varroa jacobsoni)* is a parasite of honeybees that was introduced into the United States sometime in the 1980s. Mites and other parasites of bees are a serious threat to U.S. agriculture. All one has to do is visit a local lawn with clover and notice that there are either no honeybees or very few honeybees present; some have estimated that greater than 95% of the wild honeybees in the United States have been eliminated by these parasites. Wild honeybees are no longer considered effective as providers of pollination for farmers. Within commercial hives, in the winter of 1995, losses ranged from 40% in Delaware to 80% in

Maine. Although bees produce honey valued at some $125 million, more important, they are responsible for pollinating nearly $15 billion worth of crops in the United States each year (Doebler, 2000). *V. destructor* is an external parasite of honeybees and is very large; females are 1 to 1.5 mm in diameter, reddish to dark brown, and easy to observe on bees with the naked eye. The mites suck hemolymph from both adult bees and the brood, preferring the blood of drones. A female mite enters a brood cell about 1 day before capping and becomes sealed in the brood capsule with the larval bee. The female then lays eggs, and the developing larval mites feed off the developing bee. When the adult bee emerges from the brood cell, the mites in the cell will have developed to adulthood and mated, and the females will be ready to enter a new cell. The disease is spread between hives by mites attached to worker bees. Untreated infestations of hives destroy colonies. Treatment of infested colonies is performed using formulations that contain the miticides flumethrin, fluvalinate, oxalic acid, formic acid, or thymol. It should not be forgotten that bees are food animals, and the strips should not be used during honey flow or when honey that may be removed for human consumption is present. Veterinarians need to be aware that pesticides may be used in manners that can lead to honey contamination (Harman, 1998). The development of resistance to these agents in mites is also problematic because the fact that bees are also arthropods makes it difficult to increase treatment levels because bees are usually killed through the same pharmacologic pathway.

Suborder Astigmata, Astigmatid Mites

In contrast to mesostigmatids, astigmatid mites lack stigmata, and respiration is integumental; the first and second coxae are widely separated from the third and fourth, the ventrum is devoid of conspicuous plates, some **tarsi** are equipped with **sarcoptiform pretarsi,** a sucker **caruncle** that is supported on a thin terminal stalk, the **pedicel.** Astigmatids include the mange mites, certain hair-clasping mites, two internal parasites of chickens, and the grain mites.

Mange mites (families Sarcoptidae, Knemidocoptidae, and Psoroptidae) cause mange or scabies, a dermatitis characterized by pruritus, alopecia, and epidermal hyperplasia with desquamation. Rubbing and scratching by the host frequently result in deeper wounds that ooze serum and blood. These coagulate, gluing hair, epidermal debris, and foreign matter together to form crusts and scabs. Secondary bacterial infection may complicate the situation.

The typical distribution and manner of spread of mange lesions vary with the host and parasite species and are often characteristic enough to permit accurate diagnosis by an experienced observer. However, recovery and identification of mites are necessary for positive diagnosis. Negative scrapings are inconclusive. Therefore typical mange lesions should be subjected to persistent examination until mites are found or until further scraping would do excessive injury to the patient. For lesions with minimal epidermal hyperplasia and lesions caused by deeply burrowing mites (e.g.,

Sarcoptes and *Demodex*), dip a scalpel blade into glycerin or mineral oil, pinch a fold of skin firmly between thumb and forefinger and, holding the blade at right angles to the skin, scrape until blood begins to seep from the abrasion. Much of the detritus will adhere to the layer of mineral oil on the scalpel blade and may be transferred to a microscope slide and searched for mites. For lesions with marked epidermal hyperplasia and exfoliation and lesions caused by superficially dwelling mites (e.g., *Chorioptes*) and lice, scrape the detritus into an ointment tin using the cover as a scraper. Examine the scrapings under a stereomicroscope or hand lens to find the mites crawling about. If no mites are observed directly, recourse may be had to digestion of the skin scrapings in potassium hydroxide as described in Chapter 7.

Generic differentiation of mange mites likely to be encountered in routine veterinary practice requires little more than examination of their pretarsi (Figures 2-100 and 2-101). If the pretarsus has a long, unsegmented pedicel (stalk), the specimen is most likely *Sarcoptes* or *Notoedres*. If the pretarsus has a long, three-segmented pedicel, the mite is bound to be *Psoroptes*. Pretarsi with short pedicels are found on *Chorioptes* from ungulates and *Otodectes* from dogs; the species identity of the host is a sufficiently reliable differential criterion in this case. *Knemidokoptes* females lack pretarsi, but the males have pretarsi resembling those of *Sarcoptes*. Certain particularly destructive manges, such as psoroptic mange in sheep and cattle and sarcoptic mange in cattle, should be reported to state animal disease control authorities.

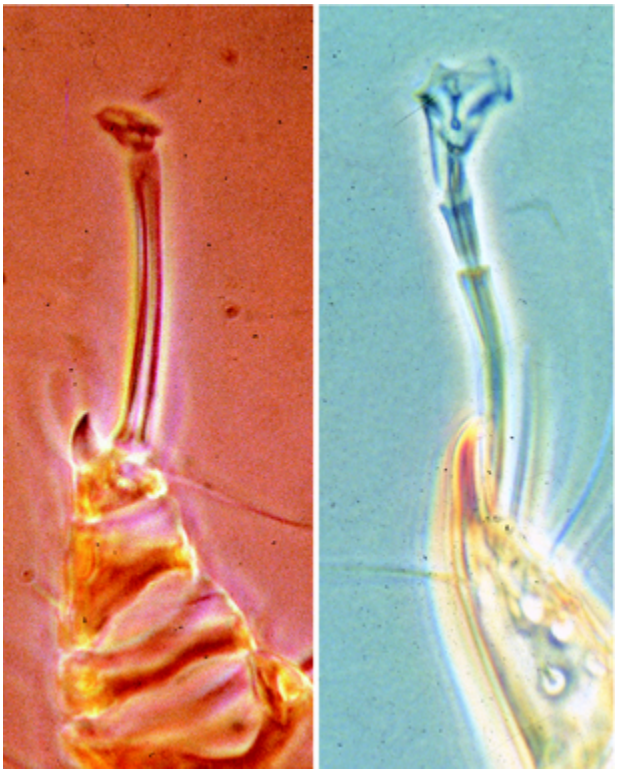

FIGURE 2-100 Pretarsi of *Sarcoptes (left)* and *Psoroptes (right)*. Both have long pedicels; the pretarsus of *Psoroptes* is jointed.

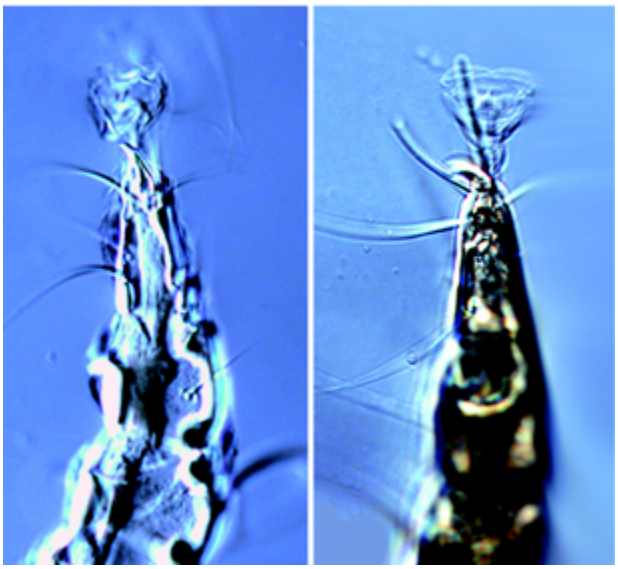

FIGURE 2-101 Pretarsi of *Otodectes (left)* and *Chorioptes (right)*. Both have short pedicels. *Otodectes* is a parasite of the ear canal of carnivorans; *Chorioptes* is a parasite of the epidermis of ungulates.

Family Sarcoptidae

Sarcoptes

The pretarsi have long, unsegmented pedicels, and the anus is at the posterior edge of the body (Figure 2-102; see also Figure 2-100). *Sarcoptes scabiei* causes sarcoptic mange or scabies of humans, dogs, foxes, horses, cattle, and others. Sarcoptic mange of cattle is reportable. Although *S. scabiei* infests a wide range of hosts, a considerable degree of host specificity has arisen among populations of this parasite so that scabies of pigs tends to spread more readily among pigs, scabies of humans tends to spread more readily among humans, and when interspecific transmission does occur, the resulting dermatitis tends to be atypical and transient. In fair-skinned human subjects with relatively mild infestations, it is possible to see the tiny serpentine tunnels that trace the wanderings of the egg-laying female mite as she burrows through the epidermis. Along the course of the burrow, dark areas representing eggs and accumulations of feces may be observed and, at the end of the tunnel, the mite may be found and lifted out with the point of a needle. Hair obscures such lesions on domestic animals, and it may be that many relatively mild cases of sarcoptic mange are overlooked. As few as 10 to 15 mites constitute a case of ordinary (but nonetheless unendurable) human scabies, but thousands to millions may be found on a mangy pig or fox. Curiously, however, *Sarcoptes* mites are frequently difficult to find on dogs, even those exhibiting advanced lesions.

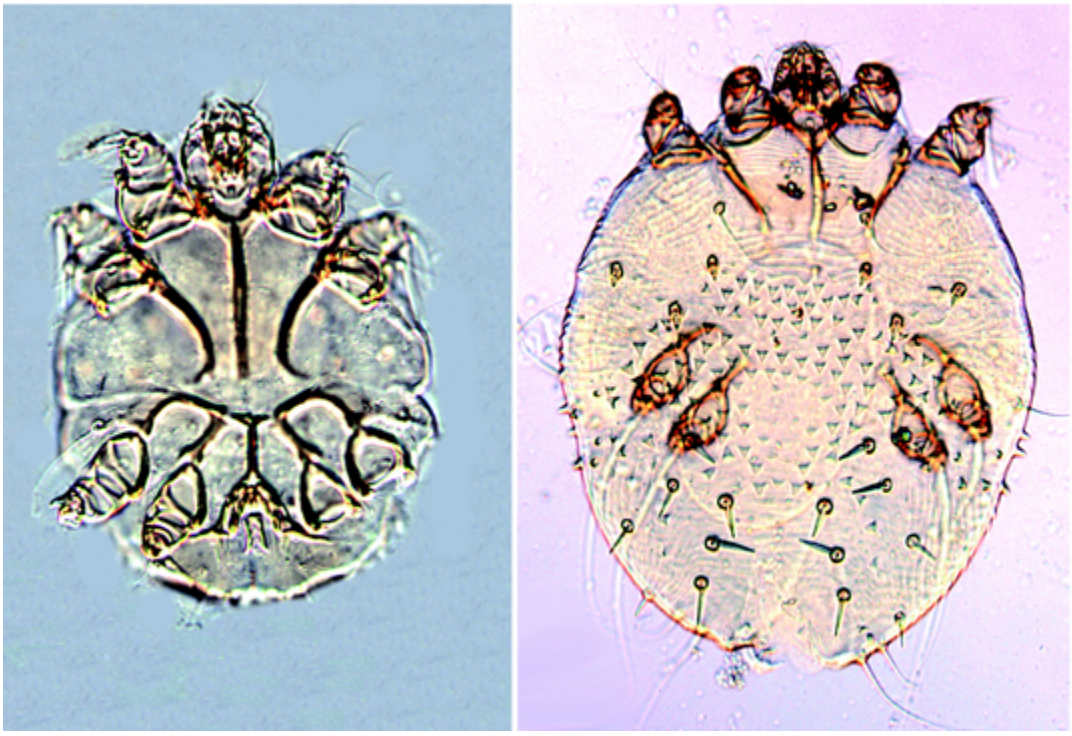

FIGURE 2-102 *Sarcoptes* male *(left)* and female *(right)*.

Sarcoptic mange of domestic animals usually starts on relatively hairless areas of skin and may later generalize. In dogs the lateral aspect of the elbow and pinna of the ear are favorite starting places; the lesions consist of follicular papules, areas of erythema, crusts of dried serum and blood, and excoriations from scratching to relieve the intense pruritus. Secondary bacterial infection is a frequent complication. In swine, sarcoptic mange usually starts around the eyes and on the nose, back, sides, and inner surface of the thighs; lesions may progress to hyperkeratosis and exfoliation of epidermal debris. The red fox, *Vulpes vulpes*, is affected by a lethal form of sarcoptic mange in which the epidermis may undergo a tenfold increase in thickness and contain countless hordes of mites. Sarcoptic mange in cattle is fortunately very rare in the United

States. Infestations in cattle can often become a horrible generalized disease that requires treatment and quarantine; the cattle can have numerous highly pruritic lesions that can cause severe self-trauma. In an outbreak of sarcoptic mange in a herd of cattle in New York state, the prevalence of udder cleft dermatitis was determined both before and after treatment of the mite infestations with eprinomectin (Warnick et al, 2002). The control of the mange in the cattle had only a moderate effect on the prevalence of udder cleft dermatitis and did not eliminate the condition from the herd.

Notoedres

A parasite of cats, rats, rabbits, and occasionally and temporarily of humans, *Notoedres* much resembles *Sarcoptes* in that the pretarsi have long, unsegmented pedicels, but it is smaller and its anus is on the dorsal surface instead of on the posterior margin of the body (Figures 2-103 and 2-104). Face mange of cats caused by *Notoedres cati* starts on the medial edge of the pinna of the ears and then spreads over the ears, face, paws, and hindquarters by contiguity and contact. The lesions of notoedric mange consist principally of alopecia and marked hyperkeratosis with abundant epidermal flakes; mites are easily demonstrated (Figure 2-105). An epizootic of notoedric mange has been reported in the Florida Keys, where more than 500 cats were examined (Foley, 1991a). Major signs included pruritus, self-mutilation dermatitis, gray crusts on the skin, secondary pyoderma, and hypertrophied skin. This is the typical causing of mange in cats.

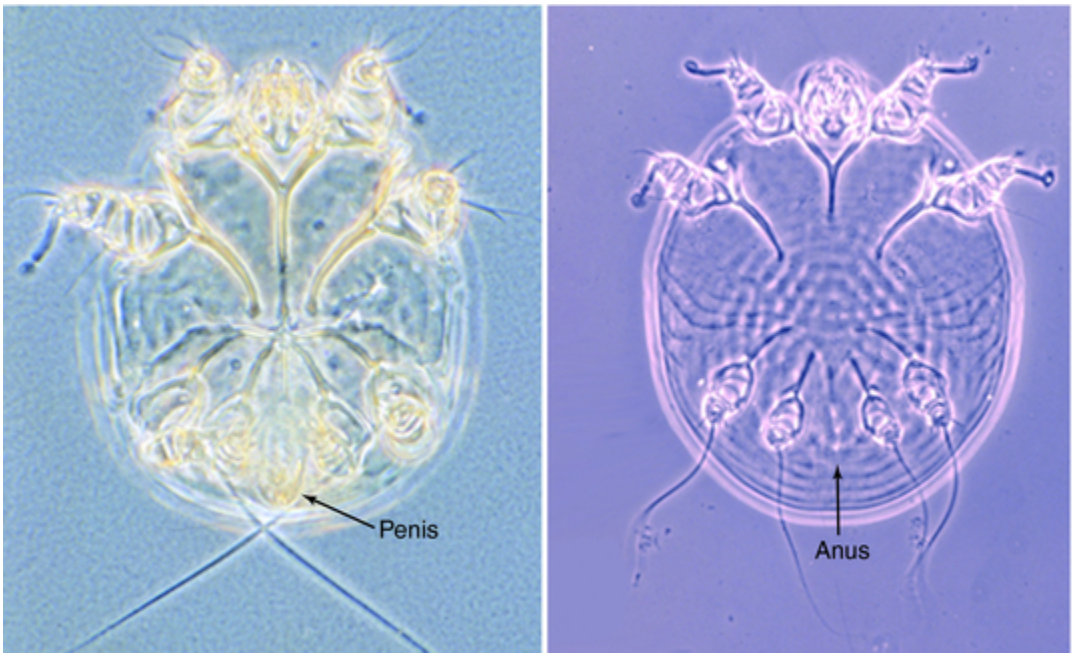

FIGURE 2-103 *Notoedres* male *(left)* and female *(right)*.

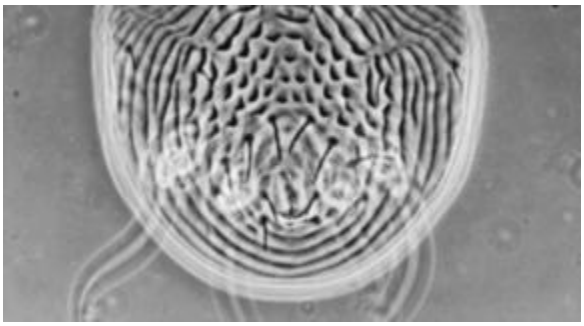

FIGURE 2-104 *Notoedres cati*. Same as Figure 2-101, *right*, but with dorsal anus of female in focus.

FIGURE 2-105 A group of kittens with typical notoedric mange lesions on the ear margins.

Not all cases of feline mange are caused by *Notoedres*. For example in the case of an exotic cat, a half dollar–sized area of dermatitis on the top of a pet ocelot's head was tentatively diagnosed as notoedric mange. However, a scraping revealed that the villain was *Sarcoptes* and raised the possibility of an infested human contact. In fact, the owner had been suffering from a severe itch below her breasts but had not connected her discomfort with her ocelot's skin lesion. In this particular case, it was not at all clear who had harbored the mites first, but that, after all, is an academic question. What is important is that correct generic identification of the parasite led to effective control through appropriate medication of both infested individuals. Cases of sarcoptic mange have also been reported in domestic cats. Most recently, four cases of crusted scabies were described, with two of the cats being from areas frequented by foxes and two from homes where a dog had or had been treated for sarcoptic mange (Malik et al, 2006).

Cosarcoptes, Prosarcoptes, Pithesarcoptes, *and* Kutzerocoptes

The first three genera are parasites of Old World monkeys (Cercopithecidae), and the last one is a parasite of New World monkeys (Cebidae). All resemble *Sarcoptes* morphologically, biologically, and pathogenetically. Mange of monkeys, at least that caused by *Cosarcoptes scanloni*, may be transmissible to humans (Smiley and O'Connor, 1980).

Trixacarus caviae

A parasite of the guinea pig, *T. caviae* closely resembles *Sarcoptes scabiei* but is only half as large; the anus is on the dorsal surface of the female and on the posterior margin of the body of the male. *Trixacarus* causes pruritus so intense that affected guinea pigs are subject to fits and seizures brought on by vigorous scratching or manipulation of the skin (Kummel et al, 1980). Mange in guinea pigs has been successfully treated with ivermectin administered subcutaneously.

Family Knemidocoptidae

Knemidokoptes

Knemidokoptes mutans causes scaly leg in chickens, turkeys, pheasants, and other gallinaceous birds. The mites burrow in the epidermis of the legs, causing the scales to lift and become loosened and the legs to become thickened and deformed (Figure 2-106). To demonstrate mites, simply remove a loose leg scale and examine the underside of it with a hand lens. The female *K. mutans* is about 0.5 mm in diameter; the legs are very short and lack pretarsi (see Figure 2-106). The males are much smaller and have longer legs equipped with pretarsi resembling those of *Sarcoptes*.

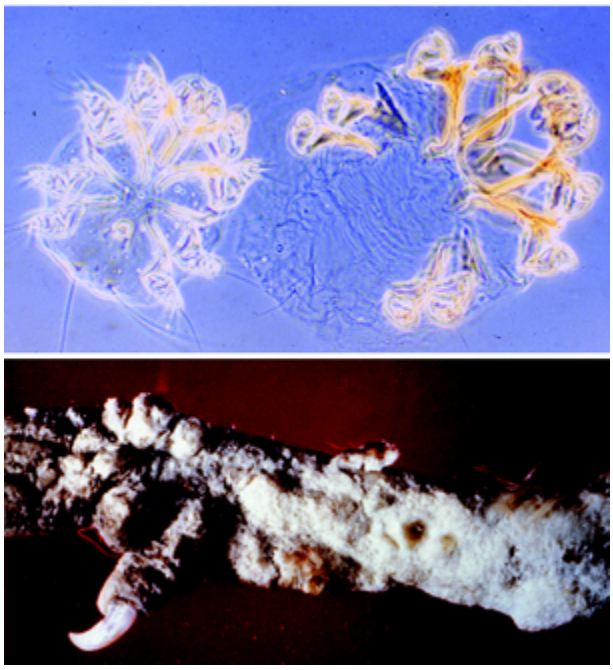

FIGURE 2-106 *Knemidokoptes* male *(left)* and female *(right)* and lesions caused to the leg of an infested chicken *(bottom)*.

Knemidokoptes pilae and *Knemidokoptes jamaicensis* cause mange of the legs, base of the beak, vent area, and back of parakeets and canaries, respectively. Lesions respond well to daily applications of mineral oil to all areas where mites are likely to be found, including the vent area. The oil tends to loosen crusts, which should be carefully removed. Rotenone-orthophenylphenol (Goodwinol ointment) or ivermectin mixed with a few drops of dimethyl sulfoxide (DMSO) and applied to lesions with a cotton swab is a suitable topical treatment. Ivermectin administered orally or intramuscularly at 0.2 mg/kg presents several advantages over topical acaricides: only one or in particularly serious cases two treatments are necessary. It does not mat down feathers or get in the birds' eyes and is apparently well tolerated (Ryan, 1986).

Knemidokoptes gallinae, the depluming mite of chickens, pigeons, pheasants, and geese, is found at the base of the feathers on the back, on top of the wing, and on the vent, breast, and thighs. It causes intense pruritus, leading in turn to feather pulling.

Family Psoroptidae

Psoroptes

The legs are long, and the pretarsi have long, three-segmented pedicels (Figure 2-107 and 2-108; see also Figure 2-100). *Psoroptes ovis* causes a very serious and reportable form of a mange (scabies or "scab") in cattle, sheep, and horses. Psoroptic mange is prevalent among cattle herds in the southwestern United States but relatively rare elsewhere in North America. *Psoroptes cuniculi* is very common and causes ear canker in rabbits and a less severe form of otic acariasis in goats and horses.

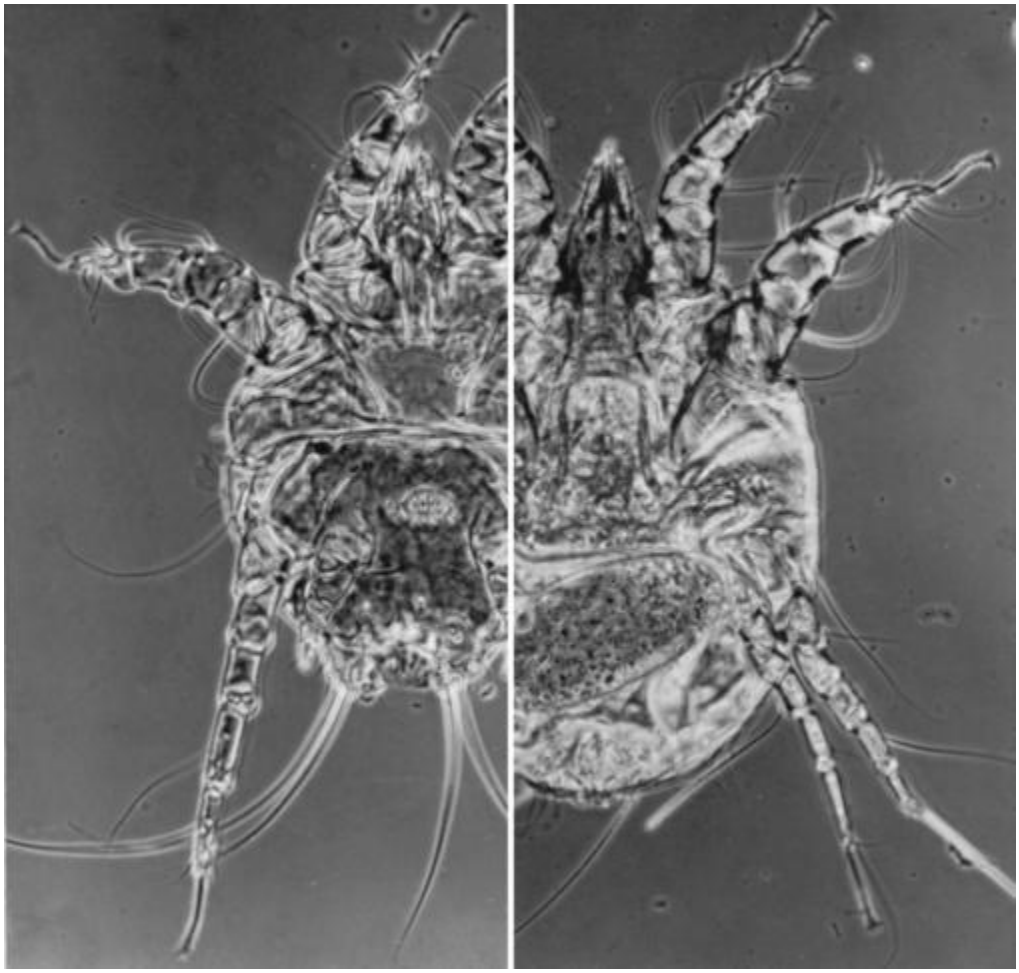

FIGURE 2-107 Psoroptes male *(left)* and female *(right)*.

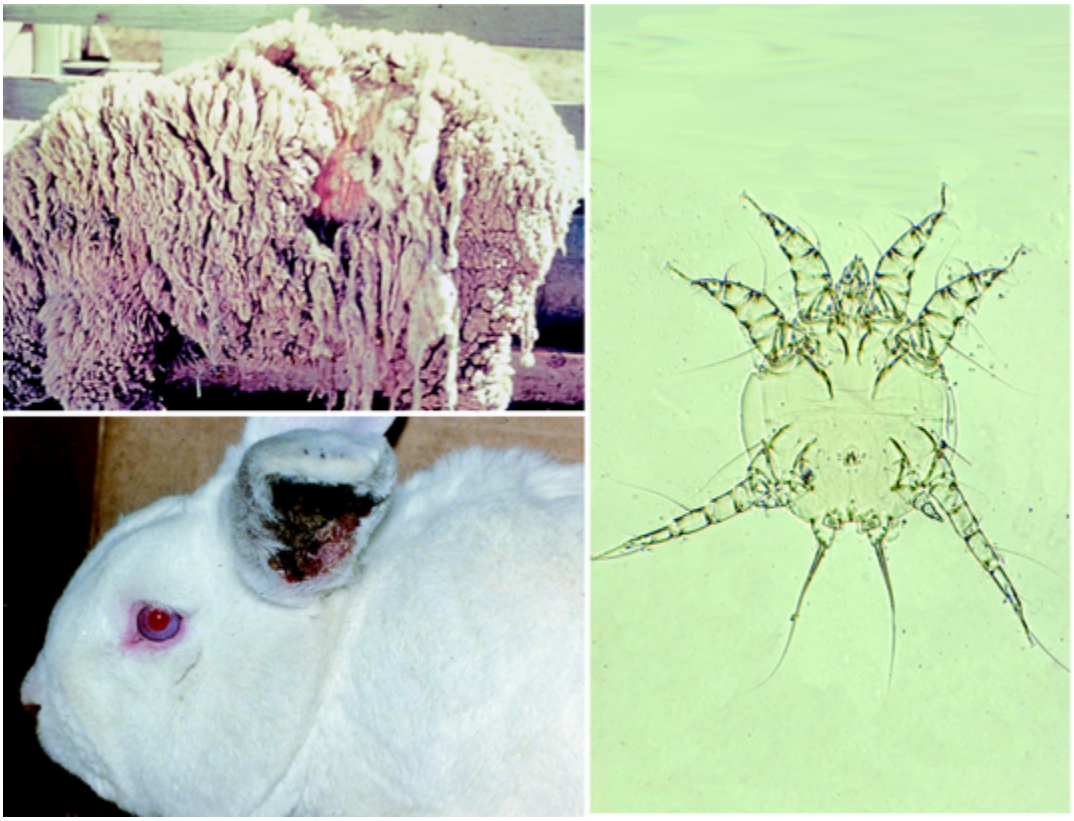

FIGURE 2-108 Psoroptic mange on a sheep *(top left)* and ear canker in a rabbit *(bottom left)*. *Right*, An adult male *Psoroptes*.

Psoroptes ovis does not burrow in the epidermis but remains at the base of the hairs and pierces the skin with its styletlike chelicerae. This manner of feeding results in exudation of serum, which hardens to form a scab. The mites are best demonstrated under the edges of these scabs, so it is inefficient to submit great wads of wool to the laboratory, especially if the scabs are not included in the shipment. Psoroptic scab is particularly devastating in sheep, especially those maintained principally for the production of high-quality wool. Pruritus is usually intense. At first, tags of wool are observed projecting from the fleece and clinging to fence posts, door jambs, trees, and other convenient objects against which

an itchy sheep might obtain some measure of relief (see Figure 2-108). Progressively more and more wool is shed or rubbed away by the frantic sheep, and pustules appear on the denuded, hardened, thickened, and excoriated skin. As the pustules become confluent and overlain by a scab of coagulated serum and foreign material, the area ceases to be suitable for the mites, and they move on to fresh territory. In this way the lesions tend to spread over the surface of the body. The sheep become greatly debilitated by psoroptic scab and may even die of it. *Psoroptes ovis* may survive off the host for several days or weeks. Therefore effective control requires both acaricidal treatment of all infested livestock and either disinfection or 2- to 4-week vacating of contaminated enclosures and vehicles (Wilson, Blachut, and Roberts, 1977).

P. cuniculi is a ubiquitous parasite of the external ear canal and can frequently be demonstrated in apparently normal rabbits. When infested rabbits are placed under stress, as for example when a doe kindles, the population of mites tends to explode and the ear canal is laid waste as a result (see Figure 2-108). A full-blown case of ear canker without secondary bacterial infection will respond amazingly well and heal in a dramatic fashion after the subcutaneous administration of ivermectin. Prevention is possible by weekly instillation of a few drops of mineral oil into the ear canal of each rabbit in the colony. *P. cuniculi* produces a less severe form of otic acariasis in goats and horses.

Chorioptes bovis

Pretarsi of *Chorioptes bovis* have short, unsegmented pedicels on the first, second, and fourth pairs of legs of the female and on all legs of the male; the male has two turretlike lobes on the posterior margin of the body (Figure 2-109). *C. bovis* is a cosmopolitan, superficially dwelling parasite, displaying a distinct preference for the tail, escutcheon, and legs of cattle, where it feeds on epithelial debris. Although cattle are the principle hosts, *C. bovis* also may be found on the tail and legs of horses, sheep, and goats and in the ear canal of rabbits. Asymptomatic infestation is far more common than obvious dermatitis.

FIGURE 2-109 *Chorioptes* male *(left)* and female *(center);* the female has pretarsi on the first, second, and fourth pairs of legs, and the male has pretarsi on all four pairs. *Right*, *Chorioptes* male and deutonymph; the deutonymph has pretarsi on the first and second pairs of legs.

Chorioptic mange in cattle usually appears during late winter as a superficial, mildly pruritic, flaky dermatitis involving the tail,

escutcheon, and hind legs (Figure 2-110). Whereas stanchioned animals are made miserable because they are unable to take appropriate action to relieve the itching, for unconfined cattle, chorioptic mange is probably not much more serious a burden than a crop of chewing lice and, like a suit of woolen underwear, may help keep them warm by encouraging physical activity. Chorioptic mange tends to disappear soon after the cattle are turned out to pasture in spring. *C. bovis*, like the pinworm *Oxyuris equi*, is an identifiable cause of tail rubbing in horses.

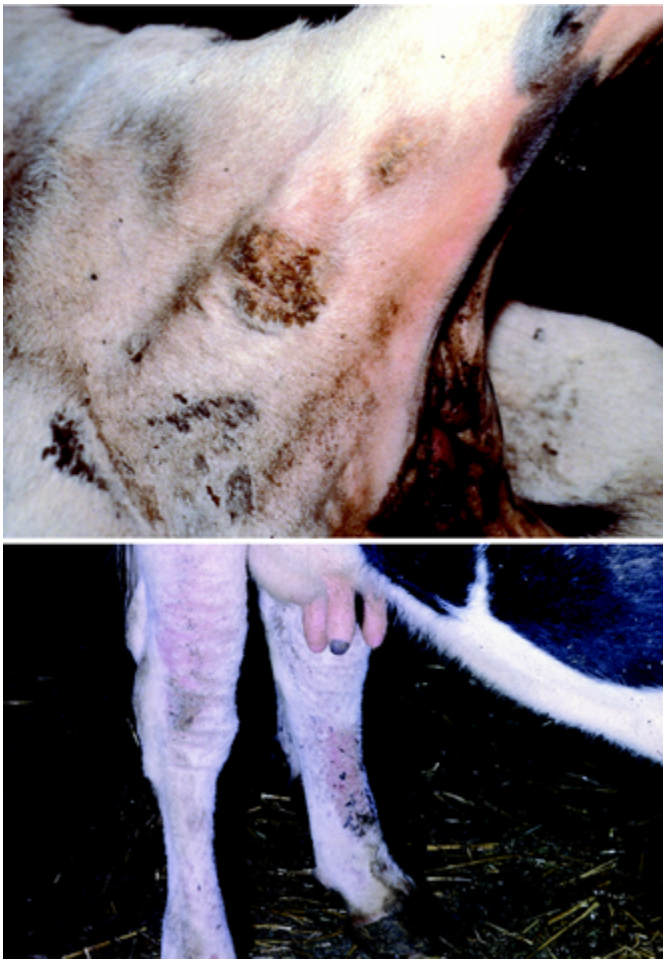

FIGURE 2-110 Chorioptic mange on cows.

C. bovis causes exudative dermatitis on the lower legs and scrota of rams. In extreme cases the crusts may be 5 cm thick. Deterioration of semen quality was associated with chorioptic mange lesions covering more than one third of the scrotum and was apparently related to elevation of testicular temperature (Rhodes, 1975).

Otodectes cynotis

Pretarsi of *Otodectes cynotis* have short, unsegmented pedicels on the first and second pairs of legs of the female and on all legs of the male; the body of the male is only weakly bilobed posteriorly (Figure 2-111; see also Figure 2-101). *O. cynotis* infests the external ear canal and adjacent skin of dogs, cats, foxes, and ferrets, causing intense irritation. Copious production of dark cerumen is characteristic of otodectic otitis. Aural pruritus sometimes causes the animal to rub and scratch its ears and shake its head violently enough to produce hematoma of the aural pinna. The mites may be demonstrated by swabbing the ear canal with a cotton applicator and then placing the applicator on a dark background under a lamp or on a sunny windowsill. The heat will drive the mites out of the debris, and they will be seen as tiny white specks moving against the dark background. The number of mites present in the cat's ear can be quite remarkable. Preisler (1985) reported more than 8500 mites in the ear canal of a cat. When large numbers of mites are present in the canal, the cat's ear tends to contain a dry, waxy, light-

colored, parchmentlike material in sheets, with large numbers of mites present in each layer.

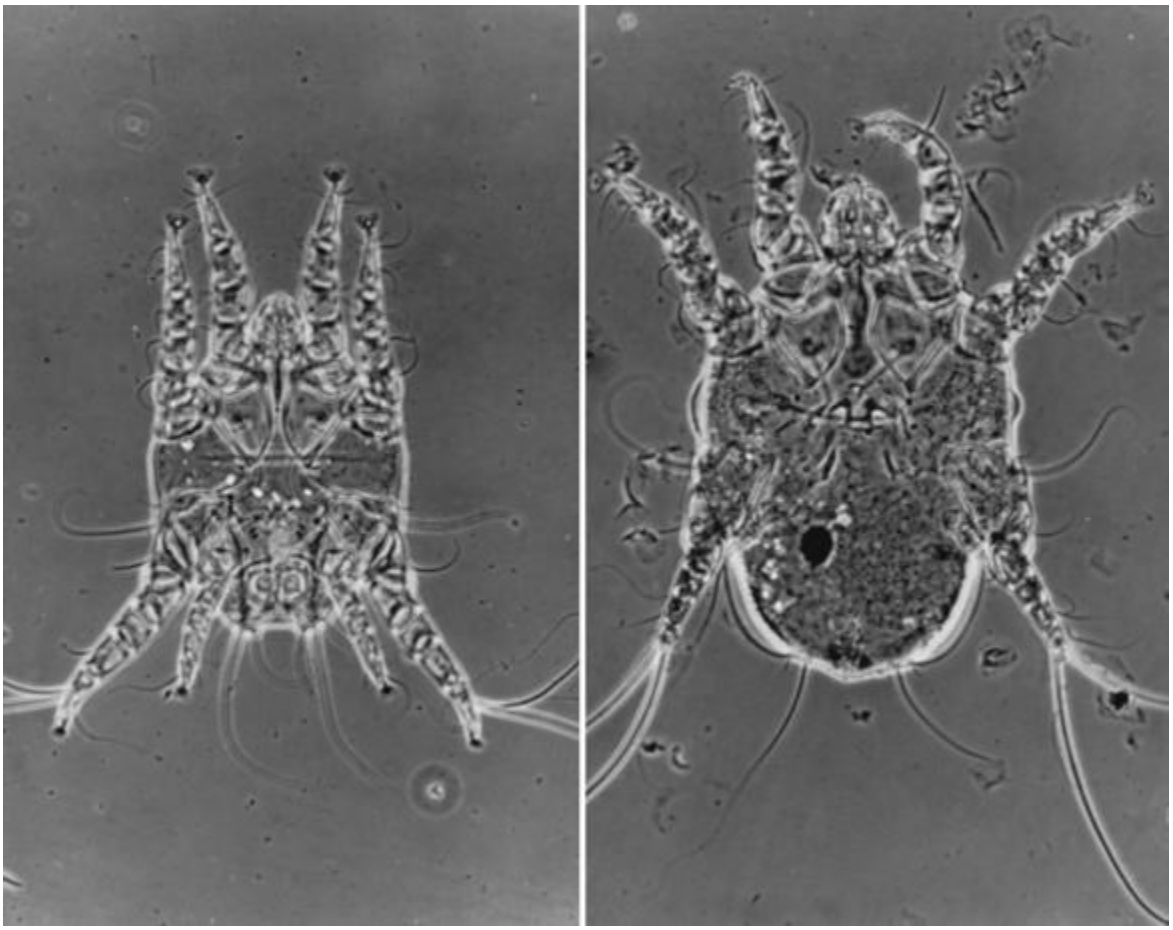

FIGURE 2-111 *Otodectes* male *(left)* and female *(right)*. The female has pretarsi on the first and second pairs of legs; the male has pretarsi on all four pairs.

Other Astigmatid Mites

Hair-clasping mites of the superfamily Listrophoroidea have one or more pairs of legs variously flattened, bowed, or otherwise modified for clasping a hair. Examples include *Chirodiscoides caviae*, a parasite of guinea pigs (Figure 2-112) and *Myocoptes musculinus*, a parasite of rodents (Figure 2-113). *Lynxacarus radovskyi* is a hair-clasping mite

of domestic cats in Florida, Puerto Rico, Hawaii, Australia, and Fiji (Figure 2-114); hordes of these tiny mites clinging to the hairs impart a scruffy appearance (Greve and Gerrish, 1981). Not all hair-clasping mites belong to the superfamily Listrophoroidea or even to the suborder Astigmata. For examples of exceptions, see *Myobia* and *Radfordia* later.

FIGURE 2-112 Chirodiscoides caviae female.

FIGURE 2-113 *Myocoptes musculinus* male *(left)* and female *(right)*, an astigmatid hair-clasping parasite of laboratory rodents. Notice how the third pair of legs of the male and third and fourth pairs of legs of the female are modified for hair clasping. The first two pairs of legs have sarcoptiform pretarsi.

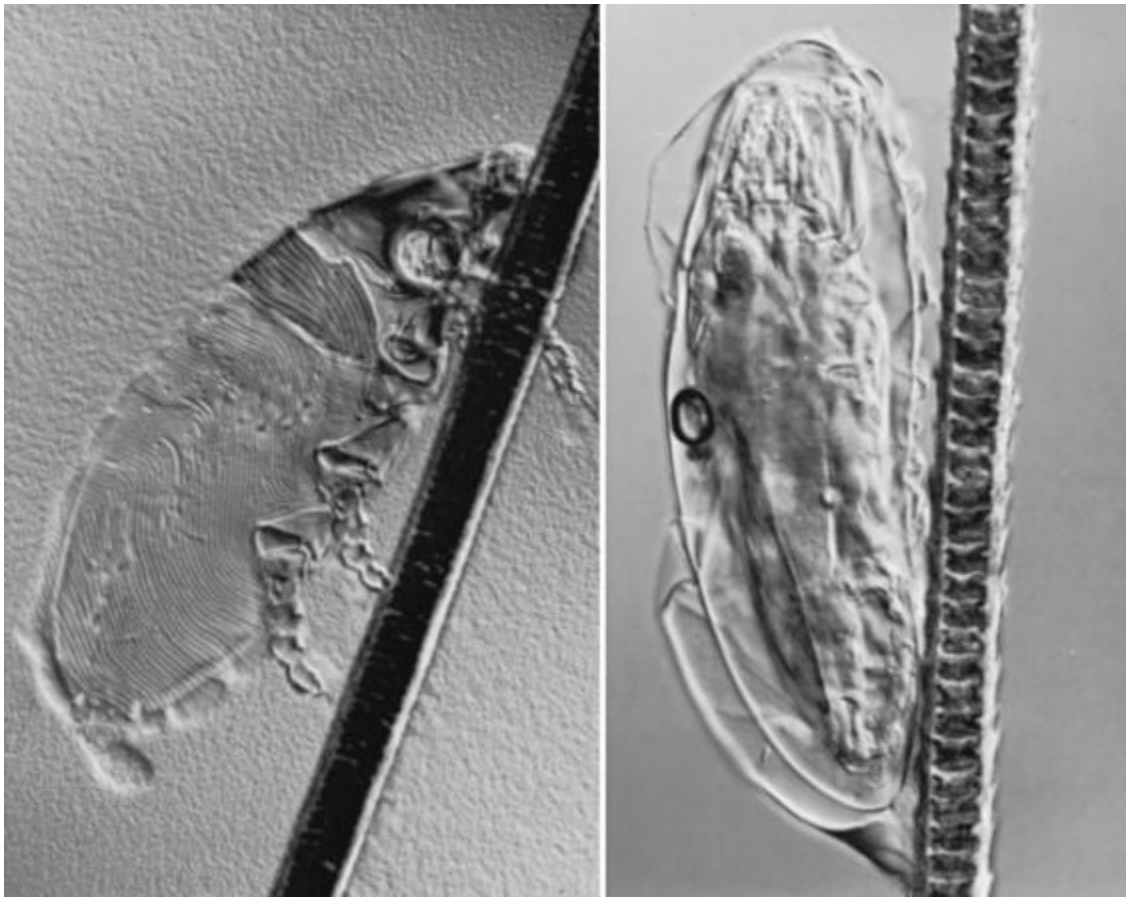

FIGURE 2-114 *Lynxacarus radovskyi* (Listrophoroidea), a hair-clasping mite of the cat. *Left*, Adult mite. *Right*, Egg with larva.

Specimens courtesy Dr. Robert Foley.

Feather mites occur in variety and abundance. Most are members of several superfamilies of Astigmata. Feather mites are usually external, but some live within the quills. Others, such as members of the family Epidermoptidae, burrow in the skin and may cause a mangelike condition. Astigmatid feather mites may be distinguished from prostigmatid feather mites such as *Syringophilus* by their sarcoptiform pretarsi.

Two families of Astigmata have evolved as internal parasites of birds: *Laminosioptes* (Laminosioptidae) occur in subcutaneous

nodules in chickens, and several genera of the family Cytoditidae are parasites of the air sacs and respiratory passages of chickens, canaries, and other birds.

Members of the families Acaridae and Glyciphagidae are free-living mites that feed on organic matter. They may be found in grain, cheeses, dried fruit, and other stored food products. Contact with these mites and their detritus may cause urticaria and dermatitis in human beings. “Grain mites” are frequently found as pseudoparasites in fecal smears. They may be distinguished from parasitic astigmatids by the shape of the female genital opening, which is a transverse or U-shaped slit in the parasites but a more or less longitudinal slit in grain mites.

Suborder Cryptostigmata, Oribatid Mites

The Cryptostigmata, or oribatid mites, are free-living inhabitants of humus, some of which serve as intermediate hosts to tapeworms of the family Anoplocephalidae. When ingested by an oribatid mite, the larva in the egg of the tapeworm *Moniezia* develops into a cysticercoid, the larval stage of which is infective for the ruminant definitive host.

Suborder Prostigmata, Prostigmatid Mites

The Prostigmata (with the stigmata if apparent located anterior to the first pair of legs) is a polyphyletic amalgamation including both free-living species and such diverse obligate parasites as pilosebaceous mites *(Demodex)*, hair-clasping mites *(Myobia)*, and “chiggers” (Trombiculidae).

Family Demodicidae

Demodex

These tiny, wormlike mites with short, stubby legs (Figure 2-115) live in the hair follicles and sebaceous glands of mammals. Several distinct species of *Demodex* often parasitize the same host animal, but each species tends to be restricted to a particular habitat. For example, two species, *Demodex folliculorum* and *Demodex brevis*, live in the skin of almost every human face, *D. folliculorum* in the hair follicles, and *D. brevis* in the sebaceous glands (Desch and Nutting, 1972), where they eat the epithelial cells. Some important pest species are as follows.

FIGURE 2-115 *Demodex canis (left)* and *Demodex cati (right)*.

Demodex canis is present in small numbers in the skin of most normal dogs (see Figure 2-115). Pups acquire *D. canis* infection from their dams during the nursing period, and most cases of demodectic mange occur between 3 and 6 months of age. Affected dogs harbor much larger than normal populations of *D. canis*, apparently as a result of immunodeficiency, and display circumscribed areas of erythema and alopecia around the eyes and mouth and over bony projections on the extremities. There is no evidence of pruritus. If the lesions remain thus localized, the prognosis for clinical recovery

is excellent; the majority of such cases are mild, and the animals recover spontaneously with the attainment of sexual maturity. However, a few cases persist, and these tend to become generalized and intractable and may prove fatal. In generalized demodicosis, the hair becomes sparse over wider expanses and the skin becomes coarse, dry, and erythematous ("red mange"). Concomitant staphylococcal pyoderma is the rule in generalized cases; pustules develop, break open, and ooze. Severe cases are associated with a disagreeable odor. Generalized canine demodicosis is difficult to ameliorate and probably impossible to cure. Two further mites of the genus *Demodex* have been described from the dog (Desch and Hilier, 2003). *D. injai* is a species that also lives in hair follicles and is about twice the length of *D. canis*. The third *Demodex* species found on the dog is as yet undescribed but appears to be shorter and stouter than *D. canis* and lives associated with the stratum corneum rather than hair follicles.

Demodex bovis mites are part of the normal fauna of bovine skin, but sometimes pinhead- to egg-sized nodules appear, usually on the neck and forequarters (see Figure 8-7). Occasionally only the eyelids, vulva, or scrotum is involved. If a fresh nodule is nicked with a sharp scalpel, a thick, toothpaste-like pus that contains masses of *D. bovis* mites can sometimes be expressed, but older lesions consist only of scar tissue and are devoid of mites. Bovine demodectic mange is practically incurable, even though individual lesions typically regress, because new nodules form to take their place. However, an unusual case of bilateral lower palpebral

demodicosis in a dairy cow, characterized by chronic eosinophilic granulomatous cellulitis but without appreciable pus formation, resolved spontaneously within 3 months (Gearhart, Crissman, and Georgi, 1981).

Demodex ovis is rarely noticed but probably rather common; mites infest the meibomian glands and the hair follicles and sebaceous glands of primary hairs of the general body skin but are most numerous on the neck, flanks, and shoulders. A second species parasitizing sheep, *Demodex aries*, appear to be confined to areas with very large sebaceous glands such as the vulva, prepuce, and nostrils (Desch, 1986).

Demodex caprae causes a nodular dermatitis in milk goats.

Demodex caballi is a harmless parasite of the meibomian glands of horses. The horse is also host to a second species, *Demodex equi*, that is about half as long (190 to 232 m) as *D. caballi* (Desch and Nutting, 1978).

Demodex cati is rarely noticed (see Figure 2-94). Dermatitis associated with *D. cati* is usually localized on the head and in the ear canals. A more superficially dwelling *Demodex*, *Demodex gatoi*, has been described from the stratum corneum of cats (Desch and Stewart, 1999); this mite is distinctly shorter and broader than *D. cati*. It appears that cats may also harbor a third species that has been seen but not yet described in detail (Desch and Stewart, 1999).

Demodex cuniculi is a relatively rare parasite of the rabbit.

Demodex phylloides is found in nodules around the eyes and on the snouts of pigs. These lesions later spread over the underside of

the body.

Family Cheyletiellidae

Cheyletiella species are easily recognized by their big palpal claws, M-shaped gnathosomal peritremes, and comblike tarsal appendages (Figure 2-116). *Cheyletiella yasguri* occurs on dogs, *Cheyletiella blakei* on cats, and *Cheyletiella parasitivorax* on rabbits. Humans may serve as an accidental or transitory host. Pups infested with *C. yasguri* develop "walking dandruff" on their backs, a dermatitis with branlike exfoliative debris that stirs with the movements of these rather large mites. The Georgis observed a caged cat that passed *C. blakei* in its feces for several weeks. Presumably this cat was ingesting these mites while grooming itself, but there was no macroscopically visible skin lesion and they could find no mites in the fur. Other genera of the family Cheyletiellidae are parasites of birds. *Cheyletiella* species survive longer off the host than other mange mites, and the premises may remain a source of reinfestation after treatment of affected animals.

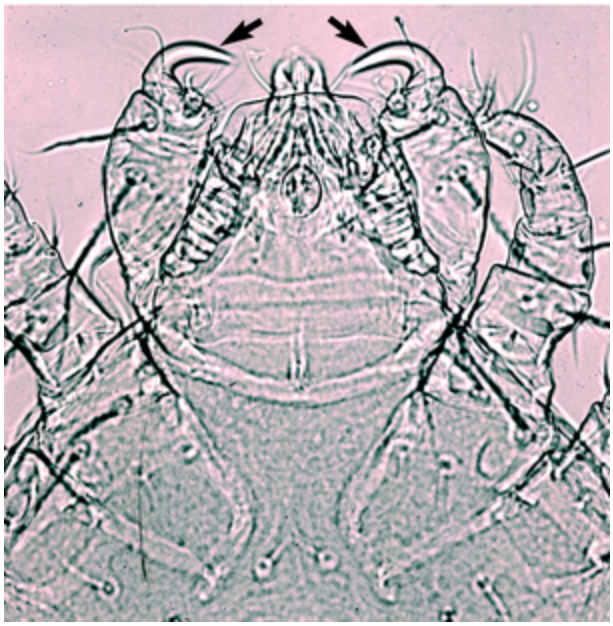

FIGURE 2-116 The anterior end of *Cheyletiella yasguri;* note the formidable palpal claws *(arrows)*.

Family Psorergatidae

Psorobia ovis, the sheep itch mite, sporadically causes pruritus and fleece derangement in sheep by rubbing and through chewing by the infested host. The course is very chronic. Lambs younger than 6 months appear unaffected, and generalization may require 3 or 4 years. The mite is minute, almost discoidal, and has radially arranged legs. *Psorobia bos* is a nonpathogenic mite of cattle. *Psorergates simplex*, the subcutaneous mite of mice, may cause a mangelike condition. To demonstrate mites, skin an infested mouse and look for pockets of mites on the underside of the dermis.

Family Myobiidae

Myobiid mites cause dermatitis in stocks of laboratory rodents. In myobiids the first pair of legs is modified for clasping hair (Figure 2-

117), whereas in *Myocoptes* species the third pair of legs of the male and third and fourth pairs of the female are so modified (see Figure 2-113). *Myobia musculi* attacks laboratory mice, and *Radfordia ensifera* attacks laboratory rats. Alopecia and erythema of the dorsal neck region are typical; severe cases are characterized by self-inflicted excoriations. Stress of overcrowding is frequently responsible for converting an asymptomatic infestation of hair-clasping mites into an outbreak of serious skin disease.

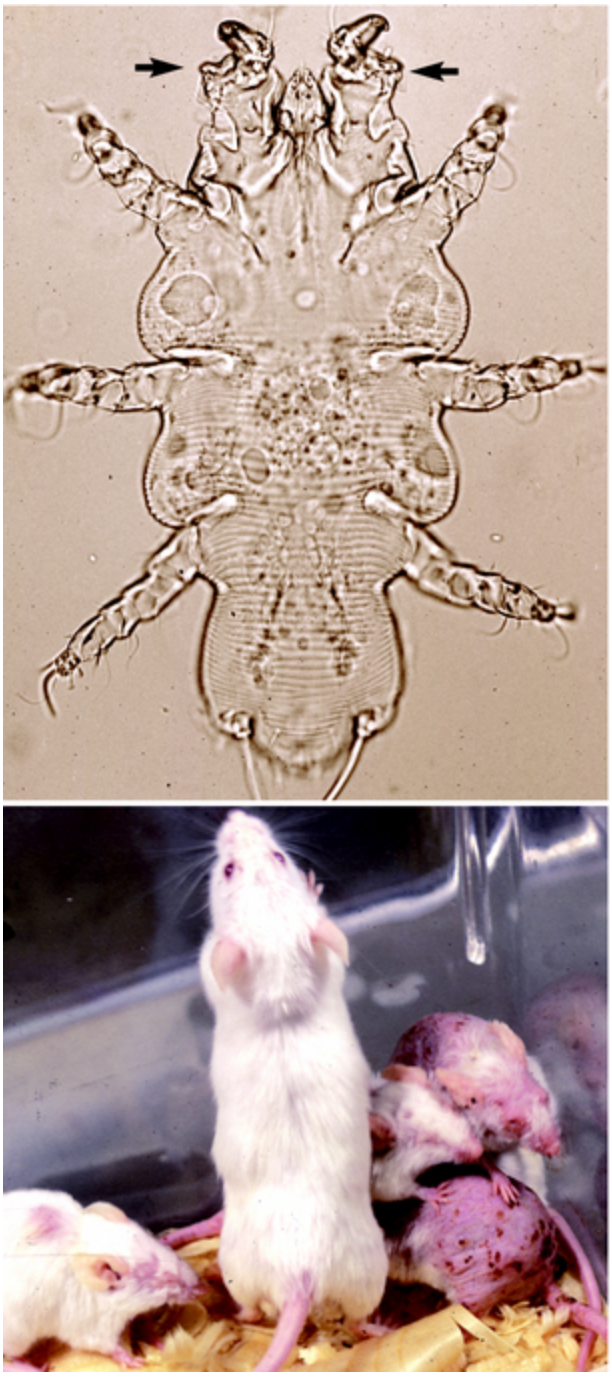

FIGURE 2-117 *Myobia musculi (top)*, a myobiid hair-clasping parasite of laboratory rodents. The first pair of legs *(arrows)* is modified for hair clasping. The mice *(bottom)* are suffering from an infestation with this mite.

Family Harpyrhynchidae

Harpyrhynchids are rounded mites, resembling psorergatids, that cause mangelike conditions in birds. Several genera include species that burrow in feather follicles or form large crusted cysts in the skin.

Family Syringophilidae

Syringophilids are nonpathogenic inhabitants of the lumen of feather quills.

Family Trombiculidae

Larvae (chiggers) of the family Trombiculidae are parasitic, but the nymphs and adults are free-living. These bright red or orange, six-legged larvae are likely to be found on the skin or in the ears of cats or dogs, on the faces or pasterns of sheep and other ungulates, and under the wings or around the vents of chickens and other birds (Figure 2-118). Infestation is usually acquired in wild or semiwild landscapes; the distribution of these nuisances is remarkably spotty, but wherever they are found, chiggers are infamous. Microscopically, the scutum is useful for recognizing a chigger as such and for generic and species identification with the help of keys. Focus on the dorsal surface (the surface opposite the one with the coxae) to see the scutum (Figures 2-119 and 2-120). Chiggers remain on the skin for several days unless dislodged by the scratching host, and their saliva, injected into the skin, disintegrates host cells and the resulting material is taken into the mite as food. The surrounding skin hardens, and a tube called a stylostome is formed in which the mouthparts remain until the chigger is replete

or dislodged. The fully developed stylostome extends from the surface of the epidermis into the dermis and is lined by necrotic cells of the stratum germinativum (see Figure 8-9). Pruritus is intense and may be protracted for many days after the chigger has been removed. Twenty-four hours after infestation with more than 2000 larvae of *Neotrombicula autumnalis*, two male Yorkshire terriers developed paresis involving first the hind legs, then the forelegs. The nervous signs disappeared within 3 days after repeated acaricidal (propoxur) and symptomatic therapy (Prosl, Rabitsch, and Brabenetz, 1985).

FIGURE 2-118 Living chigger from the ear of a cat in Maryland.

Courtesy Dr. Craig Greene, VCA Newark Animal Hospital, Newark, Delaware.

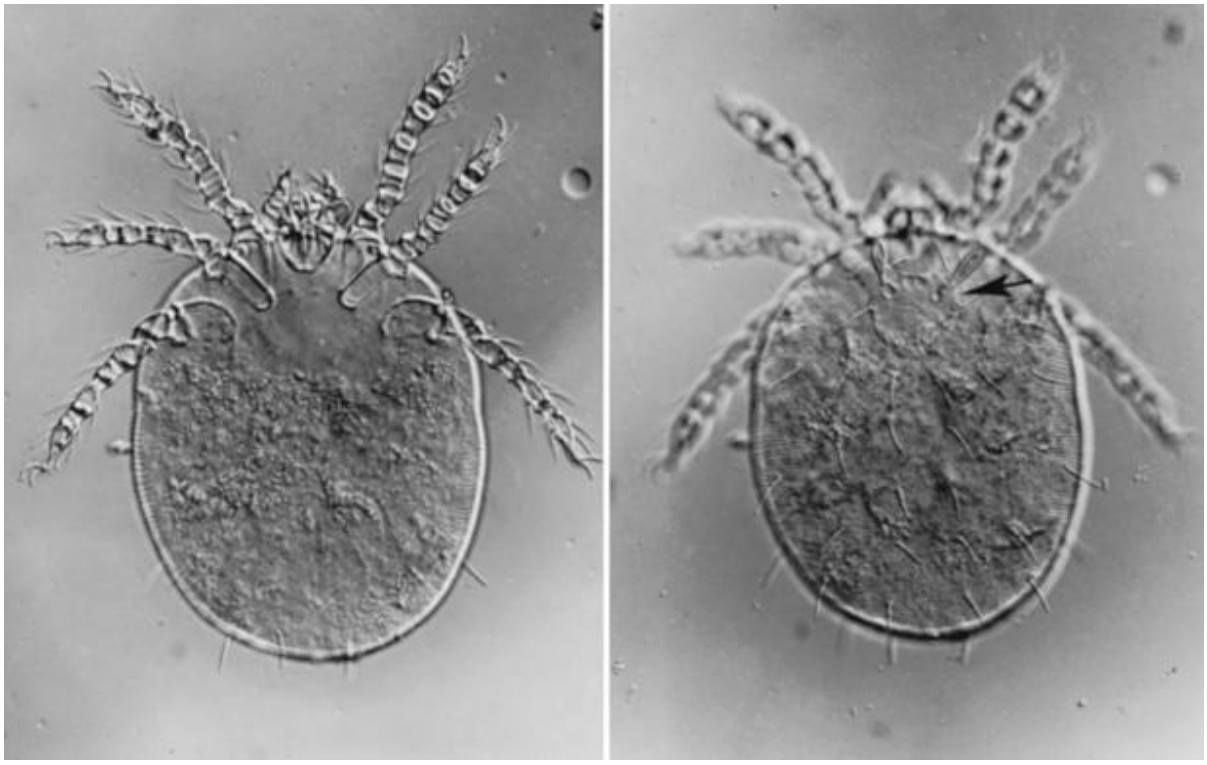

FIGURE 2-119 *Walbachia americana*, a trombiculid mite (chigger). *Left*, The ventral surface is in focus. *Right*, The dorsal surface. The scutum *(arrow)* with its two sensillae (large plumose setae) and four or five setae is helpful in identifying chiggers; it is on the dorsal surface near the anterior end of the body.

FIGURE 2-120 Scutum of *Neotrombicula* sp. (Trombiculidae: Prostigmata).

Recently a new syndrome, straelensiosis, was reported to be affecting dogs in Europe. This is due to a trombiculid mite. Some 22 dogs over a period of 5 years in the south of France were found to have a chronic, painful, extensive-to-generalized dermatitis that was associated with papular crusts and suppurations (Bourdeau et al, 2001). The mite was described as *Straelensia cynotis* by Fain and Le Net (2001). This larval trombiculid enters the hair follicle, where it stays for an extensive period with its stylostome directed into the dermis (Figure 2-121). A case has since been found in a dog in Portugal (Seixas et al, 2006).

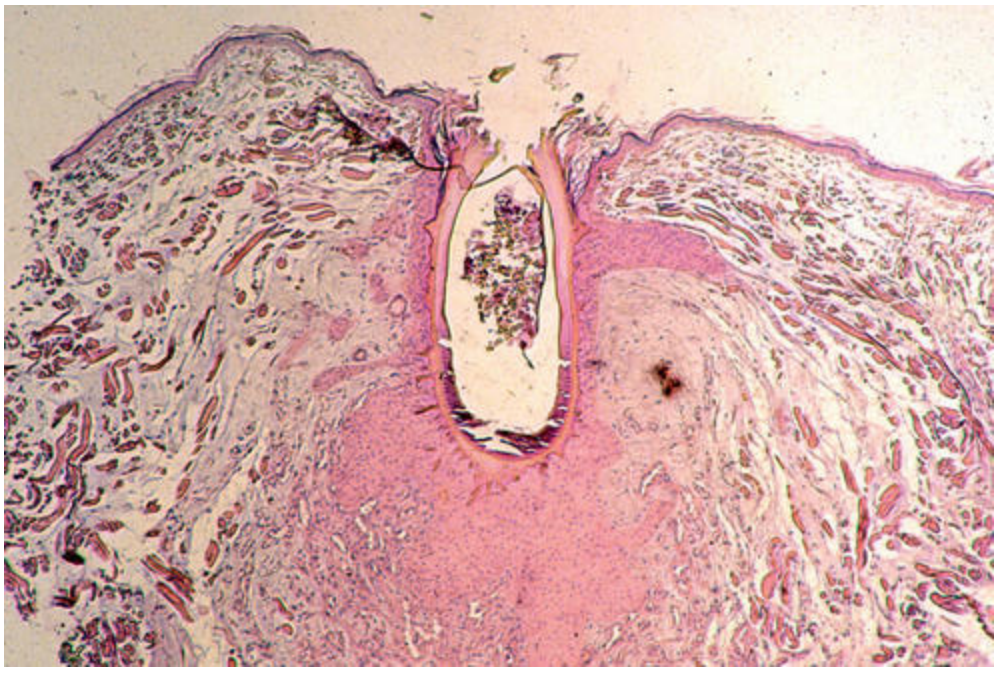

FIGURE 2-121 *Straelensia cynotis* in a hair follicle.

Courtesy Dr. Maja Suter, Institute of Animal Pathology, University of Berne, Berne, Switzerland.

Family Pyemotidae

Pyemotes

“Hay itch mites” of the genus *Pyemotes* are parasites of various insect larvae that are grain-destroying pests. *Pyemotes tritici* is a tiny elongate mite that becomes enormously distended when gravid; males and females are sexually mature at birth. People and domestic animals that come into contact with infested grains, straw, hay, and the like may be attacked by these mites and develop an erythematous and intensely pruritic papular and vesicular rash. An outbreak of dermatitis in 12 horses and many persons in Florida was attributed to *P. tritici* received in a shipment of alfalfa hay (Kunkle and Greiner, 1982).

Family Tarsonemidae

Acarapis woodi is the tracheal mite of honeybees. These mites entered the United States through Texas and Florida in 1984, coming from Mexico and Europe. These mites, along with *Varroa* and the beetle *Aethina*, have been responsible, in part—along with the currently unexplained “colony collapse disorder”—for the remarkable reduction of honeybee populations in the United States. These small mites live within the trachea of the honeybee. Female mites move from bee to bee, entering the adult bee through the first thoracic spiracle. Large numbers can build up in the tracheal tubes. The mites within the tubes cause problems with thermoregulation of hives in winter and cause bees to die outside of hives because they cannot elevate their metabolic rate high enough to stay warm when they fly on cool days. Treatment has been performed using the addition of menthol chips or oil of wintergreen to hives (Williams,

2000). Though this seems to afford some protection, it may be that most susceptible hives have already disappeared.

Treatment of Mite Infestations

Dogs and cats

Sarcoptes

Selamectin is probably the treatment of choice for sarcoptic mange in dogs and is labeled for this application (Shanks et al, 2000). Topical imidacloprid (10% w/v)/moxidectin (2.5% w/v) has also been found to be highly efficacious against sarcoptic mange in dogs (Fourie, Heine, and Horak, 2006). Subcutaneous ivermectin is also routinely used to treat sarcoptic mange. Other effective acaricides include amitraz, benzyl benzoate, lime sulfur, phosmet, and rotenone. In most cases, with these other compounds, treatment must be repeated several times over a period of weeks.

S. scabiei and other sarcoptiform parasites may temporarily infest people who come into intimate contact with mangy dogs and cats. In this case, acaricidal treatment of the pet is the key to lasting success in curing the people. On the other hand, proper scabies contracted from another human being causes very persistent dermatitis and misery unless effectively treated and, of course, has little or nothing to do with dogs and cats.

Notoedres

Selamectin topically applied to cats will treat notoedric mange (Itoh et al, 2004). Ivermectin (0.3 mg/kg) has been successfully used to treat numerous cats with notoedric mange (Foley, 1991a). The standard treatment previously for *N. cati* infestations in cats was lime sulfur. With lime sulfur the cat is first bathed and then dipped or washed with a 1:40 solution of lime sulfur in warm water. This treatment is applied weekly for at least 6 weeks.

Otodectes

Selamectin is approved for the treatment of ear mites in cats. Ivermectin and milbemycin oxime have both been formulated as otic suspensions that are approved for treating ear mites in cats. Otodectes cynotis has also been successfully treated with the topical application of moxidectin/imidacloprid (Fourie, Kok, and Heine, 2003). Subcutaneous ivermectin (0.2 to 0.225 mg/kg) injected on one or two occasions with a 3-week interval between injections has proven highly successful in treating ear mites in cats (Foley, 1991b). *Otodectes* ear infestations also respond to pyrethrin- and rotenone-containing compounds. With these products the ear canal should be thoroughly cleaned before instillation of the acaricidal solution. The application of 1 to 2 mL of mineral oil to the ear canal followed by 30 seconds of massage repeated every 2 or 3 days will often cure dogs and cats of their ear mite infestations.

Demodex

Fortunately most dogs with lesions of demodectic mange have a localized *D. canis* infestation that will respond successfully to topical treatment. The localized form of demodectic mange may be controlled by applying rotenone ointment or benzyl benzoate lotion. These drugs have very little residual activity and therefore must be applied daily.

The treatment of generalized demodectic mange is a challenge and frequently proves to be a frustrating experience for the clinician and client alike. Currently recommended therapies include amitraz rinses every 7 to 14 days and oral daily ivermectin, milbemycin, or moxidectin (Mueller, 2004). Amitraz, approved for the control of generalized demodicosis, is applied topically as an aqueous suspension (10.6 mL of concentrate per 2 gal or 7.6 L of water) at 2-week intervals for a total of three to six applications (Folz et al, 1983). It is recommended that treatment be continued until no viable mites can be found in skin scrapings at two successive treatments. A brood bitch with asymptomatic *D. canis* infection may be bred, but a bitch with demodectic mange or a history of demodectic mange should be spayed.

Cheyletiella

Infections with *C. yasguri* in dogs have been successfully treated with topical applications of imidacloprid/moxidectin (Loft and Willesen, 2007) or selamectin (Mueller and Bettenay, 2002). Infestations also responded well to the application of topical 65% permethrin, and all mites were gone within 1 week of treatment

(Endris et al, 2000). Milbemycin oxime has also been used to treat dogs with naturally occurring cheyletiellosis (White, Rosychuk, and Fieseler, 2001). Canine cheyletiellosis has also been successfully treated using fipronil (Chadwick, 1997). *Cheyletiella* is also susceptible to amitraz. In cats, infestations with *C. blakei* have been successfully treated with the topical application of fipronil (Scarampella et al, 2005) or selamectin (Chailleux and Paradis, 2002). The premises should be sprayed with a residual organophosphate insecticide such as diazinon to destroy these rather hardy mites.

C. yasguri of dogs and *C. blakei* of cats also attack people, especially those who share their beds with their pets. Curiously, *C. blakei* rarely produces obvious lesions on cats, but the owner may be aware of frequent bites. If *C. blakei* infestation is suspected, one can attempt to collect mites from the fur with a bit of Scotch tape. However, the diagnosis is more often reached fortuitously when the mites or their eggs are found in a routine fecal flotation. Because cats so meticulously groom themselves, a fecal flotation often affords a better sample of what is on the cat's exterior than direct examination does.

Ruminants

Chorioptes

Eprinomectin can be applied topically to lactating dairy cattle without withholding of milk and is approved for the treatment of

chorioptic mange. Alpacas and llamas have also been successfully treated with eprinomectin applied topically (Plant, Kutzler, and Cebra, 2007). In a severe case of mange in a herd of alpacas involving infestations with *Psoroptes*, *Sarcoptes*, and *Chorioptes*, treatment with injectable ivermectin rapidly cleared the animals of their *Psoroptes* and *Sarcoptes* mites, but the *Chorioptes* mites required further treatment with topically applied ivermectin (Geurden, Deprez, and Vercruysse, 2002). Chorioptic mange usually responds to standard louse treatments. Coumaphos or lime sulfur suspension as spray or dip controls chorioptic mange mites on lactating dairy cows.

Sarcoptes

Sarcoptic mange should be reported to state disease control authorities and treatment carried out under their supervision. Lactating dairy cows can now be treated with eprinomectin, which is labeled for *Sarcoptes* infestations of cattle. Sarcoptic mange of beef cattle and nonlactating dairy cattle is treated with avermectins, ivermectin, moxidectin, doramectin, or eprinomectin. It also can be treated with sprays or dips containing lime sulfur, phosmet, and tetrachlorvinphos.

Psoroptes

Psoroptic scabies in cattle or sheep should be reported to state disease control authorities and treatment carried out under their supervision. Coumaphos, phosmet, and hot lime sulfur are approved

by the U.S. Department of Agriculture's Animal and Plant Health Inspection Service (APHIS) as official dips for psoroptic scabies in cattle, and injectable ivermectin is approved as a systemic acaricide (Wright, 1986). Most of the macrocyclic lactones are labeled for treating psoroptic mange in cattle. Cattle treated with ivermectin must be isolated from untreated cattle for 2 weeks after treatment and withheld from slaughter for the required period. Ivermectin has not been approved for the treatment of psoroptic mange in sheep in the United States. Holding facilities vacated by sheep or cattle with psoroptic mange should be left vacant for at least 2 weeks to give the mites time to die off before new stock is housed (Wilson, Blachut, and Roberts, 1977).

Demodex

Two goats with nodular demodicosis were treated successfully without any scarring or skin depigmentation (Strabel et al, 2003). One of the goats was treated with weekly oral ivermectin; the other was treated with selamectin. It seems highly probable that these treatments will also work in sheep and in cattle under most circumstances.

Horses

Severe irritation caused by mange mites may lead to serious self-mutilation by affected horses. Treatment with macrocyclic lactones has proved efficacious (Osman, Hanafy, and Amer, 2006). Mange is contagious and sometimes communicable. Isolate mangy horses and

sterilize all water buckets, brushes, curry combs, and the like. Stalls should be thoroughly disinfected or left vacant for 2 to 3 weeks.

Swine

Ivermectin is highly effective in treating sarcoptic mange in swine.

Ferrets, lagomorphs, and pocket pets

Notoedric mange *(Notoedres douglasi)* affecting two fox squirrels *(Sciurus niger)* responded dramatically to a single subcutaneous injection of ivermectin at 0.5 mg/kg body weight (Evans, 1984). A case of notoedric mange that developed in an African pygmy hedgehog *(Atelerix albiventris)* was treated with injectable moxidectin (Pantchev and Hofmann, 2006).

O. cynotis has been effectively treated in ferrets with topical selamectin (Miller et al, 2006).

M. musculinus and *M. musculi* infestations were eliminated from laboratory mice by subcutaneous injection of ivermectin 0.2 mg/kg body weight (Wing, Courtney, and Young, 1985). More recently, a group of mutant sickle-cell–anemia mice were cleared of their infections by being cross-fostered on outbred mothers that were treated with topical ivermectin (Huerkamp et al, 2005). Topical selamectin has been shown to eliminate infestations of mice with *M. musculinus*, *M. musculi*, and *R. ensifera;* this treatment also controlled the pinworms *Syphacia obvelata* and *Aspiculuris tetraptera* (Gonenc et al, 2006). Also, a single treatment with topical moxidectin has been used successfully in the treatment of *M. musculinus* infestations

(Pullium et al, 2005). Application of 0.5 mg active permethrin per mouse as 0.25% dust mixed with the bedding was convenient and eliminated *M. musculi* infestations in experimental mice (Bean-Knudsen, Wagner, and Hall, 1986).

Guinea pigs infected with *T. caviae* have been shown to respond well to treatment with ivermectin (Mandigers, van der Hage, and Dorrstein, 1993; McKellar et al, 1992). Treatment has been administered orally, subcutaneously, or percutaneously. It seems highly likely that other avermectins would also be efficacious in the guinea pig.

Ear canker in rabbits *(P. cuniculi)* responds to two subcutaneous injections of ivermectin at 0.2 mg/kg administered 14 days apart (Bowman, Fogelson, and Carbone, 1992). Rabbits can also be treated very successfully with topical selamectin (McTier et al, 2003), topical imidacloprid/moxidectin (Hansen et al, 2005), or topical eprinomectin (Ulutas et al, 2005). The mites *C. parasitovorax* and *Listrophorus gibbus*, along with the flea *C. felis*, have been successfully treated in rabbits with a topical formulation of imidacloprid and permethrin (Hansen et al, 2006). When pesticides and anthelminthics are applied to rabbits, it must be remembered that rabbits remain in the unusual regulatory position of still being considered a minor species food animal in the United States, and the reality is that they are often still consumed as food.

CLASS CRUSTACEA

Copepods

Copepods are crustaceans of importance to veterinary medicine because they serve as intermediate hosts of both cestodes and nematodes. There are three major groups of copepods, the calanoids, cyclopoids, and harpacticoids; the cyclopoids comprise the group that typically has been found to be important intermediate hosts of the parasites of domestic animals. Copepods have shrimp-shaped bodies and five pairs of swimming legs (Figure 2-122). The antenna on each side of the head usually branches into two stalks. There may or may not be a single simple eye. Copepods reproduce sexually, and the males often have a modified antenna that is used in copulation. The females typically carry egg sacks that contain developing eggs. Most copepods are grazers of phytoplankton, but some can be carnivorous, and a few are parasites in their own right. There are 11 molts that occur, separating 12 larval stages. The first five molts produce six larval forms of the naupliar type, the next five molts produce the developmental stages called copepodites (typically a new body segment is added with each molt), and the final molt produces the adult male or female. While grazing, the copepods will ingest either the coracidia of tapeworms or the hatched larvae of nematodes. They will then serve as either transport hosts or as required intermediate hosts. Important parasites that use copepods include *Spirometra*, *Diphyllobothrium*, and *Dracunculus* species.

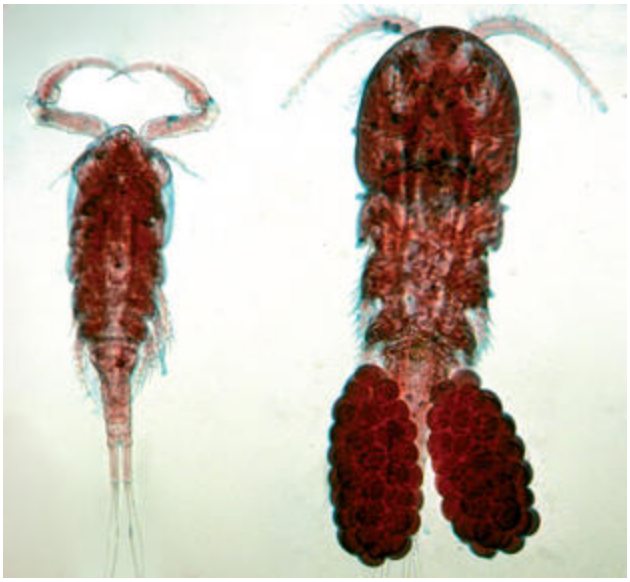

FIGURE 2-122 Copepods, male and female, stained. The female bears the two large egg sacks that are typical of many of these free-living crustaceans.

Pentastomida

Pentastomids, or tongueworms, are highly specialized crustaceans, as unlikely as that may seem. The adult parasites live in the respiratory passages of predacious reptiles, birds, and mammals. The body is annulated, and the anterior, subterminal stoma is flanked by two pairs of retractable hollow fangs or hooks (Figure 2-123). Eggs containing four- or six-legged larvae are discharged with the nasal secretions or swallowed and passed in the feces (Figure 2-124). If ingested by an appropriate intermediate host, usually a member of some species likely to fall prey to the predator in question, these larvae invade the tissues, develop, and encyst in the viscera as nymphs that resemble the adults in all particulars except for mature reproductive organs.

FIGURE 2-123 Stoma and hooks of a pentastomid nymph from a South American otter.

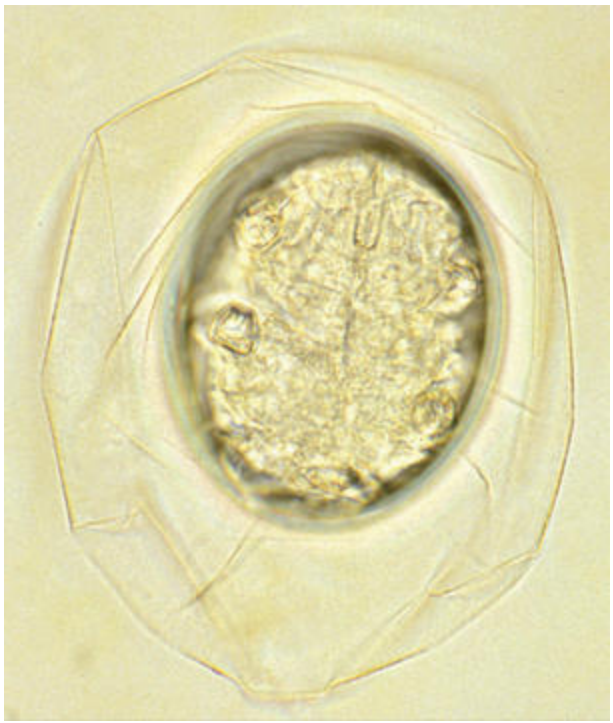

FIGURE 2-124 Egg of the pentastomid *Rheighardia sternae* from the feces of a gull.

Linguatula serrata occurs in the nasal and paranasal sinuses of dogs and cats, where it causes bleeding, catarrhal inflammation, and

some impediment to respiration. Cattle, sheep, rabbits, and other animals serve as intermediate hosts; fully developed nymphs, the form infective for carnivorans, are found encysted in the lymph nodes and serous membranes.

Kazacos et al (2000) reported on a Basenji-cross dog that had been born and spent time in Cameroon, Africa. It seems that the dog must have ingested some quantity of python feces containing the eggs of pentastomes of the genus *Armillifer*. The dog had been ill for several years, and when it became acutely ill 2 years after first admission, it was unresponsive to treatment and euthanized. It was found to have a massive visceral infection with the nymphs of this pentastomid (Figures 2-125 and 2-126).

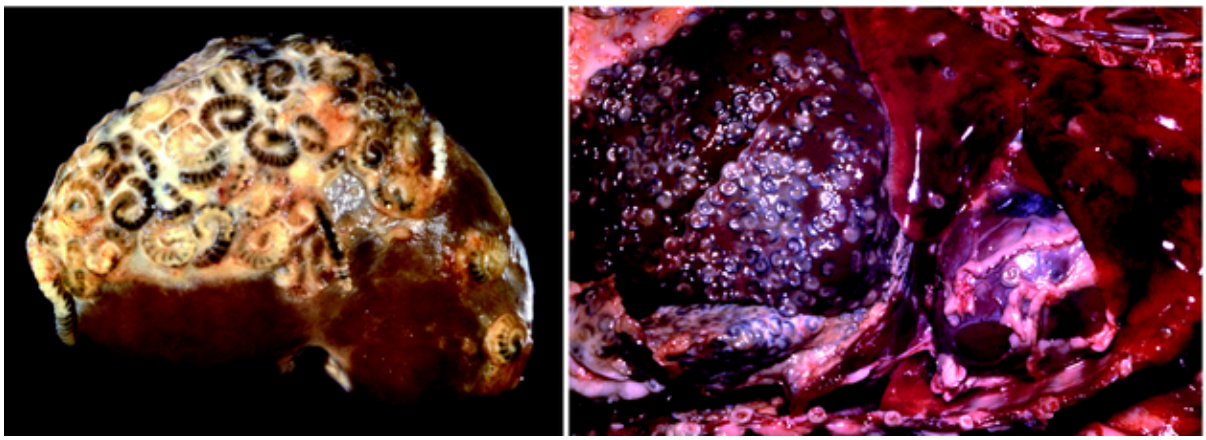

FIGURE 2-125 *Armillifer armillatus*. *Left*, A kidney removed from the infected dog whose viscera *(right)* have the liver, lungs, and heart containing large numbers of the very large coiled nymphs of this pentastomid parasite whose adults are found in pythonid snakes.

Courtesy Dr. Kevin R. Kazacos, School of Veterinary Medicine, Purdue University, West Lafayette, Indiana.

FIGURE 2-126 *Armillifer armillatus*. Nymphs of this pentastomid teased from the tissues of the dog in Figure 1-125. Several of the nymphs have been damaged during the teasing process.

Courtesy Dr. Kevin R. Kazacos, School of Veterinary Medicine, Purdue University, West Lafayette, Indiana.

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CHAPTER 3

Protozoans

Most protozoans are free-living organisms, and of those that live as parasites in the bodies of mammals, only a small proportion is associated with disease. Even then, their etiologic significance is sometimes unclear. For example, certain intestinal flagellates multiply when the host has diarrhea. In such cases the presence of large numbers of flagellates in the fecal smear is the result rather than the cause of the diarrhea. On the other hand, there are protozoans that indeed behave as primary pathogens, and these are responsible for some of the most important diseases of humans and domestic animals. These diseases are the malarias, piroplasmoses, coccidioses caused by apicomplexans, and trypanosomiases caused by sarcomastigophoran hemoflagellates.

ZOOMASTIGINA

Flagellates

Flagellates bear one or more long, slender flagella (sing., flagellum) for locomotion. The flagellum is also called an undulipodium by those engaged in protozoology to accentuate its structural differences from the flagellum of bacteria. Flagellates multiply asexually by binary fission, and certain species form resistant cysts. The parasitic flagellates can be divided into two main groups according to their location in the host's body and type of life

history. The hemoflagellates (e.g., *Trypanosoma* and *Leishmania*) live in the blood, lymph, and tissue spaces and are typically transmitted from host to host by bloodsucking insects. There is no collective term for the others, so we will call them mucosoflagellates. These mucosoflagellates live in the alimentary or genital tract, usually in intimate association with the mucous membranes, and are transmitted from host to host in the feces or genital effluvia. Certain mucosoflagellates are transmitted as trophozoites (e.g., *Trichomonas*), others as cysts (e.g., *Giardia*).

Kinetoplastida (Hemoflagellates)

Trypanosoma

A trypanosome is an elongated, spindle-shaped cell with a single nucleus lying near the middle of its length and a single flagellum that arises near a large mitochondrion with copious DNA called a **kinetoplast** and passes out of the anterior end of the cell (Figure 3-1). During development in both mammalian and arthropod hosts, trypanosomes can undergo considerable morphologic change. Four morphologic forms are distinguished in the case of *Trypanosoma cruzi*. The **amastigote** lacks a flagellum, whereas the other three forms all have a flagellum but differ with respect to the location of the kinetoplast. The kinetoplast lies posterior to the nucleus in the **trypomastigote,** immediately anterior to the nucleus in the **epimastigote,** and near the anterior end of the cell in the **promastigote.** The flagellum lies in the edge of an undulating membrane as it courses from kinetoplast to the anterior end of the cell body of the trypomastigote. Infection of the arthropod host occurs when it ingests the blood of an infected mammal. Infection of

the mammalian host occurs by one of two mechanisms, depending on the species of trypanosome involved: either through the bite of the infected arthropod or by contamination of the host's mucous membranes or abraded skin by its feces. The former are called **salivarian,** and the latter **stercorarian trypanosomes.** Most salivarians are pathogenic and most stercorarians are nonpathogenic, but the pathogenic stercorarian *T. cruzi* is an important exception to this generalization.

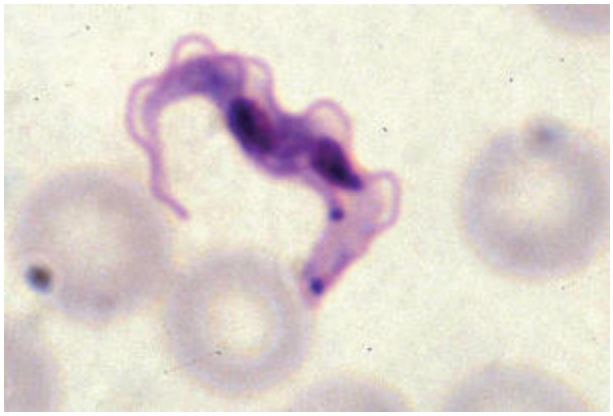

FIGURE 3-1 Giemsa-stained trypomastigote of *Trypanosoma brucei*. With tsetse-transmitted trypanosomes, dividing forms, like the one in this image, can be observed in blood smears.

Tsetse-transmitted trypanosomes are of major significance in sub-Saharan Africa (see Figure 3-1). *Trypanosoma brucei* and *Trypanosoma congolense* cause fatal nagana disease in domestic ruminants but are only mildly pathogenic in the indigenous wild ruminants. The wild ruminants thus serve as reservoirs of *T. brucei* and *T. congolense*, which are conveyed through the bites of tsetses (*Glossina* species) to domestic livestock. These trypanosomes and tsetses defend vast areas of African grazing lands against invasion by domestic livestock. Humans have been striving to introduce their

domestic animals into these areas for a long time without remarkable success, and where they have succeeded, they have often destroyed the grasslands by overgrazing and turned them into deserts.

T. brucei multiplies by longitudinal binary fission in the blood, lymph, and cerebrospinal fluid of the mammalian host. The trypomastigotes, the only stage in the mammalian host, that are ingested by the tsetse when it feeds on the blood of an infected mammal multiply in the insect's midgut, undergo metamorphosis, and migrate to the salivary glands, where they reach the infective metacyclic trypomastigote stage and are then ready to be injected into the mammalian host at the next feeding. *Trypanosoma gambiense* and *Trypanosoma rhodesiense*, the etiologic agents of African sleeping sickness in human, are closely related to *T. brucei*.

Some trypanosomes are transmitted outside of Africa by other dipteran vectors. *Trypanosoma vivax* is a form of considerable importance to livestock in West Africa. The reservoir hosts are wild ungulates. The living trypanosome is active in fresh blood films, hence the name *vivax*. In cattle the infection may be without signs, or there may be acute or chronic disease. In peracute disease there may be a high parasitemia associated with extensive hemorrhages throughout the mucosal and serosal surfaces of the body. In chronic disease, cattle will become anemic and emaciated, with signs of severe wasting. Similar disease has been reported in goats and sheep. *T. vivax* has been exported from Africa to South America, where the reservoir appears to be deer. Outside of Africa, the disease is transmitted mechanically by biting flies.

Trypanosoma evansi occurs in Asia, tropical America, and Africa north of the Sahara and causes surra of all species of domestic animals. Flies of the family Tabanidae and vampire bats serve as vectors. In South American horses, *Trypanosoma equinum* causes a disease called mal de caderas, which is similar to surra.

Sexually transmitted trypanosomes

Trypanosoma equiperdum is unique among trypanosomes in not requiring an intermediate host. Transmission among hosts occurs through direct sexual contact and results in the equine venereal disease called *dourine*. The acute stage is characterized by swelling of the genitalia and a mucoid discharge in which *T. equiperdum* can usually be demonstrated. As the acute signs subside, circular, flattened, “silver dollar” plaques appear in the skin and then disappear within several hours or days to be replaced by others. The chronic stage of dourine is marked by emaciation, paresis, intermittent fever, and finally death. Dourine was eradicated from the United States in 1920 and again in 1949 but has since reappeared at least once. The eradication of *T. equiperdum* from North America was made possible to a great extent by the work of a Canadian veterinarian, Edward Watson, who worked on the disease for some 15 years, was the first to identify the trypanosome in horses in North America, and developed a complement fixation test that could be used to identify infected horses in the field. Identified horses were then destroyed. Thus, within 16 years the disease had been identified and eradicated from the Canadian provinces (Derbyshire and Nielsen, 1997).

Nonpathogenic trypanosomes

Not all trypanosomes transmitted by the bites of arthropod vectors are exotic and tropical, but most of them are nonpathogenic. *Trypanosoma cervi* was identified in 29 of 45 Alaskan reindeer *(Rangifer tarandus)* examined over a 2-year period and in 98% of white-tailed deer *(Odocoileus virginianus)* in southern Florida examined over a 5-year period (Telford et al, 1991). *Trypanosoma cervi* also infects elk and mule deer in the United States and is apparently without pathogenic effect (Kingston, Morton, and Dietrich, 1982). *Trypanosoma theileri* (pronounced "tyler-eye") is a harmless parasite of cattle transmitted by tabanid flies, and *Trypanosoma melophagium* is an equally harmless parasite of sheep transmitted by the sheep ked, *Melophagus ovinus;* both are distributed worldwide. Occasionally, *T. theileri* contaminates culture media that have been enriched with "sterile" bovine serum, much to the surprise and confusion of the microbiologist. It is interesting that *M. ovinus*, which is first cousin to a tsetse, is almost universally infected with a trypanosome, albeit fortunately a harmless one.

T. cruzi (Figure 3-2), the etiologic agent of American trypanosomiasis (Chagas' disease) of human and dog, is transmitted by triatomin bugs of the genera *Triatoma, Rhodnius*, and *Panstrongylus* in South and Central America and in Texas, Arizona, New Mexico, California, and Oklahoma (Fox et al, 1986). Opossums, armadillos, rats, guinea pigs, cats, raccoons, and monkeys serve as reservoirs of infection in the wild. Five of 400 raccoons *(Procyon lotor)* examined in Maryland were infected (Walton et al, 1958); 104 of 221 raccoons (47%) were found to be seropositive in South Carolina and Georgia (Yabsley and Noblet, 2002). *T. cruzi* has been observed in hunting dogs in central Virginia that had

lymphadenopathy but did not yet have clinical signs of cardiomyopathy (Barr et al, 1995). Autochthonous cases of *T. cruzi* continue to occur in the United States from time to time in dogs (Nabity et al, 2006).

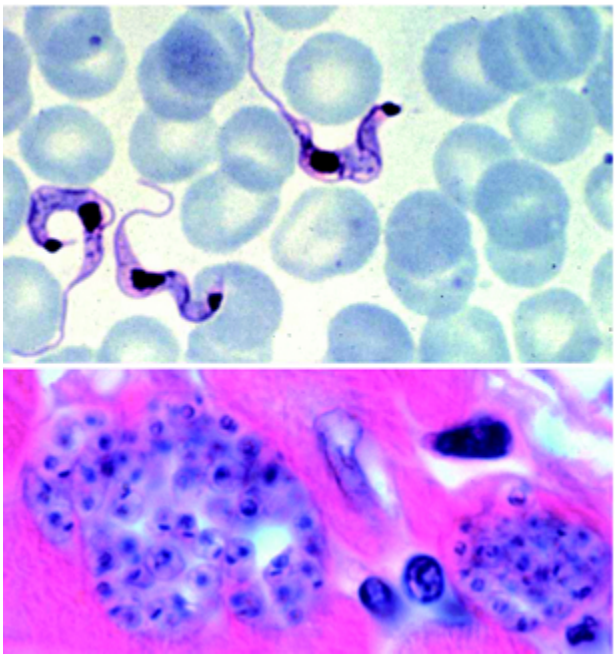

FIGURE 3-2 *Trypanosoma cruzi*. Top image is a trypomastigote in a Wright's stained buffy coat preparation from a naturally infected dog. Bottom image shows the amastigote stages in heart muscle.

Top specimen courtesy Dr. Stephen C. Barr.

In the vertebrate host, *T. cruzi* amastigotes (cells that contain a nucleus and a kinetoplast, but with either no or only a very rudimentary undulipodium) multiply by binary fission in reticuloendothelial, neural, and glial cells, and, most important, in cardiac and smooth muscle cells. Amastigotes released by rupture of the host cell change into trypomastigotes, which then appear in the circulating blood to invade other cells or to be ingested by the bug as it feeds. Trypomastigotes of *T. cruzi* are rarely, if ever, seen

dividing in blood smears prepared from circulating blood. The trypanosomes multiply and undergo metamorphosis in the bug's hindgut and are eventually passed in the feces that the bug almost invariably passes while feeding on its sleeping victim. Trypanosomes enter the body by going through the oral, nasal, and conjunctival mucosae or by infectious bug feces being rubbed into abrasions in the skin. Infection can also occur through the placenta or by blood transfusion, and accidental self-injection presents a potential hazard of infection to persons handling blood samples from infected animals, even those specimens in which trypomastigotes cannot be demonstrated in blood films. Trypomastigotes are difficult to demonstrate in the blood of long-term carriers, and one must turn to serology, culture, polymerase chain reaction (PCR), or xenodiagnosis for recourse. In xenodiagnosis, uninfected bugs are allowed to feed on the suspected individual, and their hindguts are later examined for trypanosomes, a cumbersome and inefficient procedure at best. In dogs, acute disease is characterized by lymphadenopathy and clinical signs associated with acute myocarditis: pale mucous membranes, lethargy, ascites, hepatomegaly, splenomegaly, and tachyrhythmia (Barr, 1991). The signs during the chronic stage of the disease are related to congestive myocardial failure. Megaesophagus and other megasyndromes described in humans with chronic Chagas' disease have not been reported in dogs.

Leishmania

Leishmania donovani and *Leishmania infantum* are the major causes of visceral leishmaniasis (kala-azar); *L. infantum* is often called *Leishmania chagasi* by many workers when discussing it in hosts in

the Americas. *Leishmania tropica* and related species causes several clinical forms of cutaneous leishmaniasis in humans, dogs, rodents, and wild mammals in Eurasia and Africa. *Leishmania mexicana* is a complex of species causing cutaneous lesions in the Americas that use various animal reservoir hosts. *Leishmania braziliensis* and related species cause mucocutaneous leishmaniasis in the Americas.

Leishmanial organisms live as amastigotes within macrophages throughout the body of the vertebrate host (Figure 3-3). The disease is spread by the bite a phlebotomine sandfly, with the important genera being *Phlebotomus* in the Old World (Africa and Eurasia) and *Lutzomyia* in the New World (the Americas). Europeans introduced visceral leishmaniases into the Americas during the period of colonization. The disease tends to be concentrated in areas around the Caribbean, in parts of sub-Saharan Africa, and in Brazil. Small pockets of the disease can be found in other parts of the world also.

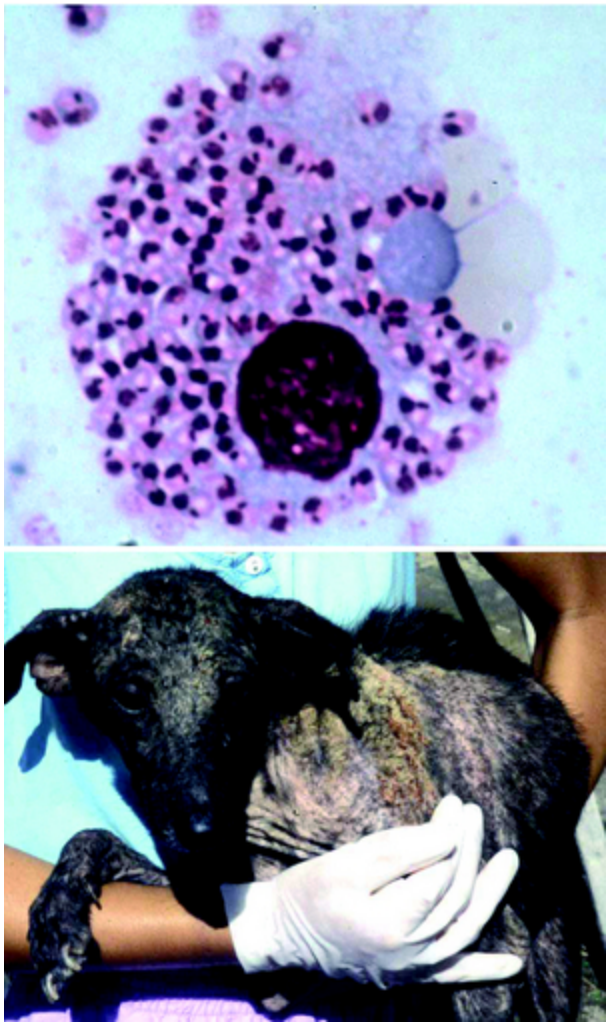

FIGURE 3-3 *Leishmania infantum*. Top image is a macrophage from bone marrow of an infected dog containing large numbers of amastigotes. Bottom image is a dog from Brazil infected with *L. infantum (L. chagasi)* showing typical cutaneous manifestation of a long-standing infection.

The stage in the macrophage of the vertebrate host is the amastigote. When an amastigote in a macrophage is ingested by the sandfly, which feeds on superficial tissues and juices of a host, the amastigotes differentiate into promastigotes. Within the fly the promastigotes multiply and produce very large numbers. Promastigotes migrate to the pharynx of the fly, and a few days later they reach the hypostome of the fly, where the promastigotes

are often in sufficient numbers to block the feeding ability of the fly. The process of development in the fly from infection to being infective takes about a week. The next time the fly bites, it will prick the skin and inject a number of promastigotes, and because the flies have difficulty feeding, they often remain hungry and feed more than when uninfected. The promastigotes will then be ingested by macrophages and carried throughout the body of the host.

Within the human host the macrophages serve to provide a means by which the parasite is disseminated throughout the body. The tissues most commonly found to harbor large numbers of parasites include the spleen, liver, bone marrow, intestinal mucosa, and mesenteric lymph nodes. The large numbers of organisms that can develop in the bone marrow can cause decreased red blood cell and platelet numbers. Dogs often also develop cutaneous lesions.

Autochthonous visceral leishmaniasis was reported in a colony of American foxhounds in Oklahoma (Anderson et al, 1982) and in a colony of English foxhounds in Ohio (Swenson et al, 1988). The Ohio outbreak involved one case of chronic illness and death, and positive serum titers in eight of 25 other colony dogs. Because the dead dog had been born and raised in the research colony and because more than a third of the other dogs in the colony carried titers, the authors concluded that transmission of the disease must have occurred in Ohio, most likely through the agency of an insect vector. In 1999 additional infections were reported from a group of working foxhounds kenneled at a hunt club in New York State. The initial presentation involved signs including bleeding, wasting, seizures, hair loss, and kidney failure. A number of the dogs died, and Dr. Breitschwerdt and colleagues at North Carolina State

University recovered *L. infantum* organisms from synovial fluid. Further testing of foxhounds from around the United States revealed that of 11,000 foxhounds in U.S. and Canadian hunt packs, some 12% had antibodies to *Leishmania* organisms, although most were without signs (Enserink, 2000). Infected dogs were found in 21 states in the United States and southern Canada, with most cases in the eastern portion of North America. It is unclear at this time how the infection is being spread between dogs, although it is being guessed that transmission is by means of sand flies when the dogs are taken to southern states for hunts. There are also a few cases of visceral leishmaniasis that have been reported to occur in dogs other than foxhounds that have never left the United States or Canada (Schantz et al, 2005).

Visceral leishmaniasis in dogs (see Figure 3-3) often is seen with cutaneous manifestations. Dogs are considered major reservoirs for human infections with this parasite and have been the targets of eradication programs similar to rabies control programs (Oliveira-dos-Santos et al, 1993). The need to develop a means of preventing canine infections on a large scale has resulted in attempts to develop vaccines that will prevent canine infections (Mayrink et al, 1996). Work has also shown that the routine monthly or biweekly spot-on application of imidacloprid and permethrin could prevent transmission in kenneled dogs in an area with a high prevalence in southern Italy (Otranto et al, 2007). Horses will also sometimes have cutaneous lesions, and horses in Puerto Rico have been found infected with this parasite (Ramos-Vara et al, 1996).

Autochthonous cases of cutaneous leishmaniasis are reported on occasion in animals from the United States. A case of dermal

leishmaniasis involving the ears of a domestic cat was reported from south-central Texas. Radical pinnectomy was performed before the cat was returned to its owners to prevent it from serving as a source of infection to sand flies (Craig et al, 1986). For both cutaneous and visceral leishmaniasis, cases are not uncommonly imported with dogs that have vacationed in areas where the diseases are enzootic. The only way to obtain the drugs for treatment is through the Centers for Disease Control and Prevention (CDC); therefore the CDC can maintain some form of surveillance on cases that are being diagnosed in the United States.

Parabasalia (Mucosoflagellates)

Trichomonads

Trichomonads are members of the protozoan phylum Parabasalia that are characteristically pear-shaped, with a single nucleus, and have a rodlike axostyle that protrudes from the more pointed posterior end. There are three to five anterior flagella and an undulating membrane with a trailing flagellum running along its free edge. Trichomonads do not have a cyst stage involved in their transmission between hosts. Special techniques are required for the differentiation of trichomonad genera on purely morphologic grounds, and currently the identification of species is aided by molecular comparisons. Therefore, practical diagnosis is based on host and site specificity and on the number of anterior and trailing flagella.

Tritrichomonas foetus (Figure 3-4) is found in the vagina, uterus, macerated fetus, prepuce, penis, epididymis, and vas deferens. The organism displays considerable pleomorphism, varies from 10 to 25

μm in length, and has three anterior flagella and a long, trailing flagellum that extends beyond the undulating membrane. In collecting samples to isolate *T. foetus*, it is important to avoid fecal contamination and consequent potential confusion with intestinal flagellates.

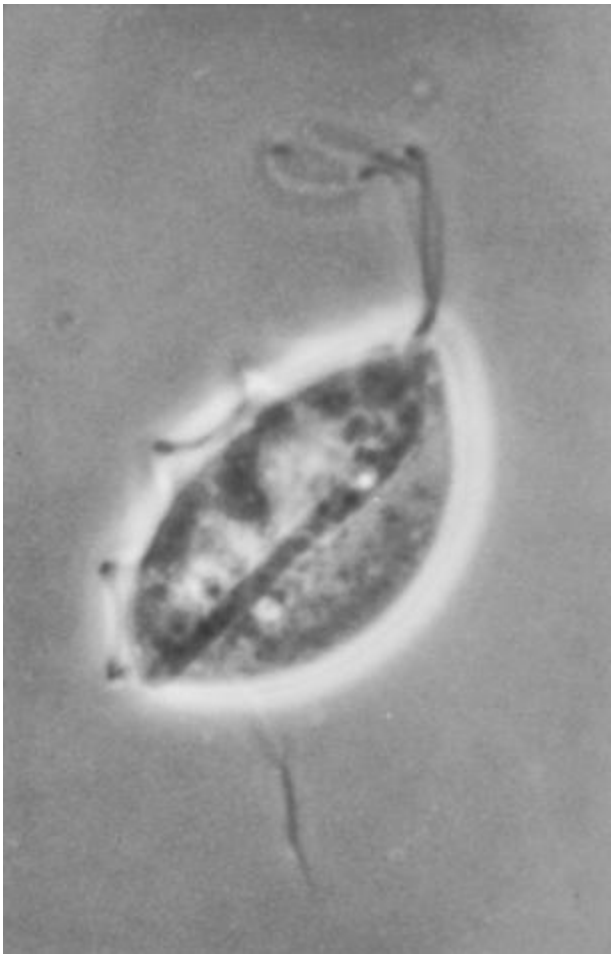

FIGURE 3-4 *Tritrichomonas foetus*. Electronic flash, phase contrast micrograph of living organism from a culture provided by Dr. S.J. Shin. The three anterior flagella, undulating membrane, trailing flagellum, and axostyle are clearly visible.

Bovine genital trichomoniasis is a venereal disease manifested in cows and heifers by infertility, abortion up to 5 months after breeding, pyometra, and occasional fetal mummification (Figure 3-

5). Infection in beef cattle remains relatively common in some parts of the United States; 16% of 57 herds sampled in California had at least one infected bull (BonDurant et al, 1990). Although infection is inapparent in bulls, *T. foetus* trophozoites can be demonstrated by direct microscopic examination or by culture of preputial swabs or washings. The infected bull is usually responsible for spreading trichomoniasis in the herd, and artificial insemination is recommended as a control measure when feasible. The *T. foetus* trophozoites are transferred from the penis to the vagina during copulation. However, semen is usually not infectious unless contaminated with preputial fluid during artificial collection. Semen contaminated in this way will remain infectious despite the addition of diluents, antibiotics, and freezing (Fitzgerald, 1986). Infected bulls should be culled, and in those situations in which artificial insemination is impractical, they should be replaced with younger, uninfected bulls. However, failure on the part of the artificial insemination technician to observe effective hygienic precautions in conducting vaginal examinations for the detection of estrus may totally negate the benefits of artificial insemination as a control measure (Goodger and Skirrow, 1986). *T. foetus* can usually be demonstrated in the vaginal secretions or washings of virgin heifers 14 to 20 days after service by an infected bull. Infected cows should be given at least 4 months of sexual rest, during which time *T. foetus* trophozoites usually disappear from the reproductive tract. Whether inseminated naturally or artificially, cows and heifers must first be given sexual rest so their reproductive tracts will be cleared of *T. foetus* before gestation begins; otherwise the infection will be perpetuated in the developing embryo (Fitzgerald, 1986). Diagnosis

has been aided by the use of the InPouch TF transport and culture kit, available from Biomed Diagnostics, San Jose, California (Parker, Campbell, and Gajadhar, 2003).

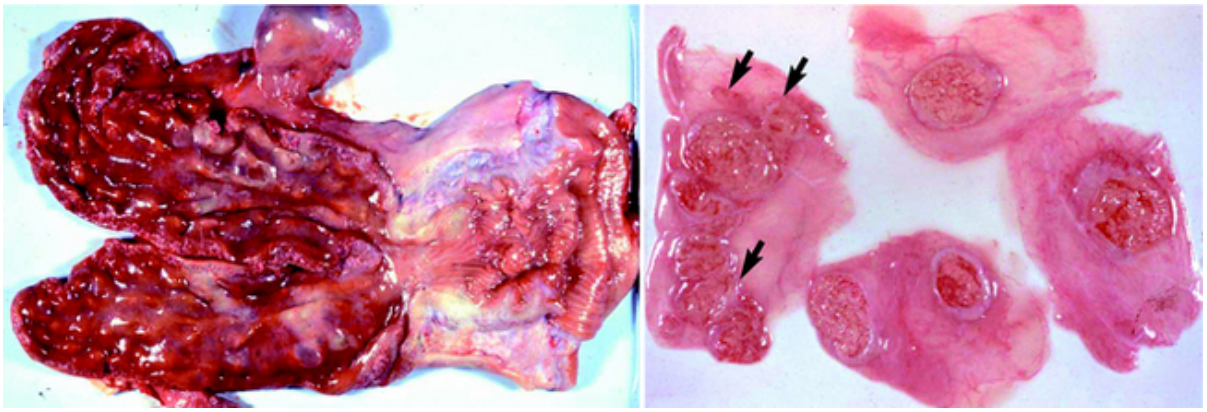

FIGURE 3-5 *Tritrichomonas foetus*. *Left*, Opened bovine uterus showing mild diffuse endometritis and inflammatory exudate in the form of a cloudy exudate on the endometrial surface. *Right*, Bovine chorioallantois. Cotyledons with placental edema; arrows indicate areas of adventitial placentation.

Romatowski (2000) described pentatrichomoniasis with diarrhea in four kittens. Gookin et al (1999) examined the effect of pentatrichomoniasis in a large number of cases and found most infections in cats younger than 1 year, with the feces being pasty to semiformed. More recently, Levy et al (2003) identified the agent causing diarrhea in cats to be *T. foetus* and have gone on to state that *T. foetus*, not *Pentatrichomonas hominis*, is the causative agent of feline trichomonal diarrhea. These authors have since shown (Gookin, Stauffer, and Levy, 2007) that a few cats infected with *T. foetus* are also occasionally infected with *P. hominis* that does not cause clinical signs. The diagnosis of this infection is also facilitated by the use of the InPouch TF transport and culture kit (Gookin et al, 2003).

Trichomonas vaginalis causes vaginitis in women; it is transmitted by sexual intercourse, with men playing the role of asymptomatic carriers. This is one of the more common sexually transmitted diseases of people around the world. *Trichomonas gallinae* causes necrotic ulcerations in the esophagus, crop, and proventriculus of pigeons, turkeys, and chickens and occasionally in hawks that are fed infected birds. *Trichomonas* species occur as oral parasites on various hosts and tend to multiply in the presence of pyorrhea, much as their intestinal counterparts multiply in the presence of diarrhea. Nonpathogenic species of *Tritrichomonas, Trichomitus, Tetratrichomonas*, and *Pentatrichomonas* occur in the cecum and colon of various domestic animals. These organisms tend to multiply in fluid feces, and many cases of diarrhea are mistakenly attributed to them for this reason. Their abundance in fluid feces is often the effect of and not the cause of the diarrhea. However, it is hard to ascertain whether they cause disease. *Monocercomonas* species resemble *Trichomonas* but lack an undulating membrane. *Monocercomonas* species are nonpathogenic; *Monocercomonas ruminantium* is found in the rumen of cattle.

Histomonas meleagridis is a cosmopolitan parasite of the cecum and liver of turkeys, chickens, pheasants, guinea fowl, and the like. The cecal nematode *Heterakis gallinarum* serves as transport host for *H. meleagridis*. When a bird ingests an infective *H. gallinarum* egg, it acquires a nonpathogenic nematode and a pathogenic protozoan parasite at one stroke. The protozoan, released from the nematode larva, spends about a week as a flagellate resident of the cecal lumen before it loses its flagella and invades the subepithelial tissues of the wall as an ameboid organism. Inflammation and

necrosis of the cecal wall and the liver are particularly severe and cause a high mortality in turkeys. *H. meleagridis* trophozoites discharged in bird droppings perish within hours, but they remain infective for years within the larvated eggs of *H. gallinarum* in soil. Earthworms serve as paratenic hosts for *H. gallinarum* larvae, and because birds like to eat them, they actually facilitate infection with both this nematode and its protozoan guest. The disease is typically of little consequence in chickens, but it can cause high mortalities in turkeys.

Treatment

For cattle, metronidazole administered intravenously at 75 mg/kg three times at 12-hour intervals is indicated for the treatment and control of *T. foetus* infections in cows. *Trichomonas* infections in puppies may be controlled with metronidazole administered orally at 66 mg/kg once daily for 5 consecutive days (Buckner and Ewing, 1977). Romatowski (2000) treated cats with both metronidazole and enrofloxacin and suggested that the long-term daily administration of enrofloxacin stopped the soft stools. Gookin and colleagues (2006) showed ronidazole and tinidazole to be of significant benefit in the treatment of intestinal trichomoniasis in cats. However, the drug should be used with caution because there have been some neurologic signs developing in cats treated with ronidazole, although ultimately the infection and diarrhea were resolved after treatment (Rosado, Specht, and Marks, 2007).

Diplomonada (*Giardia* and relatives)

Giardia

The number of species of *Giardia* that exist is open to question, and the names of species in current usage are in a state of flux (Thompson et al, 2000; Bowman, 2005). The species in people currently has been called *Giardia lamblia, Giardia duodenalis, Giardia intestinalis*, or *Giardia enterica*. There are some species that are recognized as distinct, e.g., *Giardia muris* in mice, *Giardia agilis* in amphibians, and *Giardia psittaci* in birds. Currently based on molecular biology, the groups of *Giardia* are discussed in terms of assemblages. In most cases, when *Giardia* is isolated from a host and examined via molecular methods, the association is such that assemblages A and B are considered to be mainly those found in human beings, assemblages C and D make up the majority of organisms found in dogs, assemblage E makes up the group most typically found in hoofed stock (cattle, sheep, goats, pigs, horses, and so on), assemblage F consists of the forms from cats, and assemblage G represents the form from rats. Sometimes assemblage A may be found in a cat (Vasilopulos et al, 2007) or a dog (Hopkins et al, 1997). This should be a simple and boring academic question, but it unfortunately is currently a major point of confusion and discussion. A few years ago we considered almost all the isolates to be zoonotic, but we were not very good at detecting the infection. Now, with improved diagnostics that detect cyst wall proteins as antigens in the feces and increased awareness of the fact that *Giardia* can cause disease, the question is very commonly whether or not to treat the asymptomatic dog, cat, pony, calf, goat, and so on. Do you sell a puppy if it is shedding *Giardia* cysts in its feces? Can a shelter adopt out an infected kitten? In a survey from around the United States using the IDEXX SNAP test, some 15% of dogs and

10% of cats were shedding antigen in their feces (Carlin et al, 2006). Also, about 7% of the world's human population harbors *Giardia* in the small intestines, but little is known about the epidemiology of this organism, especially with regard to the possible role of other mammals as sources of human infection. It seems that animals can sometimes be shedding A and B and thus may be a source of zoonotic infection to humans; however, it also appears that usually people get infected with *Giardia* from other people. However, members of the public would prefer to blame animals rather than their associates.

Giardia trophozoites are adapted for attachment to the mucous epithelial cells of the small intestine (Figure 3-6). The *Giardia* trophozoite is shaped like a teardrop (see Figure 3-6), with one side pushed in to form a sucking disc. Within the cell are two nuclei, each with a large endosome (Feulgen-negative nucleolus) that makes the organism look like a tennis racket with eyes when viewed bottom side up under the compound microscope. Other subcellular structures include two slender axonemes, four pairs of flagella, and a pair of median bodies. All of the other intestinal flagellates are found in the cecum and colon, but *Giardia* parasitizes the small intestine, in which the trophozoites attach to the mucosal cells by their sucking discs. Trophozoites usually form infective cysts before passing out with the feces. The mature cyst containing two potential trophozoites is the form usually found in the feces of infected hosts (see Figure 3-6). Although trophozoites may also be passed, especially with diarrheal stools, they are incapable of causing infection and soon die; if they go into fresh water they will lyse owing to their inability to osmoregulate.

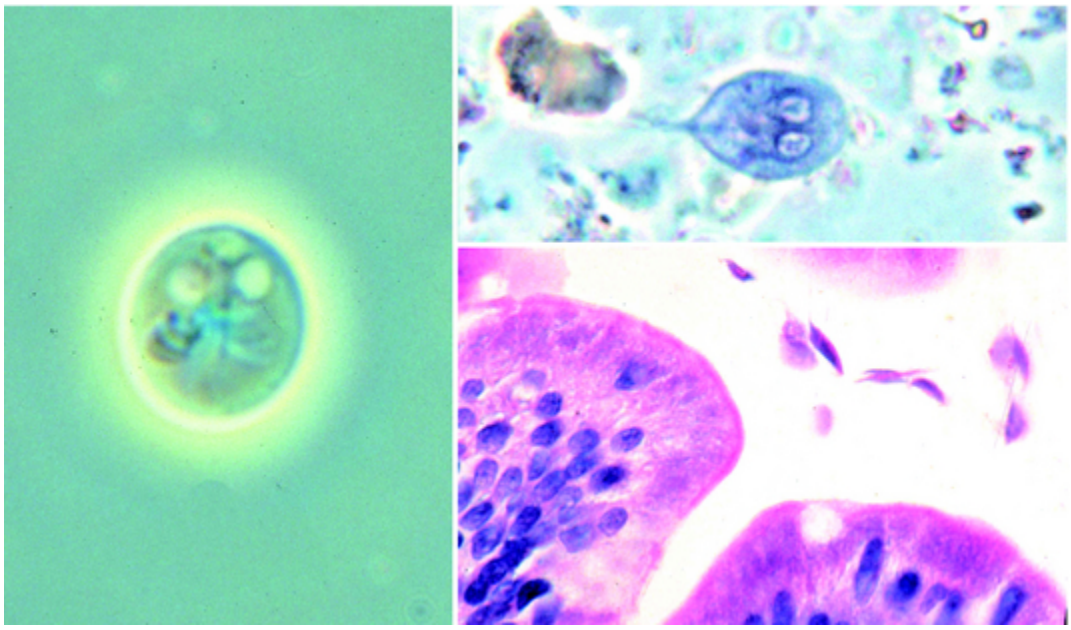

FIGURE 3-6 *Giardia*. *Left*, Cyst passed in feces. Phase contrast micrograph showing two of the four nuclei near the top of the image. *Top right*, *Giardia* trophozoite in trichrome-stained fecal smear. *Bottom right*, Section through intestinal mucosa of an infected animal with detached trophozoites present within the lumen.

In dogs, diarrhea may begin as early as 5 days after exposure to infection (Abbitt et al, 1986); cysts first appear in the feces after about a week or two. In cats, *Giardia* trophozoites are found in the jejunum and ileum instead of the duodenum. The principal clinical sign is persistent diarrhea resulting from intestinal malabsorption; the feces of infected cats are often mucoid, pale, soft, and more than usually malodorous (Kirkpatrick, 1986). In calves, *Giardia* was associated with chronic diarrhea marked by high morbidity, negligible mortality, absence of response to electrolytes and antibiotics, and clinical and parasitologic response to dimetridazole within 48 hours (St Jean et al, 1987). In lambs the careful examination of production parameters in bottle-reared and experimentally infected animals showed that neonatal giardiasis caused extended times for lambs to reach slaughter weight and

decreased carcass weight (Olson et al, 1995). The enumeration of cysts in the feces of ewes around lambing time revealed that there was a periparturient increase in cyst production by ewes that peaked between the time of lambing and 4 weeks afterward (Xiao, Herd, and McClure, 1994). In an outbreak in central Italy, lambs with naturally acquired giardiasis developed a malabsorption syndrome, decreased weight gain, and impaired feed efficiency that responded to treatment with fenbendazole at 10 mg/kg for 3 days (Aloisio et al, 2006) *Giardia* infection in humans may be inapparent or may cause severe enteritis.

Diagnosis

Trophozoites may be demonstrated in direct smears of diarrheal feces (see Figure 3-6); trophozoites often cannot be demonstrated in formed stools. Cysts (see Figure 3-6) may be concentrated by fecal flotation in zinc sulfate of specific gravity 1.18 but tend to shrink and become distorted beyond recognition in sucrose and other flotation media. Phase contrast microscopy is helpful in identifying *Giardia* trophozoites and cysts. If phase contrast microscopy is unavailable, a drop of Lugol's solution of iodine at the edge of the coverslip will stain the trophozoites and cysts and make them easier to identify by increasing the contrast of the nuclei within the organisms. *Giardia* cysts are frequently found in the normal stools of asymptomatic hosts, but in occasional cases of clinical giardiosis neither cysts nor trophozoites can be found in the feces. There are several antigen detection kits that are designed for use on the feces of animals and people (Garcia and Shimizu, 1997), and the IDEXX SNAP test is now used in-house routinely by veterinarians (Carlin et al, 2006).

Treatment

Dogs may be treated for giardiasis with fenbendazole at the same dosage used for helminths (Barr, Bowman, and Heller, 1994; Zajac et al, 1998). Dogs have also been treated with a combination febantel-pyrantel-praziquantel (37.8 mg/kg, 7.56 mg/kg, 7.56 mg/kg, respectively) product for 3 days withsuccessful clearance of cysts from most dogs (Payne et al, 2002). Treatment with albendazole (25 g/kg every 12 hours for a total of four doses) has been shown to stop the shedding of *Giardia* cysts by infected dogs (Barr et al, 1993). Albendazole therapy has the potential of inducing bone marrow toxicosis in dogs and cats; therefore veterinarians should observe caution in using this drug for treating giardiasis (Stokol et al, 1997). Other treatments that have been used for canine giardiasis include quinacrine (6.6 mg/kg twice a day for 5 days), metronidazole (22 mg/kg orally twice a day for 5 days), and tinidazole (44 mg/kg once daily for 3 days) (Zimmer and Burrington, 1986).

Giardia infections in cats may be treated safely and effectively with metronidazole, 22 to 25 mg, orally twice a day for 5 to 7 days (Scorza and Lappin, 2004; Zimmer, 1987). Cats have also been successfully treated with a combination of febantel (37.8 mg/kg), pyrantel (7.56 mg/kg), and praziquantel (7.56 mg/kg) for 5 days (Scorza, Radecki, and Lappin, 2006).

There are vaccines for *Giardia* from Fort Dodge Animal Health, the canine GiardiaVax and feline Fel-O-Vax *Giardia* that are approved for use in preventing giardiasis in dogs in the United States and for which prelaunch efficacy data were submitted to the U.S. Department of Agriculture (USDA) as part of the approval package

(Olson et al, 2000). Unfortunately, the efficacy of these vaccines is questioned by many veterinarians in the field; the majority of veterinarians find them of little value, but a number believe the vaccines efficacious. Trials of the effects of the administration of these vaccines on the clearance of dogs and cats with existing infections have failed to eliminate the organisms from the feces of these animals (Anderson et al, 2004; Payne et al, 2002; Stein et al, 2003).

Fenbendazole and albendazole administered to calves at varying doses for different periods have both been proved efficacious against *Giardia* (O'Handley et al, 1997; Xiao, Saeed, and Herd, 1996). For fenbendazole, all treatments with a single dose of 10 mg, with 10 or 20 mg administered daily for 3 days, or with 0.833 mg administered daily for 6 days were effective. For albendazole, a dose of 20 mg administered daily for 3 days was effective.

Dimetridazole was administered orally to infected calves in 250 mL of water at a dosage of 50 mg/kg for 5 days. The feces of calves administered dimetridazole were cleared of cysts and their diarrhea stopped within 48 hours (St Jean et al, 1987).

For treatment of giardiasis in parakeets, three doses of dimetridazole at 1.5 mg/30 g of body weight at 12-hour intervals by stomach tube were more effective than supplying drinking water containing 200 ppm of this chemical to the birds for 5 days. Metronidazole therapy was not effective (Scholtens, New, and Johnson, 1982).

Control of *Giardia* infection involves prevention of fecal contamination of feed and water supplies and sanitation and

disinfection of the environment with Lysol (2% to 5%), Sterinol (1%), or chlorine bleach (sodium hypochlorite, 1%) (Kirkpatrick, 1986).

Rhizopoda (Amebas)

Intestinal Amebas

Entamoeba histolytica is principally a parasite of the large intestine and causes amebic dysentery in humans, an endemic disease of the tropics that occurs sporadically in the temperate regions. Amebic abscess of the liver is a serious, frequently life-threatening sequela. Humans also host a few nonpathogenic amebas *(Entamoeba dispar, Entamoeba hartmanni, Entamoeba coli, Iodamoeba buetschlii*, and *Endolimax nana)*, some of which are shared with domestic animals. *E. histolytica* and other amebas appear to cause little if any harm to domestic animals. Amebic trophozoites and cysts frequently appear in fresh fecal smears of perfectly healthy cattle, sheep, goats, horses, and swine but are usually overlooked. These have been described in the past as separate species (e.g., *Entamoeba bovis* and *Entamoeba ovis*) but have received almost no attention in recent years.

However, special cases exist in which amebas are of clinical importance, notably in primates. For example, a case of gastric amebiasis characterized by anorexia, diarrhea, and weight loss was reported in the silvered leaf monkey (*Presbytis cristatus;* Palmieri, Dalgard, and Connor, 1984). The normal high pH level (5.0 to 6.7) of the stomach of leaf monkeys and the stress of capture, shipment, and confinement were considered to have contributed to the extensive gastric involvement observed. *Entamoeba invadens* causes severe disease and death in captive reptiles. For example, 200 of

500 red-footed tortoises *(Geochelone carbonaria)* imported into southern Florida died over a period of 2 months, showing signs of anorexia, listlessness, and diarrhea. Necropsy examination revealed necrosis of the duodenal mucosa and multifocal hepatic necrosis. Amebas were found in both duodenal and hepatic lesions histologically (Jacobson, Clubb, and Greiner, 1983).

The parasitic amebas reproduce asexually, usually by binary fission. Actively parasitic forms, called *trophozoites*, display ameboid motion when recovered from fresh feces and kept at body temperature. Most species form cysts, which in certain cases are multinuclear. Trophozoites are more likely to be found in fluid feces, and cysts in formed feces.

Treatment of *Entamoeba histolytica* infections

Little is known about the treatment of canine amebiasis. In humans, metronidazole is the drug of choice in the treatment of intestinal and hepatic amebiasis and is therefore a logical choice for treating canine amebiasis. Roberson (1977) suggests oral administration of 50 mg of metronidazole per kilogram body weight daily for 5 days.

Facultative Amebiasis

Facultative amebas are free-living most of the time but can cause serious disease if they enter human hosts. These pathogens are best known for causing disease in humans (e.g., fulminate primary amebic meningoencephalitis [*Naegleria fowleri*, mainly], chronic amebic encephalitis [*Acanthamoeba culbertsoni* and other species; Figure 3-7], and acanthamoeba keratitis) (Barnett et al, 1996; Schaumberg et al, 1998; Schuster and Visvesvara, 2004; Sell et al, 1997). However, cases of amebic encephalitis have been reported

from other animals, including dogs, gibbons, sheep, cattle, beavers, and tapirs (Kinde et al, 2007; Lozano Alarcon et al, 1997; Morales et al, 2006). The ameba, *Balamuthia mandrillaris*, was found to cause disease in a mandrill from the San Diego Zoo (Visvesvara et al, 1993). This parasite has also killed gorillas, an orangutan, a horse, and dogs (Canfield et al, 1997; Finnin et al, 2007; Foreman et al, 2004; Kinde et al, 1998, 2007; Rideout et al, 1997). Human cases have also been reported (Deol et al, 2000; Tavares et al, 2006).

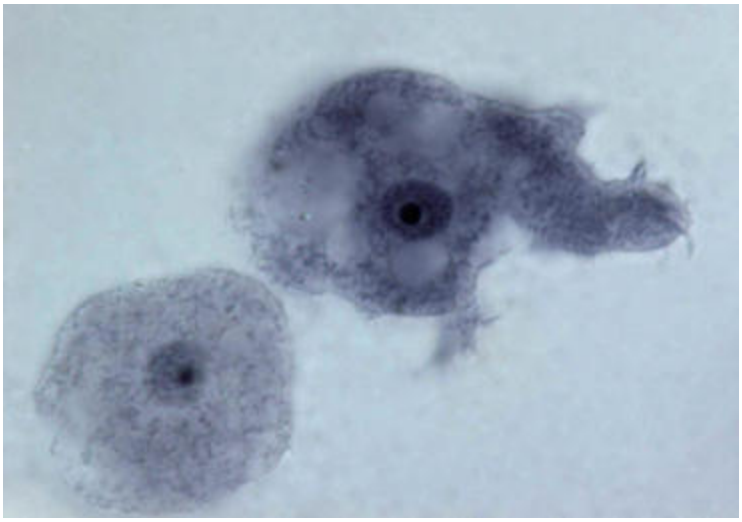

FIGURE 3-7 *Acanthamoeba* trophozoites from culture. Note the filamentous pseudopods and the large central karyosome within the nucleus.

CILIOPHORA (CILIATES)

Balantidium coli

B. coli, a normal element of the intestinal fauna of the pig and rat, is very large as single cells go, measuring up to 150 μm in length (Figure 3-8). The cell surface is covered with cilia (sing., cilium) arranged in rows with a tuft of longer ones surrounding the peristome, or "cell mouth." Prominent organelles include a large

macronucleus, a smaller micronucleus, two contractile vacuoles, and a number of food vacuoles in the cytoplasm. *B. coli* reproduces by transverse fission and forms cysts up to 60 μm in diameter.

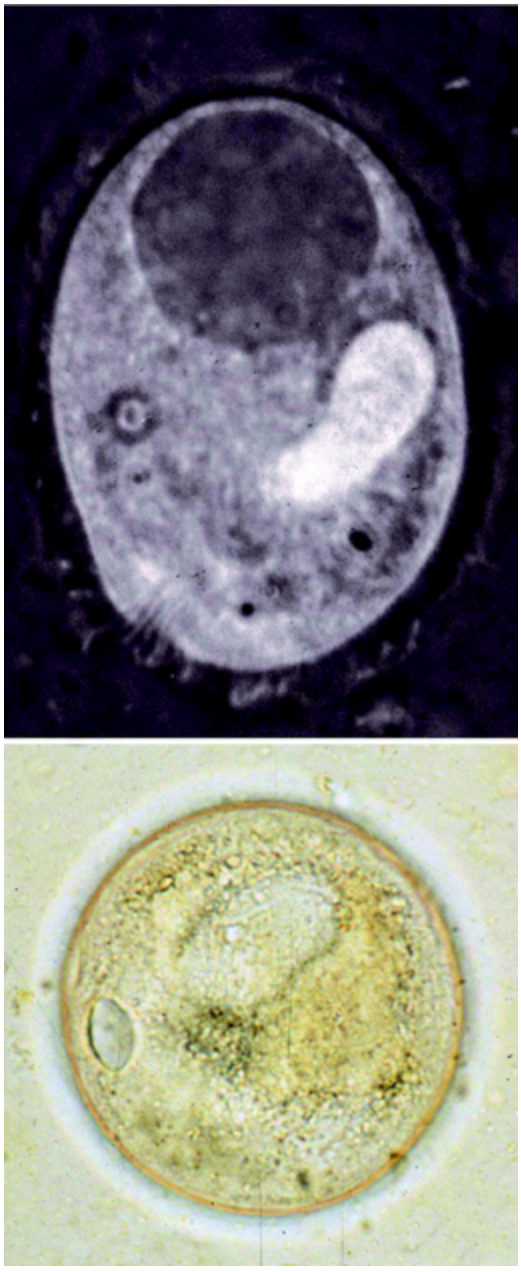

FIGURE 3-8 *Balantidium coli*. *Top*, Trophozoite (electronic flash photograph) of motile ciliate. *Bottom*, Cyst. Trophozoites abound in the large intestine of normal swine, and cysts are passed in their feces. *B. coli* has been incriminated in human colonic disease ranging from mild colitis to an ailment resembling amebic dysentery.

Although harmless to the pig and usually harmless to humans, *B. coli* occasionally causes ulceration of the human large intestine, manifested clinically as diarrhea and occasionally as dysentery (diarrhea with abdominal pain, straining, and blood and mucus in the stools). Diagnosis of *B. coli* infection is based on the demonstration of motile trophozoites in direct smears of diarrheal feces or cysts in flotation preparations of formed feces. Acute enteritis characterized by watery diarrhea and lethargy involving four gorillas in the Los Angeles Zoo was attributed to *B. coli* infection (Teare and Loomis, 1982). Lowland gorillas affected with balantidiasis did not accept metronidazole well and were treated with intramuscular injections of dehydroemetine dihydrochloride (Gual-Sill and Pulido-Reyes, 1994).

Symbiotic Ciliates

The forestomachs of ruminants and the ceca and colons of horses abound with large, somewhat bizarre ciliates that are neither pathogenic nor indispensable to their hosts (Figure 3-9). Sometimes they are found in the lungs of ruminants at necropsy, the result of agonal inspiration of ruminal contents and nothing more.

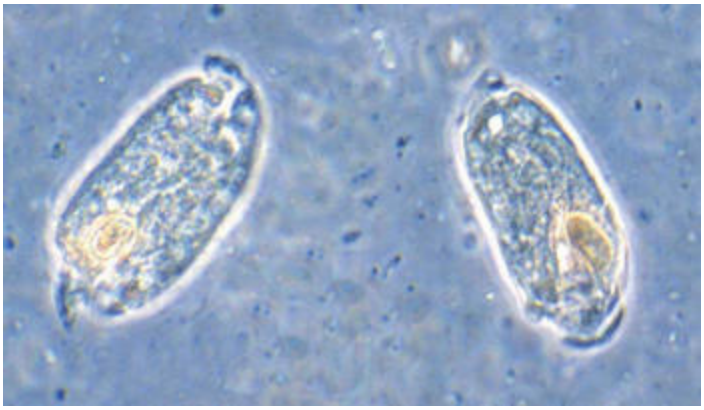

FIGURE 3-9 Ciliates from the large intestine of a horse.

APICOMPLEXA

The Apicomplexa (Sporozoa) of interest to us are all obligate intracellular parasites that cause disease by destroying their host cells. The most important members are the coccidians, many of which develop in epithelial cells of the alimentary canal and cause a form of enteritis called *coccidiosis*, and the hemosporidians, which develop in erythrocytes and cause hemolytic anemia. Coccidians are transmitted mainly by fecal contamination and reproduce by rigid sequences of asexual and sexual phases of multiplication and development that, in an important minority of cases, require an alternation of hosts. Hemosporidians are transmitted by bloodsucking arthropods and include the piroplasms, which are transmitted by ixodid ticks, and the plasmodia, which are transmitted by dipterans, in which they complete the sexual phases of their life histories.

Coccidians

The functional unit of coccidian ontogeny is the zoite, a motile, banana- or cigar-shaped cell, rounded at one end and pointed at the other (apical) end (Figure 3-10). It is the zoite that migrates in the host and invades cells, and it is the zoite that represents the beginning and end point of every coccidian life process. Relationship to a particular portion of the life history is denoted by a prefix. Thus, sporozoites are infective forms found in sporulated oocysts (pronounced “oh’oh-sists”); sporozoites are the result of the reduction divisions that occur in the oocyst that is the result of fusion of gametes. Sporozoites invade host cells, in which they form many merozoites by a kind of multiple internal fission called

schizogony (pronounced “ski-zog o-ne”; synonym, merogony); tachyzoites divide rapidly, bradyzoites divide slowly, and so on. The genera *Eimeria, Cystoisospora, Hammondia, Sarcocystis*, and *Toxoplasma* present an orderly sequence of increasing biologic complexity and therefore are taken up in that order.

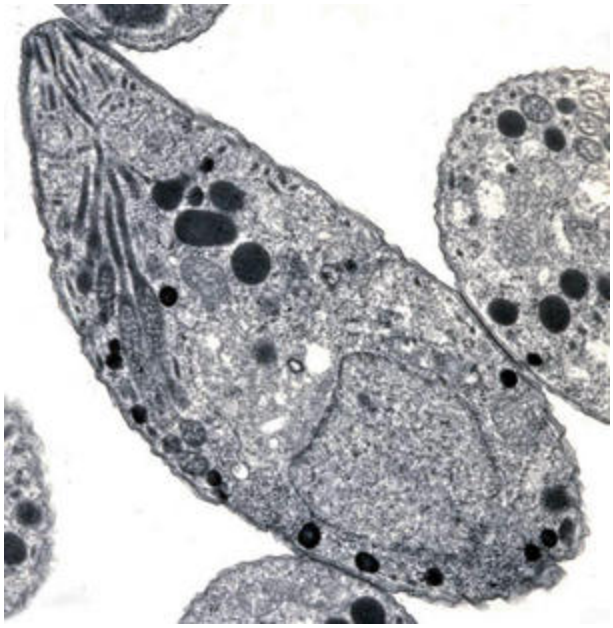

FIGURE 3-10 Tachyzoite of *Toxoplasma gondii* from a mouse.

TEM courtesy of Dr. John F. Cummings.

Eimeria

The general form of coccidian life history is represented by the genus *Eimeria*, species of which are gastrointestinal parasites of a wide range of vertebrate hosts. This life history includes both asexual multiplication and sexual multiplication. Sexual multiplication culminates in the formation of oocysts, which are discharged with the feces, and in the development, within each of these oocysts, of eight infective organisms, sporozoites. The life history of *Eimeria* should be learned by heart because it serves as a

basis for all of the other coccidians. Figure 3-11 may prove helpful in mastering the following details.

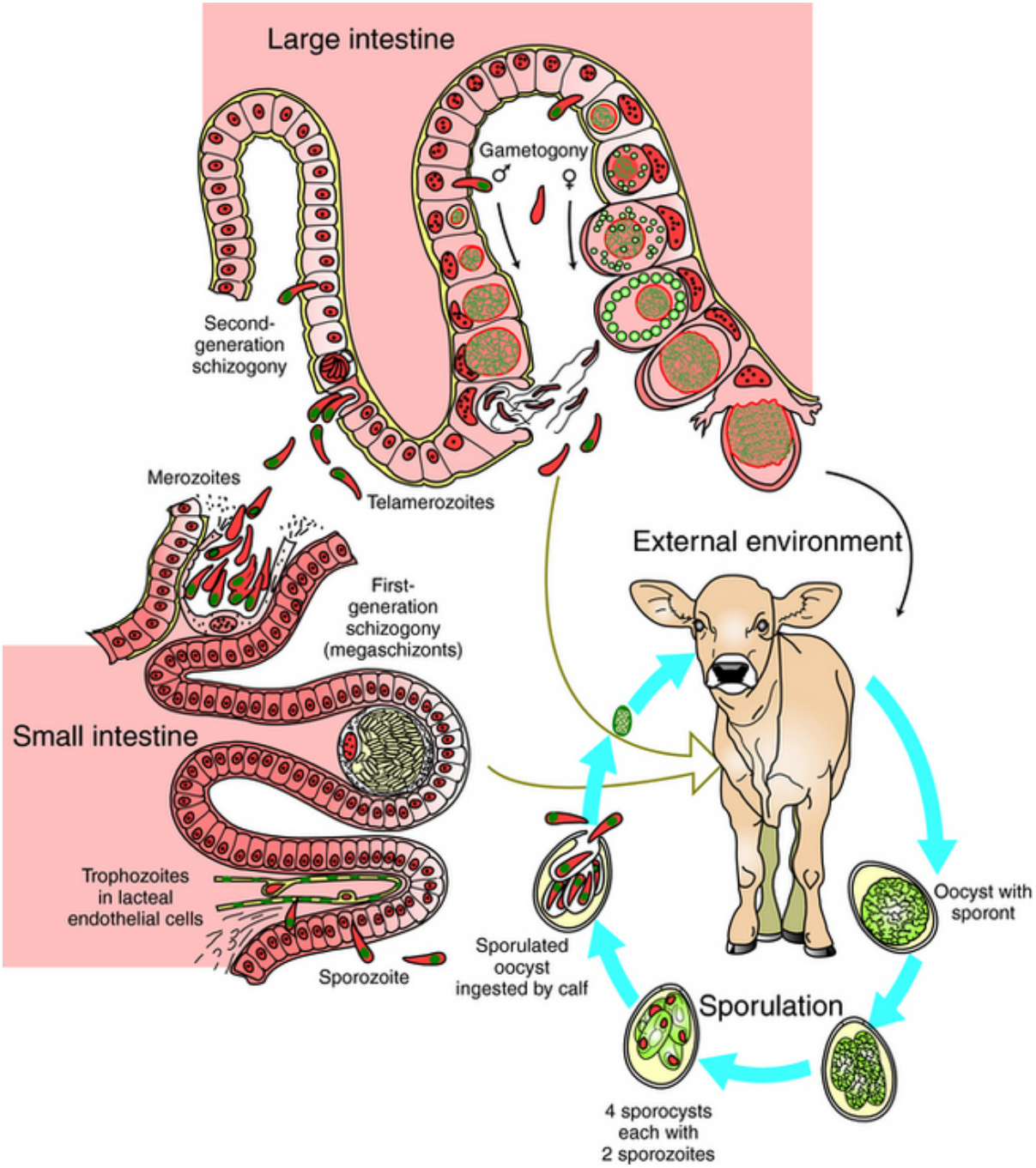

FIGURE 3-11 Life history of *Eimeria bovis*. The detail of eimerian ontogeny are set forth in the text. *E. bovis* first-generation schizonts are megaschizonts and develop in central lacteal cells of the small intestine. Second generation schizogony and gametogony

occur in epithelial cells of the large intestine. Clinical signs are associated with the large intestinal phase of the infection.

Schizogony (merogony)

If the infective, sporulated oocyst is ingested by a suitable host, the sporozoites emerge, and each may enter an epithelial or lamina propria cell, round up as a trophozoite, grow larger, and become a first-generation schizont (pronounced “skiz ont,” [meront]). The trophozoite, schizont, and all other intracellular stages of *Eimeria* are surrounded by a membrane-lined parasitophorous vacuole in the host cell cytoplasm or, in some cases, nucleoplasm. This schizont produces first-generation merozoites that burst the cell and invade fresh cells to become second-generation schizonts. There may be several more schizogonic generations, but two or three are the limit for many of the important species of *Eimeria*. The number of asexual generations, the type and location of the host cells parasitized, and the number of merozoites formed at each generation depend on the species of coccidium in question. The salient attributes of schizogony are (1) an exponential increase in the number of zoites arising from a single sporozoite, (2) destruction of host cells in proportion to the degree of infection, and (3) automatic suspension of the asexual process after a fixed number of repetitions.

Gametogony

A merozoite produced by the final schizogony (i.e., a telomerozoite) enters a fresh host cell and develops into either a male or a female (microgamont or macrogamont, respectively) or developing sex cell. The female macrogamont enlarges, stores food materials, and induces hypertrophy of both cytoplasm and nucleus of its host cell.

When mature, it is called a *macrogamete* or *female sex cell*. The male microgamont undergoes repeated nuclear division and becomes multinucleate. Each nucleus is finally incorporated into a biflagellate microgamete or male sex cell. Of the many microgametes formed by the microgametocyte, only a small fraction finds and fertilizes macrogametes to form zygotes. A wall forms around the zygote by the coalescence of hyaline granules at its periphery to form an oocyst.

Sporogony

The oocyst is released by rupture of the host cell and passes out with the feces to undergo sporulation. Within a day or two, if provided with adequate moisture, moderate temperatures, and sufficient oxygen, the single cell (sporont) in the oocyst divides into four sporoblasts. Each sporoblast develops into a sporocyst, which contains two haploid sporozoites, thus becoming an infective, sporulated oocyst and completing the cycle (Figure 3-12). The life history of *Eimeria* is presented again in schematic form in Figure 3-13.

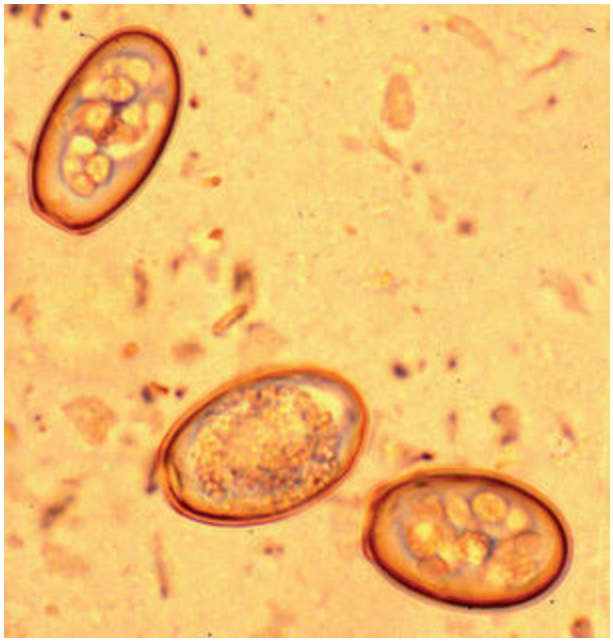

FIGURE 3-12 *Eimeria magna* oocysts, sporulated, from the feces of a domestic rabbit.

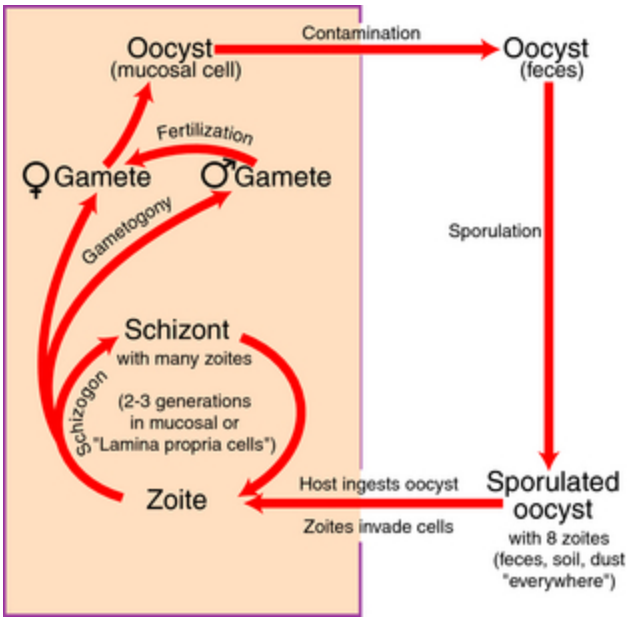

FIGURE 3-13 Life history of a typical *Eimeria* species.

Cystoisospora

The common canine and feline coccidia used to be placed in a genus called *Isospora* ("i-sos por-rah"). Recently, there was a taxonomic revision of the names and species, and the genus *Isospora* was shown to represent species in birds that are relatives of the Eimeriidae (Barta et al, 2005). The species affecting dogs and cats, now called the *Cystoisospora*, are species parasitic in carnivores and related to other genera—*Hammondia, Toxoplasma, Besnoitia*, and *Sarcocystis*—that have similar sporulated oocysts and typically use carnivores or omnivores as a final host (Figure 3-14). In the case of *Cystoisospora*, the sporont develops into two sporoblasts with two resulting sporocysts that each contain four sporozoites. The life history of *Cystoisospora felis*, for example, resembles that of *Eimeria bovis* except that its sporozoites may encyst (singly without any multiplication) in the tissues of a mouse or bird. As Figure 3-15 indicates, a cat may become infected with *Cystoisospora felis* by ingesting either sporulated oocysts or sporozoite-infected mice. In this case the mouse thus serves as a facultative paratenic host for *Cystoisospora felis*.

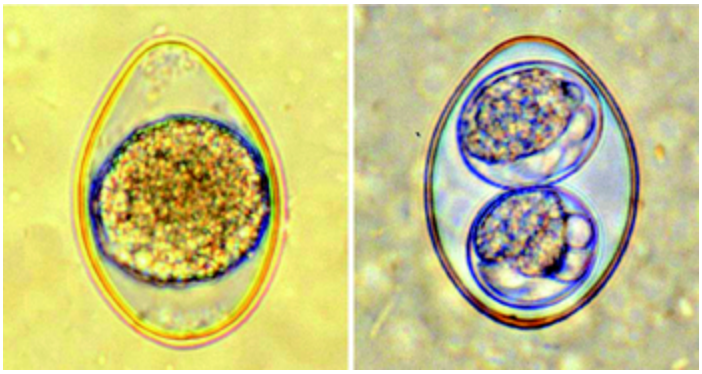

FIGURE 3-14 *Cystoisospora felis* unsporulated oocyst *(left)* and sporulated oocyst *(right)*.

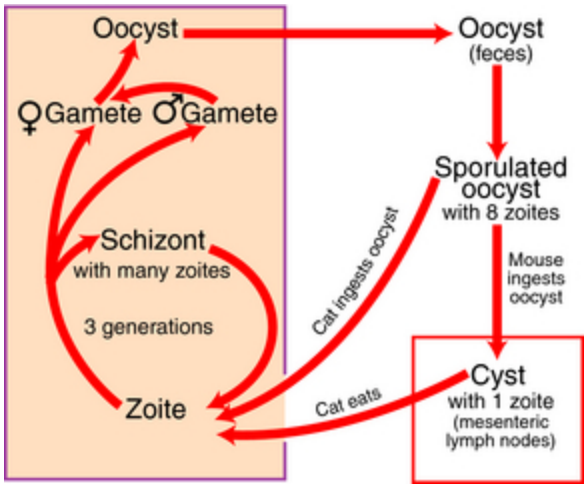

FIGURE 3-15 Life history of *Cystoisospora felis*.

Enteric coccidiosis

A particular species of *Eimeria* or *Cystoisospora* tends to be restricted to a narrow range of hosts, but each host species may be parasitized by a number of different species of coccidians simultaneously. Antemortem diagnosis of coccidian infection (i.e., coccidiosis) is based on identification of oocysts in the host's feces. Host specificity and the form of the oocyst usually suffice for identification to the species level, but micrometry and sporulation of the oocysts must occasionally be resorted to in order to distinguish among certain species (see Chapter 7). Postmortem diagnosis is based on gross and microscopic lesions, which vary considerably with the host and parasite species involved, and on the demonstration of the sexual or asexual stages of the parasites. Schizonts, gamonts, oocysts, and intermediate stages lie surrounded by their parasitophorous vacuoles in the cytoplasm (or nucleus, in a few cases) of enterocytes, lamina propria cells, or endothelial cells of the central lacteal of the villus. Although these are most elegantly displayed by histologic techniques, direct smears or squash preparations are just

as dependable as hematoxylin and eosin (H&E) slides and are quicker and less expensive. Oocysts and merozoites can often be demonstrated in smears or concentrates of the intestinal contents. Contrast microscopy or staining with Wright's or Giemsa stain is helpful in demonstrating sporozoites.

It is important to understand that the mere identification of coccidian oocysts in the feces of a host does not justify a diagnosis of the disease coccidiosis unless the history and clinical signs are in accord. Large numbers of oocysts may be counted in the feces of perfectly healthy hosts, and surveys reveal prevalence rates on the order of 30% to 50% in a wide range of host species. On the other hand, severe and even fatal coccidiosis sometimes occurs during the early asexual stages of infection before oocysts have had time to develop. In such cases, disease is manifest, but oocysts have not yet appeared in the feces. Chronic diarrhea is the cardinal sign of coccidiosis and results from the destruction of intestinal epithelium by hordes of multiplying organisms. Diarrhea has many causes, only one of which is coccidian infection, so the diagnosis of coccidiosis is always uncertain in individual cases. In other words, diarrhea plus oocyst shedding does not infallibly equal coccidiosis. However, as regularly recurring episodes of illness characterized by diarrhea in successive populations of young puppies, kittens, calves, lambs, kids, piglets, chicks, ducklings, poults, or other domestic or wild animals, outbreaks of coccidiosis become predictable events and leave the diagnostician in little doubt as to the cause. Given a closed breeding colony with reasonably steady environmental conditions, clinical coccidiosis will regularly appear in each new wave of young

mammals or birds unless effective prophylactic measures have been exercised.

It is often repeated that coccidian infection is self-limiting, implying that the population of infecting organisms grows to a maximum and then more or less abruptly fades away to extinction or to a low level as the host develops immunity. Small numbers of oocysts may be shed in the feces for several weeks or even months, but infection remains otherwise inapparent. Should the now relatively immune host be exposed to a different species of coccidian, the same pattern will be repeated. Thus immunity to coccidian infection tends to be highly specific and reasonably protective but incomplete. Some animals shed oocysts while remaining healthy for months or years. Such animals have sufficient protective immunity to limit but not exclude infection in the presence of continued exposure.

The disease coccidiosis results from either overwhelming infection or the interaction of moderate levels of infection and stress. The level of environmental contamination with oocysts is best affected by removing all manure and getting all surfaces as clean as feasible. There is no reliable and practical disinfectant. Drying and direct sunlight are most effective in destroying oocysts when these agents happen to be available. Administration of anticoccidial drugs (coccidiostats) during exposure of young susceptible animals permits infection to occur and immunity to develop but limits infection sufficiently to abort disease. Such drugs are virtually indispensable to intensive systems of poultry, goat, cattle, sheep, dog, and cat production.

Dogs and cats

True infection of dogs and cats with species of *Cystoisospora* must be distinguished from pseudoparasitism arising from the various gustatory habits of these hosts. A dog with a history of recurrent diarrhea and oocyst shedding seems like an "open-and-shut case" until the oocysts turn out to belong to a parasite of the squirrel *Sciurus carolinensis*. It would then seem that dietary indiscretion and not protozoan infection is probably to blame for the diarrhea. In fact, almost all puppies and kittens experience infection with *Cystoisospora* at some time during the early months of their lives. More than once I have observed *Cystoisospora* oocysts in the feces of puppies and kittens raised in elaborately controlled gnotobiotic colonies, and infection always occurs in well-managed colonies in which less stringent levels of sanitation are practiced.

Cystoisospora canis, Cystoisospora ohioensis, and *Cystoisospora burrowsi* in dogs and *Cystoisospora felis* and *Cystoisospora rivolta* in cats are the species most commonly involved in coccidian infection and disease in these hosts. Clinical signs may precede oocyst shedding in particularly acute infections. Diarrhea is copious and watery and may persist for several weeks. Response to treatment is seldom dramatic.

Cattle

All calves experience infection with one or more species of *Eimeria* during their first year of life, so finding a few oocysts in the diarrheal feces of a sick calf does not itself justify a diagnosis of coccidiosis. However, authentic outbreaks of coccidiosis do occur, especially in cattle up to 2 years of age, and these outbreaks are

most often attributed to either *Eimeria zuernii* or *Eimeria bovis*. Both of these species undergo two asexual cycles; the first culminates in the formation of schizonts in the lamina propria cells *(E. zuernii)* or endothelial cells of the lacteals *(Eimeria bovis)* of the villi of the lower ileum. The megaschizonts of *Eimeria bovis* are macroscopically visible (about 250 μm) and contain more than 100,000 merozoites. The schizonts of *E. zuernii* are unobtrusive because of their small size and deeper location. The second-generation schizonts are microscopic and occur in the epithelial cells of the cecum and colon, which is also the site of gametogony. The onset of clinical signs coincides with the beginning of gametogony and results from the mechanical disruption of mucosal cells by the sexual stages. In severe cases, so few epithelial cells remain that serum and blood are lost from the capillaries of the denuded lamina propria. The prepatent period (time from infection until the diagnostic stages appear in the feces) for *Eimeria bovis* is 16 to 21 days; the prepatent period for *E. zuernii* is 12 to 14 days. *Eimeria alabamensis* and *Eimeria auburnensis* are occasionally incriminated in outbreaks of clinical coccidiosis (Radostits and Stockdale, 1980).

Winter coccidiosis in calves characterized by bloody diarrhea and tenesmus is a distinctive clinical entity. Severe cold weather and other stresses may precipitate clinical disease at infection levels that might otherwise not produce symptoms.

Nervous coccidiosis may affect as many as one third of the cattle in some herd outbreaks of coccidiosis, especially in beef cattle in the northwestern United States and western Canada. In addition to acute diarrhea, affected animals display muscular tremors, convulsions, opisthotonus, nystagmus, blindness, and a mortality

rate of about 50%. The pathogenesis of nervous coccidiosis is unknown, but more than 90% of the cases occur during the coldest months of the year, from January to March. Canadian workers have reported the presence of a heat-labile toxin in the serum of calves with nervous coccidiosis that can transfer neurologic signs to inoculated mice (Isler, Bellamy, and Wobeser, 1987); of interest, there has been no follow-up to this report in the past 20 years.

Sheep and goats

At one time, sheep and goats were thought to share the same species of *Eimeria;* however, gradually two complete sets of species names are emerging to reflect the predominant opinion that sheep and goats harbor similar but distinct sets of coccidian species. Specific diagnosis is based on morphologic identification of oocysts in sugar flotation concentrates of feces. Micrometry and sporulation of oocysts in 1% of potassium dichromate solution may be resorted to if necessary for differentiating similar species.

In sheep, clinical coccidiosis is especially likely to occur after shipping and is probably precipitated by the associated stress. In lambs experimentally infected with *Eimeria ovinoidalis*, oocysts appear in the feces about 14 days after infection, and if the infections are severe, deaths will occur beginning about 3 weeks after infection. Goats appear to be much more susceptible to their *Eimeria* infections, and coccidiosis is a serious problem in raising kids in many goat herds. Clinical signs typically follow weaning by 2 to 3 weeks, but coccidiosis should be suspected whenever diarrhea is observed in kids older than 2 weeks. Weaker, heavily infected kids are likely to die; the stronger and less heavily infected survive

but fail to grow normally. Pasty to watery diarrhea and dehydration are typical. Bloody stools and tenesmus, frequently observed in calves with coccidiosis, are not typical of the disease in sheep and goats. Diarrhea may precede oocyst shedding by several days. In such cases of suspected prepatent coccidiosis, examine direct fecal smears for merozoites. Necropsy examination reveals many 3- to 6-mm irregular, whitish, raised lesions. Smears or squash preparations made from these lesions reveal *Eimeria* in various stages of development.

Horses

Eimeria leuckarti is the only species of enteric coccidian reported from North American horses. A survey of naturally acquired *E. leuckarti* infection conducted on 13 Kentucky breeding farms revealed *E. leuckarti* in 67 (41%) of the foals on 11 of those farms. Oocysts, demonstrated by flotation in concentrated sucrose (SG 1.275), were first shed in the feces when the foals were 15 to 123 days old and continued to be shed sporadically for as long as 4 months (Lyons, Drudge, and Tolliver, 1988); a similar survey of three farms in Kentucky in 2004 revealed oocysts in 36%, 41%, and 85% of the 79 foals examined on the farms (Lyons et al, 2007).

Oral administration of 50,000 to 2 million oocysts to yearling ponies led to patent infections in 33 to 37 days, and oocyst shedding continued for as long as 12 days. Schizonts were not observed; gametocytes developed in lamina propria cells of the villi in the small intestine. No clinical signs of disease were observed in these artificially infected ponies (Barker and Remmler, 1972). *E. leuckarti*

infection therefore appears to be prevalent, at least in foals in Kentucky, but relatively harmless.

Swine

Pigs are host to eight species of *Eimeria* and one of *Cystoisospora*, of which only the latter appears to be of significant clinical importance (Vetterling, 1965). *Cystoisospora suis* causes neonatal coccidiosis in 1- to 2-week-old pigs. Clinical signs include diarrhea, dehydration, and weight loss; morbidity tends to be high, and mortality low or moderate. Susceptibility to infection falls rapidly with age. Although 400,000 oocysts of *C. suis* may kill a 1-day-old pig, only mild and transient diarrhea ensues if infection is postponed until the pig reaches 2 weeks of age. The prepatent period is 5 days, and oocyst shedding lasts 1 to 3 weeks. Pigs surviving infection with *Cystoisospora suis* are solidly immune to reinfection with this species. Porcine neonatal coccidiosis is to be differentiated from enteritides associated with *Strongyloides ransomi*, toxigenic *Escherichia coli*, transmissible gastroenteritis virus, rotavirus, and *Clostridium perfringens* type C. *Cystoisospora suis* infection is rarely observed in adult swine, and the epidemiology of porcine neonatal coccidiosis remains problematic (Lindsay Blagburn, and Powe, 1992; Stuart et al, 1980).

Rabbits

Rabbits are host to a number of *Eimeria* species, and one, *Eimeria stiedae*, can be highly pathogenic. This is a relatively unusual *Eimeria* species in that it often will be found in the epithelium of the biliary system, it can cause marked hypertrophy of the epithelium and significant pathogenic changes on the surface of the liver as

large white foci that may be visible on necropsy, and it often it is fatal.

Llamas

Llamas and alpacas are host to a number of species of *Eimeria*, and they can develop coccidiosis, especially as crias. Species include *Eimeria lamae, Eimeria alpacae, Eimeria punoensis, Eimeria macusaniensis*, and *Eimeria peruviana*.

Birds

The subject of coccidiosis in domestic poultry forms too large and complex a body of information to be accommodated on these pages. The reader is referred to standard texts on avian diseases.

Treatment and control

Treatment of isolated cases of fully developed coccidiosis is a matter of supportive therapy because by the time oocysts are detected in the feces, no available drug will have much effect on the population of coccidians infecting that particular host. Controlling coccidiosis in populations of susceptible animals is a challenging proposition, and heavy reliance is placed on chemicals administered prophylactically. The objective of anticoccidian prophylaxis is to afford sufficient protection to the exposed animal to allow it to develop immunity without getting sick in the process. The chemicals reduce the magnitude of challenge and thereby prevent coccidiosis; they do not prevent the infection. However, do not expect the chemical to perform miracles. Too much contamination of the environment with oocysts and, even more important, too much

stress placed on the hosts are conditions that cannot be overcome by the best of chemicals.

Dogs and cats

Coccidiosis outbreaks in dogs and cats involving *Cystoisospora* species can be controlled with sulfonamide drugs. Sulfadimethoxine is administered to dogs for the treatment of coccidian enteritis according to the following schedule: 55 mg/kg for the first day and 27.5 mg/kg for the next 4 days or until the dog is symptom free for at least 2 days. More recently, triazine-derivative drugs have been used off-label for the treatment of canine and feline coccidiosis (Daugschies et al, 2000; Lloyd and Smith 2001).

Dosages that have been used for this class of drugs include 10 to 30 mg of toltrazuril per kilogram for 1 to 3 days in dogs; 25 mg of diclazuril per kilogram once in cats; and 20 mg of ponazuril per kilogram daily for 1 to 3 days in dogs and cats. It must be remembered that in all these cases this in an off-label use of these products.

Ruminants

Whatever chemical agent is chosen, efficient control of coccidiosis requires that exposure of ruminants to oocysts and stressful conditions be minimized. Adequate stall space, clean mangers, plenty of clean air, and dry footing are as essential as they are rare. Never mix calves, sheep, or goats of different ages or sizes in the same pen. As a matter of regular routine, all animals should be observed attentively for several minutes a day at a time when neither the stockman nor his stock has other urgent business. If any sick animals are observed, they should be removed to a separate pen

for supportive treatment. This measure is doubly beneficial; it reduces exposure of the sick to unnecessary stress and of the healthy to extra oocysts. As soon as coccidiosis has been diagnosed in one or a few of the animals, all of the other young ruminants on the premises should be treated prophylactically with an anticoccidial agent. Coccidial infection (coccidiasis) is inevitable. Coccidial disease (coccidiosis) can be prevented or at least ameliorated by sound husbandry and appropriate medication.

Cattle

Clinical coccidiosis in calves caused by *Eimeria bovis* and *E. zuernii* may be treated with amprolium (thiamine antagonist), monensin (ionophore), or sulfa drugs (e.g., sulfamethazine, sulfadimethoxine, and sulfaquinoxaline). Actually, once oocysts have appeared in the feces, it is too late in the course of infection for specific chemotherapy to benefit the animal appreciably. Chemotherapy is certainly outweighed in importance by supportive therapy, especially that directed toward maintenance of fluid balance. Amprolium may be administered for 5 days in the drinking water at a concentration intended to deliver a dose of 10 mg/kg body weight per day. Usually it is better to administer medication individually to clinically ill animals because the sickest and neediest animals are the least likely to receive their share with mass treatment methods. Sulfamethazine is administered orally at a dosage rate of 140 mg/kg body weight daily for 3 days (Radostits and Stockdale, 1980). Include amprolium (10 mg/kg/day for 5 days) and sulfaquinoxaline. Sulfaquinoxaline (6 mg/lb/day for 3 to 5 days) may also prove useful in treating cattle with clinical signs of coccidiosis.

For prophylaxis, amprolium is administered to calves in the feed or drinking water for 21 days during natural exposure to oocysts at a concentration intended to deliver 5 mg/kg per day. Decoquinate is recommended as an aid in the prevention of coccidiosis caused by *Eimeria bovis* and *E. zuernii* in ruminating calves and older cattle. Decoquinate is fed at a dosage level of 0.5 mg/kg for at least 28 days during periods when there is risk of exposure to oocysts; it is ineffective in the treatment of already established infections. Lasalocid is sold as a feed additive and administered at 1 mg/kg daily. Horses must not be allowed to ingest feed that contains lasalocid. Monensin is sold as a feed additive for improved feed efficiency and the control of coccidiosis and is fed at the rate of 100 to 360 mg per head per day. Horses must never be allowed access to feed containing monensin because the toxic dose for this species is only about one tenth of that for cattle (Langston et al, 1985). There are also several sulfa-based products available for coccidiosis control.

Sheep

The animals most at risk are lambs at weaning in grazing pens or when placed in feedlots; it is often important to begin treatment before or immediately after moving the animals into one of these environments. Decoquinate, lasalocid, and sulfaquinoxaline are approved for coccidiosis control in sheep. Sulfaquinoxaline is to be administered in the water for 3 to 5 days. Decoquinate is administered as for cattle at 0.5 mg/kg for at least 28 days. Lasalocid is administered to sheep in feed so that they get between 15 and 70 mg per head per day. Again, do not let horses get at feed containing lasalocid.

Goats

Decoquinate and monensin are approved for preventing coccidiosis in nonlactating goats. For prophylaxis, herd conditions may require that kids be medicated continuously from 2 weeks until they are several months of age. Decoquinate may be mixed with the feed to supply 0.5 mg/kg per day or mixed with salt (4 lb of 6% decoquinate premix with 100 lb of salt). Monensin is fed at the rate of 20 g of monensin sodium per ton on a 90% dry matter basis. This is offered as the sole ration. Do not let horses get into feed containing monensin. Amprolium is not approved for goat kids in the United States. Experimentally, amprolium may be administered to goat kids with coccidiosis at a considerably higher dose rate than is recommended for calves (25 to 50 mg/kg of body weight). Overdose with amprolium may lead to fatal polioencephalomalacia from thiamine deficiency. Sulfa drugs may be used for treating coccidiosis only in sufficiently hydrated kids because sulfa drugs damage the kidneys if insufficient water is available to keep them in solution.

Older goats, while remaining free of clinical signs, may shed oocysts for extended periods and serve as the ultimate source of infection for kids. In problem herds it may prove necessary to isolate kids at birth from their dams, feed them artificially, and include a coccidiostat in the starter ration for several months. In more favorable situations it may suffice to provide a clean, disinfected stall and wash the does' udders carefully before kids are allowed to nurse. Stress or exposure to a previously unencountered species of *Eimeria* may lead to temporary bouts of diarrhea in adult goats.

Much of the information and perspectives on goat coccidiosis presented here are those of Smith and Sherman, 1994.

Horses

E. leuckarti appears to be nonpathogenic, which is fine because no treatment is available for this infection.

Swine

Medication of piglets with neonatal coccidiosis appears to be futile. Rigorous sanitation probably represents the most effective investment. “The following sanitation program has been recommended: steam clean farrowing crates; wet down the crates with an ammonia-orphenol-containing disinfectant and let them stand overnight; and steam clean the following day” (Stuart and Lindsay, 1986). In Europe today and until 2005 in Canada, Baycox (ponazuril) from Bayer HealthCare was approved for the treatment of coccidiosis in piglets. Use in Canada was discontinued at the request of Health Canada based on the concern that Canadian scientists could not rule out the possibility that it might have health effects on consumers. In Europe, Baycox is also approved for the treatment of chickens and cattle with coccidiosis.

Rabbits

In laboratory settings, rabbits are being treated with toltrazuril or ponazuril. Similarly, some pet rabbits are being treated with ponazuril. It must be remembered that the rabbit is considered a food animal by many people still in the United States; therefore when treatment is administered, there must be concern as to the ultimate fate of the animal being treated.

Cryptosporidium

The genus *Cryptosporidium* is currently considered by many parasitologists to be less closely related to the other coccidia than to a group of the Apicomplexa known as the gregarines rather than the coccidia and malarias (Carreno, Martin, and Barta, 1999). Again, this seems a purely academic exercise, but it helps explain the superficial relationship between these organisms and the mucosal cells that they parasitize and why almost all the anticoccidials and antimalarials have proven inadequate in the control of infections with this parasites. Of course, in 10 years we might change our minds again.

The genus *Cryptosporidium* has undergone a proliferation of species in the last few years at a fairly frantic clip (Fayer Santin, and Xiao, 2005). The important species in veterinary medicine that are now recognized include the following as parasites of the small intestine: *Cryptosporidium parvum* in calves less than 30 days of age, *Cryptosporidium bovis* in older calves and adult cows, *Cryptosporidium suis* in swine, *Cryptosporidium canis* in dogs, *Cryptosporidium felis* in cats, *Cryptosporidium meleagridis* and *Cryptosporidium bayleyi* in birds, and *Cryptosporidium wrairi* in guinea pigs. The parasites of the stomach include in the mouse, *Cryptosporidium muris*, in the snake, *Cryptosporidium serpentis*, and in the abomasum of the cow, *Cryptosporidium andersoni*. The important species in people is *Cryptosporidium hominis*. The common zoonotic species that infects people, and often veterinary students, is *C. parvum*. The other species that show up in people as rare zoonoses are *Cryptosporidium canis, Cryptosporidium felis, C. meleagridis, C. muris*, and *Cryptosporidium suis*. Sheep, goats, horses, and related animals seem

to share *C. parvum* with calves, at least right now. There are also a number of species from cervids that will probably be described sometime soon.

Life history

The transmission stage is the infective oocysts (5 to 8 μm in diameter depending on the species (Figures 3-16 and 3-17) containing four sporozoites that are discharged in the feces and serve to disseminate the infection. The oocysts remain viable for months unless exposed to extremes of temperature (below 0° C, above 65° C), desiccation, or impracticably concentrated disinfectants (5% ammonia, 10% formalin). When ingested by a suitable host, the oocyst opens along a preexisting suture line to release the four sporozoites that invade the microvillous border of the gastric glands (*C. muris;* Tyzzer, 1907, 1910) or lower half of the small intestine (*C. parvum;* Tyzzer, 1912). In parasitophorous vacuoles in the microvillous border, the cryptosporidia undergo schizogony, gametogony, fertilization, and sporogony. Some oocysts go through excystation internally, providing the mechanism for autoinfection that accounts for the chronicity of certain cases in immune-sufficient hosts and lethal hyperinfection in immune-deficient hosts.

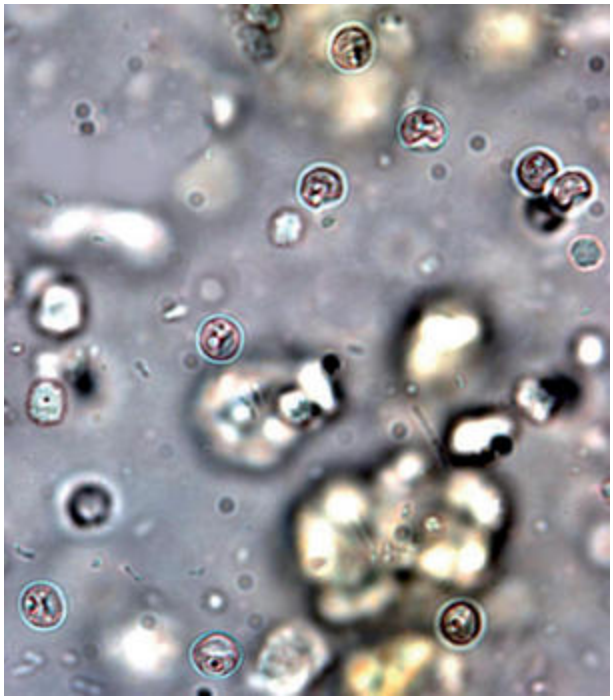

FIGURE 3-16 Oocysts of *Cryptosporidium parvum* in a sugar flotation preparation from calf feces.

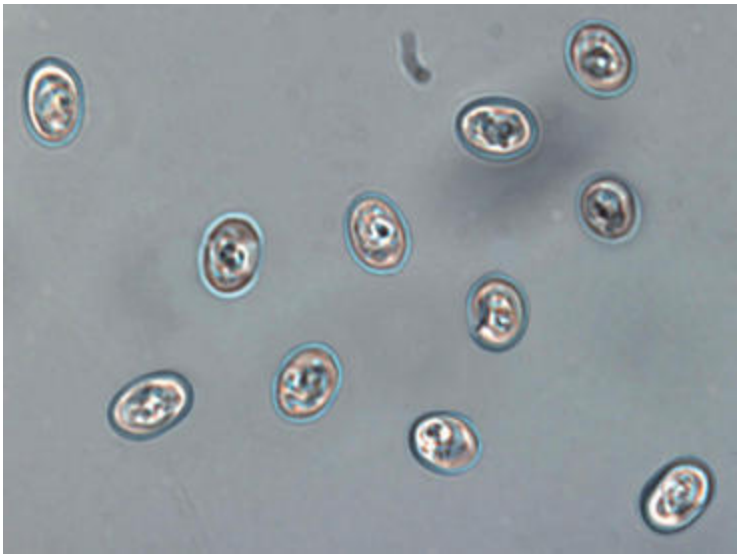

FIGURE 3-17 *Cryptosporidium andersoni* oocysts in a sugar preparation from infected cow feces.

Clinical signs

Inapparent infection is common in many mammalian, avian, reptilian, and piscine hosts. For example, *Cryptosporidium* was found in the microvillous borders of enterocytes of 5% (184 of 3491) of 1- to 30-week-old pigs submitted for diagnostic necropsy, but according to Sanford, "Only 26 per cent of the cryptosporidia-infected pigs had diarrhea and most of those had other primary diarrheagenic agents or lesions capable of causing their diarrhea" (Sanford, 1987). On the other hand, debilitating diarrhea may be associated with infection (e.g., in calves within the first 3 weeks of life). Although *C. parvum* is usually the culprit in clinical cryptosporidiosis in mammals, *C. andersoni* may cause mild diarrhea in cattle of all ages, especially young adults. Immunocompromised hosts may develop a life-threatening hyperinfective form of cryptosporidiosis, as is the case with many human acquired immunodeficiency syndrome (AIDS) patients (Ma and Soave, 1983). Severe cryptosporidiosis has been reported to be associated with immunocompromise induced by feline leukemia virus (FeLV) in a cat (Monticello et al, 1987) and in Arabian foals with inherited combined immunodeficiency. In the latter case, however, it was not possible to separate the effects of *Cryptosporidium* and concurrent adenoviral infection (Snyder, England, and McChesney, 1987).

Diagnosis

Cryptosporidium oocysts are difficult to see on fecal slides because they are colorless, transparent, and small; *C. parvum* is 5.0 by 4.5 μm (see Figure 3-16), and *C. andersoni* is 7.4 by 5.6 μm (see Figure 3-17) (Upton and Current, 1985). Concentrated sucrose solution (specific gravity 1.33) is the flotation medium of choice for concentrating oocysts of *Cryptosporidium*. The coverslip variant of

the flotation concentration technique, which is described in Chapter 7 in the section on qualitative fecal examination, can be used. The oocysts appear as tiny subspheric objects that may be dented by osmotic extraction of water by the hypertonic medium. They tend to lie immediately below the coverslip, so focus on the top of an air bubble to find the best focal plane for *Cryptosporidium* oocysts. The oocyst walls may have a pinkish hue that helps in finding them; the pinkish hue is caused by chromatic aberration and is best developed by objective lenses of modest quality. The cyst walls are clear and colorless under a highly corrected objective lens. Questionable objects may be examined under the highest magnification to demonstrate the sporozoites. Phase contrast microscopy is helpful, and a number of staining procedures (e.g., methylene blue, Giemsa stain, iodine wet mount, modified Kinyoun acid-fast smear) have been recommended to increase the optical contrast and stain-confusing yeasts differentially. However, the most serious obstacle to the correct microscopic diagnosis of cryptosporidiosis is inexperience and insecurity on the part of the microscopist. The best procedure is to keep examining feces from 1- to 3-week-old calves with the 40× objective and suitably stopped brightfield illumination until you see *Cryptosporidium* oocysts. If in doubt, check for sporozoites under higher power. Once you have seen the oocysts, you will have acquired the most essential ingredient of accurate diagnosis. Exacting microscopic technique pays dividends, especially as one nears the resolution limits of the light microscope. Köhler illumination, described in all microscope manuals, is indispensable. Also useful for laboratories are various fluorescently labeled antibodies that bind to the oocyst, but these methods require the

availability of a microscope equipped with an ultraviolet light source and appropriate filter sets. Several assays designed for in-office use are approved for the detection of the *C. parvum* antigen in human feces, and the test, although expensive, appears to work well on bovine samples.

Treatment

There is no effective specific treatment for *Cryptosporidium* infection in animals. For people, the U.S. Food and Drug Administration (FDA) has approved the use of nitazoxanide in oral suspension for the treatment of diarrhea caused by *Cryptosporidium* (and *Giardia*). Other drugs that have been used in dogs and cats include paromomycin 150 mg/kg once a day for 5 days for dogs and cats; tylosin at 10 to 15 mg/kg three times a day for 14 to 21 days for cats; and azithromycin at 5 to 10 mg/kg twice a day for 5 to 7 days for cats.

Toxoplasma

Life history

Toxoplasma gondii is an enteric coccidian of the domestic cat *(Felis catus)* and other members of the family Felidae. Cats are the only known definitive hosts (hosts in which microgametes and macrogametes are formed), and therefore only infected cats shed oocysts of this parasite in their feces. The oocyst is small (11 to 13 μm; Figure 3-18), contains a single sporont, and is noninfective when passed in the feces. Sporulation is completed in 1 to 5 days and results in formation of two sporocysts, each of which contains four sporozoites. Fully sporulated oocysts are infective on ingestion

to essentially all warm-blooded animals including cats (Figure 3-19). Therefore almost any warm-blooded animal may serve as a paratenic host of *T. gondii* (Dubey, 1986a, 1986b). A paratenic host is a host in which a parasite may grow or multiply, but the growth or development is not required by the parasite to complete its life cycle.

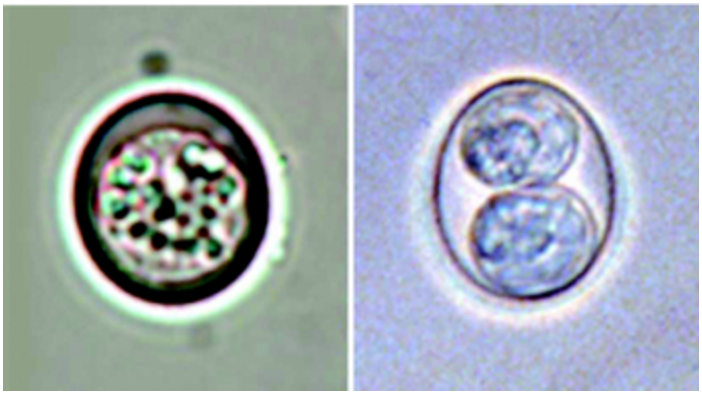

FIGURE 3-18 Oocysts of *Toxoplasma gondii*, unsporulated *(left)* and sporulated *(right)*.

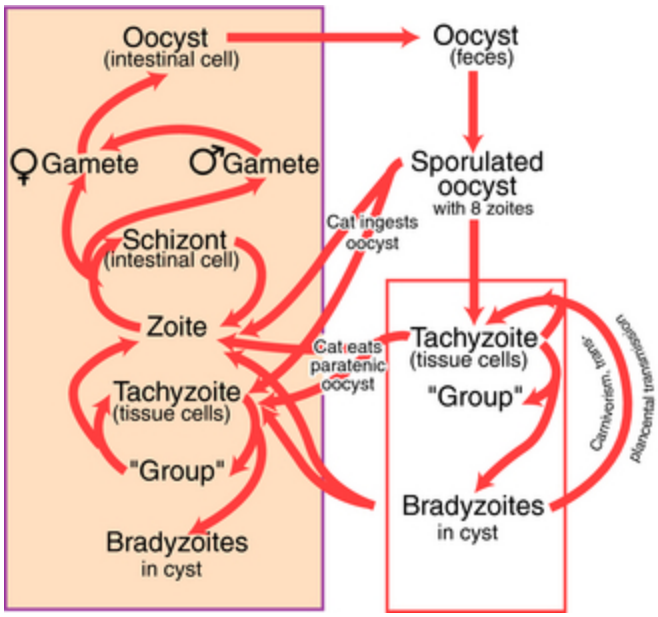

FIGURE 3-19 Life history of *Toxoplasma gondii*.

On ingestion, sporulated oocysts rupture in the intestine and release the sporozoites. These enter and multiply in cells of the intestine and associated lymph nodes to form rapidly multiplying stages, tachyzoites, which spread to all other tissues of the body; there they invade cells and continue to multiply (Figure 3-20). Eventually, tissue cysts containing slowly dividing forms, bradyzoites, are formed in the brain, striated muscles, and liver and remain viable for the life of the host (Figure 3-21). Bradyzoites are infective on ingestion to essentially all warm-blooded animals and behave in the manner similar to that just described for sporozoites. Historically, bradyzoites were differentiated from tachyzoites by the fact that they stained with the periodic acid–Schiff's reagent, indicating that they contain glycogen and are able to withstand pepsin digestion fluids. Thus, paratenic hosts become infected with *T. gondii* by ingesting sporulated oocysts from cat feces or bradyzoites in the tissues of other paratenic hosts. Transplacental transmission of tachyzoites from dam to fetus in utero also occurs but varies in importance depending on the species of host involved (Dubey, 1986a, 1986b).

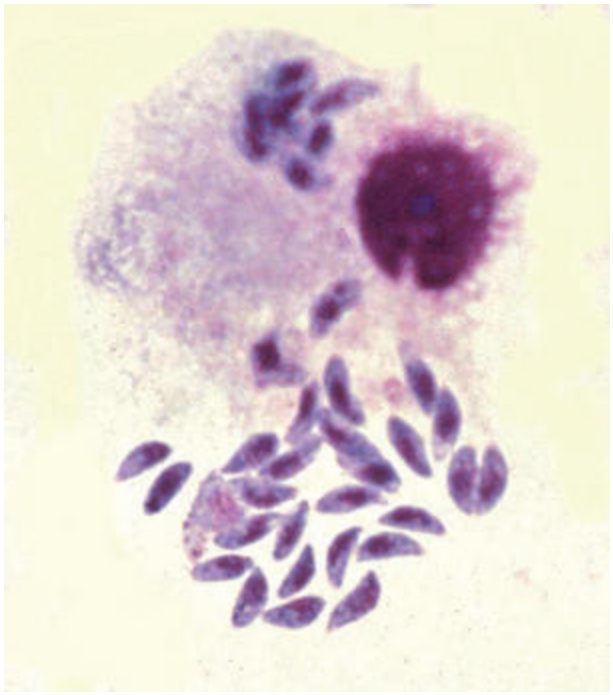

FIGURE 3-20 Tachyzoites of *Toxoplasma gondii* and the pulmonary macrophage of a naturally infected cat (Giemsa stain).

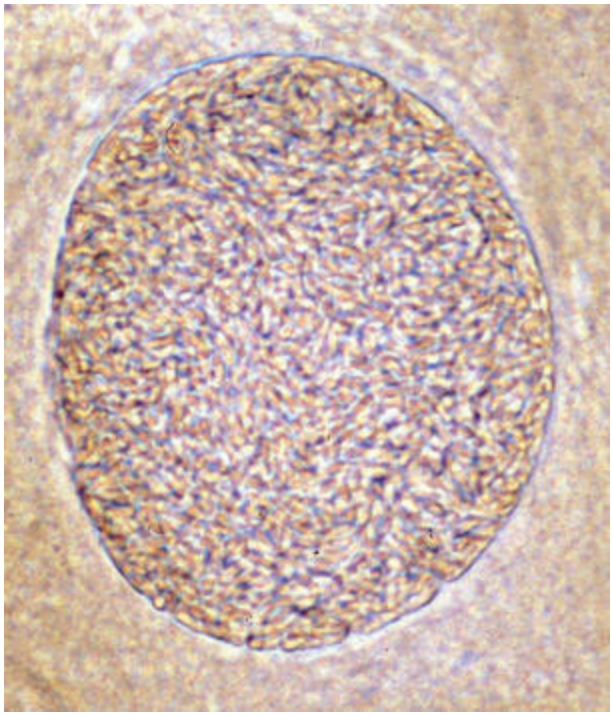

FIGURE 3-21 *Toxoplasma gondii* cyst in a mouse's brain. This is a fresh temporary mount prepared by simply squashing the brain tissue between the coverslip and slide.

When a member of the cat family ingests tissue cysts of *T. gondii* (see Figures 3-19 and 3-21), the bradyzoites penetrate the epithelial cells of the small intestine, undergo a series of asexual cycles, and finally undergo the sexual cycle, which culminates in the shedding of oocysts. Cats shed *Toxoplasma* oocysts in their feces 3 to 10 days after eating mice infected with encysted bradyzoites but not until 19 to 48 days after ingesting sporulated oocysts (Dubey and Frenkel, 1976). Apparently, the asexual reproduction preceding formation of bradyzoites in the paratenic host satisfies a major portion of the developmental requirements preceding sexual reproduction. Cats may also serve as paratenic hosts inasmuch as multiplication of tachyzoites and cyst formation occur in their extraintestinal tissues (Dubey, 1986b); cats are also capable of developing systemic disease (Meier et al, 1957).

Importance

Like other coccidians, *T. gondii* destroys cells, and the explosive multiplication of tachyzoites of this organism is potentially devastating to the host. On first exposure to *T. gondii* infection, adult humans with intact immune systems suffer a brief if unpleasant illness marked by variable combinations of fever, myalgia, lymphadenopathy, anorexia, and sore throat that is probably rarely diagnosed as to exact cause. The situation is far more grave for hosts with deficient immune responses such as fetuses, neonates, older adults, and those with congenital or acquired immunodeficiency diseases. The greatest concern attaches to exposure of human fetuses to the hazard of death, congenital malformation, or mental retardation that may result from exposure of the nonimmune mother to *T. gondii* infection during pregnancy. Although women

with circulating antibody to *T. gondii* need not worry about exposing their unborn babies to congenital toxoplasmosis, such women account for only about 30% of the population at risk. The other 70% must be careful to avoid cat feces and uncooked meat during pregnancy (Dubey, 1986a, 1986b).

Adult cattle appear to be resistant to toxoplasmosis, whereas sheep and goats are susceptible, usually manifesting toxoplasmosis as abortion due to focal placentitis (Dubey, 1986d, 1987). Aborting ewes and does need not be culled because they probably will not repeat the performance. *T. gondii* infection is highly prevalent in pigs, and uncooked pork may be an important source of human infection (Dubey, 1986a, 1986c).

Treatment

Humans may contract toxoplasmosis either by ingesting sporulated oocysts from the feces of an infected cat or by eating uncooked meat of animals containing *T. gondii* cysts. “Pregnant women should eat only adequately cooked meat and either leave the cleaning of cat litter pans to someone else or wear disposable gloves” (Frenkel and Dubey, 1972). They are also well advised to wash lettuce and other fresh vegetables carefully; avoid contact with newborn lambs, kids, and fetal membranes; and shun unpasteurized goat’s milk. The meats that probably pose the greatest risk of infection are lamb and range-fed chicken if eaten undercooked. The risk of acquiring infection from most meat purchased in the United States is fairly low. A survey by the USDA of meat from supermarkets in the United States (2094 samples each of commercially raised beef, chicken, or pork from 698 retail meat stores) revealed no toxoplasmosis in the

beef or chicken and toxoplasmosis in only seven pooled (six samples per pool) pork samples (Dubey et al, 2005b).

A cat shedding oocysts of *T. gondii* should be hospitalized to prevent exposure of its owner until it stops shedding oocysts, usually in less than 2 weeks. Reinfection, if it occurs, results in low-grade shedding of oocysts of short duration. Intercurrent *Cystoisospora* infection may also trigger a brief output of *T. gondii* oocysts. However, in general, having once passed through a patent *T. gondii* infection, the particular cat remains a relatively minor source of infection. Thus the cat that has a history of shedding *T. gondii* oocysts and/or is serologically positive is probably a safer pet than the cat that has never been exposed to this organism (Dubey, 1986b).

According to Dr. S.C. Barr, cats clinically ill with toxoplasmosis can be treated with clindamycin hydrochloride. The drug should be given orally with food. Start at 25 mg/kg twice daily and work up to 50 mg/kg twice daily. If the cat goes off its feed, withhold the drug for 24 hours and then start the clindamycin again at the level of 25 mg/kg. Cats should be treated for a minimum of 2 weeks. Cats can also be treated with clindamycin phosphate intramuscularly at 12.5 to 25 mg/kg twice daily, pyrimethamine orally at 0.25 to 0.5 mg/kg with 30 mg of sulfonamide per kilogram given twice daily, or trimethoprim and sulfadiazine orally at 15 mg/kg twice daily, all for 4 weeks (Lindsay et al, 1997). Pyrimethamine causes megaloblastic anemia or leukopenia, and therapy should be discontinued if there is no response in 30 days. Based on the efficacy of treatment of toxoplasmosis in mice with ponazuril (Mitchell et al,

2004), this product may offer a means of reducing the shedding of oocysts in the feces of cats.

Neospora

Neospora caninum was originally described as a parasite of the domestic dog (Dubey et al, 1988). It was initially identified in littermates dying of signs related to polyradiculitis (Bjerkås, Mohn, and Presthus, 1984; Core, Hoff, and Milton, 1983). The cysts seen in neural tissues (Figure 3-22) were characterized by the possession of a cyst wall thicker than that of *T. gondii*, which is the apicomplexan it is thought to most closely resemble. In transplacentally infected puppies, the typical presentation is a flaccid hindlimb paresis. In cases where there is adult onset of the disease, presentation includes neurologic signs, nodular dermatitis, pneumonia, urine and fecal incontinence, hepatitis, myocarditis, and myositis. More recently, *N. caninum* was recognized as a major cause of bovine abortion among dairy cows around the world (Anderson et al, 1991; Barr et al, 1997). Abortions due to this parasite are common, and between 10% and 20% of abortions in dairy cows probably are caused by *N. caninum*. *Neospora* abortions tend to peak at midgestation, and calves infected in utero after this time tend to survive. Abortions may occur in subsequent pregnancies, but more typically, future births produce calves that are congenitally infected. It seems that serologically positive calves will ultimately give birth to calves that are infective and seropositive. It has been suggested that seropositive cows produce less milk than seronegative cows and are more likely to be culled earlier (Thurmond and Hietala, 1996 and 1997).

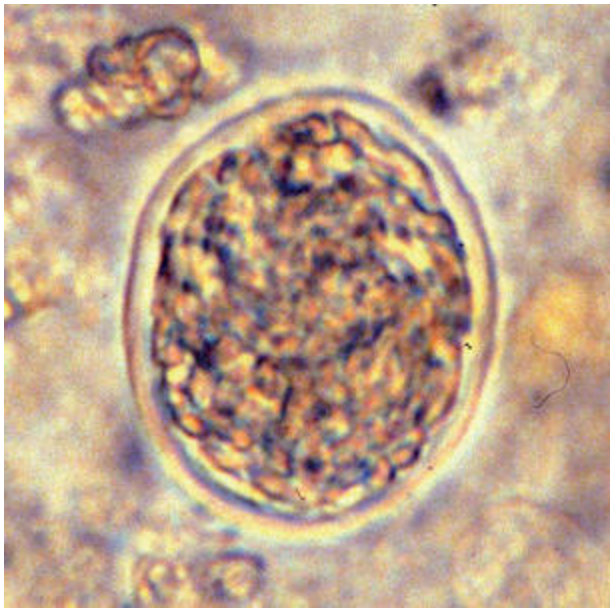

FIGURE 3-22 *Neospora caninum* cyst from a homogenate of the brain of a naturally infected dog. Note the thickness of the cyst wall compared with that of *Toxoplasma gondii*.

In 1998 the *N. caninum* of cattle was shown to use dogs as definitive hosts (McAllister et al, 1998). The oocysts shed in the feces of dogs are indistinguishable from those of *T. gondii* and *Hammondia* species, but they can be distinguished by molecualr methods (Hill et al, 2001). Oocyst shedding by dogs was confirmed (Lindsay, Dubey, and Duncan, 1999), but it has been hard to get dogs to produce large numbers of oocysts on a regular basis. This has made it difficult to study means of prevention or to more fully understand the importance of dogs relative to environmental contamination. Several diagnostic assays, immunologic and molecular, are now available for the detection of *N. caninum* infections. It appears that cattle do not typically serve as hosts of *T. gondii*, and there have been no cases of neosporosis reported from humans. Thus, at this time, it would appear that the ingestion of rare beef does not pose a threat of human infection with either of

these parasites. Treatment of lactating dairy cows is especially problematic, and no drug therapy is currently available. Intervet offers a vaccine that aids in the prevention of infection with bovine neosporosis.

Neospora hughesi was described in 1998 from material collected from a horse (Marsh et al, 1998). The differentiation was based on molecular differences among the equine, bovine, and canine isolates. The differences between *N. hughesi* and the bovine and canine isolates were later confirmed with material collected from a horse in Oregon (Dubey et al, 2001a).

Hammondia

The oocysts of species of *Hammondia* are morphologically virtually indistinguishable from one another and from those of *Toxoplasma* and *Neospora*. *Hammondia hammondi*, a parasite of the cat that unlike *Cystoisospora felis* multiplies in the tissues of an intermediate host, pigs, rats, mice, goats, hamsters, and dogs. *Hammondia heydorni* is a similar parasite that uses dogs, foxes, and coyotes as the final host and cattle, sheep, goats, camels, water buffalo, guinea pigs, and dogs as intermediate hosts. The zoites first multiply rapidly (tachyzoites); they then form cysts in which they multiply slowly (bradyzoites). The net result is the multiplication and storage of zoites in cysts in the tissues of an animal that is likely to fall prey to a cat or dog final host. As indicated in Figure 3-23 for *H. hammondi*, only sporulated oocysts from cat feces are infectious for mice, and only bradyzoites from mouse tissues are infectious for cats. Thus *H. hammondi* has an obligatory two-host life history. Tachyzoites are neither infectious to cats nor transmittable to the

progeny of pregnant female mice via the placenta, as is true of *T. gondii*.

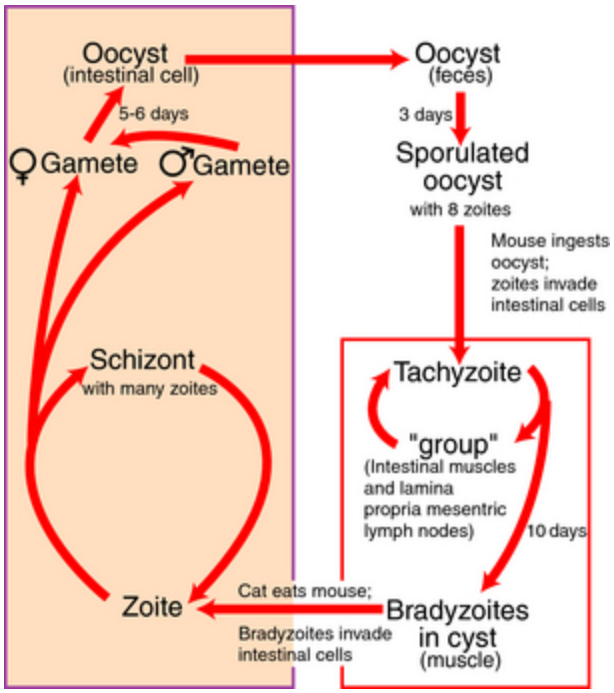

FIGURE 3-23 Life history of *Hammondia hammondi*.

Sarcocystis

Species of *Sarcocystis*, like *H. hammondi*, have an obligatory two-host life history but differ in that only sexual reproduction occurs in the definitive host and that sporogony is completed there. Fully sporulated oocysts and sporocysts are discharged in the host's feces, and no development occurs in the external environment. Asexual reproduction, including schizogony and sarcocyst formation, occurs only in the intermediate host. The bradyzoites in sarcocysts differ from those in *Hammondia* cysts in that they develop into gametocytes instead of schizonts when ingested by the definitive host. Bradyzoites represent a state of arrested development, or hypobiosis. Like sporozoites in a sporulated oocyst, bradyzoites in a

sarcocyst must enter a definitive host to develop further. The life history of *Sarcocystis* is portrayed diagrammatically in Figure 3-24.

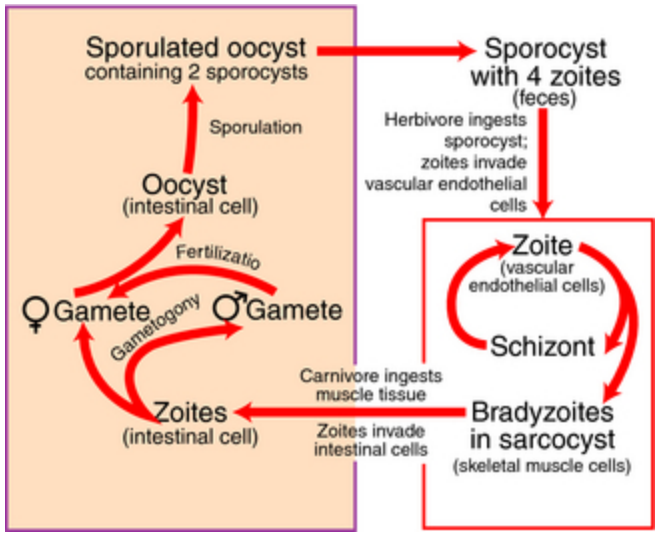

FIGURE 3-24 Life history of *Sarcocystis* species.

The host relationships of several species of *Sarcocystis* are summarized in Table 3-1. Normally the carnivorous host becomes infected by eating the infected flesh of the herbivorous host, and the herbivorous host becomes infected by ingesting sporocysts from the feces of the carnivorous host. Schizogony and encystment occur exclusively in the herbivorous host, and gametogony, fertilization, and sporulation occur exclusively in the carnivorous host. Sarcocystis usually causes no illness in the carnivore, but schizogony in the endothelium of the herbivore may result in serious or fatal disease.

TABLE 3-1 Host Relationships of Some Species of *Sarcocystis*

Intermediate Hosts	Definitive Hosts		
	Dog	Cat	Human
Cattle	*Sarcocystis cruzi*	*Sarcocystis hirsuta*	*Sarcocystis hominis*
Sheep	*Sarcocystis tenella*	*Sarcocystis areticanis*	*Sarcocystis medusiformis*
Goat	*Sarcocystis capracanis*	—	—
Swine	*Sarcocystis miescheriana*	*Sarcocystis porcifelis*	*Sarcocystis suihominis*
Horse	*Sarcocystis bertrami*	*Sarcocystis fayeri*	*Sarcocystis equicanis*
Cottontail rabbit	*Sarcocystis leporum*	—	—
Mouse	—	*Sarcocystis muris*	—
Mule deer	*Sarcocystis hemionilatrantis*	—	—

Cattle become infected with *Sarcocystis cruzi* when they ingest its sporocysts discharged in dog feces. Two schizogonic generations occur in the vascular endothelium, the first generation principally in the endothelium of the mesenteric arteries and the second in the endothelium of capillaries throughout the body. At least one more schizogonic generation occurs in circulating mononuclear cells. Merozoites released from second- or later-generation schizonts enter striated muscle cells and, in certain cases, nerve cells to form sarcocysts. Sarcocyst formation is a slow process requiring several months. The dog becomes infected when it consumes uncooked beef containing sarcocysts of *S. cruzi*. Thus the cycle of infection can be interrupted either by cooking beef scraps to be fed to dogs or by preventing canine fecal contamination of cattle feedstuffs. The economic importance of subclinical bovine sarcocystosis remains to be assessed, but clinical disease and death losses have occurred in cases in which 10,000 or more sporocytes were ingested over a short time period (Dubey and Fayer, 1983; Frelier, 1977). Clinical signs in cattle are associated with release of the second wave of merozoites about 4 to 6 weeks after infection and consist of protracted fever, anemia, lymphadenopathy, anorexia, diarrhea,

hypersalivation, weakness, and hair loss about the eyes, the neck, and, perhaps most noticeably, the tail switch.

Infection of sheep with 10,000 to 50 million *Sarcocystis tenella* sporocytes was studied experimentally. A total of 25 to 50 million sporocysts led to death in 16 to 19 days from occlusion of the mesenteric arteries by first-generation schizonts. Sheep infected with 10 million and fewer sporocysts had anemia, hepatitis, and myocarditis related to the second schizogonic generation. Neurologic signs and lesions of encephalomyelitis were also observed in these artificial *S. tenella* infections in sheep (Dubey, 1988).

Sarcocystis neurona

S. neurona causes severe neurologic disease in horses of both sexes and all ages. Clinical signs include stumbling, paresis, lameness, ataxia, recumbency, constipation, urinary incontinence, diaphoresis, muscle atrophy, and other manifestations of neural degeneration depending on the location of the lesions (Mayhew and Greiner, 1986; MacKay, 1997). The equine protozoal myeloencephalitis (EPM) organism has been identified as *S. neurona* (described by Dubey et al, 1991). Opossums are the host shedding sporocysts into the environment (Figure 3-25). Recent work has shown that opossums shed sporocysts of *S. neurona* and four other distinct sporocysts in their feces as determined morphologically and molecularly (Cheadle et al, 2001). One characteristic of this infection is the formation of schizonts by the dividing cells in the equine tissues (Figures 3-26 and 3-27). It is also now known that cats, striped skunks, and nine-banded armadillos can be infected

with muscle stages of *S. neurona* (Cheadle et al, 2001a and b; Tanhauser et al, 2001). It has also been discovered that raccoons are capable of having myocarditis and encephalitis that are due to *S. neurona* infections (Hamir and Dubey, 2001). It seems that sarcocysts may develop in some infected horses (Mullaney et al, 2005), but this still needs to be verified.

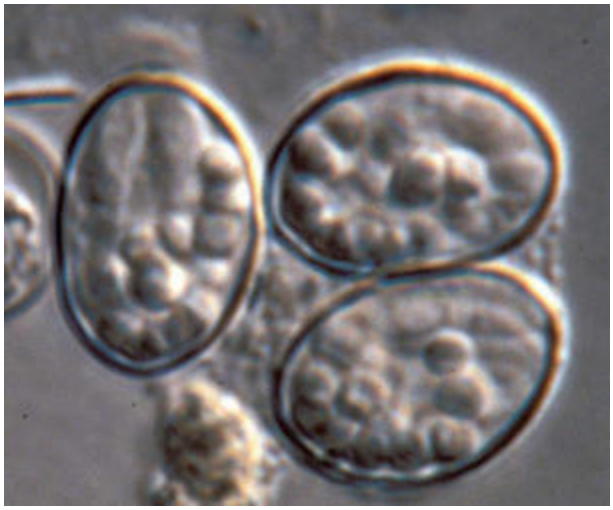

FIGURE 3-25 Sporulated sporocysts of *Sarcocystis neurona* passed in the feces of an opossum fed infected muscle from an experimentally infected cat.

Courtesy Dr. J.P. Dubey, USDA, Beltsville, Maryland.

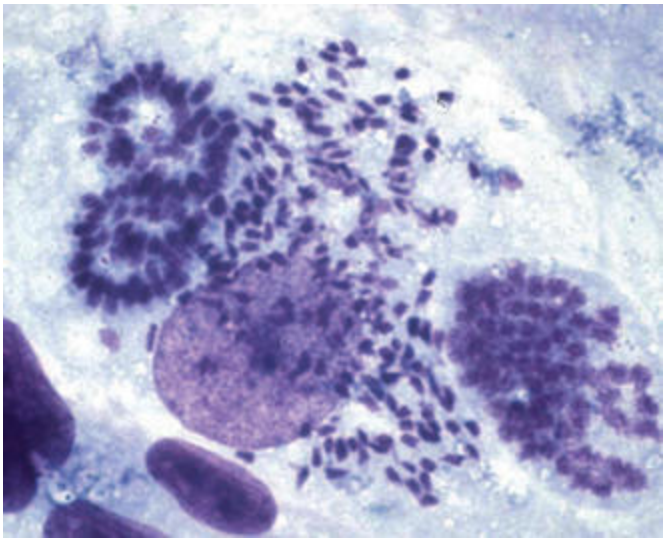

FIGURE 3-26 Schizonts of *Sarcocystis neurona* in a culture of bovine turbinate cells (Giemsa stained). Culture was initiated with merozoites from the nervous tissue of a naturally infected horse.

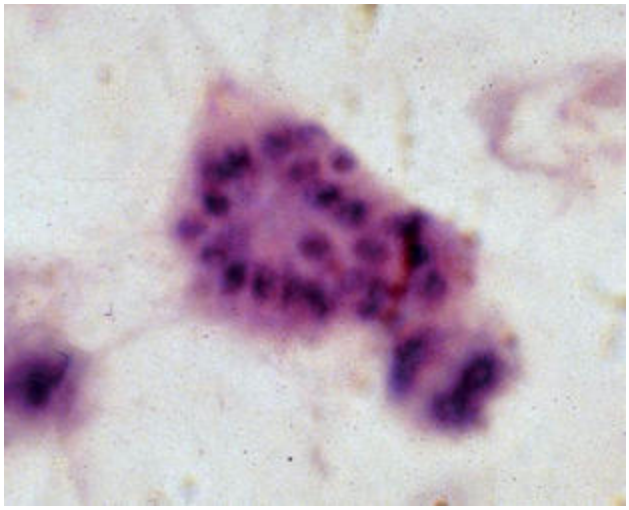

FIGURE 3-27 Section of nervous tissue from a horse showing the characteristic rosette of organisms that is not uncommonly seen in infections with *Sarcocystis neurona*, the causative agent of equine protozoal myeloencephalitis (EPM).

Diagnosis

An antemortem diagnosis is based solely on clinical signs of neurologic disease, and none of these is pathognomonic. Several laboratories provide diagnostic tests consisting of Western blot analysis of serum or cerebrospinal fluid or molecular methods using PCR to assist with a diagnosis. A positive diagnosis is based on histopathologic demonstration of the EPM organisms in association with lesions in the central nervous system (see Figure 3-27).

Treatment

There are several treatments now approved by the FDA for the treatment of EPM. These are ponazuril 5 mg/kg for 7 days (Marquis with 15% W/W ponazuril) and nitazoxanide for 5 days at 11.36

mg/kg followed by 23 days at 22.72 mg/kg (Navigator with 32% nitazoxanide). Also available from Fort Dodge Animal Health is a killed protozoal *S. neurona* vaccine.

Protozoal Encephalomyelitis Organisms

Sheep

Apicomplexan encephalomyelitis of adult sheep may be caused by *S. tenella* and other *Sarcocystis* species (Dubey, 1988).

Cattle

Dubey, Perry, and Kennedy (1987) described a case of encephalitis in an 18-month-old steer apparently caused by a *Sarcocystis*-like organism.

Toxoplasma and *Sarcocystis* in Sea Otters and Other Aquatic Mammals

There have been a number of reports of *Toxoplasma* and *Sarcocystis* inducing antibody responses or causing serious disease in seals, walruses, otters, dolphins, and sea lions (Conrad et al, 2005; Dubey et al, 2001b, 2003, and 2005a; Honnold et al, 2005. Infection is due to oocysts washing into the aquatic environment and perhaps being concentrated by filter-feeding shellfish on which some of these animals feed. The challenge is how to minimize the exposure of these aquatic animals, some of which are on the endangered species list, to the oocysts shed in the feces of terrestrial carnivores that are then washed into various tidal basins and estuaries.

Besnoitia

Large cysts (0.5 mm) containing bradyzoites occur in the skin of cattle, where they cause scleroderma, and in various tissues of other animals. Oocysts resembling those of *Toxoplasma* are shed in the feces of cats.

Klossiella

Klossiella equi is a parasite of the renal epithelium of the horse, and *Klossiella muris* is a parasite of the renal epithelium of the mouse (see Fig. 5-165). The life histories of these parasites have yet to be worked out in detail; neither species appears to be pathogenic under ordinary circumstances. However, Anderson et al (1988) reported tubular necrosis and nonsuppurative interstitial nephritis in an older, immune-compromised pony. Reinmeyer, Jacobs, and Spurlock (1983) were first to demonstrate the sporocysts of *K. equi* in the urine of a 2-year-old standardbred gelding with immune deficiency. These transmission stages are rarely observed; they, like the pathologic changes reported by Anderson et al (1988), were observed in immunodeficient horses.

Hepatozoon

The *Hepatozoon* species commonly causing disease in dogs in the United States is now recognized as *Hepatozoon americanum* (Macintire et al, 1997; Panciera et al, 1997, Vincent-Johnson et al, 1998). Throughout the rest of the world the disease seems to be caused by a different species, *Hepatozoon canis* (Smith, 1996). The vector of *H. americanum* is now known to be *Amblyomma maculatum* (Mathew et al, 1998, 1999); reservoirs are known to include the coyotes (Garrett et al, 2005). In the case of *H. canis*, dogs acquire

their infections by ingesting an infected tick, *Rhipicephalus sanguineus*.

In the life cycle of this parasite, ticks become infected by ingesting a blood meal that contains neutrophils and monocytes that harbor the gamonts of the parasite. Sexual replication in the gut of the tick results in the production of oocysts containing infective sporozoites. After dogs become infected by ingesting the tick, schizonts occur in various tissues, and finally, the gamonts occur in white blood cells.

H. canis typically seems to cause subclinical infections, and the diagnosis is typically made by finding gamonts in the peripheral blood. In the case of infection with *H. americanum*, there is typically severe disease, with dogs having marked neutrophilic leukocytosis. Dogs with *H. americanum* often have significant joint pain associated with myositis and periosteal bone proliferation, which can be revealed in radiographs. Lesions occur primarily on the diaphysis of the more proximal long bones of the limbs; however, flat and irregular bones are frequently involved (Panciera et al, 2000). Lesions involving metacarpals, metatarsals, and digits are infrequent. The earliest observed periosteal lesions in experimentally infected dogs were observed 32 days after exposure to sporulated oocysts of *H. americanum*, with hypertrophy and hyperplasia of osteoprogenitor cells, and osteoblasts appearing in the cellular zone of the periosteum. The osseous lesions are similar to those of hypertrophic osteopathy in domestic dogs and other mammalian species.

Diagnosis of *H. americanum* infection typically requires the examination of muscle tissue collected at biopsy or during necropsy to reveal the schizonts. With *H. americanum* infection there is a large

cystic form of the organism that occurs in skeletal muscles that has not been observed in other parts of the world. Also, the meronts typically seen in multiple organs of the body with the occurrence of *H. canis* infection in dogs from other parts of the world are not seen in dogs infected in the United States.

In a report of two cases of infection in the United States, treatment with toltrazuril failed to prevent relapse in most of the 11 treated dogs; treatment of three dogs with a combination of trimethoprim sulfate, pyrimethamine, and clindamycin also failed to prevent relapse (Macintire et al, 1997). Macintire et al (1997) suggested that primaquine phosphate has proven efficacious in treating dogs infected with *H. canis* in Africa. Of the 22 dogs reported in the study by Macintire et al (1997), seven were humanely killed because of chronic wasting, six died of the disease, three were lost to follow-up, and six were alive at the time of the report. Three of the living dogs were free of clinical signs, whereas the other three dogs had chronic wasting disease with intermittent periods of remission and relapse.

Hemosporidians

Piroplasmoses

Babesia

Babesia species are apicomplexan parasites of the erythrocytes of their vertebrate hosts (Figure 3-28); the erythrocyte is the only vertebrate host cell infected. For the members of the genus *Babesia*, sexual conjugation occurs within the intestinal lumen of the tick, and sporogony occurs within the epithelium of the tick's intestinal wall. Sporogony occurs within the hemocoel of the tick. The

sporozoites multiply in the ovary of the female tick and thereby infect the larvae that hatch from her eggs. Sporozoites are found in the salivary glands of the ticks in high numbers and enter the next host when the tick bites.

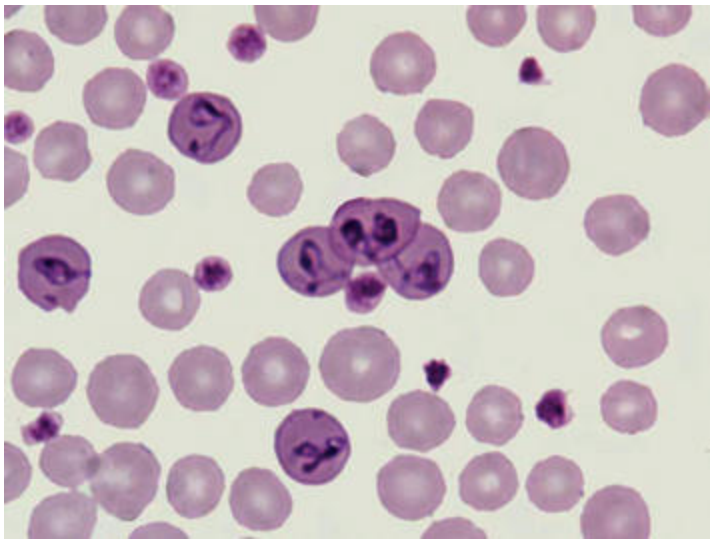

FIGURE 3-28 *Babesia bigemina* in Giemsa-stained blood film from a cow.

Texas fever

Babesia bigemina causes bovine piroplasmosis (Texas fever), a disease characterized in the acute phase by pyrexia (up to 42° C), hemoglobinuria, anemia, icterus, and splenomegaly. The apple-seed–like piroplasms are found in pairs in the erythrocytes, which they destroy, releasing hemoglobin in the process and giving rise to the characteristic clinical manifestations. Transmission of infection among cattle occurs through the bite of the one-host ticks *Rhipicephalus (Boophilus) annulatus* and *Rhipicephalus (Boophilus) microplus;* the piroplasms multiply in the ovary of the female tick and thereby infect the larvae that hatch from her eggs. Calves are much less susceptible than older cattle. The greater susceptibility of

older hosts holds for all species of *Babesia* and is greatly increased by splenectomy.

Texas fever was once endemic south of the thirty-fifth parallel in the United States, but a cattle-dipping campaign launched in 1906 to eradicate *R. annulatus* virtually eliminated the disease by 1940. This prodigious effort was successful mainly because of the high degree of specificity displayed by *R. annulatus* for its bovine host. Other mammals can serve as hosts, but most *R. annulatus* ticks are found on cattle. Therefore when the cattle were rounded up for dipping, most of the feeding tick population was rounded up with them. *R. microplus*, on the other hand, infests a broad range of hosts. When *R. microplus* is involved, eradication of bovine piroplasmosis is virtually impossible with contemporary methods.

Other *Babesia* species of livestock

Babesia bovis, Babesia divergens, and *Babesia argentina* cause bovine piroplasmosis in various parts of the world. In the United Kingdom, piroplasmosis is transmitted between cattle by *Ixodes ricinus*. Each species of *Babesia* tends to use one or more different species of tick vectors. Other species of *Babesia* infect sheep *(Babesia ovis)*, horses *(Babesia caballi)*, and swine *(Babesia trautmanni)*.

Canine babesiosis

This disease is cosmopolitan in distribution (Lobetti, 1998). Dogs are infected with two species of these parasites, *Babesia canis* and *Babesia gibsoni. B. canis* is the larger form, with pear-shaped trophozoites, 4 to 5 μm long, typically being found in pairs in the erythrocytes. *B. gibsoni* is smaller, 3 μm long, and usually round to oval in shape. *B. gibsoni* is transmitted by *R. sanguineus,*

Haemaphysalis bispinosa, and *Haemaphysalis longicornis*. The species *B. canis* has been divided into three subspecies: *B. canis canis* of Europe, transmitted by *Dermacentor reticulatus; B. canis vogeli* of northern Africa and North America, transmitted by *R. sanguineus;* and *B. canis rossi* of southern Africa, transmitted by *Haemaphysalis leachi*. Fortunately, the subspecies in North America and Europe do not produce the fulminant form of disease seen in southern Africa (Jacobson, 2006). A survey of greyhounds in Florida has shown that large numbers (46% of 383 greyhounds) have antibodies to *B. canis* (Taboada et al, 1992), but most do not have clinical signs. Clinical signs when present include depression, anorexia, anemia, and splenomegaly. The strain of *Babesia* in Florida appears mainly to cause disease in puppies, for which the major diagnostic feature is anemia. The disease when present in dogs in the United States typically manifests with anemia, anorexia, and lethargy. In a recent survey of 673 canine blood samples tested for *Babesia* DNA by PCR, the 144 positive samples came from 29 states and one Canadian province (Birkenheuer et al, 2005). Of these samples, 91% (131) were recognized as the small form *Babesia, B. gibsoni*, and 10 were recognized as the larger *Babesia* form, *B. canis vogeli* (three samples did not match current recognized species). Almost all the samples representing *B. gibsoni* (122 of 131) were from American pit bull terriers. Six of the 10 *B. canis vogeli* cases were in greyhounds. We now also have a new species of small form of *Babesia, Babesia conradae*, that occurs in California in dogs and seems to be related to forms found in people and wildlife (Kjemtrup et al, 2006). *B. conradae* seems to be more pathogenic in dogs than *B. gibsoni* (Kjemtrup and Conrad, 2006). Diagnosis is based on demonstrating

trophozoites of the parasites in the erythrocytes in Giemsa-stained blood films or serology; of course, PCR is being used more and more commonly for the diagnosis of infections, especially with blood parasites.

Theileria

The genus *Theileria* differs from *Babesia* in that there are schizonts that occur in lymphocytes and induce the infected lymphocytes to undergo division and proliferation. Also, there is typically no transovarial transmission in the case of ticks infected with *Theileria* species. *Theileria parva*, the causative agent of East Coast fever of African cattle, occurs in the erythrocytes, lymphocytes, and endothelial cells and is transmitted interstadially by *Rhipicephalus* and *Hyalomma* species.. East Coast fever is characterized by dyspnea, emaciation, weakness, tarry feces, and exceptionally heavy mortality. *Theileria* (formerly *Babesia*) *equi* of the horse has been demonstrated to have schizont stages in lymphocytes. There are also species of *Theileria* in deer in the United States, such as *Theileria cervi*, which is transmitted by *Amblyomma americanum* (Reichard and Kocan, 2006)

Cytauxzoon

The genus *Cytauxzoon* is defined as distinct from *Theileria* in that the schizonts that occur in the vertebrate occur in macrophages rather than lymphocytes. There are some who would prefer to combine the genus under *Theileria*, and this might make good sense. However, the name *Cytauxzoon* does such a marvelous job of describing the disease and its effects on the feline host cell with the resulting pathogenesis that it would be sad to lose the name to synonymy.

The disease cytauxzoonosis, caused by *Cytauxzoon felis*, is a sporadic but rapidly and usually fatal disease of domestic cats occurring predominantly in the south central United States (Blouin et al, 1984; Bondy et al, 2005; Jackson and Fisher, 2006). Clinical signs consist of pyrexia, anemia, icterus, and dehydration; death occurs within a few days. Wright's- or Giemsa-stained blood smears reveal 1- to 2-μm organisms with light blue cytoplasm and dark red nucleus in the erythrocytes (Figure 3-29). Late in the course of cytauxzoonosis, enormous reticuloendothelial cells packed with schizonts appear in the peripheral blood. Histologically, parasitized reticuloendothelial cells nearly occlude the lumens of small- and medium-sized veins in the lungs, spleen, and lymph nodes (Haber and Birkenheuer, 2005; Wightman, Kier, and Wagner, 1977). The bobcat *Lynx rufus* has a parasitemia but no clinical signs of disease and may be the natural reservoir host of *Cytauxzoon felis* (Glenn, Rolley, and Kocan, 1982; Kier, Wagner, and Morehouse, 1982). Of interest, blood from parasitemic bobcats injected intraperitoneally into domestic cats led to a persistent erythroparasitemia but no clinical signs of disease. However, when *Dermacentor variabilis* nymphs were fed on a splenectomized parasitemic bobcat, allowed to molt to the adult stage, and then fed on two splenectomized domestic cats, the latter died in 13 and 17 days with typical lesions of cytauxzoonosis (Blouin et al, 1984). Thus, experimentally at least, *D. variabilis* serves as a transtadial vector of *Cytauxzoon felis* from the reservoir host *L. rufus* to the highly susceptible accidental host *F. catus* and leads to lethal infection with the schizogonic stages of this piroplasm. Iatrogenic cytauxzoonosis has been induced in a specific pathogen-free cat by the inoculation of mononuclear cells from a

Florida panther *(Felis concolor coryi)*, in an attempt to determine whether the panther was infected with feline immunodeficiency virus (Butt et al, 1991). The cat died 12 days after inoculation with typical schizonts of *Cytauxzoon felis* occluding the pulmonary veins (see Figure 8-39). In a recent survey of cases from the mid-Atlantic states, of 34 cats infected with *Cytauxzoon felis*, 32 succumbed to the infection (Birkenheuer et al, 2006). The most common signs of the infection were pancytopenia and icterus.

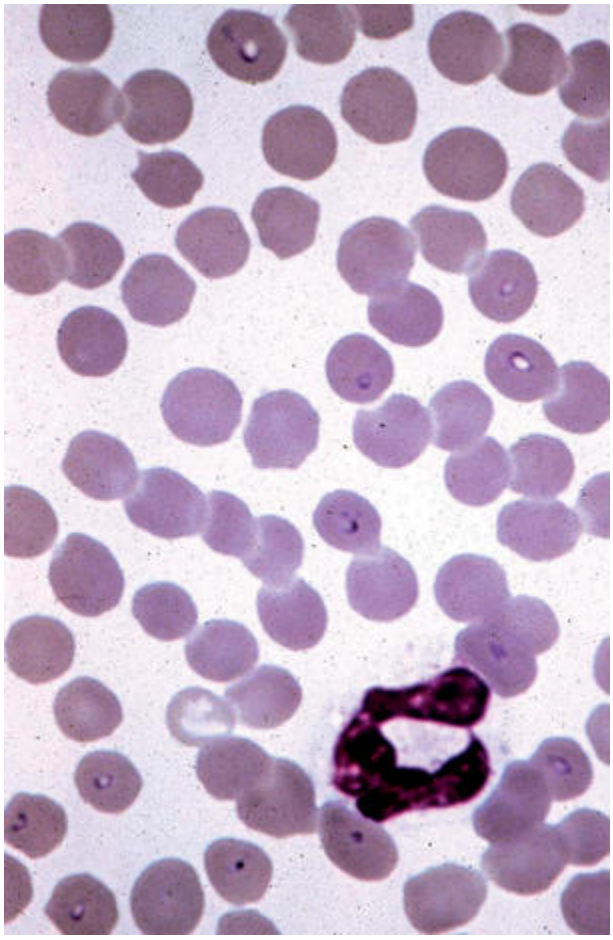

FIGURE 3-29 Giemsa-stained blood film from a cat showing the appearance of the *Cytauxzoon felis* organisms within the red blood cells.

Courtesy Dr. Tracy W. French.

Treatment of piroplasmoses

Dogs and cats

B. canis infection usually responds to a single intramuscular injection of 3.5 mg diminazene (Berenil) per kilogram or to subcutaneous injections of 15 mg phenamidine (Ganaseg) per kilogram (Lewis and Huxsoll, 1977; Roberson, 1977). *B. gibsoni* infections are not as readily curable with these drugs as is *B. canis* (Ruff et al, 1973). In Okinawa, diminazene aceturate (3 mg/kg injected intramuscularly on 2 consecutive days) and pentamidine isethionate (16.5 mg/kg injected intramuscularly on 2 consecutive days) appeared to cure *B. canis* infection and effected satisfactory clinical response in *B. gibsoni*–infected dogs but did not clear their blood of parasites (Farwell, LeGrand, and Cobb, 1982). None of these drugs are available for routine clinical use in the United States. Trypan blue and acridine derivatives (e.g., acriflavine) also have been used in the treatment of babesiosis. A combination of atovaquone and azithromycin has been recently recommended as a treatment for dogs with *B. gibsoni* (Birkenheuer, Levy, and Breitschwerdt, 2004).

For cytauxzoonosis, attempts to treat experimentally infected cats with parvaquone and buparvaquone, two drugs used to treat bovine theileriosis, failed to prevent the death of the infected cats (Motzel and Wagner, 1990). A cat that had a 2-day history of lethargy and anorexia rapidly progressed to become seriously icteric with dark-brown urine and began a 10-day course of enrofloxacin, followed by a 5-day course of tetracycline (Walker and Cowell, 1995). *Cytauxzoon felis* organisms were present in the blood of the cat after

the 10-day course of enrofloxacin but were not present in blood samples collected 6 and 15 weeks after discharge. Greene et al (1999) successfully treated six of seven cats with two intramuscular injections (2 mg/kg body weight) of diminazene (five cats) or imidocarb (one cat); one cat died after the first injection of diminazene. More recently, cats have been identified surviving natural infections with *Cytauxzoon felis* (Meinkoth et al, 2000). Eighteen cats from northwestern Arkansas and northeastern Oklahoma were initially identified through piroplasms in blood smears. Clinical signs in most cats were similar to those described for cytauxzoonosis, but four did not have signs. The parasitemia was generally persistent throughout follow-up (i.e., for up to 154 days). Only one cat was treated with imidocarb, and all cats survived. The authors postulate that they may be dealing with a less virulent strain of this parasite.

Horses

B. caballi and *T. equi* are susceptible to many antiprotozoal drugs, but in the United States none are approved for use in horses. Imidocarb dipropionate is administered subcutaneously at 2 mg/kg repeated once after 24 hours for the treatment of *B. caballi*, and at 4 mg/kg repeated at 72-hour intervals for *T. equi*.

Malarias

Plasmodium

Plasmodium species are the causative agents of malarias of humans, nonhuman primates, rodents, birds, and reptiles (mainly lizards). Mammalian malarias are transmitted by anopheline mosquitoes and

avian malarias by culicine mosquitoes; the vectors of reptilian malarias are largely unknown.

Life history

Sporozoites injected into the host by the infected mosquito during feeding enter cells such as hepatocytes, become trophozoites, and undergo schizogony. This first multiplication of plasmodia in hepatocytes is termed *preerythrocytic schizogony*. Merozoites released when the hepatocyte ruptures invade erythrocytes or reticulocytes of the circulating blood, pass through a trophozoite phase, and then undergo erythrocytic schizogony. In certain species of *Plasmodium*, some of these merozoites reinvade hepatocytes to continue exoerythrocytic schizogony, which is held accountable by some authorities for relapses after therapeutic elimination of erythrocytic infection by chloroquine, quinine, and the like. Merozoites released when the infected erythrocytes rupture reinvade other erythrocytes and again undergo schizogony. Each generation of erythrocytic merozoites occupies approximately 24, 48, or 72 hours, depending on the species of *Plasmodium* involved. Synchronization of schizogony and consequent erythrocyte destruction leading to cyclic bouts of chills and fever is typical of certain malarias, particularly those of humans. The terms *quotidian, tertian*, and *quartan* refer to recurrence of fever daily, on the third day (i.e., at 48 hours), and on the fourth day (i.e., at 72 hours), the anomaly in nomenclature arising from inconsistency in the inclusion of zero in the system of natural numbers as applied to the reckoning of time. Eventually some merozoites develop into either microgametocytes or macrogametocytes, which are the stages infective for the mosquito. When a suitable species of mosquito feeds on a malarious host, the

microgametocytes and macrogametocytes in the blood meal mature, and the microgametes fertilize the macrogametes to form zygotes. The zygotes then elongate to form motile ookinetes, which migrate to the hemocoel side of the mosquito's midgut, where each develops into an oocyst. Thousands of sporozoites develop within each oocyst by a budding process similar to schizogony and are released into the hemocoel when the oocyst ruptures. Those sporozoites that reach the salivary glands are ready to infect another host next time the mosquito takes a blood meal and thus complete the rather involved life history of *Plasmodium*. In humans the symptoms of malaria are extremely variable, and diagnosis depends on the demonstration of plasmodia in fixed, stained blood smears. Fatality can usually be attributed to cerebral involvement, renal failure, or pulmonary hemorrhage.

Identification

Differentiation of species of *Plasmodium* is based on study of Giemsa-stained thin blood smears and recognition of rather subtle morphologic features of the early trophozoite ("ring form") (Figure 3-30), ameboid late trophozoite, schizont, and male and female gametocytes. The color and distribution of hematin in the cytoplasm of the parasite, as well as cytoplasmic stippling and other morphologic alterations of the infected erythrocyte, are also taken into account. The diagnosis of malaria is clearly a job for an expert. For human malarias there are now also available antigen detection methods similar to those used in animal medicine for heartworm and viruses.

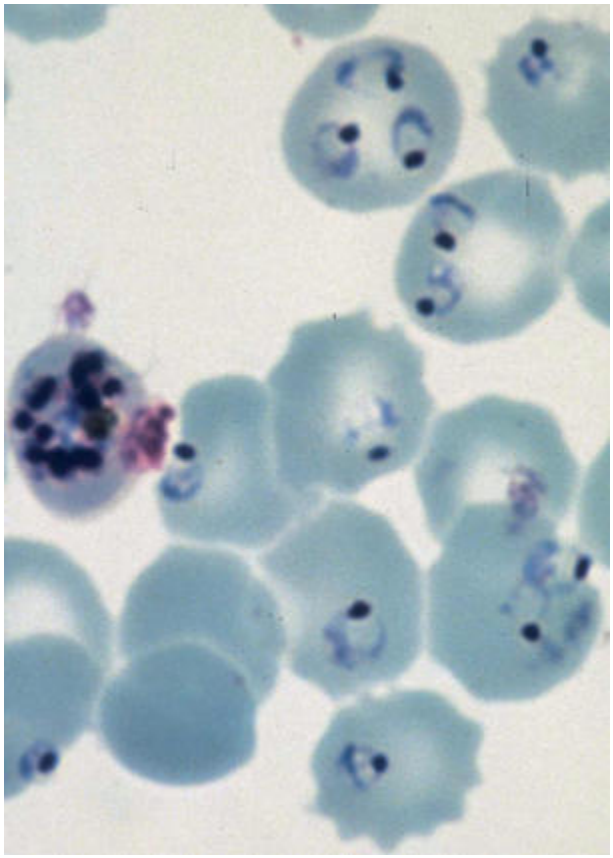

FIGURE 3-30 *Plasmodium falciparum*, human malaria, ring-stage trophozoites in red blood cells.

Simian malaria

About 20 species of *Plasmodium* have been described from nonhuman primates, some of which (e.g., *Plasmodium knowlesi*, *Plasmodium cynomolgi*) are transmissible to humans through the bites of infected anopheline mosquitoes. The diagnosis of simian malaria is of particular interest to laboratories where imported primates are experimental animals (Coatney et al, 1971). Old World monkeys may also be infected with *Hepatocystis*.

Avian malaria

Avian malaria is a complex of diseases caused by many species of *Plasmodium* (Figure 3-31). *Haemoproteus* and *Leucocytozoon*, considered later, also cause malaria-like infections in birds.

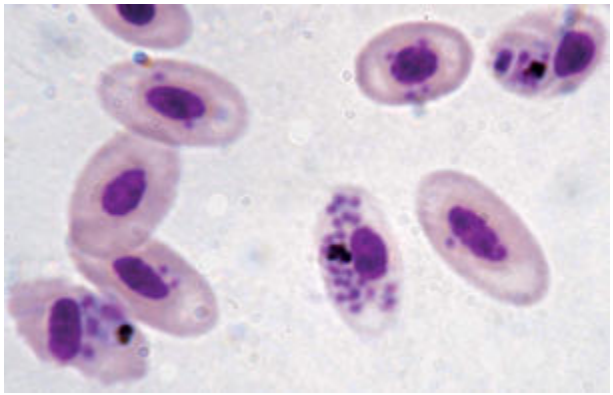

FIGURE 3-31 Schizonts of *Plasmodium gallinarum* in chicken red blood cells

Specimen courtesy of Priscilla Maldonado, New York University.

Haemoproteus

Haemoproteus species are parasites of birds, turtles, and lizards. Schizogony occurs in vascular endothelial cells of various organs, and only gametocytes appear in circulating erythrocytes. In blood films fixed with methanol and stained with Giemsa, the gametocytes appear as elongated, sometimes horseshoe-shaped cells embracing the erythrocyte nucleus; the cytoplasm of the gametocyte contains pigment granules accumulating as a result of the incomplete digestion of hemoglobin (Figure 3-32). Various species of *Haemoproteus* are transmitted by *Culicoides*, Hippoboscidae, or *Chrysops*, which become infected when they ingest erythrocytes containing gametocytes. Fertilization, development of oocysts, and salivarian transmission of sporozoites to the vertebrate host

resemble the corresponding events in the life history of *Plasmodium*. *Haemoproteus* is essentially nonpathogenic.

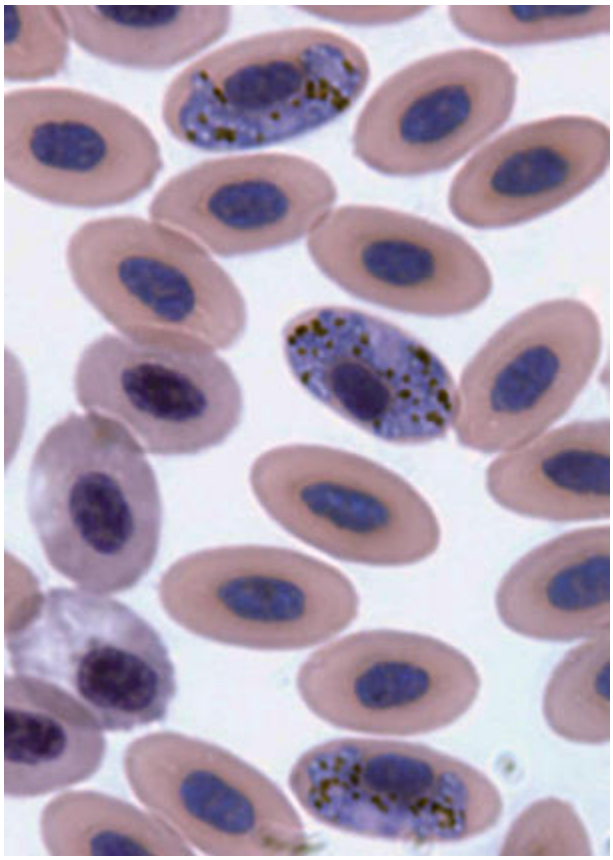

FIGURE 3-32 *Haemoproteus* sp. in avian red blood cells (Giemsa stain).

Leucocytozoon

Leucocytozoon species are parasites of domestic and wild birds; *Leucocytozoon simondi* causes acute, fatal disease in ducks and geese, as do *Leucocytozoon caulleryi* in chickens and *Leucocytozoon smithi* in turkeys. Schizogony occurs in hepatocytes and vascular endothelial cells of various tissues, producing merozoites that invade erythroblasts, erythrocytes, lymphocytes, and monocytes, and there develop into gametocytes. Leucocytozoon gametocytes differ from those of *Plasmodium* and *Haemoproteus* in not containing pigment

granules and in greatly distorting the host cell (Figure 3-33). Some gametocytes are round and push the host cell nucleus to one side so that it forms a cap on the parasite. Others are oval or elliptic in cells that become elongated and bizarre in appearance as the parasite grows. *Simulium* species serve as intermediate hosts.

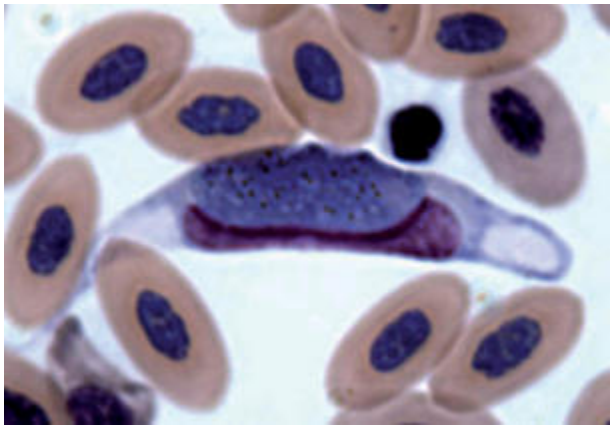

FIGURE 3-33 *Leucocytozoon* sp in a blood smear from a red-tailed hawk (Giemsa stain).

Hepatocystitis

Hepatocystis species are parasites of the lower monkeys, fruit bats, and squirrels of the Old World. Schizogony occurs in hepatocytes, requires 2 months, and results in large schizonts called *merocysts*. Merozoites released from merocysts invade erythrocytes and develop into gametocytes. *Culicoides* species are the probable vectors.

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CHAPTER 4

Helminths

The parasitic worms belong to the phyla Platyhelminthes (flat worms, flukes, and tapeworms), Nemathelminthes or Nematoda (roundworms), Acanthocephala (thorny-headed worms), and Annelida (segmented worms, night-crawlers). Tongueworms of the parasitic class Pentastomida are also wormlike in appearance, but being of the phylum Arthropoda, are discussed in Chapter 2. This list of helminth taxa does not exhaust Nature's bounty of "small, elongate, and slender, creeping or crawling animals, usually soft-bodied, naked, and limbless or nearly so; any animal having a real or fancied resemblance to an angleworm or earthworm" (*Webster's New International Dictionary*, ed 2, Springfield, Mass, 1935, G & C Merriam Co). However, it does include all of the worms in which veterinarians are particularly interested.

PHYLUM PLATYHELMINTHES

The phylum Platyhelminthes contains three classes: Turbellaria, Trematoda, and Cestoda. All are typically soft-bodied, flattened dorsoventrally, and hermaphroditic. The Turbellaria (planarians) are mostly free-living, carnivorous flatworms. Aquarists finding planarians in fish tanks may mistake them for parasites, but otherwise they are of only passing interest to veterinarians. The trematodes (flukes) of importance to veterinary medicine may be found as adults in the intestine, bile ducts, lungs, blood vessels, or

other organs of their vertebrate final hosts. Adult cestodes (tapeworms) are parasites of the intestine of vertebrates, and their larvae are parasites of different vertebrates or of invertebrates. The class Cestoda includes many important parasites of domestic animals and is the subject of the second portion of this section.

Class Trematoda

The class Trematoda contains three orders: Monogenea, Aspidogastrea, and Digenea. Monogeneans and most aspidogastreans undergo direct development and are parasites of aquatic and amphibious animals. *Gyrodactylus* and *Dactylogyrus*, for example, are common and pathogenic monogenean parasites of the skin and gills of aquarium fishes. These two orders of parasites are of interest to few veterinarians. The trematodes of importance to most veterinarians are the digenetic trematodes.

Order Digenea

Life history

The order Digenea is so called because its members undergo indirect development with sexual and asexual generations parasitizing alternate hosts. All flukes infecting dogs, cats, ruminants, horses, and swine are digeneans. The life history of *Fasciola hepatica*, depicted in Figure 4-1, is typical of the order.

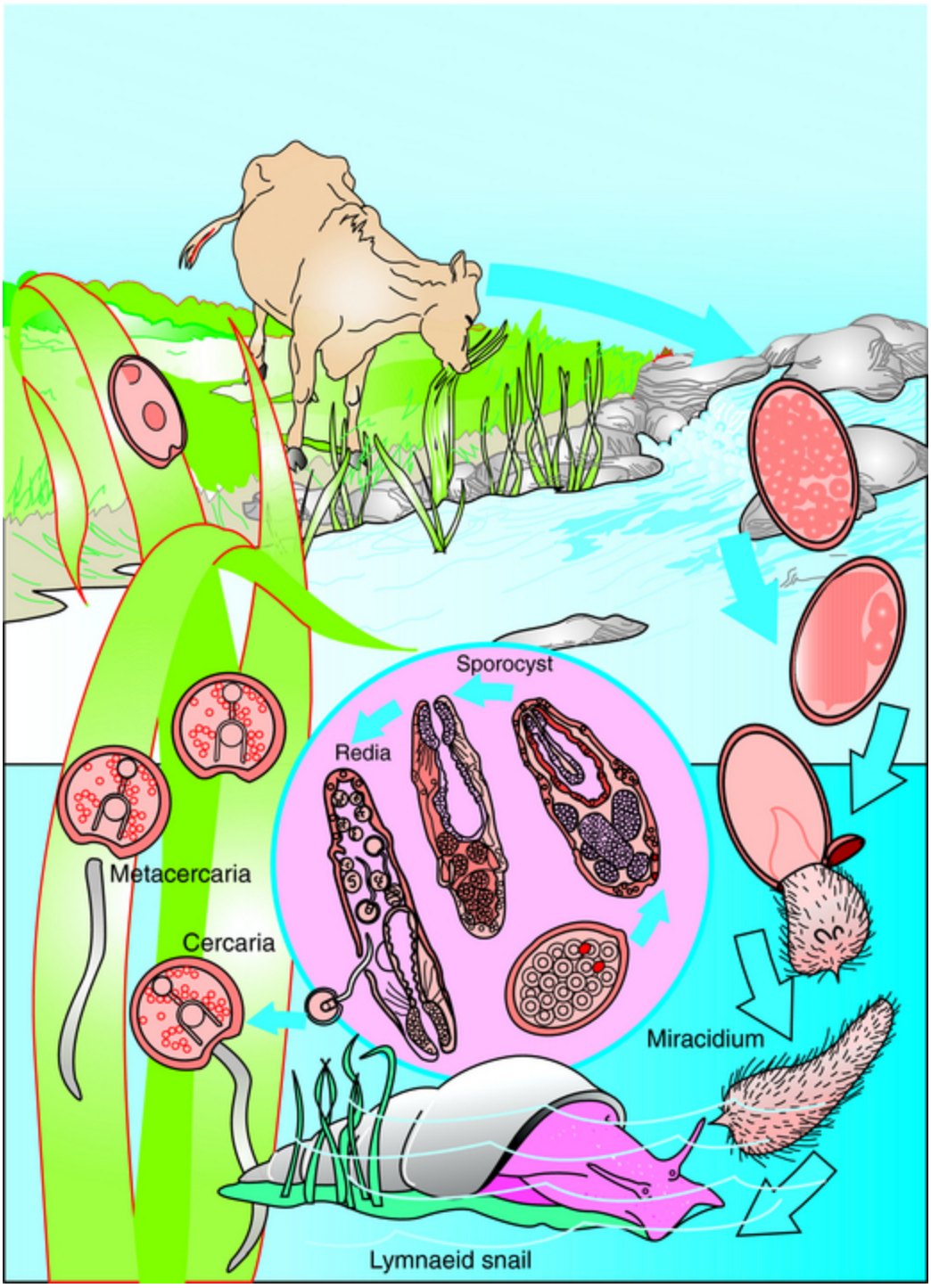

FIGURE 4-1 Life history of *Fasciola hepatica.* The adult liver flukes produce fertile eggs that leave the host by way of the common bile duct and intestinal tract. If these eggs are carried to water, a ciliated miracidium develops within them over a period of several weeks or months, depending on the temperature of the water. On hatching, the miracidia seek certain species of lymnaeid snails, in which they develop and multiply through one

generation of sporocysts and two of rediae. The second generation of rediae produce free-swimming cercariae that leave the snail and encyst as metacercariae on various submerged objects, including aquatic vegetation. Ruminants and other animals become infected with *F. hepatica* when they ingest aquatic plants contaminated with metacercariae.

Adult *F. hepatica* flukes (Figure 4-2) live in the bile ducts of ruminant and other mammalian hosts. Their eggs are carried first to the bowel lumen with the bile and then to the exterior with the feces. When deposited, each of these eggs consists of a fertilized ovum and a cluster of vitelline cells enclosed in an operculated capsule (Figure 4-3). Only if the egg falls into water will a ciliated larva called a **miracidium** develop inside it (Figure 4-4). The miracidium is completely covered with cilia and has a conical papilla at its anterior end for boring into the snail intermediate host, a pair of eye spots, a brain, a rudimentary excretory system, and a cluster of germinal cells, the progenitors of the next generation of larvae (Figure 4-5). The miracidium, which is fully developed and ready to hatch after 2 to 4 weeks at summer temperatures, escapes from the egg capsule by pushing aside the operculum and swims about in search of a suitable species of snail (e.g., *Lymnaea truncatula*). If it fails to find such a snail within 24 hours, the miracidium exhausts its energy stores and dies.

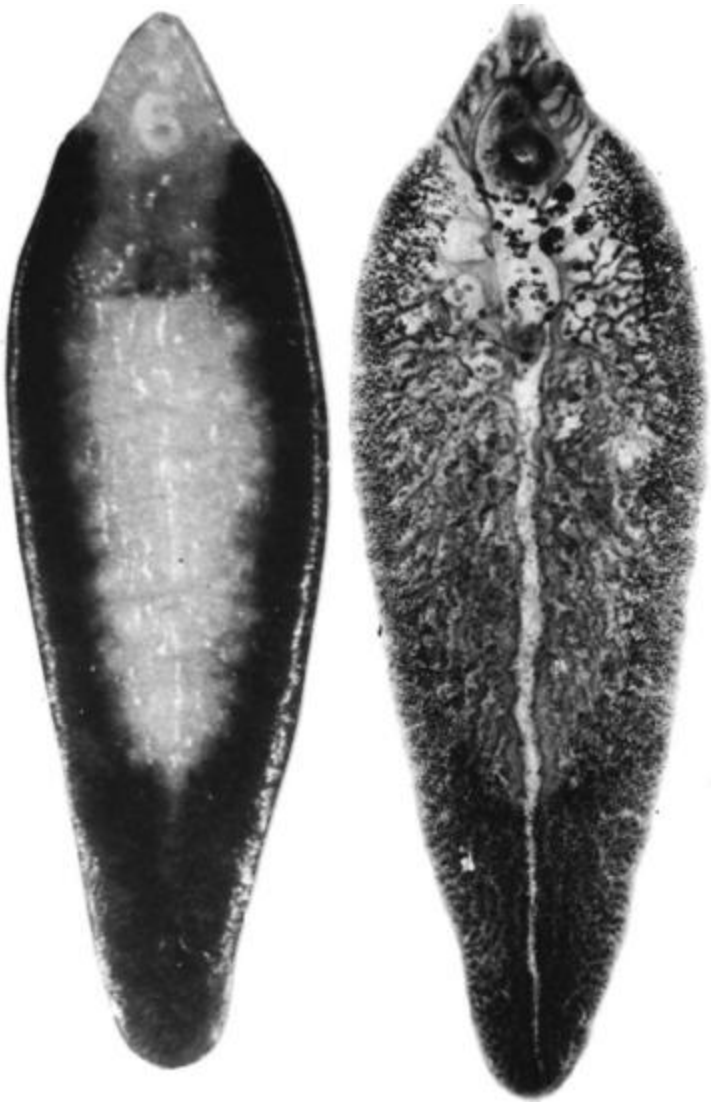

FIGURE 4-2 Adult *Fasciola hepatica* liver fluke. *Left,* An uncleared specimen. *Right,* A cleared, stained specimen.

FIGURE 4-3 Egg of *Fasciola hepatica* from feces.

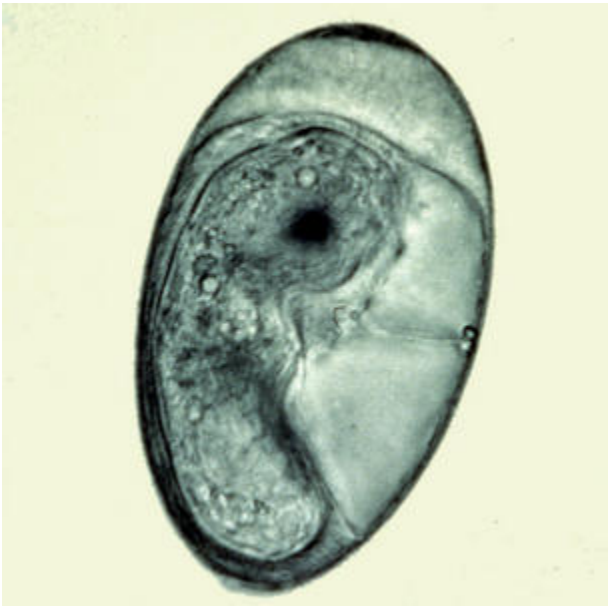

FIGURE 4-4 Egg of *Fasciola hepatica* containing a fully developed miracidium.

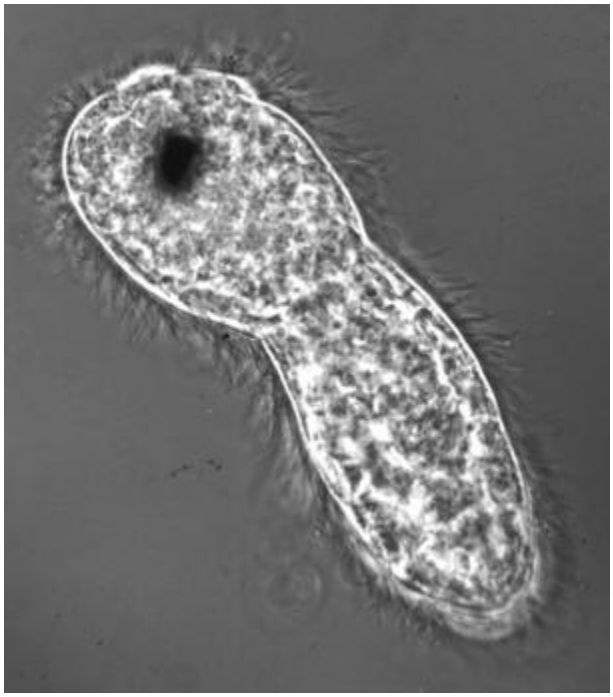

FIGURE 4-5 Miracidium of *Fasciola hepatica* swimming; electronic flash photomicrograph.

If the miracidium is more fortunate, it bores into the snail's body, loses its ciliated covering, migrates to the gonad or digestive gland (often referred to as the liver), and forms a **sporocyst**. Each germinal cell, by growth and repeated divisions, becomes a germinal ball, and each germinal ball develops into a redia (Figure 4-6).

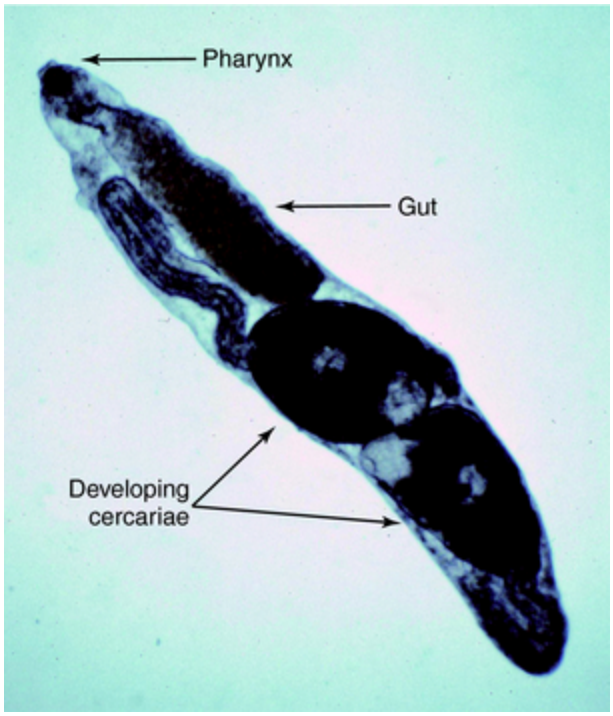

FIGURE 4-6 Redia of *Fascioloides magna* from a snail showing developed cercariae inside.

Courtesy Dr. Gary A. Conboy, Atlantic Veterinary College, University of Prince Edward Island, Canada.

The rediae grow until they burst the sporocyst wall and are thus liberated into the tissues of the snail. The redia has a mouth and digestive organs and eats its way through the snail's tissues. Like the sporocyst, the redia is packed with germinal balls, these being the progenitors of a second generation of rediae. Each germinal ball of second-generation rediae develops into yet a third kind of larva, the **cercaria** (Figure 4-7).

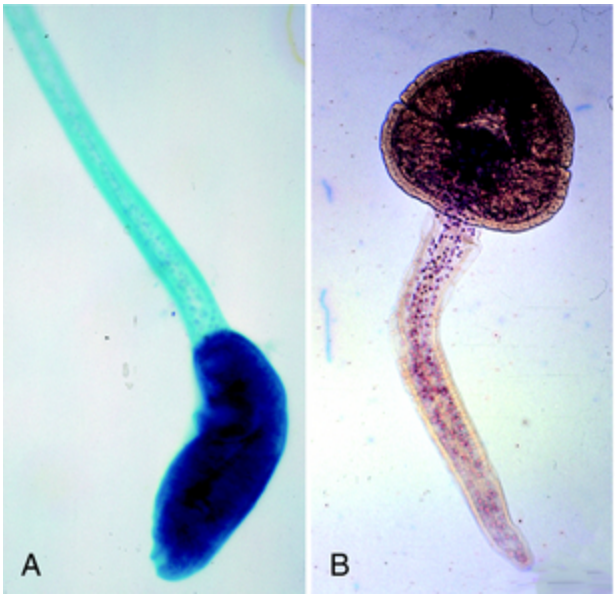

FIGURE 4-7 Cercariae of *Fasciola hepatica.*

The cercaria is a tadpolelike larva with a discoidal body and a long tail for swimming. The cercaria displays certain adult organs (e.g., oral and ventral suckers, mouth, pharynx, forked intestine, and excretory canals with flame cells) and primordia of the reproductive organs. Special secretory cells alongside the pharynx are purely larval structures; they secrete a cyst wall within which the final larval stage will lie in wait for a grazing ruminant. When fully developed in a month or two of summer temperatures, the cercaria leaves the redia through a birth pore and makes its way out through the snail's tissues and into the surrounding water. After a brief swim the cercaria migrates a short distance above the water level on the surface of some plant and encysts, losing its tail in the process to become a **metacercaria**, the stage that is infective to sheep and other grazing mammals (Figure 4-8).

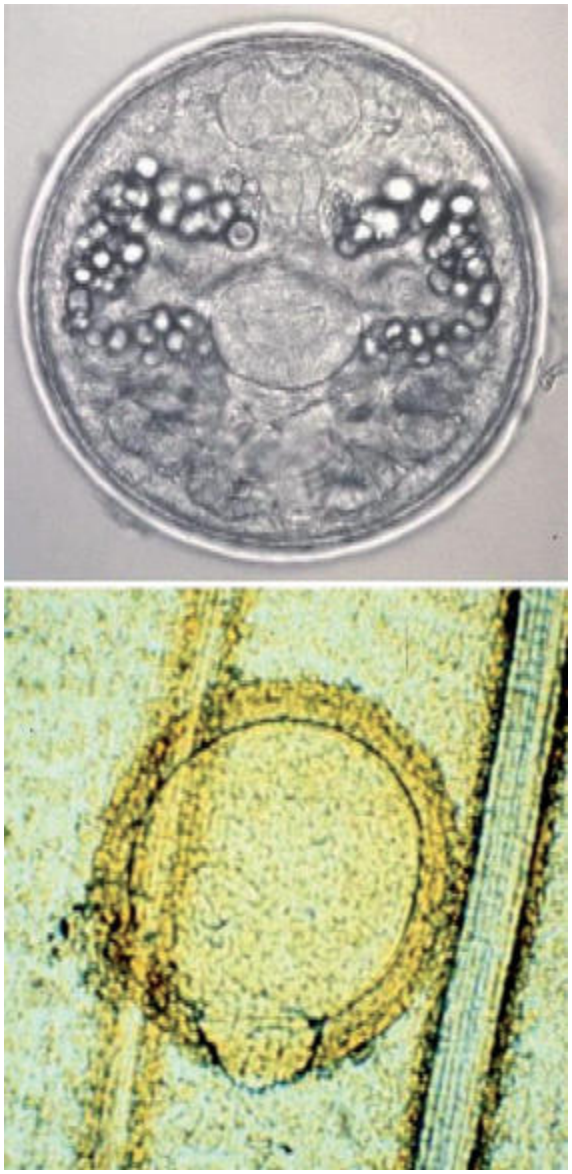

FIGURE 4-8 Metacercariae of *Fasciola hepatica*. *Top,* Free cyst. *Bottom,* Cysts on vegetation.

When ingested, the metacercarial cyst wall is digested in the host's small intestine. The young fluke, now called a **marita**, penetrates the wall of the intestine and crosses the peritoneal space to the liver, which it penetrates (see Figure 8-41). After several weeks of boring about in the hepatic parenchyma, the maritas enter the bile ducts, mature into adult flukes, and begin laying eggs at about a month

and a half after infection. The complete life cycle of *F. hepatica* thus encompasses 3 or 4 months under favorable conditions. Therefore exposure to this parasite and patent infection tend to be rather more widely separated in time than is the case of most ruminant parasitisms.

Digenean trematodes are very discriminating in their choice of snail hosts, and the geographic distribution of trematode species is therefore largely dictated by the geographic distribution of suitable species of snails. Adult trematodes, on the other hand, seem to be able to make do with a rather broad range of definitive host species.

The metacercarial stage determines what food the host must eat to obtain an infection with an adult fluke. The strategies used by different trematodes vary (Figure 4-9). The metacercariae of fasciolids and paramphistomatids encyst on vegetation and have a strategic advantage when it comes to getting into grazing ruminants. For the troglotrematids, heterophyids, and opisthorchiids, the metacercariae encyst in intermediate hosts such as fish, crayfish, and crabs, and fish-eating mammals tend to serve as the final hosts. The diplostomatids are found within amphibians or other vertebrate paratenic hosts, whereas the dicrocoeliids encyst in arthropods. The schistosomatids differ from other trematodes in that there is no metacercarial stage; rather, the cercariae penetrate the skin of the final host. Sometimes humans eat foodstuffs that put them in contact with possible trematode infections (e.g., *F. hepatica* has found its way into humans by way of watercress, and *Dicrocoelium dendriticum* has entered humans through the ingestion of ants containing metacercariae).

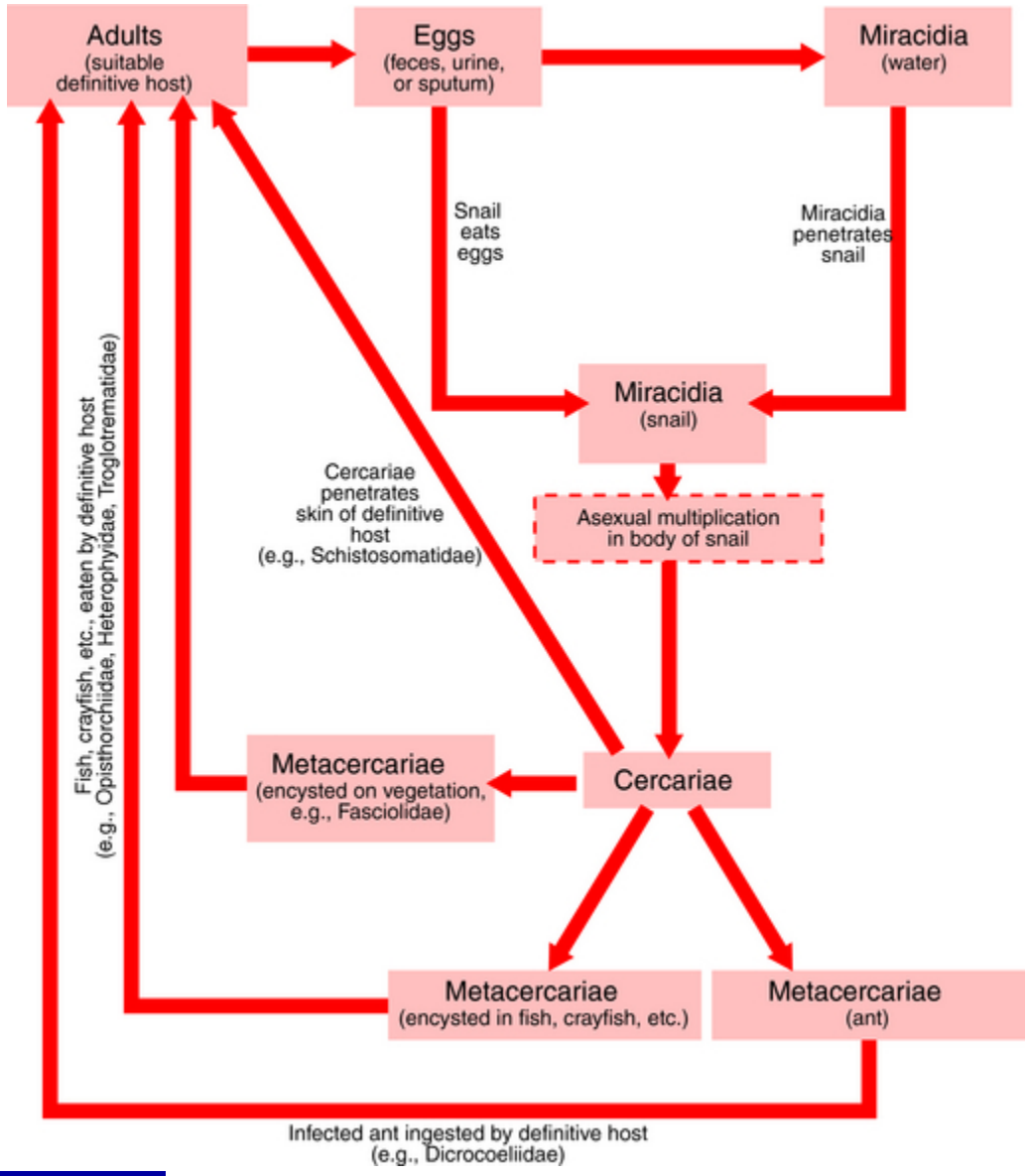

FIGURE 4-9 Some life history variations followed by trematode parasites of domestic animals.

Identification

An adult trematode is typically little more than a bag of reproductive organs with both sexes represented. Typically there are two testes and one ovary, the anatomic positions of which provide diagnostic criteria. The genital pore may be identified by the convergence of male and female reproductive ducts. Usually the

presence of a cirrus, or intromittent organ, helps to identify the male duct, and a procession of well-tanned eggs the female duct. The oral sucker surrounds the mouth, which is connected by way of the esophagus to a pair of blind ceca. The ceca are simple tubular sacs in most species but are intricately branched in the family Fasciolidae. The ventral sucker or acetabulum is often but not always near the genital pore. In the family Heterophyidae, both the ventral sucker and the genital pore are enclosed in an invagination, the ventrogenital sac, and an extra genital sucker or gonotyl surrounds the genital opening. The anatomic structures most used as taxonomic characters are labeled in Figure 4-10. Diagnostic criteria sufficient for identification of these families are presented in the following discussion. In general, identification of trematodes to family level combined with the host and organ listings provided in Chapter 7 will result in sufficiently precise diagnosis to serve practical needs. An excellent guide to the identification of families and genera of trematodes of North America north of Mexico is S.C. Schell's *Handbook of Trematodes of North America North of Mexico* (Moscow, Idaho, 1985, University Press of Idaho). Because only a limited set of trematode species is likely to be found in domestic animals in any particular locality, knowledge of the endemic species is valuable. Sometimes the only way to acquire this information is to submit collections for expert identification. The specimens should be relaxed by overnight storage at 5° C and fixed in formaldehyde and acetic acid in alcohol (FAA) or shipped fresh and packed in plenty of ice in a well-insulated container.

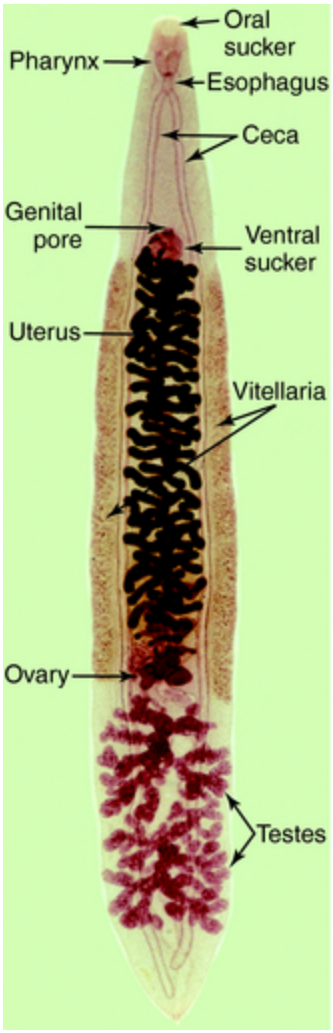

FIGURE 4-10 *Clonorchis sinensis* (Opisthorchiidae).

A Few Representative Families of Trematodes

Information on the geographic distribution and biology of some trematodes of veterinary importance can be found in Table 4-1.

TABLE 4-1 Information on Some Trematodes of Veterinary Importance

Family	Genera and Species	Geographic Distribution	Hosts	Location in Host	Disease	Length of Adult	Length of Egg	Second Intermediate Host	Prepatent Period
Fasciolidae	*Fasciola hepatica*	Tropics and U.S.	Herbivorus mammals and	Bile ducts	Hepatic fibrosis	3 cm	120 µm	Metacercariae on vegetation	60 days
	Fasciola gigantica	Africa	humans	Bile ducts	Hepatic fibrosis	5 cm	120 µm	Metacercariae on vegetation	60 days
	Fasciolopsis buskii	Asia	Pigs and humans	Intestine	Intestinal upset	8 cm	120 µm	Metacercariae on vegetation	90 days
	Fascioloides magna	U.S. and Europe	White-tailed deer	Liver (cysts)	Hepatitis, kills other cervids and small ruminants, nonpatent cysts in cattle	10 cm	120 µm	Metacercariae on vegetation	270 days
Paramphistomidae	*Paramphistomum* and *Cortylophoron*	Worldwide	Ruminants	Rumen	Intestinal damage by immature flukes	10 mm	120 µm	Metacercariae on aquatic vegetation	80 days
Troglotrematidae	*Nanophyetus salmincola*	North Pacific rim	Dogs and cats	Intestine	Transmits *Neorickettsia helminthoeca*	1 mm	80 µm	Fish	7 days
	Paragonimus kellicotti	Eastern U.S.	Minks, dogs, cats	Lungs	Cysts in lungs	6 mm	90 µm	Crayfish	30 days
Heterophyidae	*Cryptocotyle*	U.S.: East coast	Birds	Intestine	Enteritis	2 mm	30 µm	Fish	14 days
	Heterophyes	Middle East	Dogs and cats	Intestine	Enteritis	2 mm	30 µm	Fish	14 days
Opisthorchidae	*Opisthorchis*	Asia and Europe	Dogs and cats	Bile ducts	Very little	6 mm	30 µm	Fish	30 days
	Metorchis	U.S.	Foxes, pigs	Bile ducts	Very little	6 mm	30 µm	Fish	17 days
	Clonorchis	Asia	Dogs and cat	Bile ducts	Very little	6 mm	30 µm	Fish	60 days
Dicrocoelidae	*Dicrocoelium dendriticum*	New York, Quebec, British Columbia, Europe	Sheep, cattle, pigs, deer, woodchucks	Bile ducts	Fibrosis with chronic disease	10 mm	40 µm	Ants	80 days
	Platynosum fastosum	Caribbean and southern U.S.	Cats	Bile ducts and gall bladder	Hepatitis, fibrosis, vomiting, jaundice, diarrhea	7 mm	45 µm	Lizards	30 days

Family	Genera and Species	Geographic Distribution	Hosts	Location in Host	Disease	Length of Adult	Length of Egg	Second Intermediate Host	Prepatent Period
Diplostomatidae	*Alaria canis*	Northern U.S. and Canada	Dogs and foxes	Intestine	Very little	4 mm	100 µm	Frogs, paratenic hosts	35 days
	*Alaria marciana*e	Southern U.S.	Raccoons and opossums						
	Fibricola texensis								
Schistosomatidae	*Schistosoma mansoni*	Worldwide	Humans	Mesenteric veins	Hepatic fibrosis	10-20 mm; sexes separate	55-145 µm; lateral spine	None, penetrate skin	60 days
	Schistosoma haematobium	Africa	Humans	Veins of urinary bladder	Erosion of bladder wall	10 mm; sexes separate	60 × 140 µm; terminal spine	None, penetrate skin	70-84 days
	Schistosoma japonicum	Asia	Humans, cats, mammals	Mesenteric veins	Hepatic fibrosis	10 mm; sexes separate	58 × 85 µm; no spine	None, penetrate skin	35-42 days
	Schistosoma bovis	Africa	Cattle	Mesenteric veins	Hepatic fibrosis	10 mm; sexes separate	62 × 207 µm; terminal spine	None, penetrate skin	42 days
	Schistosoma margrebowiei	Africa	Horses, ruminants	Mesenteric veins	Hepatic fibrosis	10 mm; sexes separate	60 × 80 µm; no spine	None, penetrate skin	38 days
	Bivitellobilhania loxodontae	Africa	Elephants	Mesenteric veins	Hepatic fibrosis	10 mm; sexes separate	71 × 87 µm; no spine	None, penetrate skin	Not known
	Heterobilharzia americana	U.S.	Raccoons, dogs, opossums	Mesenteric veins	Hepatic fibrosis	10 mm; sexes separate	70 × 87 µm; no spine	None, penetrate skin	60 days
	Bird genera	Worldwide	Birds	Skin	Dermatitis in mammals	10 mm; sexes separate	Varied	None, penetrate skin	

Trematodes acquired by eating metacercariae encysted on vegetation

Family Fasciolidae

Identification

The body is large and leaflike, with suckers close together at the anterior end; the ceca have numerous diverticula; and the ovary and testes are dendritic (Figure 4-11; see also Figure 4-2). *F. hepatica* and *Fasciola gigantica* are parasites of the liver and bile ducts of herbivorous mammals and man, with *F. gigantica* being more restricted to the tropics. *Fascioloides magna* is a parasite of the liver of the white-tailed deer but also will infect other ruminants. *Fasciolopsis buski* is a parasite of the small intestine of pigs and humans in Asia; the ceca of this species do not have diverticula. Antemortem diagnosis of chronic fascioliasis is by demonstration of the large operculate eggs (see Figure 4-3) in the feces. Saturated sucrose floats but distorts the eggs, which nevertheless remain recognizable. Sedimentation techniques are preferred, however.

FIGURE 4-11 Liver flukes of ruminants. *Fasciola hepatica, Fasciola gigantica,* and *Fascioloides magna* belong to the family Fasciolidae. The small flukes scattered about are *Dicrocoelium dendriticum* of the family Dicrocoeliidae.

Life history

The life history of *F. hepatica* as presented in the preceding section is typical of the family. The geographic distribution of *F. hepatica* is worldwide but discontinuous. In North America, *F. hepatica* is found in the Gulf Coast States, the Pacific Northwest, the Caribbean, and eastern Canada. The lymnaeid snails that serve as intermediate hosts require neutral soils that remain reasonably moist throughout the year and tend to flourish where winters are not so cold as to destroy the eggs and juvenile stages, thus permitting the parasite population to survive its season of hardship in both definitive host and

environment. Because soil characteristics may vary dramatically within very short distances, it is not uncommon for one “fluky pasture” to contain all of the *F. hepatica* snails and metacercariae, whereas the rest of the farm may afford safe grazing. Small streams, ponds, and marshy areas are obvious snail-breeding areas, but any depression (e.g., rut, dead furrow) that can hold a bit of water for a while can serve as a source of infection during periods of adequate rainfall.

Transmission of fascioliasis occurs between February and July in Louisiana (Malone et al, 1984), but in the northwestern states transmission gradually builds through the pasture season and reaches a peak during November (Hoover et al, 1984). Summer drought tends to interrupt the cycle on the Gulf Coast, whereas winter cold tends to do the same in the Northwest. However, special circumstances may produce unexpected results. For example, outbreaks of fascioliasis during periods of drought form an apparent paradox that can be explained as follows. When drought has laid waste to the rest of the pasture, green vegetation is still to be found at the water hole, and livestock may be forced to graze on aquatic plants, which they ordinarily eschew as unpalatable. Such plants are likely to be heavily contaminated with the resistant metacercariae of *F. hepatic,* and concentrated grazing on them may result in serious levels of infection. Because metacercariae are extremely resistant to drying, infection may follow feeding of hay grown on infested meadows far removed from the scene of an outbreak.

F. magna, one of the largest known trematodes, is widely scattered over North America. Adult *F. magna* organisms are found in cysts that communicate with the bile ducts of its normal definitive host,

the white-tailed deer *(Odocoileus virginianus)*. In cattle, these cysts usually do not communicate with the bile ducts, and in sheep and goats *F. magna* maritas fail to mature and the juvenile flukes wander aimlessly and destructively in the liver tissue (see Figure 7-68). Therefore *F. magna* infection is nonpatent in cattle, sheep, and goats and cannot be diagnosed by fecal examination in these hosts. Aimlessly migrating *F. magna* maritas are likewise very destructive in llamas, *Dama* deer, sika deer, and other cervids in game farms and petting zoos where white-tailed deer probably serve as the source of infection.

Importance

Several clinical syndromes may be associated with liver fluke infection, depending on the numbers and stage of development of the parasite and on the presence or absence of *Clostridium novyi*. **Acute fluke disease** occurs during invasion of the liver by recently ingested metacercariae. In heavy invasions the trauma inflicted by the maritas tunneling about in the liver and consequent inflammatory reaction result in highly fatal clinical illness characterized by abdominal pain with a disinclination to move. Postmortem examination reveals an abdominal cavity containing blood-stained exudate and an enlarged, friable liver covered with fibrin tags; large numbers of maritas can be recovered from the cut surfaces. Heavy invasions of the sort associated with acute fluke disease may occur when lambs are turned into pastures containing marshy areas that were heavily contaminated the previous season.

In certain cases all that is needed to precipitate rapidly fatal disease is a minor trauma that provides clostridial organisms with

some damaged and poorly oxygenated tissue in which to multiply and secrete their deadly toxins. Even the minor trauma associated with the migrations of a few *F. hepatica* (or *Taenia hydatigena* larvae) is enough to provide an appropriate environment for *C. novyi.* As is typical of clostridial infections, sheep die so fast that they hardly have time to be sick. Necropsy reveals focal liver necrosis and extensive subcutaneous hemorrhage; the latter is possibly responsible for the colloquial name "black disease." *C. novyi* also causes a lethal condition called "big head" in young rams, but here the precipitating trauma results from contests of physical prowess instead of parasite migrations.

Chronic fluke disease is associated with the presence of adult trematodes in the bile ducts and is characterized by the classical clinical signs of liver fluke infection. There is gradual loss of condition, progressive weakness, anemia, and hypoproteinemia with development of edematous subcutaneous swellings, especially in the intermandibular space and over the abdomen. Necropsy reveals distended, thickened bile ducts packed with adult trematodes. In cattle the fibrotic ducts later calcify to produce what looks like a branching system of clay pipes. Isseroff, Sawma, and Reino (1977) demonstrated that the bile duct hyperplasia of fascioliasis is related to the excretion of large amounts of the amino acid proline by *F. hepatica*. Isseroff, Spengler, and Charnock (1979) have adduced evidence to the effect that proline synthesis and excretion by *F. hepatica* may account, at least in part, for the anemia that often accompanies infection with this fluke.

The presence of one fluke leads to condemnation of the liver in slaughtering establishments inspected by the U.S. Department of

Agriculture (USDA). Tindall (1985) reported that almost one third of livers from cattle raised in Puerto Rico were condemned during the year ending in October 1984. Following Puerto Rico, in order of percentage of livers condemned, were Florida, Nevada, Oregon, Idaho, Utah, Washington, and California. Probably, liver condemnations far outweigh losses caused by clinical fascioliasis in economic importance. Briskey, Scroggs, and Hurtig (1994) examined livers from seven slaughterhouses in 17 of the western United States and found 368 of 1913 livers positive for liver flukes. *F. magna* causes considerable economic loss by producing wasted cattle livers condemned as unfit for human consumption, and its destructive migrations in the livers of sheep and goats virtually preclude small ruminant production in endemic areas.

Treatment and control

Clorsulon (Curatrem) is administered to cattle orally as 8.5% suspension at a dosage rate of 7 mg/kg for treatment of immature and adult *F. hepatica* infections (Malone, Ramsey, and Loyacano, 1984; Courtney, Shearer, and Plue, 1985; Yazwinski et al, 1985). The dose of clorsulon (2 mg/kg) administered with ivermectin as Ivomec Plus is only fully efficacious against the adults of *F. hepatica*. Clorsulon is not licensed for use in dairy cattle of breeding age, and cattle must not be treated within 8 days of slaughter.

Albendazole is indicated for the removal of liver fluke from cattle at a dosage rate of 10 mg/kg of body weight and from sheep at 7.5 mg/kg. Albendazole is not licensed for use in dairy cattle of breeding ages, and cattle must not be treated within 27 days of slaughter. Albendazole (15 mg/kg) was effective in eliminating

adult *F. hepatica* and in reducing the death rate among naturally infected goats in Montana (Leathers et al, 1982).

Other effective flukicides (diamphenethide, nitroxynil, oxyclozanide, rafoxanide, triclabendazole) are not available in the United States.

F. magna presents a more difficult problem in domestic ruminants. Both clorsulon (24 mg/kg) and albendazole (26 mg/kg) were reasonably effective against immature and adult *F. magna* in its natural host, the white-tailed deer (Foreyt and Drawe, 1985). However, a drug must kill essentially all immature *F. magna* to benefit infected sheep and goats because survival of only a few maritas is potentially lethal in these hosts. In sheep a single treatment with clorsulon (15 mg/kg) 8 weeks after inoculation with metacercariae of *F. magna* was not sufficiently effective to be of practical value (Conboy, Stromberg, and Schlotthauer, 1988), whereas closantel (15 mg/kg orally or 7.5 mg/kg intramuscularly) was considered to "meet the need" (Stromberg et al, 1985). Unfortunately, closantel is unavailable to veterinarians in the United States.

Theoretically, aquatic snails can be controlled by draining swamps or by broadcasting molluscicides on the snail-infested waters. However, the continued existence of flukes where they have always been indicates that snail control measures are impracticable in many cases. Areas connected by streams with other snail-infested regions are generally not amenable to snail control measures. Periodic anthelmintic medication may help to reduce contamination of pastures with fluke eggs. When periods of drought or cold destroy *F. hepatica* eggs and snails weakened by infection with this parasite,

control measures based on anthelmintic medication alone may produce satisfactory results. On the other hand, when large populations of eggs and infected snails are able to survive the year around, these must be attacked directly as well.

Family Paramphistomadtidae

Identification

The ventral sucker is at the posterior end of the body; the ventral sucker of other trematodes is either on the ventral surface of the body or absent (Figure 4-12). Genera and species include *Paramphistomum*, *Calicophoron*, and *Cotylophoron* (rumen flukes), *Gastrodiscoides hominis* (a parasite of the intestine of humans, monkeys, and apes), and *Megalodiscus* species (parasites of the colon and cloaca of frogs).

FIGURE 4-12 A rumen fluke of the family Paramphistomatidae.

Life histories

Eggs of *Paramphistomum cervi* are undeveloped when passed in the feces of cattle, sheep, and goats. Miracidia develop in eggs deposited in water and hatch to invade snails of the genera *Physa*, *Bulinus*, *Galba*, and *Pseudosuccinea*, in which cercariae develop through one sporocyst and two redial stages. On emergence from the snail, the cercaria swims away to encyst on aquatic vegetation. Thus the extramammalian portion of the life history of a fluke in the genus *Paramphistomum* is very much like that of one in *Fasciola*. Metacercariae of *Paramphistomum* species excyst in the upper small intestine and migrate through the abomasum back to the rumen. In

heavy infections, migration to the rumen tends to be prolonged, and disease of several months' duration may result. Once arrived in the rumen and reticulum, the adult paramphistomes are relatively harmless (Rolfe and Boray, 1987).

Instead of encysting on aquatic vegetation as do other paramphistomatids, *Megalodiscus* cercariae encyst on the skin of frogs and tadpoles. The frogs become infected when they eat pieces of molted epidermis or tadpoles bearing metacercariae.

Treatment

Clorsulon at 2 mg/kg in combination with ivermectin at 0.2 mg/kg was ineffective in treating immature rumen flukes (Rolfe and Boray, 1993). Hexachlorophene in a single dose of 20 mg/kg and oxyclozanide in two doses of 19 mg/kg 3 days apart were both highly efficient against juvenile and adult paramphistome flukes, predominantly *Calicophoron calicophorum*, in cattle (Rolfe and Boray, 1987). Unfortunately, neither of these chemicals is available for use in domestic ruminants in the United States.

Trematodes acquired by eating fish, crayfish, crabs, and other intermediate hosts

Family Troglotrematidae

Identification

The genital pore is immediately posterior to the ventral sucker; the genital pore of other trematodes is located elsewhere. The location of the genital pore and the fact that the testes lie opposite one another are the only characteristics that unite the diverse assemblage of genera thrown together in the family

Troglotrematidae. Troglotrematids of veterinary importance are parasites of the intestines (*Nanophyetus* sp., Figure 4-13) or lungs (*Paragonimus* sp., Figures 4-14 and 4-15).

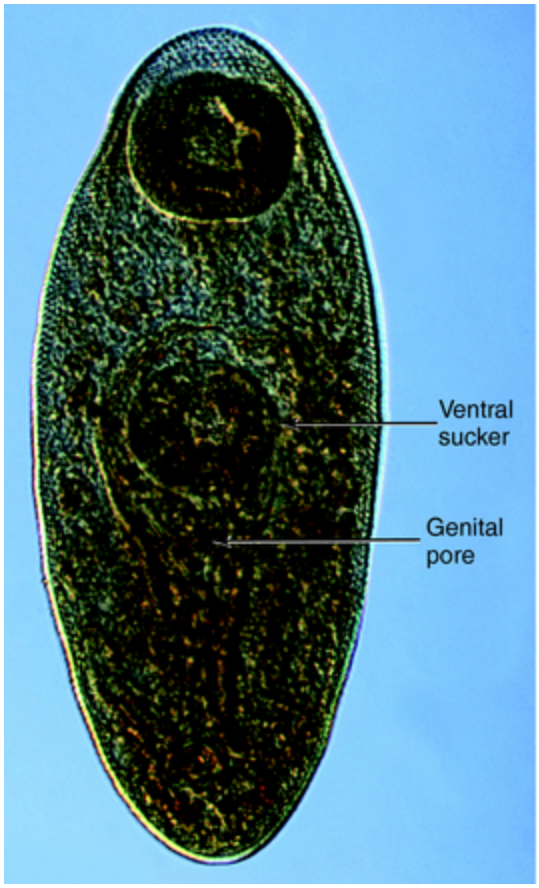

FIGURE 4-13 *Nanophyetus salmincola* (Troglotrematidae).

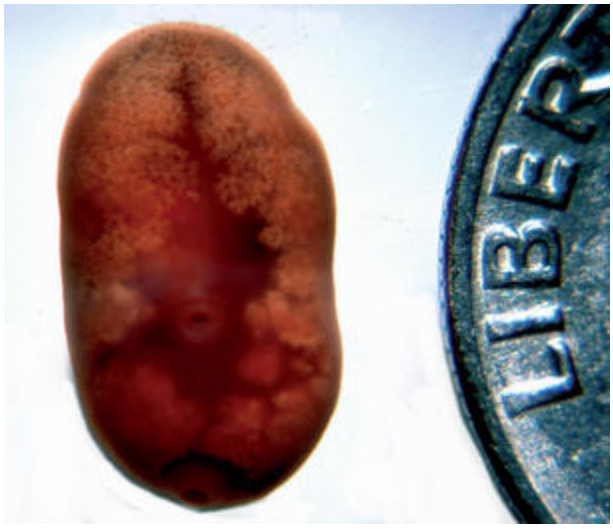

FIGURE 4-14 *Paragonimus kellicotti.* Living adult worm recovered at necropsy from a cyst in the lung of a cat.

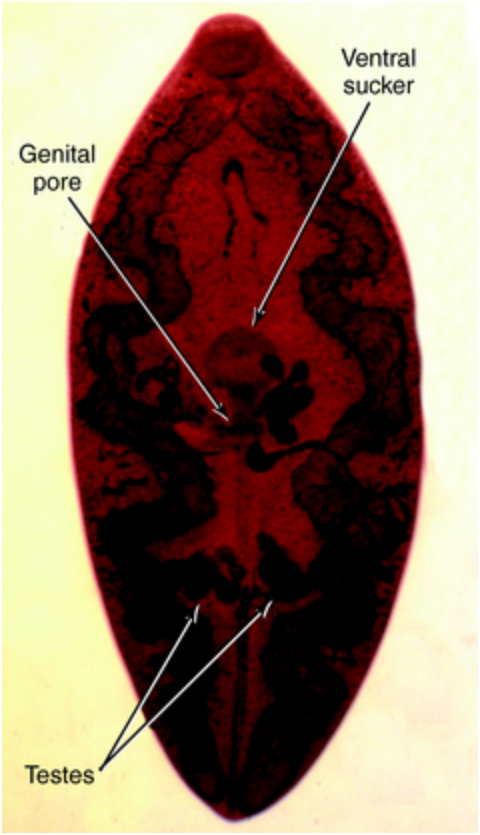

FIGURE 4-15 *Paragonimus kellicotti.*

Life histories

Nanophyetus salmincola adults parasitize the small intestine of piscivorous carnivorans of the Pacific Northwest. Eggs are undeveloped when passed in the host's feces. Miracidia require about 3 months to develop in eggs laid in water and hatch spontaneously still later. The miracidia penetrate the freshwater snail *Oxytrema silicula*, in which cercariae develop in rediae. After emergence from the snail, these cercariae penetrate the skin of salmonid fishes and encyst in various tissues. Eating salmon or trout infected with metacercariae of this trematode infects the dog, cat, coyote, fox, bear, raccoon, or mink. *N. salmincola* is host in turn to a rickettsial agent, *Neorickettsia helminthoeca*, the causative agent of "salmon poisoning" in dogs. Salmon poisoning, characterized by hemorrhagic enteritis and lymph node enlargement, is diagnosed by the presence of trematode eggs in the patient's feces and is usually fatal unless treated with broad-spectrum antibiotics.

Paragonimus kellicotti occurs, usually in pairs, in pulmonary cysts (see Figure 8-44). Cats, dogs, and many species of wild mammals in North America may become infected by eating crayfish containing the encysted cercariae or by eating animals that have recently fed on crayfish. The large, vase-shaped eggs (see Figures 7-36, *B,* and 8-45Figure 7-36, *B*Figure 8-45) are swept up the tracheobronchial tree, swallowed, and passed out with the feces. If the eggs arrive in water, miracidia develop and hatch in about 2 weeks and enter an operculate snail, *Pomatiopsis lapidaria*, in which cercariae develop through one sporocyst and two redial stages. The cercariae leave the snail and encyst as metacercariae in crayfish. Radiographically demonstrable cysts develop in the lungs of cats at 28 days, and eggs

are first shed in the feces about a month after infection. Signs of respiratory disease may be associated with *P. kellicotti* infection.

Treatment

Praziquantel, 23 mg/kg three times a day for 3 days, has been shown to be highly efficacious in removing *P. kellicotti* from the lungs of cats and dogs (Bowman et al, 1991). Fenbendazole, 50 mg/kg for 10 to 14 days, is also highly effective against these lung flukes (Dubey, Miller, and Sharma, 1979), as is albendazole, at a dosage rate of 25 mg/kg twice daily for 14 days. Praziquantel, 7 mg to 38 mg administered subcutaneously or intramuscularly, has also been shown to be highly effective in the removal of *N. salmincola* from dogs and coyotes (Foreyt and Gorham, 1988).

Family Heterophyidae

Identification

The ventral sucker and genital pore are withdrawn in a ventrogenital sac; one or more gonotyls (muscular suckers surrounding the genital pore) may be present (Figure 4-16).

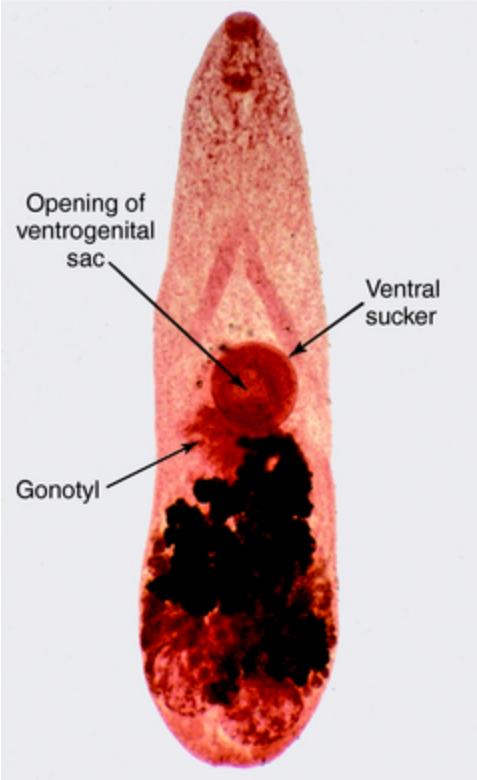

FIGURE 4-16 *Heterophyes* sp. From a dog in Lebanon.

Metagonimus yokogawai and *Heterophyes heterophyes* are parasites of cats, dogs, pigs, and humans in East Asia; infection is acquired by eating insufficiently cooked fish in which metacercariae have encysted.

Cryptocotyle lingua, a parasite of gulls and terns, produces severe enteritis in dogs, foxes, and minks a few days after they have eaten a small North Atlantic fish, the cunner, in which metacercariae are found in the subcutaneous tissues surrounded by black host capsules. The appearance of infected fish leads to the colloquial name “black spot disease.” A black host capsule is also observed surrounding various other species of trematode metacercariae and is not peculiar to *C. lingua*. Cercariae of *C. lingua* develop in the periwinkle *Littorina littorea*, a marine snail.

Family Opisthorchiidae

Identification

The uterus and ovary are anterior to the testes. There is no cirrus sac, and the genital pore is immediately anterior to the ventral sucker of these flat, translucent, fusiform, or oval parasites of the bile and pancreatic ducts of mammals, birds, and reptiles (Figure 4-17; see also Figure 4-10). Opisthorchiids might be confused with dicrocoeliids because they are similar in size, shape, and location in the host, but in dicrocoeliids, the ovary is posterior to the testes. Species include *Opisthorchis tenuicollis, Opisthorchis felineus*, *Metorchis conjunctus, Metorchis albidus*, *Parametorchis complexus*, *Clonorchis sinensis*, and others.

FIGURE 4-17 *Parametorchis* sp. (Opisthorchiidae).

Life history of opisthorchis tenuicollis

The adult trematodes are parasites of the bile and pancreatic ducts and small intestine of dogs, cats, foxes, pigs, and humans. When deposited in the host's feces, eggs containing miracidia are eaten by a snail *Bithynia tentaculata*, in which cercariae develop in rediae. The cercariae encyst as metacercariae in carp, bream, and roach. The definitive host becomes infected by eating these freshwater fish.

Importance

Opisthorchids display a rather low order of host specificity, and each species is capable of infecting many species of fish-eating mammals. Uncomplicated infection with moderate numbers of opisthorchiids is usually asymptomatic, but chronic infection with heavy worm burdens may lead to severe hepatic insufficiency.

Treatment

Praziquantel at 100 mg/kg should be efficacious (Hong et al, 2003).

Trematodes acquired by eating arthropods or vertebrate paratenic hosts

Family Dicrocoeliidae

Identification

The body is translucent. The ovary is posterior to the testes of these parasites of the gallbladder and bile and pancreatic ducts of mammals, birds, and reptiles (Figures 4-18 and 4-19; see also Figure 8-47).

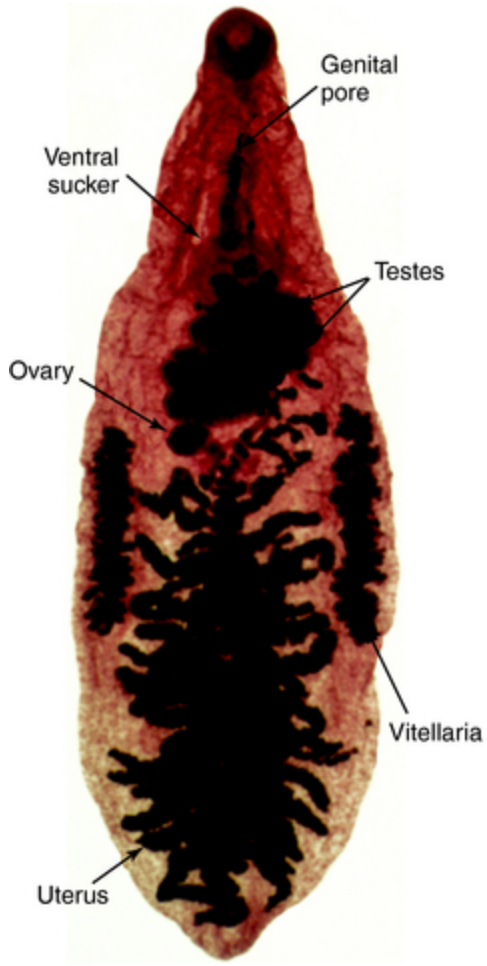

FIGURE 4-18 *Dicrocoelium dendriticum* (Dicrocoeliidae).

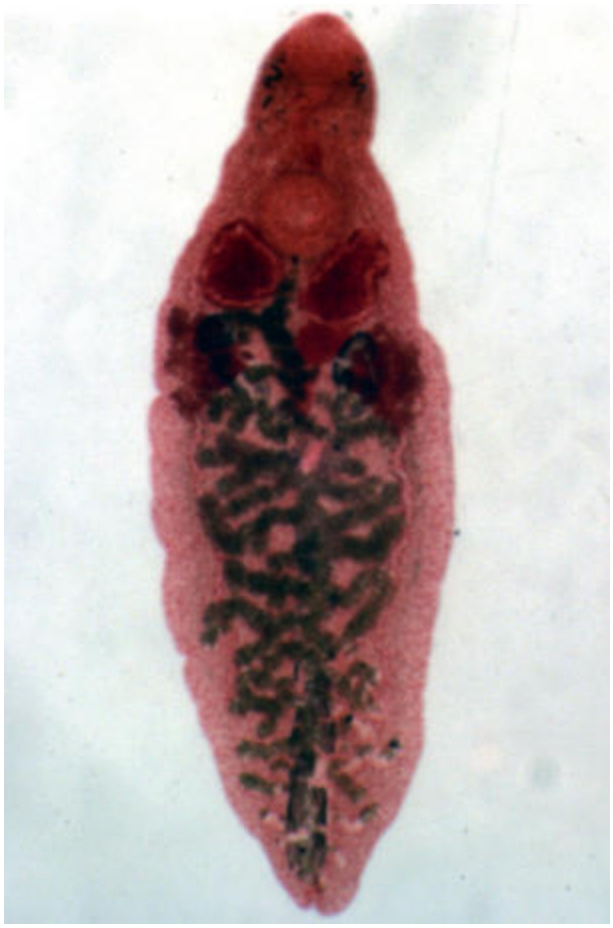

FIGURE 4-19 *Platynosomum fastosum* (Dicrocoeliidae).

Life history of *Dicrocoelium dendriticum*

Whereas most trematode life histories involve water, this species is adapted to a sequence of hosts that frequent dry habitats. Adult *D. dendriticum* are parasites of the bile ducts of sheep, cattle, pigs, deer, woodchucks, and cottontail rabbits. Embryonated eggs deposited in the host's droppings are ingested by the terrestrial snail *Cionella lubrica*, in which long-tailed cercariae develop in daughter sporocysts. As the cercariae leave the sporocysts, the snail secretes mucus around masses of them to form so-called slime balls in which they are expelled from the snail. The slime balls are apparently esteemed as food by the ant *Formica fusca*, in which the cercariae

encyst as metacercariae. The definitive host becomes infected by inadvertently ingesting infected ants while grazing; the metacercariae excyst in the small intestine and migrate up the common bile duct into the finer ramifications of the biliary tree.

Importance

D. dendriticum causes no clinical illness in cattle, lambs, or yearling sheep, but these trematodes are long-lived and the pathologic changes in the liver increase in severity and extent with the duration of the infection. Therefore in older sheep, *D. dendriticum* infection causes progressive hepatic cirrhosis manifested clinically as cachexia, lowered wool production, decreased lactation, and premature aging. In short, *D. dendriticum* makes sheep husbandry unprofitable by curtailing the reproductive life of the ewe flock.

Treatment

Albendazole administered orally to sheep at 15 to 20 mg/kg is highly effective against adult *D. dentriticum* (Theodorides, Freeman, and Georgi, 1982).

Platynosomum fastosum

This parasite of the bile and pancreatic ducts of cats occurs in the southeastern United States and the Caribbean (see Figure 4-19). Infection is acquired by eating lizards, toads, geckos, and skinks containing metacercariae (Chung, Miyahara, and Chung, 1977; Eckerlin and Leigh, 1962). The infection has been taken to Hawaii in introduced anoles (Goldberg and Bursey, 2000).

Treatment

Praziquantel, 20 mg/kg, markedly reduced the number of *Platynosomum* eggs passed in the feces of cats (Evans and Green, 1978). On the suggestion to a practitioner in Florida that it might be possible to treat platynosomiasis with elevated doses of praziquantel, the reply was that the last infected cat with hepatic dysfunction died when so treated. Thus it was thought that surgical removal of the flukes was the best course of therapy. Albendazole is another logical choice.

Eurytrema procyonis

This common parasite of the pancreatic duct of the raccoon was reported from a New York State domestic cat with a 2-year history of weight loss and vomiting probably resulting from pancreatic fibrosis and atrophy (Anderson, Georgi, and Car, 1987). A cat infected with *E. procyonis* stopped shedding eggs in its feces after a 6-day course of 30 mg/kg of fenbendazole (Roudebush and Schmidt, 1982).

Trematodes acquired by eating amphibia or vertebrate paratenic hosts

Family Diplostomatidae

Identification

The body of these intestinal parasites of birds and mammals is divided into a flattened or spoon-shaped forebody containing oral and ventral suckers and a bulbous tribocytic organ, and a cylindric hindbody containing the reproductive organs (Figure 4-20). The forebody will wrap around the mucosa of the intestinal tract, forming a firm attachment between the fluke and the host's

intestinal epithelium (Figure 4-21; see also Figure 8-49). Diplostomatids are most likely to be confused with members of the families Strigeidae, which have cup-shaped forebodies and leaflike tribocytic organs, and Cyathocotylidae, which have bulbous tribocytic organs but undivided bodies.

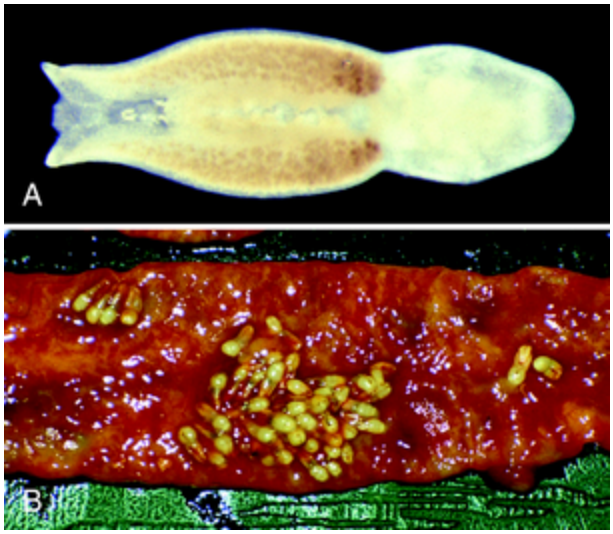

FIGURE 4-20 *Alaria canis* (Diplostomatidae). **A,** Living specimen detached from mucosal epithelium showing the forebody and hindbody, with the forebody having a ventral groove for wrapping around a bit of host mucosa. **B,** Flukes attached to the intestinal mucosa.

FIGURE 4-21 *Alaria* sp. (Diplostomatidae) attached to the mucosa of a dog's small intestine.

Life history of *Alaria*

The large, unembryonated egg (see Figure 7-36, *A*) is passed in the feces of the infected canid (Figure 4-22). If the egg is deposited in water, a miracidium develops and hatches in about 2 weeks to penetrate a snail of the genus *Helisoma* in which cercariae develop in daughter sporocysts. Each cercaria that succeeds in penetrating the skin of a tadpole transforms into a special larval stage called a mesocercaria, which is limited to *Alaria* species and a few closely related genera. If the tadpole is eaten by a frog, snake, or mouse, the mesocercariae take up residence and wait for their new host to fall prey to a dog or other suitable definitive host. The frog, snake, or

mouse that harbors these mesocercariae is called a **paratenic host** or **collector host**, which, by definition, is a host in which immature stages may survive indefinitely but undergo no essential development. The paratenic host helps to distribute the parasite in space and time and often bridges the gap of food preferences or overcomes some other obstacle to the union of parasite and definitive host. When a dog eats a paratenic host, the mesocercaria migrates directly through the diaphragm to the lungs, where it transforms into a metacercaria. In a few weeks, the metacercaria migrates up the trachea, is swallowed, and matures in the intestine. Eggs appear about 3 to 5 weeks after ingestion of mesocercariae (see Figure 4-22).

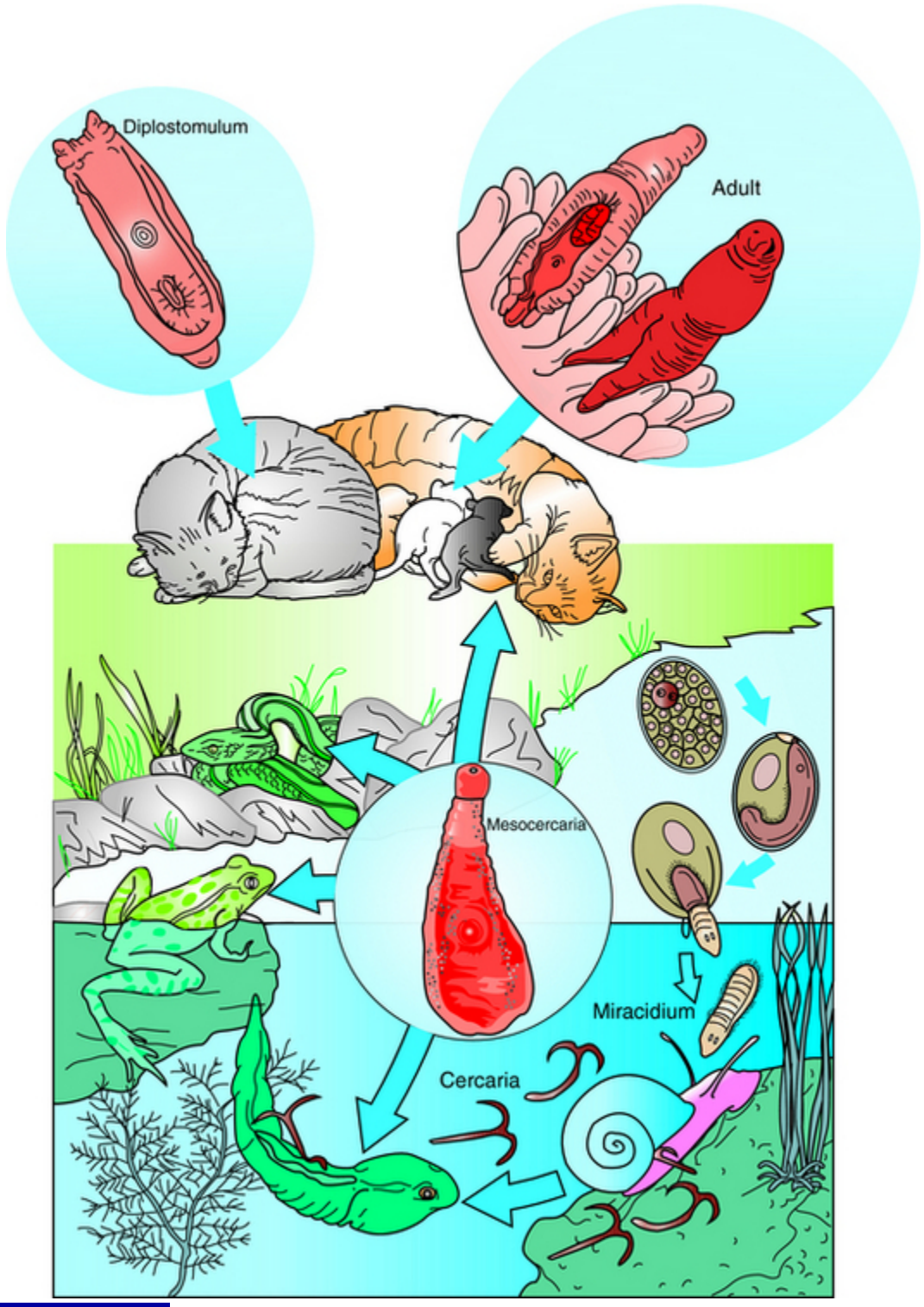

FIGURE 4-22 Life history of *Alaria marcianae* (Diplostomatidae). Miracidia develop in eggs deposited in water, hatch, and enter planorbid snails of the genus *Helisoma* where they develop into forked-tailed cercariae. Cercariae penetrate the skin and enter the tissues of tadpoles of the leopard frog *Rana pipiens* where, undergoing only minor

changes, they remain as mesocercariae. If the tadpole is eaten by a frog, snake, bird, or mammal, the mesocercariae invade the tissues of these paratenic hosts but again remain mesocercariae. However, when mesocercariae in tadpoles or any of the paratenic hosts are ingested by a male or nonlactacting female cat, they penetrate the diaphragm and develop into metacercariae of the diplostomulum type in the lungs. Finally, diplostomula pass up the trachea and down the esophagus to mature and reproduce in the small intestine. If mesocercariae are ingested by a lactating queen, they migrate to the mammary glands and are shed in the milk to develop into adult worms in the kittens. Some mesocercariae remain in the tissues of the queen to infect future litters.

Diagram and notes modified from Pearson [1956] and Shoop and Corkum [1984].

Mice infected with mesocercariae transmit *Alaria marcianae* to their sucklings through the milk, and when mature these offspring can transmit the infection in the same fashion. If a female cat becomes infected with *A. marcianae* during lactation, the mesocercariae will not develop into metacercariae in her lungs but instead will migrate to her mammary glands to infect her kittens. The kittens then behave as definitive hosts and develop patent infections (Shoop and Corkum, 1984).

Importance

Adult *Alaria* organisms are attached to the mucous membrane of the small intestine but apparently do their host little harm. However, because the mesocercariae migrate through the lungs and sometimes wander into other tissues, they may at times cause clinical illness. For example, a case of human infection with mesocercariae of *Alaria americana* terminated fatally as a result of extensive pulmonary hemorrhage. The circumstances suggested that the person had eaten inadequately cooked frogs' legs while hiking (Freeman et al, 1976).

Treatment

Infections with the adult trematode within the intestinal tract of dogs and cats can be treated with praziquantel and probably epsiprantel. The typical cestocidal dosage will be efficacious in most cases.

Families Allocreadiidae, Hemiuridae, and Lecithodendriidae

In the case of Potomac horse fever caused by *Neorickettsia risticii*, it is thought that horses are becoming infected by the ingestion of caddisflies or mayflies containing the metacercariae of various trematodes (Madigan et al, 2000); one of six horses fed pools of aquatic insects became infected with *N. risticii* after being fed pools of mature caddisflies *(Dicosmoecus gilvipes)*. Operculate snails, *Elimia livescens* of the family Pleuroceridae, that were shedding virgulate cercariae (typically cercariae of the Lecithodendriidae) were dissected, and the trematode cercariae and sporocysts were examined in pools for the presence of *N. risticii* DNA by amplification using the polymerase chain reaction (PCR). Of 209 pools of trematodes so examined, 50 were found to be positive for *N. risticii* DNA with PCR (Kanter et al, 2000). Trematodes of the family Lecithodendriidae are typically found in bats, so it is suspected that the cercariae from the snails go on to form metacercariae (Figure 4-23) in the aquatic larvae of various flies (e.g., caddisflies and mayflies) that are infectious to the bats after they become flying adults. Horses become infected when the adult flies fall into and are consumed with feed or water.

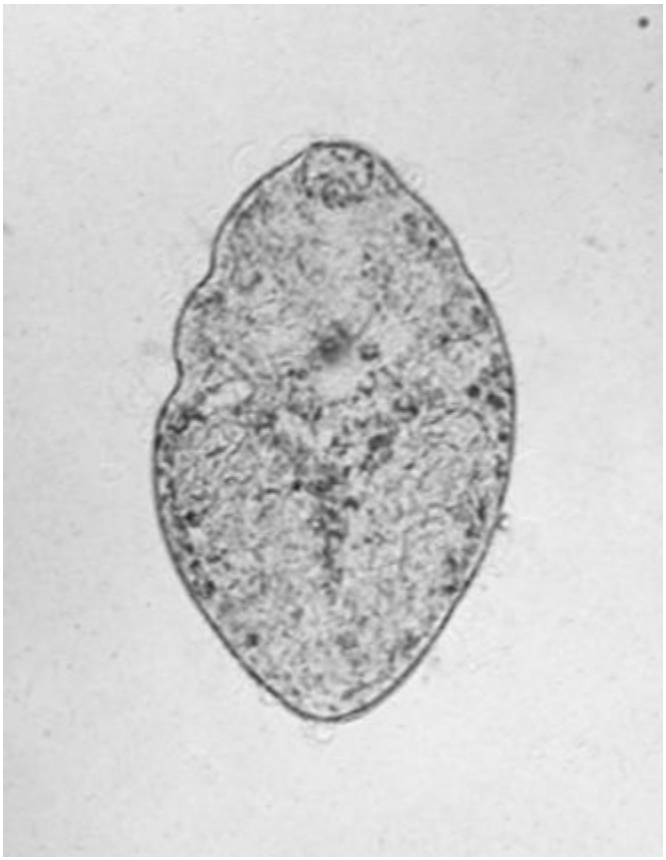

FIGURE 4-23 Lecithodendriid metacercaria recovered from a caddisfly in California incriminated as a vector of Potomac horse fever.

Courtesy Dr. John E. Madigan, School of Veterinary Medicine, University of California, Davis, California.

Another bit of the puzzle showed that an *Ehrlichia* sp. very closely related to *N. risticii* could be isolated from both the tissues and trematodes recovered from rainbow trout *(Oncorhynchus mykiss)* from a creek in northern California (Pusterla et al, 2000). The trematodes in this case were members of the genera *Deropegus* (family Hemiuridae) and *Crepidostomum* and *Creptotrema* (family Allocreadiidae). These trematodes live in the intestine and gallbladder of the trout as adults. The metacercarial stage is probably found in the larval stages of various aquatic flies (e.g., caddisflies and mayflies), although members of the family

Hemiuridae are thought to have larval stages mainly in crustacea. If this agent infects horses, it is thought that as with the trematodes of bats, the horses are infected by the ingestion of adult flies harboring the metacercarial stages of this parasite.

Trematodes acquired by skin penetration

Family Schistosomatidae

Schistosomiasis caused by *Schistosoma mansoni*, *Schistosoma haematobium*, and *Schistosoma japonicum* is second only to malaria as a scourge of mankind, especially in the Caribbean area, South America, Africa, and Eastern Asia. Domestic animals in various tropical areas may be affected with *Schistosoma bovis* (cattle and sheep), *Schistosoma indicum* (horses, cattle, goats, and, in India, buffalo), *Schistosoma nasale* (cattle in India), *Schistosoma suis* (swine and dogs in India), and *Schistosoma matheei* (sheep, southern Africa). In Japan and the Philippines, *S. japonicum* is a serious parasite of humans and animals alike. In North America, schistosomes present only two isolated problems: *Heterobilharzia americana,* a parasite of raccoon, nutria, bobcat, rabbit, and dog in the area extending from Florida along the Gulf Coast into Texas and north at least as far as Kansas, and "swimmer's itch," a dermatitis caused by cercariae of wild waterfowl schistosomes (*Trichobilharzia*, *Austrobilharzia*, and *Bilharziella* species) penetrating and abortively migrating in human skin. Of course, many cases of human schistosomiasis exist in North America among immigrants from endemic localities, but human schistosomiasis is unlikely to become endemic in the United States because the snail intermediate hosts (*Biomphalaria*, *Tropicorbis*, *Oncomelania,* and *Bulinus* species) do not occur here.

Identification

Sexes are separate, with the slender female lying in the gynecophoric canal of the somewhat stouter male (Figure 4-24). Adult schistosomes are parasites of veins of the digestive and urinary tracts of birds and mammals. Other trematodes are hermaphroditic and parasitize tissues other than blood vessels. Eggs lack an operculum and contain a fully developed miracidium when discharged in the feces (e.g., *Schistosoma mansoni*, *S. japonicum*) or urine (e.g., *S. haematobium*); eggs of some species are armed with a spine. Other trematode eggs have a polar operculum and lack a spine. Schistosome eggs hatch on exposure to water, so feces must be suspended in 0.85% sodium chloride (NaCl) solution when sedimenting eggs of these parasites. A miracidium hatching technique (Goff and Ronald, 1980) increases the probability of detecting patent *H. americana* infection in dogs. The eggs of *H. americana* are rather spheric and possess only a slight bump on one side rather than a spine as seen in *Schistosoma mansoni* and *S. haematobium*.

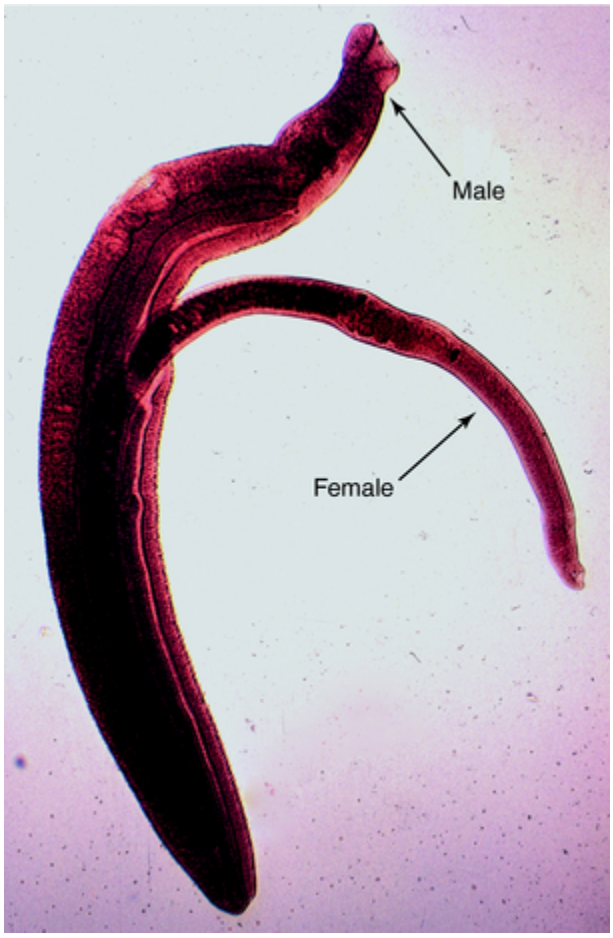

FIGURE 4-24 *Schistosoma mansoni* (Schistosomatidae). The body of the slender female can be seen protruding from the gynecophoric groove of the stouter male.

Life history of *Heterobilharzia americana*

The miracidium hatches soon after the egg comes in contact with water and then enters a freshwater snail, *Lymnaea cubensis*, in which cercariae develop in daughter sporocysts. On emergence from the snail, the cercariae penetrate the skin of a raccoon, nutria, bobcat, rabbit, or dog and migrate by way of the lungs to the liver. After a period of development in the liver, mature males and females make their way to the mesenteric veins and mate, the more or less cylindric female lying in the gynecophoric groove of the male (see Figure 8-50). The eggs, laid in the terminal branches of the

mesenteric veins, passively work through the bowel wall to the lumen and escape with the feces (see Figures 8-51 and 8-52Figure 8-51Figure 8-51). The eggs evoke a granulomatous reaction that eventually prevents their egress and favors their carriage to other organs, with the consequent production of widely disseminated granulomas. The life histories of other schistosomes differ only in detail from that of *H. americana*.

For treatment of *H. americana* infection, fenbendazole administered orally at 40 mg/kg for 10 days completely removed *H. americana* from one artificially infected dog, whereas an untreated control dog remained infected (Ronald and Craig, 1983). Praziquantel and epsiprantel are also logical choices for treating *H. americana* infection.

Class Cestoda

Information on the geographic distribution and biology of some cestodes of veterinary importance can be found in Table 4-2.

TABLE 4-2 Information on Some Tapeworms of Veterinary Importance

Cestode	Final Hosts	Geographic Distribution	Egg	Intermediate Hosts	Larval Stage	Scolex	Segment	Prepatent Period	Comments
PSEUDOPHYLLIDEA									
Diphyllobothriidae									
Diphyllobothrium	Dogs, cats, humans, bears, pigs, seals	Cold climate, fresh water	Operculate 66 × 44 µm	Copepod*; fish†	Plerocercoid	Slitlike, no hooks	Square, medial uterine pore	40 days	Humans can be infected with adult form
Spirometra	Dogs, cats, lynx, raccoons	US, Australia, Asia	Operculate 66 × 44 µm	Copepod*; tadpoles, snakes, rodents†	Plerocercoid "sparganum"	Slitlike, no hooks	Square, medial uterine pore	15-30 days	Causes human sparganosis
CYCLOPHYLLIDEA									
Taeniidae									
Taenia pisiformis	Dogs	Worldwide	Taeniid egg, 30 µm	Cottontail rabbits	Cysticercus	Muscular, 4 suckers, Hooks claw hammer–shaped	Square segments, single lateral pore	56 days	
Taenia hydatigena	Dogs	Worldwide	Taeniid egg, 30 µm	Mainly sheep	Cysticercus	Muscular, 4 suckers, Hooks claw hammer–shaped	Square segments, single lateral pore	51 days	
Taenia ovis	Dogs	Worldwide, absent in US	Taeniid egg, 30 µm	Mainly sheep	Cysticercus	Muscular, 4 suckers, Hooks claw hammer–shaped	Square segments, single lateral pore	42-63 days	
Taenia saginata	Humans	Worldwide	Taeniid egg, 30 µm	Cattle—muscle	Cysticercus	No hooks on scolex	Square segments, single lateral pore	70-84 days	Scolex without hooks
Taenia solium	Humans	Worldwide	Taeniid egg, 30 µm	Pigs—muscle	Cysticercus	Muscular, 4 suckers, Hooks claw hammer–shaped	Square segments, single lateral pore	35-84 days	Causes human cysticercosis
Taenia asiatica	Humans	Southeast Asia	Taeniid egg, 30 µm	Pigs and cattle—liver	Cysticercus	No hooks on adult scolex	Square segments, single lateral pore	70-84 days	Adult scolex without hooks
Taenia taeniaeformis	Cats	Worldwide	Taeniid egg, 30 µm	Mice and rats	Strobilocercus	Muscular, 4 suckers, Hooks claw hammer–shaped	Square segments, single lateral pore	40 days	
Taenia serialis	Dogs	Worldwide	Taeniid egg, 30 µm	Cottontail rabbits	Coenurus	Muscular, 4 suckers, Hooks claw hammer–shaped	Square segments, single lateral pore	1-2 months?	Cats have had coenurosis
Taenia multiceps	Dogs	Worldwide, absent in US and New Zealand	Taeniid egg, 30 µm	Mainly sheep	Coenurus	Muscular, 4 suckers, Hooks claw hammer–shaped	Square segments, single lateral pore	30 days	
Echinococcus granulosus	Dogs, canids	Sheep areas	Taeniid egg, 30 µm	Mainly sheep	Unilocular hydatid cyst	Muscular, 4 suckers, Hooks claw hammer–shaped	Worms and segments very small, usually not seen	45-60 days	Causes human unilocular hydatidosis
Echinococcus multilocularis	Foxes, dogs	Holarctic	Taeniid egg, 30 µm	Mice and rats	Multilocular hydatid cyst	Muscular, 4 suckers, Hooks claw hammer–shaped	Worms and segments very small, usually not seen	28 days	Causes human alveolar hydatidosis
Anoplocephalidae									
Moniezia benedeni	Cattle	Worldwide	Square	Oribatid mites	Cysticercoid	Unarmed	Much wider than long	40 days	
Moniezia expansa	Sheep	Worldwide	Square to round	Oribatid mites	Cysticercoid	Unarmed	Much wider than long	25-45 days	
Moniezia caprae	Goats	Worldwide	Square to round	Oribatid mites	Cysticercoid	Unarmed	Much wider than long	???	
Thysanosoma actinoides	Ruminants—not cattle	Mountainous North and South America	Elongate, small	Book lice (Psocidae)	Cysticercoid	Unarmed	Fringed	???	
Anoplocephala magna	Equids	Worldwide	Round	Oribatid mites	Cysticercoid	Unarmed	Much wider than long	4-6 weeks	Eggs hard to find in feces; segments usually not seen
Anoplocephala perfoliata	Equids	Worldwide	Round	Oribatid mites	Cysticercoid	Unarmed with lappets	Usually see whole worm	4-6 weeks	
Paranoplocephala mammillana	Equids	Worldwide	Round	Oribatid mites	Cysticercoid	Unarmed	Much wider than long	4-6 weeks	

Cestode	Final Hosts	Geographic Distribution	Egg	Intermediate Hosts	Larval Stage	Scolex	Segment	Prepatent Period	Comments
Dipylidiidae									
Dipylidium caninum	Dogs, cats, other felids and canids	Worldwide	Eggs passed in egg packets	Fleas	Cysticercoid	4 suckers, retractable rostellum	Pumpkin seed–shaped segments with lateral pores on both sides	21 days	Occasionally, adult worms in children
Mesocestoididae									
Mesocestoides spp.	Raecoons, dogs, cats	Worldwide	Eggs confined to parauterine organ	First host still unknown; reptiles and mammals†	Tetrathyridium	Muscular 4 suckers; no hooks	Small, sesame seed–like, with contained parauterine organ	20-30 days	Dogs can be infected with tetrathyridia. Rare human infections.

*First intermediate host.
†Second intermediate host.

Tapeworms belong to the class Cestoda of the phylum Platyhelminthes and resemble trematodes in having acoelomate parenchymatous bodies and in having both sexes represented in the same individual. An adult tapeworm is essentially a chain **(strobila)** of independent, progressively maturing reproductive units, one end of which is capable of attachment to the wall of the host's intestine by a **holdfast** organ or **scolex**. In a fully developed adult tapeworm, all stages of development are displayed in a linear array starting at the scolex and terminating at the distal end. Although from a reproductive viewpoint a tapeworm appears to be a colony instead of an individual, all segments are served by common osmoregulatory and nervous systems, and the animal moves in a rhythmic and coordinated manner by means of the concerted activity of two zones of muscle fibers found in each segment. There are no organs of prehension or digestion; all nutrients are absorbed through the tapeworm's specialized integument. The body of an adult tapeworm is so flattened that for the purposes of argument it can be said to have two surfaces and two edges. This shape affords maximum surface area per unit volume, a distinct asset for an animal that absorbs all of its nourishment through its skin. Some tapeworms grow to considerable size. The strobila of *Taenia*

saginata, for example, may contain as many as 2000 segments and reach a length of 3.6 m (30 feet) in the human small intestine (Arundel, 1972).

Of the 14 orders within the class Cestoda, the two orders that are of typical interest to veterinarians are the Pseudophyllidea and the Cyclophyllidea. The order Pseudophyllidea is represented by only two genera of importance to most veterinarians: *Diphyllobothrium* and *Spirometra*. Both use copepods as the first intermediate host in which the **oncosphere** develops into a second larval stage called a **procercoid**. The second intermediate host may be a fish, amphibian, or reptile and supports development of the **procercoid** into a third larval stage called a **plerocercoid**. The definitive host becomes infected when it ingests a second intermediate host or any of a series of paratenic hosts containing plerocercoids. Pseudophyllideans are associated with aquatic food chains. The order Cyclophyllidea contains five families of veterinary importance: Taeniidae, Mesocestoididae, Anoplocephalidae, Dipylidiidae, and Hymenolepididae. Most cyclophyllideans require only one intermediate host. Depending on the family of tapeworm, the intermediate host may be a mammal (Taeniidae) or an arthropod (Anoplocephalidae, Dipylidiidae, Hymenolepididae). Members of the Mesocestoididae are thought to require two intermediate hosts, the second of which may be a mammal, bird, or reptile, but so far the hypothesized second larval stage and first intermediate host have not been identified. Cyclophyllideans produce oncospheres with a protective capsule of embryonic membrane origin and are associated with terrestrial food chains.

Almost all tapeworms require at least two and some require three hosts to complete their life histories. *Vampirolepis* (*Hymenolepis*, *Rodentolepis*) *nana*, a cyclophyllidean parasite of mice and sometimes of humans, is exceptional in being able to complete its life history within the confines of a single individual.

Cestodes produce eggs that when fully developed contain a first-stage larva called an **oncosphere**. Oncospheres develop into a second larval stage in the body cavities or tissues of an intermediate host. Usually the second larval stage is infective for the definitive host on ingestion. However, in certain prominent cases, the second larval stage must first develop into a third larval stage in a second intermediate host before it is ready to infect the definitive host. The oncosphere is the first larval stage and is infective for the first (or only) intermediate host. The oncosphere consists of a **hexacanth embryo** surrounded by two embryonic membranes. The first larval stage, or hexacanth embryo, is infective to the first intermediate host and develops in this host into a second larval stage. In most cyclophyllideans of interest to us, there is only one intermediate host, and the second larval stage is the stage infective to the definitive host in which it matures. In the Mesocestoididae (in which the second larval stage is still hypothetical) and in the Pseudophyllidea, the second larval stage organisms are infective to the second intermediate host, in which they develop into a third larval stage. The third larval stage of mesocestoidids and pseudophyllideans is the form infective for the definitive host. The second and third larval stages of these various tapeworms have their own names, which are presented later in the discussion of their respective life histories.

In a teleologic sense, the objective of larval development is to form a scolex in a kind of intermediate host that is likely, for one reason or another, to be ingested by a suitable definitive host. Because this objective has been reached in such diverse hosts as mites and cattle, there is considerably more variation in size and form among larval cestodes than among adults. It is at this point that uniformity of structure and function gives way to diversity. Therefore details of larval development are discussed in connection with life histories in the following characterization of cestode families.

When an infective tapeworm larva first arrives in the intestine of its definitive host, most of the infective larva's body is digested away, leaving only the scolex and a bit of undifferentiated tissue called the neck. The scolex attaches to the intestinal wall, and the neck begins to bud off segments. These segments remain attached to one another to form the chain mentioned previously. At first the segments remain undifferentiated, but ovaries, testes, vitellaria, and other reproductive organs gradually begin to take shape in the segments some distance removed from the neck. These reproductive organs gradually mature, eggs and sperm are formed, and fertilization occurs. Depending on the kind of tapeworm, the fertilized eggs either are discharged through a uterine pore or accumulate in the segment. Therefore the terminal segments of a mature tapeworm are found to be empty in the former case and packed full of eggs like ripe seedpods in the latter.

The anatomic details and nomenclature of the genitalia are important in detailed taxonomic work but need not be emphasized here because a reliable identification usually can be made on the basis of host identity and somewhat more accessible morphologic

features as outlined later. However, differences do exist between cyclophyllideans and pseudophyllideans that are important in diagnosis and in understanding their particular life histories.

Pseudophyllidean Tapeworms

The holdfast of pseudophyllideans has only two shallow, longitudinally grooved bothria for locomotion and attachment (Figure 4-25). The two most important genera, *Diphyllobothrium* and *Spirometra*, have no hooks to assist the weak grip of the bothria. The considerable area of contact between the long chain of broad segments and the intestinal mucosa apparently affords sufficient traction to maintain the tapeworm in place.

FIGURE 4-25 *Diphyllobothrium latum* (Diphyllobothriidae), scolex of stained, permanent mount.

Pseudophyllidean segments have a uterine pore that permits the escape of eggs (Figure 4-26). Segments over a considerable length of the strobila discharge their eggs until their supply is exhausted. The terminal segments of pseudophyllidean tapeworms become senile rather than gravid and are usually detached in short chains rather than individually. Thus the diagnosis of pseudophyllidean infection depends on distinguishing the operculate eggs in fecal sediments from those of trematodes, which sometimes is not an easy matter.

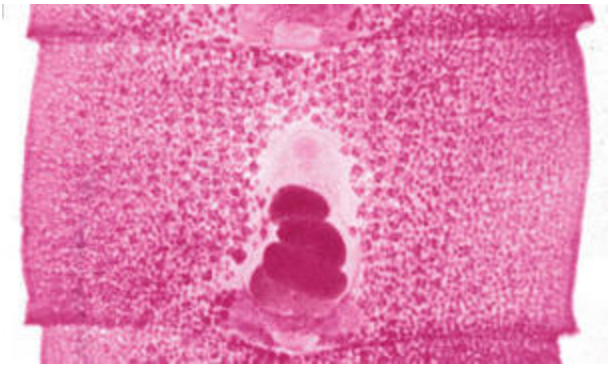

FIGURE 4-26 Mature segment of *Diphyllobothrium latum*.

The pseudophyllidean oncosphere and its two membranes are surrounded in turn by an operculate shell (Figure 4-27). The outermost membrane remains behind in the shell when the oncosphere, now surrounded only by its ciliated inner membrane or **embryophore,** pops open the operculum of the shell and swims away (Figure 4-28). The ciliated pseudophyllidean oncosphere is called a **coracidium.**

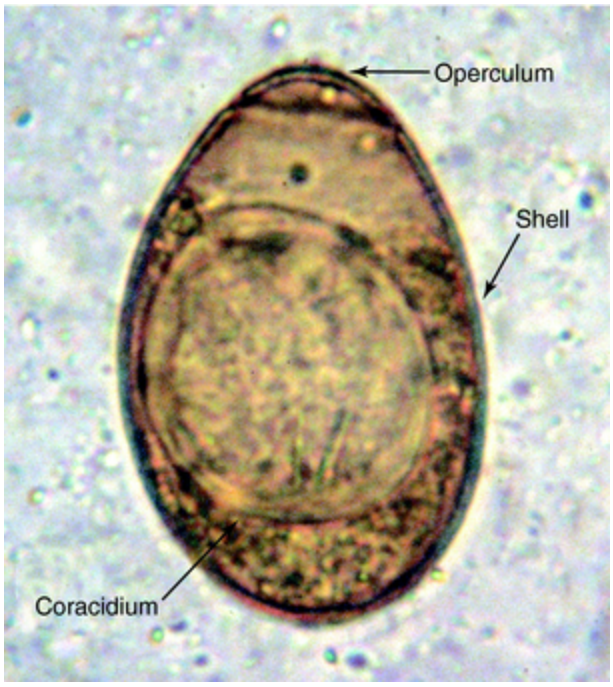

FIGURE 4-27 Egg of *Spirometra mansonoides* (Diphyllobothriidae). The capsule of diphyllobothriid eggs is operculate; this one contains a fully developed coracidium.

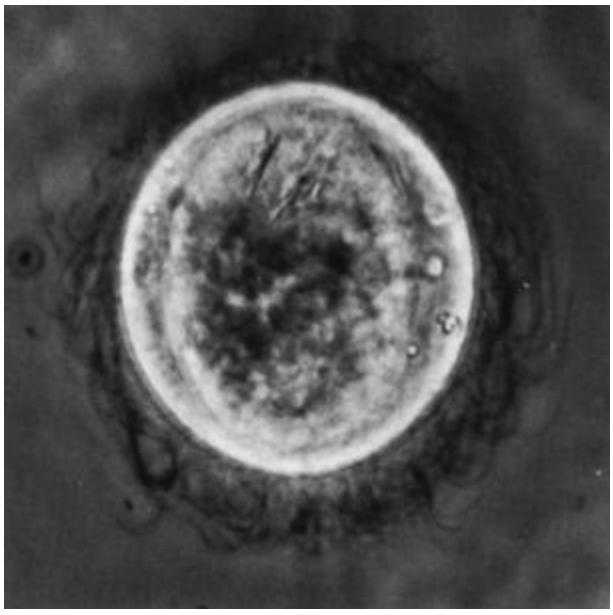

FIGURE 4-28 Coracidium of *Spirometra mansonoides.* Phase contrast electronic flash photomicrograph of the free-swimming organism.

Courtesy Dr. Justus Mueller.

Family Diphyllobothriidae

Identification

The scolex of *Diphyllobothrium latum* and *Spirometra mansonoides* has two slitlike grooves (see Figure 4-25). Mature segments are broader than long (Figure 4-29; see also Figure 4-26). The uterus consists of a spiral tube with four to eight loops on each side and opens to the outside through a midventral uterine pore behind the genital pore. The reproductive organs are concentrated at the centers of the segments (see Figure 4-29). Operculated eggs are discharged through the uterine pore.

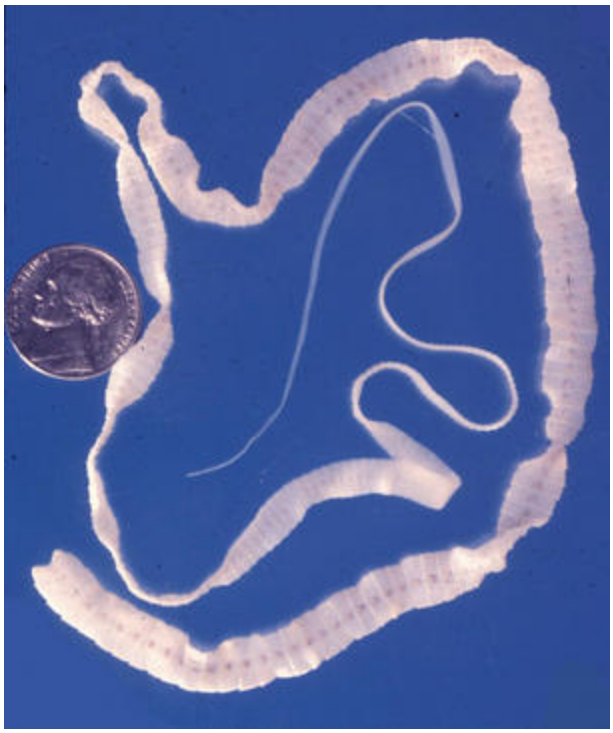

FIGURE 4-29 *Spirometra mansonoides* (Diphyllobothriidae), entire specimen from a cat. Note how small the scolex is relative to the mature segments and also the central location of the genitalia throughout the length of the tapeworm.

Life history

The two important genera of Diphyllobothriidae in veterinary medicine, *Diphyllobothrium* and *Spirometra*, differ in that one exclusively uses aquatic intermediate hosts and the other uses amphibious and terrestrial intermediate hosts. *Diphyllobothrium* species use copepods and fish. *Spirometra* species use copepods, amphibians, reptiles, birds, and mammals.

D. latum has a life cycle similar to that of other pseudophyllidean tapeworms that requires two intermediate hosts, of which the first is a copepod and the second is a vertebrate, whereas cyclophyllidean development involves only one intermediate host. When ingested by a copepod, the **coracidium** (oncosphere with ciliated embryophore) develops into a solid wormlike **procercoid** within the body cavity (Figure 4-30). When the infected copepod is ingested by a second intermediate host, the procercoid enters its musculature or connective tissues and develops into a **plerocercoid** (Figure 4-31). The plerocercoid is notable for its ability to parasitize a series of predatory paratenic hosts until a suitable definitive host is found. Thus when a pike eats a minnow infected with the plerocercoids of *D. latum,* these merely invade the flesh of the pike and remain plerocercoids. However, when a human, a dog, or a cat eats either the minnow or the pike, the plerocercoid matures into an adult tapeworm, with the **prepatent period** (i.e., the time between infection and the appearance of detectable stages, which in this case are eggs found in the feces) being about 5 or 6 weeks. *D. latum* procercoids develop in copepods of the genus *Diaptomus*, and its plerocercoids develop in fish. Definitive hosts of *D. latum* include humans, dogs, mongooses, walruses, seals, sea lions, bears, foxes, and minks (Wardle and McLeod, 1952).

FIGURE 4-30 Copepod *(Cyclops vernalis)* with body cavity filled with three different procercoids *(arrows)* of *Spirometra mansonoides;* electronic flash photomicrograph of living organisms.

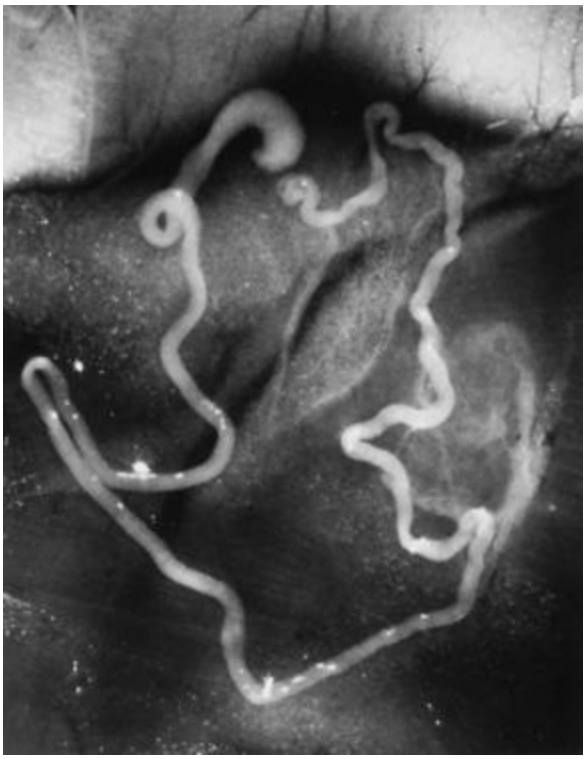

FIGURE 4-31 *Spirometra mansonoides* plerocercoid larva in the subcutaneous tissues of a white mouse.

Photograph [about twice natural size] courtesy Dr. Robert Smith; culture courtesy Dr. Justus Mueller.

Spirometra mansonoides procercoids develop in copepods of the genus *Cyclops*. Its plerocercoids develop in "any class of vertebrates

except fishes"; even kittens fed procercoids support development of plerocercoids, which appear in the flat muscles of the body wall and subcutaneous fascia (Mueller, 1974). The natural intermediate host is probably the water snake *Natrix*, and the natural definitive host is probably the bobcat *Lynx rufus*. Other definitive hosts of *S. mansonoides* include the domestic cat and dog and the raccoon (Mueller, 1974). The life history is illustrated in Figure 4-32; animals can begin shedding eggs in the feces as soon as 10 days after the ingestion of the larval plerocercoid stage.

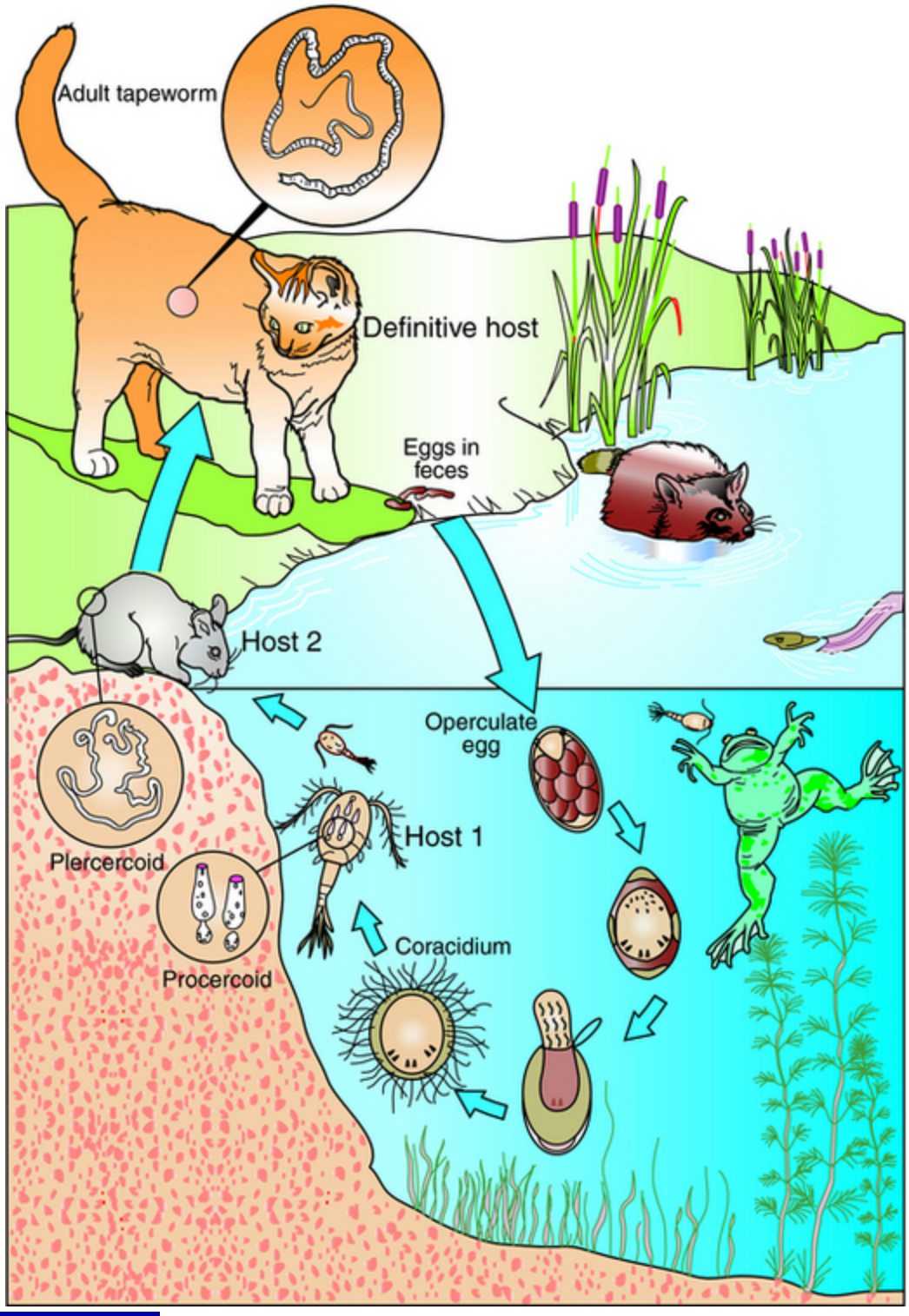

FIGURE 4-32 Life history of *Spirometra mansonoides*, a pseudophyllidean tapeworm. Coracidia develop and hatch from eggs deposited in water and swim about until they are ingested by copepods of the genus *Cyclops*. Shedding its ciliated coat, the hexacanth embryo develops into a procercoid larva in the body cavity of the copepod. If an infected

copepod is swallowed by any vertebrate except a fish, the procercoids develop into plerocercoids, which tend to locate in the subcutaneous tissues and flat muscles of the body wall. Plerocercoids survive predation of their hosts and remain plerocercoids in their new hosts unless the new host happens to be a cat. Plerocercoids develop into adult *S. mansonoides* tapeworms in the small intestine of the domestic cat and bobcat.

An Eastern Asian species, *Spirometra mansoni*, does use frogs, rabbits, and birds for development of the plerocercoid (see Figure 8-68). Not so very long ago, it was the custom in parts of the Eastern Asia to apply the incised body of a freshly caught frog as a poultice to wounds, sore eyes, and the like. (This behavior is not so unlike the once common application of a raw steak to "reduce the bruising" associated with a black eye.) The plerocercoids *of Spirometra mansoni*, if present in the tissues of the frog, would then transfer to the human host and migrate about in the subcutaneous connective tissues, a condition dubbed **sparganosis** in the human medical literature. The plerocercoids **(spargana)** of *S. mansonoides* are also capable of causing human sparganosis, as Mueller and Coulston (1941) demonstrated by experiments on themselves where they inserted spargana into the tissues of their arms.

D. latum and *S. mansonoides* are usually less obtrusive than other tapeworm parasites of dogs and cats because they do not detach segments but release their eggs more or less continuously through the uterine pores of their mature segments. Therefore the client usually is unaware of *Diphyllobothrium* and *Spirometra* infection unless a whole tapeworm or a long chain of senile segments is discharged at once. *Diphyllobothrium* infection is acquired by eating uncooked predatory freshwater fish. *S. mansonoides* can be passed experimentally from the copepod through such diverse second

intermediate hosts as frogs and mice. In the type locality (Syracuse, New York), *Natrix*, a water snake, is frequently found infected with *S. mansonoides* plerocercoids.

Families of Cyclophyllidean Cestodes

Compared with the rest of the mature worm, which may be several meters long in the larger species, the **scolex** is minute, frequently measuring less than a millimeter. The cyclophyllidean scolex has four radially disposed muscular suckers that serve for attachment and locomotion (Figure 4-33). These suckers and the tissue immediately surrounding them are quite mobile. Dr. Georgi described watching a severed scolex of *Taenia pisiformis* "walk" with remarkable agility across the bottom of a Petri dish. Each sucker in turn was advanced on a stalk of tissue and fixed to the bottom of the dish. Then the scolex was drawn toward the point of fixation by contraction of the stalk of tissue, another sucker advanced, and so on. At the apex of most cyclophyllidean scolices there is a dome-shaped projection, the **rostellum**, which is sometimes retractable into the scolex and may be armed with small hooks. In the family Taeniidae a nonretractable rostellum is armed with two concentric rows of hooks. Strong muscles operate these hooks in a concerted and rhythmic clawing motion. The points are projected in a manner similar to a cat baring its claws, but in a centrifugal direction. This clawing motion ceases once the scolex has found safe anchorage in the intestinal wall (see Figure 7-45). Cyclophyllidean families that lack rostellar hooks (e.g., Anoplocephalidae, Mesocestoididae) tend to have more strongly developed suckers to make up for it.

FIGURE 4-33 Holdfast and neck of *Taenia* sp., showing four suckers and nonretractable rostellum with hooks.

Segments of cyclophyllidean strobila have genital pores for fertilization but no opening to allow the eggs to escape from the uterus. Therefore the eggs accumulate until the segment becomes packed full like a ripe seedpod. As they reach the end of the chain, these gravid segments are detached and pass out with the feces or crawl out the anus onto the perianal skin. Therefore cyclophyllidean infections are usually diagnosed by identifying gravid segments on the host or in its environment.

Cyclophyllidean oncospheres are fully developed when passed in the feces of the definitive host and are immediately infective for the intermediate host. These oncospheres lack a true shell and technically should not be called eggs, but most authors call them this and so shall we. The outer membrane of the cyclophyllidean

oncosphere serves as a protective capsule in some species. However, the outer membrane of taeniid oncospheres is delicate and usually has been lost by the time they appear in a host's feces. The inner embryonic membrane (embryophore) serves as a protective coat for the taeniid oncosphere. In anoplocephalids, the embryophore is a distinctive pear-shaped body (pyriform apparatus), and in taeniids it consists of a rather thick layer of prismatic blocks. The eggs of *Dipylidium caninum* are clustered in packets formed by outpocketings of the uterine wall.

Teratologic development of cestode larvae is not at all uncommon, and occasionally cases are observed in which larval tapeworm tissue behaves much like a malignant neoplasm. For example, Williams, Lindsay, and Engelkirk (1985) reported a fatal case of peritoneal cestodiasis in a dog from which parasites actually passed out through a poorly healing laparotomy incision, and 500 mL of parasite tissue was recovered from the peritoneal cavity at necropsy. The parasites were too abnormal both grossly and histologically to identify, even by careful comparison with specimens of the most likely candidates, *Mesocestoides corti*, *Taenia crassiceps*, and *Taenia multiceps*.

Family Taeniidae

Taenia

Identification

Adult tapeworms of the genus *Taenia* measure from tens to hundreds of centimeters in length, depending on the species in question and degree of maturity of the specimen. The scolex has four suckers and

a nonretractable rostellum armed with two rows of hooks (Figure 4-34; see also Figure 4-33). The segments are more or less rectangular, with unilateral genital pores alternating irregularly from one side to the other along the strobila (Figure 4-35). The eggs in gravid segments are typical of the family (Figure 4-36). Differentiation of genera and species is based on number and sizes of rostellar hooks and on morphology of mature segments and may require the services of an expert (Verster, 1969). Taeniid tapeworms of the genus *Echinococcus* are recognized by their very small bodies, millimeters in length, composed of only four or five segments, along with hooks and eggs that are morphologically similar to those of other taeniid tapeworms. Species of the genus *Taenia* are fairly restricted in their final host usage, where the adult worm is found in the small intestine. *Taenia* species commonly occurring as adults in dogs include *T. pisiformis*, *T. hydatigena*, *Taenia ovis*, *Taenia serialis*, and *T. multiceps*. *Taenia* species occurring as adults in human beings include *Taenia solium*, *T. saginata*, and *Taenia asiatica*. The common *Taenia* species occurring in adult form in the domestic cat is *Taenia taeniaeformis*. Common species of *Echinococcus* in canids include *Echinococcus granulosus* and *Echinococcus multilocularis* (also found on occasion in domestic cats). In South America a species of *Echinococcus* in felids is *Echinococcus oligarthus; Echinococcus vogeli* is a species that cycles between the bush dog, *Speothos venaticus*, and the paca, *Cuniculus paca*. In Tibet the species *Echinococcus shiquicus* cycles between the Tibetan fox, *Vulpes ferrilata,* and the plateau pika, *Ochotona curzoniae*.

FIGURE 4-34 *Taenia taeniaeformis* (Taeniidae); scanning electron micrograph by Dr. Ronald Minor. The rostellum of taeniid tapeworms is nonretractable and is armed with a row of long hooks and a concentric row of short hooks.

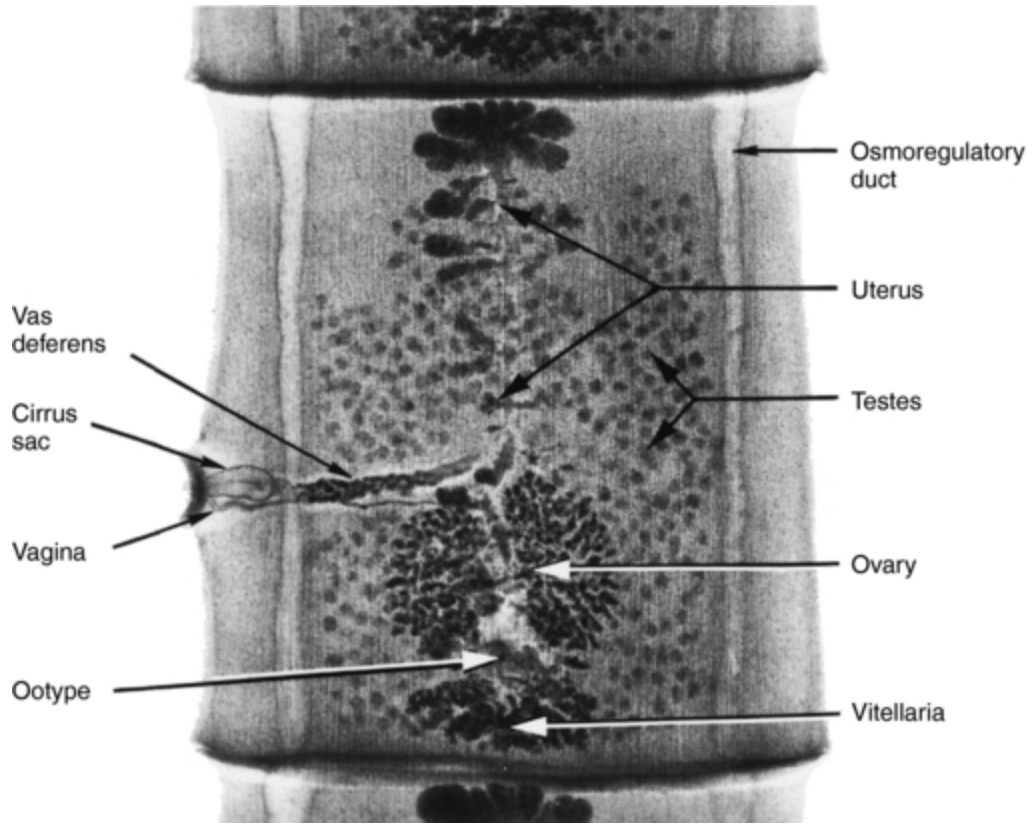

FIGURE 4-35 Mature *Taenia* segment.

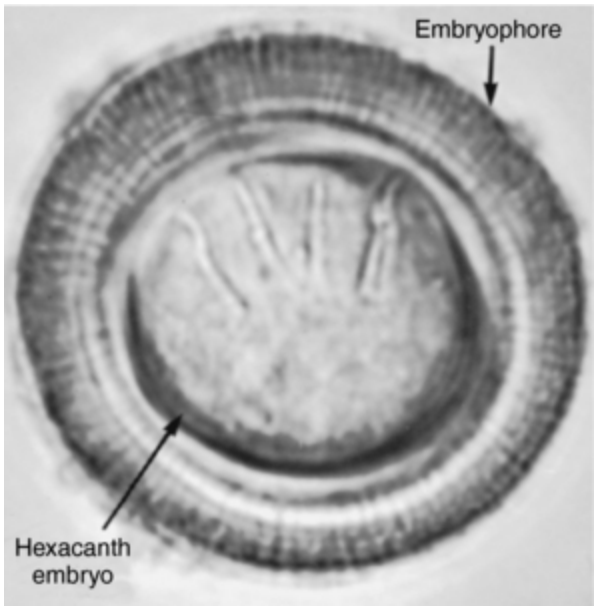

FIGURE 4-36 Egg of *Taenia taeniaeformis* (Taeniidae) of the cat. The capsule of taeniid eggs is fragile; eggs in fecal smears have usually lost their capsules.

Life history

Gravid taeniid segments (Figure 4-37) are shed and exit from the carnivorous definitive host through the anus; the segments of *Echinococcus* species are so small that they are never observed, and often only free eggs are passed in the feces. The segments crawl about on the pelage of the host or surface of the fecal mass, emptying themselves of their eggs (oncospheres) in the process. Therefore any segment collected after it has been out for more than a few minutes may contain few if any eggs. If ingested by a suitable vertebrate intermediate host (usually a species normally taken as prey by the definitive host), the egg hatches and the hexacanth embryo enters the wall of the intestine and migrates to its organ of predilection, usually the liver and peritoneal membranes or the skeletal and cardiac muscles. Here the **hexacanth embryo** grows, cavitates, and differentiates to form the second larval stage, which is

infective to the definitive host. The fully developed second larval stage of the family Taeniidae consists of a fluid-filled bladder with one or more scolices (often called a **bladderworm**) and is surrounded by a connective tissue capsule formed by the vertebrate intermediate host.

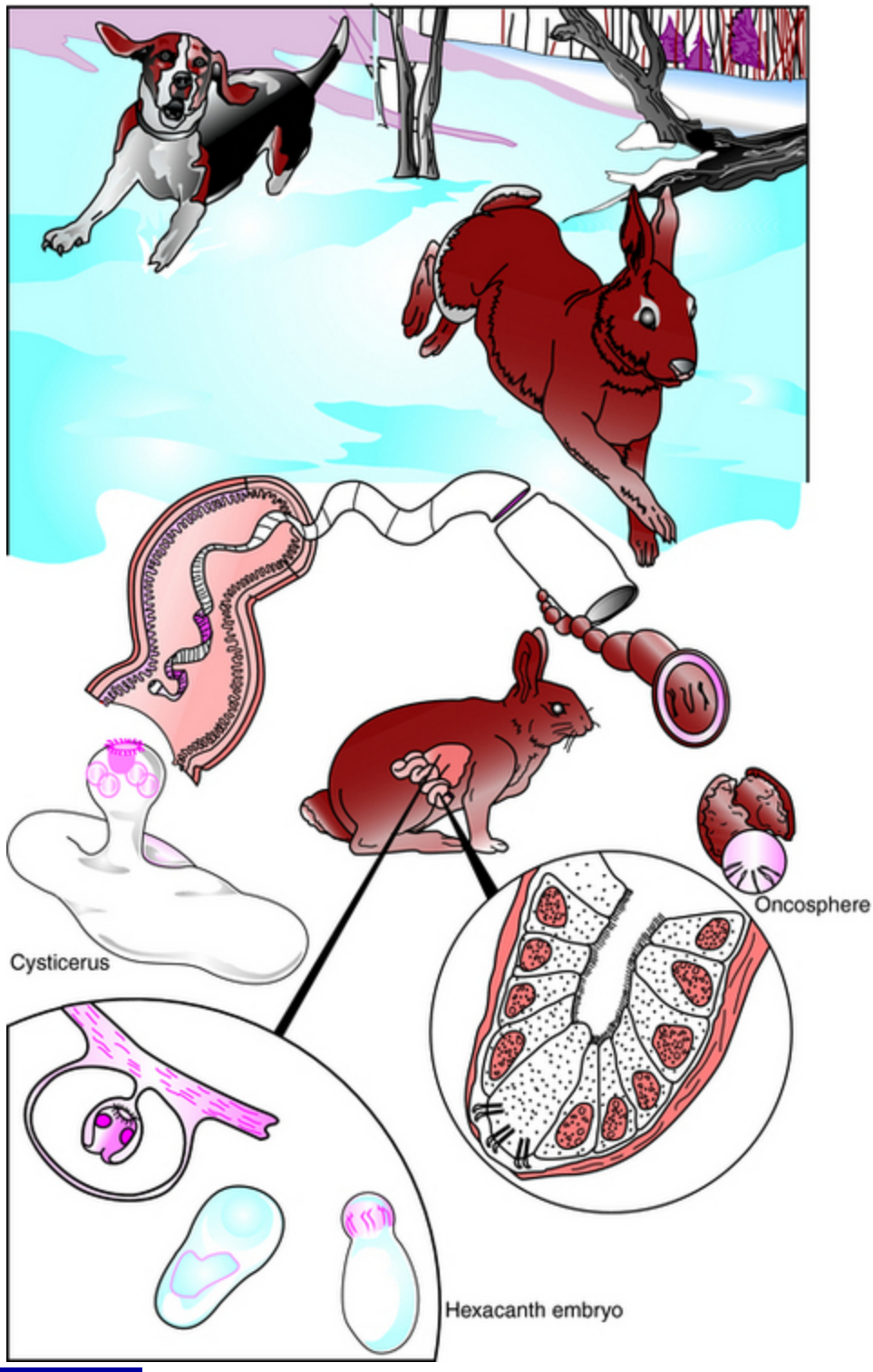

FIGURE 4-37 Life history of *Taenia pisiformis,* a cyclophyllidean tapeworm. Oncospheres (eggs) of *T. pisiformis* are shed in the feces of dogs. If ingested by a cottontail rabbit, *Sylvilagus floridanus,* the hexacanth embryo hatches, invades the mucosa of the small intestine, and makes its way to the liver. Tunneling through the liver, the hexacanth

grows, cavitates to form a bladder, and develops a holdfast organ complete with two rows of hooks and four suckers. Fully developed cysticerci may remain in the liver, but they are more often found encapsulated on the peritoneal surfaces of the mesentery. When a dog eats an infected rabbit, the bladder is digested, leaving only the holdfast and adjacent neck. The holdfast attaches to the wall of the small intestine, and segments begin to form at the neck.

Until the middle of the nineteenth century, the relationship of bladderworms to tapeworms was not recognized. Therefore different stages of the same species were described and named as distinct species belonging to separate phyla. For example, *Cysticercus cellulosae* was placed in the now defunct phylum Cystica, whereas its parent, *T. solium*, was referred to the defunct phylum Vermes. The older names of the larval stages are still occasionally used to identify the morphologically different larval stages of tapeworms. Such usage is helpful in describing pathologic specimens because it eliminates the need for writing "the cysticercus of *Taenia* such-and-such." However, because the specific names of the adult and larval stages often differ, these additional names can add to the confusion that sometimes surrounds the events in the development of different species of tapeworm. Therefore their use has been minimized herein as much as possible.

When a second larval stage of a taeniid tapeworm is ingested by a suitable definitive host, the bladder is digested away, the scolex embeds itself in the mucosa of the small intestine, and the neck begins to bud off segments to form the strobila. Eggs of taeniid tapeworms first appear in the feces 6 to 9 weeks after ingestion of the larva. Williams and Shearer (1982) observed a prepatent period of 34 to 80 days for *T. taeniaeformis* in cats, and the infections remained patent for 7 to 34 months.

There are four basic kinds of taeniid second-stage larvae: the **cysticercus, strobilocercus, coenurus,** and **hydatid.** Members of the genus *Taenia* typically form cysticerci, strobilocerci, and coenuri, depending on the species in question. A **cysticercus** (Figures 4-38, 4-39, and 4-40; see also Figure 8-60) consists of a single bladder with one scolex. A **strobilocercus** (Figure 4-41; see also Figure 8-61) is a cysticercus that has already begun to elongate and segment while still in the intermediate host, and a **coenurus** (Figure 4-42) consists of a single bladder with many scolices, each with the potential for developing into a mature tapeworm (see Figure 8-62). Hydatids are formed by members of the genus *Echinococcus* and are of two kinds, **unilocular hydatid cysts** (see Figure 8-64) and **alveolar hydatids** (see Figure 8-57), both of which often contain thousands of scolices. Usually, one *Taenia* oncosphere develops into only one bladderworm. However, in the case of *T. crassiceps*, asexual multiplication (budding) results in many cysticerci surrounded by a single host-tissue capsule (see Figure 8-63). Such a structure may easily be mistaken for a hydatid cyst by the unwary observer. Many coenuri branch and ramify extensively to form very complex structures, and teratologic malformations may result in diverse and complex structures.

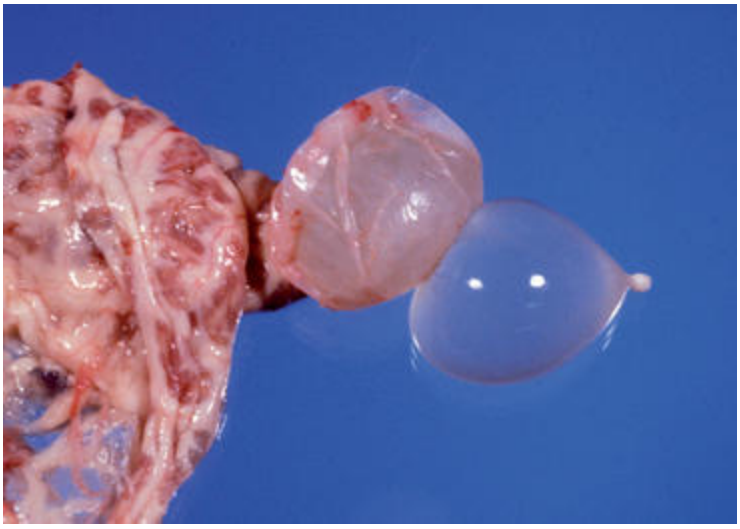

FIGURE 4-38 Cysticercus of *Taenia hydatigena* (Taeniidae) from the mesenteries of a sheep.

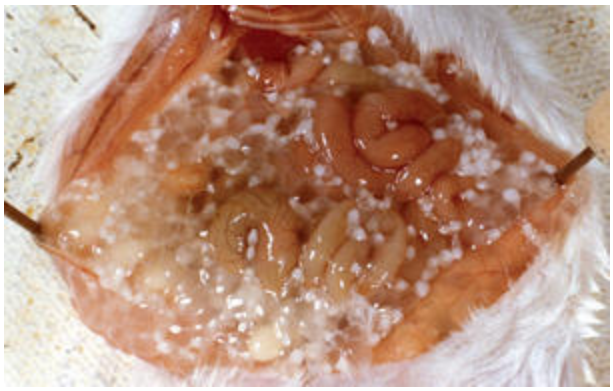

FIGURE 4-39 Cysticerci of *Taenia crassiceps* in the abdominal cavity of an albino mouse that was injected with 10 of these self-replicating cysticerci.

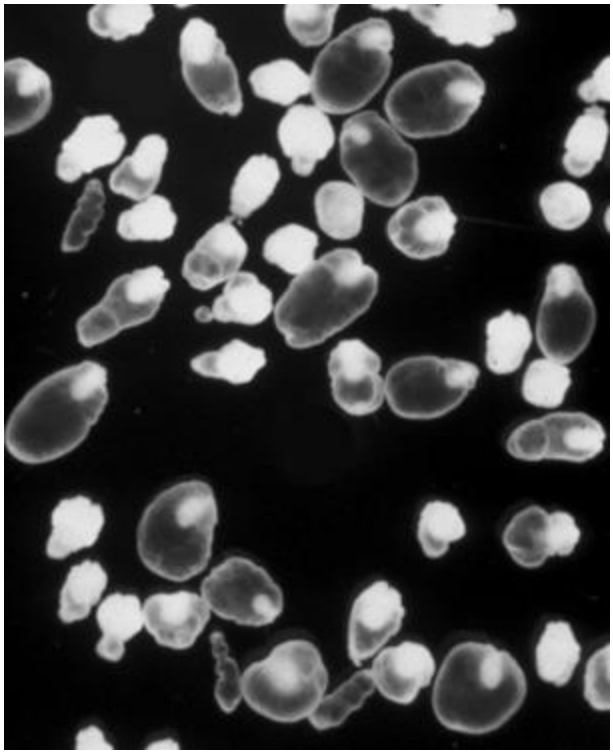

FIGURE 4-40 Cysticerci of *Taenia crassiceps* as they appear in a petri dish.

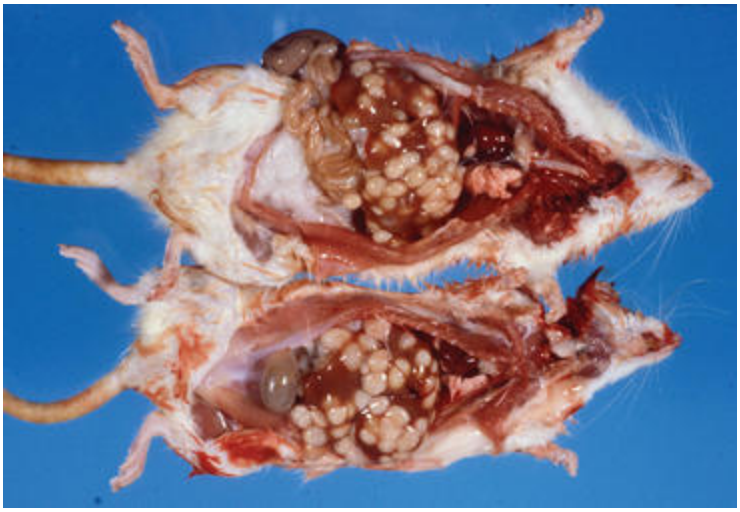

FIGURE 4-41 Strobilocerci *Taenia taeniaeformis* in the liver of two experimentally infected rats.

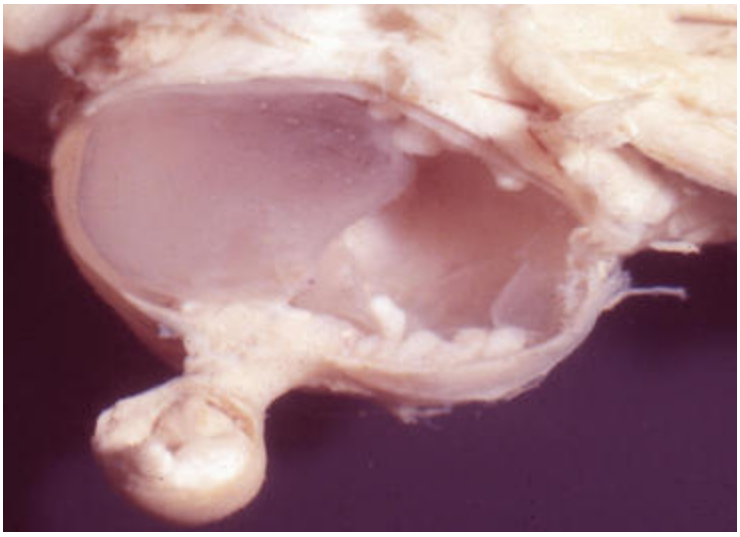

FIGURE 4-42 A coenurus of *Taenia serialis* from the subcutaneous axillary region of a chinchilla.

Cysticercosis

T. hydatigena is a canine taeniid tapeworm with a cysticercus (see Figure 4-38) that migrates through the liver tissue and encysts on the peritoneal membranes of cattle, sheep, swine, and certain wild ungulates. Massive invasions, such as when entire tapeworm segments are ingested, result in acute traumatic hepatitis, and even small numbers of migrating *T. hydatigena* larvae are capable of precipitating "black disease" in the presence of *C. novyi*. However, frank disease is rarely caused by this larval tapeworm, and the principal economic loss results from condemnation of infected livers by meat inspection authorities. Rare cases of human cysticercosis and coenurosis are also caused by larvae of canine taeniids.

Taenia ovis is a second canine taeniid tapeworm with a cysticercus that infects the cardiac and skeletal muscles of sheep and represents the most important pathologic lesion found by United States inspectors in imported Australian mutton. In one instance

$1,540,000 worth of boneless mutton (12.5% of the total shipment) had to be sold as pet food or shipped back to Australia (Arundel, 1972). This tapeworm is no longer found in the United States. Vaccines for sheep have been developed with very good efficacy against the development of the cysticercoid stage, but unfortunately they have yet to be commercially employed to any great extent.

T. pisiformis is a third canine taeniid tapeworm, with the cysticercus being found in the liver and peritoneal cavity of rabbits. This tapeworm is the most common taeniid tapeworm of dogs in the United States. It also indicates how well the process works, because every dog that is so infected must have eaten a rabbit or parts of a rabbit, and this means that many rabbits are infected by grazing near where *T. pisiformis* segments have been shed.

T. saginata is a taeniid tapeworm of human beings that has an "unarmed" scolex, i.e., the scolex has no hooks. The cysticercus of *T. saginata* encysts in the striated muscles of cattle, especially the heart and muscles of mastication. The cystericus, like the adult form, has an unarmed scolex. Taeniid eggs survive the rigors of the septic tank, as well as many contemporary municipal sewage treatment processes, and because defecating out-of-doors is unavoidable when hunting or camping out (and because the segments can leave the host by crawling out through the anal opening), it is easy to see how cattle pastures become contaminated with *T. saginata* eggs. The cysticerci that develop when these eggs are ingested by cattle are relatively inconspicuous and easily overlooked by the lover of rare or raw ("cannibal sandwich") beef. Consequently, *T. saginata* is a common parasite in the United States and would be far more common but for the vigilance of our meat inspectors. Condemnation

of carcass meats for the presence of *T. saginata* cysticerci can result in great economic loss. Sometimes this loss is concentrated in a particular lot of cattle and borne by a single producer. Under such circumstances the economic loss caused by *T. saginata* ceases to be an abstract number and becomes of immediate concern, not only to the unlucky producer, but to his veterinarian, too. The problem is that some person, most likely a farm or feedlot employee, has a tapeworm and has defecated or shed segments in or near the cattle feed. People are generally uncooperative under such circumstances, and the culprit is rarely identified.

T. asiatica is a taeniid tapeworm of human beings in southeast Asia (e.g., Thailand, Indonesia, Korea, Taiwan, and the Philippines). The cysticercus has hooks and is found in the liver of pigs (occasionally cattle) and does not occur in muscle. When this form develops to the adult stage in humans, the hooks are lost, and the tapeworm appears morphologically and molecularly very similar to *T. saginata*. This form has caused significant economic losses in pigs in the area where it occurs and is thought to be maintained by the habit of humans eating raw liver. This form may be considered a separate species but has been designated a separate subspecies with the name *Taenia saginata asiatica* (Fan et al, 1995; Hoberg et al, 2001).

T. solium is the "armed" taeniid tapeworm of human beings. The cysticercus of the human tapeworm *T. solium*, unlike those of *T. saginata* and *T. asiatica*, represents a significant hazard to human health. People become infected with *T. solium* by ingesting the cysticerci in undercooked pork. After the tapeworm matures, the person's feces contain a steady supply of eggs, which may be conveyed to the mouth at any time by a lapse in personal hygiene.

When the eggs reach the stomach, the oncospheres hatch out, enter the gut wall, and wander far and wide in the body, slowly developing into cysticerci. Apparently the milieu intérieur of humans resembles that of swine closely enough to satisfy the development requirements of the cysticercus. In humans the signs depend on where the cysticerci localize, and sites may include most typically muscle, but also, eye, brain, or spinal cord. Dogs can also on rare occasions be infected with these cysticerci (see Figure 8-60).

Strobilocercus

T. taeniaeformis, the common taeniid tapeworm of the domestic cats, has a larval stage that is termed a *strobilocercus* (see Figure 4-41; see also Figures 8-54 to 8-56 and 8-61). This larval stage is not of any significant zoonotic potential.

Coenurosis

T. multiceps is a canine taeniid tapeworm, with the larval stage being a coenurus that invades the cranial cavity of sheep, goats, and sometimes cattle. As the cyst grows over a period of 6 or 8 months, neurologic signs of progressive space occupation slowly develop. There may be blindness, incoordination, walking in circles, and pressing the head against walls, tree trunks, and the like. Finally, the animal lies down and dies. The most common diseases that might be confused with cerebral coenurosis are bacterial encephalitis (listeriosis) and parelaphostrongylosis. Intracranial surgery is the only cure for cerebral coenurosis but lies beyond economic reality for sheep unless the shepherd is very skillful with his jackknife. The location of the larva within the skull makes some people wonder how the scolices ever reach a dog's stomach, but

they must not realize that a good stout dog can crush a sheep's skull with one bite. As in the case of *T. hydatigena* and *Taenia ovis*, control can be based only on excluding dogs and other canids from sheep pastures. Unfortunately, this is often next to impossible.

T. serialis is another taeniid tapeworm of canids with a larval stage that is a coenurus. In this case the larval stage typically develops in the subcutaneous tissues or the viscera of rabbits. Cerebral coenurosis in cats appears in isolated cases (Georgi, de Lahunta, and Percy, 1969; Hayes and Creighton, 1978; Kingston et al, 1984; Smith et al, 1988). Marked by severe neurologic disturbances, it is invariably fatal. The responsible species is probably *T. serialis* owing to the disappearance of *T. multiceps* from the United States.

Echinococcus

Identification

The genus *Echinococcus* contains two species of special importance to veterinary medicine, *E. granulosus* and *E. multilocularis*, which are very small (2 to 8 mm long) adult tapeworms having only four or five segments, of which only the terminal segment is gravid (Figure 4-43). In *E. granulosus*, 45 to 65 testes are generally distributed, and the genital pore is located at or posterior to the middle of the segment. In *E. multilocularis*, 17 to 26 testes are found posterior to the genital pore, which is located anterior to the middle of the segment. Caution: Human hydatid infection may be acquired by ingesting the eggs of *Echinococcus* species; wear gloves and wash carefully when handling the feces of potentially infected carnivores.

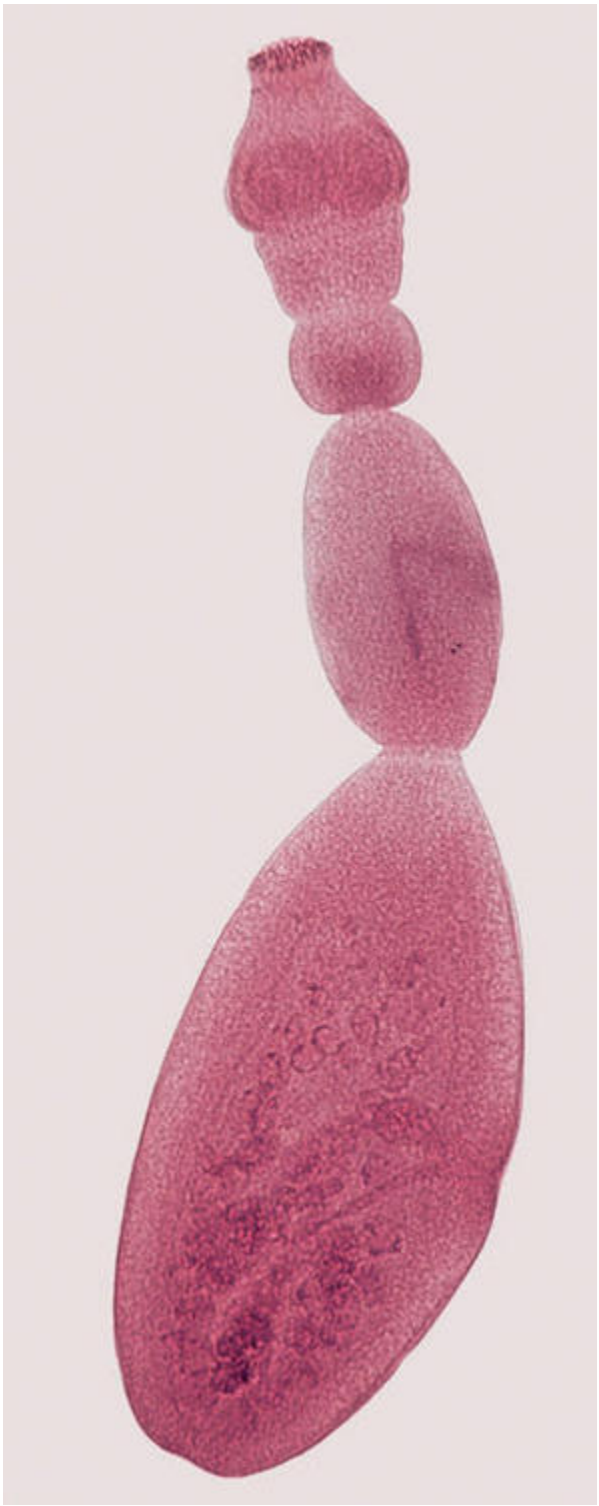

FIGURE 4-43 *Echinococcus granulosus* (Taeniidae), entire worm.

E. granulosus is endemic in North and South America, England, Africa, the Middle East, Australia, and New Zealand. *E. multilocularis* is endemic in north-central Europe, Alaska, Canada, and the central United States as far south as Illinois and Nebraska (Ballard and Vande Vusse, 1983).

Life history

E. granulosus is a parasite as adults of the dog, coyote, wolf, and dingo. Its larva is a **unilocular hydatid cyst** in sheep, swine, cattle, humans, moose, caribou, kangaroos, and others. Species vary in their suitability as intermediate hosts. Hydatid cysts found in sheep are usually fertile, whereas those in cattle tend to be sterile. Subspecies of *E. granulosus* differ in their preferences for intermediate hosts. For example, *E. granulosus granulosus* hydatids belong to the subspecies adapted to sheep and humans, whereas *E. granulosus equinus* is the subspecies found in horses, asses, and mules. The hydatid membrane may bud off daughter cysts either internally or externally. The whole structure occupies progressively more space as it grows, but hydatid cysts do not infiltrate, in contrast to alveolar hydatids. Pathogenic effects of hydatid cysts include pressure atrophy of surrounding organs and allergic reactions to hydatid fluid leaks. Rupture of a fertile hydatid cyst may scatter bits of germinative membrane, scolices, and brood capsules throughout the pleural or peritoneal cavity and result in multiple hydatidosis. Pulmonary hydatid cysts may rupture into a bronchus, the contents may be coughed up, and the lesion may be healed. Hydatid cysts that remain intact eventually die and degenerate, but the course is protracted.

E. multilocularis is a parasite of canids, mainly foxes and wolves in arctic regions. The larval stage, the **alveolar hydatid cyst**, develops in the liver of voles and lemmings (see Figures 8-57 and 8-58Figure 8-57Figure 8-58). The alveolar hydatid is characterized by exogenous budding that continuously proliferates and infiltrates surrounding tissue. As with unilocular hydatid cysts, the alveolar hydatid contains many small scolices, each of which is termed a **protoscolex** (plural, **protoscolices**). People become infected when they ingest the egg of *E. multilocularis*.

Unilocular hydatid disease

The unilocular hydatid cyst is the second-stage larva of *E. granulosus* and is infective to dogs and other canids that serve as definitive hosts (Figure 4-44). Starting as an oncosphere less than 30 μm in diameter, the larva grows very slowly and infrequently exceeds more than a few centimeters in diameter in slaughtered sheep and cattle. Because humans live longer, a fertile hydatid infecting man may grow very large and interfere with the function of neighboring organs by pressing against them. The hydatid membrane is surrounded by, but usually not attached to, an inflammatory connective tissue capsule (see Figure 8-64). The space between the host and the parasite generally contains a small volume of clear, colorless, or light-yellow liquid. Brood capsules, each containing many scolices, develop from the germinal epithelium lining the laminated hydatid membrane (Figure 4-45). Some of these rupture, releasing scolices to form a sediment of so-called “hydatid sand” in the hydatid fluid (Figure 4-46). Endogenous daughter cysts may be found free in the fluid-filled cyst cavity or attached to the germinal epithelium. Exogenous daughter cysts are relatively unusual; they

may be found in the pericystic space between the hydatid membrane and the host connective tissue capsule. “Sterile” hydatids, so-called because they lack protoscolices, often form in cattle and swine, making the diagnosis sometimes difficult and presumptive.

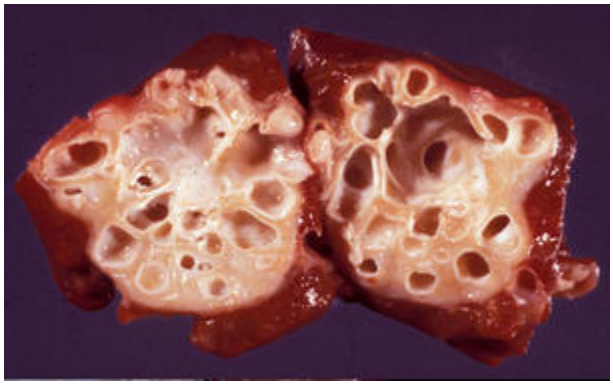

FIGURE 4-44 A hydatid cyst *(Echinococcus granulosus)* in the liver of a horse. This horse displayed no clinical signs of hepatic involvement despite the presence of 20 to 30 cysts like the one illustrated.

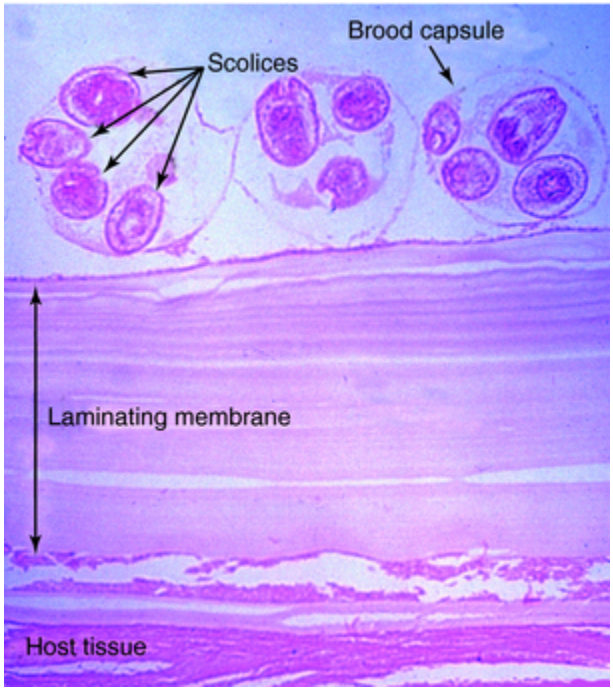

FIGURE 4-45 *Echinococcus granulosus* hydatid cyst with three brood capsules, each containing three or more protoscolices.

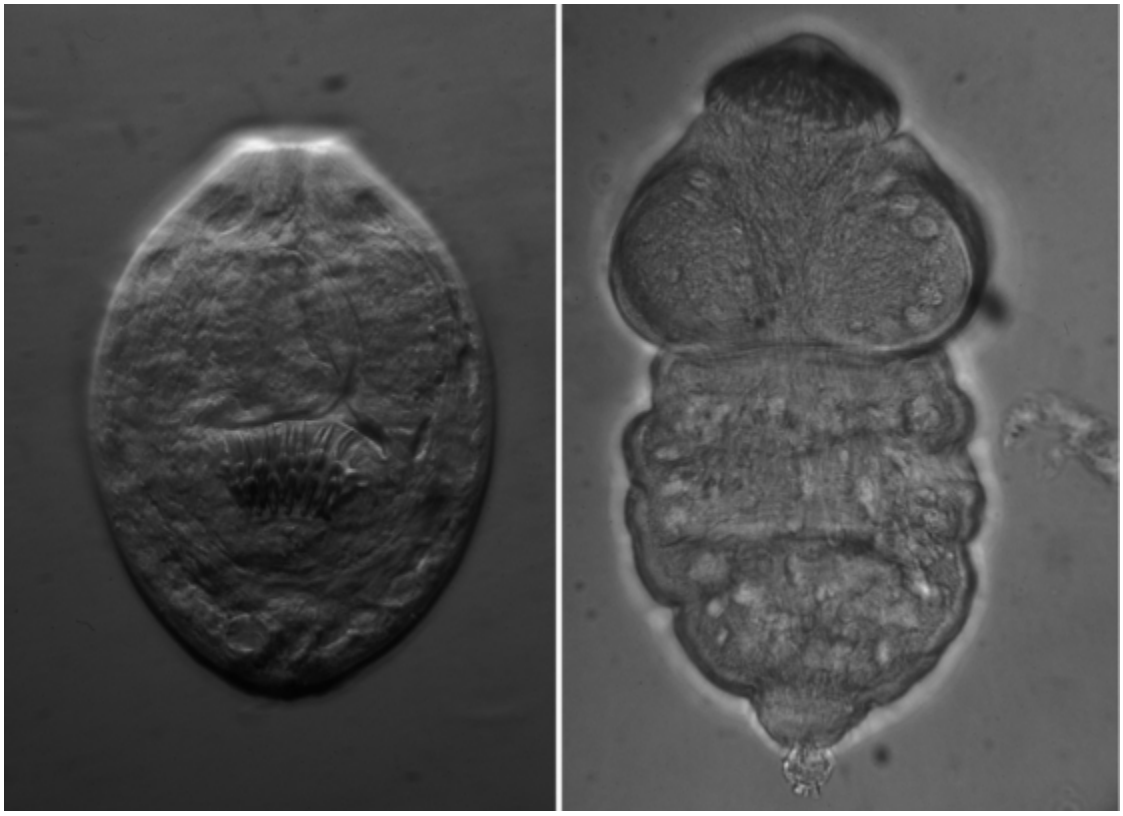

FIGURE 4-46 Protoscolices of *Echinococcus granulosus* from a hydatid cyst. The one on the left is invaginated, whereas the one on the right is evaginated.

Alveolar hydatid disease

Alveolar hydatid cysts are the second larval stage of *E. multilocularis* (the first being the hexacanth embryo within the egg) and contain protoscolices that are infective to dogs, foxes, and cats, which serve as definitive hosts (Figure 4-47). Alveolar hydatids may develop in voles, lemmings, cattle, horses, swine, and humans. In humans the cysts are typically "sterile" and become a proliferating germinal membrane that continuously proliferates and infiltrates surrounding tissue like a malignant neoplasm. Alveolar hydatid infection proves

invariably fatal in a few years. In North America the largest numbers of cases in human beings have occurred in areas where the parasite has entered the peridomestic cycle by infecting dogs and rodents in native American villages. This occurred in St. Lawrence Island, Alaska, where a large number of villagers were infected with this parasite. Cases continue to be reported from Alaska; and there has been one case reported from the lower 48 United States, in Minnesota. In central Europe, almost 600 cases have been reported in recent years, with most being from eastern France to western Switzerland. Often in people the entire cyst cannot be removed by surgical resection because of its indiscrete boundaries, making it harder to treat than the discrete cysts of unilocular hydatidosis. Patients are often placed on long-term anthelmintic therapy with products such as albendazole. Of 408 patients who were alive in 2000 whose cases were reported to the central European hydatid registry, only 4.9% were considered to have been cured of their infection.

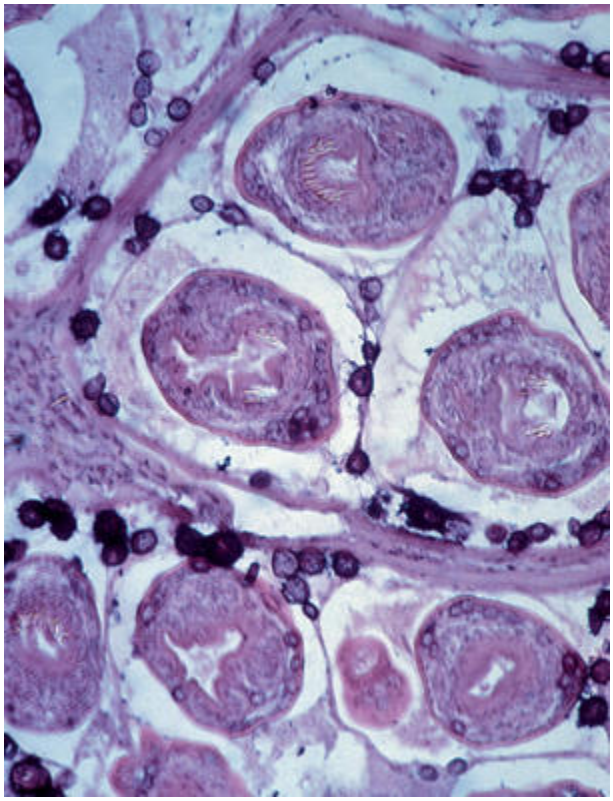

FIGURE 4-47 *Echinococcus multilocularis* alveolar hydatid.

Control

Both *E. granulosus* and *E. multilocularis* tend to establish sylvatic cycles when suitable predator-prey relationships exist in the wildlife population of a region. Therefore *E. granulosus* cycles are maintained among wild ruminants and wolves in the Canadian north woods and among wallabies and dingoes in Australia. Natural nidi of *E. multilocularis* are maintained in various rodents and foxes. The sylvatic cycle reaches humans through their domesticated animals. Dogs that scavenge the entrails of wild game infected with *Echinococcus* species become direct sources of hydatid infection to humans and their domestic animals. Contamination of pastures with the feces of infected wild carnivorans also results in hydatid infection of domestic ruminants and swine. The establishment of a

pastoral cycle may then result from the feeding of uncooked offal from these domestic animals to dogs and, in the case of *E. multilocularis*, to cats (Figure 4-48).

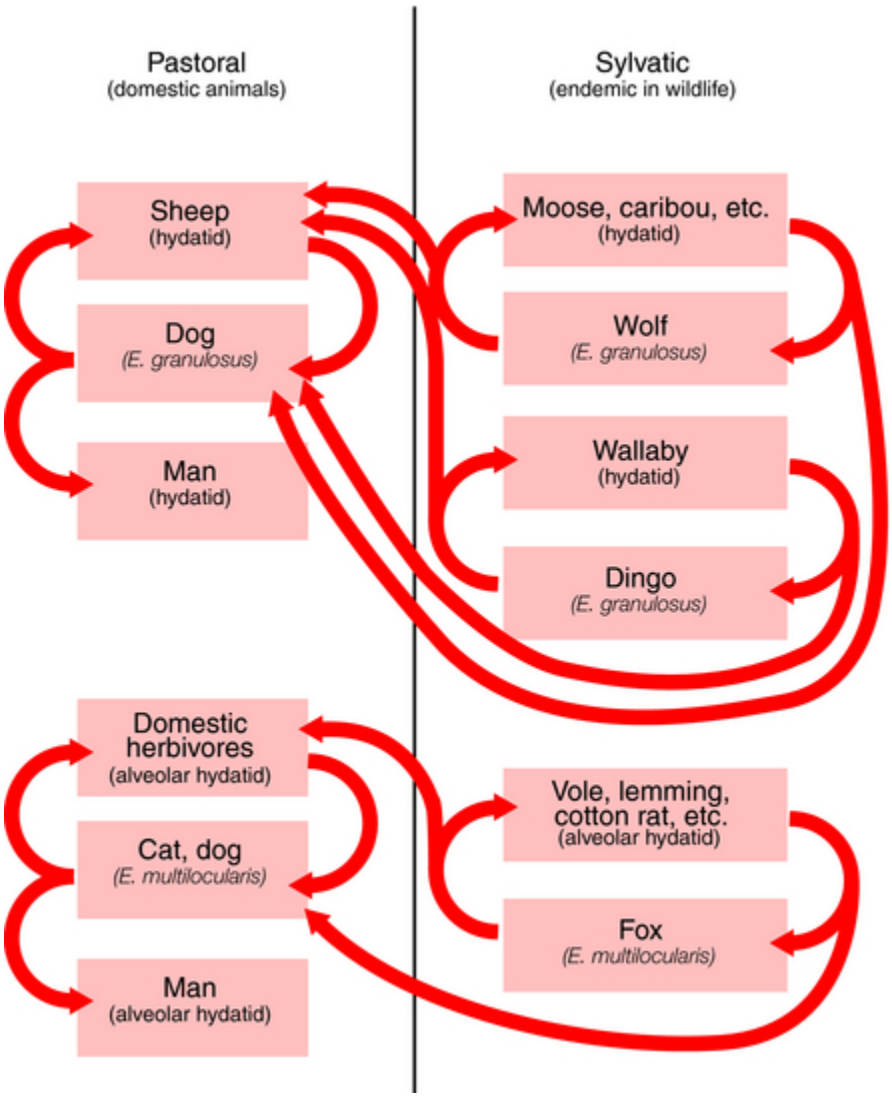

FIGURE 4-48 Pastoral and sylvatic cycles of *Echinococcus granulosus* and *Echinococcus multilocularis*.

The direct source of human infection is, in most instances, the domestic dog or cat, and scrupulous hygiene is the first line of defense. Periodic anthelmintic medication of dogs or cats,

depending on the species of tapeworm involved, carries the threat one step further away. In the case of a well-established sylvatic cycle, this is about as far as it is practical to go. *Echinococcus* infection may be reduced to insignificant incidence in cases in which it is limited to a pastoral cycle and thus accessible to manipulation by humans. Destruction of all stray dogs, regimented anthelmintic medication of the rest, and prohibition against feeding uncooked offal to dogs and cats are mandatory.

A campaign against hydatid disease was begun in Iceland 1864. At the outset, about one in six or seven people and virtually all ages of slaughter sheep and cattle harbored hydatid cysts, and about one fourth of the dogs were infected with the adult worm. By 1900 the human infection rate had fallen dramatically and has basically reached the point of nonexistence. The campaign, devised by Dr. Harald Krabbe of the Royal Veterinary and Agricultural University of Copenhagen, consisted of alerting the public to the need to observe strict hygiene in dealing with dogs, destroying all cysts and infected offal, and administering mandatory anthelmintic medication to all dogs (Palsson, 1976). Thus salutary results in *Echinococcus* control can be achieved in a century or so, provided there is no sylvatic cycle to complicate the issue. In Australia, for example, a sylvatic cycle involving kangaroos and *Canis dingo* would have to be considered in any eradication attempt. “Obviously the denial of sheep offal to domestic dogs will not eliminate infection if dogs have access to macropods in dingo-infested areas” (Herd and Coman, 1975). In the United States, *E. granulosus* appears to be most prevalent in sheep-raising areas of Utah (Loveless et al, 1978) and California. In California the spread of echinococcosis appears to be

related to a quaint transhuman form of husbandry in which bands of sheep migrate from place to place under the control of contract Basque shepherds from Spain and France. These shepherds, for the most part, are ignorant of the epidemiology of hydatid disease and feed their dogs mostly on dead sheep (Araujo et al, 1975).

There have been vaccines for sheep produced that have been successful in preventing the development of hydatid cysts in sheep. These vaccines are currently undergoing field trials in various parts of the world and may go a long way in providing new means for the eradication of this parasite in certain locals.

Other Cyclophyllidean Tapeworms

The second larval stage of all of the following cyclophyllidean families are **cysticercoids** of one kind or another. A cysticercoid may be thought of as a cysticercus small enough to fit into the body of an arthropod. It is small and solid rather than cavitated (the cysticercoid is solid; the cysticercus has a fluid-filled bladder) but has an inverted (or at least introverted) scolex. The cysticercoids of *Mesocestoides* species have yet to be identified, remarkable as that may seem in this enlightened age. However, the specialists nevertheless seem certain that a cysticercoid stage of *Mesocestoides* must precede the well-known tetrathyridium found in a wide range of mammals, birds, and reptiles.

Family Anoplocephalidae

Identification

Moniezia organisms have unarmed scolices with four large suckers and very wide segments with bilateral genitalia. They are found in

the small intestine of cattle, sheep, and goats *(Moniezia benedeni, Moniezia expansa,* and *Moniezia caprae)*. Interproglottidal glands at the posterior margin of each segment extend the full width of *M. expansa* but occupy only the midzone of the *M. benedeni* segment (Figure 4-49). The egg of *M. benedeni* found in cattle feces is one of the few eggs that appears square, and internally the pear-shaped (pyriform apparatus) characteristic of anoplocephalid eggs can be seen (Figure 4-50).

FIGURE 4-49 Mature segments of *Moniezia expansa* (Anoplocephalidae).

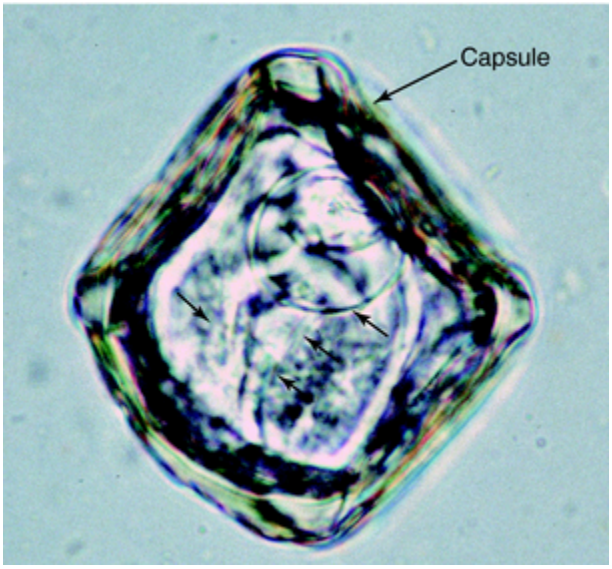

FIGURE 4-50 Egg of *Moniezia* sp. (Anoplocephalidae) of ruminants. The pear-shaped embryophore *(arrows)* is typical of anoplocephalid eggs.

Thysanosoma actinioides, the fringed tapeworm, is found in the common bile duct and duodenum of virtually all ruminant species except cattle. Ligature of the bile duct within 5 minutes of slaughter has revealed that these worms are probably found almost exclusively in the intestine of the living animal (Boisvenue and Hendrix, 1987). The endemic areas of *T. actinioides* are the western parts of North and South America, especially mountainous areas. *Wyominia tetoni* is found in mountain sheep *(Ovis canadensis)*. *T. actinioides* has wide segments with bilateral genitalia and a fringe of outgrowths at the posterior border of each segment. *W. tetoni* resembles *T. actinioides*, but its segments are not fringed. *Thysaniezia*, *Stilesia*, and *Avitellina* species are exotic anoplocephalids of ruminants.

Anoplocephala magna and *Paranoplocephala mamillana* (Figure 4-51) are relatively harmless parasites in the small intestine of horses. *Anoplocephala perfoliata* (Figure 4-52) is found mainly in the cecum but also tends to cluster in the ileum near the ileocecal valve, where it is associated with ulceration and reactive inflammation of the ileal wall. This clustering results in ulceration of the mucous membrane and inflammation with thickening and induration of the deeper layers of the intestinal wall. These pathologic changes probably account for some cases of persistent diarrhea and may predispose to intussusception of the ileum into the cecum or rupture of the bowel wall in the vicinity of the ileocecal valve (Barclay, Phillips, and Foerner, 1982; Beroza et al, 1983). Proudman and Edwards (1993) published work showing an association between

infection with *A. perfoliata* and ileocecal colic in horses. Diagnosis of *A. perfoliata* infection is based on distinguishing the eggs from those of *A. magna* and *P. mamillana*. *A. perfoliata* eggs and segments frequently cannot be demonstrated, either by flotation or sedimentation techniques, in the feces of horses known to be heavily infected with this parasite, a paradox for which we are unable to offer a satisfactory explanation. For this reason, an enzyme-linked immunosorbent assay (ELISA) has been used to examine the immunoglobulin G (IgG) of horses to determine infection with this parasite. In a case-controlled study with this means of detection, horses with tapeworms had a 26 times greater risk of developing spasmodic colic (Proudman, French, and Trees, 1993). What is important is that horses be treated occasionally with something other than ivermectin (i.e., something that will kill tapeworms).

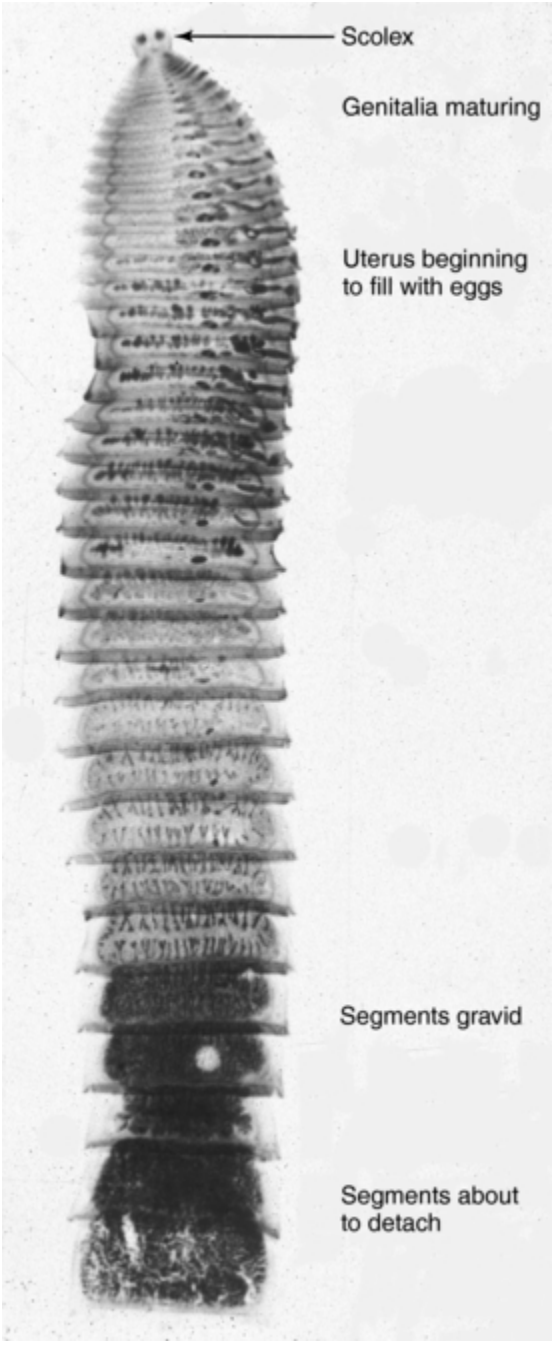

FIGURE 4-51 *Paranoplocephala mamillana* (Anoplocephalidae), entire tapeworm.

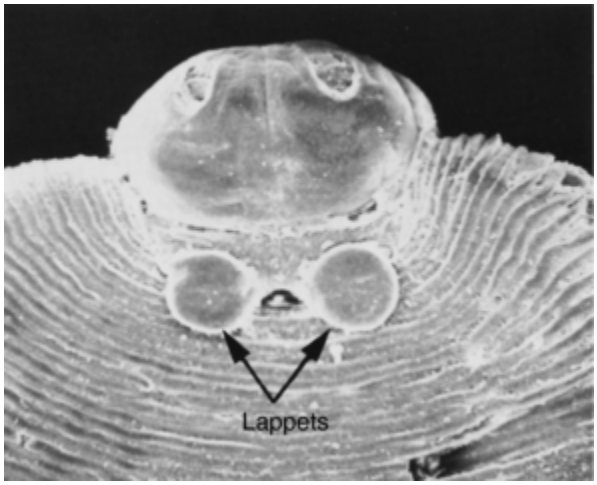

FIGURE 4-52 *Anoplocephala perfoliata* (Anoplocephalidae), scanning electron micrograph. The scolex of *A. perfoliata* is about 2 mm in diameter and has four large suckers and four projections called *lappets*.

Life history

The life histories of only a few anoplocephalids have been documented, but those that have involve an arthropod intermediate host in which the infective cysticercoid develops. Infection purportedly results from the incidental ingestion of these infected arthropods by the grazing animal. Free-living oribatid mites serve as hosts for cysticercoids of *Moniezia* species of sheep and cattle, *Bertiella* species of primates, and *Cittotaenia* species of the European wild rabbit. *T. actinoides* is apparently transmitted by "booklice" or "barklice" of the family Psocidae, order Psocoptera. Psocopterans resemble mallophagan lice but are entirely free living and have no other known relationship to parasite life histories.

Control

The tapeworms of cattle, sheep, and goats all belong to the family Anoplocephalidae. Pasture renovation is recommended to destroy the surface layer of humus and thus the habitat of oribatid mites,

which are the intermediate host of at least some of these cestodes. However, there seems to be little experimental basis to support this recommendation. Fortunately, adult tapeworms are relatively nonpathogenic. Those species that invade the bile ducts cause condemnation of the liver at slaughter and in this way lead to considerable economic loss. However, the most common reason for a veterinarian's wish for a drug to remove adult tapeworms from ruminants seems related to the difficulty of persuading the average client that those big white worms are relatively harmless. It is easier to worm the stock than to convince the stockman.

Family Dipylidiidae

Identification

In *Dipylidium caninum*, *Diplopylidium* species, and *Joyeuxiella* species, the scolex has four suckers and a retractable rostellum armed with several circles of thornlike hooks (Figure 4-53). Segments are shaped like cucumber seeds and have bilateral genital pores. The genital apertures of *D. caninum* lie slightly behind the middle of the segment (i.e., away from the scolex), and each egg capsule may contain from 5 to 30 eggs (Figure 4-54). The genital apertures of the Middle Eastern, African, and Australasian parasites *Diplopylidium* and *Joyeuxiella* lie before the middle of the segment (i.e., toward the scolex), and each capsule contains a single egg.

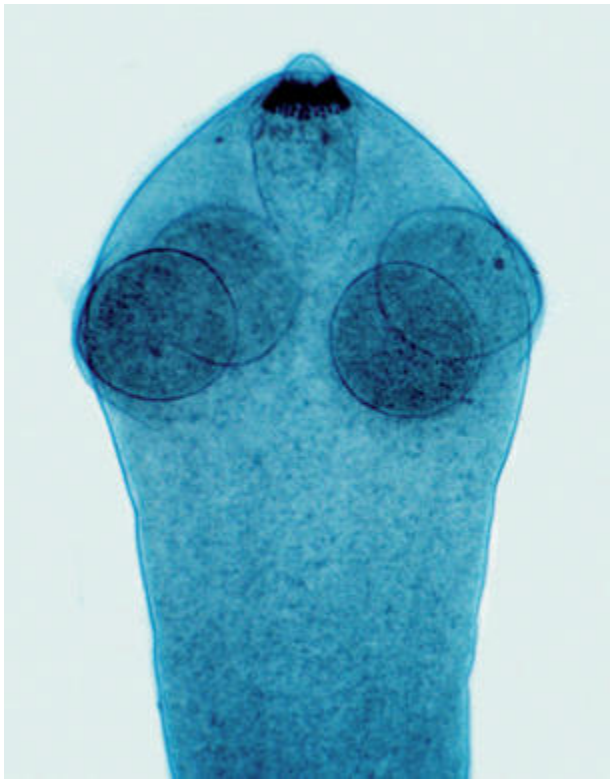

FIGURE 4-53 *Dipylidium caninum* (Dipylidiidae); scolex of fresh stained specimen. The scolex of *D. caninum* is less than 0.5 mm in diameter; the rostellum is retractable and armed with small thornlike hooks.

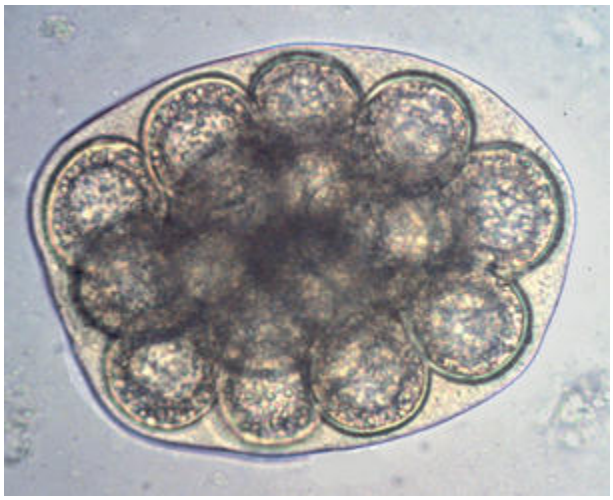

FIGURE 4-54 Egg packet of *Dipylidium caninum*.

Life history

Cysticercoids of *D. caninum* develop in fleas (*Ctenocephalides* species) and biting lice *(Trichodectes canis)*, and the dog acquires this tapeworm while nipping its insects (Figure 4-55). Children also may become infected in this way. Cysticercoids of *Diplopylidium* and *Joyeuxiella* develop in coprophagous beetles; reptiles and small mammals serve as second intermediate hosts.

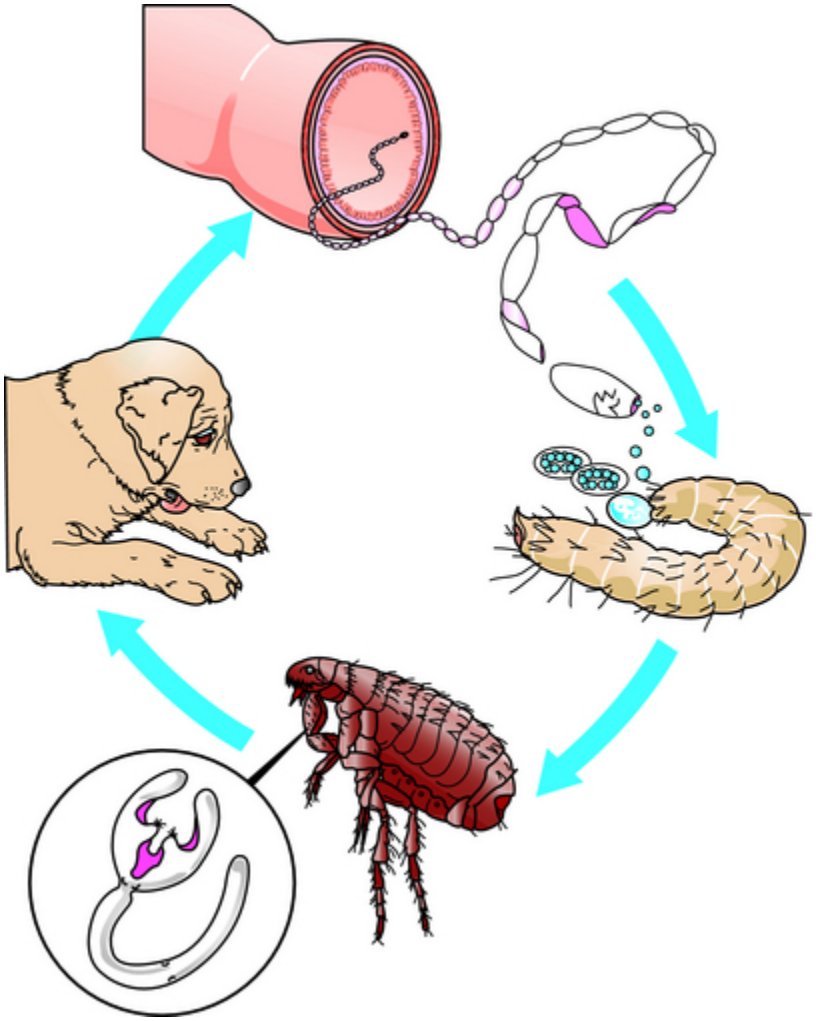

FIGURE 4-55 Life history of *Dipylidium caninum*. Gravid segments discharge their egg packets as they move about. Larvae of *Ctenocephalides* chew their way into egg packets and ingest the oncospheres of the tapeworm. The hexacanth embryo enters the body cavity of the flea larva and remains there through its metamorphosis. After the adult flea emerges from the cocoon, the hexacanth develops into a cysticercoid in 2 or 3 days.

If such a flea is ingested by the definitive host as during self-grooming, the cysticercoids develop into adult tapeworms in the small intestine.

D. caninum requires only 2 to 3 weeks to develop from a cysticercoid into a segment-shedding tapeworm. Therefore the benefits of anthelmintic therapy are particularly short-lived unless fleas and biting lice also are brought under control. It has been shown that the developing cysticercoids require a day or so in a flea that has found a mammalian host to be warm enough to finish their ultimate development to the infective stage (Pugh, 1987).

Family Hymenolepididae

The family Hymenolepididae contains many species that occur in birds and two mammalian parasites. *Hymenolepis diminuta* is a parasite of the small intestine principally of rodents but occasionally also of dogs and even humans (Ehrenford, 1977). The eggs of this tapeworm can be found in the feces (Figure 4-56). The cysticercoid of *H. diminuta* develops in fleas, flour beetles, and a rather wide range of other insects (Figure 4-57). *Vampirolepis* (*Hymenolepis*, *Rodentolepis*) *nana* is also a parasite of rodents and humans, and its second larval stage is a cysticercoid in fleas and flour beetles or in the intestinal mucosa of its definitive host. *V. nana* can complete its life history within the intestinal tract of a mouse or a human. Some of the eggs hatch within the intestine, and the hexacanth embryos burrow into the mucous membrane to form cysticercoids that later reenter the lumen to complete their development as mature tapeworms. The rest of the eggs pass out with the feces to await ingestion by flour beetles or fleas, in which the cysticercoids develop. Thus *H. diminuta* requires fleas, flour beetles, or other

insects as intermediate hosts, whereas *V. nana* may or may not. Because the eggs discharged in feces are infective to humans, *V. nana* infection in laboratory rodent stocks constitutes something of a health hazard to personnel. Because *H. diminuta* infection requires ingestion of an infected insect, human infection with this tapeworm is less probable but does occur. Hymenolepids have three testes and a single ovary; *V. nana* has a single circle of hooks on its scolex, whereas *H. diminuta* has no hooks.

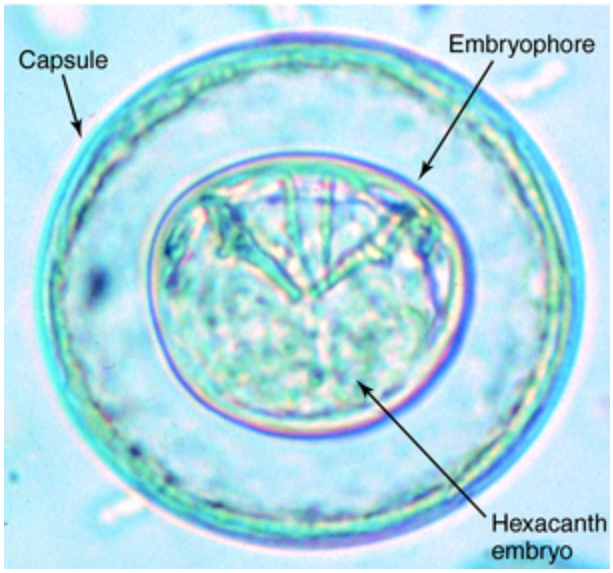

FIGURE 4-56 Egg of *Hymenolepis diminuta* (Hymenolepidae), a common parasite of rodents.

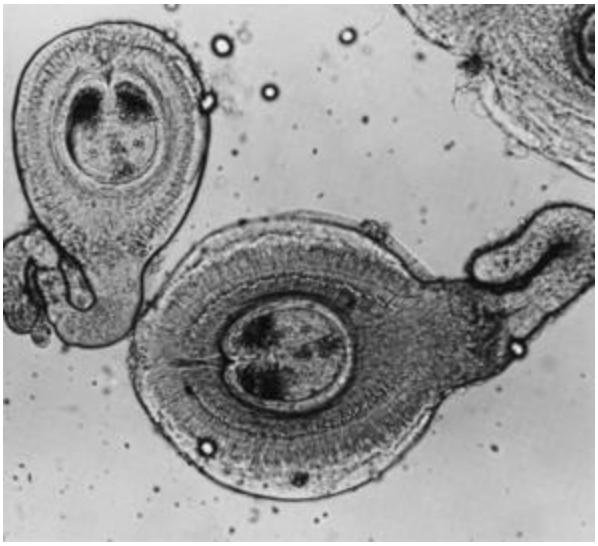

FIGURE 4-57 Cysticercoids of *Hymenolepis diminuta*.

Family Mesocestoididae

Identification

The scolex of *Mesocestoides* species has four suckers but no hooks. Mature segments have a mediodorsal genital pore, and eggs accumulate in a special, thick-walled parauterine organ as the segments mature (Figure 4-58). Gravid segments detach from the strobila and carry their relatively small burden of oncospheres to the outside world.

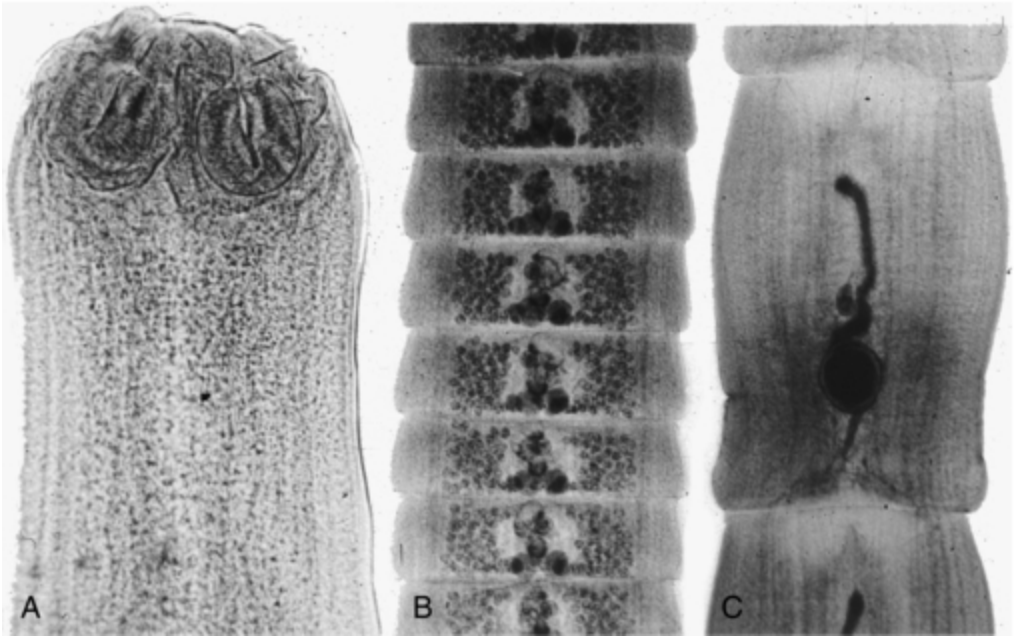

FIGURE 4-58 *Mesocestoides* sp. **A,** Scolex. **B,** Mature segments. **C,** Gravid segments.

Life history

The complete life history of the genus *Mesocestoides* has yet to be worked out. The larval form infective for the definitive host is a third larval stage called a **tetrathyridium** and is found in the peritoneal cavity of mammals and reptiles and in the lungs of birds (see Figures 8-65 to 8-67Figure 8-65Figure 8-67). A cysticercoid larval stage is hypothesized to precede the tetrathyridium, possibly developing from the oncosphere in a coprophagic insect (Loos-Frank, 1991).

Mesocestoides infection of dogs and cats results from predation on snakes, birds, and small mammals. Some clients find it difficult to accept that their civilized pets are using their long, sharp teeth in an atavistic way, especially sportsmen with expensive bird dogs and vegetarians with cats. However, the carnivoran must be denied prey if *Mesocestoides* infection is to be prevented. Most taeniids have

about a 2-month prepatent period, but *Mesocestoides* organisms may start discharging segments in hardly more than 2 weeks after infection, thereby imparting the impression that the anthelmintic has not worked at all. To make matters worse, *M. corti* tapeworms multiply asexually in the intestines of dogs. If this species is not totally eliminated by anthelmintic medication, it will repopulate the intestine even without further exposure (Eckert, von Brand, and Voge, 1969).

Treatment of Adult Tapeworm Infections

Dogs and cats

Adult tapeworm infections cause little harm or inconvenience to dogs and cats. It is true that infected dogs frequently sit down and drag their bottoms, but so do uninfected dogs. No doubt a tapeworm segment wandering about the perineum tickles. Although this phenomenon must certainly be included in the list of causes for pruritus ani, distended anal sacs are more frequently to blame. The veterinarian who treats pruritus ani by expressing anal sacs will obtain better results than another who prescribes anthelmintics for this condition.

A tapeworm segment crawling about on a pet's tail or freshly passed feces offends most clients, and the civilized world makes quite a business of poisoning tapeworms. For lasting results to be obtained, the source of infection must also be dealt with, or the segments will reappear and the client may not.

There are many drugs with proven efficacy against the tapeworms affecting dogs and cats. Praziquantel and epsiprantel both show

activity against one or more tapeworm genera, but almost all fail against one or another genus.

The cestocidal drug praziquantel, in a single 5-mg/kg oral or subcutaneous dose, eliminates 100% of both immature and adult *T. hydatigena*, *T. pisiformis*, *Taenia ovis*, *T. taeniaeformis*, *E. granulosus*, *E. multilocularis*, *M. corti*, and *D. caninum* from dogs and cats (Anderson, Conder, and Marsland, 1978; Dey-Hazra, 1976; Rommel, Grelck, and Hörchner, 1976; Thomas and Gönnert, 1978). Praziquantel at a dosage of 7.5 mg/kg for 2 consecutive days eliminated 100% of *Diphyllobothrium erinacei,* and a single dose of 35 mg/kg eliminated all *D. latum* from infected cats (Sakamoto, 1977). Praziquantel in combination with pyrantel pamoate and febantel also has been shown efficacious in removing infections with *E. granulosus* and *E. multilocularis*. Epsiprantel at 2.75 mg/kg in cats and 5.5 mg/kg in dogs is efficacious against *D. caninum*, *T. pisiformis*, and *T. taeniaeformis*. Doses of 7.5 mg/kg were required to clear all dogs of infections from adult *E. multilocularis* (Arru, Garippa, and Manger, 1990).

Fenbendazole administered for 3 days at 50 mg/kg is effective against *T. pisiformis*.

Ruminants

For *Moniezia* infection in the United States, fenbendazole has been approved as a cattle anthelmintic at 5 mg/kg. Overseas, fenbendazole is marketed for *Moniezia* control at a higher dose of 7.5 mg/kg. Albendazole also can be used in cattle in the United States for treatment of *Moniezia* infection at the approved dose of 10

mg/kg. Oxfendazole is also approved for treating *Moniezia* infection in cattle at a dose of 4.5 mg/kg.

Albendazole is effective against *Thysanosoma* infection in sheep at 7.5 mg/kg. Fenbendazole at 10 mg/kg also appears to be effective (Bergstrom, Taylor, and Presgrove, 1988), as also is praziquantel at 40 mg/kg (Martinez, 1984).

Stilesia (exotic) infections are difficult to treat. Praziquantel at a dose of 2.5 mg/kg was extremely effective against *Moniezia* infection in sheep, but doses of 8 to 15 mg/kg were required for the treatment of *Avitellina centripunctata, Stilesia globipunctata*, and *Stilesia hepatica* (Bankov, 1975, 1976; Thomas and Gönnert, 1978).

Horses

Lyons et al (1992) found praziquantel at 1 mg/kg to be highly effective in the removal of *A. perfoliata* from horses. Slocombe (1979) found pyrantel at 13.2 to 19.8 mg base per kilogram highly effective. The daily feeding of pyrantel tartrate (2.64 mg/kg) to horses significantly reduces tapeworms in both adult horses and yearlings, with most treated animals becoming free of this parasite (Greiner and Lane, 1994; Lyons et al, 1997).

PHYLUM NEMATODA

Body form is remarkably constant among nematodes, a fact that may simplify the anatomy lesson but that somewhat aggravates the difficulties of identification and taxonomic classification. It is helpful in understanding nematode anatomy and physiology to appreciate the significance of the nematodes' unique high-turgor pressure method of maintaining sufficient corporeal rigidity to

permit rapid locomotion by sinusoidal undulation. Crofton (1966) brilliantly expounded these relationships in his book *Nematodes*, and the following discussion represents a summary of his exposition.

Nematodes have a relatively large body cavity **(pseudocoelom)** containing fluid under pressure that varies up to one half atmosphere above that of the surrounding medium (see Figures 8-78, 8-85, 8-96 to 8-98Figure 8-78Figure 8-85Figure 8-96Figure 8-98). The body cuticle contains inelastic collagen fibers so arranged that an increase in internal pressure causes an increase in length but minimal change in diameter. This anisometric cuticle and high internal pressure thus maintain a relatively constant body diameter. Nematodes do not have a circular muscle layer. Rather, all of the somatic musculature is oriented longitudinally and divided into dorsal and ventral fields by lateral expansions of the hypodermis, the **lateral chords**. A muscle cell of either field is connected by a cytoplasmic process to its respective (dorsal or ventral) median nerve. Thus dorsal and ventral flexion of the body are made possible by independent contraction of the corresponding muscle field, and longitudinal waves of contraction result in the sinusoidal pattern characteristic of nematode locomotion.

The high internal pressure also exerts its influence on the structure and organization of the internal organs. For the lumen of the intestine to be filled with food, some sort of pump is essential to overcome the tendency of the pseudocoelomic fluid pressure to collapse it, and most nematodes have a well-developed muscular esophagus for this purpose. Defecation, on the other hand, is accomplished by the contraction of a dilator ani muscle (there is no

sphincter) that opens the end of the digestive tube and allows it to empty.

The basic **excretory system** consists of paired unicellular glands with a common midventral excretory pore in the neck region (near the circumesophageal nerve ring) and ducts that, in some forms, run nearly the full length of the body in the substance of the lateral chords. In the Ascaridoidea and related groups, the excretory system is composed of a single very large cell with a very large nucleus, with the pore being located near the nerve ring or anteriorly between the subventral lips.

Male nematodes are smaller than the females of their species. Their caudal ends may terminate in a cuticular expansion supported by muscular rays. This so-called **copulatory bursa** reaches its highest development among the strongylids and is used to grasp the female (Figure 4-59). The Strongylida are therefore considered the "bursate" nematodes, whereas the Oxyurida, Ascaridida, and Spirurida comprise a group of nematodes considered to be the "abursate" nematodes. The **copulatory spicules**, used to dilate the vulva of the female, are cuticular structures that develop by sclerotization of folds of the dorsal wall of the cloaca. Spicules are often paired, but some species have only one (e.g., *Trichuris* species) or none (e.g., *Trichinella* species); they vary greatly in size and shape among species and are often used as diagnostic characters. In many species, accessory sclerotizations of the cloacal wall serve as guides for the spicules. A spicule guide in the dorsal wall is called a **gubernaculum**, and one located in the ventral wall is called a **telamon**. The primary male reproductive organs consist of a single convoluted tube with regions structurally and functionally

differentiated as testis, seminal vesicle, and vas deferens. The terminal portion of the vas deferens with its strong muscular coat is called the **ejaculatory duct**, which empties into the **cloaca**. Some male nematodes have two reproductive ducts, but none of these are animal parasites.

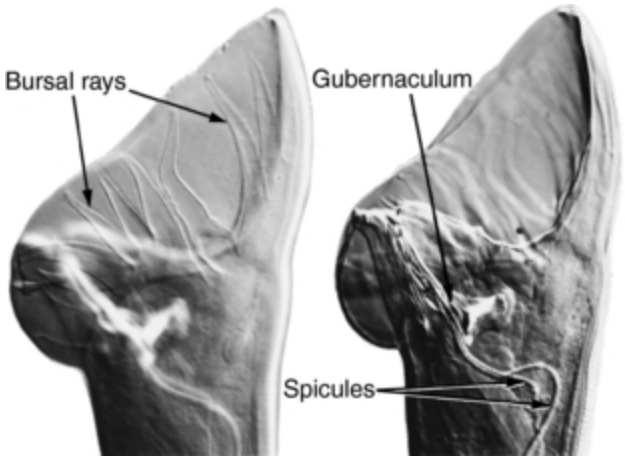

FIGURE 4-59 Surficial *(left)* and sagittal *(right)* aspects of the copulatory bursa of *Cyathostomum labiatum,* a typical member of the order Strongylida, superfamily Strongyloidea.

The female reproductive system is also tubular and usually has two branches (i.e., **didelphic**) but may be monodelphic or even multidelphic. Regions structurally and functionally differentiated as ovary, oviduct, uterus, and vagina communicate through the vulva with the exterior. The vulva is ventral in position and may be located near the oral end **(opisthodelphic)**, caudal end **(prodelphic)**, or the middle of the body **(amphidelphic)**. The location and special anatomic features of the vulva are useful in identification (Figure 4-60). In female strongylids, a muscular ovijector regulates the discharge of eggs from the uterus. The eggs contained in the terminal portion of the uterus are valuable aids in

identifying nematodes. See Chapter 7 for illustrations of nematode eggs.

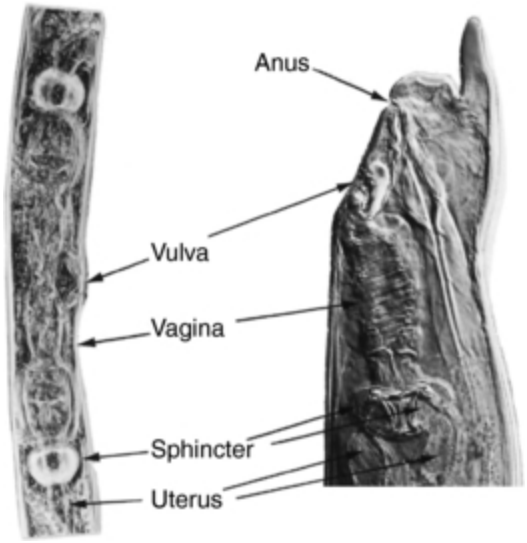

FIGURE 4-60 Ovijectors of a representative of the superfamily Trichostrongyloidea *(left)* and of the superfamily Strongyloidea *(right)* (×64).

All rational control efforts are based on an understanding of the life history and behavior of both host and parasite. A general outline of the ontogenetic development of a nematode is shown in Figure 4-61. What appears to be a rich and confusing diversity of life histories among various orders of nematodes can all be related and rationalized according to this basic pattern. Embryonic development is, of course, a continuous process, with change accompanying every cell division. The “one-cell,” “morula,” and “vermiform embryo” stages are arbitrarily chosen from this continuum because they are the stages of egg development most frequently encountered in diagnostic procedures. The difference between a vermiform embryo and a first-stage larva is that the former contains only cell clusters as organ primordia, whereas the latter displays clearly recognizable organs such as esophagus, intestine, and excretory glands. A

microfilaria is an example of a vermiform embryo, developing into a larva only after it has been ingested by a mosquito. Each larval stage is separated from the next by a molt marked by metamorphosis of the larva and ecdysis or a casting off of the cuticle from the preceding stage.

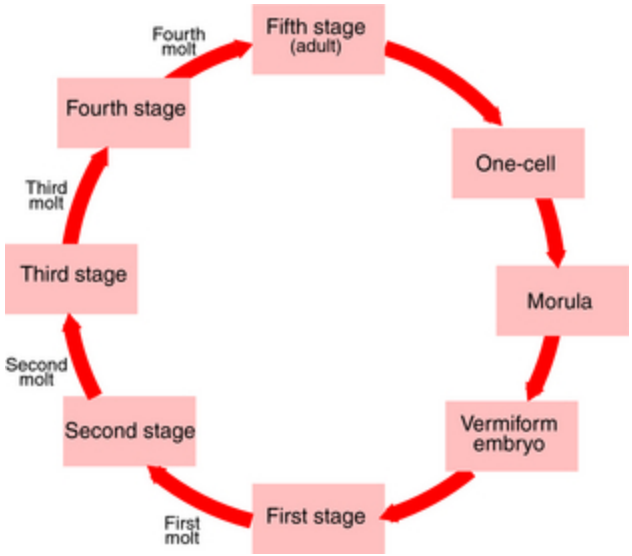

FIGURE 4-61 Stages and transitions in the ontogenetic development of a nematode.

The nematode life history also can be generalized from the standpoint of the important events related to diagnosis, treatment, and control. Figure 4-62 represents these events as four stages (adult, preinfective, infective, preadult) separated by four transitions (contamination, development, infection, and maturation). In the mastering of the details of any particular nematode life history, the process of integrating these two schemes is a profitable intellectual exercise. The prepatent periods of the more important veterinary species of nematodes are presented in Table 4-3.

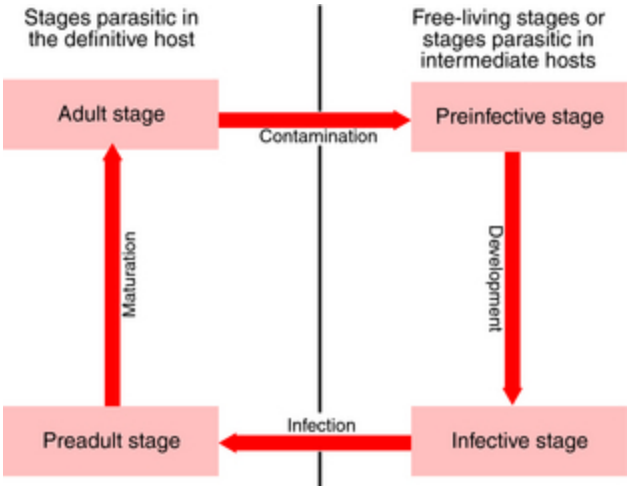

FIGURE 4-62 A generalization of nematode life histories, emphasizing the stages and transitions of greatest importance to diagnosis, treatment, and control. As used here, the term *preadult stage* refers to all stages of parasitic larval development from entry of the parasite into the host to the attainment of sexual maturity. Maturation represents the length of time required for this transition. Similarly, preinfective stage represents all developmental stages leading up to the infective stage, and development represents the time required for that transition.

TABLE 4-3 Some Nematode Prepatent Periods*

Parasite	Prepatent period	Comments
SECERNENTEA		
STRONGYLIDA		
Trichostrongyloidea		
Trichostrongylus	¾ month	Arrested larvae
Ostertagia	¾ month	Arrested larvae
Haemonchus placet	1 month	
Haemonchus contortus	¾ month	
Cooperia	½ month	
Nematodirus	¾ month	

Hyostrongylus	¾-1 month	
Dictyocaulus	1-1¼ month	
Strongyloidea		
Cyathostominae	2½-4 months	Arrested larvae
Strongylus vulgaris	6-7 months	
Strongylus equinus	9 months	
Strongylus edentatus	11 months	
Triodontophorus	3-6 months	
Chabertia	l¼ months	Arrested larvae
Oesophagostomum	1½ months	Arrested larvae
Stephanurus dentatus	9-16 months	
Ancylostomatoidea		
Ancylostoma caninum	½ month	Arrested larve/transmammary infection
Ancylostoma tubaeforme	½ month	Arrested larvae
Uncinaria stenocephala	½ month	Arrested larvae
Unicinaria levcas	½ month	Arrested larve/transmammary infection
Bunostomum	1½-2¼ months	
Metastrongyloidea		
Crenosoma	¾ month	
Filaroides hirthi	1¼ months	Potential autoinfection
Filaroides osleri	6 months	Potential autoinfection
Aelurostrongylus abstrusus	l¼-1½ months	

Protostrongylus	l¼-1½ months	
Metastrongylus	¾-1 month	
Muellerius	l½ months	
Parelaphostrongylus tenuis	2¾-3 months	Not patent in most domestic animal hosts
RHAMBDITIDA		
Strongyloides stercoralis	½ month	Transmammary infection
Strongyloides papillosus	¼-½ month	Transmammray infection
OXYURIDA		
Oxyuris equi	4-5 months	
ASCARIDIDA		
Ascaris suum	2 months	
Parascaris equorum	2½ months	
Toxocara vitulorum	¾ month in calves	Transmammary infection
Toxascaris leonina	2 months	Paratenic hosts
Toxocara canis	1-2 months	Transplacental infection, paratenic hosts
Toxocara cati	2 months	Paratenic hosts
SPIRURIDA		
Gongylonema	2 months	Intermediate host, dung beetle or cockroach
Draschia	2 months	Intermediate host, *Musca*
Habronema	2 months (?)	Intermediate host, *Musca/Stomoxys*
Thelazia	¾-1 month	Intermediate host, *Musca* or fruit flies

Setaria	8-10 months	Vector: mosquitoes
Onchocerca	10 + months	Vector: blackflies or ceratopogonids
Elaeophora	4½ months	Vector: tabanids
Dirofilaria	6½-7 months	Vector: mosquitoes
Dipetalonema reconditum	2-3 months	Vector: fleas
ADENOPHOREA		
Trichinelloidea		
Trichuris vulpis	2½-3 months	
Trichinella spiralis	¼-½ month	Find adults in diarrheic feces
Dioctophymatoidea		
Dioctophyme renale	4-5 months	Eggs in urine

* All periods are presented as months postinfection in a naive animal.

Order Strongylida

The order Strongylida is composed of four superfamilies: (1) Strongyloidea, the large bowel strongyles of horses and the nodular worms of ruminants, swine, and primates; (2) Trichostrongyloidea, the abomasal and small intestinal hairworms of ruminants; (3) Ancylostomatoidea, the hookworms of diverse mammals; and (4) Metastrongyloidea, the lungworms. One of the most important genera of nematodes *(Dictyocaulus)* that live in the lungs, hence *lungworms*, falls within the Trichostrongyloidea rather than the Metastrongyloidea superfamily, but there are always exceptions to be resolved.

Morphology

The strongylid mouth, or **stoma**, presents important diagnostic characteristics that are the same for both male and female and usually sufficient for generic identification. Strongyloids have well-developed **buccal capsules** often armed, at the base, with teeth (Figure 4-63). Ancylostomatoids also have well-developed buccal capsules, but these are permanently flexed dorsally and armed on their ventral (leading) edge with formidable pointed **teeth** or rounded **cutting plates** (Figure 4-64). In the Trichostrongyloidea, the buccal capsule usually is reduced in size but may be equipped with a tooth or lancet in bloodsucking species (Figure 4-65). In the typical metastrongyloid, the buccal capsule is absent.

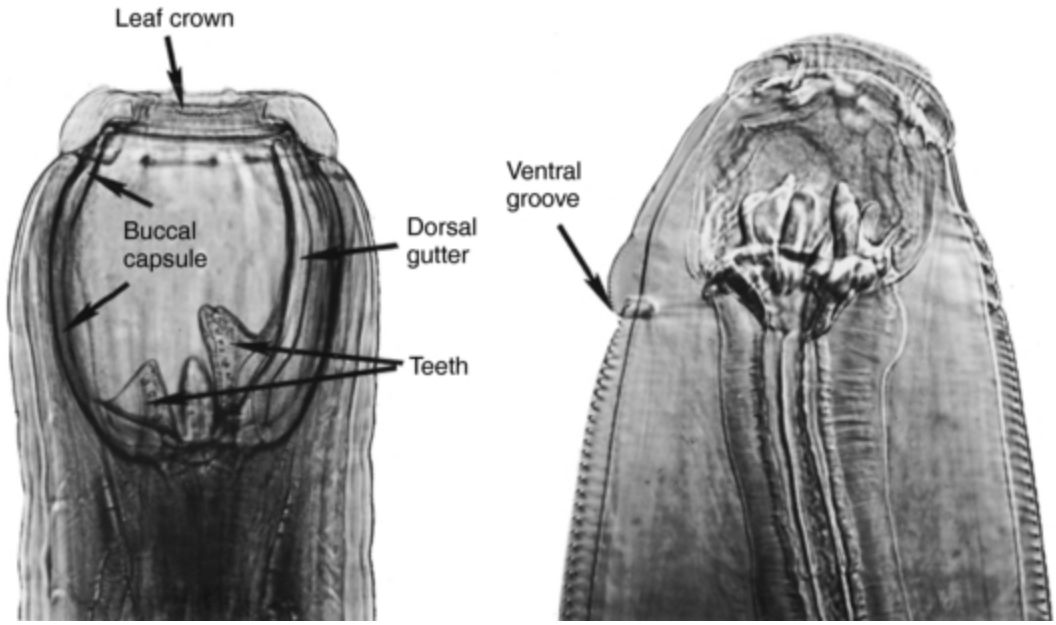

FIGURE 4-63 Superfamily Strongyloidea. Left, *Strongylus equinus*. Right, *Ternidens deminutus*.

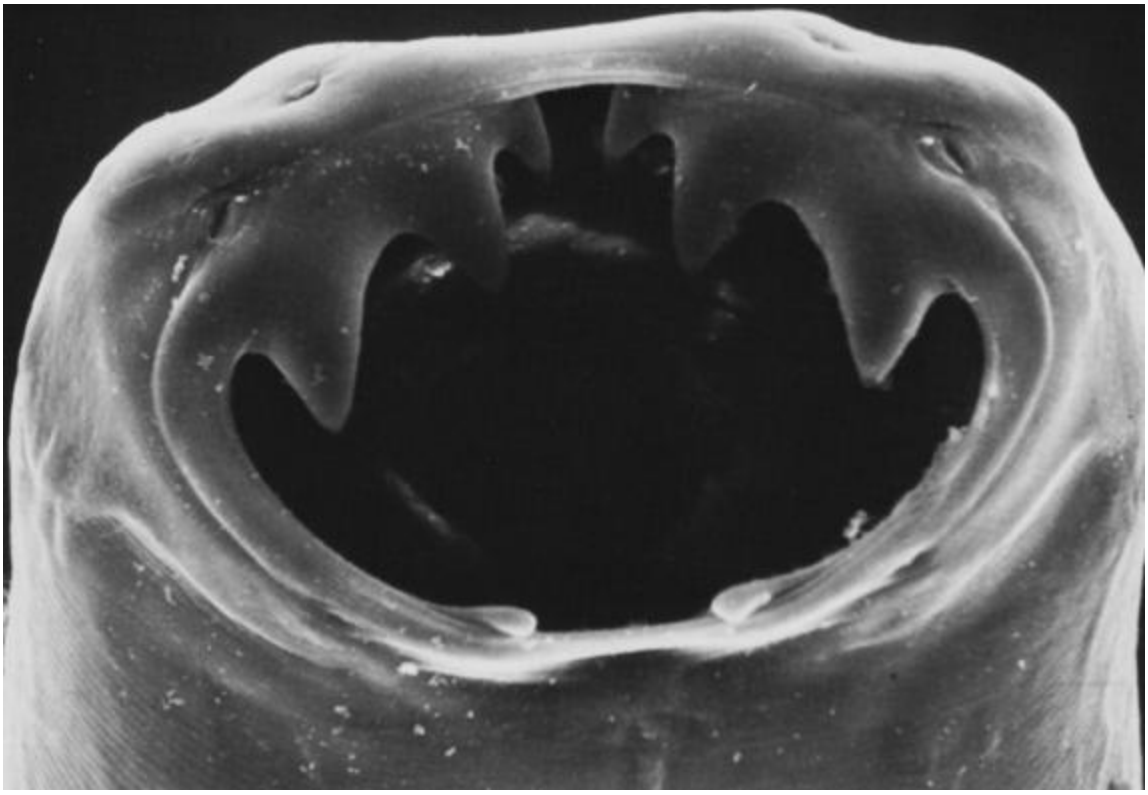

FIGURE 4-64 Superfamily Ancylostomatoidea. Dorsal aspect of the buccal capsule of *Ancylostoma caninum*, the common hookworm of the dog. The three pairs of pointed teeth are at the ventral margin of the stoma.

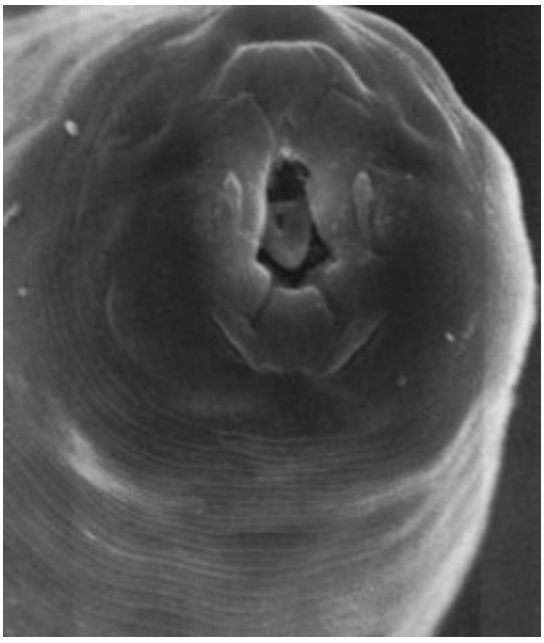

FIGURE 4-65 Superfamily Trichostrongyloidea. En face view of the stoma of *Haemonchus contortus,* the stomach worm of sheep. This voracious bloodsucking nematode uses its lancet to puncture the mucous membrane of the abomasum.

Courtesy Dr. Marguerite Frongillo, Cornell University, Ithaca, New York.

Male nematodes of the order Strongylida have a caudal **copulatory bursa** that consists of dorsal, lateral, and ventral expansions of the body cuticle **(lobes)** supported by muscular processes called **rays** (Figure 4-66). The dorsal lobe contains one ray that is usually median in position and variously branched. The lateral lobes each contain an externodorsal ray adjacent to the dorsal lobe and three rays arising in a group: the posterolateral, the mediolateral, and the anterolateral. The ventral lobes each contain two rays. The disposition and configuration of these rays are used in classification and identification of strongylids. In typical members of the superfamilies Strongyloidea and Ancylostomatoidea the dorsal and lateral lobes are about equally developed (Figure 4-67; see also Figure 4-59); in Trichostrongyloidea the lateral lobes predominate (see Figure 4-66), and in Metastrongyloidea the bursa tends to be reduced in size (Figure 4-68). In some metastrongyloids (e.g., *Filaroides* species), the bursa is completely absent (Figure 4-69).

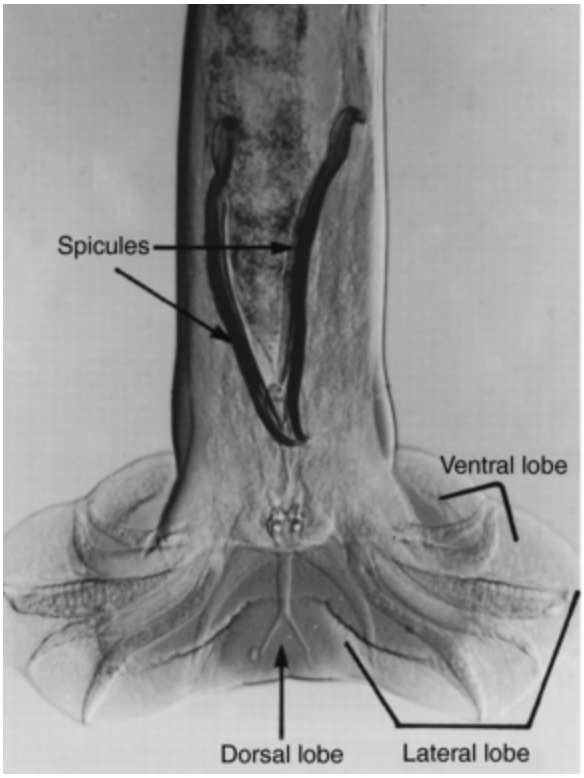

FIGURE 4-66 Superfamily Trichostrongyloidea. Bursa and spicules of *Teladorsagia circumcincta,* an abomasal parasite of sheep.

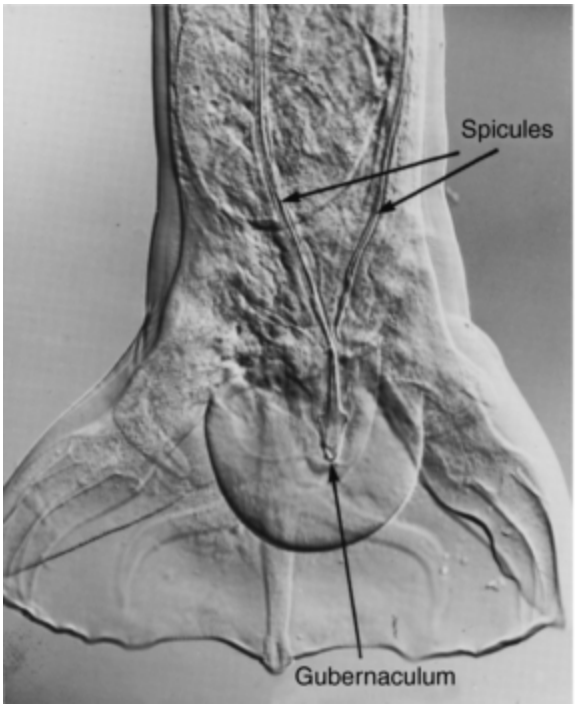

FIGURE 4-67 Superfamily Ancylostomatoidea. Bursa and spicules of *Placoconus lotoris,* a hookworm of the raccoon, *Procyon lotor*.

FIGURE 4-68 Superfamily Metastrongyloidea. Bursa and spicules of *Protostrongylus rufescens*.

FIGURE 4-69 Superfamily Metastrongyloidea. Caudal ends of male *Filaroides hirthi (left)* and *Filaroides milksi (right),* showing reduction of bursal structures to mere papillae. The spicules of *F. hirthi* are shorter, are broader in relation to their length, and have broader knobs for the attachment of the retractor muscles than the spicules of *F. milksi*.

The **spicules** of males of the superfamilies Strongyloidea and Ancylostomatoidea tend to be long, thin, and flexible (see Figures 4-59 and 4-67), whereas those of the Trichostrongyloidea tend to be shorter and substantially stouter (Figure 4-70; see also Figure 4-66). In the Metastrongyloidea, spicules vary so widely in size and shape that generalization is unprofitable.

FIGURE 4-70 Superfamily Trichostrongyloidea. Bursa and spicules of *Trichostrongylus axei,* a parasite of the abomasum of ruminants and of the stomach of horses.

The strongylid uterus has two horns and is equipped with a well-developed muscular ovijector (see Figure 4-60). In typical trichostrongyloids and ancylostomatoids, the vulva is located near the middle of the body, and the two horns of the uterus extend in opposite directions **(amphidelphic)**. In strongyloids and metastrongyloids, the vulva is typically located close to the anus, and both horns of the uterus extend anteriorly **(prodelphic)**.

Life History

The life histories of superfamilies Strongyloidea, Trichostrongyloidea, and Ancylostomatoidea are typically direct, with free-living microbivorous first and second larval stages and an infective third larval stage (Figure 4-71). Females of all three superfamilies lay typical **strongyle eggs** (i.e., eggs with smooth-surfaced, ellipsoidal shells that contain an embryo in the morula stage of development when laid and passed out with the feces). Such eggs are produced by all members of the order Strongylida, except certain genera in the superfamily Metastrongyloidea, and are therefore properly termed *strongylid eggs*. However, "strongyle" conveys the same meaning to most and is commonly used. Often in ruminants, where eggs of the trichostrongyloids predominate, such eggs are called "trichostrongyle eggs," even though it is clear that some of the eggs might be those of the rarer strongyloids present in these hosts. Similarly, in dogs and cats such eggs are often called "hookworm eggs" because these are the predominant strongylid worms present in these hosts.

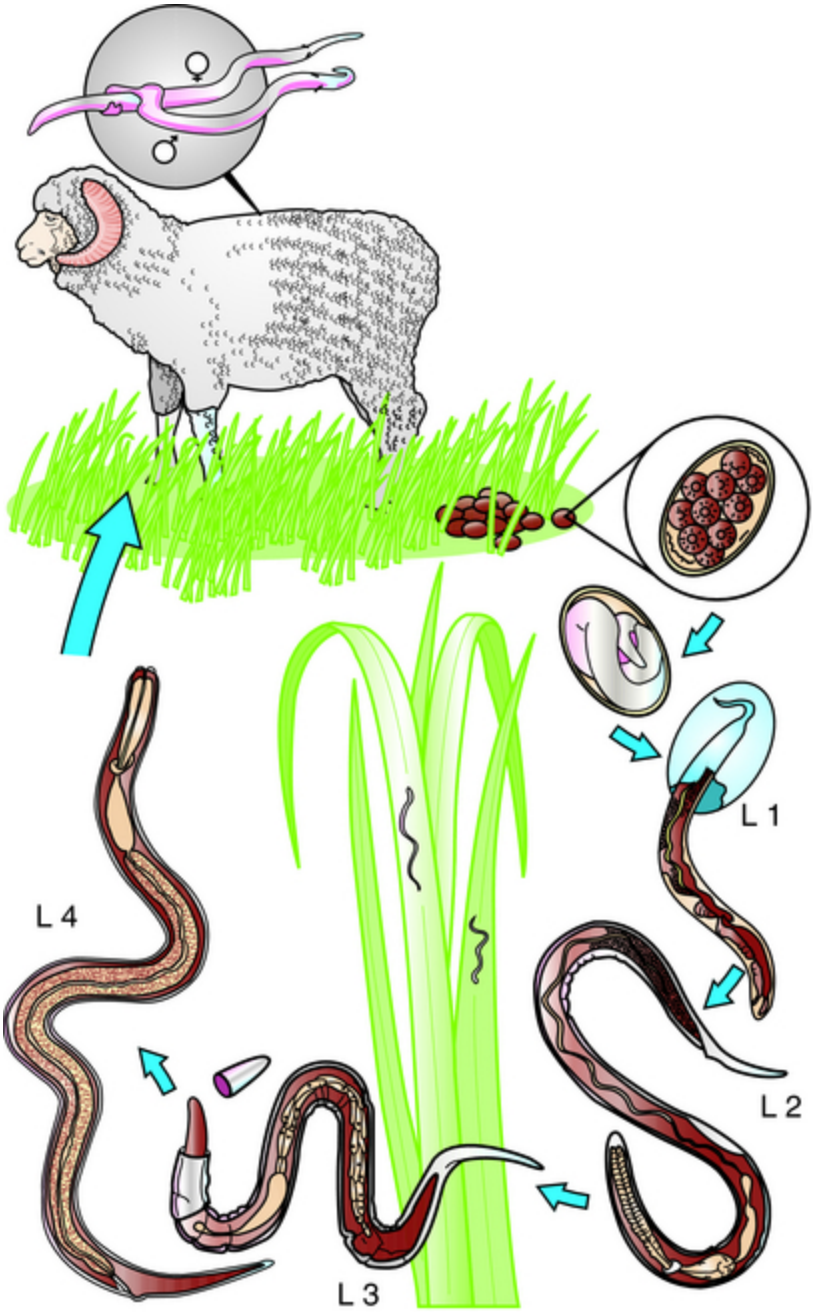

FIGURE 4-71 Life history of a typical strongylid nematode, *Haemonchus contortus*. Eggs are shed in the feces in the morula stage of development. First-stage larvae develop and hatch in a day or two to feed on microorganisms in the feces. After a molt, the resulting second-stage larva also feeds on microorganisms. The second molt is started but not completed in the external environment, so the infective third-stage larva remains encased in the cuticle of the second stage until it is ingested by a sheep. The sheath is cast off in the abomasum of the sheep, and the now parasitic third-stage larva undergoes a

molt to the fourth stage. The fourth stage sooner or later molts to the fifth or adult stage, depending on whether it enters a period of arrested development.

Typically, in the developing eggs the morula develops into a first-stage larva that hatches from the egg within a day or two. After feeding, this larva undergoes its first molt to become a second-stage larva. Both first- and second-stage larvae remain in the feces, where they feed on bacteria. In the second molt the cuticle of the second stage is temporarily retained as a protective sheath about the infective third-stage larva and will not be shed until this larva enters a suitable host. In about a week these sheathed third-stage larvae begin to migrate out of the fecal mass and into the water film covering the surrounding soil particles and vegetation. Infection occurs when these sheathed larvae are ingested by grazing animals. Variations on this basic life history pattern are discussed later in connection with the several genera.

Various representatives of the superfamily Metastrongyloidea lay eggs in all stages of development from a single cell (e.g., *Aelurostrongylus* species) to an egg containing a first-stage larva (e.g., *Filaroides* species). However, sufficient development occurs within the host that the form found in the feces is either a first-stage larva or an egg containing a first-stage larva. Metastrongyloids typically require a molluskan or annelid intermediate host for development from the first stage to the infective third stage, and infection of the definitive host occurs through ingestion of snails, slugs, or earthworms containing infective third-stage larvae. *Filaroides osleri* and *Filaroides hirthi*, both directly infective to the dog in the first larval stage, are important exceptions to this rule.

Superfamily Trichostrongyloidea

Trichostrongyloid nematodes are especially common and pathogenic in grazing ruminants, but swine, horses, cats, and birds also host important species. The abomasum and small intestine are the usual locations in ruminants, but one aberrant genus, *Dictyocaulus*, reaches maturity in the air passages. It is sufficient, for practical purposes of effective treatment and control, to identify trichostrongyloids at the generic level of the older classification schemes (Yorke and Maplestone, 1926).

Trichostrongylus

Identification

These are very small, hairlike worms less than 7 mm long, without cephalic inflations, and virtually without a buccal capsule; spicules are short, twisted, and usually pointed (Figure 4-72; see also Figure 4-70). *Trichostrongylus axei* parasitizes the simple stomach or abomasum of a wide range of hosts including ruminants, horses, and leporids. Other species are parasites of the small intestine of ruminants and display a higher order of host specificity. Even heavy infections with *Trichostrongylus* will be overlooked on necropsy examination unless care is taken to thoroughly examine washings or scrapings of the stomach and the first 6 meters of the small intestine, preferably with a hand lens or stereoscopic microscope. *Trichostrongylus* species are most likely to be confused with *Strongyloides* species or with the smaller species of *Cooperia*.

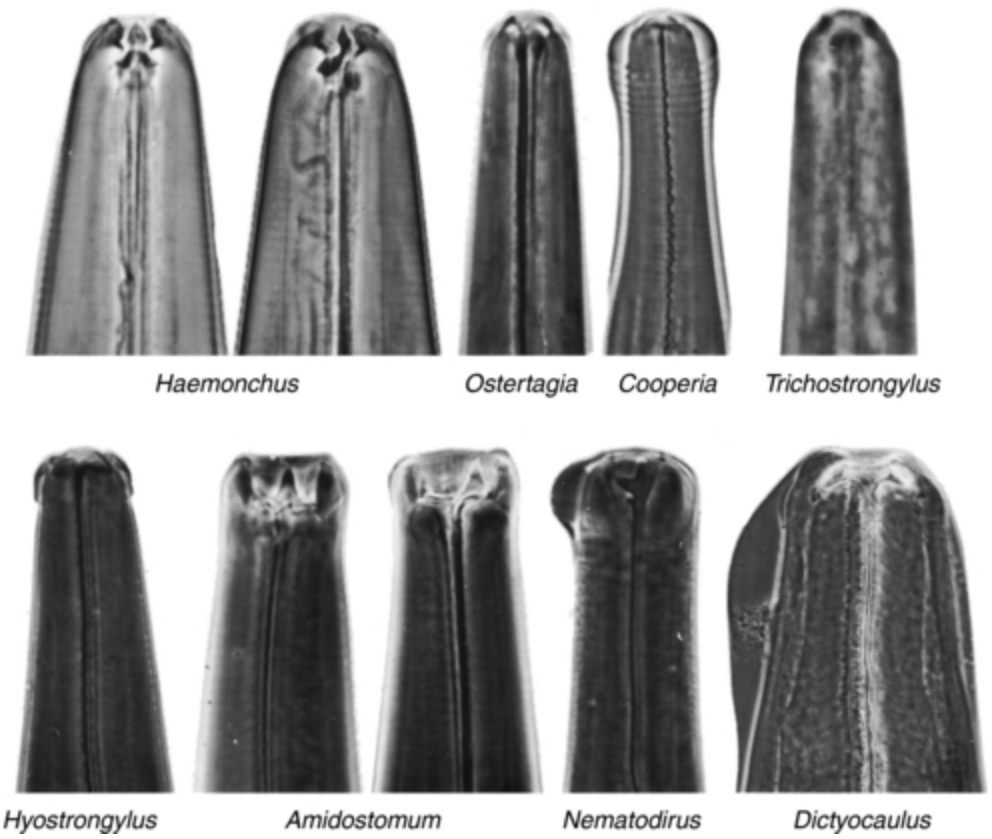

FIGURE 4-72 Stomas of eight genera of the superfamily Trichostrongyloidea. *Amidostomum* is a parasite of geese and ducks but not of mammals; its large, toothed buccal capsule is not typical of trichostrongyloids.

From Whitlock JH: Diagnosis of veterinary parasitisms, Philadelphia, 1960, Lea & Febiger.

Life history

The infective third-stage larvae of *Trichostrongylus* species survive the winter on pasture, and ruminants are exposed to infection when they are turned out to pasture in spring. As the weather becomes warmer, the infective larvae die off, and by summer the overwintering generation is essentially gone. However, egg production from new infections rapidly recontaminates the pasture and continues well into fall to produce the next season's overwintering population of *Trichostrongylus* organisms.

Importance

Although *Trichostrongylus* infections are often asymptomatic, when present in large numbers (10,000 to 100,000 or more), these parasites are capable of producing protracted and debilitating watery diarrhea, especially in stressed or malnourished sheep, cattle, and goats. At first the feces remain semisolid but soon become watery and dark green in color ("black scours"), staining the fleece of the hindquarters. Some of the feces accumulate in pea- to egg-sized masses ("dingleberries," "dags") that dangle from the fleece and grow by accretion as fluid feces continue to pour over and dry on their surfaces. The resulting foul condition tends to attract blowflies such as *Lucilia cuprina* and to result in myiasis. Egg counts rarely exceed 5000 eggs per gram because *Trichostrongylus* organisms are very small worms that lay few eggs and because the feces are greatly diluted with water. Necropsy examination reveals a wasted carcass without obvious lesions even in the affected small intestine; the parasites themselves are easy to overlook because they are so small. Protracted diarrhea is sufficient to account for the weakness and emaciation typically observed in trichostrongylosis, but it is important to remember that less than massive burdens of *Trichostrongylus* organisms do not usually cause serious illness in well-nourished, unstressed ruminants. Therefore it may be important to consider the quality of the environment and animal husbandry in identifying the ultimate causes of particular outbreaks.

Ostertagia and *Teladorsagia*

Identification

Ostertagia and *Teladorsagia* are indistinguishable by the criteria outlined as follows; however, *Teladorsagia* are parasites of sheep and goats (e.g., *Teladorsagia circumcincta*) whereas *Ostertagia* are parasites of cattle (e.g., *Ostertagia ostertagi*). Usually less than 14 mm long and brownish in color, with a short, broad buccal cavity (see Figure 4-72) and short, two- or three-pronged spicules (Figure 4-73; see also Figure 4-66), parasites of these genera are found in the abomasum of ruminants. The tip of the mature female's tail is usually annulated (Figure 4-74); the eggs in the amphidelphic ovijector are typical strongylid eggs; and the vulva is guarded by a cuticular expansion called a *vulvar flap*.

FIGURE 4-73 Spicules of *Ostertagia ostertagi*.

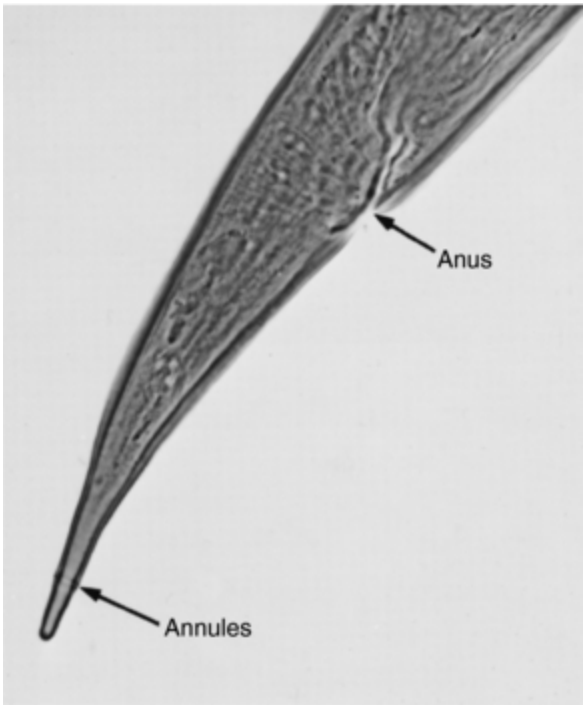

FIGURE 4-74 Tail of female *Ostertagia* organism.

Life history

Ostertagia- and *Teladorsagia*-infective third-stage larvae resemble those of *Trichostrongylus* in overwintering on northern pastures and in thus infecting ruminants during the early grazing season. However, arrested development of parasitic larvae is also very well developed in *Ostertagia* species, and this is of both epidemiologic and pathologic importance. **"Type I"** or **"summer" ostertagiosis** usually occurs in pastured young cattle, the worms maturing without first passing through a developmental arrest (i.e., hypobiotic or latent phase). By contrast, **"type II"** or **"winter" ostertagiosis** typically occurs in late winter when larvae that have remained in arrested development since fall once again become metabolically active and proceed to develop into adults. Such

behavior is part and parcel of the normal mechanism used by *Ostertagia* species and certain other trichostrongyloids for overwintering. However, when mistimed or overdone to such an extent as to overcome the compensatory mechanisms of the host, it leads to winter ostertagiosis.

Importance

O. ostertagi causes chronic abomasitis in young cattle, a disease marked by profuse watery diarrhea, anemia, and hypoproteinemia manifested clinically as submaxillary edema. The animal is typically hidebound and emaciated. The appetite remains intact, which seems paradoxic in view of the advanced pathologic changes taking place in the abomasum. The hydrogen ion concentration of the gastric juice approaches neutrality. Necropsy examination reveals a wasted carcass with depletion of fat deposits typical of extreme malnutrition. The rumen, reticulum, and omasum may be full of good feed, but the alimentary tract from the cardia onward is virtually empty owing to malfunction of the abomasums—the animal has starved to death in the midst of plenty. The "Morocco leather" appearance of the abomasal mucosa is pathognomonic; the whole mucosa is studded with grayish white, pinhead- to pea-sized nodules with a worm protruding from a small opening at the summit of each (see Figures 7-60, 8-76, and 8-77Figure 7-60Figure 8-76Figure 8-77). *O. ostertagi* is the most important helminth parasite of cattle in the United States. Young cattle infected with large numbers of this parasite waste away and die in a matter of weeks. Those infected with sublethal parasite burdens fail to achieve their full potential for growth and development or require substantially more time to do it. Either is economically

disadvantageous. *Teladorsagia* specie of sheep and goats may also cause serious endemic disease in certain localities.

Haemonchus

Identification

Up to 30 mm in length, these parasites of the abomasum of ruminants have a buccal cavity armed with a **lancet** (see Figure 4-65). The male has an asymmetric dorsal ray in its bursa (Figure 4-75) and short, wedge-shaped spicules. The white, egg-filled uterus of the female spirals around the blood-filled gut, giving rise to the so-called barber pole appearance. The vulva is located about a quarter body length from the tail and may or may not be guarded by variously shaped cuticular inflations (vulvar flaps). The prevalence of various vulvar flap configurations varies among species and subspecies of *Haemonchus* (Figure 4-76).

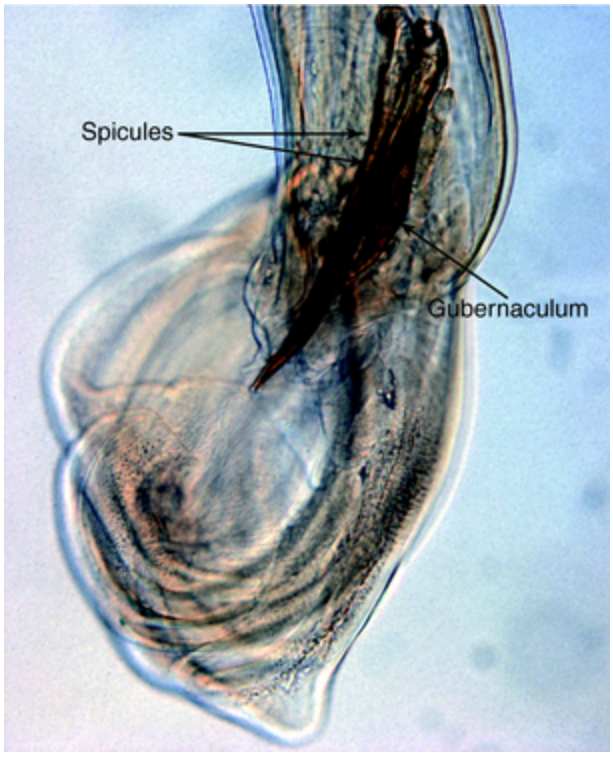

FIGURE 4-75 Spicules of *Haemonchus contortus*.

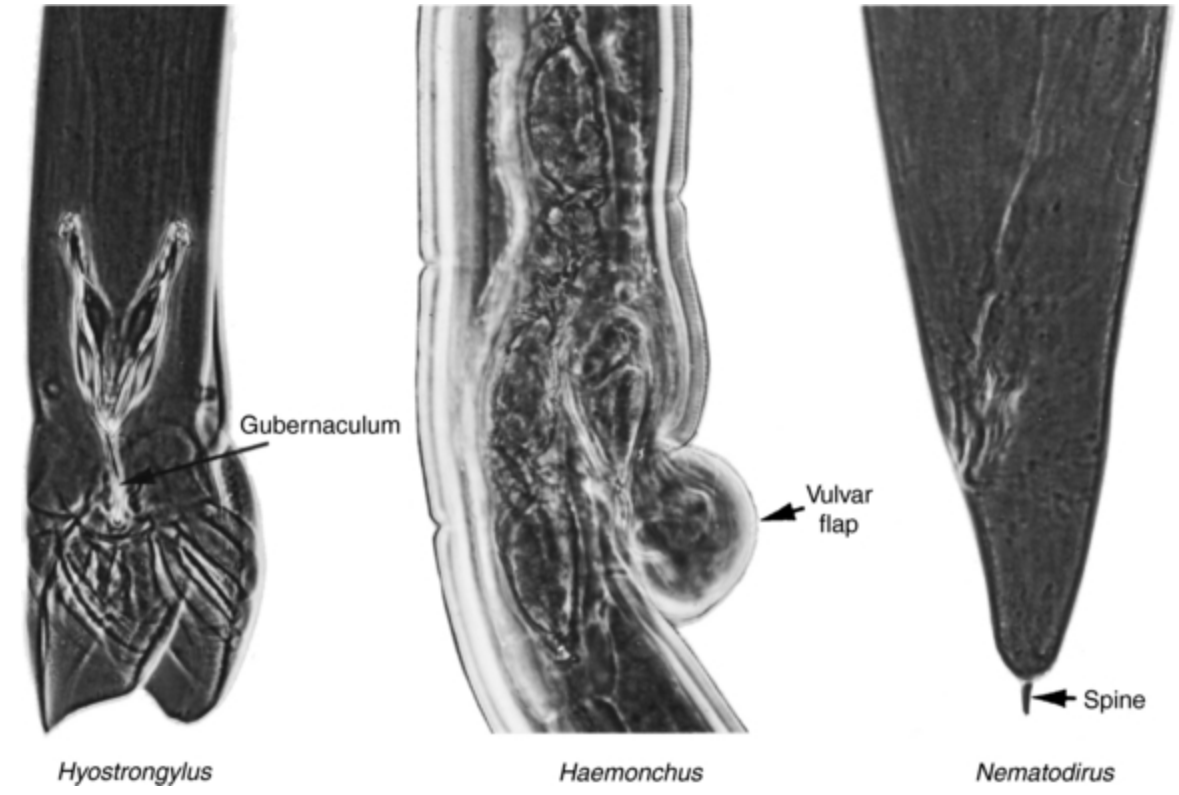

FIGURE 4-76 Three genera of the superfamily Trichostrongyloidea.

From Whitlock JH: Diagnosis of veterinary parasitisms, Philadelphia, 1960, Lea & Febiger.

Importance

The disease haemonchosis is characterized by anemia. At peak infection, naturally acquired populations of *Haemonchus contortus* may remove one fifth of the circulating erythrocyte volume per day from lambs and may remove an average of one tenth of the circulating erythrocyte volume per day over the course of nonfatal infections lasting 2 months. These are round numbers drawn from observations of a flock of 100 to 175 lambs with erythrocyte loss estimated by the whole-body radioiron retention technique (Georgi, 1964; Georgi and Whitlock, 1965). The pathogenic effects of *H. contortus* result from the inability of the host to compensate for blood loss. If the amount of loss is small and restitution by the host complete, no measurable illness results. “It is doubtful, indeed, whether in such circumstances (i.e., satisfactory nutrition) infection with up to 500 worms has any effect on growth or wool production” (Clunies Ross and Gordon, 1936). However, if the rate of blood loss exceeds the host’s hematopoietic capacity, because either the challenge is overwhelming or the response is handicapped by poor nutrition, defective phenotype, or stress, a progressive anemia leads rapidly to death. The cardinal sign of haemonchosis is pallor of the skin and mucous membranes. A hematocrit reading of less than 15% is always accompanied by extreme weakness and shortness of breath and warrants a grave prognosis. A simple means of measuring the amount of anemia in sheep and goats due to haemonchosis along with an indication of which animals require treatment is the use of a

FAMACHA chart, which shows images of eyes of animals with different hematocrit levels along with an indication of which to treat (Kaplan et al, 2004). Loss of plasma protein results in anasarca frequently manifested externally as submaxillary edema (bottle jaw). The appetite typically remains good, and in acute outbreaks affected animals may not lose appreciable weight. Feces are well formed, diarrhea occurring only in infections complicated by the presence of such species as *Trichostrongylus* and *Cooperia*. Lambs are often the most seriously affected members of a flock, but older sheep under stress also may have fatal anemia. Individual older ewes may succumb in late spring to the overwhelming challenge imposed by hordes of larvae simultaneously emerging from developmental arrest. High egg counts, 10,000 eggs per gram or higher, are typical of haemonchosis.

Mecistocirrus

Identification

Mecistocirrus species are parasites of the abomasum of ruminants and the stomach of pigs in Central America, India, and the Far East. They are similar in morphology to *Haemonchus* species, except that the vulva is close to the anus and the spicules are long and thin (Figure 4-77).

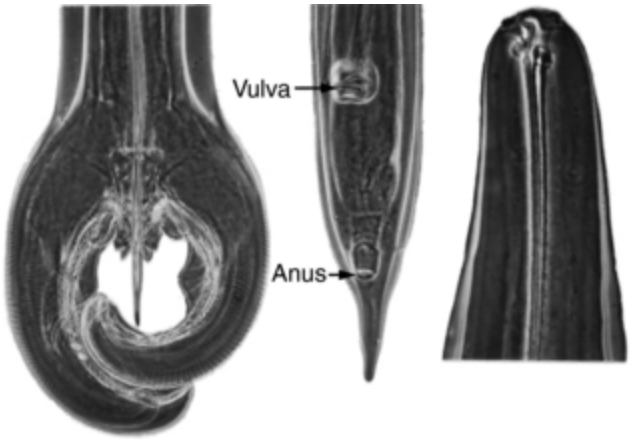

FIGURE 4-77 *Mecistocirrus* spp.

From Whitlock JH: Diagnosis of veterinary parasitisms, Philadelphia, 1960, Lea & Febiger.

Cooperia

Identification

Parasites of the small intestine of ruminants, species of *Cooperia* are less than 9 mm long. The cuticle of the stomal region is transversely striated and slightly inflated, the buccal cavity is very small, the spicules are short and blunted at their tips, and the dorsal ray of the bursa is lyre-shaped (Figures 4-78 and 4-79; see also Figure 4-72). *Cooperia* species are most likely to be confused with *Trichostrongylus* or *Strongyloides* species because of similarity in size and location in the host.

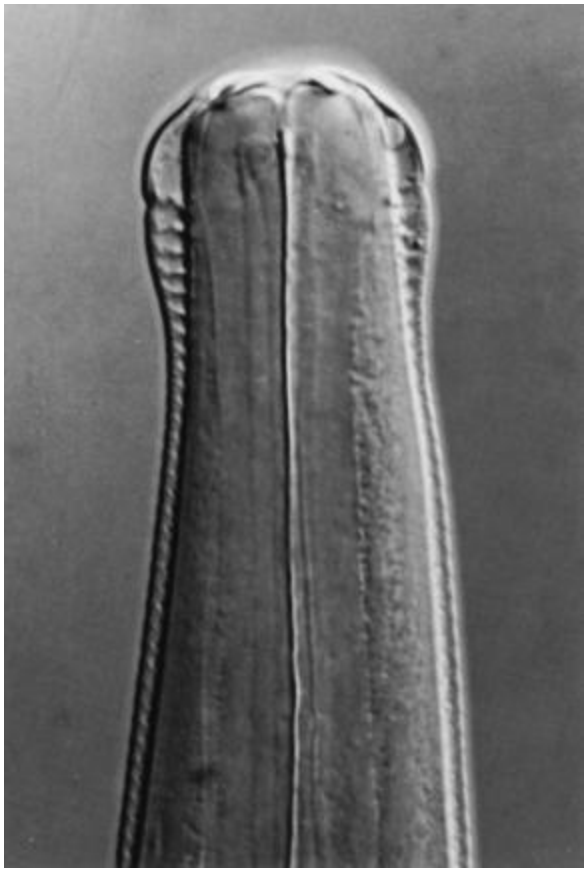

FIGURE 4-78 Stomal end of *Cooperia*.

FIGURE 4-79 Spicules of *Cooperia*.

Importance

The relationship of *Cooperia* species to disease production is similar to that presented for *Trichostrongylus* species earlier.

Nematodirus

Identification

Species of *Nematodirus* vary considerably in size; the largest grows to a length of 25 mm. The cuticle of the stomal region is transversely striated and may be inflated; the stoma is armed with a dorsal, triangular tooth (see Figure 4-72). The neck is usually coiled, the spicules are long and thin, the uterus contains very large eggs, and the female has a spine at the tip of her tail (see Figure 4-76).

Life history

The life history and epidemiology of *Nematodirus* species infecting domestic ruminants are distinctly different from those of most other trichostrongyloids. The larva develops to the infective third stage within the eggshell, and hatching depends on extrinsic stimuli, at least in certain species. For example, the infective larva of *Nematodirus battus* must usually be subjected to freezing followed by warmer weather before it will hatch. This property tends to concentrate hatching of infective larvae in the spring, to limit reproduction to one generation per year, and to generate a single wave of infection and disease in late spring. As a result, the severity of infection is typically directly proportional to the previous year's pasture contamination, and timing of the outbreak depends on weather favorable for mass hatching of eggs. However, a second wave of larvae on pasture and consequent infection of sheep has been observed to occur in the fall (Gibson and Everett, 1981; Rodger, 1983; McKellar et al, 1983; Hollands, 1984; Hosie, 1984). Development and hatching of the infective larvae of *Nematodirus spathiger* and *Nematodirus fillicollis* tend not to be seasonally constrained in this manner, and these species are common parasites of sheep.

Importance

Although *Nematodirus* species infections usually are not associated with clinical disease, *N. battus* causes a specific strongylosis characterized by very restricted seasonal incidence and by extremely severe and debilitating diarrhea. Most of the lamb flock display a sudden loss of thrift quickly followed by profuse diarrhea. Deaths begin from 2 days to 2 weeks after onset of clinical signs and continue for several weeks, after which survivors gradually recover;

mortality may reach 30%. Egg counts average 600 and rarely exceed 3000 eggs per gram of feces. Necropsy reveals a dehydrated carcass, enlarged pale edematous mesenteric lymph glands, and mild catarrhal enteritis, but very little else in the way of lesions. A count of 10,000 *N. battus* worms is considered significant (Thomas and Stevens, 1956). Originally described from Great Britain (Crofton and Thomas, 1951, 1954), *N. battus* appeared in Oregon in 1985 (Hoberg, Zimmerman, and Lichtenfels, 1986) and has since been identified in sheep fecal samples from Washington, New York, Vermont, and Maryland (Zimmerman et al, 1986).

Hyostrongylus

Identification

A parasite of the stomach of swine, *Hyostrongylus rubidus* is less than 9 mm long and has a small, annular buccal collar, short spicules with two points, and a long narrow gubernaculum (see Figures 4-72 and 4-76). *Hyostrongylus kigeziensis* is a parasite of the mountain gorilla (Durette-Desset et al, 1992).

Life history and pathogenesis

H. rubidus is a typical trichostrongyloid nematode somewhat resembling *Ostertagia* species in its habits. The adult worms parasitize the stomach and produce typical strongylid eggs that closely resemble those of the *Oesophagostomum* species that infect swine. Ensheathed third-stage larvae develop within a week under optimum conditions; these larvae are infective when swallowed by swine. Like *Ostertagia* species, *H. rubidus* invades the gastric glands, where the third and fourth molts take place. *H. rubidus* evokes a

catarrhal, sometimes diphtheritic, gastritis with ulceration and secretion of a tenacious mucus. Clinical signs include anemia and inappetence with occasional melena as evidence of gastric hemorrhage. Hyostrongylosis is mainly a disease of adult pigs at pasture, but transmission can be markedly reduced during dry summers (Roepstorff and Murrell, 1997). It has been shown, however, that transmission can occur under confinement conditions (Bladt-Knudsen et al, 1994).

Anthelmintic medications

Fenbendazole, ivermectin, and doramectin are approved for treatment of or have been shown to successfully treat infections of pigs with *H. rubidus*.

Ollulanus

Identification

A parasite of the stomach of the pig, cat, and other felids including the cougar and tiger, *Ollulanus tricuspis* is minute (less than 1 mm long). The anterior end is rolled up, the vulva is near the anus, the female tail terminates in three or more sharp points, and the spicules are short, equal, and bifurcated (Figure 4-80). These worms can be diagnosed using endoscopy specimens (Cecchi et al, 2006).

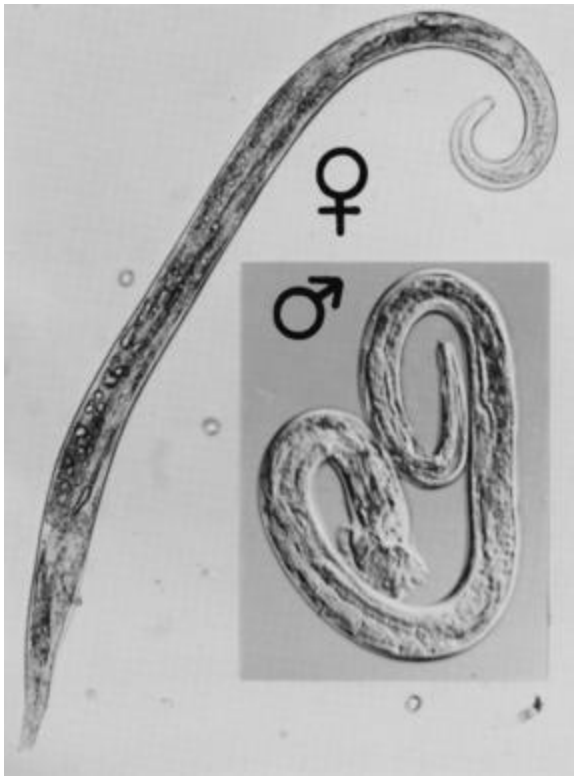

FIGURE 4-80 *Ollulanus tricuspis* from a leopard. Diagnosis is usually based on finding adult specimens of this viviparous species in vomitus.

Life history

O. tricuspis is **ovoviviparous** (the eggs develop and hatch within the uterus of the female), and the larvae develop to maturity in the stomach of the host. It is a rare example of a nematode capable of completing its life history within a single host. Ingestion of vomitus from an infected host is the most likely means of transmission of *O. tricuspis*.

Importance

In cats these worms are capable of causing chronic gastritis that can prove fatal (Hänichen and Hasslinger, 1977). Chronic gastritis also has been observed in a tiger (Breuer et al, 1993) and in captive

cheetahs (Collett et al, 2000). In stomachs of infected cats, there is a significant increase in mucosal fibrous tissue and mucosal lymphoid aggregates (Hargis, Prieur, and Blanchard, 1983).

Anthelmintic medication

It has been reported that tetramisole (a 2.5% formulation administered at 5 mg/kg) has proved efficacious and without side effects (Hasslinger, 1984).

Dictyocaulus

Identification

Up to 80 mm long, white adult *Dictyocaulus* worms are found in the respiratory passages of ruminants and horses, *Dictyocaulus viviparus* in cattle, *Dictyocaulus filaria* in sheep, and *Dictyocaulus arnfieldi* in equids. The buccal cavity is small; the bursa is somewhat reduced; the spicules are short, dark, and granular in appearance; the vulva is near the middle of the body; and the egg contains a first-stage larva when laid (Figure 4-81; see also Figure 4-72).

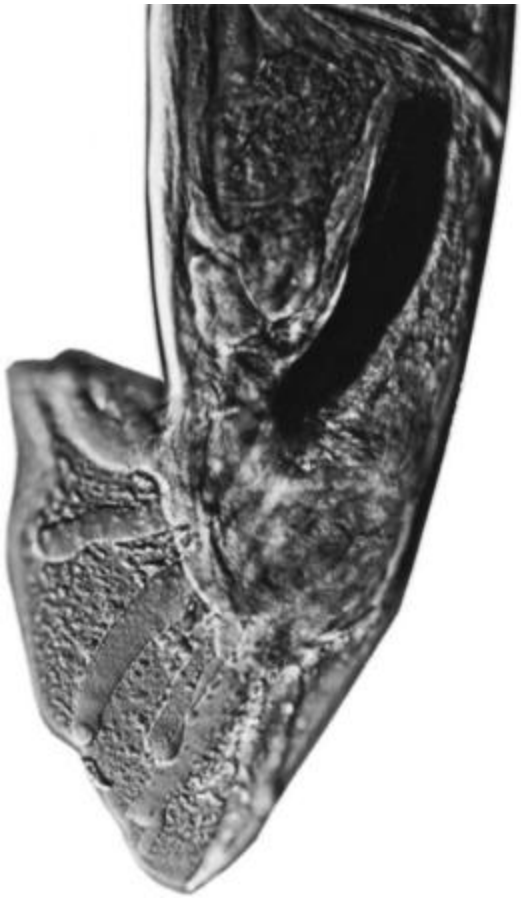

FIGURE 4-81 Bursa and spicules of *Dictyocaulus*.

Life history

Adult *Dictyocaulus* organisms live in the lumen of the bronchial tree, where they cause chronic bronchitis and localized occlusion of the bronchial tree with atelectasis. *Dictyocaulus viviparus* is the only nematode that reaches maturity in the lungs of cattle. The freshly laid egg contains a vermiform embryo that usually hatches before being eliminated in the feces (see Figure 7-61). The free-living stages probably derive their energy from stored food materials instead of ingested bacteria because they can develop to the doubly ensheathed infective stage in aerated clean water and because the characteristic “food granules” in the intestinal cells of the first-stage

larva become less conspicuous and finally disappear as development proceeds. Development to the infective stage requires about 5 days under optimum conditions. When ingested, the infective larvae migrate by way of the mesenteric lymph nodes and thoracic duct and arrive in the lungs about 5 days later (Jarrett et al, 1957). Egg-laying starts about 4 weeks after infection.

Importance

Light infections with *D. viviparus* are borne without obvious physiologic embarrassment; calves cough occasionally and may breathe slightly faster than normal. Heavier infections lead to partial or complete obstruction of the air passages, and clinical disease develops in proportion to the degree of obstruction. A progressive increase in respiration rate starts at about the fifth day after ingestion of several thousand infective larvae, and the animal coughs occasionally. During the third week, respirations become forced and reach a rate of 100 per minute. Auscultation reveals harsh bronchial sounds and occasional crepitation. Until the fourth week, no larvae are shed in the feces, and the diagnosis rests entirely on the history and clinical signs. During the fourth week, first-stage larvae appear in the feces, and the severity of the clinical signs reaches a maximum. The respiratory rate exceeds 100 per minute, coughing is frequent, crepitation and harsh bronchial sounds can be heard, and air hunger becomes acute. The calves do not feed because they cannot spare the time needed for breathing. Clinical improvement can be noted in survivors after the fifth week.

D. filaria in sheep and goats has a life history similar to that of *D. viviparus* (Daubney, 1920). However, unless unusually large

infections are acquired, the clinical signs are usually mild. Most cases of severe clinical illness associated with *D. filaria* are complicated by the presence of less obvious but more pathogenic parasites in the alimentary tract.

D. arnfieldi is a relatively well-adapted parasite of donkeys *(Equus asinus)* but tends to be quite pathogenic in horses. Where this parasite is endemic, it is hazardous to pasture horses and donkeys together.

Ecology and Epidemiology of Strongylid Infections of Ruminants

The following discussion refers principally to ruminants because the ecology and epidemiology of ruminant strongylids have been subjects of intensive research for the best part of a century. The lessons learned from sheep can be applied at least qualitatively to horses. The typical strongylid life history as outlined in Figure 4-82 is generally applicable to members of the superfamilies Trichostrongyloidea, Strongyloidea, and Ancylostomatoidea. Important embellishments on this scheme, such as the skin penetration of hookworm infective larvae and the atypical larval development of *Dictyocaulus* species, do not significantly alter the qualitative ecologic and epidemiologic relationships portrayed.

1. The rate of environmental contamination with eggs is in direct proportion to the degree of infection of the host population with adult worms.

2. Development and survival of the infective stage depend on the prevailing conditions of temperature and moisture. Optimum

requirements vary distinctly among worm species.

3. Host resistance varies as a function of age, vigor, genetic constitution, presence or absence of an already established infection, and, in some instances, acquired immunity.

4. The maturation of the fourth-stage larvae may be held temporarily in abeyance by as yet poorly understood influences. Populations of arrested larvae may be harbored for months before some unknown stimulus restarts their final development.

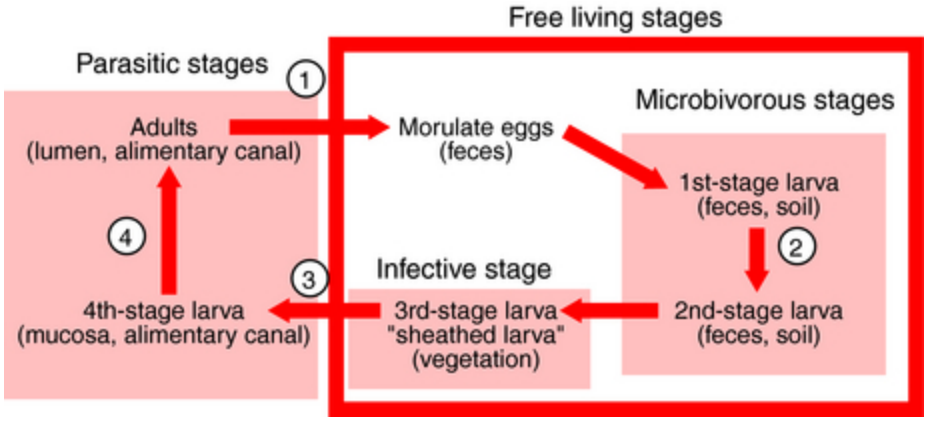

FIGURE 4-82 A typical strongyloid life history. Stages 1 through 4 are explained in the text.

Adult worm populations

Although some infective larvae may survive for weeks or months under suitable environmental conditions, it is the carrier host that often perpetuates strongylid infections from year to year. The infection may be maintained as a small population of adult worms, as a latent population of histiotropic larvae, or as both. Strongylids, like cold viruses and daffodils, display marked seasonal variations. The worm population normally is regulated in a way that spares the

host and perpetuates the parasite. Only when this regulation breaks down do outbreaks of disease occur.

During their first season at pasture, calves, lambs, and kids acquire strongylid burdens rapidly by ingesting third-stage larvae as they graze. If the vegetation is heavily contaminated with pathogenic species (e.g., *O. ostertagi* or *H. contortus*), disease and deaths may occur among these young and inexperienced hosts. The accumulation of infection is manifested by a corresponding increase in fecal egg output and by further contamination of the pasture. Provided with sufficient warmth and moisture for larval development, the number of infective stages on vegetation will tend to increase exponentially, at least during the early part of the grazing season. However, the hosts now begin to develop resistance to further infection. The principal component of this developing resistance is a peculiar phenomenon called **premunition:** "a state of resistance to infection which is established after an acute infection has become chronic and which lasts as long as the infecting organisms remain in the body" (*Dorland's Illustrated Medical Dictionary,* ed 27, Philadelphia, 1988, Saunders). The mechanism of premunition is unknown, but the phenomenon can be readily demonstrated by a variety of simple experiments. For example, if we decide to impose a severe *H. contortus* burden on a sheep that is already harboring a moderate population of these parasites, we must first remove the already established population by anthelmintic medication. Otherwise, part or all of the dose of larvae that we administer experimentally will fail to take. As premunition and other forms of host resistance develop, individual strongylid burdens reach a peak and then begin to decline. Normally the calf, lamb, or

kid enters its first winter with a substantially reduced population of adult strongylids.

What becomes of the infective larvae that the now-premunized host continues to ingest as it grazes? There are three possibilities: such larvae may be rejected, replace established adult worms, or become arrested in their development as fourth-stage larvae, but the total number of adult worms tends to remain at a plateau. The **arrested larvae** (also referred to as **latent, inhibited,** or **hypobiotic larvae**) remain in the alimentary mucous membranes until some stimulus related to the coming of spring, to the reproductive cycle of the host, or to both, restarts their development. For example, in spring a substantial increase in the output of strongylid eggs is observed in the feces of ewes, rams, and wethers. A more pronounced rise also commonly occurs in lambing ewes from 2 weeks before until 8 weeks after parturition at any season. Both "**spring rise**" and "**periparturient rise**" (Crofton, 1954) in fecal egg counts are related principally to the maturation of the larvae that have overwintered as arrested fourth stages in the alimentary mucosae of adult sheep (Herd et al, 1983). "The production of a large number of eggs about two months after parturition ensures that infective stages will be available in large numbers at a time when the sheep population is not only enlarged by lambing but also has a high proportion of susceptible individuals which have not been exposed to infection previously" (Crofton, 1963). The periparturient rise in fecal egg counts can be abrogated by protein supplementation of the ewe (Donaldson, van Houtert, and Sykes, 1997).

In summary, calves, lambs, and kids tend to carry large parasite burdens, whereas adult cattle, sheep, and goats usually harbor lighter infections. One peak of strongylid reproductive activity is observed during the grazing season. This occurs in both mature and growing ruminants but tends to be more marked and pathogenic in the latter. A second peak occurs in mature females a few weeks after parturition and is marked by the "postparturient rise" in egg output. This increase is most marked in ewes lambing in spring, at which season a modest spring rise also is observed in wethers and barren ewes.

The **biotic potential** or **reproductive capacity** of strongylids depends jointly on the rate of production of fertile eggs and on the **generation time** (i.e., the time required for these eggs to develop into egg-producing adults). The normal degree of realization of the biotic potential tends to maintain stable worm populations that display marked periodicity but neither explode nor fade away to extinction. Normally the probability of any individual strongylid egg reaching reproductive age is only one in thousands, so the worms must compensate by producing enormous numbers of eggs. *Haemonchus* species are the most fecund, with *Oesophagostomum, Chabertia, Bunostomum*, *Ostertagia*, *Cooperia*, *Trichostrongylus,* and *Nematodirus* species following roughly in that order. The species with low per-individual reproduction rates tend to compensate either by maintaining larger adult populations (*Trichostrongylus* and *Cooperia* species) or by producing eggs more resistant to inclemencies of the external environment (*Nematodirus* species).

Development and survival of the infective stage

Most strongylids are capable of developing and maintaining significant populations of infective larvae over considerable ranges of temperature and moisture. Minimum conditions are of interest because they dictate the point at which the environment ceases to harbor significant infection, and optimum conditions are of interest because it is during periods favorable for the development and survival of preparasitic stages that outbreaks of clinical strongylosis usually occur.

No strongylid life history can be completed in totally arid environments, and parasitism with strongylids is correspondingly rare in desert regions. Even under apparently dry conditions, however, microhabitats may exist that contain enough moisture to allow survival if not development of eggs and larvae.

The temperature necessary for development varies with the species, and in each case the rate of development varies with the temperature. With the very significant exceptions of *N. filicollis*, *N. battus*, and *Ostertagia* species, which appear to be well adapted to cold climates, the egg and larva populations of most strongylids experience marked reductions or even disappear from northern pastures during winter. Such pastures become recontaminated in spring. *Nematodirus*-infective larvae develop and remain viable in the eggshell during winter in climates about as harsh as possible for the profitable practice of cattle, sheep, or goat husbandry. *Ostertagia* overwinters both as infective larvae on pasture and as arrested larvae in the host population; the pasture larvae begin to die off as warmer and dryer conditions supervene.

Host resistance

Age

A general increase in resistance to strongylid infection with age is well marked in cattle, slightly less so in sheep, and least in goats. Age resistance may break down in the face of overwhelming challenge or as a secondary result of malnutrition or disease. Old ewes may succumb to strongylidosis when their teeth fail them, and limited milk production by ewes predisposes their nursling lambs (Whitlock, 1951). Examination of the teeth and udders of ewes should accompany any investigation of parasitic disease in sheep (Love and Biddle, 2000).

Phenotype

Whitlock (1955b, 1958) reported an inherited resistance to trichostrongylidosis in sheep. The progeny of a ram called Violet harbored smaller populations of worms and suffered less reduction in hematocrit than did the progeny of other rams. Unfortunately, one dark and stormy night the electric transmission lines fell on Violet and blew him to glory. Years later, when he retired and turned over his Zeiss photomicroscope, Dr. Whitlock had a brass plate engraved in Violet's memory and mounted on the microscope. Currently the process has been used in Australia and New Zealand, whereby the resistance status of rams is included in their records. Thus this aspect of genetics is currently being applied on a regular basis to aid in preventing nematode-related disease in sheep.

Premunition

The presence of a stable population of adult strongylids in the alimentary canal tends to inhibit further infection or, at least, further maturation of larvae. Removal of this stable adult population by anthelmintic medication vacates an ecologic niche that is promptly filled through maturation of arrested larvae, uninterrupted development of recently ingested infective larvae, or both. Whatever the underlying reason for premunition—that is, ecologic or immunologic—a ruminant with a subclinical strongylid infection should not be treated with anthelmintics unless an uncontaminated environment can be provided after treatment. The loss of premunition resulting from removal of the stable and established infection will permit rapid reinfection, perhaps with a heavier parasite load than before.

The following seeming paradox lends a measure of symmetry to this argument. If sheep are removed during peak exposure from an *H. contortus*–infested pasture to a parasite-free environment, they will develop more serious infections than if left on the pasture. Interrupting the flow of larvae apparently throws the regulation out of balance in some way. The inhibition of larval development by adult worms is manifested as premunition. It appears that the larvae in turn exercise a measure of control over the adults. At any rate, the practical advice to be gleaned from this is as follows: Be sure to administer an anthelmintic to *H. contortus*–infected sheep before

transferring them to an uncontaminated environment, at least during the parasites' normal period of rapid population growth.

Although host immunity is often credited for the state of premunition, it might also be due to interactions between the parasites. An ecologic explanation of premunition might be kin selection—that is, once established, worms exploit the chosen niche and somehow directly or with the manipulation of the host make the niche inhospitable to other worms from different parental stocks. When sheep are infected first with one group of worms and then infected with brothers and sisters or cousins after the first group has matured, there is some evidence that the genetic relatedness of the existing and incoming populations have an effect on the number of worms that will develop to adulthood (Ketzis et al, 2001).

Self-cure

There are few examples showing immunity that protects the host against reinfection after the initial strongylid population is gone. Stoll (1929) reported an experiment "in which two helminth-free lambs, upon fenced-in pasturage permitting natural repeated infection, during the summer developed, following an initial dose of *Haemonchus contortus* larvae, first an accumulation of parasites and then a self-cure which expelled the worms and protected the animals thereafter against any significant amount of further infestation with this stomach worm." Thus was born the celebrated phenomenon called *self-cure*.

Stewart (1950) observed seven periods of self-cure within 18 months in a flock of grazing sheep, demonstrated that an identical response could be elicited by giving large doses of infective *H. contortus* larvae, and concluded that self-cure taking place after periods of rain could be attributed to the intake of large numbers of *H. contortus*–infective larvae. He subsequently related the rejection of the previously established adult worm population to an acute hypersensitivity reaction in the alimentary mucous membrane.

An edematous change was evident in the mucous membrane of the abomasum or small intestine, depending on the site of attachment of the adults, on the day on which a rise of blood histamine occurred after the administration of larvae. The intake of *H. contortus* larvae produced this change only in the abomasum of a sheep that had been infested with *H. contortus* and only in the small intestine of a sheep that had been infested with *Trichostrongylus* spp. (Stewart, 1953).

The lack of permanent protection against reinfection observed by Stewart does not necessarily invalidate Stoll's observations, but examples of functional acquired sterile immunity are rare where *H. contortus* is concerned. Drs. Georgi and Whitlock had no difficulty reinfecting lambs of the New York State Veterinary College flock with *H. contortus cayugensis* after their naturally acquired worm burdens had been removed by anthelmintic therapy. Similar results are commonly observed in other parts of the world with other subspecies of this parasite.

There is at least one definite practical consequence of self-cure. Sheep or goats may die in the throes of evicting their worms and confuse the diagnosis by being found "uninfected" at necropsy when the clinical signs and history correctly pointed to haemonchosis. Profound anemia in grazing sheep or goats is haemonchosis unless positive evidence of another cause (e.g., acute radiation sickness) can be produced. The absence of *H. contortus* worms from the abomasum of an anemic sheep or goat in no way rules out the diagnosis of haemonchosis.

Active immunity

A durable sterile immunity is conferred in cattle by infection with the lung nematode *D. viviparus*, and considerable success has been achieved by means of artificial immunization with irradiated larval vaccines (see the review by Poynter, 1963). The practical application of vaccines is of course limited to areas of endemic dictyocaulosis, and although *D. viviparus* infection is cosmopolitan in distribution, clinical parasitic disease tends to be sporadic. Clinical dictyocaulosis is common in the British Isles, and that is where the vaccine has found ready acceptance and effective application.

Delayed maturation of larvae

Arrested development of larvae not only helps perpetuate certain strongylids from year to year but spares the host during the period of winter (or dry season) stress, when energy invested in the reproduction of worms with free-living larvae would be a losing

proposition biologically. Normally these larvae mature the following spring. However, outbreaks of severe strongylidosis may result from the unseasonable maturation of arrested larvae during winter and early spring. It is important to recognize the parasitic cause of such outbreaks despite their unseasonable incidence.

Treatment and Control of Strongylid Infections in Ruminants

The first step in dealing with an outbreak of strongylidosis in a herd of cattle, sheep, or goats is to identify the source of infection and to separate the animals from it. For purposes of observation and nursing, it is usually more convenient to confine the herd in a barn or drylot, and restriction of activity may help prevent losses precipitated by exertion. Never hurry patients acutely ill with haemonchosis; they may drop dead at your feet. Segregate all animals showing anemia, diarrhea, weakness, or depression to facilitate therapy and to prevent their being bullied to death by their stronger fellows, but do not separate nurslings from their dams unless the owner is willing and able to cosset them.

Administration of an anthelmintic may hasten the death of very sick animals, and the owner should be forewarned of possible further losses precipitated by drenching. However, the benefit of an effective anthelmintic drench in primary haemonchosis is usually dramatic. Strongylid nematodes continue to infect our cattle, sheep, and goats despite the plethora of safe and efficacious anthelmintic drugs. The use of anthelmintic drugs should be based on thorough

knowledge of the biology of the worms and the area's climatic conditions. The entire herd may be treated at regular "strategic" intervals in the hope of preventing the buildup of infective larvae in the pastures and thus preventing outbreaks of clinical strongylosis. When contamination is particularly severe, strategic treatments preceding parturition and turnout to pasture, at midsummer and in fall, may need to be supplemented by "tactical" treatments at times when infection pressure may be particularly severe, for example, after a period of moist, warm weather particularly favorable for larval development.

Strongylids of the alimentary canal

Ruminant anthelmintics include fenbendazole, albendazole, ivermectin, doramectin, moxidectin, eprinomectin, levamisole, and morantel. All of these drugs are available in a variety of pharmaceutical forms to suit all types of farm and feedlot management systems.

Abomasal parasites such as *Haemonchus* species, *Ostertagia* species, and *T. axei* tend to be more susceptible to anthelmintic medication than related parasites of the small intestine such as *Trichostrongylus*, *Cooperia*, and *Nematodirus* species. Normally, these latter genera tend to concentrate in the first quarter of the small intestine, and only a few specimens are found lower down. It is thought that poisoned small intestinal parasites have a greater opportunity to recover and reestablish infection lower down in the small intestine, whereas poisoned abomasal parasites have left the

abomasum before they have had a chance to recover. Therefore unless experiments designed to evaluate the efficacy of anthelmintics against parasites of the small intestine are based on postmortem examination of the entire small intestine, the results reported are likely to be biased in favor of the anthelmintic (Bogan et al, 1988).

Fall or early winter treatment ideally should be carried out with anthelmintic drugs active against the immature, arrested parasitic stages of *Ostertagia* species (Armour, Duncan, and Reid, 1978; Duncan et al, 1976; Williams et al, 1977). In northern temperate, nonarid areas of the United States, treatment of ewes with a larvicidal anthelmintic at the time they are put indoors in fall prevents periparturient rise, at least in fall- and early spring–lambing ewes (Herd et al, 1983).

Resistance

A population of parasites under more or less continuous chemical attack must alter its genetic composition through selection or mutation or be driven to extinction. Increased resistance of the parasites to the chemical, the more frequent outcome, is most common when antiparasitic chemicals are most needed and therefore most frequently used. Purchased livestock also may introduce resistant strains of parasites. However, it must be borne in mind that most cases of apparent anthelmintic failure are due either to continued exposure to infective larvae or to errors in selection and administration of an appropriate anthelmintic chemical (Coles,

1988). *H. contortus*, *T. circumcincta*, and *Trichostrongylus colubriformis* of sheep and goats in widely scattered parts of the world have displayed resistance to ivermectin, benzimidazoles, and levamisole/morantel. Resistance to anthelmintics has been slower to appear in relation to cattle parasites, but it seems that sporadic cases of resistance to benzimidazoles or macrocyclic lactones may occur (McKenna, 1996; Vermunt, West, and Pomroy, 1995). The genus most typically incriminated in the case of cattle is *Cooperia*, but it appears that *Ostertagia* and *Trichostrongylus* may also sometimes be involved.

Resistance to the different antiparasitics in the United States is of greatest concern in goats, but reports of resistance have also occurred with sheep and cattle. Resistance to ivermectin was first reported in the United States for *H. contortus* in Angora goats (Craig and Miller, 1990). Resistance of this same parasite was also observed in cattle in Texas (DeVaney, Craig, and Rowe, 1992). Resistance has now also been seen in *Haemonchus* and *Trichostrongylus* in goats in the southern United States (Kaplan et al, 2007). It seems that resistance of the gastrointestinal nematodes of goats is now a very common event in the United States, with resistance having been seen with respect to albendazole, levamisole, ivermectin and moxidectin (Mortensen et al, 2003).

Lungworms

Clinical outbreaks of dictyocaulosis are treated with fenbendazole, ivermectin, dormectin, levamisole, oxfendazole, or albendazole.

These are highly efficacious against both adult and immature stages of *Dictyocaulus* species.

Subclinical parasitism of adult dairy cattle

The need to treat adult dairy cattle for the helminths that may be present still remains an open-ended question. Herd et al (1983) compared 26 trials in which milk production was examined and found that in 14 trials there was no change, in seven trials there was an increase after treatment, and in five trials there was an increase in the control group. In a large trial of 9721 lactations examined in Britain over a 305-day lactation period, there was a 42-kg gain in milk production (Michel et al, 1982). The authors thought that this was not a cost-effective increase, whereas others interpreted the gain as cost effective (Theodorides and Free, 1983).

In a New Zealand trial, half of 5556 cows on 47 dairies were treated twice with oxfendazole when dry (Bisset, Marshal, and Morisson, 1987). During the next 251-day lactation, the treated cows produced an average of 2.24 kg more butterfat or 52.9 kg more milk. A positive response was seen in 36 of the 47 treated herds, but only one herd had a significant increase. The authors noted a greater response to treatment in cows that had been grazed previously on pastures that had been occupied with calves and with cows that were historically higher milk producers.

Two trials were performed in the Netherlands (Ploeger et al, 1989, 1990). In the first trial, 285 of 527 dry cows were treated with ivermectin. The milk yield over a hypothetical 305-day

lactation increased an average of 205 kg in the treated cows. In this trial, 17 of the 31 treated herds had a positive response, and again greater responses were noted in cows that had historically higher milk yields. In the second trial, 676 of 1385 cows in 81 herds were treated with albendazole within a week of calving. The milk yield during the hypothetical 305-day lactation of the treated cows increased 133 kg, and 49 of the 81 herds had a positive response.

In an Australian trial, half of 498 cows in five pasture-fed herds were treated with ivermectin when dry (Walsh, Younis, and Morton, 1995). The milk yield increased 74 L during the first 100 days of lactation, whereas the yield over the entire lactation was 86 L. All of the herds had a positive response, but the increase was significant in only one herd. No increased response was observed among cows that previously had been noted to have a high lactation production index. There was no difference in the cows as to time from calving to first service, but the calving to conception time was reduced in the treated cows by 2 to 8 days. As is typical of lactating dairy cows, there were few eggs present in the feces of the Australian cows, and there was no correlation between egg reduction and the observed increases in milk production (see the excellent review by Reinemeyer, 1995).

Eprinomectin, an avermectin that can be applied to lactating dairy cattle, has now been examined for its effects on adult dairy cattle in several trials where it was administered at the time of calving. In the case of pastured dairy cattle in Canada, the treatment did seem to produce an economic increase in milk production

(Ndtvedt et al, 2002). In a similar trial in Canada looking at breeding parameters, there was a marginally significant improvement in the calving to conception interval, but not calving to first service interval, and there was a reduction in the number of breedings to conception in treated animals (Sanchez et al, 2002). In two studies in cattle in Canada and the United States with cattle having limited outdoor exposure, there were not apparent advantages to treatment at calving either in milk production or in reproduction parameters (Sithole et al, 2005, 2006). These studies would suggest that when cattle are at risk of continued infection pressure from pasture, treatment may be warranted but likely will be of little value in most confinement systems.

Young cattle

Unlike the case for treating adult dairy cattle, there is fairly unanimous agreement among parasitologists that the treatment of yearlings and 2-year-olds is a profitable undertaking (see a second excellent review by Reinemeyer, 1990). These are the ages of cattle that tend to suffer significantly from parasitism. Parasitized replacements grow more slowly and often fail to reach their full growth potential. Such performance results in real financial loss of which the producer may well be completely unaware.

Subclinical parasitism of sheep

The effects of moderate parasitism in lambs were investigated by administering 5000, 10,000, or 20,000 infective *T. colubriformis*

larvae and comparing weight gains and feed efficiency of these artificially infected lambs with the performance of uninfected controls. Although about one half of the larvae administered became adult worms, and group average fecal egg counts of 536 to 2236 eggs per gram were observed, these levels of infection apparently caused no significant differences in average daily gain or feed efficiency (Bergstrom, Maki, and Kercher, 1975).

Integrated control of ruminant strongylid infections

Much has been written about prevention and control of strongylidoses. Every scheme has its proponents and detractors, but there is no unique formula that applies in all situations.

Parasitism should be considered as a year-round game among the livestock, the strongylids, and the stockman. Certain moves at propitious times are capable of biasing the game in the stockman's favor, but these moves must not violate the rules of the game or the results may be disappointing or even disastrous. The ultimate criterion for success in any control effort is the net profit that accrues, not the number of worms fatally poisoned. The purchase of a livestock scale, as suggested by Whitlock (1955a), and the maintenance of adequate production records provide objective measures of success.

Control efforts may be classified under selective breeding for resistant stock, rotational grazing, and anthelmintic medication. The first of these has been used the longest. Long before worms were recognized as disease agents, shepherds selected productive

livestock for breeding, and worms claimed the lives of weaklings (against the shepherd's wishes perhaps, but to his eventual benefit) (Whitlock, 1966). There exist, in many parts of the world and under certain systems of husbandry, cattle, sheep, and goats capable of thriving without help from science and technology. These animals have parasites and handle them effectively as a population. Individual animals occasionally die of parasitism, just as individuals occasionally get killed by predators, hung up in fences, or drowned in watering places, but the effect of minor losses such as these on the general population is minimal. On the other hand, there are also parts of the world and systems of husbandry in which the economic production of food and fiber requires intelligent intervention to suppress strongylid populations. Host resistance continues to be of paramount importance here, even though conscious selection of resistant stock is seldom part of the breeding program. The reason is that resistant hosts contribute less to the growth of the parasite populations than do more susceptible animals, and their presence thus tends to benefit the flock as a whole.

In theory, rotational grazing seeks to prevent or limit the intake of infective larvae by permitting animals to graze on a particular area of pasture no longer than a week so that eggs passed in their feces do not have time to develop into infective larvae, and then not allowing the animals to return until all the larvae have died off. The considerable investment in fence construction required by rotational grazing schemes usually discourages strict observance of the rules, so the theoretic ideal is seldom realized in practice. However, any

practicable rotation scheme undoubtedly increases the productivity of the pasture and may prolong the parasite generation, if only slightly (Levine and Clark, 1961).

Modern anthelmintics are efficient and comparatively nontoxic. There are places in the world where efficient livestock production is virtually impossible without them, and they are of undoubted benefit in increasing productivity wherever significant parasite losses occur. However, there are limitations, hazards, and expenses that we cannot afford to ignore. No anthelmintic can overcome excessive exposure to infection, just as no amount of bailing can overcome too large a leak. Crofton (1958) concluded that periodic treatment with interim reinfection merely delayed attainment of the full parasite potential. He suggested concentrating treatments early in the pasture season to obtain maximum delay in the parasite population increase because an adult worm in spring is a potential forebear of a whole series of generations that season.

Currently it is widely believed that, at least in temperate climates, only one generation of ruminant trichostrongylids capable of causing disease is produced (Herd et al, 1984). However, Crofton's basic premise is supported by Herd, Parker, and McClure (1984), who found that "prophylactic treatments in the spring were just as effective as suppressive treatments throughout the entire grazing season and resulted in significant ($P < 0.001$) increases in weight gain." The prophylactic treatments used by Herd, Parker, and McClure (1984) consisted of four doses of ivermectin (0.02 mg/kg) administered 3, 6, 9, and 12 weeks after spring turnout. In

New York State, we freely admit, 12 weeks after turnout is getting pretty close to fall.

Probably the most important type of host resistance is premunition. The development of premunition in a grazing flock tends to truncate the growth curve of the parasite population by preventing the maturation of new waves of larvae and thus in effect prolonging the generation time. Although interference with the development of premunition is obviously to be avoided, periodic anthelmintic medication may have precisely this effect.

FAMACHA and refugia

It has been strongly suggested that a way to prevent resistance within *Haemonchus contortus* from developing in a flock of sheep is to treat only those animals needing therapy. This leaves the remainder of the sheep shedding feces into the environment containing eggs from worms that are still fully susceptible to whatever drug or drugs that have been used. In the case of haemonchosis, the relationship between worm burden and anemia is well established (Whitlock et al, 1966). The FAMACHA technique combines the ability to detect anemia in sheep (and goats) using the mucous membranes around the eyes with the need to treat sheep that have apparent anemia to reduce their burdens of *Haemonchus contortus* (Vatta et al, 2001). Thus, in the warmer areas where haemonchosis is typically the major disease threatening sheep and goats, the FAMACHA chart system provides a means of easily recognizing those sheep in need of treatment. It must be

remembered that this system is for areas where haemonchosis is the major helminth causing disease in a sheep flock; the system is not designed to work where the major parasites are *T. circumcincta* or species of *Trichostrongylus*, *Cooperia*, or *Nematodirus*.

Superfamily Strongyloidea

Morphology

Strongyloids tend to be larger and stouter-bodied than trichostrongyloids, and most of them have a large buccal cavity surrounded by a sclerotized wall (buccal capsule) that is usually rigid but may be jointed or thin and flexible. The stomal structures of strongyloids are sufficiently distinct to permit identification of species with occasional reference to other characters. Greater dependence must be placed on these other characters when it is impossible to examine both dorsal and lateral aspects of the stoma, as is the case with permanently mounted specimens.

The **buccal cavity** of strongyloids is large and directed anteriorly (see Figure 4-63). The stomal opening is surrounded by a row or two of what appear to be leaves or palings of a stockade, depending on the imagination of the observer. These are called **leaf crowns** (corona radiata), and much is made of them in the taxonomy of strongyloids. In some species, the duct of the dorsal esophageal gland is carried to the rim of the buccal capsule in a sclerotized ridge (**dorsal gutter;** see Figure 4-63) on the inner wall of the buccal capsule. In other species the dorsal gutter is absent (Figure 4-83). Teeth, when present, lie at the base of the buccal

cavity, where they lacerate the plug of mucous membrane that is drawn into the buccal cavity by the sucking action of the muscular esophagus. The copulatory bursa is well developed, the spicules long and thin. The vulva is close to the anus, and the uterus is prodelphic in most strongyloids.

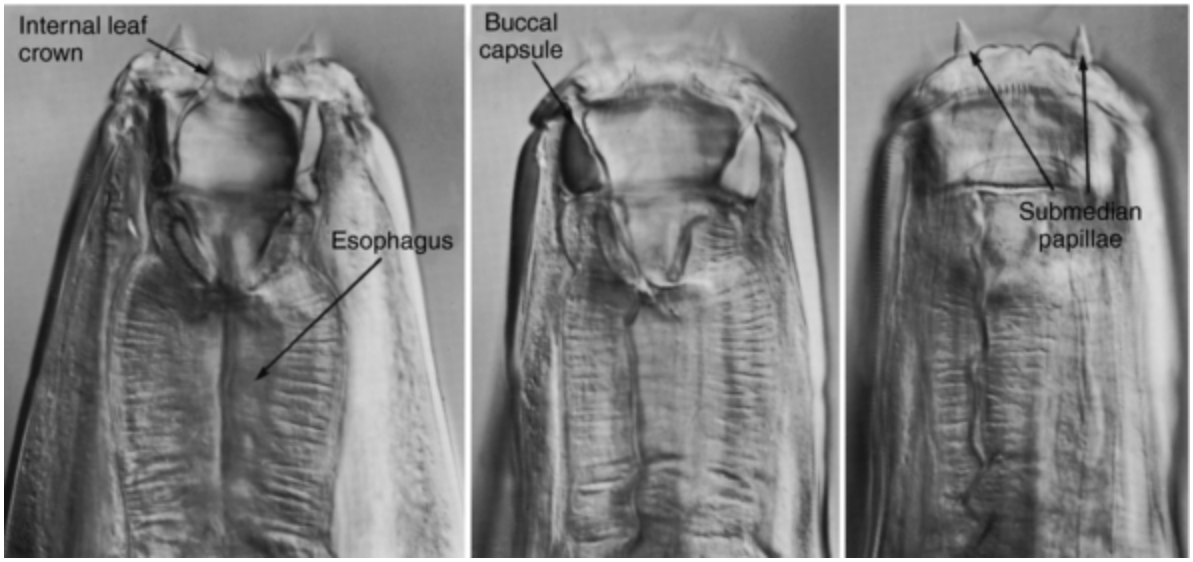

FIGURE 4-83 *Murshidia dawoodi* (Strongylidae: Cyathostominae) from an African elephant.

Life history

Strongyloid life histories are typical of the order Strongylida—that is, they are direct with an infective third-stage larva—but significant variations occur in certain groups. For example, *Syngamus* species, the gapeworm of domestic and wild birds, and *Stephanurus* species, the kidney worm of swine, use earthworms as paratenic hosts.

Family Strongylidae

Subfamily Strongylinae

Identification

Members of the subfamily Strongylinae, often referred to as "large strongyles," are chiefly parasites of the large intestine of equines *(Strongylus, Triodontophorus, Oesophogodontus,* and *Craterostomum)*, elephants *(Decrusia, Equinurbia,* and *Choniangium)*, macropodid marsupials *(Macropicola* and *Hypodontus)*, and ostriches *(Codiostomum)*. Identification of genera and species of strongylin parasites of horses is a matter of comparing the microscopic appearance of the stomal region of specimens with the series of illustrations of equine parasites found in Chapter 7. There are two leaf crowns, but because the elements of each are similar in size and number, the two crowns appear as one.

Importance

Strongylus vulgaris, *Strongylus edentatus*, and *Strongylus equinus* are among the most destructive parasites of the horse. All three are bloodsuckers as adult worms in the cecum and colon, but even more important, their larvae undergo migrations that inflict even greater damage, especially in foals and yearlings. *Triodontophorus* organisms appear, by the ferocious teeth at the base of their buccal cavities (see Figure 7-76), to be bloodsucking parasites. Clusters of *Triodontophorus tenuicollis* worms cause localized ulceration of the colonic mucous membrane.

Life history of *Strongylus vulgaris*

The extrahost development of *S. vulgaris* is typical of strongylids in general (see Figure 4-71). Development to the infective stage

requires adequate moisture and temperatures in the range 8° to 39° C; the time required is inversely related to temperature (e.g., about 8 to 10 days at 18° C, 16 to 20 days at 12° C). In arid regions, scattering the droppings with a tractor and harrow reduces strongylid larva populations by breaking up the manure and causing it to dry out before the larvae have reached the desiccation-resistant third stage. However, in more humid regions, the interior of even scattered manure remains sufficiently moist long enough for development to the third stage. Once *S. vulgaris* larvae have arrived at the third stage, they are very resistant to cold and desiccation and can survive on pasture through a northern winter or in stored dry hay for many months. The longevity of *S. vulgaris* third-stage larvae depends mainly on the food reserves in their intestinal cells; the greater the activity of the larvae, the more rapidly these reserves become exhausted. However, it is imprudent to depend on *S. vulgaris* to wear itself out no matter how warm and humid the weather may be. Any pasture that has held a horse within a year can be assumed to be contaminated with *S. vulgaris* infective larvae.

In 1870 Otto Bollinger hypothesized that occlusion of the intestinal arteries by verminous thrombi and emboli could account for most equine colic cases, both fatal and nonfatal. Since then, the causative relationship between *S. vulgaris* and colic has been extensively debated and somewhat investigated, although not to an extent commensurate with its scientific and practical importance.

The meticulous experimental observations and well-thought-out conclusions of Enigk (1950b, 1951) provide the basis for the following outline. For the reader interested in greater detail than can be presented here, Dr. Georgi has published an English translation of Enigk's papers (Georgi, 1973), and all serious students of equine medicine and pathology should study the review by Ogbourne and Duncan (1977).

When ingested by a horse, the infective third-stage larvae of *S. vulgaris* cast off their sheaths in the lumen of the small intestine and enter the wall of the cecum and ventral colon. Here the larvae penetrate to the submucosa, where they undergo the third molt, which is completed by the seventh to eighth day after infection. Leaving their third-stage cuticles surrounded by round cells, the fourth-stage larvae penetrate nearby small arterioles that lack an internal elastic lamina and wander in the intima of these vessels and progressively larger branches of the cranial mesenteric artery.

Enigk observed that *S. vulgaris* cannot penetrate the internal elastic lamina, which thus confines the larvae to the intima and helps keep them on their proper course. Thus constrained, the rapidly migrating larvae reach the colic and cecal arteries by the eighth to the fourteenth day after infection and the cranial mesenteric artery by the eleventh to the twenty-first day (Enigk, 1950b; Duncan and Pirie, 1972). Some of the larvae push on into the aorta and its branches, where they may cause important pathologic changes (see Figure 7-88). However, larvae proceeding beyond the cranial mesenteric artery are probably lost to their

species because of the improbability of their finding their way back to the cecum and ventral colon to breed.

After 2 to 4 months of migrating in the intima, the fourth-stage larvae that have not gone astray or become trapped deep in thrombi are carried by the bloodstream to the small arteries in the subserosa of the intestinal wall. The larvae, now grown large, occlude these small arteries, whose walls then become inflamed and in due course are destroyed. The larvae thus liberated from the arterial tree then enter the surrounding tissue and become encapsulated in pea- to bean-sized nodules wherein the final molt occurs. Some larvae complete the final molt even before returning to the intestinal wall. According to Duncan and Pirie (1972), most of the larvae found in the cranial mesenteric lesions at 4 months after infection have molted to the fifth stage, although the fourth-stage cuticle is still retained as a sheath. This sheath is cast off before these immature adults return to the intestinal wall. Finally, the immature adults enter the lumen of the cecum and ventral colon, mature, and commence reproductive activity at about 6 months after infection. It is rare to find more than 100 or 200 adult *S. vulgaris* worms in a horse, and their egg production usually constitutes 10% or less of the total strongylid output.

The migrations of fourth-stage *S. vulgaris* larvae cause arteritis, thrombosis, and embolism of the cranial mesenteric artery and its branches. Although these arterial lesions exist to some degree in almost every horse, and principal branches are frequently completely occluded by them, fatal infarction of the bowel wall is

relatively infrequent. This seeming paradox suggests a Darwinian interpretation. Of all domestic animals, the horse has by far the most elaborate system of anastomoses in the arterial supply to the large intestine. The colic vessels are particularly well supplied with the means for rapidly establishing effective collateral circulation (Dobberstein and Hartmann, 1932). In an evolutionary context, this may be interpreted as evidence that *S. vulgaris*, which has no direct counterpart in other domestic animals, has probably been occluding horses' intestinal arteries and thus exerting selection pressure for ages.

However, despite this exceptional adaptation, obstruction of the intestinal arteries does occasionally lead to fatal infarction of the bowel. Even temporary curtailment of blood flow pending establishment of collateral circulation may account for a high proportion of clinical colic cases from which the patient recovers. Furthermore, the fatal intestinal displacements often interpreted at necropsy examination to be the cause of colic symptoms are more likely to be the result of abnormalities of intestinal tone and motility brought about by verminous thromboembolism and the horse's violent efforts to obtain relief.

After the larvae have migrated back to the intestinal lumen, the arterial lesions heal (Duncan and Pirie, 1975; Pauli et al, 1975). These lesions also heal dramatically after destruction of the larvae by medication with any of several newer anthelmintics, including ivermectin (Holmes et al, 1990). Development and resolution of verminous arteritis can be studied radiographically in young foals

by injecting contrast medium through a catheter that has been introduced into the aorta by way of a peripheral artery (Slocombe et al, 1977). Two such radiographs comprise Figure 4-84. The upper radiograph of a 2-month-old pony foal was taken 1 month after 500 *S. vulgaris* larvae were administered through a nasogastric tube. The cranial mesenteric and ileocecal arteries are enlarged, and blood flow through the colic arteries is greatly diminished, as evidenced by the lack of contrast medium flowing through them. The lower radiograph of the same foal was taken 1 month after albendazole therapy. Now the stem arteries have returned to nearly normal size, and the contrast medium clearly outlines the colic arteries, indicating a greatly increased flow through those vessels (Rendano et al, 1979b).

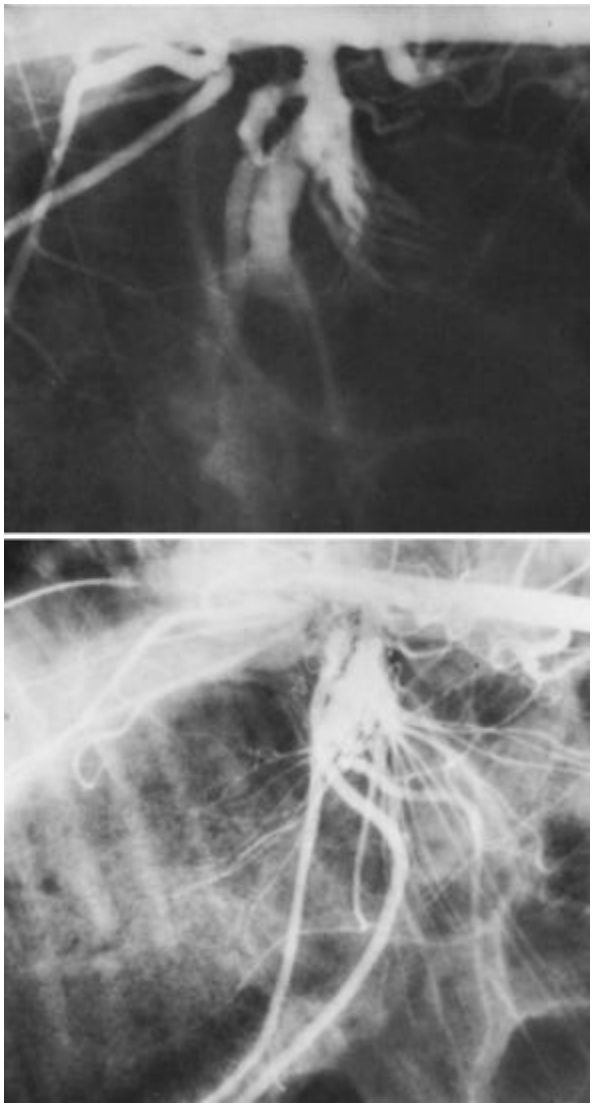

FIGURE 4-84 Resolution of equine verminous arteritis after larvicidal therapy with albendazole. The ramifications of the cranial mesenteric artery are made visible by contrast arteriography. The upper radiograph was taken 1 month after infection with 500 *Strongylus vulgaris* larvae, and albendazole therapy was started immediately afterward. The lower radiograph was taken 1 month after albendazole therapy.

Life histories of *Strongylus edentatus* and *Strongylus equinus*

Adult *S. edentatus* and *S. equinus* are about twice as large as *S. vulgaris,* probably twice as bloodthirsty, and considerably more difficult to remove with anthelmintic drugs, but their larvae are not

quite as pathogenic. The migration routes followed by larvae of *S. edentatus* and *S. equinus* have been elucidated by Wetzel (1940b), Wetzel and Kersten (1956), and McCraw and Slocombe (1974, 1978).

The third-stage larvae of *S. edentatus* burrow into the wall of the large intestine and reach the liver through the portal veins. Enclosed in nodules in the hepatic parenchyma, they molt to the fourth stage in about 2 weeks. The fourth-stage larvae then wander about in the hepatic tissue for about 2 months, growing larger as they go. Leaving the liver by way of the hepatic ligaments, the larvae wander for months in the parietal retroperitoneal tissues and eventually make their way to the base of the cecum and thence to the bowel lumen. The prepatent period usually is cited as 11 months but may be as short as 6 months (McCraw and Slocombe, 1978).

The third-stage larvae of *S. equinus*, like those of *S. vulgaris*, undergo their third molt in nodules in the wall of the cecum and colon. About 11 days after infection, the newly molted fourth-stage larvae leave their intestinal nodules, cross the peritoneal space, and enter the right half of the liver, which in the living horse lies in contact with the cecum. These larvae wander about in the hepatic tissue for 2 months or longer before emerging and entering the pancreas or abdominal cavity, where they complete their development to the fifth stage. The fourth molt occurs about 4 months after infection. Finally these adult worms penetrate the wall

of the large intestine and reenter the lumen to mate. The prepatent period of *S. equinus* is 9 months.

Triodontophorus

Triodontophorus species (and the 40-odd species of cyathostomes) do not migrate far beyond the mucous membrane of the colon; therefore the pathogenic effects of their larvae are considerably less dramatic than those inflicted by larvae of *Strongylus* species. However, *T. tenuicollis* adults are frequently observed clustered in ulcerated areas in the large intestine.

Subfamily Cyathostominae

Identification

These "small strongyles" are parasites of the large intestine of horses, elephants, pigs, marsupials, and turtles, and there is a multitude of them. About 40 species of cyathostomes parasitize the cecum and colon of horses, and it is commonplace to find as many as 15 to 20 of these species infecting an individual host at the same time. Cyathostomins have somewhat smaller buccal cavities than strongylins. All have distinct inner and outer leaf crowns, the elements of which differ in size and number (see Figure 4-83). In some species the inner leaf crown elements are inconspicuous and can be seen only in well-cleared specimens. Identification of species of equine cyathostomes can be accomplished by comparing dorsal and lateral aspects of the buccal regions of fresh or cleared, fixed specimens with the photomicrographs of strongylins and

cyathostomins portrayed in Chapter 7. All of the more common species are represented in that collection.

Importance

From 75% to 100% of the eggs passed in the feces of naturally infected horses are produced by the small strongyles (Cyathostominae) because these greatly outnumber the large strongyles (Strongylinae) both in numbers of species and in numbers of individuals. Cyathostomin larvae do not migrate beyond the mucous membrane of the cecum and colon, so their pathogenic effects are usually less dramatic than those inflicted by the larvae of *Strongylus* species. However, infection by large numbers of arrested cyathostomin larvae causes a distinct clinical disease that usually is observed in late fall, winter, or early spring (Mirck, 1977). This form of cyathostominosis is characterized by watery diarrhea associated with severe inflammation of the mucous membrane of the cecum and colon, and often terminates fatally. Affected horses display persistent diarrhea, progressive emaciation, and marked hypoalbuminemia sometimes attended by anasarca. The feces may be negative for strongylid eggs, and the history often includes regular and vigorous anthelmintic medication without effect (Church, Kelly, and Obwolo, 1986; Jasko and Roth, 1984). There are many more larvae than can be accommodated as adult parasites, and as they mature, many are swept out with the manure. Lesions consist of granulomatous colitis, and masses of cyathostomin larvae are embedded in the mucous membrane (Figure 4-85). Massive

invasions of the bright red fourth-stage larvae of *Cylicocyclus insigne* riddling the mucosa of the large intestine are particularly impressive in this regard. Most of the worms are immature, and egg counts are therefore misleadingly low. Anthelmintic therapy has no influence on the course of the disease, although continued treatment will reduce the numbers of worms being passed in the feces (Deprez and Vercruysse, 2003). Church, Kelly, and Obwolo (1986) diagnosed their two cases heroically by taking full-thickness biopsies of the jejunum and cecum or ventral colon, and cured both patients with steroid therapy directed at the inflammatory reaction. In one case, dexamethasone (20 mg) was administered intramuscularly each day for 4 days and on alternate days thereafter, with the dose reduced by 4 mg every fourth day. In the second case, dexamethasone (20 mg) was administered intramuscularly for 10 days. In both cases, response to steroid therapy was dramatic, with improvement in fecal consistency noted within 24 hours and return to normal serum albumin levels within 1 week.

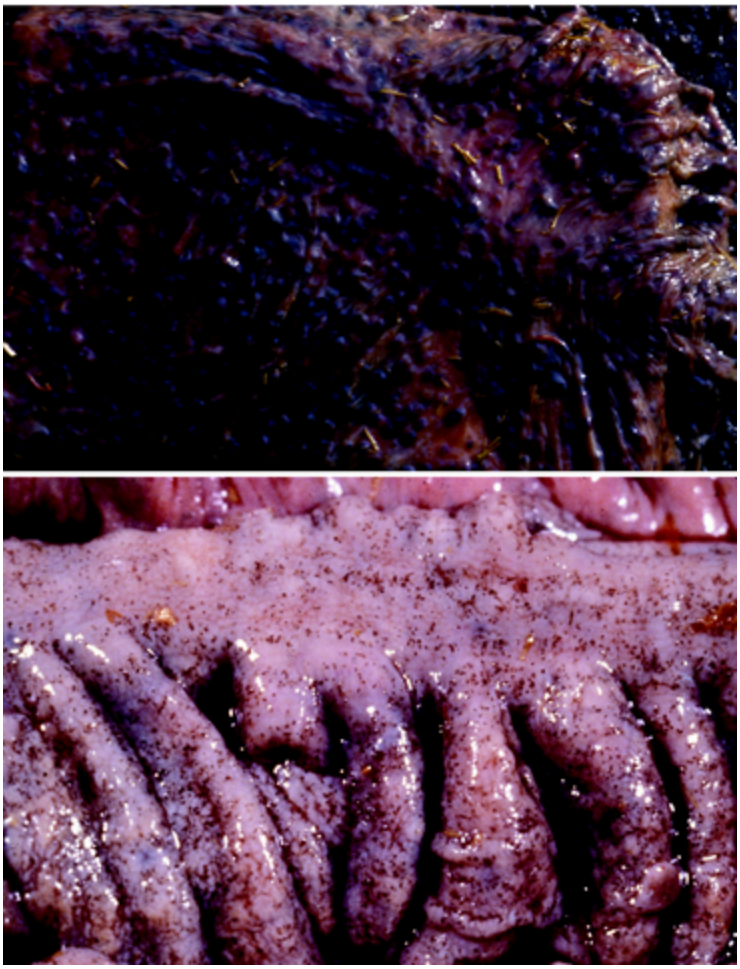

FIGURE 4-85 Fourth-stage larvae and juvenile adult "small strongyles" (Cyathostominae) in the colonic mucosa of a horse. Massive invasions such as this usually cause severe diarrhea.

The cyathostomin larvae encysted in the mucosa are basically unaffected by routine pyrantel, fenbendazole, or oral ivermectin at 0.2 or 1.0 mg/kg (Klei et al, 1993). Moxidectin at 0.3 or 0.4 mg/kg has effects against the more mature encysted larvae but is less efficacious against the younger third-stage larvae (Bairden et al, 2006; Xiao, Herd, and Majewski, 1994). Fenbendazole at a dose of 10 mg/kg/day for 5 days has been labeled as effective against both

encysted early third-stage larvae and against older encysted third-stage and fourth-stage larvae.

Treatment and Control of Strongylid Infections in Horses

Horses, asses, and mules host a far greater variety of strongylid parasites than ruminants and other domestic animals do. Even an apparently healthy horse may be infected with tens or even hundreds of thousands of small strongylid worms (Cyathostominae). Most equine parasites are distributed wherever horses are kept all over the world. The relative abundances of individual species may vary from place to place, but the group as a whole seems well adapted to a wide range of climates. In fact, the conditions under which horses are kept and the uses to which they are put seem to have far more influence on the mix of strongylid parasites they harbor than does the part of the world they happen to inhabit. This is in stark contrast to the situation in ruminants. For example, two sheep farms lying a few miles apart but at substantially different altitudes may have completely different parasite problems because the ecologic conditions at pasture favor development and survival of the infective larvae of different species of trichostrongyloids at different elevations.

With horses, it is a case of management more than of weather. Backyard ponies, livery horses, show and race horses, and horses kept for breeding purposes follow distinctly different careers and therefore present distinctly different problems for parasite control. “Because management of horses is so variable and the uses to which

horses are put are so different, recommendations as far as control of horse parasites should be tailored to the particular horse establishment rather than to a set of universal recommendations" (Craig and Suderman, 1985). "What's a good worming schedule for horses?" is a common but naive question.

About the most strongylid-contaminated environment ever devised for a horse is the neat little paddock that, in wealthy neighborhoods at least, is surrounded by a white board fence. There is rarely enough grass in such an enclosure to satisfy the horse's nutritional needs for more than a few weeks each year, so hay and grain must be fed to make up the difference. Great masses of horse manure accumulate, and thriving hordes of strongylid infective larvae develop in them and spread out onto the surrounding grass. The horse enjoys nibbling whatever grass is available and is capable of cutting it closer than a lawnmower. In such a situation a horse cannot fail to ingest large numbers of infective strongylid larvae. A sensible solution to this problem might be to provide horses the exercise and fresh air they need in bare paddocks containing no green plants at all. However, the almost universally adopted "solution" is to keep the horses in their green exercise lots and try to trim the worm population to subclinical levels by periodic administration of anthelmintic drugs. This program has been pursued so energetically that the strongylid parasites of horses excel over those of all other hosts relative to benzimidazole resistance, at least in North America.

On many breeding farms, all horses older than 2 months are routinely dewormed every 4 to 8 weeks (Drudge and Lyons, 1965). The objective of this program is to prevent contamination of the pasture with strongylid eggs, and that is why it is essential that all horses on the premises be treated. Piperazines are effective against both ascarids and cyathostomes and are therefore the logical choice for worming foals aged up to 6 months. Thereafter, drugs effective against *Strongylus* species should be substituted. On the basis of epidemiologic evidence, the most essential of all strategic treatments is that administered in spring, around foaling time. It is during this period that the adult worm population is greatly augmented through maturation of arrested and migrating larvae. The fecundity of these worms is also increased, and larger numbers of larvae reach the infective stage, thus posing a threat to young, susceptible horses. Elimination of these egg-laying worms in spring renders the pastures safer for grazing horses (Duncan, 1974).

Adult *S. vulgaris*, *S. edentatus*, *S. equinus*, cyathostomes, *Oxyuris* species, and *Parascaris* species are susceptible to febantel, fenbendazole, ivermectin, oxibendazole, and pyrantel pamoate. Administration of a macrocyclic lactone in fall and early spring affords control of ascarids and stomach bots.

Larvae of *S. vulgaris* migrating in the cranial mesenteric artery and its ramifications are accessible to attack by several anthelmintics. Ivermectin is highly effective in a single dose at 0.2 mg/kg (Klei et al, 1984; Lyons, Drudge, and Tolliver, 1982; Slocombe and McCraw, 1980, 1981; Slocombe et al, 1983).

Fenbendazole may be administered in a single dose of 30 to 60 mg/kg (Duncan et al, 1977) or in five daily doses of 7.5 to 10 mg/kg (Duncan, McBeath, and Preston, 1980). Oxfendazole is effective at a dose of 10 mg/kg (Duncan, McBeath, and Preston, 1980; Kingsbury and Reid, 1981; Slocombe et al, 1986).

Anthelmintic resistance

Phenothiazine, thiabendazole, cambendazole, mebendazole, fenbendazole, oxfendazole, and febantel are no longer as effective against small strongylids as they were when first introduced (Drudge and Elam, 1961; Drudge and Lyons, 1965; Drudge, Lyons, and Tolliver, 1977, 1979; Hagan, 1979; Slocombe et al, 1977). Drudge, Lyons, and Tolliver (1979) identified five species *(Cyathostomum catinatum*, *Cyathostomum coronatum*, *Cylicocyclus nassatus*, *Cylicostephanus goldi*, and *Cylicostephanus longibursatus)* that exhibited cross-resistance to cambendazole, fenbendazole, mebendazole, oxfendazole, and thiabendazole. However, all of these worms were highly susceptible to 10 mg/kg of oxibendazole, a 2-amino substituted benzimidazole. Later trials after repeated dosing of the herd for 14 years with oxibendazole showed that these five species of worms were resistant to other benzimidazoles but still affected by ivermectin and piperazine (Lyons et al, 1996). Resistant populations also may be controlled with pyrantel pamoate, with ivermectin, or with a benzimidazole administered with piperazine. The selection of populations of these five cyathostome species resistant to benzimidazole anthelmintics was rapid, although the

large strongylids and other nematode parasites of horses are still readily killed with these products. In response to the developing resistance, Duncan (1982) suggested that in any worm control program, drugs of different chemical structures should be alternated every 6 to 12 months to reduce the likelihood of the development of resistant worm populations; however, as Dr. Kaplan has recently stated, the currently accepted opinion is that the traditional rotation program is probably no longer the best approach (Briggs et al, 2004).

Because resistance is the inevitable result of frequent, regular anthelmintic medication, a better course might be to worm only those horses with significant fecal egg counts (e.g., 100 eggs per gram). Such a process of selective chemotherapy has been tried with horses in a polo string (Hamlen-Gomez and Georgi, 1991). This work showed that certain horses may have had a predisposition to infection and that strategic deworming of chronic egg shedders resulted in a significant savings over regular, routine deworming. The possible combination of selective chemotherapy with the use of a daily deworming product such as Strongid-C (pyrantel tartrate) could possibly lead to significant improvements in parasite management in certain herds of horses.

Coles et al (1999) reported on the discovery of large strongyles that were resistant to pyrantel. Strongyle eggs were collected from the feces of the three horses that had high numbers of eggs after treatment, and they were found by in vitro methods to apparently

be resistant. A second treatment of one horse had very little effect on the fecal egg counts after treatment. Culture of the larvae to the infective stage allowed it to be determined that all three horses were shedding some eggs of *S. edentatus* and one horse was shedding mainly the eggs of *S. edentatus*. This appears to be the first report of large strongyle resistance to any anthelmintic.

Remarkably, and to the great advantage of the horse, avermectin resistance has not yet been documented among any of the small strongyles. Recent work has indicated that there may be a trend toward resistance in some populations, but there is still no definite evidence that resistance is present (von Samson-Himmelstjerna et al, 2007). The lack of avermectin resistance in the equine cyathostomes remains a mystery to most parasitologists. Possible theories include no resistance gene(s) to be selected by treatment pressure (considered the least likely by many); the avermectins as dosed having only a minimal "tail" effect (a period when worms are surrounded by less than curative doses of drug); ivermectin having no effect on encysted cyathostomes, leaving them intact as an untreated refugia (thought the benzimidazoles may have all had some effect on the encysted forms); and maybe just luck. We can hope that this continues to be the case forever, but, even with all the evidence to the contrary, it is expected that sooner or later the small strongyles of the horse will become resistant to this class of compounds. Therefore it is a good idea to keep periodically doing egg counts before and after treatment to verify product efficacy.

Pasture management

Dr. Georgi used to say something to the effect that "the king's horses probably had fewer worms." The reason was simply that the fecal matter was always immediately picked up after deposition—that is, with sufficient manpower it is theoretically possible to completely break the life cycle of the common horse parasites. This is exactly the concept behind the development by Herd of both a mechanical pasture vacuum and a pasture sweeper (Herd, 1986). Horses also will often refuse to graze in areas where they defecate, dividing a pasture into areas called roughs and lawns. It has been suggested that this may be a means by which most horses reduce their intake of strongyle larvae, although this may not be true in smaller pastures (Medica et al, 1996). Dragging and harrowing pastures when occupied will reduce roughs but may spread infected feces over the entire pasture, increasing the chance for a horse to ingest larvae. Composting of horse manure before spreading will kill any parasite eggs that are present.

Family Chabertiidae

Subfamily Oesophagostominae and Chabertiinae

Identification

There is a transverse fold of cuticle ("ventral groove," see Figure 4-63) on the ventral side of the body just posterior to the buccal cavity. The buccal cavity varies in size from small (e.g., *Oesophagostomum columbianum*, Figures 4-86 and 4-87) to very large

(e.g., *Chabertia ovina*, Figures 4-88 and 4-89). Oesophagostomins are parasites of the large intestines of ruminants (*O. columbianum*, *Oesophagostomum venulosum*, *Oesophagostomum radiatum*, and *C. ovina*), swine (*Oesophagostomum dentatum*, *Oesophagostomum brevicaudum)*, and primates (*Conoweberia* species and *Ternidens deminutus*).

FIGURE 4-86 *Oesophagostomum columbianum,* dorsoventral view of buccal and anterior esophageal regions.

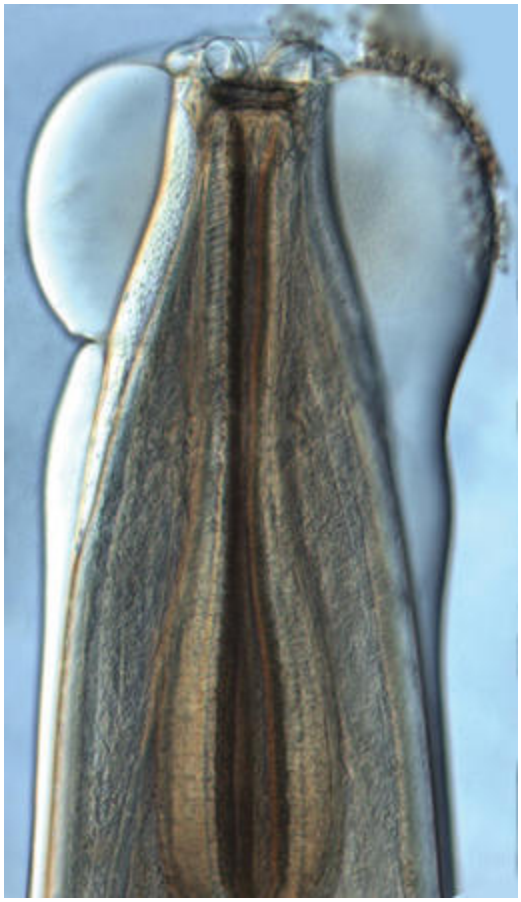

FIGURE 4-87 *Oesophagostomum columbianum,* lateral view of buccal and anterior esophageal regions.

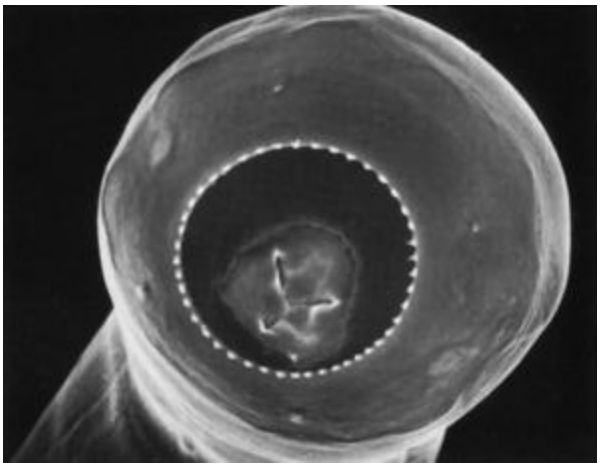

FIGURE 4-88 *Chabertia ovina,* head-on. The oral end of the esophagus with its triradiate lumen is visible at the base of the buccal cavity.

FIGURE 4-89 *Chabertia ovina,* lateral view of buccal cavity and anterior esophageal regions.

Importance

Oesophagostomins are called *nodular worms* because their parasitic larvae tend to become encapsulated by a somewhat excessive reactive inflammation on the part of the previously sensitized host. Acute inflammation may lead to clinical disease characterized by fetid diarrhea that may be fatal. The nodules later caseate and calcify, and severe involvement may interfere mechanically with normal intestinal motility. Clinical signs in ruminants and swine usually are associated with these reactions to the larval stages in the wall of the bowel and not to adult worms in the lumen. Therefore clinical disease is likely to be associated with nonpatent infection,

and diagnosis must depend on correct interpretation of clinical signs or postmortem findings. The feces are watery, dark, and very fetid. Weakness is marked, and emaciation rapid. Necropsy examination conducted during an outbreak of nodular worm disease reveals an inflamed intestine studded with active nodules filled with creamy pus, each containing a living larva (Figure 4-90). Caseated and calcified nodules should not be held accountable for current acute parasitic enteritis but may occasionally cause intussusception or other mechanical abnormality.

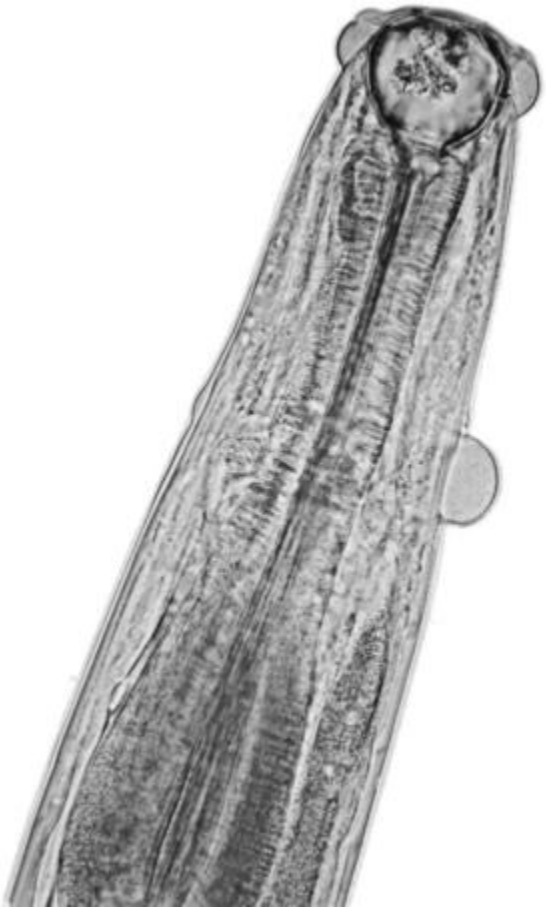

FIGURE 4-90 *Oesophagostomum radiatum* fourth-stage larva from a nodule in the intestinal wall of a calf. *Oesophagostomum* species fourth-stage larvae are unusual in having buccal cavities relatively larger than those in the adult stage.

The most important effect of *Oesophagostomum* species in swine is the formation of nodules in the gut wall by developing third-stage larvae. The fourth-stage larvae emerge from these nodules as early as 2 weeks after infection, or they remain for several months. Nodule formation may be accompanied by catarrhal enteritis, spoils sausage casings, and probably interferes with maximum growth of young swine. A rise in egg output by sows peaks at 6 or 7 weeks after farrowing and then drops off rapidly. This could be an important epidemiologic factor in situations favorable for the development of infective larvae.

Conoweberia apiostomum, *Conoweberia stephanostomum*, and *T. deminutus* are pathogenic, especially in recently captured primates with the unaccustomed stresses of confinement and transportation (see Figures 8-83 and 8-84Figure 8-83Figure 8-84). Acute and chronic disease syndromes caused by *C. stephanostomum* occurred in gorillas from the thirteenth to fortieth days after capture (Rousselot and Pellissier, 1952). The chronic syndrome consisted of intermittent diarrhea, paleness of the mucous membranes, and the presence of eggs in the feces. In the acute form, the gorilla refuses to eat or nibbles a little and suffers some diarrhea but very soon passes only small quantities of glairy mucus streaked with blood, much like that observed in acute amebic dysentery of humans. The gorilla remains either lying down or sitting with both hands on its head in an attitude of human desperation.

Anthelmintic medication

Many different products are approved for treating infection with the adults of *Oesophagostomum* and *Chabertia* species in cattle and sheep and *Oesophagostomum* species in swine.

Family Stephanuridae, Subfamily Stephanurinae

Identification

Stephanurus dentatus, the kidney worm of swine, is a stout (up to 2 by 40 mm) parasite of the hepatic, renal, and perirenal tissues, axial musculature, and spinal canal of swine and sometimes of cattle. The buccal cavity is cup-shaped and directed straightforward with 6 to 10 triangular teeth at its base (Figure 4-91). The gut is convoluted, the spicules equal and short, and the bursa reduced.

FIGURE 4-91 *Stephanurus dentatus*.

Earthworms serve as intermediate hosts. The life history may be direct or could involve earthworms as facultative intermediate hosts, infection occurring by ingestion or skin penetration of third-stage larvae or by ingestion of infected earthworms. Once in the body of the pig, the larvae enter the liver and spend 4 to 9 months wandering destructively there. Some are trapped by an encapsulating tissue reaction, but the rest migrate to the retroperitoneal tissues surrounding the kidneys and ureters. Eggs appear in the urine 9 to 16 months after infection and persist for 3 years or longer. Piglets may become infected in utero (Batte, Harkema, and Osborne, 1960; Batte, Moncol, and Barber,1966).

S. dentatus larvae migrate abortively in other hosts (e.g., cattle) and frequently lose their way in pigs. Not only liver and kidney but also choice loin chops are frequently condemned because of these destructive larvae. Although migration of *S. dentatus* larvae in the spinal cord may cause posterior paralysis, otherwise the clinical signs of infection are not distinctive. Extensive liver damage may lead to emaciation and death.

Anthelmintic medication

Levamisole and fenbendazole are the approved anthelmintics for the treatment of *S. dentatus* infections. Ivermectin in a mixture as a feed additive designed to deliver a dosage of approximately 0.1 mg/kg daily for 7 days is also approved for the treatment and control of *S. dentatus* infection. Ivermectin (0.3 mg/kg body weight subcutaneously) has a marked effect on *S. dentatus* infections

(Becker, 1986). Albendazole is very active against both adult and immature *S. dentatus* but is not approved for use in swine in the United States.

Family Syngamidae

The subfamily Syngaminae includes the genera *Syngamus* and *Cyathostoma* (not *Cyathostomum*) in birds and *Mammomonogamus* in mammals (see Figure 7-57). All three have large buccal capsules (Figure 4-92), and all are parasites of the upper respiratory tract. Males and females of *Syngamus* and *Mammomonogamus* species are fused permanently in copula. Earthworms serve as paratenic hosts for *Syngamus*. *Syngamus trachea* infections have caused the deaths of farmed rheas, and in these birds, treatment with fenbendazole at 25 mg/kg was successful therapy (de Witt, 1995). Ivermectin also is highly effective in the treatment of *Syngamus* infections.

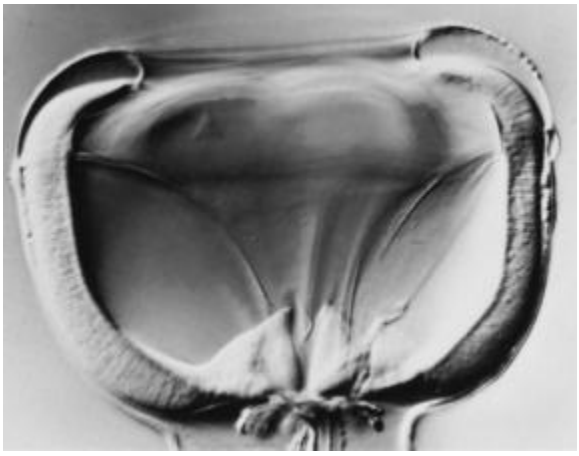

FIGURE 4-92 *Cyathostoma* (family Syngamidae) buccal capsule.

Superfamily Ancylostomatoidea

Family Ancylostomatidae

Identification

Adult hookworms are parasites of the small intestine. Some species such as *Ancylostoma caninum* cause the loss of large quantities of blood from their hosts, whereas others such as *Uncinaria stenocephala* remove very little. Fresh specimens of *A. caninum* tend to be dark in color, whereas those of *U. stenocephala* are quite pale. All hookworms have a large buccal cavity directed obliquely dorsally, so the anterior end of the worm is more or less "hooked," but, again, this trait is variably developed as can be appreciated from a comparison of *Bunostomum* (Figure 4-93) and *Globocephalus* species (Figure 4-94). The male hookworm, provided with well-developed bursa, is often found in copula with the female, the two worms forming a T because the vulva is located some little distance from the caudal extremity. The female lays typical strongylid eggs, and these appear in the feces during the morula stage of development.

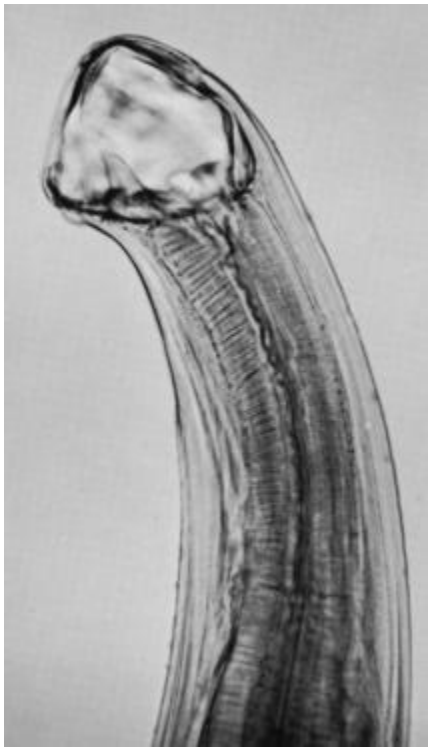

FIGURE 4-93 *Bunostomum* sp.

FIGURE 4-94 *Globocephalus urosubulatus*, a hookworm of swine; dorsal *(left)* and lateral *(right)* aspects.

Courtesy Dr. E.I. Braide.

Two subfamilies are distinguished: Ancylostomatinae and Bunostominae. “Carnivorous hosts are parasitized only by the Ancylostomatinae, herbivorous hosts by the Bunostominae, and omnivorous hosts by both subfamilies” (Lichtenfels, 1980).

The subfamily Ancylostomatinae includes the genera *Ancylostoma*, *Uncinaria*, *Globocephalus*, and *Placoconus*.

The most common hookworms of the dog and cat are species of *Ancylostoma* and *U. stenocephala*. Species of *Ancylostoma* have buccal cavities with sharp teeth, whereas those of *Uncinaria* have cutting plates (Figure 4-95). The ventral margin of the stoma of *Ancylostoma* is armed by one *(Ancylostoma braziliense)*, two *(Ancylostoma duodenale)*, or three *(A. caninum, Ancylostoma tubaeforme)* pairs of sharp teeth. *A. braziliense* matures in dogs and cats, *A. duodenale* in humans, *A. caninum* in dogs (see Figures 4-64 and 4-95), and *A. tubaeforme* in cats (Figure 4-96). The ventral margin of the stoma of *Globocephalus urosubulatus* of swine has neither plates nor teeth (see Figure 4-94). The buccal capsule of *Placoconus lotoris* of raccoons is formed of five articulating plates (Figure 4-97).

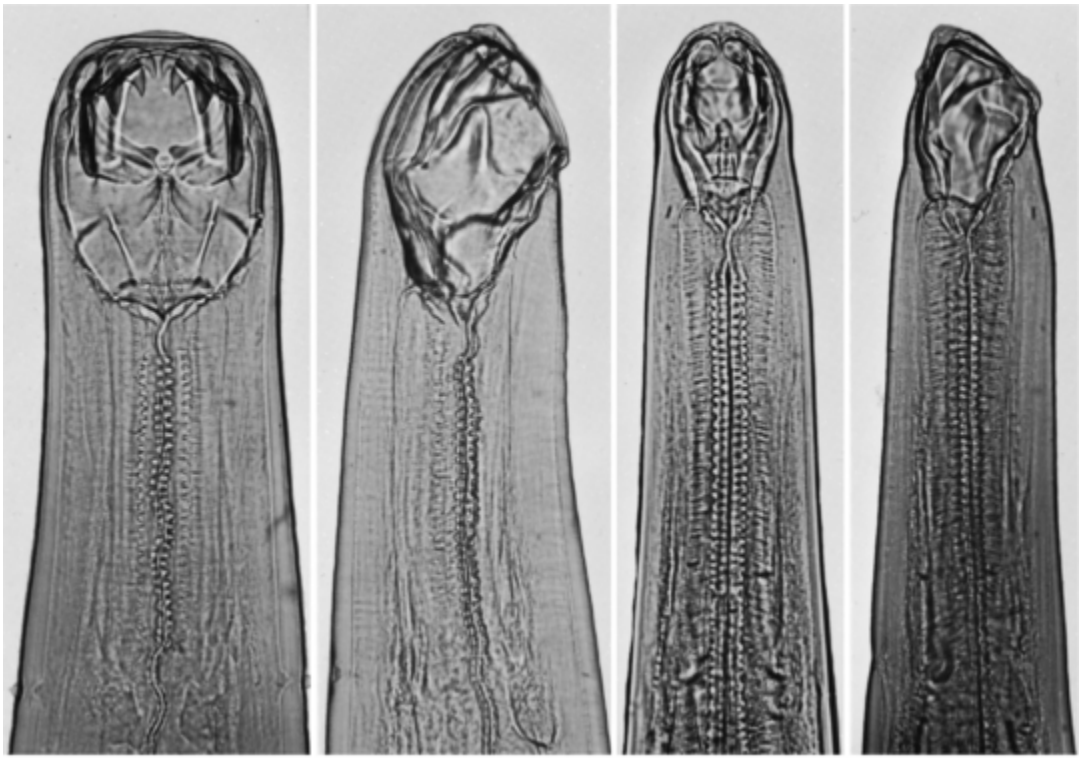

FIGURE 4-95 Dorsoventral and lateral aspects of the buccal and esophageal regions of *Ancylostoma caninum* and *Uncinaria stenocephala*.

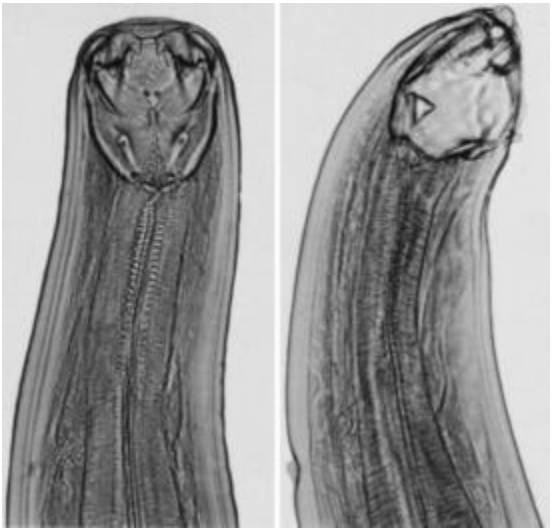

FIGURE 4-96 *Ancylostoma tubaeforme*. At left is the dorsoventral aspect of the stoma, and at right, its lateral aspect.

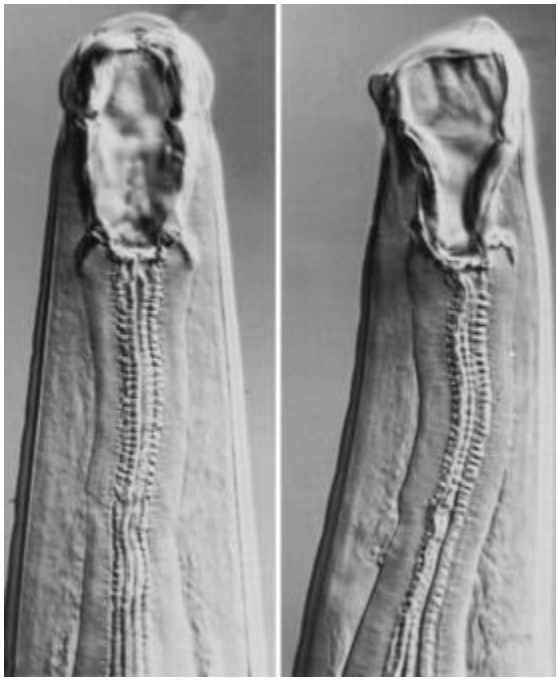

FIGURE 4-97 *Placoconus lotoris*, hookworm of the raccoon; dorsoventral *(left)* and lateral *(right)* aspects of the buccal and esophageal regions.

The subfamily Bunostominae includes the genera *Bunostomum* of ruminants (see Figure 4-93), *Necator* of humans, *Bathmostomum* of elephants, and *Grammocephalus* of elephants and rhinoceroses.

Life history

Infection typically occurs through either ingestion or skin penetration by infective larvae, which then undergo more or less extensive migrations through the tissues of the host before developing into adult hookworms in the small intestine (Figure 4-98; see also Figure 7-44). Hookworms in sea lions, seals, and dogs are capable of infecting neonates through transmammary transmission; transmammary transmission does not appear to occur with the hookworm of the cat.

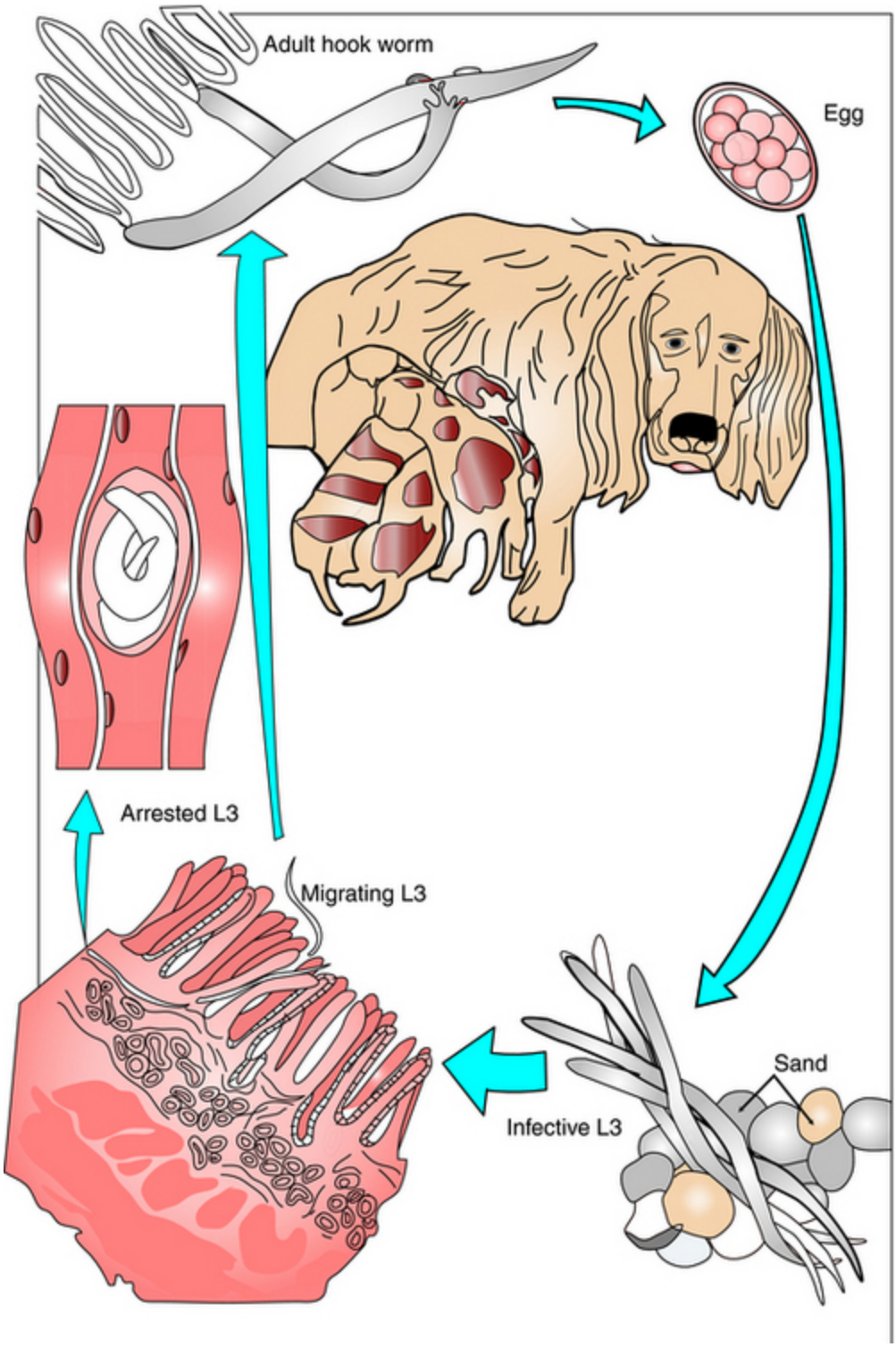

FIGURE 4-98 Life history of *Ancylostoma caninum*. The actively motile sheathed larva develops in 2 to 8 days. Shaded, well-drained soils, warmth, and humidity provide optimum conditions for development and survival of this stage, which may infect the host either on being swallowed or by penetrating its skin. Eggs are shed in the feces about 2

weeks after ingestion of larvae and about a month after penetration of skin by larvae. However, not all larvae mature. Some invade skeletal muscle cells (Little, 1978) or gut wall (Schad, 1974, 1979) and enter an arrested state of development. Arrested larvae later become reactivated in response to obscure cues and migrate either to the small intestine, where they mature, or to the mammary glands, where they are shed in the milk and infect the pups. Arrested larvae are regularly reactivated during the last 2 weeks of pregnancy.

Anthelmintic medication

In ruminants, hookworms can be treated with avermectins, levamisole, or various benzimidazoles. In pigs, treatment is usually performed using an avermectin. Cats can be treated with labeled products containing ivermectin, selamectin, moxidectin, milbemycin oxime, pyrantel pamoate, emodepside, or febantel. Dogs can be treated with many available products that contain pyrantel pamoate, febantel, fenbendazole, milbemycin oxime, and moxidectin.

In Australia there is concern that the hookworm of the dog, *A. caninum*, is becoming resistant to treatment with pyrantel. This was first suggested by a report from New Zealand of a dog imported from Australia that had a hookworm infection that would not clear with pyrantel (Jackson et al, 1987). Larvae grown from eggs in the feces of this dog were used to infect two other dogs that could not be cleared of their infections with a 5× dose of pyrantel. There have since been other reports of reduced efficacy from Australia (Hopkins and Gyr, 1991; Hopkins, Gyr, and Schimmel, 1998). Most recently, there has been a controlled trial in Australia that has shown poor efficacy against worms in experimentally infected dogs

(Kopp et al, 2007). This appears to provide additional rationale for practitioners to order posttreatment fecal examinations to monitor the effects of therapy.

Hookworm disease of dogs

The principal importance of hookworms is associated with their ability to cause anemia. Hookworm disease varies in severity from asymptomatic infection to rapidly fatal exsanguination, depending on the magnitude of the challenge and the resistance of the host. Magnitude of challenge is determined by the virulence and number of hookworms. Virulence depends on the species of hookworm involved. *A. caninum* is much more pathogenic for dogs than *A. braziliense* or *U. stenocephala* because it causes much greater blood loss per worm. The number of hookworms infecting a particular host depends very heavily on the degree of exposure to infective larvae. Exposure, in turn, depends on the extent to which infected hosts have contaminated the environment by shedding eggs in their feces, and on the suitability of the substrate (gravel and sand are ideal), temperature, and moisture for development and survival of infective larvae.

Infection of nursling pups with *A. caninum* occurs through the mammary gland via **transmammary transmission** (Kotake, 1929a, 1929b; Stone and Girardeau, 1966, 1968). Transplacental transmission, if it occurs at all, is overshadowed by transmammary infection (Stoye, 1973). A bitch exposed to only one substantial oral or percutaneous infection will shed *A. caninum* larvae in her milk for

the next three lactations, although the larval output will diminish with each lactation. Currently available anthelmintics administered at dosages to treat and control adult hookworm infections lack significant efficacy against hookworm larvae arrested in the tissues. The arrested larvae of *A. caninum* may be present in dogs receiving monthly treatment with a combination heartworm preventive, and they are thus still available to move through the mammary gland to the intestines of the nursling pups (see Figure 4-98).

Host resistance is resolvable into two abilities: (1) The ability to limit the number of hookworms maturing in the small intestine is influenced by age, premunition, and acquired immunity. As dogs grow older, they become more resistant to hookworms whether or not they experience infection. Immunity acquired from previous infection confers increased resistance, but this is difficult to disentangle from the influences of advancing age and from the marked inhibition of further infection exerted by a residual population of hookworms (premunition). (2) The ability to compensate for blood loss caused by hookworms is influenced by the hematopoietic capacity and state of nutrition of the individual and by the presence or absence of other stresses.

Clinical forms of disease

Four different forms of canine hookworm disease can be distinguished. Peracute disease occurs in the neonatal pup. Acute disease occurs in older pups and mature dogs. Chronic hookworm

infection is not uncommon in adult dogs and may or may not be associated with clinical signs.

Peracute hookworm disease results from the passage of infective larvae from dam to nursing pups in the milk. Transmammary infection of very young pups with as few as 50 to 100 adult *A. caninum* may prove fatal. Typically, the pups appear healthy and sleek the first week, then sicken and deteriorate rapidly the second week. The visible mucosae are very pale, and the soft to liquid feces are very dark in color because the blood shed by the hookworms in the small intestine has been partially digested on the way out. The worms do not lay eggs until the sixteenth day of infection, so diagnosis must rest on the clinical signs of disease. Prognosis is guarded to poor with or without treatment.

Treatment is often to little avail in peracute neonatal hookworm disease. Blood transfusion is essential to keep affected pups alive long enough for anthelmintic medication to take effect, and anthelmintic medication must be administered immediately to stop the loss of blood as soon as possible. On no account should anthelmintic therapy be delayed. It is impracticable to attempt replacement of hookworm blood losses by transfusion for any appreciable length of time.

Routine cage, pen, and run sanitation and periodic anthelmintic medication of all adult dogs are essential to reduce the level of environmental contamination with hookworm larvae. When neonatal losses have already been experienced, it is essential to

examine the visible mucosae of each pup daily from about the seventh day of life until weaning and to administer an anthelmintic at the first sign of anemia. Alternatively, antihookworm therapy should begin 2 weeks after pups are whelped and continue weekly for 3 months (Kelly, 1977).

Bitches that have lost litters may be treated with fenbendazole, 50 mg/kg per day, from the fortieth day of gestation to the fourteenth day of lactation, to prevent further losses (Burke and Roberson, 1983; Düwel and Strasser, 1978). This treatment attacks the reactivated larvae and is effective but rather expensive. It also has been shown that ivermectin treatment of the bitch (0.5 mg/kg body weight administered 4 to 9 days before whelping followed by a second treatment 10 days later) can also prevent puppies from being infected by larvae passed in the milk (Stoye, Meyer, and Schneider, 1987). Treatment of four bitches with a single 1 mg/kg subcutaneous injection of doramectin failed to prevent transmammary infection of all their puppies, with five of the 23 puppies, representing three of the four litters, becoming infected (Schnieder et al, 1996).

Acute hookworm disease results from sudden exposure of susceptible older pups to large numbers of infective larvae. Even mature dogs may be overwhelmed if exposure is sufficiently great. Usually, many eggs will be found in the feces of affected animals, but clinical signs may precede the appearance of eggs by about 4 days in particularly heavy infections. In acute hookworm disease and in chronic (compensated) hookworm infection, response to

simple anthelmintic therapy is usually dramatic. Supportive therapy beyond provision of an adequate diet is unnecessary.

Chronic (compensated) hookworm infection is usually without signs. Diagnosis rests on the presence of hookworm eggs in the feces and measurable reductions in erythrocyte count, blood hemoglobin, or packed cell volume. Occasionally, however, incomplete adjustment between parasite and host produces a state of chronic ill health.

Secondary (decompensated) hookworm disease usually involves older dogs that have more ailing them than just hookworms. The cardinal sign again is profound anemia, usually in a malnourished or even emaciated animal. The hookworms may indeed kill the dog, but it is important in this case to recognize that they play a secondary role. An accurate diagnosis, for example, of "malnutrition with secondary hookworm infection" logically leads to effective therapy. The efficacy of mebendazole and fenbendazole was dramatically reduced in iron- and protein-deficient rats infected with *Nippostrongylus brasiliensis* (Duncombe et al, 1977a, 1977b). Clinical experience indicates that protein sufficiency is also essential to efficient anthelmintic action against hookworms and other parasites. Cases of malnourished dogs that have secondary hookworm disease and dogs that seem adequately nourished but fail to respond to anthelmintic medication should first be given a course of supportive therapy (e.g., high-protein diet, ferrous sulfate orally or parenteral iron injections, vitamins, and, if necessary, blood transfusion) and then remedicated with a suitable anthelmintic.

Arrested larvae and the refractory egg shedder

Arrested *A. caninum* larvae are found in the intestinal wall and skeletal muscle tissue of the adult dogs, and these arrested larvae are not killed by routine treatment. Little (1978) found that larvae of *A. caninum* are continually migrating from the muscles to the intestine through the lungs. When adult worms were already present in the intestine, few if any of these larvae developed to maturity, but when the adult worms were eliminated by treatment, these larvae from the muscles were able to mature and start producing eggs in about 4 weeks. A second course of treatment then eliminated the new adults, and these in turn were replaced by more larvae from the muscles. Schad found that if infective larvae were chilled before being administered orally to dogs, they became arrested in the gut wall. When reactivated, these larvae were able to become established in the intestine in the presence of adults, and neither removal of adult worms with anthelmintic nor immunosuppression with prednisolone initiated resumed development of the arrested *A. caninum* larvae (Schad, 1974, 1979; Schad and Page, 1982). Thus, besides arrested larvae serving as a source of infection for nursing puppies, they also serve to repopulate the intestine with adults that contaminate the environment. Practicing veterinarians frequently encounter dogs with hookworm infections that refuse to "clean up" even after repeated treatments with a variety of drugs over the course of many months. This "larva leak" phenomenon provides a plausible explanation for these refractory cases.

Environmental contamination

Because hookworm infection is common and the females are prodigious egg layers, populations of infective larvae are likely to bloom whenever the weather becomes favorable for their development and survival. Therefore most frank hookworm disease cases occur during late spring, summer, and early autumn in temperate climates, particularly when mild weather is accompanied by adequate rainfall. The infective challenge may become overwhelming in carelessly managed kennels and pet shops where feces are allowed to accumulate long enough to permit infective larvae to develop. Unpaved runs are particularly favorable for the perpetuation of the parasite because the feces mixes with the soil. This not only makes sanitation difficult but provides more favorable cultural conditions, especially when the soil is light, open textured, and well drained.

From 2 to 8 days are required for the morula in the hookworm egg to develop into an infective third-stage larva. Shirt-sleeve temperatures (23° to 30° C) and a moderately moist, well-aerated medium are optimal. Thus hookworm larvae develop well in shaded areas of well-drained soils but not in heavy, water-logged soils or where they are exposed to direct sunlight and desiccation. *Ancylostoma* eggs and larvae are destroyed by freezing, whereas those of *Uncinaria* are very resistant to cold. *A. caninum* larvae will not develop to the infective stage at temperatures consistently below 15° C. Above the optimum temperature for development (30° C),

larvae rapidly develop to the infective stage. It can be reached in 48 hours at 37° C, the highest temperature compatible with development (McCoy, 1930). Thus, compared with *Toxocara* eggs, soil pollution by hookworm infective larvae may be viewed as a temporary problem that a good hard freeze will probably solve.

People are always looking for ways to kill the larvae on soil or lawns, but there is no good method. During mild weather, sodium borate, broadcast at the rate of 10 lb/100 sq ft (0.5 kg/m^2) and raked in, will destroy hookworm larvae in gravel- or loam-surfaced runs. This treatment destroys vegetation as well as hookworm larvae and is therefore unsuitable for lawns. Resinated dichlorvos, an organophosphate, was reported to interfere with the development of first- and second-stage larvae of *A. caninum* (Kalkofen, 1971). Paved surfaces, cages, and the like should first be cleaned thoroughly and then mopped or sprayed with 1% sodium hypochlorite solution (Clorox). This solution kills the larvae or at least induces them to cast off their sheaths, after which they are more susceptible to drying and other unfavorable environmental stresses. Large commercial dog-rearing operations make extensive use of wire-bottomed cages and pens to effect the physical separation of the dogs from the bulk of their feces.

In most situations environmental protection is performed by the routine treatment of pet dogs and cats. Anthelmintic medication may be used to reduce the output of hookworm eggs in the feces and thus limit the degree of contamination of the environment with infective larvae. Therapeutic dosages may be administered monthly,

periodically, or when indicated by positive fecal examinations. Most monthly heartworm preventives will also do an excellent job in protecting the environment from hookworm eggs.

Cutaneous larva migrans

"Creeping eruption" (human cutaneous larva migrans) is a linear, tortuous, erythematous, and intensely pruritic eruption of the human skin usually caused by migration of a nematode larva (Kirby-Smith, Dove, and White, 1926). *A. braziliense* larvae are most frequently involved in the typical protracted cases, especially in the coastal regions of the southeastern United States (White and Dove, 1926). Accidental sporadic or experimental cases involving *A. caninum*, *U. stenocephala*, *Bunostomum phlebotomum*, *Strongyloides stercoralis*, and *Gnathostoma* spp. have also been reported, and the larvae of those species that normally mature in man *(A. duodenale*, *Ancylostoma ceylonicum*, and *Necator americanus)* produce a transient but otherwise typical creeping eruption in previously sensitized individuals. It should also be noted that larvae of *Gasterophilus* and *Hypoderma* species also migrate in human skin (James, 1947), producing a clinical condition properly termed *cutaneous larva migrans*. There is every reason to believe that after the larvae disappear from the skin that they will enter deeper tissues, where they will persist for extended periods (see Figure 8-86).

Probably no nematode larva capable of penetrating the skin is above suspicion in individual cases, but the epidemiologic importance of any particular species depends on many influences

beyond its intrinsic capabilities. For example, the etiologic prominence of *A. braziliense* may have much to do with the defecation behavior of dogs and cats, as may be surmised from the following description of circumstances surrounding infection, lesions, and symptoms by Kirby-Smith, Dove, and White (1926).

At least 50 percent of the cases of creeping eruption seen by the senior author are believed to have originated at the beach, the probable origin being traced to the soft damp sand in front of the beach buildings at points slightly above the high water mark. Such patients reported with lesions varying in numbers. They were not the most extensively infected ones. Persons with hundreds of lesions definitely attributed the origin of their infection to contact with damp sand when they were wet with perspiration while working: repairing an automobile, doing brick work, or making plumbing connections underneath houses, and the like.

The most recent visible lesion is a very narrow erythematous formation along the course traveled by the worm. Soon a slightly raised line representing the location of the burrow can be palpated. This line becomes visibly elevated, more or less continuous and vesicular. Sometimes bullae are formed. The surface of the lesion dries, resulting in a thin crust. When the parasite travels it moves from a fraction of an inch to several inches a day, advancing, as a rule, more rapidly at night.

To some patients the itching sensation resulting from infection is almost intolerable, whereas others endure it with less suffering. The

severity of the lesions, too, is more pronounced in some than in others.

The severity and persistence of the lesions are at least partly related to hypersensitivity resulting from previous exposure. The lungs may be invaded, but intestinal infection with mature worms ensues only in cases involving those species that are normal parasites of humans.

Human enteric infections with *Ancylostoma caninum*

Prociv and Croese (1996) reported on a series of human cases with eosinophilic enteritis from northern semitropical Queensland, Australia. Most of these cases came from typical suburban housing developments. An adult *A. caninum* was recovered at colonoscopy from the terminal ileum of one patient, and an unidentifiable adult hookworm was found on a portion of ileum resected from a second patient. There have since been additional cases reported from Australia and the United States in which adult *A. caninum* have been recovered and cases that have signs and serology suggestive of *A. caninum* infection (Prociv and Croese, 1996; Vikram-Khoshoo et al, 1995). Signs of infection have included obscure abdominal pain that may or may not be associated with an increased level of circulating eosinophils. Worms are not observed in most seropositive patients. It appears that these people became infected with infective-stage larvae by the cutaneous route as they went about parks and yards without shoes and socks. These cases provide yet another good reason why veterinary practitioners must insist that clients submit

fecal samples from their pets for annual evaluation and work with their clients to practice hookworm prevention and control.

Superfamily Metastrongyloidea

Metastrongyloids are parasites of the respiratory, vascular, and nervous systems of mammals. Most species whose life histories have been investigated require a snail or slug intermediate host. However, *Metastrongylus* species develop to the infective stage in earthworms, and *F. osleri* and *F. hirthi* infect their definitive hosts directly. The copulatory bursa is of the basic strongylid pattern but has suffered varying degrees of reduction in the evolution of different families. For example, the bursa is best developed in the family Metastrongylidae (Figure 4-99) but is reduced to mere papillae in the family Filaroididae. The vulva is close to the anus except in the family Crenosomatidae, in which it is located in the midregion of the body. The diversity of structure and biology displayed by members of the superfamily Metastrongyloidea makes further generalization precarious.

FIGURE 4-99 *Metastrongylus apri.*

Family Metastrongylidae

The family Metastrongylidae contains only one genus, *Metastrongylus*, all species of which are large white parasites of the bronchi and bronchioles of swine.

Identification

The mouth is flanked by a pair of trilobed lips. The spicules are long and thin, the bursa is well developed, and the vulva is near the anus (see Figure 4-99). When passed in the feces of infected swine, the egg contains a larva.

Life history

Oviparous females lay eggs containing first-stage larvae. The standard view is that these eggs do not hatch or develop into infective larvae unless they are ingested by an earthworm. However, continued high prevalence (50%) in Iowa swine despite confinement rearing and improved sanitation indicates that the earthworm may not be an obligatory intermediate host of *Metastrongylus* species (Ledet and Greve, 1966).

Metastrongylus species are of only modest pathologic and economic importance. It was once supposed that they acted as vectors of swine influenza virus, but substantial proof for this idea is lacking (Wallace, 1977).

Anthelmintic medication

Fenbendazole, levamisole, and ivermectin are approved anthelmintics with activity against swine lungworms.

Family Protostrongylidae

Identification

Protostrongylids have a well-developed bursa, spicule, and spicule guide, and the vulva is near the anus (Figure 4-100; see also Figure 4-68).

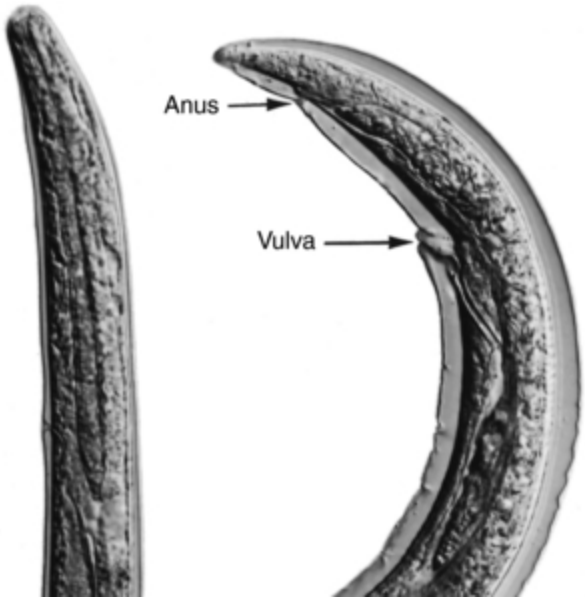

FIGURE 4-100 *Muellerius capillaris* female.

Life history

The oviparous protostrongylid females deposit unsegmented eggs in the surrounding lung, vascular, or neural tissues. These eggs develop into first-stage larvae before they appear in the feces. If these first-stage larvae are ingested by any of a wide range of snails and slugs, they develop in these intermediate hosts into doubly ensheathed

third-stage infective larvae. The protostrongylids considered here are all parasites of sheep and goats.

Protostrongylus

Protostrongylus rufescens lives in the smaller bronchioles, where they may cause localized lesions. Males of this brownish red species can be distinguished from *D. filaria* by their longer, comblike spicules (see Figure 4-68). The female *Protostrongylus* organism is prodelphic, whereas the female *Dictyocaulus* organism is amphidelphic. Fenbendazole-medicated salt has been used successfully to control protostrongylid lungworms in free-ranging Rocky Mountain bighorn sheep in Montana (Jones and Worley, 1997).

Muellerius

Muellerius capillaris (see Figure 4-100) is a tiny species so deeply embedded in lung tissue or reactive nodules that specimens are extremely difficult to dissect out intact. Antemortem diagnosis is less difficult because the active first-stage larvae are easily separated from the host's feces by the Baermann technique and are not difficult to distinguish from those of *Protostrongylus* and *Dictyocaulus* species (see Figure 7-61). *Muellerius* species are usually nonpathogenic at the levels of infection normally encountered in nature and agriculture, but heavy infections may have serious consequences, especially in goats.

Treatment

M. capillaris infection has been treated successfully in sheep with moxidectin (1% injectable solution at 0.2 mg/kg) and in goats with topical eprinomectin (0.5 mg/kg) (Geurden and Vercruysse, 2007; Papadopoulos et al, 2004). Also, levamisole, fenbendazole, albendazole, and ivermectin have been used to treat *M. capillaris* infections in sheep and goats, but results have been less than would be hoped for all these products.

Parelaphostrongylus

Parelaphostrongylus tenuis is normally a parasite of the meninges of the white-tailed deer, *O. virginianus*, in which species it rarely if ever causes disease (Figure 4-101). However, in abnormal hosts such as sheep, goats, llamas, camels, moose, caribou, reindeer, wapiti, fallow deer, and mule deer, *P. tenuis* tends to invade the nervous tissue proper, causing serious or fatal neurologic disease (Baumgärtner et al, 1985; Krogdahl, Thilsted, and Olsen, 1987; Mayhew et al, 1976; Nichols et al, 1986) (see Figures 8-93 and 8-94Figure 8-93Figure 8-94). Because *P. tenuis* rarely matures in these hosts, larvae are not shed in the feces. Therefore diagnosis is presumptive and based on the appearance of neurologic signs in ruminants that share their pastures with white-tailed deer. Cattle are now known to also succumb to infection with this parasite, and at least two cases have been reported (Duncan and Patton, 1998). Six horses had neurologic signs apparently associated with parelephostrongylosis, and worms were seen in the nerve tissue of two of these animals (Biervliet et al, 2004). A 6-month-old colt from

New York State developed severe encephalitis, was humanely killed, and was found to be infected with a worm that was consistent in morphology with *P. tenuis* (Tanabe et al, 2007).

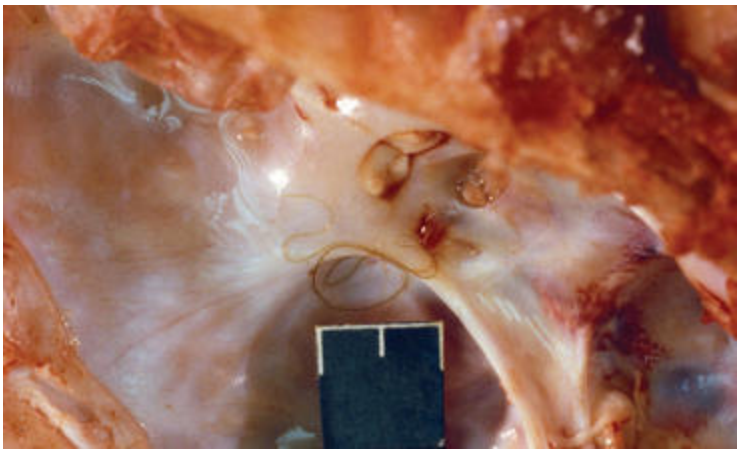

FIGURE 4-101 Adult *Parelaphostrongylus tenuis* in the brain cavity of a deer. The end of the scale is 2 cm across.

Family Crenosomatidae

Identification

Crenosomatids have well-developed bursae with a large dorsal ray, the uterus is amphidelphic with a prominent ovijectoral sphincter, and the cuticle is thrown into crenated folds, especially anteriorly (Figure 4-102). *Crenosoma vulpis* is less than 16 mm long and found in the bronchi and bronchioles of foxes *(Vulpes vulpes)*, wolves *(Canis lupus)*, raccoons *(Procyon lotor),* and dogs. *Troglostrongylus* species are parasites of Felidae.

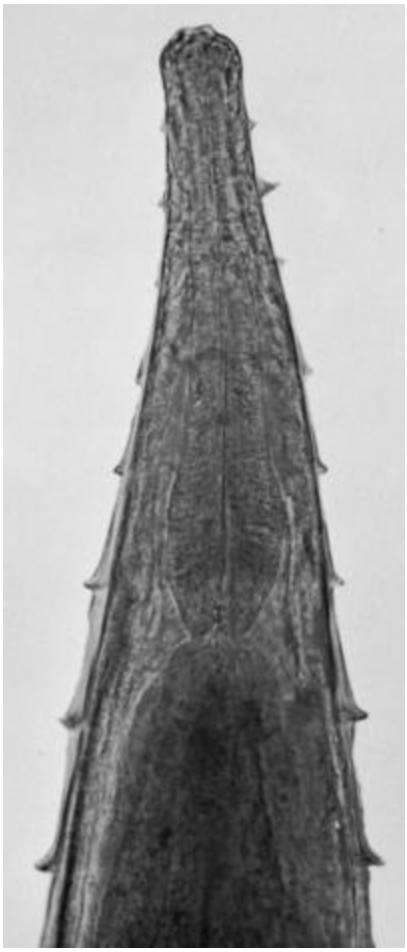

FIGURE 4-102 *Crenosoma* sp. from the lung of a bear.

Life history

The ovoviviparous females deposit first-stage larvae or thin-shelled eggs containing first-stage larvae. These ascend the trachea and descend the alimentary tract to exit in the host's feces (see Figure 7-27) and develop into infective third-stage larvae in snails and slugs. The definitive host becomes infected by ingesting infected mollusks; the prepatent period is 19 days (Wetzel, 1940a).

Treatment

Fenbendazole (50 mg/kg daily for 3 days) was apparently successful in curing an infection of *C. vulpis* in a Labrador retriever (Peterson et al, 1993). A survey of 55 afebrile dogs with chronic cough in Prince Edward Island, Canada, revealed that 15 (27.3%) were infected with *C. vulpis* (Bihr and Conboy, 1999). The dogs were successfully treated with a course of fenbendazole therapy (50 mg/kg daily for 3 to 7 days). A single treatment with milbemycin oxime cleared 32 naturally infected dogs of their *C. vulpis* infection (Conboy, 2004).

The high percentage of dogs positive for *C. vulpis* in Canada with the only sign being chronic cough indicates the need to carefully consider this worm in the differential for such a sign in regions where this worm is prevalent. As foxes become more and more abundant in North America because of reduced amounts of hunting, it is expected that this infection will become more prevalent.

Crenosoma species require a molluskan intermediate host. Control depends on preventing the dog's access to these intermediate hosts.

Family Angiostrongylidae

The angiostrongylid bursa may be somewhat reduced, but the rays conform to the typical strongylid pattern and are well defined. The vulva is near the anus, and the uterus is prodelphic. *Aelurostrongylus abstrusus* is a parasite of the lung parenchyma in cats, *Gurltia paralysans* is a parasite of the leptomeningeal veins in South American cats, and *Angiostrongylus vasorum* is a widely distributed

parasite of the pulmonary arterial tree of foxes and dogs in western Europe. Recently this worm was found for the first time to occur in dogs in North America in Newfoundland, Canada (Conboy et al, 1998). *Angiostrongylus cantonensis* is found in the pulmonary arteries of rats, whereas *Angiostrongylus costaricensis* is found in the mesenteric arteries of rodents. Both *A. cantonensis* and *A. costaricensis* can also cause disease in other mammalian hosts including dogs and primates, including humans. Some place the species *A. cantonensis* and *A. costaricensis* in the genus *Parastrongylus*.

Aelurostrongylus abstrusus

Life history

The oviparous female of *A. abstrusus* deposits unsegmented eggs in "nests" in the lung parenchyma (see Figure 8-87). These appear as small, grayish white subpleural nodules. It is hard to tease intact worms out of tissues, but the males have fairly stout spicules (Figure 4-103). In histologic sections or squash preparations of such nodules, all degrees of development from one-celled eggs to hatched first-stage larvae are in evidence. The first-stage larvae are carried up the tracheobronchial tree and swallowed, appearing later in the cat's feces (see Figure 7-52). These larvae are very active and can be readily demonstrated by the Baermann technique, which was found to detect 18 of 20 cases of infection with this parasite (Willard et al, 1988). Further development occurs only if these first-stage larvae enter any of a wide variety of snails and slugs (Blaisdell, 1952; Hobmaier and Hobmaier, 1935). Two molts without cuticle

shedding occur in the mollusk's foot tissues so that the infective larvae, which develop in 2 to 5 weeks, are enclosed in two sheaths. Cats may be infected experimentally by being fed snails containing third-stage larvae, but the natural mode of infection is probably through predation of paratenic hosts that normally eat snails. Mice and possibly birds may serve as paratenic hosts. The third-stage larvae merely encyst in their tissues and undergo no further development until they are ingested by a cat. Larvae appear in the cat's feces 5 to 6 weeks after infection.

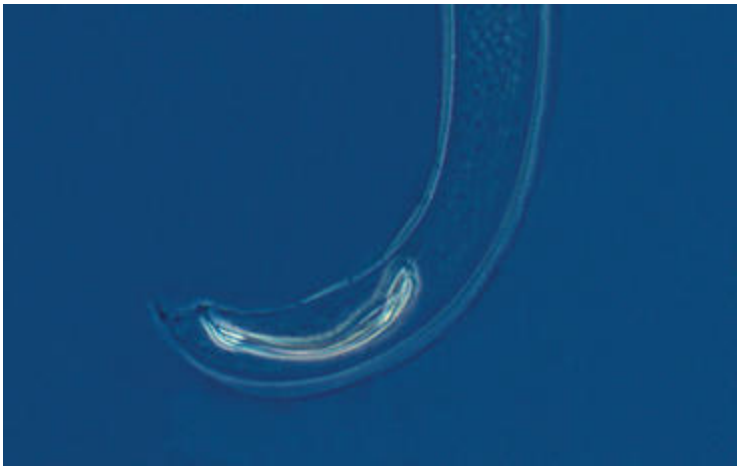

FIGURE 4-103 *Aelurostrongylus abstrusus*, posterior end of a male tail showing the spicules.

Infection with *A. abstrusus* usually involves individual rural cats that like to hunt. Control consists of preventing the cat's access to infected intermediate hosts. Unfortunately, we cannot specify what these might be, except for a wide range of snails and slugs that few cats would deign to eat anyway. Probably the cats get their *A. abstrusus* infective larvae from paratenic hosts such as mice and

voles, but our knowledge of the epidemiology of *A. abstrusus* and other carnivoran metastrongyloids is incomplete.

Importance

Although many cats with *A. abstrusus* infection are free of clinical signs, coughing and anorexia may be associated with moderate infections. Severe infections are manifested by cough, dyspnea, and polypnea, all of which may terminate fatally (Blaisdell, 1952).

Treatment

Kirkpatrick and Megella (1987) successfully treated a case of *A. abstrusus* infection with a single parenteral dose of ivermectin (0.40 mg/kg), whereas of two cats in Turkey treated with this regimen, only one cleared (Burgu and Samehmetoglu, 2004), and in another case this treatment was not efficacious (Grandi et al, 2005). In Germany, topical selamectin (6 mg/kg) was used to treat one cat twice, a month apart, with success (Reinhardt et al, 2004), but the same treatment failed in two out of three cats in Italy (Grandi et al, 2005). Fenbendazole (50 mg/kg daily for 3 days) also has been proved efficacious in the treatment of a cat infected with *A. abstrusus* (Schmid and Düwel, 1980) and in four of four cats treated at 50 mg/kg daily for 15 days (Grandi et al, 2005). Prednisone (1 mg/kg orally twice a day for 5 days) may help alleviate many of the clinical signs during recovery.

Angiostrongylus vasorum

Life history

First-stage larvae shed in the feces of infected dogs resemble those of *A. abstrusus*. These larvae invade a wide range of molluskan intermediate hosts and develop to the infective third stage, but the practical epidemiology of canine angiostrongylosis has yet to be worked out in detail. After ingestion of the mollusk, the larvae migrate to the visceral lymph nodes where they molt to the adult stage before making their way into the lungs and the pulmonary arteries, where they mature and live (see Figure 8-88). The prepatent period is around 7 weeks.

Importance

The parasite has made its way from Europe into the Atlantic coastal provinces of Canada. Previously, cases had been present in imported dogs as in a fatal case in a greyhound from Ireland, with extensive pulmonary thrombosis and interference with clotting leading to multiple subcutaneous hemorrhages (Williams et al, 1985). In a survey of dogs from coastal Canada, 202 dogs from the provinces of New Brunswick, Newfoundland, Nova Scotia, and Prince Edward Island were examined, and *A. vasorum* was found in only 16 of 67 dogs from the Avalon peninsula of Newfoundland (Conboy, 2004). This parasite has now also been found in a coyote from the Avalon peninsula (Bourque, Whitney, and Conboy, 2005). Besides causing lung disease from the deposition of eggs and larvae into the lungs, these infections induce clotting disorders that can manifest as in the imported greyhound with subcutaneous hemorrhages or with more deadly intracranial hemorrhage (Garosi et al, 2005).

Treatment

The 16 dogs that were diagnosed as naturally infected in Newfoundland were treated with four weekly oral doses of 0.5 mg of milbemycin oxime per kilogram. In 14 of the dogs the clinical signs resolved and shedding of larvae ceased, whereas one dog with severe signs died during the course of treatment; one dog was reported to have improved clinical signs, but a posttreatment fecal sample was not available (Conboy, 2004). Fifty naturally infected dogs in Denmark were treated either with a single topical application of 0.1 mL of imidacloprid 10%/moxidectin 2.5% per kilogram of body weight (27 dogs) or with 25 mg of oral fenbendazole per kilogram of body weight for 20 days (23 dogs), and 85.2% and 91.3% of the dogs, respectively, were cleared of larvae in the feces (Willesen et al, 2007). *A. vasorum* has also been treated with ivermectin at 0.2 mg/kg (Martins et al, 1993; Migaud, Marty, and Chartier, 1992), fenbendazole at 20 mg/kg twice daily for 2 or 3 weeks (Migaud, Marty, and Chartier, 1992; Patteson et al, 1993), or levamisole at 7.5 mg/kg for 2 consecutive days, followed by 10 mg/kg for 2 days, and if the infection does not clear, each of the individual regimens is repeated (Bolt et al, 1994).

Angiostrongylus cantonensis

Life history

First-stage larvae are shed in the feces of infected rats and invade molluskan intermediate hosts, where they develop to the infective stage. When the mollusk is eaten by a rat, the liberated third-stage

larvae make their way to the brain of the rat, where they molt and grow to young adults that are about 1 centimeter long. They then enter a vein and are carried to the heart and pulmonary arteries, where they mature and mate, and the female lays eggs that embryonate and hatch. Paratenic hosts involved include crustacea and amphibians.

Importance

If people, dogs, or other mammals ingest snails or paratenic hosts, the worms may undergo their migration into the brain, causing eosinophilic meningitis and encephalomyelitis. During the past few decades this worm has spread across the Pacific with one of its intermediate hosts, the giant African snail *Achatina fulica*. Infection is typically acquired by eating infected raw snails or slugs or freshwater prawns, which serve as paratenic hosts (Alicata, 1988). In a series of 55 natural cases of canine neural angiostrongylosis from Brisbane, Australia, infection was characterized by ascending paresis involving the tail and urinary bladder and lumbar hyperalgesia. Three grades of clinical illness were characterized. Grade 1 consisted of caudal paresis and ataxia of one or both pelvic limbs and pain on deep pressure over the lumbar muscles. Grade 2 began as grade 1, but posterior paresis and inability to stand unaided developed quickly. Manual expression of urine was necessary. Dogs with both grade 1 and grade 2 illness responded satisfactorily to nursing care and immunosuppressive corticosteroid therapy. However, when the anthelmintics levamisole and

mebendazole were administered in grade 1 and grade 2 cases, either alone or in combination with corticosteroids, a death rate of 75% ensued. Clearly, anthelmintic medication is contraindicated in canine neural angiostrongylosis. Grade 3 illness was characterized by rapidly developing ascending paralysis and extreme hyperalgesia. The prognosis was very poor, and all seven dogs were euthanized (Mason, 1987).

In 1986 and 1987, rats in New Orleans, Louisiana, were found to be infected with *A. cantonensis* (Campbell and Little, 1988) A few years later, a howler monkey in the New Orleans zoo had fatal cerebral disease and was ultimately diagnosed as having been infected with this worm (Gardiner et al, 1990). In 1995 a nonfatal case was reported from New Orleans in an 11-year-old boy who ate a snail on a dare (New, Little, and Cross, 1995). In 1996 a miniature horse in Baton Rouge, Louisiana, had meningoencephalitis and was euthanized (Costa et al, 2000). At necropsy, the horse was found to be infected with *A. cantonensis*. As of 1997, around one quarter of rats, *Rattus norvegicus*, examined in Baton Rouge were found to be infected with this parasite. The worm has been found in additional animals in Louisiana, a lemur, a wood rat, and opossums (Kim et al, 2002), and it has killed a white-handed gibbon in a zoo in Miami (Duffy et al, 2004). It is expected that additional cases will begin to turn up in dogs and possibly cats.

Treatment

Treatment seems to be mainly supportive, with immunosuppression to prevent reaction to the migrating worms, and in Australia the development of an ELISA for the detection of the infection allows for diagnosis before therapy is begun (Lunn et al, 2003).

Angiostrongylus costaricensis

A. costaricensis is a parasite of rodents in Central and South America, where the adult worms live in the mesenteric arteries; it was reported once from cotton rats in Texas (Ubelaker and Hall, 1979). Eggs are laid by the females, and the first-stage larvae occur in the feces of the rodents. Snails are the intermediate hosts. People have become infected with this worm on the ingestion of snails, and they develop pain in the lower right abdomen, fever, and often vomiting. Recently it was reported that infections with this worm caused the death of two Ma's night monkeys *(Aotus nancymaae)* and the surgical resection of a portion of the intestine of a siamang *(Hylobates syndactylus)* housed in zoos in Florida (Miller et al, 2006). Raccoons and opossums trapped around the zoos were also found to be infected.

Family Filaroididae

The Filaroididae family of worms differs from the others within the superfamily Metastrongyloidea in that these worms are without a bursa. (Do not confuse the Filaroididae family of Metastrongyles with the very distantly related superfamily Filarioidea, the superfamily that contains the mosquito-transmitted canine

heartworm, *Dirofilaria immitis*.) There are species within the Filaroididae in a number of carnivores that use snail intermediate hosts (*Filaroides martis* and *Filaroides rostratus*). There is also a species, *Filaroides decorus*, in the lungs of the California sea lion that uses fish as the intermediate host. The two most well known species in veterinary medicine are canine parasites that have direct life cycles, i.e., *F. osleri* and *F. hirthi* (Figure 4-104). Some place the species *F. osleri* and *F. rostratus* in the genus *Oslerus*, but although accepted by some and possibly correct, this placement is not accepted by all.

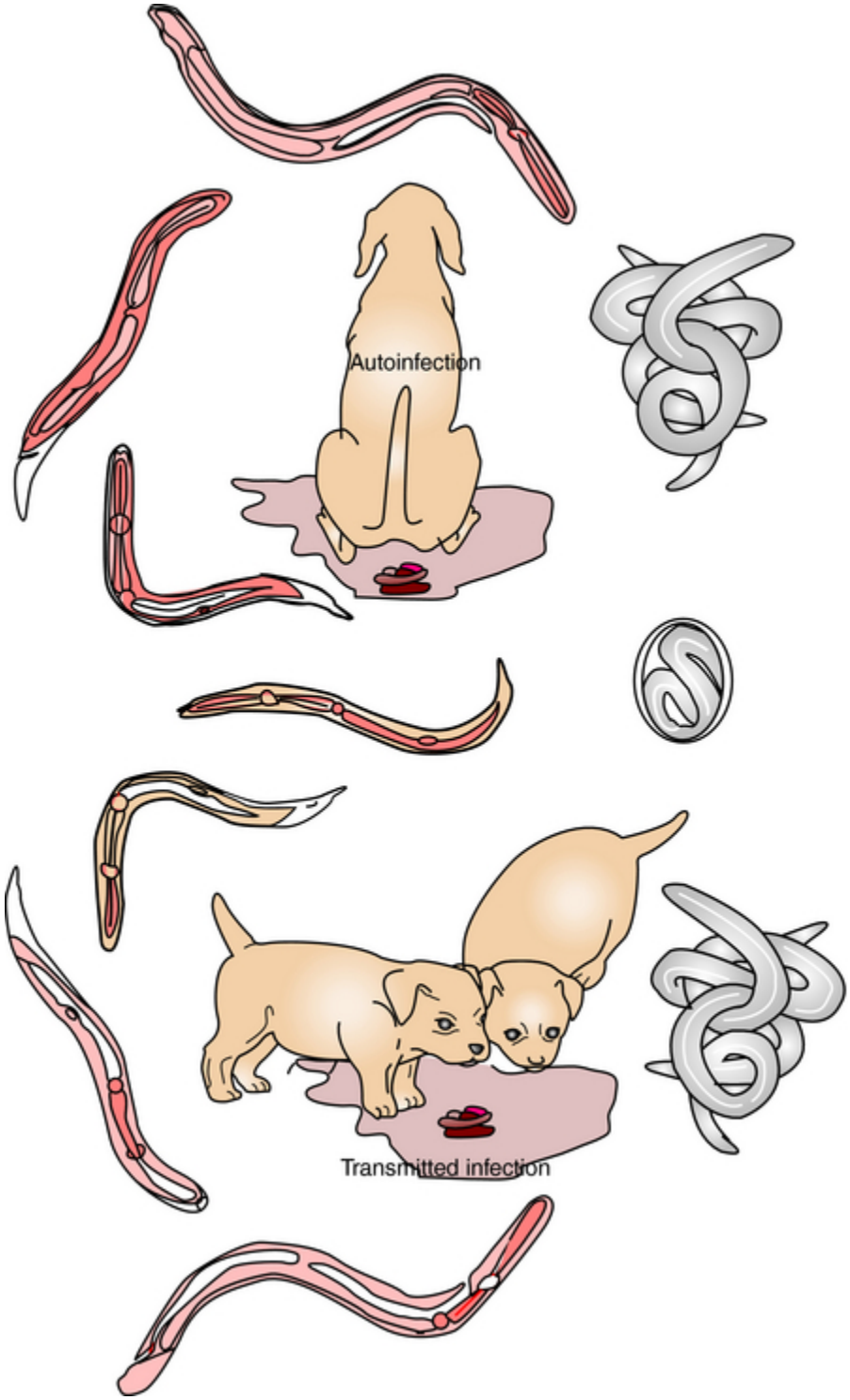

FIGURE 4-104 Life history of *Filaroides hirthi*. The female worm in the lung parenchyma of the dog lays eggs containing infective first-stage larvae. Because these larvae are released within the host, autoinfection is inevitable and the degree of resulting infection is apparently governed solely by the host's immune reactions. First-stage larvae

pass up the trachea and out with the feces, and transmission of *F. hirthi* infection occurs principally by coprophagy. Cannibalism and regurgitative feeding provide other mechanisms.

Identification

The bursal lobes are reduced to mere papillae (see Figure 4-69). The spicules are short and arcuate, the vulva is preanal, the uterus is prodelphic, and the body cuticle is inflated to form a diaphanous teguminal sheath (see Figure 4-60). *F. osleri* occurs in nodules within the epithelium of the trachea and bronchi. *F. hirthi* lives threaded through the lung parenchyma.

Filaroides osleri

Life history

Adult *F. osleri* occur in nodules in the trachea and bronchi of dogs and certain wild canids such as the Australian dingo (Figure 4-105; see also Figures 8-91 and 8-92Figure 8-91Figure 8-92). The females deposit delicate, thin-shelled eggs containing first-stage larvae that hatch before being voided in the host's feces (see Figure 7-27). The first-stage larvae are directly infective, and development through all five stages is completed in the lung tissue of the dog. Infection is acquired through the ingestion of regurgitated stomach contents, lung tissue, or feces of infected dogs. John Dorrington, a South African veterinary practitioner, was the first to succeed in transmitting *F. osleri* infection to dogs by feeding them first-stage larvae obtained from female worms (Dorrington, 1968). It has been postulated that transmission of *F. osleri* occurs directly from bitches

to their pups by salivary contamination during licking (Dorrington, 1968) and from parent dingoes to their pups during the period of regurgitative feeding (Dunsmore and Spratt, 1976).

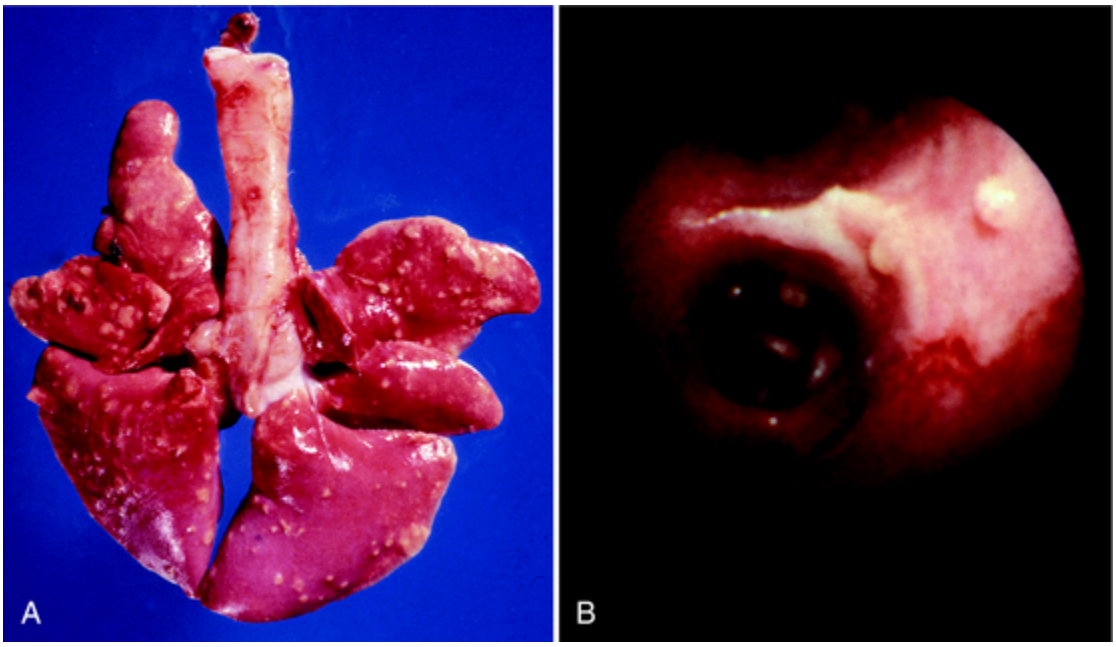

FIGURE 4-105 Lesions of *Filaroides* species. At left, the lung of a dog with *Filaroides hirthi* infection. Foci of inflammatory reaction to dead and dying worms are scattered over the lungs. Live *F. hirthi* worms excite little if any tissue reaction and, because they are so very small, are scarcely visible to the unaided eye. At right, early *Filaroides osleri* nodules near the tracheal bifurcation of a dog photographed through a fiberoptic endoscope.

Courtesy Dr. James Zimmer.

F. osleri infection develops slowly. Nodule formation can be detected with the bronchoscope at about 2 months, and larvae can first be demonstrated in the feces by zinc sulfate flotation at 6 to 7 months after experimental feeding of larvae.

Importance

Milks (1916) summarized the clinical signs manifested in his three cases of *F. osleri* infection as follows:

The only common symptom . . . was the spasmodic attack of a hard, dry cough which could be started by exercise or exposure to cold air. These attacks could not be started by pressure upon the larynx as in most cases of bronchitis. The dogs would cough several times and finally retch after which the attack would usually cease . . . the disease runs a very chronic course and does not materially interfere with the health of the animal until the knots become so numerous as to seriously obstruct the air passages.

F. osleri displays rather low prevalence in spite of its worldwide distribution. It tends to become entrenched in breeding stock and resists all efforts to expel it. Public knowledge that *F. osleri* is present in a kennel can destroy the kennel's reputation.

Treatment and control

Criteria for successful chemotherapy of *F. osleri* infection include (1) disappearance of cough and air hunger on exercise, (2) resolution of tracheal and bronchial nodules as demonstrated by bronchoscopy, and (3) cessation of fecal larval output. These criteria have rarely been satisfied, and authors disagree as to the efficacy of various treatments. Some treatments that have been used include fenbendazole, ivermectin, and doramectin. Fenbendazole (50 mg/kg daily for 7 days) was reported to stop coughing in a dog with an *F. osleri* infection (Lamb, 1992). Also, ivermectin has been reported to clear dogs of the signs of *F. osleri* infections (Boersema, Baas, and

Schaeffer, 1989; Valet-Picavet, 1991). There have been two reports from India, where individual dogs have been successfully treated with a single injection of doramectin (0.2 mg/kg) (Gahlod, Kolte, and Kurkure, 2002; Jana, 2002).

Filaroides hirthi

Life history

F. hirthi, like *F. osleri*, is infective in the first larval stage and requires no period of development outside the host (Georgi, 1976a; see Figure 4-104). Transmission has been shown to occur among cagemate puppies through the ingestion of first-stage larvae in freshly passed feces, and it has been hypothesized that transmission from brood bitches to their litters occurs by the same mechanism after the fourth or fifth week of the nursing period (Georgi et al, 1979b). First-stage larvae arrive in the lungs as early as 6 hours after oral infection, traveling by way of the hepatic portal circulation, the mesenteric lymphatic drainage, or both. Molts occur at 1, 2, 6, and 9 days in the lung tissue, and larvae can be demonstrated in the feces by zinc sulfate flotation at 32 to 35 days after infection (Georgi, Georgi, and Cleveland, 1977; Georgi et al, 1979a) (see Figure 7-27).

Importance

F. hirthi is important because the lesions it induces in the lungs of dogs used in toxicologic research interfere with the interpretation of experiments (see Figures 4-105, 8-89, and 8-90 Figure 8-89 Figure

8-90). In 1973, Hirth and Hottendorf described pathologic changes in commercially reared beagle dogs that were associated with *F. hirthi*. The presence of these minute lungworms in the alveoli and bronchioles evoked a focal granulomatous reaction and other pulmonary changes, including some that resembled drug-induced and neoplastic lesions. Research dogs still appear on occasion with *F. hirthi* in their lungs (Bahnemann and Bauer, 1994; Vajner et al, 2000).

Usually, *F. hirthi* infection is not attended by clinical signs of disease, and antemortem diagnosis is based on demonstrating first-stage larvae in the feces (see Figure 7-27), although very severe infections may be suspected from radiographic changes (Rendano et al, 1979a). However, fatal cases of hyperinfection with this parasite have developed in severely stressed and immune-deficient animals (August et al, 1980; Craig et al, 1978). Massive hyperinfection with *F. hirthi* was observed in two Beagle pups experimentally treated with prednisolone at a dosage rate of 4 mg/kg/day for more than 4 months (Genta and Schad, 1984). Dr. Georgi encountered several other cases of fatal *F. hirthi* hyperinfection in dogs experimentally maintained on corticosteroids for long periods. However, because these occurred in commercial pharmaceutical laboratories observing strict proprietary secrecy, the particulars were unavailable.

Treatment and control

For treatment of *F. hirthi* infection, albendazole administered orally at a dosage of 25 mg/kg of body weight twice daily for 5 days is

highly effective (Georgi, Slauson, and Theodorides, 1978). Fenbendazole, 50 mg/kg daily for 2 weeks, did not clear a dog of its *F. hirthi* infection, whereas a single subcutaneous injection of ivermectin (0.05 mg/kg) given at a later time appeared to clear the dog of its infection (Bourdeau and Ehm, 1992). Treatment of 40 dogs with subcutaneously administered ivermectin once at 1 mg/kg or ivermectin twice at 1 mg/kg a week apart reduced infections with *F. hirthi* by 44.8% and 74.1%, respectively, as revealed by necropsy (Bauer and Bahnemann, 1996). Fecal examination of these treated dogs revealed that only 5% to 10% of the dogs were shedding larvae in their feces, although higher percentages of the dogs still had worms in their lungs.

Order Rhabditida

The order Rhabditida is a very large group of small nematodes with a rhabditoid or rhabditiform esophagus consisting of corpus, isthmus, and bulb (Figure 4-106). Many species are free-living inhabitants of soil or parasites of lower vertebrate or invertebrate animals. The most famous member of this group is the free-living, model genetic organism, *Caenorhabditis elegans*. There are only three genera in this order Rhabditida that parasitize domestic animals: *Rhabditis* (syn., *Pelodera*), *Halicephalobus* (syn., *Micronema*), and *Strongyloides*.

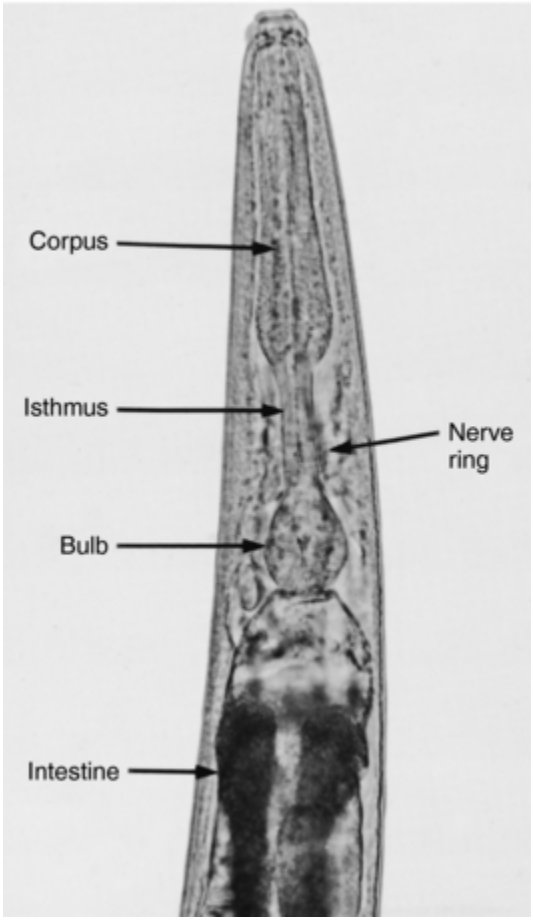

FIGURE 4-106 Anterior end of a *Strongyloides papillosus* free-living adult with a typical rhabditiform esophagus.

Rhabditis (Pelodera)

Rhabditis (Pelodera) strongyloides is a free-living inhabitant of decaying organic matter but occasionally produces a pruritic, hyperemic dermatitis of cattle, swine, dogs, horses, people, and rodents that have been exposed to an excess of the nematode's normal habitat. Damp straw bedding has been incriminated repeatedly in canine dermatitis caused by this parasite and was associated with larvae-associated lesions in 11 hounds in Finland (Saari and Nikander, 2006). Similarly, damp and dirty straw with

high humidity were responsible for the lesions in a large number of heifers on a dairy in Israel (Yeruham and Perl, 2005), Diagnosis is based on finding nematode larvae with a rhabditiform esophagus in skin scrapings or histologic sections (Figure 4-107; see also Figure 8-72); sometimes adults are also present. If *R. strongyloides* larvae are placed on nutrient agar, they will develop into adults in a day or so. These adults are 1 to 2 mm long and will promptly fill the Petri dish with their offspring. Ivermectin was used to treat a number of the hounds in Finland with success.

FIGURE 4-107 *Rhabditis strongyloides* rhabditiform larva from a nutrient agar culture. The culture was grown from scrapings of an acute erythematous dermatitis affecting a dog.

In cattle, especially in the tropics, a parasitic otitis externa can develop that is caused by a nematode described as *Rhabditis bovis.*

Once the infection is established in the ear canal, there appears to be a destruction of the ear epithelium resulting in ulcerations (Msolla, 1989). These ulcerations predispose the ears to secondary bacterial infection. The cattle have a condition that appears as chronic wasting. There is some indication that treatment of cattle with ivermectin may help with these infections, but typically they are treated by the topical application of various agents.

Halicephalobus

Halicephalobus gingivalis (syns. *Halicephalobus deletrix* and *Micronema deletrix*) is tiny (250 to 450 by 15 to 20 μm) and has a rhabditoid esophagus and only one egg in its uterus. A male of this species has yet to be reported. The other seven species of *Halicephalobus* apparently are all free-living in soil, manure, or humus, but *H. gingivalis* is a highly pathogenic facultative parasite of horse and man (Anderson, Linder, and Peregrine, 1998; Nadler et al, 2003) (see Figure 8-73). *H. gingivalis* also has been seen in a section of skin from the scrotum of a bull. *H. gingivalis* was first observed in a nasal swelling in a horse (Anderson and Bemrick, 1965) and from the nasal and maxillary sinuses, gums, jaws, kidneys, heart, brain, spinal cord, and meninges in 12 equine cases reported subsequently (Blunden, Khalil, and Webbon, 1987). The paper by Blunden and colleagues deserves recognition as a model case report that students and clinicians would do well to emulate. There have been three fatal human infections with this nematode (Gardiner, Koh, and Cardella, 1981). The first reported human case of fatal

meningoencephalomyelitis caused by *H. gingivalis* involved a 5-year-old boy who sustained extensive injuries heavily contaminated with manure when he fell into a running manure spreader and passed through its mechanism (Hoogstraten, Connor, and Neafie, 1976).

Strongyloides

Strongyloides is an unusual genus in terms of morphology and life history. (Be careful not to confuse the genus name *Strongyloides* with the species name of *R. strongyloides* or with the superfamily name Strongyloidea. Also be warned that the adjective "strongyloid" as used by many authors is more likely to refer to properties of members of the superfamily Strongyloidea than to those of the genus *Strongyloides.* The ubiquitous prefix derives from the Greek word *strongylos,* meaning round and compact, and apparently has great appeal to taxonomists of every stripe. *Strongyl-* has not been restricted to the christening of worms but has been applied to such diverse animals as sponges *[Strongylophora]*, bugs *[Strongylodemas]*, and fishes *[Strongyliscus]*, among others.)

Identification

The tiny **parthenogenetic** parasitic female lies deep in the mucosal crypts of the alimentary tract, particularly the small intestine (see Figure 8-74); parasitic males do not exist. The esophagus of the female is nearly cylindric and at least one fourth as long as the body (Figure 4-108); the elongate shape of the esophagus is the reason why the female is termed "**filariform**." Other small nematodes in this location include members of the superfamily

Trichostrongyloidea, which have a very much shorter esophagus, and species of *Trichinella* and *Capillaria*, both of which have a stichosome esophagus. The embryonated egg, **rhabditiform** larva (so called because it has the typical corpus, isthmus, and bulbus of the Rhabditida), and infective **filariform** third-stage larva (with a long esophagus) are the stages most important in diagnostic procedures. Of the significant species of *Strongyloides* in veterinary medicine, only those of dogs (also humans) and cats produce eggs that routinely hatch before leaving the body such that first-stage larvae rather than embryonated eggs are found in the feces. The free-living adults (see Figures 4-106 and 4-108) frequently develop in cultures of feces from *Strongyloides*-infected animals.

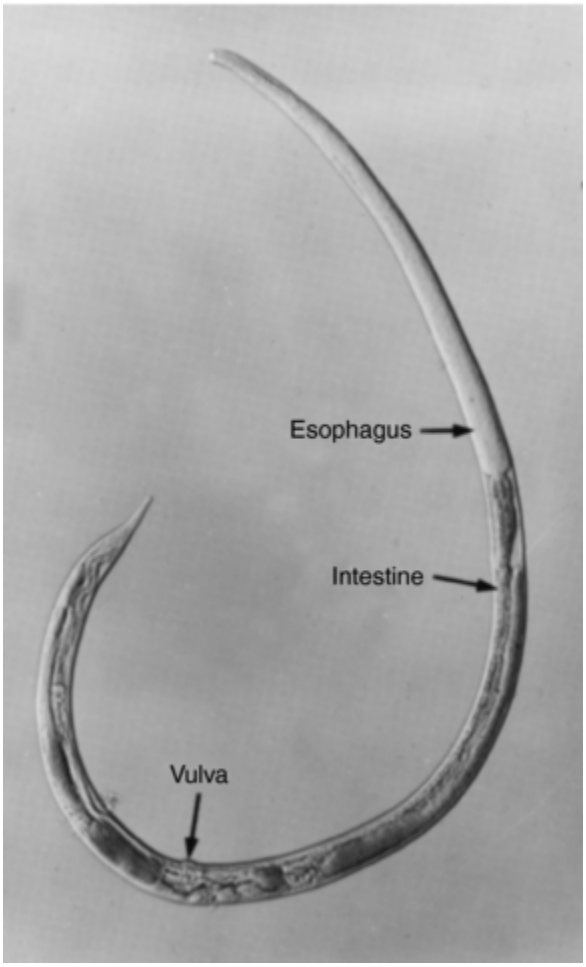

FIGURE 4-108 *Strongyloides stercoralis* parasitic female.

Prominent species of *Strongyloides* parasitizing domestic animals and humans include *S. stercoralis* of humans and dogs; *Strongyloides papillosus* of ruminants; *Strongyloides ransomi* of swine; *Strongyloides westeri* of horses; *Strongyloides fuelleborni* of African and Asian primates and of humans; *Strongyloides cebus* of American primates; and *Strongyloides ratti* and *Strongyloides venezuelensis* of rats. Cats in Australia and India are parasitized by *Strongyloides felis,* and on rare occasions in the southeastern United States, cats are infected with *Strongyloides tumefaciens*, which is probably naturally a parasite of

the bobcat and which causes fibrotic lesions in the colon. Thus all species of domestic animals have a species of *Strongyloides*, as do many species of wild mammals and birds (Little, 1966a, 1966b).

Life history

The genus *Strongyloides* is unique among parasites of domestic animals in having alternate free-living and parasitic generations. The filariform parasitic female produces eggs by mitotic parthenogenesis, and the larvae from these eggs are termed **homogonic** offspring to distinguish them from the **heterogonic** offspring of the free-living, sexual generation. Homogonic rhabditiform larvae in the external environment may develop through two molts into infective filariform larvae or through four molts into free-living males and females where all stages have rhabditiform esophagi. If the third-stage filariform larva enters a suitable host, usually by penetrating its skin, development proceeds through third and fourth molts to the filariform parasitic female. The free-living rhabditiform males and females mate to produce heterogonic rhabditiform larvae that, with minor exceptions, develop only into infective filariform larvae (Basir, 1950; Triantophyllou and Moncol, 1977). The life history of *Strongyloides* species is portrayed in Figure 4-109.

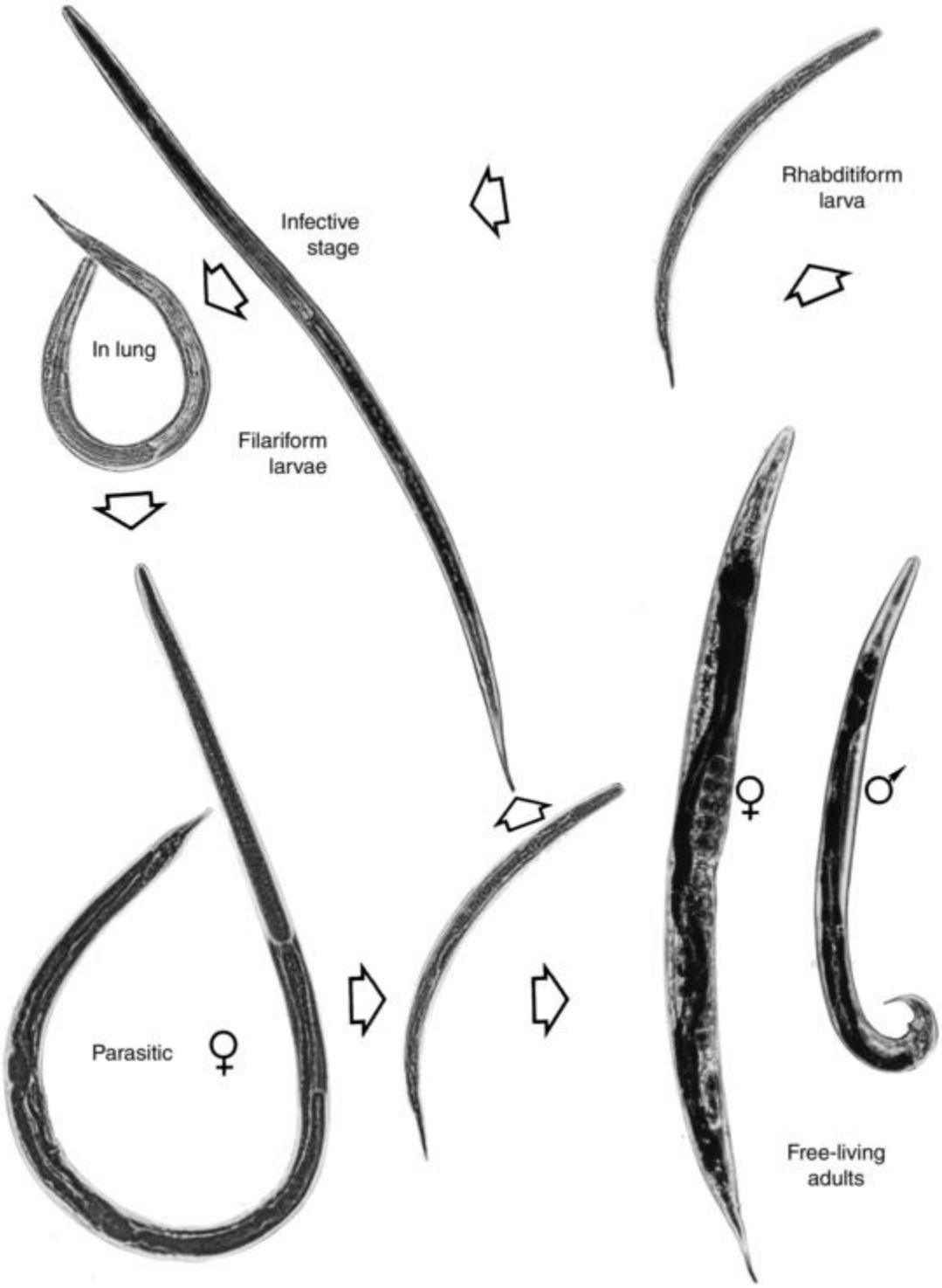

FIGURE 4-109 Life stages of *Strongyloides stercoralis.* Not to same scale.

The major mode of transmission of *Strongyloides* species in mammals appears to be transmammary. This occurs in dogs, horses, pigs, and ruminants. After an initial infection has been established, additional larvae tend to migrate to deeper body tissues, from which they are then passed to offspring in the colostrum and milk; this **transmammary transmission** has important implications for disease induction and control.

Importance

Strongyloides infections are moderate and asymptomatic in most individuals of all domestic species, and when disease does occur, it usually is confined to massively challenged neonates and nurslings. The other exception has been in immunocompromised or immunosuppressed animals.

Dogs

S. stercoralis infection may be asymptomatic, or it may cause any grade of clinical illness. Serious cases involve signs of bronchopneumonia and severe watery or mucous diarrhea that may easily be confused with the generalized viral diseases of puppyhood. In massive invasions the lungs of young pups may be sprinkled with petechial and ecchymotic hemorrhages caused by migrating larvae breaking out of the alveolar capillaries. The prepatent period is about 1 week. These worms routinely show up in kennels, and infections of pups can be life threatening (Dillard, Saari, and Anttila, 2007).

S. stercoralis infection in man is unique in its chronicity (Gill et al, 2004). This infection may persist for decades or for life owing to the development to the infective filariform larval stage within the patient's digestive tract. These infective larvae may reinvade the host by penetrating either the bowel wall **(internal autoinfection)** or perianal skin **(external autoinfection)**. Autoinfection accounts for the extreme chronicity of infection and, in part, for the explosive development of massive disseminated infection **(hyperinfection)** that may overwhelm patients with depressed cell-mediated immunity. Hyperinfection with *S. stercoralis* has caused the deaths of many persons who have immunodeficiency diseases or are undergoing immunosuppressive therapy or immunosuppression for transplantation (Dwork, Jaffe, and Lieberman, 1975); the worm has even been transplanted in the donor organ (Patel, Arvelakis, and Sauter, 2008). Dogs can also develop autoinfection when immunosuppressed (Schad, Hellman, and Muncey, 1984). The ability of *S. stercoralis* to undergo internal autoinfection is probably due in part to the passage of larvae rather than eggs as occurs with the other species of *Strongyloides* parasites in domestic animals.

S. stercoralis is a parasite that is zoonotic, and infections may be shared between dogs and people. Galliard (1951) had no difficulty producing durable infections in dogs by using 19 strains of *S. stercoralis*, 11 obtained from Europeans infected in different regions of French Indochina (Vietnam) and eight from natives of Tonkin, but he found dogs to be quite refractory to strains imported from the West Indies and Africa. The epidemiologic role of the dog in

human *S. stercoralis* infection has actually been documented by only one report of natural transmission from dog to man (Georgi and Sprinkle, 1974). A recent survey of kenneled dogs and kennel workers in Brazil found some dogs infected, but none of the workers infected, although some workers were serologically positive for antibodies to *S. stercoralis* on ELISA (Gonçalves et al, 2007). In kennels the infections often go unnoticed, are maintained through transmammary transmission and skin penetrating larvae, and should always be considered a potential zoonotic agent for kennel employees if a diagnosis of infection has been made.

Horses

S. westeri, as with other members of the genus, develops rapidly in passed feces to the infective filariform stage, which usually enters the host by penetrating its skin or oral mucous membranes. *S. westeri* eggs are encountered almost exclusively in suckling and weanling foals; the dam of an infected foal sheds no *S. westeri* eggs even though she is the source of infection via the mammary gland (Lyons, Drudge, and Tolliver, 1969, 1973). The foals will begin to shed eggs in their feces at 10 days to 2 weeks after birth. Diarrhea rather frequently afflicts foals between the ninth and thirteenth day of life, thus occurring coincidentally with the first postparturient estrus of the mare. Enigk, Dey-Hazra, and Batke (1974) presented convincing evidence that this so-called foal-heat diarrhea is caused by *S. westeri* and is not related to any alteration in the chemical composition of the mare's milk. Heavy infections in foals persist for

10 weeks; lighter infections may last 2 or 3 times as long. Occasionally, very light infections are observed in yearlings and older horses. These may represent percutaneous infections in hosts that were not exposed as sucklings (Enigk, Dey-Hazra, and Batke, 1974). Fortunately, the use of ivermectin has probably markedly reduced the presence of *S. westeri* on many farms, and a recent survey in Kentucky thoroughbred foals found a prevalence of only 1.5%, whereas decades ago in the same area the prevalence was greater than 90% (Lyons and Tolliver, 2004).

Ruminants

S. papillosus has long been considered to behave typically as a commensal or at the least causing significant disease only when present in very large numbers. In a recent report on a series of studies performed in the late 1960s and early 1970s, it was shown that even relatively light infections with this parasite can cause severe disease in goats (Pienaar et al, 1999). In these studies with 89 goats infected with various dosing regimens, some kids died after three infections with as few as 2000 to 5000 larvae per exposure. The most susceptible age group was kids 6 weeks to 6 months of age, although older goats, 6 to 12 months of age, also succumbed. Death typically occurred within 9 to 30 days of receiving 75,000 larvae. The clinical signs included dehydration, inappetence, emaciation, weakness, cachexia, diarrhea, anemia, respiratory distress, and abnormal stools. Fever was not seen in any of the animals. Nervous signs were exhibited from day 43 after exposure

onward, and about 22% of the goats that died had histopathologic lesions in the brain and spinal cord. Sudden death from hepatic rupture occurred in 6% of the goats. In a different set of studies (Nakamura et al, 1994), it was shown that the inoculation of live parthenogenetic females into the duodenum of susceptible lambs produced continuous sinus tachycardia immediately after inoculation, with the result being death due to cardiac arrest. Thus the effects of adults in the one study and the numerous lesions seen in varied tissues of the goats in the other set of studies would suggest that *S. papillosus* may be more pathogenic than previously considered.

Pigs

The *S. ransomi* female lies deeply embedded in the mucous membrane of the small intestine. The larvae in eggs shed develop into infective third-stage filariform larvae in 2 or 3 days that infect the next host via penetration of the skin or oral mucosae. These may follow a tracheal migration route to maturation in about 6 days or a somatic migration route to accumulate as arrested larvae in the adipose tissues, especially those of the mammary area. Tracheal migration and maturation are the usual outcome in piglets and occur to some extent in older pigs. Mature gilts tend instead to store *S. ransomi* larvae in their adipose tissues and to shed them later in the colostrum and milk. The third-stage larvae in the colostrum and milk are said to be “advanced” as compared with the third-stage larvae that originally infected the gilt because they are slightly

larger and their genital primordia longer, wider, and more conspicuous, and because they mature in suckling pigs in only 2 to 4 days instead of 6 days. Transmammary infection is the key to the epidemiology of *S. ransomi* infection. Piglets separated at birth from their dam and reared artificially were free of *S. ransomi* infection, whereas piglets allowed to nurse began to shed eggs in their feces 2 to 4 days after birth (Moncol and Batte, 1966). This initial transmammary infection thus serves to contaminate the environment of the sow and litter, thereby augmenting the mature worm burdens of the piglets and rebuilding the sow's tissue store of arrested larvae for subsequent litters (Moncol, 1975).

Strongyloidosis of piglets is an acute enteritis with bloody diarrhea (dysentery), rapid emaciation, anorexia, anemia, and stunting. There may be death losses, but from an economic standpoint these may be economically less significant than the retarded growth of the survivors.

Treatment

Ivermectin seems to be the treatment of choice for almost all species of *Strongyloides*, including dogs and humans (Lindo et al, 1996; Mansfield and Schad, 1992); in people it is marketed as Stromectol (tablets containing 3 mg ivermectin). In dogs with experimental infections of *S. stercoralis,* treatment with ivermectin at 0.8 mg/kg body weight failed to remove larvae from the tissues of the dogs (Mansfield and Schad, 1992). *S. ransomi*, *S. papillosis*, and *S. westeri* are also treated with ivermectin (in some cases other avermectins

are also so labeled). It has also been shown that the treatment of mares at foaling with ivermectin can prevent the infection of suckling foals (Ludwig et al, 1983). *Strongyloides* in pigs can also be treated with levamisole. *S. westeri* in horses can also be treated with oxibendazole (15 mg/kg).

Order Oxyurida

Although the order Oxyurida is named for *Oxyuris equi*, the common and unusually large pinworm of the horse, most pinworms are very much smaller than *O. equi*. The oxyurid esophagus has a more or less spheric bulb immediately anterior to its junction with the intestine; this bulb often has a valve in its lumen (Figure 4-110). One or both sexes have a long, tapering tail, and it is for this that they are called pinworms. All oxyurids are highly host-specific parasites of the large intestine.

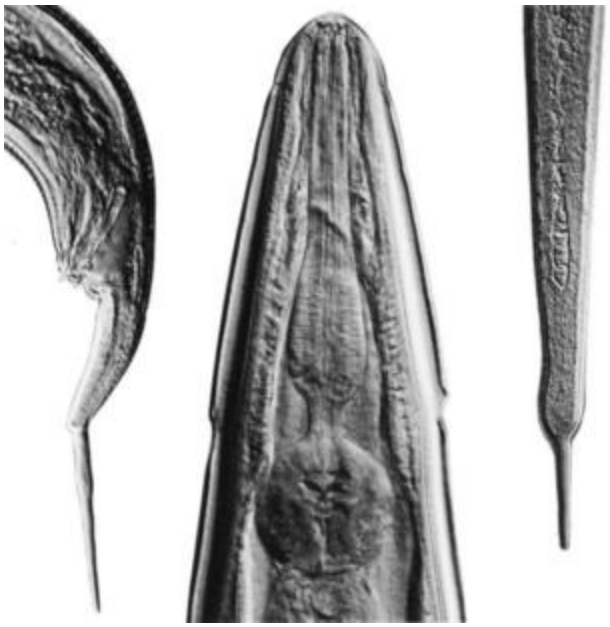

FIGURE 4-110 *Passalurus ambiguus* (a pinworm of the rabbit). Tail of male *(left)*, stomal end *(center),* and tail of female *(right)*.

Oxyuris equi

Adult *O. equi* (Figure 4-111; see also Figure 7-75) are found principally in the small colon, although occasional specimens may be found in the large colon. Instead of simply discharging her eggs in the fecal stream, the gravid female *O. equi*, which may be anywhere from 40 to 150 mm long, migrates down the colon and rectum and out through the anus to cement her eggs in masses to the skin of the anus and its immediate surroundings. These egg masses consist of a tenacious yellowish gray fluid containing 8000 to 60,000 eggs. The eggs develop to the infective stage in 4 or 5 days, during which the cementing fluid dries, cracks, and detaches from the skin in flakes. These flakes, which contain large numbers of infective eggs, adhere to mangers, water buckets, walls, and the like, thus contaminating the environment of the stable. Paper towels or disposable cloths are to be preferred for cleansing the perineum of horses because any nondisposable object, such as a sponge or towel, will inevitably become heavily contaminated with *O. equi* eggs. Then when the sponge or towel is applied to a horse's muzzle after a workout or is used to clean the bit, the future brightens up for *O. equi*. The prepatent period is 5 months.

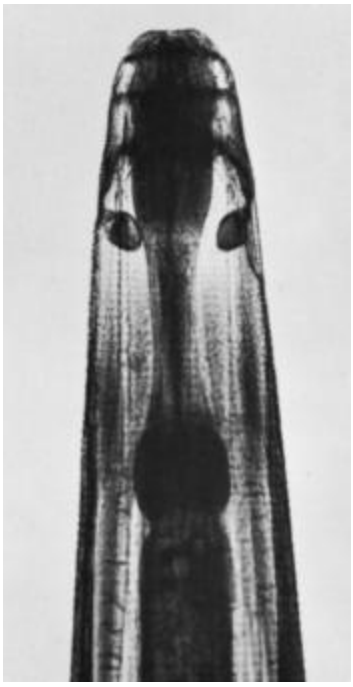

FIGURE 4-111 *Oxyuris equi* anterior end showing the esophageal bulb.

Severe infection with third- and fourth-stage *O. equi* (Figure 4-112) may produce significant inflammation of the cecal and colonic mucosa manifested by vague signs of abdominal discomfort. However, the most common affliction perpetrated by *O. equi* on the horse is pruritus ani caused by the adhesive egg masses deposited on the perianal skin by the female worm. In its efforts to relieve the itching, the horse will persistently rub its tail against posts, mangers, and the like until the tail head becomes disheveled, bare of hair, or even scarified.

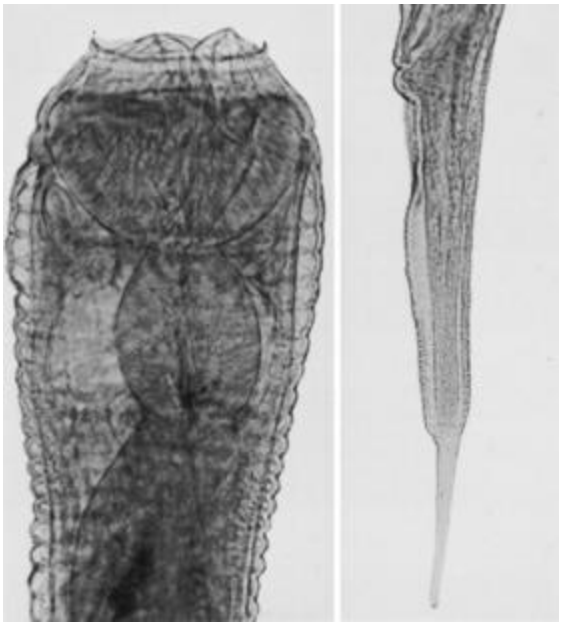

FIGURE 4-112 *Oxyuris equi* fourth-stage larva. *Left,* The anterior end shows the temporary buccal capsule-like modification of the esophageal corpus that permits attachment to the mucous membrane. *Right,* The tail.

Treatment

O. equi is an easy parasite to control. All of the available equine anthelmintics are highly effective against both immature and adult large pinworms. Ivermectin appears to continue to work very well (Klei et al, 2001). Pinworms also are controlled by the daily administration of pyrantel tartrate.

Probstmayria vivipara

Probstmayria vivipara is a tiny (less than 3 mm long) pinworm that gives birth to infective larvae and is therefore capable of completing its life history within the confines of its host's large intestine (Figure 4-113).

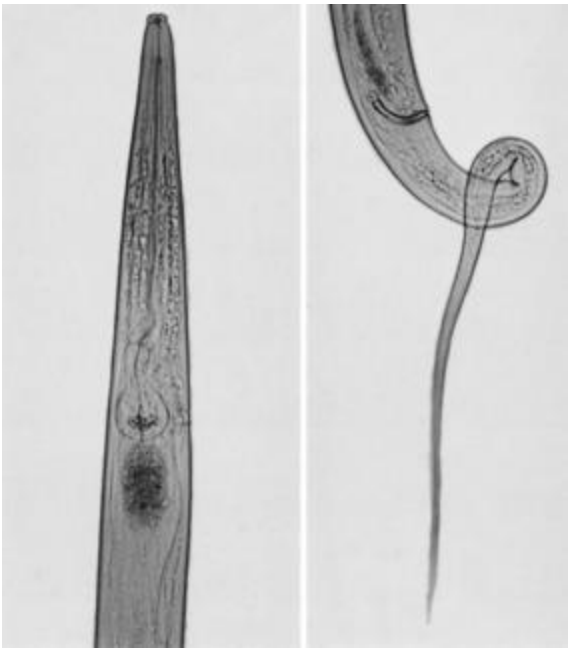

FIGURE 4-113 *Probstmayria vivipara* adult male anterior end *(left)* and tail *(right)*.

Skrjabinema

Skrjabinema ovis and *Skrjabinema caprae*, harmless parasites of sheep and goats, respectively, are 8 to 10 mm long. The genus name is pronounced “Skreeyabinema.”

Enterobius vermicularis

Enterobius vermicularis is a small (up to 13 mm long) pinworm of humans and great apes and still has an extensive distribution among civilized man despite cooking and washing, the nemeses of many other parasites (see Figure 7-105). Infection rates vary up to 40%, depending on age and race. White elementary school children display the greatest intensity and prevalence of infection. The gravid *E. vermicularis* female migrates through the anal opening to cement her eggs to the host’s perianal skin. The eggs develop to the

infective stage within hours and are ready to reinfect the host by contamination of the hands, to infect other individuals by contamination of bedclothing or other fomites, or to become airborne on dust particles.

Infection may be suspected in children who have pruritus ani and insomnia. Diagnosis is reached by observing the female worm in the act of depositing her eggs on the perianal skin or by demonstrating the eggs. This can best be accomplished by momentarily pressing the adhesive side of a piece of cellophane tape against the anus and then sticking the tape to a slide to prepare it for microscopic examination. Conventional fecal examination techniques almost uniformly fail to demonstrate the eggs of *Enterobius* species and many other pinworms (e.g., *Oxyuris* species). The important practical point for veterinarians is that *E. vermicularis* is a parasite of humans and apes (apes have other species of *Enterobius* as well), but never of dogs or cats. Occasionally a physician prescribes removal or euthanasia of the family pet to help control pinworms. The finest degree of tact is required in dealing with this situation.

Infection of apes with species of *Enterobius* is usually asymptomatic. However, sporadic cases of fatal ulcerative enteritis with extensive invasion of the intestinal submucosa and even of the mesenteric lymph nodes by the adult pinworms have been reported in chimpanzees (Holmes, Kosanke, and White, 1980; Keeling and McClure, 1974; Schmidt and Prine, 1970). Both *Enterobius*

anthropopitheci, a natural parasite of apes, and *E. vermicularis* of humans have been implicated.

Order Ascaridida

Ascarids are among the largest and most familiar of nematode parasites infecting the intestinal tract of domestic animals. The worms found in domestic animals range from several inches up to 2 feet in length. The mouth is surrounded by three fleshy lips, one dorsal and two subventral (Figure 4-114), and the tail of the male is usually curved ventrally. Some genera have lateral cervical alae that make the anterior end of the worm resemble an arrowhead, thus such generic names as *Toxocara* and *Toxascaris*.

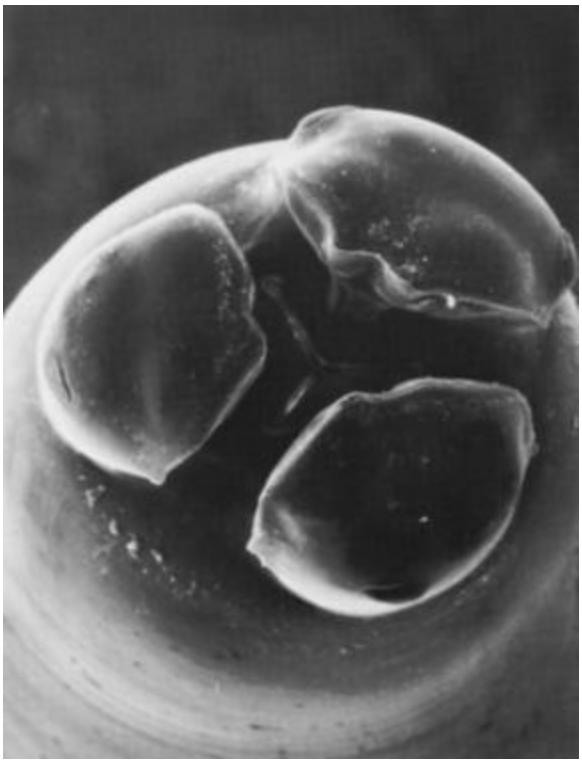

FIGURE 4-114 *Ascaris suum* lips and stoma.

Development to the infective stage differs only in detail for the various ascarid genera. The single cell develops into an infective larva inside the eggshell within several days or weeks, depending on the species of worm and the ambient temperature. There are many genera of ascaridoid nematodes that parasitize aquatic vertebrates (e.g., fish, crocodilians, birds, and sea mammals), and these genera typically have free-swimming larval stages initially and various required intermediate hosts. The ascaridoids found in domestic animals have adapted to their terrestrial existence by changing the typical life history pattern. Thus the life cycles of the ascaridoids in domestic animals are direct with or without various migrations in the body of the host or through transplacental or transmammary pathways. Another adaptation to the terrestrial environment has been the development of an eggshell capable of withstanding the extremes of harsh environments. Ascarid eggs are remarkably resistant to chemical and physical insults. The single most important fact to remember in relation to the epidemiology of ascariasis is that the eggs remain infective in soil for many years. Various ascarid genera display remarkable differences in patterns of intrahost development; however, for the terrestrial species, almost without exception it is now accepted by most that part of the adaptation to the terrestrial environment has been the incorporation of two molts within the eggshell so that the larval stage hatching from the egg of these ascaridoids is a third-stage larva.

Identification

For the purposes of practical identification, adult ascarids are quite host-specific. Thus *Ascaris suum* infects swine, *Parascaris equorum* infects horses, *Toxocara vitulorum* infects cattle, *Toxocara canis* infects dogs, and *Toxocara cati* infects cats. Dogs and cats also share a second ascarid, *Toxascaris leonina*, which must be distinguished from their respective species of *Toxocara* (see Figures 7-39 to 7-42Figure 7-39Figure 7-42).

Ascarid eggs are relatively thick walled, contain a single cell when passed in the feces, and are usually sufficiently distinctive to permit identification of the species (see Figures 7-8 to 7-10, 7-25, 7-52, 7-71, and 7-91Figure 7-8Figure 7-9Figure 7-10Figure 7-25Figure 7-52Figure 7-71Figure 7-91).

Ascaris

A. suum is a ubiquitous and pathogenic parasite of swine. The adult worms are about 30 cm long, white to cream colored, with three large lips typical of the ascaridoids (Figure 4-115; see also Figure 4-114). Long considered a variety of the morphologically indistinguishable human ascarid *Ascaris lumbricoides*, *A. suum* is considered a distinct species by most contemporary authors. However, *A. lumbricoides* can mature in swine, and *A. suum* can mature in humans. Typically, however, these two species maintain separate cycles, with the swine species staying in swine and the human species in humans even when both hosts live very closely together (Anderson, 1995; Anderson, Romero-Abal, and Jaenike, 1993).

FIGURE 4-115 *Ascaris suum,* adult worms collected from naturally infected pigs.

Although the eggs of both species will hatch and their larvae will migrate extensively in a wide range of hosts, the infective egg in polluted soil or stuck to the mammary skin of the sow is the key element in the epidemiology of *A. suum* infection. The infective egg hatches in the stomach and small intestine (Figure 4-116), releasing the third-stage larva (Geenen, Bresciani, and Boes, 1999), which enters the wall of the cecum and colon and proceeds to the liver, arriving there in a matter of hours by way of the portal vein (Murrell et al, 1997). After tunneling about in the liver for several days, the larva arrives in a pulmonary capillary by way of the caudal vena cava, heart, and pulmonary artery. At this point, the larva either may remain in the circulation to be carried to the somatic tissues or may lodge temporarily in the pulmonary capillary and then break out into an alveolus. In the case of *A. suum*, the latter course appears to be much more probable because the larva will typically proceed up the bronchial tree and trachea to the

pharynx, there to be swallowed, then will arrive once again in the small intestine, where it will mature.

FIGURE 4-116 *Ascaris suum* mechanically hatched infective larva with retained cuticle of previous stage.

In their migrations through various tissues, ascarid larvae at first inflict only mechanical damage, but hypersensitivity rapidly develops, and allergic inflammation with eosinophilic inflammation characterizes the host reaction to subsequent invasions. In pig livers, the inflammation heals by fibrosis, giving rise to the so-called milk spot lesions (see Figure 7-92) that cause the organ to be condemned by meat inspectors as unfit for human consumption.

The lesions of early migrations in the lungs are likewise mechanical in nature, and once again the initial focal hemorrhages are followed by hyperemia, edema, and eosinophilic infiltration as hypersensitivity develops. In young pigs, extensive lung lesions give

rise to severe respiratory embarrassment. Breathing is rapid, shallow, and marked by audible expiratory efforts (“thumps”) and coughing; pigs may die. A report from Norway where 40 pigs purchased for fattening and placed in a room containing highly contaminated litter died or were killed owing to acute respiratory disease related to *A. suum* migration highlights the continued need for vigilance against this infection (Gjestvang, 2005).

The pathologic effects of adult *A. suum* infections in the small intestine are less dramatic than those of the larval migrations, but they are undoubtedly significant. There may be diarrhea, but the most important effect is interference with proper nutrition and normal growth. Heavily infected pigs fail to make economically profitable gains. Occasional bizarre accidents such as occlusion of the bile duct or perforation of the bowel wall result from the tendency of ascarids to wander.

Diagnosis of clinical ascarosis frequently depends on clinical and necropsy findings because the main pathologic events occur during the prepatent stage. Clinical signs of severe respiratory distress in a group of growing pigs and the discovery of extensive petechial and ecchymotic pulmonary hemorrhages and edema contribute to a diagnosis of acute ascarosis. Pieces of lung tissue should be minced and placed in a Baermann apparatus to demonstrate the migrating larvae. Less acute cases are marked by respiratory distress, varying degrees of malnutrition, and lesions of interstitial pneumonia. Chronic ascarosis is marked by stunting, emaciation, a copious outpouring of *A. suum* eggs in the feces, and lesions of chronic

interstitial pneumonia and hepatic fibrosis. Such pigs are hopeless from an economic point of view.

Anthelmintic medication

A. suum, the economically most important nematode of swine, continues to menace the swine industry despite its susceptibility to piperazines, dichlorvos, fenbendazole, levamisole, ivermectin, and pyrantel tartrate. It is obvious that drugs alone are not successful in controlling this ubiquitous parasite. However, treating and cleaning sows with soap and warm water 2 weeks before moving them to the farrowing crates will materially reduce the contamination to which the piglets will be exposed. Treating again at weaning with continuing attention to the hygienic conditions of the premises should keep the growing pigs reasonably free of *A. suum*. Continuous provision of feeds containing pyrantel tartrate prevents the migration and establishment of *A. suum*. Pyrantel tartrate is the only approved drug that kills the infective larva immediately after it hatches in the small intestine.

In summary, control efforts should be directed at preventing infection of pigs during the first few weeks of life. Anthelmintic medication of the sow before farrowing, careful sanitation at farrowing time, and avoidance of exposure of young pigs to contaminated soils all serve to limit early infection. A method has been described for moving pigs into a new breeding facility without the movement of their parasites (Epe and Blomer, 2001). The described method included using pigs known to have a low level of

A. suum infection; treatment with ivermectin 2 weeks before and the day of transport in a clean trailer to a disinfection platform, where each pig was washed using a high-pressure sprayer for 10 minutes with tap water and 10 minutes with a 2% Venno Oxygen wash (a combination of 2-[2-butoxyethoxy]-ethanol, a nonionic surfactant [isotridecanol ethoxylates in an emulsifier, sulfochlorinated paraffin oil]); transport in another clean trailer to the facility; and leading through a bath of 2% Neopredisan solution. A total of 1203 fecal samples examined 4, 6, and 10 weeks after transfer were all negative for *A. suum*.

Parascaris

P. equorum, the very large ascarid parasite of the horse, can be up to 2 feet long and has large distinctive lips (Figures 4-117 and 4-118). *P. equorum* resembles *A. suum* both epidemiologically and with respect to the route adopted by its larvae in migrating through the tissues. When the infective egg of *P. equorum* is swallowed by a foal, the larva hatches, burrows into the wall of the small intestine, and is carried to the liver by the portal vein. After migrating about in the hepatic tissues, the larva enters a hepatic vein and is carried by the caudal vena cava, heart, and pulmonary artery to the lungs, where it enters an alveolus. After completing a molt in the lungs, the larva ascends in the expectorant mucus of the tracheobronchial tree and returns by way of the lumen of the esophagus and stomach to the intestine, where it completes a final molt and matures.

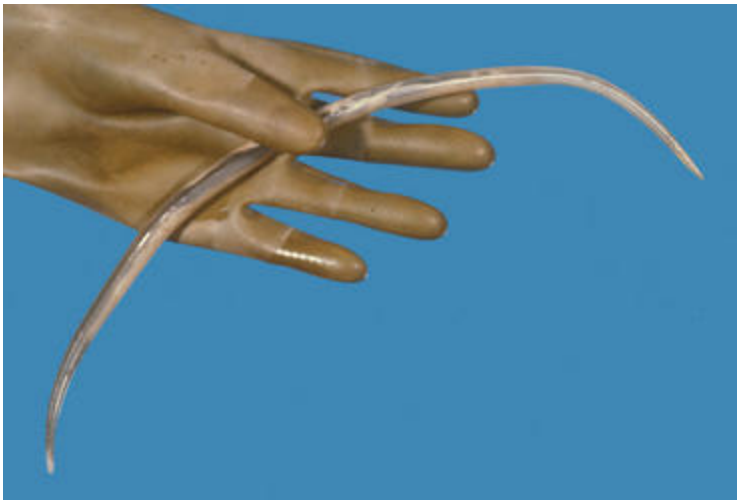

FIGURE 4-117 Adult *Parascaris equorum*.

FIGURE 4-118 *Parascaris equorum*, anterior end of adult female showing the shape of the characteristic lips.

The first waves of invading larvae inflict mainly mechanical injury, and little more than petechial hemorrhages can be observed.

However, as the host becomes sensitized to *Parascaris* antigens, the tissues respond to the presence of larvae with infiltrations of eosinophilic leukocytes and other inflammatory cells. The damage done to the liver and lungs eventually heals, but the chronic reduction in functional capacity suffered during what normally is a period of rapid growth leaves its mark on the yearling. It never will be what it could have been.

The durable infective egg is the key element in the epidemiology of *P. equorum* infection. These eggs accumulate as a growing reservoir of infection in polluted soils, and they adhere by their sticky shell covering to the teats and udder of the brood mare and wait there for the foal to be born.

Heavy infection with adult ascarids causes moderate enteritis and subnormal growth through interference with digestion and absorption of nutrients. Ascaridosis produces a malnourished, undersized, sickly individual with little stamina and reduced resistance to disease: its haircoat is dull, its skin dry and leathery, and its abdomen too large for its frame. It is not unusual to find a half-pail of *P. equorum* in the small intestine of a foal, a sufficient mass of parasites actually to compete with the host for nutrients. Occasionally, adult *P. equorum* perforate the bowel wall and cause fatal peritonitis. Administration of anthelmintics that tend to paralyze ascarids (e.g., pyrantel pamoate, piperazine, and ivermectin) to a foal with a heavy *P. equorum* burden may occasionally cause impaction or complete obstruction of the bowel (Cribb et al, 2006; Schusser, Kopf, and Prosl, 1988).

Control

The thick eggshell of *P. equorum* protects the egg from temperature extremes and ultraviolet irradiation and makes the egg resistant to desiccation and most chemical disinfectants. The epidemiology of *P. equorum* infection therefore differs considerably from that of strongylids with their free-living infective larvae. Therefore effective stall sanitation for the control of ascarids involves weekly removal of all manure and bedding and thorough cleaning of all surfaces with a high-pressure cleaner or steam jenny. Most horsemen find such a program excessively laborious and rely instead on anthelmintics to suppress production and environmental contamination with the eggs of *P. equorum*. However, because of the extraordinary longevity and hardihood of ascarid eggs, contamination, however gradual, tends to be cumulative, and thorough cleaning at least of the foaling stall and of the mare's udder and teats before foaling is well worth the effort.

Anthelmintic medication

Piperazine compounds (100 mg/kg), fenbendazole (10 mg/kg), pyrantel (6.6 mg/kg), ivermectin (0.2 mg/kg), moxidectin (0.4 mg/kg), and a number of other anthelmintics both current and obsolete are highly effective against the intestinal stages of *P. equorum*. Pyrantel tartrate used as a feed additive prevents ascarid infections in horses.

Over the past few years there have been several reports of resistance of *P. equorum* to ivermectin and moxidectin. These reports

have come from the United States, Canada, and Europe (Boersema, Eysker, and Nas, 2002; Craig, Diamond, and Ferwerda, 2007; Hearn and Peregrine, 2003; von Samson-Himmelstjerna et al, 2007; Schougaard and Nielsen, 2007; Slocombe, de Gannes, and Lake, 2007; Stoneham and Coles, 2006). In all these trials horses were not cleared of their infections by treatment with a macrocyclic lactone. For the purpose of clearing the horses of their infection, it was necessary to use pyrantel pamoate or fenbendazole (in one case a 2× dose of pyrantel pamoate was required for clearance [Craig, Diamond, and Ferwerda, 2007]). The macrocyclic lactones still appeared highly efficacious against strongyle and *Strongyloides* infections.

Development of Strongylid, Ascarid, and *Strongyloides* Infections in Foals

Around 60 years ago, Ann F. Russell (1948) reported on her study of the sequential changes in the composition of worm populations in 26 foals from seven different thoroughbred studs. She performed fecal egg counts and identified infective larvae developing in fecal cultures of samples collected from these foals every week from the age of 4 weeks to at least 6 months and, in a few cases, to more than 1 year. These studies remain of interest because they indicate what happens without the pressure of modern anthelmintics. The interesting thing is that the curves would probably still appear about the same; the only things that might change would be that the number of eggs per gram would be less and there would probably be

almost no larvae of *Strongylus vulgaris* recovered from the cultures. However, these two graphs and their interpretation remain an excellent primer in equine parasitology.

In Figure 4-118, egg counts are plotted against age for *S. westeri*, for *P. equorum*, and for the family Strongylidae collectively. Note that *S. westeri* infection reached a maximum early in life, then rapidly dropped to a low level and finally disappeared at about 5 months of age. This accords perfectly with what we now know about the mammary transmission of *S. westeri*.

P. equorum eggs first appeared at about 12 weeks of age, after which egg counts rose steeply to a peak and then rapidly fell but, instead of disappearing completely, persisted at a low level indefinitely. The 12-week delay in appearance of *P. equorum* eggs corresponds closely to the prepatent period of this parasite, and we may deduce from this that the infection was acquired soon after birth. Thus anthelmintic medication of the pregnant mare, careful bathing of her udder and teats, and thorough cleaning of the foaling box are logical measures for the prevention of significant infection of foals with *P. equorum*. The persistence of infection at a low level in horses of all ages and the extraordinary resistance of the egg to the rigors of the external environment make *P. equorum* a difficult parasite to control.

The third and most important curve shown in Figure 4-119 represents a gradual increase in the composite strongylid egg counts during the first year of life. To interpret this curve, one must take

into account the relative abundances of *S. vulgaris*, *S. edentatus,* and the "small strongylids" as determined by fecal culture and identification of the infective larvae. These findings are portrayed in Figure 4-120, which shows that the eggs of the small strongylids always predominated, representing, at various ages, between 80% and 100% of the total strongylid eggs shed in the feces of these foals. This is to be expected in view of the 6- to 11-month prepatent periods of *Strongylus* species and the general predominance of cyathostomes in horses. It is curious, therefore, that small numbers of *S. vulgaris* and *S. edentatus* eggs appear in fecal samples of foals up to 12 weeks of age. Russell (1948) observed this phenomenon in every one of 26 foals studied and interpreted it as evidence of coprophagia. This ingestion of feces by foals is probably related to the normal process of "seeding" the cecum and colon with beneficial microorganisms essential for the digestion of cellulose, but it also presents a clear opportunity for invasion by parasites.

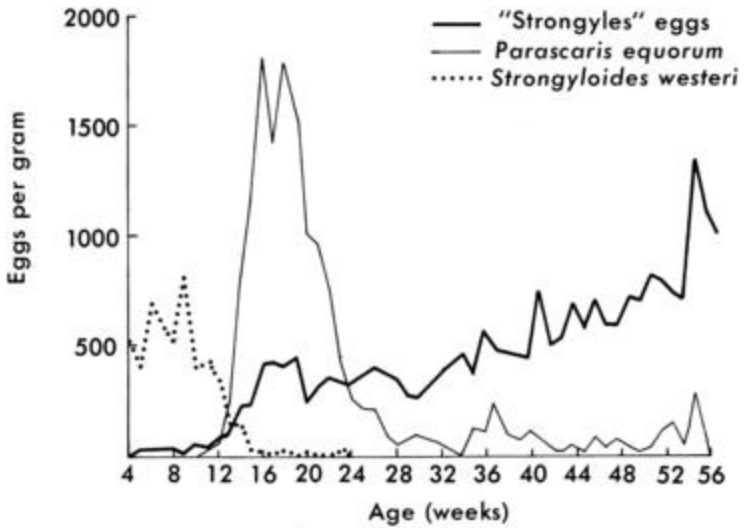

FIGURE 4-119 Average number of eggs of *Parascaris equorum,* "strongyles," and *Strongyloides westeri* counted per gram of manure. Data obtained from weekly observations of 26 foals.

Modified from Russell, 1948; reproduced from Evans JW, Barton A, Hintz HF, et al: The horse, New York, 1977, WH Freeman.

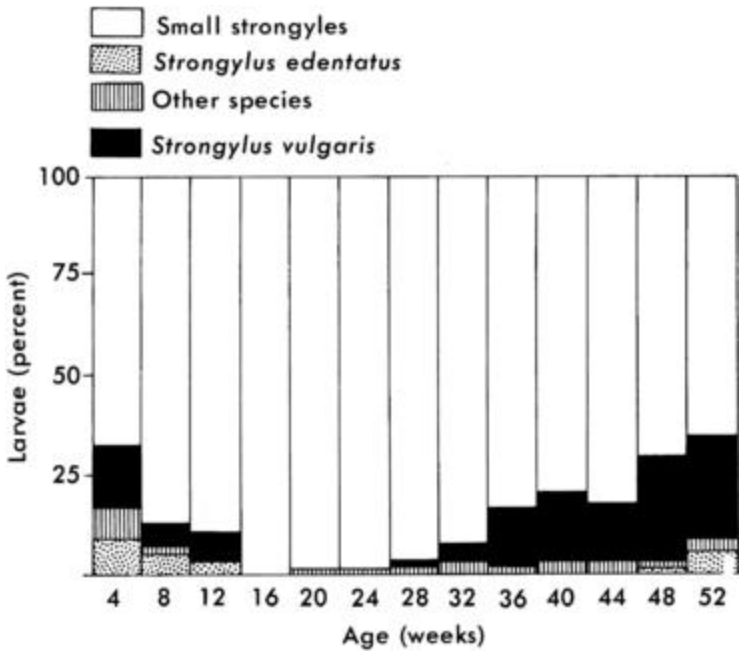

FIGURE 4-120 Percentage of larvae of different species of strongyles in fecal cultures. Data obtained from weekly observations of 26 foals.

Modified from Russell, 1948; reproduced from Evans JW, Barton A, Hintz HF, et al: The horse, New York, 1977, WH Freeman.

As Figures 4-119 and 4-120 show, strongylid egg output increases steadily, and *S. vulgaris* and *S. edentatus* eggs appear on schedule at 6 months and 11 months, respectively. This clearly indicates that strongylid infection begins shortly after birth of the foal and proceeds without interruption thereafter. Because young foals are much more susceptible to the pathogenic effects of these parasites than are older horses, it follows that the greatest efforts

should be directed toward preventing excessive exposure, especially during the first months of life.

Toxascaris

T. leonina is a parasite of cats and dogs in the cooler climates of the world. The adult female can be 10 or so cm long. The egg of *T. leonina* develops rapidly, usually reaching the infective stage in about a week. If the egg is ingested by a rodent or an animal other than the final host, the larva hatches and invades the wall of the intestine, where it remains for about a week before proceeding to other tissues, where it encysts and remains arrested in the infective stage. When the infective egg or an infected rodent is ingested by a dog, cat, or other suitable definitive host, the larva invades the mucosa of the small intestine. There it develops and molts before returning to the lumen of the intestine to mature. Cats and dogs can thus acquire *T. leonina* infection by ingesting infective eggs or rodents with infective larvae encysted in their tissues (Figure 4-121).

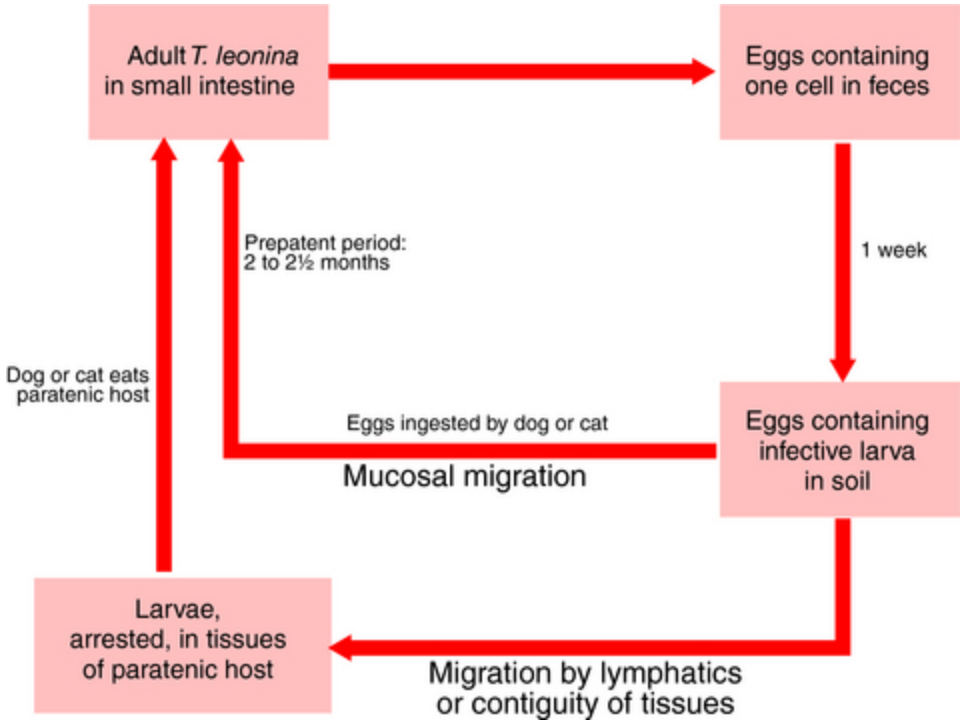

FIGURE 4-121 Alternative life histories of *Toxascaris leonina*.

The eggs of *T. leonina* develop to the infective stage in only 1 week as compared with 4 weeks for *Toxocara* species (see Figure 7-9). This rapid development might explain the persistence of *T. leonina* infection in reasonably well-sanitized cage colonies of dogs. The life cycle of *T. leonina* with its rapid infective-larval development and ability to use mice as paratenic hosts is such that this ascaridoid also often becomes a problem of felids or canids housed in zoologic gardens.

Toxocara

Toxocara is a genus of rather large ascaridoids that as adults are parasites in the small intestine of various mammals. The worms have three large lips and a glandular esophageal bulb (the

ventriculus) located at the junction of the esophagus and intestine. They tend to have cervical alae, and their eggs have pitted surfaces. *Toxocara canis* and *T. cati* are two of the most commonly observed parasites of the dog and cat, respectively. *T. vitulorum* of calves is commonly seen in developing parts of the world, and the egg still can be observed occasionally in feces from calves in the United States. Other species of *Toxocara* include those found in elephants, hippopotami, bats, civet cats, rats, coati mundis, and mongooses.

Toxocara canis

The *Toxocara canis* worm is commonly seen in puppies during the few months after birth. The adults tend to be 10 to 15 cm long and cream colored (see Figure 7-43), with the internal reproductive organs appearing white when viewed through the cuticle in fresh worms. Sometimes when worms are passed in the feces the gut tends to appear rather gray or black, and the worms appear darker than when still quite lively. Adult dogs infected with this parasite that are shedding the eggs in their feces can be found.

Importance

Heavy prenatal *Toxocara canis* infections cause severe abdominal discomfort in nursling pups. The pups whimper and shriek almost continuously and adopt a peculiar straddle-legged posture of the hind limbs when standing or walking. Alarming numbers of immature and adult worms may appear in the feces or vomitus. Death may result from rupture or obstruction of the intestine as the

ascarids, reacting to some irritant, thrash about and become tangled into knots. Obstruction of the bile or pancreatic duct occasionally provides prize exhibits for pathology museums.

Life history

The adolescent wanderings of nematode larvae are influenced not only by their intrinsic capabilities for penetrating tissues and responding to various chemical and physical stimuli, but also by the suitability of the host invaded. If a *Toxocara canis* egg hatches in a dog's stomach, the larva invades the bowel wall and arrives in a pulmonary capillary by the same route outlined earlier for *A. suum*. Unlike *A. suum*, however, the *Toxocara canis* larva is considerably more prone to remain in the circulation than to break into the alveolus, especially if its host is a mature dog. If the larva fails to enter the alveolus, it will be returned to the heart by the pulmonary veins and carried away by the systemic circulation, perhaps to lodge in a kidney or some other somatic tissue, where it will encyst as an arrested infective larva.

The direction taken at the alveolus is crucial in determining whether the larva will undergo a tracheal migration and develop to sexual maturity or a somatic migration to remain arrested as an infective larva in that particular dog. The probability of tracheal migration is high in a newborn puppy. However, by the time the pup is 1 or 2 months old, the probability that a newly hatched *Toxocara canis* larva will develop into an adult ascarid in that particular pup has fallen to a very low level and remains so

indefinitely. During the same period of the pup's life, the probability of somatic migration progressively increases, and arrested infective larvae accumulate in the tissues.

Somatic migration also accounts for the accumulation of arrested infective *Toxocara canis* larvae in the tissues of a wide range of other paratenic intermediate hosts, including rodents, sheep, pigs, monkeys, humans, and earthworms (see Figures 7-51 and 8-99Figure 7-51Figure 8-99). If a mouse with arrested infective larvae in its tissues is eaten by a dog, somatic migration is not observed, and in some instances at least, development proceeds to maturity in the alimentary tract (Sprent, 1958). The mouse not only has saved the larvae but apparently has changed them, too. Migration and encystment in paratenic hosts and exploitation of the prey-predator relationship is an epidemiologic norm for carnivoran ascarids in general. Both *T. cati* and *T. leonina* can be transmitted in this manner, as can ascarid parasites of certain wild carnivorans such as *Baylisascaris procyonis* of the raccoon *P. lotor*.

It should be remembered that adult dogs can be infected with *Toxocara canis*. In a national survey of fecal samples from dogs in shelters around the United States, although the lowest level of roundworm infections occurred in dogs over 7 years of age, greater than 5% of dogs in this age group were infected (Blagburn et al, 1996). It has also been shown that adult dogs can be infected with *Toxocara canis* routinely, as well as repeatedly after anthelmintic clearance, if they are given only a relatively few infective eggs, 100 to 200, at once (Dubey, 1978; Fahrion et al, 2008; Maizels and

Meghji, 1984). There have been no studies on whether larvae in paratenic hosts may more successfully develop in adult dogs than larvae in infective eggs.

From the perspective of the dog and the veterinarian, the most important arrested larvae of *Toxocara canis* are those to be found in the tissues of the female dog (see Figure 7-50). Transmission of infection from bitch to pups occurs almost exclusively by way of **transplacental transmission**. During the last trimester of pregnancy, arrested larvae are reactivated and migrate from the tissues of the bitch to the pups in utero (Fülleborn, 1921). After parturition, small numbers of reactivated larvae also may be shed in the milk, but this is a minor form of transmission for this parasite. The alternative life histories of *Toxocara canis* are summarized in Figure 4-122.

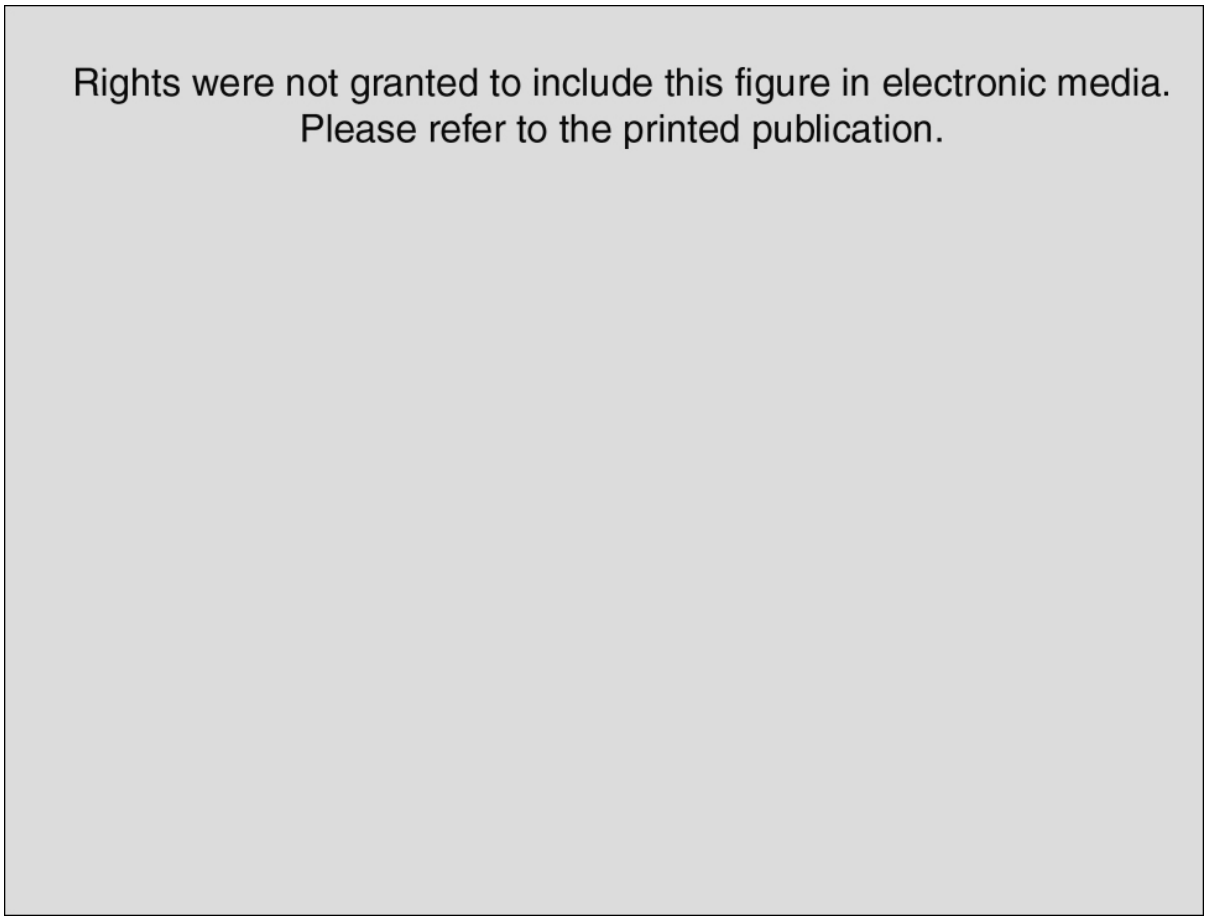

FIGURE 4-122 Alternative life histories of *Toxocara canis*. *1,* A paratenic host is any in which a larval parasite may survive and remain infective for its definitive host without undergoing development. Any of a wide range of animal species including rodents, sheep, pigs, monkeys, humans, earthworms, and adult dogs may serve as paratenic host for *Toxocara canis* larvae. *2,* Arrested infective larvae are also found in the tissues of male dogs, but these are supposed to be of little if any epidemiologic importance. *3,* The larvae that have entered the pups through the placenta molt once in the fetuses but defer further development until after birth.

Redrawn from Sprent JFA: Observations on the development of Toxocara canis [Werner, 1782] in the dog, Parasitology 48:184, 1958.

Treatment

Owing to transplacental transmission, unless heroic measures have been taken to prevent infection, pups may be assumed to be

infected. About the only anthelmintic labeled for the treatment of 2-week-old puppies is pyrantel pamoate. Medication should start routinely as early as the second week of life and be repeated every 2 weeks until the pup is 3 months old. Young puppies are also regularly treated with piperazine compounds (110 mg piperazine base per kilogram), which is considered safe and highly effective against ascarids in the lumen of the alimentary tract and therefore ideally suited to removing *Toxocara canis* as they arrive and develop in the intestinal lumens of perinatally infected pups. Many of the labels for piperazine products, however, state that they should not be used in puppies under 6 weeks of age. Drontal Plus (febantel, praziquantel, and pyrantel pamoate) is labeled for use in puppies older than 3 weeks and weighing over 2 pounds. Milbemycin oxime (with or without lufenuron) is labeled for puppies over 4 weeks of age and 2 pounds in weight. Puppies over 6 weeks of age can be treated with fenbendazole or ivermectin with pyrantel pamoate. At 7 weeks of age, puppies can be treated topically with moxidectin and imidacloprid. At 8 weeks the formulation of ivermectin with pyrantel pamoate and praziquantel is labeled for use in puppies.

The question is often asked if the puppy placed on a monthly heartworm preventive also needs to be treated every 2 weeks as per the Centers for Disease Control and Prevention (CDC) guidelines (www.cdc.gov/ncidod/dpd/parasites/ascaris/prevention.htm), which state, “In areas where both ascarids and hookworms are common, begin treating both puppies and their mothers with an

age-appropriate anthelmintic at 2, 4, 6, and 8 weeks of age. Some recommend extending this to 12 weeks and then treating monthly until the pet is 6 months old. To treat for ascarids alone, begin by 2½-3 weeks and treat every 2 weeks for at least three additional treatments." In one study in the United Kingdom, 104 puppies from three kennels where *Toxocara canis* was common were given either milbemycin oxime with lufenuron (Sentinel) or febantel, pyrantel pamoate, and praziquantel (Drontal Plus) beginning at 2 weeks of age, with the Sentinel dogs being treated monthly until the dogs were 26 weeks old and the Drontal Plus dogs being treated every other week for 12 weeks and then again when the dogs were 26 weeks old (Schenker et al, 2006). There was very little difference in the amount of egg shedding between the two groups, and the Sentinel-treated dogs in this study actually shed slightly fewer eggs and had more negative fecal samples. There are two additional points that need to be considered relative to this question. First, in light of the CDC recommendation, it may be wisest to treat between the first few monthly treatments of a puppy in order to stay in compliance. Second, it should be remembered that monthly products are safety tested by the U.S. Food and Drug Administration (FDA) as though they are going to be given once a month for the life of the pet, whereas other products are tested as though they are going to be given once per indication of infection. So, the question remains a complicated one.

In breeding situations, the role of the bitch in the epidemiology of *Toxocara canis* is paramount because she harbors the better part

of the reservoir of infection not contained in the soil. Clients should be advised that bitches bestowing pathogenic *Toxocara canis* burdens on their litters will likely repeat the performance once or twice again, even after the uptake of infective eggs has ceased. Clients should also be made aware that the environment of a bitch with a litter of nurslings is likely to contain veritable clouds of eggs from 3 weeks postpartum onward, and it is during this period that anthelmintic medication and sanitation can be applied most effectively and efficiently. Rather heavy patent infections are regularly observed in nursing bitches for a short period beginning about 1 month after parturition. This has been explained as follows (Sprent, 1961). Some reactivated larvae fail to establish themselves in the pups' intestines and are passed with their feces. Brood bitches eat their pups' feces to clean the nest and, in so doing, afford these jettisoned larvae a second chance to mature.

Treating to clear arrested larvae

The phrase "*Toxocara canis*–free dogs" implies that the dogs are devoid of both adult and larval parasites. However, it is nearly impossible to detect small numbers of arrested larvae in the tissues of even a small pup, so the status "*Toxocara canis*–free" is always to be taken with a grain of salt. The sort of measures required to produce *Toxocara canis*–free dogs are usually beyond the resources (and requirements) of commercial breeders.

Griesemer and Gibson (1963) obtained *Toxocara canis*–free pups from colostrum-deprived bitches raised in isolation that had been

maintained on wire through several gestations without anthelmintic medication. The somatic larval burden apparently was eliminated through the placenta over the course of several pregnancies.

Bitches with *Toxocara canis* and *A. caninum* infections were medicated daily with fenbendazole from the fortieth day of gestation to the fourteenth day of lactation at a dosage rate of 50 mg/kg. Their pups were found free of both parasites (Düwel and Strasser, 1978). Burke and Roberson (1983) obtained 89% fewer ascarids and 99% fewer hookworms in pups from dams subjected to the same regimen. The timing of medication coincided with the period of reactivation and migration of arrested *Toxocara canis* larvae in these parturient females.

Ivermectin administered during gestation has been shown to cause marked reductions in the number of *Toxocara canis* organisms in puppies born to experimentally infected bitches (Shoop et al, 1988). Treatments of 1.0 mg/kg body weight on days 20 and 42 or 0.5 mg/kg body weight on days 38, 41, 44, and 47 of gestation both caused marked reductions in the number of worms recovered from puppies of treated bitches. These dosages are well above the level of ivermectin used in heartworm prophylaxis.

Toxocara cati

The worm *T. cati* is slightly smaller than *Toxocara canis*, with females up to 12 cm long, and has very elegant cervical alae (Figure 4-123 and see Figure 7-56). When the fresh worm is observed, the ventral curvature of the anterior end along with the large cervical

alae gives the front end of the worm a cobralike appearance. These worms are commonly delivered to practitioners after they have been observed in vomitus by owners. If in doubt about the worm's identity, the practitioner can always break the worm open about one third of the body length behind the head and look for the more familiar *Toxocara* eggs with a microscope. This will work, of course, only if the worm presented is a female.

FIGURE 4-123 *Toxocara cati* stomal end showing the broad cervical alae.

Life history

The migration patterns of *T. cati* differ qualitatively from those of *Toxocara canis* in that (1) prenatal infection through the placenta does not occur and (2) the probability of tracheal migration in egg infections remains high throughout the cat's life (Figure 4-124). Neonatal infection through the mammary glands had been

considered an important route of infection in kittens (Swerczek, Nielsen, and Helmbolt, 1971); however, more recent work has shown that transmammary transmission does not occur in cats with chronic infections, although it can occur if cats are infected acutely during the last part of pregnancy (Coati, Schnieder, and Epe, 2004). Infected paratenic hosts unquestionably represent an important reservoir of infection for adult cats, at least those with well-developed predatory habits. In larvae from cats infected acutely during pregnancy and from paratenic hosts, the migration in the cat and their arrested development in the paratenic host appear in some way to satisfy the larval wanderlust and, although a small proportion of the larvae may wander as before, most develop to maturity after a sojourn in the wall of the stomach (i.e., a mucosal migration; Sprent, 1956).

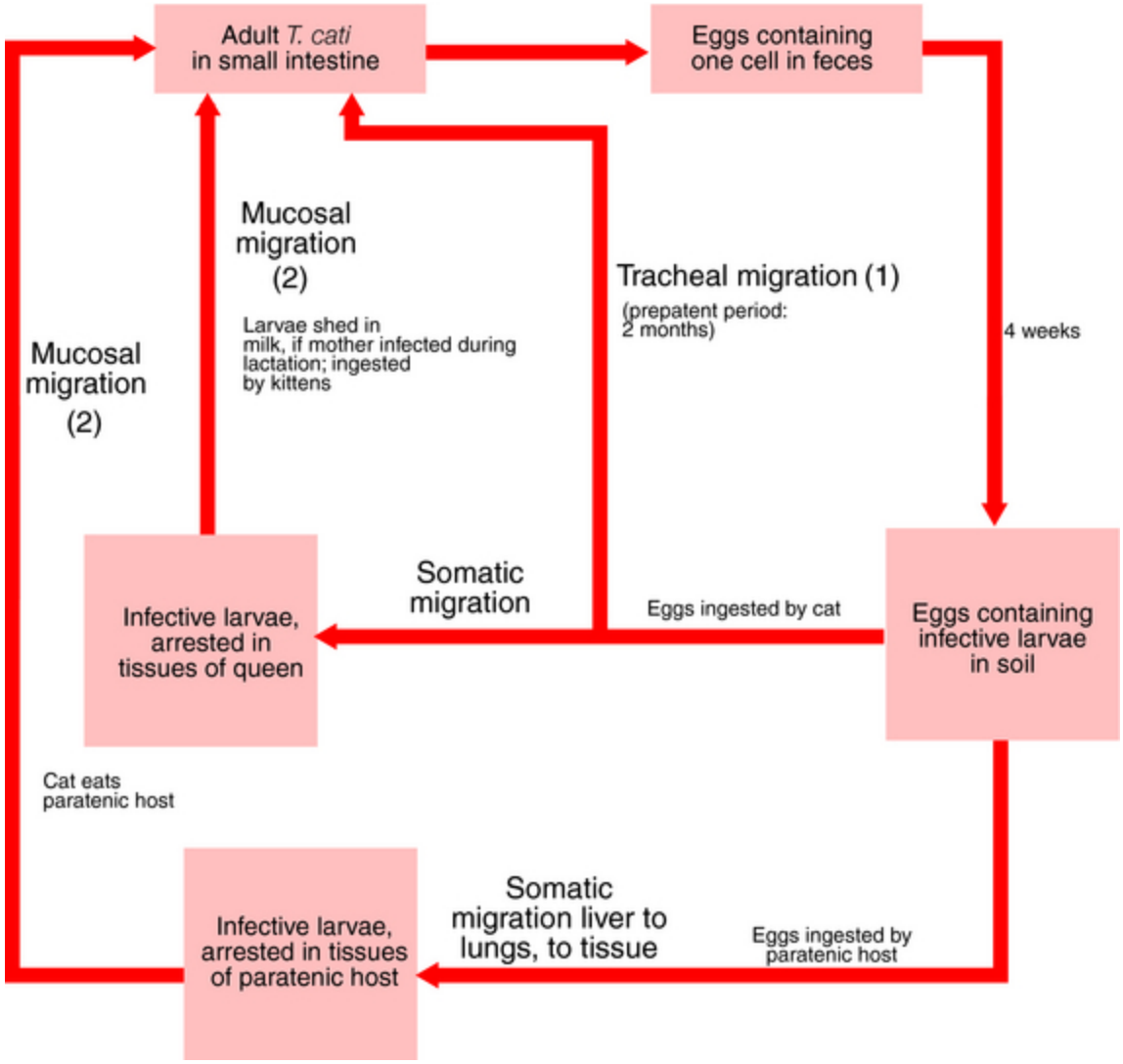

FIGURE 4-124 Alternative life histories of *Toxocara cati*. *1,* The probability that ingestion of infective eggs will lead to patent infection remains substantial throughout the life of the cat. *2,* Larvae that have already undergone somatic migration in a paratenic host, including the queen, satisfy their histotrophic requirements with a mucosal migration. Transmammary transmission seems to occur only if the queen is acutely infected during late pregnancy. The relative epidemiologic importance of these alternatives will depend on the kind of environment, the abundance of suitable paratenic hosts, and the sex and habits of the cats

Redrawn from Coati N, Schnieder T, Epe C: Vertical transmission of Toxocara cati Schrank 1788 (Anisakidae) in the cat, Parasitol Res 92:142, 2004; Sprent JFA: The life history and development of Toxocara cati (Schrank, 1788) in the domestic cat, Parasitology 46:54, 1956; Swerczek TW, Nielsen SW, Helmbolt CF: Transmammary passage of Toxocara cati in the cat, Am J Vet Res 32:89, 1971.

Treatment

The fact that cats get neither hookworms nor roundworms routinely from their mother by transmammary or transplacental transmission means that treatment of the very young kitten is not as critical as the early treatment of young puppies. The only product in the United States labeled for 2-week-old kittens is pyrantel pamoate; when this is formulated with praziquantel (Drontal), the age limit on the label is 4 weeks and the weight requirement is 1½ pounds. Piperazine in various formulations is also often administered to young kittens; although as with the dog, many of the labels on these products say they should not be given to kittens younger than 6 weeks of age. The other products that are approved for cats have labels that are quite conservative relative to the dosing of kittens, with some being approved for treatment beginning at 6 weeks of age (ivermectin and milbemycin oxime), 8 weeks (selamectin), and 9 weeks (emodepside and praziquantel); some of these have weight restrictions as well.

Environmental Control of Roundworms

Soil pollution

Toxocara and *Toxascaris* eggs are very resistant to environmental extremes and remain infective for years, especially in poorly drained clay and silt soils, hence their accumulation in soil and filth and the threat they pose to successful dog-rearing progress with time. A reasonable explanation for the heavy ascarid infections so frequently encountered in hound pups might be sought in the common practice

of chaining the hounds almost permanently to doghouses, a practice particularly conducive to soil pollution. Because the infective eggs are virtually immune to any reasonable measures taken to destroy them, the most effective measure is to entomb them under a concrete or bituminous asphalt slab. Once the slab is installed and provided that feces are not allowed to accumulate for more than a week at a time, the probability of the confined dog ingesting infective ascarid eggs becomes quite small. The next best way of decontaminating polluted soil is to replace the top foot or so with fresh gravel.

Contaminated kennel areas

All surfaces must first be made physically clean. High-pressure washers like those in car washes are very effective, and inexpensive mobile units are quite satisfactory. Wood and wire construction is difficult to clean properly with any kind of equipment or amount of effort. After surfaces are physically clean, they may be mopped or sprayed with 1% sodium hypochlorite (3 cups Clorox per gallon of cool water) to strip off the outer protein coat of the ascarid eggs so they will not stick to surfaces and can be rinsed away. The preliminary cleaning is absolutely essential because any appreciable amount of residual organic matter will neutralize the sodium hypochlorite and render it ineffective in stripping the ascarid eggs. Notice that nothing has been said about killing the ascarid eggs. The preceding treatment does not kill ascarid eggs; it just knocks them loose. Ascarid eggs are killed by heat. Raising the temperature of a

cage or bedding above 60° C (140° F) for 5 minutes will kill all eggs, but this temperature may be difficult to reach under many circumstances when different housing structures are involved.

Paratenic hosts

Mice and other small paratenic hosts may play a significant role in the epidemiology of *Toxocara* and *Toxascaris* infection, especially with regard to predacious cats. If you dissect the mice, voles, moles, shrews, and snakes that your cat drags in, you will probably find *Toxocara* larvae encysted in many of them. A survey in rural England of brown rats found larvae of *Toxocara* in 15% of the rats examined (Webster and Macdonald, 1995). In a rural setting there is probably little that can be done about this source of infection except to confine the dogs and cats indoors. Rodents are attracted to the abundance of food in kennels and catteries and are not put off by the presence of their ferocious predators; a mouse is quite willing to risk its life for a kibble. There seems to be little information about the importance of rodents in transmitting ascarids and other parasites to dogs and cats confined to buildings and outdoor enclosures. However, considering the facts gathered here, an investment in rodent control could be partly written off against the cost of controlling parasites.

Human Toxocarosis (Visceral Larva Migrans)

The widespread distribution of dog feces and the prevalence of *Toxocara canis* eggs therein led Fülleborn (1921) to wonder about the pathologic significance in man of nodules containing larvae of this parasite. These nodules occurred principally in the liver, lungs, kidneys, and brain. Beaver et al (1952) recognized the causative role of *Toxocara canis* larvae in cases of sustained eosinophilia (above 50%), pneumonitis, and hepatomegaly in children younger than 3 years old and dubbed the condition visceral larva migrans. As a horrible sequela occurring at 3 to 13 years, the larvae may produce granulomatous retinitis. Misdiagnosis of *Toxocara canis*–induced granulomatous retinitis as retinoblastoma has prompted the unnecessary enucleation of children's eyes in at least 36 reported cases.

The typical epidemiologic situation around symptomatic cases involves a toddler eating soil heavily contaminated with infective *Toxocara canis* eggs. Such soil is likely to be found wherever dogs habitually defecate and, in particularly high concentration, in the nests of maternal bitches and their litters. The soil of public parks in cities tends to be heavily contaminated with infective *Toxocara canis* eggs (Dubin, Segall, and Martindale, 1975; Woodruff and Burg, 1973). Although dirt eating is often considered to be a manifestation of depraved appetite (i.e., pica) resulting from dietary deficiency or emotional insecurity, even well-nourished, well-adjusted babies should not be trusted to forgo whatever delicacies may be at hand.

Children must not be allowed to play where dogs habitually defecate, and dog feces must never be used to fertilize vegetable gardens.

The vast majority of infections in humans around the world are without recognized symptoms. People act like other paratenic hosts, and the larvae can persist in the tissues of primates for at least 10 years (Beaver, 1966). A recent survey of human sera in the United States from people over 6 years of age (n = 20,395) revealed that some 13.9% were serologically positive for the infection, and because of the biology of the larvae (Won et al, 2007), it is highly likely that this means that they are currently infected. *T. cati* appears somewhat less important than *Toxocara canis* as a cause of human infection, with some cases being diagnosed serologically (Petithory and Beddock, 1997; Virginia et al, 1991), but there is as yet no consensus as to whether specific infections can be reliably distinguished serologically. For people, there is no other logical source of infection in most cases other than infective eggs in the environment, and in the United States, owing to the lack of other common intestinal parasites in people, concerns about cross-reaction with antibodies to other parasites is considered minimal. Thus it seems that people are getting infected from the ingestion of eggs that have embryonated in soil after having been passed in the feces of dogs and cats. This means that the veterinary profession has a clear responsibility to identify and eliminate *Toxocara canis* and *T. cati* infection at every opportunity and to provide the public with

objective scientific information about the epidemiology and prevention of human toxocarosis.

Cases have been reported of children infected with adult *T. cati* (Eberhard and Alfano, 1998), but it is believed that these children may have ingested intact adult worms recovered from litter boxes.

Visceral Larva Migrans in Nonhuman Hosts

In veterinary medicine, it should not be forgotten that other hosts besides people and other primates can develop disease due to the migrations of the larvae of *Toxocara canis* (and *T. cati*) in their tissues. Cats infected with *Toxocara canis* develop elevated eosinophil counts and massive eosinophilic granulomas in their kidneys and livers and have lungs with severe medial hypertrophy of the pulmonary vessels (Parsons et al, 1988). There is a long list of other hosts that can develop disease due to *Toxocara canis* that includes sheep, pigs, and tortoises (Parsons, Bowman, and Grieve, 1989). The larvae of *Toxocara canis* and *T. cati* can cause white-spot disease in the livers of pigs similar to those caused by *A. suum* (Ronéus, 1966).

Baylisascaris

Species of *Baylisascaris* common in North American wildlife include *B. procyonis* of the raccoon, *Baylisascaris columnaris* of the skunk, and *Baylisascaris laevis* of the woodchuck. The raccoon has been introduced into Europe, where it has proliferated quite successfully, and the raccoon roundworm is also now present in Europe. *B. procyonis* causes a particularly serious form of visceral larva migrans

in a wide range of hosts including humans (Kazacos, 2001), and zoonotic infections have also occurred Europe as well (Küchle et al, 1993). Unlike *Toxocara* larvae, the larvae of *B. procyonis* grow larger as they migrate. However, they resemble *Toxocara canis* larvae in that they tend to invade the central nervous system of intermediate hosts and, because they grow as they migrate (see Figure 8-100), only one to three *B. procyonis* larvae in the brain may prove fatal. These properties render them very pathogenic to more than 100 species of animal, including woodchucks, rabbits, ground squirrels, chickens, turkeys, partridges, pigeons, cockatiels, chukar partridges, emus, quail, and humans (Kazacos, 2001; Kazacos et al, 1983; Myers, Monroe, and Greve, 1983; Roth et al, 1982). Unfortunately, human cases continue to occur (Pai et al, 2007; Park et al, 2000), and it is imperative that veterinarians be aware of the risk posed by raccoons either being held in captivity or within a community. Raccoons infected with *B. procyonis* can be treated with most of the anthelmintics active against *Toxocara canis* (Bauer and Gey, 1995).

Hay, straw, and other feedstuffs and bedding materials contaminated with raccoon feces are often found to be the source of infective eggs (Figure 4-125) of this parasite. Haylofts and attics may be attractive places for children to play during inclement weather, but such areas should be inspected beforehand to make sure that raccoons have not been nesting in them. Ground-feeding birds such as doves, pigeons, and robins are particularly at risk

when they feed on nondigested seeds in dried raccoon feces (Evans and Tangredi, 1985).

FIGURE 4-125 Infective egg of *Baylisascaris procyonis.*

Dogs can be hosts of the adult worms. Greve and O'Brien (1989) diagnosed infection with adult *B. procyonis* in a 5-month-old Labrador Retriever (patent) and a 6-month-old Golden Retriever (nonpatent) by administering piperazine and identifying the adult and juvenile worms when these were passed in the feces. Eggs of this worm also have been observed in the feces of dogs in Minnesota, Indiana, Michigan, and Prince Edward Island (Conboy, 1996; Kazacos 2001). Dogs naturally infected with adult worms have been treated for their *B. procyonis* infections using milbemycin oxime (Bowman et al, 2005). The eggs of this worm are slightly smaller than those of *Toxocara canis* and *Trichuris vulpis* (Figure 4-126).

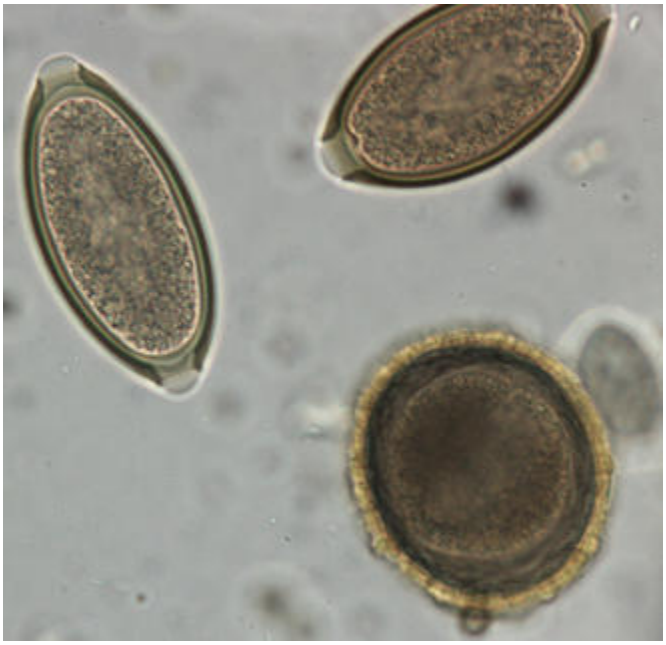

FIGURE 4-126 An egg of *Baylisascaris procyonis* and two eggs of *Trichuris vulpis* in the feces of a naturally infected dog.

Order Spirurida

The order Spirurida contains two suborders: Camallanina and Spirurina. Members of both suborders require an arthropod, either a crustacean or an insect, intermediate host for development to the infective stage. The definitive host acquires spirurid infections by ingesting infected arthropods or paratenic hosts that have fed on such arthropods. The suborder Spirurina also includes the superfamily Filarioidea, for which the intermediate host is a blood-feeding arthropod that becomes infected while taking its blood meal and that vectors the parasite when taking another blood meal.

Suborder Camallanina

Dracunculus

The suborder Camallanina contains only one genus of veterinary significance, *Dracunculus*, a parasite of the subcutaneous tissues of carnivorans and man (Figure 4-127 and see Figure 7-49). The female *Dracunculus* is very large (up to 120 cm), and the male is smaller (up to 40 mm). When a female has been fertilized, the anus and vulva atrophy, and a shallow ulcer forms in the host's skin at the location of the anterior end of the worm. When water wets this ulcer, the female projects her body and prolapses a length of uterus, which then bursts to discharge a horde of larvae (Figure 4-128). Her body then slowly moves toward the opening to await the next wetting.

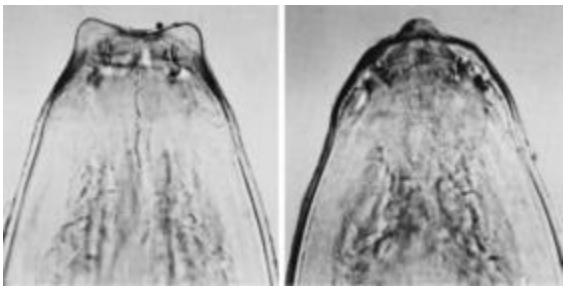

FIGURE 4-127 *Dracunculus insignis* from the axillary connective tissue of a dog. *Left,* The lateral aspect of the stomal end. *Right,* The dorsoventral aspect.

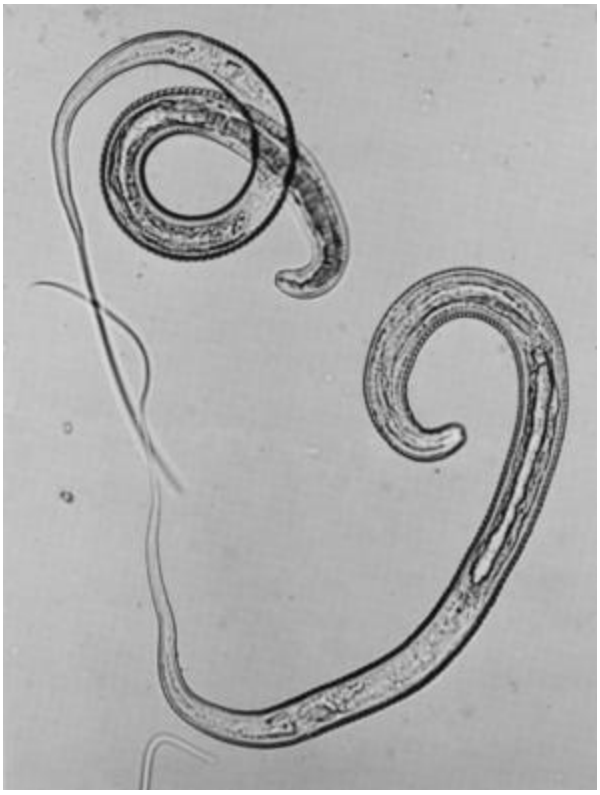

FIGURE 4-128 *Dracunculus insignis* first-stage larvae.

Humans are infected with their own species of *Dracunculus*, *Dracunculus medinensis*. This is a parasite that is on the ropes in its bout with extinction owing to a massive international campaign aimed at its eradication, and only about 10,000 cases a year are now reported in about nine countries in Africa (Hopkins et al, 2007). A primitive technique for extracting *D. medinensis* from humans consisted of grasping the worm and winding it up on a stick a little at a time. The winding takes days because if the worm is broken in the process, a severe reaction may develop. Surgical excision is the modern treatment of choice.

Veterinarians in the United States are liable to come across *Dracunculus insignis*, a parasite of the raccoons and other

carnivorans, including the dog and cat in North America (see Figure 8-108). *Dracunculus* species have also been reported from snakes and snapping turtles in the United States. In the life cycle of this genus of worms, the larvae liberated from the female that is slowly inching out of the body will become infective if ingested by a copepod of the genus *Cyclops*. Development in the copepods takes about 3 weeks. The definitive host becomes infected by ingesting these *Cyclops* organisms in the drinking water. It appears in the case of *D. insignis* that frogs can serve as paratenic hosts (Eberhard and Brandt, 1995), which increases the chance for dogs to become infected by the ingestion of frogs.

Suborder Spirurina

The suborder Spirurina contains 10 superfamilies; six are of interest as parasites of domestic animals. The stoma and surrounding structures of spirurins are distinctive. Comparison of specimens with the illustrations of this section should suffice for generic identification. The one exception here are the Filarioidea, which for the most part have very plain and simple stomas.

Superfamily Gnathostomatoidea

Gnathostoma species have a doughnut-shaped collar of spines surrounding the oral opening (Figure 4-129). Adult specimens are found in cystic nodules in the stomach walls of wild and domestic carnivores. Eggs are passed in the one- to two-cell stage and develop to the second larval stage in water. These larvae hatch and develop to the infective third stage only if ingested by copepods *(Cyclops)*. A

variety of amphibians, snakes, and fishes may serve as paratenic hosts to convey the gnathostome from the copepod to the definitive host. The migrations of gnathostome larvae in the liver and other organs of the definitive host are destructive. The cystic nodules housing adult *Gnathostoma spinigerum* may break open into the peritoneal cavity with fatal outcome. Larvae of *G. spinigerum* ingested by human beings tend to wander aimlessly without maturing.

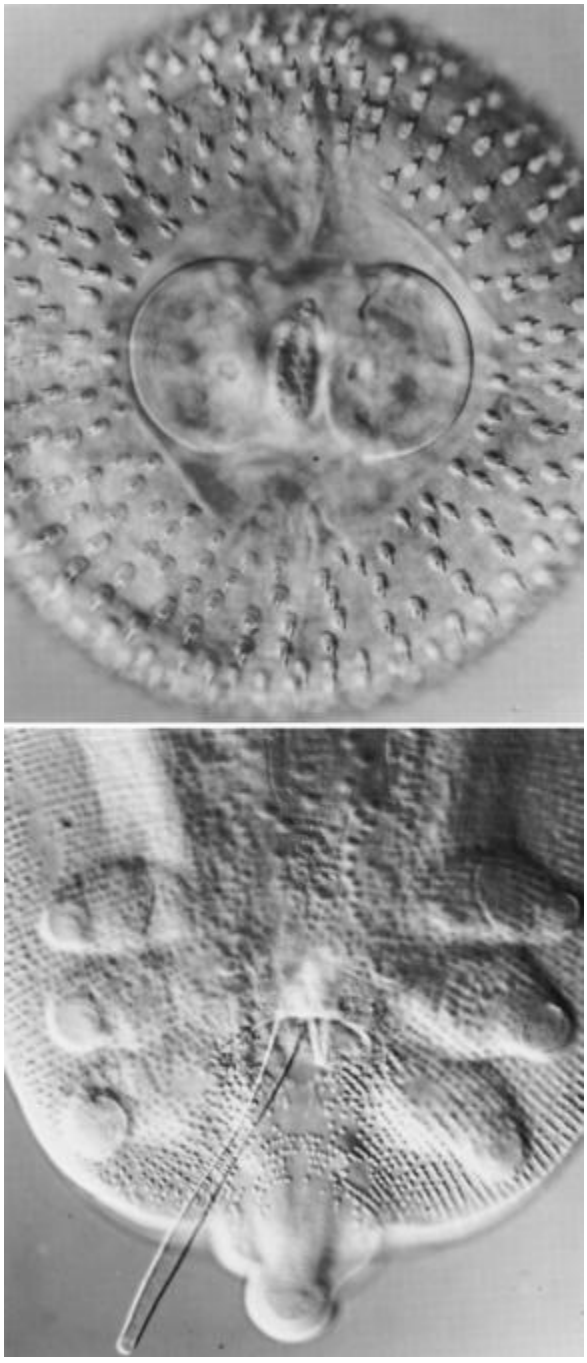

FIGURE 4-129 *Gnathostoma* stomal end (*upper)* and caudal extremity of the male *(lower)*.

Superfamily Physalopteroidea

Identification

Physaloptera species are parasites of the stomach of carnivorans. The mouth is flanked by pseudolabia and surrounded by a cuticular collar (Figures 4-130 and 4-131). The adult worms are white or pinkish in color and tend to live with the anterior end embedded in the mucosa (see Figure 7-55). In the dog the adult worms often are present also in the very anteriormost portion of the duodenum at the level of the gastric valve. Infections with these worms in dogs and cats often are associated with vomiting, and the adults are often viewed during endoscopy (Jergens and Greve, 1992).

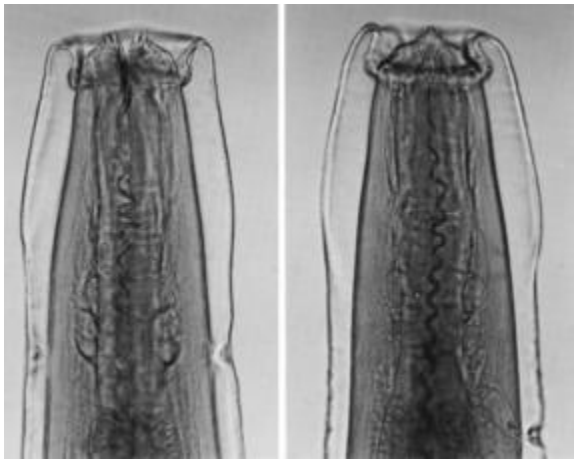

FIGURE 4-130 *Physaloptera* sp. *Left,* The dorsoventral aspect of the anterior extremity. *Right,* The lateral aspect of the anterior extremity.

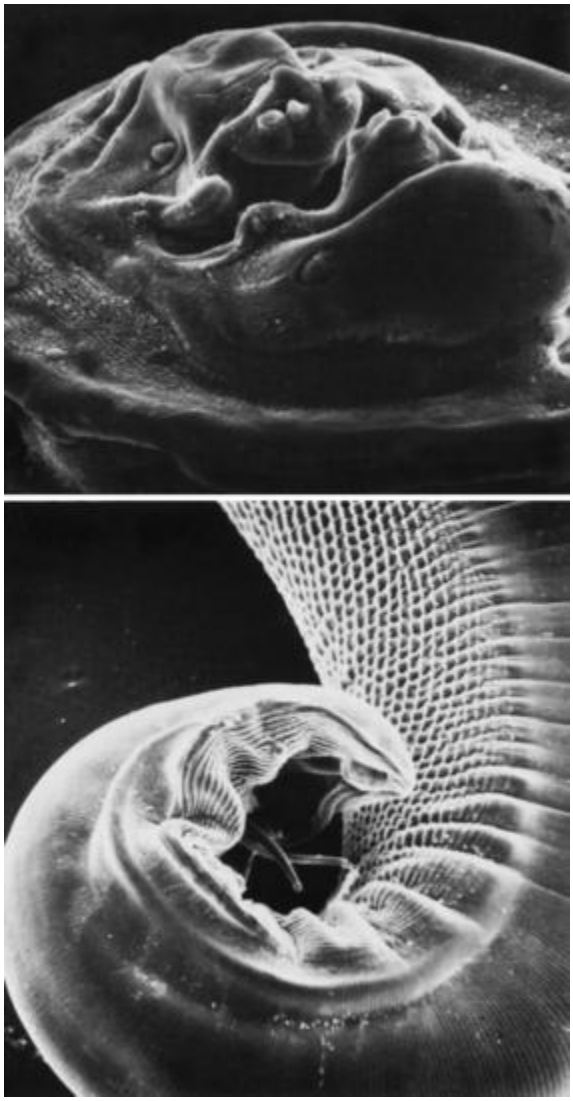

FIGURE 4-131 *Physaloptera* sp. stoma *(upper)* and caudal extremity of male *(lower)*.

Life history

The female worm lays small, thick-walled, larvated eggs. The larvae in the eggs will develop to the infective stage in various coprophagous beetles, crickets, and other insects. The larvae will also use various cold-blooded vertebrates as paratenic hosts.

Treatment

Dogs have been treated with fenbendazole at 50 mg/kg for 3 days (Jergens and Greve, 1992). Infected cats have been treated with ivermectin at 0.2 mg/kg (Gustafson, 1995) and with two doses of pyrantel pamoate at 5 mg/kg given 3 weeks apart (Santen, Chastain, and Schmidt, 1993). A summary of *Physaloptera* infections in 29 dogs and six cats in Iowa concludes with the recommendation that animals be given a trial course of pyrantel pamoate at 20 mg/kg that may be repeated if signs of vomiting do not cease (Campbell and Graham, 1999). These authors also suggest that the different anthelmintics used in their series of cases (fenbendazole, pyrantel pamoate, and pyrantel pamoate, praziquantel, and febantel) all appeared efficacious, but some required elevated doses or longer treatment times than suggested for typical labeled use.

Superfamily Thelazioidea

Family Pneumospiruridae

Pneumospirurids are parasites of the lungs of wild carnivorans and appear occasionally in domestic dogs and cats. *Pneumospirura* and *Metathelazia* are representative genera.

Family Thelaziidae

Thelazia species (Figure 4-132) are parasites of the conjunctival and lachrymal sacs of domestic animals. North American species include *Thelazia lacrymalis* in horses, *Thelazia skrjabini* in cattle and horses, *Thelazia gulosa* in cattle, and *Thelazia californiensis* in dogs, sheep, and various wild mammals. Slightly less than half of the horses

surveyed in Kentucky were found infected with *T. lacrymalis* (Lyons et al, 1986). *Thelazia* species apparently do little harm to cattle and horses in North America, but exceptional cases requiring treatment may arise.

FIGURE 4-132 *Thelazia* sp. from the conjunctival sac of a horse.

Life history

The female *Thelazia* worm deposits thin-shelled eggs containing larvae that develop to the infective stage in the face fly, *Musca autumnalis*. The Oriental face fly, *Musca hervei*, serves as intermediate host of *Thelazia* species in Japanese cattle (Shinonaga et al, 1974). A great deal of work over the past few years, carried out mainly in China and Italy with a canine and human Eurasian

species of *Thelazia*, *Thelazia callipaeda*, has revealed that the vectors of this species are drosophilid fruit flies of the genera *Phortica* and *Amiota* (Shen et al, 2006). *T. californiensis* has been considered as being vectored by the muscoid latrine flies, *Fannia canicularis* and *Fannia benjamini,* but the fruit flies may explain ocular cases that have occurred in the western United States that have been associated with people getting gnats in their eyes (Kirschner, Dunn, and Ostler, 1990).

Treatment

Doramectin at 0.2 mg/kg given either subcutaneously or intramuscularly has been approved for the treatment and control of *Thelazia* infections in cattle. A single dose of tetramisole subcutaneously at 12.5 to 15 mg/kg produced rapid clinical recovery in infected cattle. Levamisole at a rate of 5 mg/kg administered subcutaneously or 1% aqueous solution as an eye lotion was also effective (Aruo, 1974; Corba, Scales, and Froyd, 1969; Vassiliades et al, 1975). *T. callipaeda* infections in dogs have been successfully treated by subcutaneous injections of 0.2 mg ivermectin per kilogram body weight (Rossi and Peruccio, 1989), direct instillation of 1 or 2 drops of 1% moxidectin into each eye (Lia et al, 2004), or the topical application to the back of the neck of topical moxidectin (2.5%) with imidacloprid (10%) providing a dose of moxidectin of 2.5 to 6.5 mg/kg (Bianciardi and Otranto, 2005). Brooks, Greiner, and Walsh (1983) successfully treated conjunctivitis in a Senegal parrot caused by *Thelazia* sp. by instilling

one drop of a 0.125% demecarium bromide, a cholinesterase inhibitor, into the conjunctival sac and subsequently flushing three paralyzed worms with sterile saline solution.

Superfamily Spiruroidea

Gongylonema species are parasites of cattle and other ungulates. The cuticle is covered with wartlike cuticular bosses (Figure 4-133), especially near the anterior end, and the nematode can usually be found woven into a remarkably regular sinusoidal tract in the mucous membrane of the host's esophagus *(Gongylonema pulchrum)* or rumen *(Gongylonema verrucosum)* (Figure 4-134). Eggs containing first-stage larvae are passed on the host's feces and, if ingested by a dung beetle or a cockroach, develop to the infective stage in about a month. The definitive host becomes infected by ingesting the infected insect. *Gongylonema* species are usually harmless.

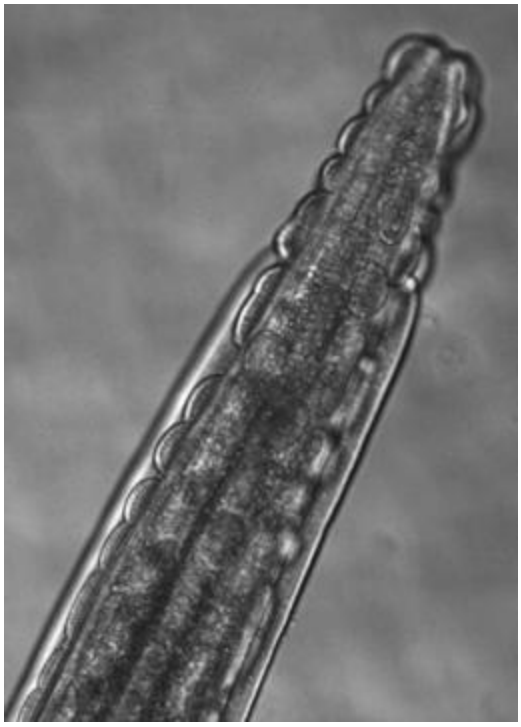

FIGURE 4-133 *Gongylonema pulchrum,* anterior end of worm showing bosses on cuticle.

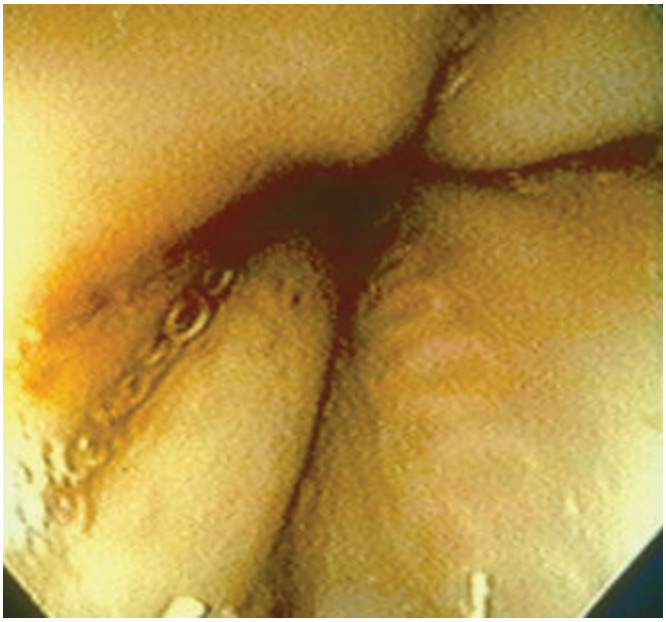

FIGURE 4-134 *Gongylonema pulchrum.* Sinusoidal worm under esophageal mucosa as viewed with an endoscope.

Courtesy Dr. Thomas Divers, College of Veterinary Medicine, Cornell University, Ithaca, New York.

Spirocerca lupi, a parasite of canids, is found in fibrous nodules in the wall of the esophagus or stomach (see Figures 8-103 to 8-105Figure 8-103Figure 8-105). The very small (12 × 30 μm) egg contains a vermiform embryo when shed in the feces (see Figures 7-25 and 8-105Figure 7-25Figure 8-105). If ingested by a coprophagous beetle, this vermiform embryo develops into a larva capable of infecting dogs and a broad range of paratenic hosts, including lizards, chickens, and mice. When infective larvae are ingested by a dog, they migrate in the adventitia of the visceral arteries and aorta to the walls of the esophagus and stomach. Some go astray and encyst in ectopic locations, but reproductive adults are normally found in cystic nodules that communicate with the lumen of the esophagus or stomach through fistulas. Dysphagia and vomiting, esophageal neoplasia, aortic aneurysm or rupture, and secondary pulmonary osteoarthropathy may be associated with chronic *S. lupi* infection.

For *S. lupi* in dogs the treatment of choice is currently doramectin. It has been given subcutaneously every other week for 4 to 6 total treatments at 0.2 or 0.4 mg/kg with additional treatments given monthly until lesions had resolved (subcutaneously at 0.4 mg/kg) or orally (0.5 mg/k daily) for an additional 6 weeks (Berry, 2000; Lavy et al, 2002). The treatment appears efficacious, and the lesions in the esophagus resolve remarkably well.

Other examples of spiruroids are *Ascarops* and *Physocephalus* species (Figure 4-135), parasites of swine, and *Streptopharagus* species (see Figure 7-105), parasites of primates.

FIGURE 4-135 *Physocephalus sexalatus*.

Superfamily Habronematoidea

Identification

Draschia megastoma, *Habronema muscae,* and *Habronema microstoma* are parasites of the equine stomach, where the adult worms stay remarkably close to the margo plicatus. *D. megastoma* is about 13 mm long and has a funnel-shaped buccal cavity, whereas *Habronema* species are larger (22 to 25 mm) and have cylindric buccal cavities (Figure 4-136). The left spicule of *H. muscae* is five times as long as the right one, whereas only a twofold disparity exists between the spicules of *H. microstoma*. *D. megastoma* excites the formation by the host of fibrous nodules riddled with intercommunicating galleries

filled with a creamy puslike material in which the worms live (see Figure 7-74). *Habronema* species are not associated with nodules.

FIGURE 4-136 *Draschia megastoma* and *Habronema muscae*.

Life history

Larvae hatch from the tiny eggs (see Figure 7-71) soon after they are laid, and larvae or eggs may be present in the feces. If larvae are ingested by maggots *(Musca domestica* for *D. megastoma* and *H. muscae; Stomoxys calcitrans* for *H. microstoma),* these develop to the infective third-stage larvae in a little more than a week. The infective larvae migrate to the head of the fly and collect in the labium. When a fly alights on a warm, moist surface such as the muzzle, ocular conjunctiva, or cutaneous wounds of a horse, the larvae change hosts. Those larvae that are swallowed presumably complete their life histories, whereas those that enter wounds have probably reached an impasse. However, from a veterinary standpoint, these aberrant larvae are extremely important because of the granulomas they induce.

Importance

Although *Draschia* and *Habronema* species are unimportant as stomach parasites, their larvae are responsible for persistent cutaneous granulomas called *cutaneous habronemiasis* and a variety of colloquial names ("swamp cancer," "bursatti," "summer sores," "esponja"). These granulomas develop in minor wounds and in areas of skin subjected to more or less continuous wetting. In pastured horses the skin adjacent to the medial canthus of the eye may be drenched in tears stimulated by the presence of flies and also very attractive to them. Typical cutaneous habronemiasis lesions are characterized by an initial rapid production of granulation tissue that steadfastly refuses to resolve during fly season, by the subsequent appearance of caseocalcareous nodules in this granulation tissue, and by the presence of *Draschia* or *Habronema* larvae. Pruritus is intense, and secondary injury may result from the horse's efforts to find relief. Habronemic conjunctivitis usually assumes the form of an ulcerated nodule containing caseocalcareous foci and situated near the medial canthus. Such nodules tend to abrade the cornea and must be removed surgically to prevent or alleviate keratitis (Underwood, 1936; Rebhun et al, 1981).

Treatment

Ivermectin and moxidectin are the treatments of choice for adult *Habronema* and *Draschia* species. Ivermectin is approved for the treatment of summer sores caused by larvae of *Habronema* and *Draschia* species. Infections, although rather rare, still occur in the

United States, with 63 of 12,720 horses entering the Equine Field Service of the University of California–Davis Veterinary Medical Teaching Hospital between January 1988 and June 2002 (Pusterla et al, 2003). These horses were treated by surgical excision (seven) or medically (56); all the horses were also treated with ivermectin. Gritty masses on conjunctival membranes must be excised to prevent injury to the cornea.

Superfamily Filarioidea

The dog heartworm, *D. immitis*, is the filarioid of most importance in veterinary medicine. The filarioids also include some of the most important nematode parasites of man in tropical climates. *Wuchereria bancrofti* and *Brugia malayi* cause the acute lymphangitis and chronic elephantiasis of bancroftian filariasis, and *Onchocerca volvulus* causes the ophthalmitis of "river blindness."

Filarioids tend to be rather long and thin white- to cream-colored worms. They are found typically in tissue spaces and body cavities, or sometimes within the vasculature or lymphatic system. They tend to be without marked cuticular ornamentation or lips and have almost no buccal capsule. Often the tail of the male has a spiral flexure. All filarioids are transmitted by bloodsucking insects in which vermiform embryos called **microfilariae** develop into infective third-stage larvae. The microfilariae either circulate in the blood of the definitive host (e.g., *Wuchereria*, *Brugia*, *Dirofilaria*, *Dipetalonema,* and *Setaria* species) or accumulate in the dermal connective tissues (e.g., *Onchocerca*, *Elaeophora* species). In either

case the microfilariae are ingested and the infective larvae deposited when the insect feeds on the definitive host.

Dirofilaria

Identification

These worms are parasites of the pulmonary arteries. The adult males are 12 to 20 cm long, and the females are 25 to 31 cm long (10 to 12 inches). The faces of these large (up to 30 cm long) white worms are very plain indeed (Figure 4-137). The dog and its close relatives are the natural hosts, but infection also occurs in cats (Calvert and Mandell, 1982; Dillon et al, 1982) and ferrets *(Mustela putorius furo)*. As few as five adult *D. immitis* may prove lethal to a ferret (Campbell and Blair, 1978; Miller and Merton, 1982; Moreland, Battles, and Nease, 1986; Parrott, Greiner, and Parrott, 1984). Human infection is abortive and results in radiographic changes referred to as "coin lesions," which have been misinterpreted as representing neoplasia and can lead to unnecessary thoracic surgery (Theis, 2005).

FIGURE 4-137 *Dirofilaria immitis*, stomal end.

Life history

The life history, as outlined in Figure 4-138, may involve many different species of mosquitoes as intermediate hosts. Today, mosquito-borne human diseases such as malaria and filarial infections are popularly viewed as tropical diseases, but not too long ago malaria accompanied every summer in the United States. Malaria disappeared when the population density of suitable mosquitoes fell below the level necessary for transmission. Reduction in mosquitoes came with the drainage of swamps for agricultural purposes, with the construction of roads, and with intentional efforts at mosquito abatement. Heartworm manages to remain endemic and even to spread to regions where malaria has disappeared, possibly because this parasite is less discriminating in its choice of mosquito hosts. Mosquito control, although invisible to the public and most veterinarians, still plays a large part in preventing human disease and probably plays a major role in keeping heartworm infection levels lower than they would be otherwise.

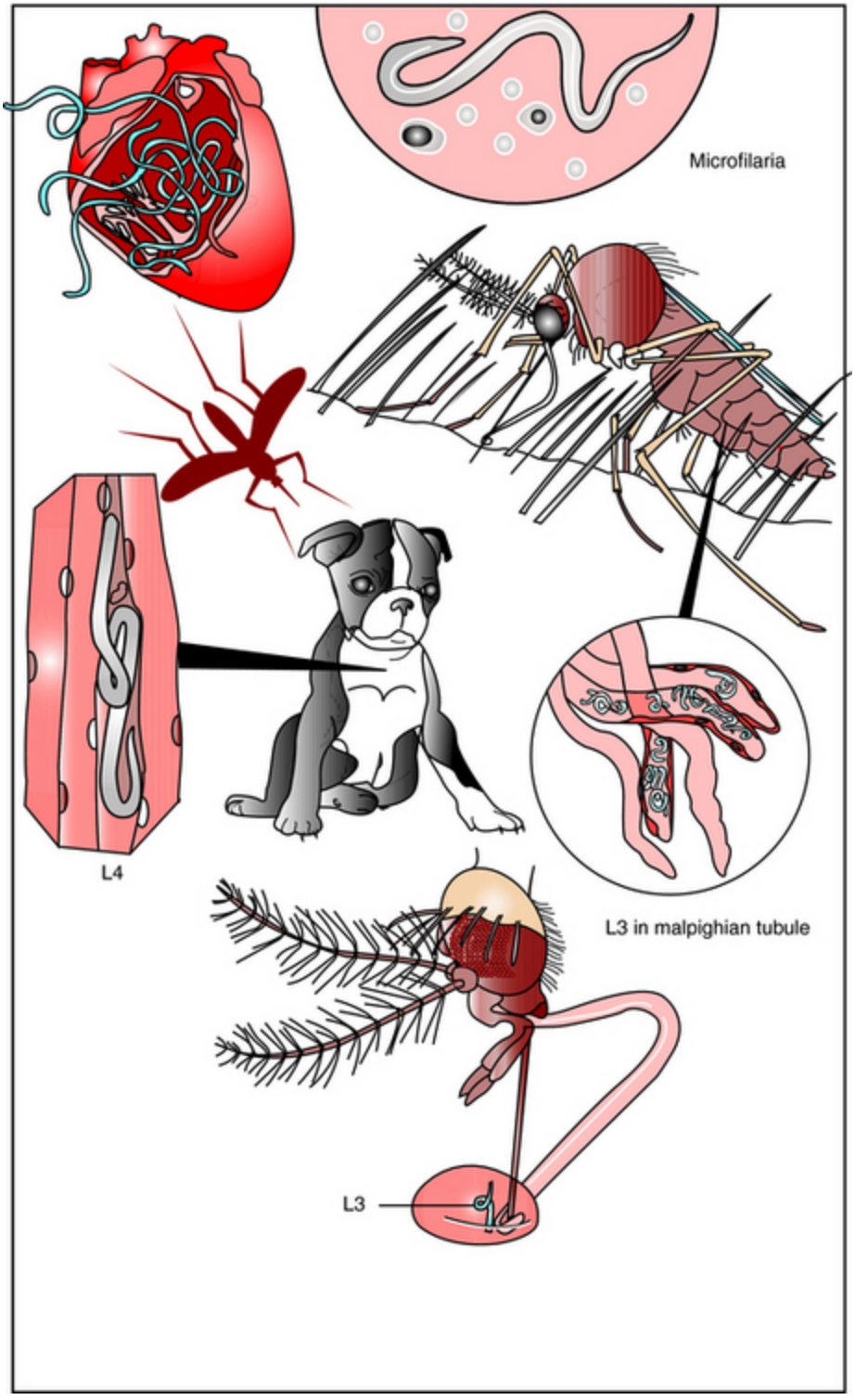

FIGURE 4-138 Life history of *Dirofilaria immitis,* the canine heartworm. Adult heartworms may survive and produce microfilariae for as long as 5 years. Microfilariae circulate in the blood, where they may be ingested by a feeding mosquito. About half of the species of North American mosquitoes are possible intermediate hosts, but significant

vector roles have been demonstrated for only a few. Larval development occurs in the malpighian tubules, after which infective third-stage larvae migrate to the salivary glands of the mosquito. The third-stage larvae enter the bite wound when the mosquito feeds on a dog. The molt from third-stage larva to fourth-stage larva occurs within 3 days after the bite of the infecting mosquito. Fourth-stage larvae remain in the connective tissues for several months, with the molt from fourth-stage larva to young adult occurring 2 to 3 months after infection. After the final molt the immature adults (fifth stage) migrate to the pulmonary arteries, apparently by way of the venous circulation. After reaching the right side of the heart, the young adults mature and start producing microfilariae at 6 to 9 months after infection.

The life cycle of *D. immitis* is initiated when the dog is bitten by an infected mosquito. The cycle is summarized in detail in the excellent review of Abraham (1988). The microfilaria (Figure 4-139) is taken up by a female mosquito with her blood meal. The larva develops to the infective third stage in the mosquito. When the mosquito takes another blood meal, the third-stage larva leaves the mouth parts and enters the bite wound and takes up residence in the skin (Figure 4-140). The third-stage larva that enters the bite wound molts to a fourth-stage larva within 3 days after infection. The young fourth-stage larvae are about 1.5 mm long at this time. The fourth-stage larvae reside in the subcutaneous connective tissues and muscles of the abdomen or thorax for the next 2 to 3 months after infection. Orihel (1961) reported that the molt from the fourth-stage larva to adult occurred 60 to 70 days after infection. Lichtenfels et al (1985) reported that the molt occurred at 50 to 58 days after infection.

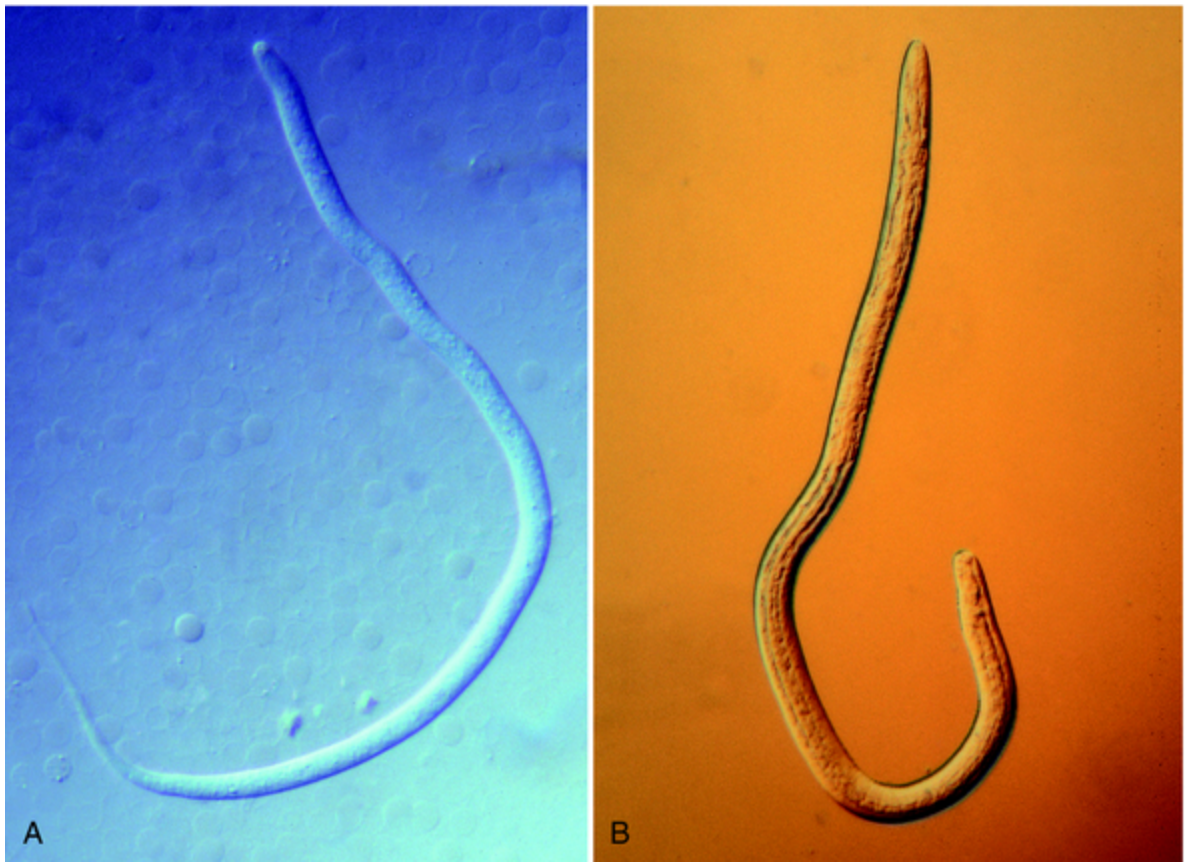

FIGURE 4-139 *Dirofilaria immits*. Microfilaria **(A)** in an unstained Knott's preparation (the red blood cell ghosts are visible), and an infective third-stage larvae from a mosquito **(B)**.

FIGURE 4-140 *Dirofilaria immitis* third-stage larva protruding from the end of the proboscis of an infected mosquito.

The worms are 12 to 15 mm long when they molt to become juvenile adults. The worms enter the pulmonary arteries and heart after being in the dog for 70 days (Kotani and Powers, 1982). When worms first reach the right side of the heart and pulmonary arteries, they are 20 to 40 mm (about an inch) long (Orihel, 1961). By 85 to 120 days after infection they reach lengths of up to 3.2 to 11 cm (Kume and Itagaki, 1955).

Fertilized females appear by 120 days after infection of the dog, and they contain fully developed microfilariae within the sixth month after infection (Orihel, 1961). Microfilariae typically are not found in the peripheral blood for several more weeks. Thus the prepatent period (i.e., the period between the infection and the first appearance of microfilariae in the blood) is between 6 and 9 months long. Once worms begin to produce microfilariae, they can continue to do this for over 5 years. The microfilariae circulate in the blood of the dog and are capable of living for up to 2½ years (Underwood and Harwood, 1939).

Mosquitoes are infected when they bite an infected dog. The microfilariae, after remaining in the midgut of the mosquito for a day, make their way to the malpighian tubules where they penetrate the cytoplasm of the primary cells. Under optimal conditions the larvae reenter the lumen of the malpighian tubules about 5 days after infection and molt to second-stage larvae about 10 days after infection and to third-stage larvae by 13 days after infection. The infective third-stage larvae then migrate through the body of the

mosquito to the cephalic spaces in the head and proboscis, where they await the chance of gaining entry into a new canine host.

Importance

The canine heartworm, *D. immitis*, is by far the most important filarioid parasite of domestic animals in North America. Adult heartworms normally are found in the pulmonary arteries. In heavy infections worms may be found in the right side of the heart. Worms probably are more common in the right side of the heart at necropsy than in living dogs because of the reduced pressure that occurs as the blood stops flowing into the pulmonary arteries. When defunct the worms are carried deeper into the lungs, where they occlude the pulmonary arterial branches and produce infarcts. Endemic areas exist in all parts of the United States (Rothstein, 1963). Heartworm infection is particularly common along the Atlantic and Gulf Coasts where salt marsh mosquitoes are prevalent, and in some localities half the dogs not on preventives that are examined will be found to be infected. There is also an increased prevalence along the course of the Mississippi River and its major tributaries such as the Ohio and the Missouri Rivers. A lower prevalence is encountered in the midwestern and north-central states. Heartworm is present and transmitted in the western United States (Bowman et al, 2007). Heartworm transmission is also occurring in southern Canada (Klotins et al, 2000; Slocombe and Villeneuve, 1993). One state in the United States, Utah, has made heartworm disease reportable to the State Veterinarian's office.

The 6- to 7-month prepatent period is free of any evidence of infection, and the developing and migrating worms cause no disturbance. The patent period, when microfilariae (see Figure 7-38) may be detected in the circulating blood, is the time of clinical illness. In the conventional view, the physiologic burden imposed on the host is attributed in part to the physical obstruction of vessels, heart chambers, and valves by the adult worms and in part to the development of a progressive pulmonary endarteritis and obstructive fibrosis leading to pulmonary hypertension and right-sided heart failure (Adcock, 1961). There is also a remarkable villous proliferation that occurs on the endothelium of the pulmonary arteries that grossly causes the surface of the vessel to appear as though it is covered with a lawn of villi (Figure 4-141). Repeated embolisms of the finer arterial branches by defunct adults with infarction and inflammatory response eventually lead to permanent damage of the vascular bed. However, obstruction of capillaries by microfilariae may also play a part in the pathogenesis of heartworm disease.

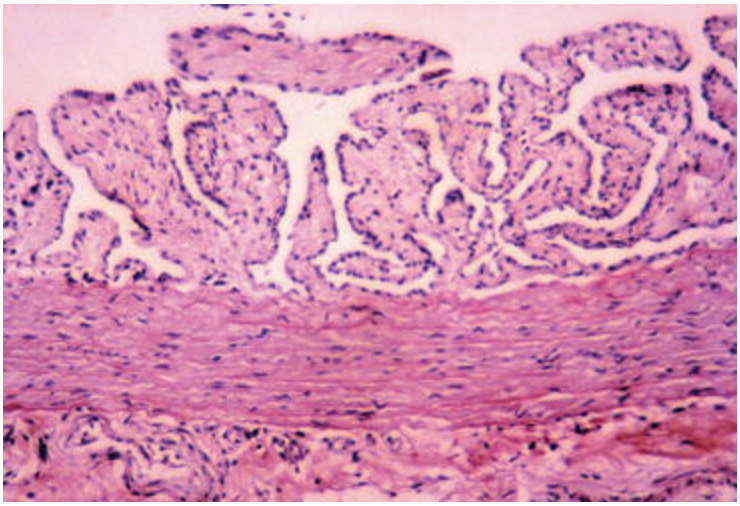

FIGURE 4-141 Histologic section (hematoxylin and eosin [H&E] stained) of the pulmonary artery of a dog infected with *Dirofilaria immitis* showing the villous proliferation present on the endothelium.

Jackson et al (1966) found that dogs with no signs of disease harbored an average of 25 worms, and that about 50 worms were associated with moderate-to-severe heartworm disease. In dogs with signs of acute hepatic failure, about 100 worms were concentrated in the venae cavae and right atrium. Dogs with typical heartworm disease fatigue easily, cough, and appear unthrifty. Decompensation of the right side of the heart leads to chronic venous congestion, with hepatic cirrhosis and ascites. Pulmonary embolism precipitates acute episodes of respiratory distress, during which blood and worms from ruptured vessels may be coughed up. Postcaval occlusion causes sudden collapse followed by death within a few days from acute hepatic insufficiency. A surgical procedure has been devised for relieving the caval occlusion by way of a jugular vein (Jackson et al, 1977; Jackson, von Lichtenberg, and Otto, 1962).

Based on a survey of U.S. veterinarians (12,173 reporting clinics), more than 250,000 dogs in the United States tested positive in 2004 for heartworms (Guerrero, Nelson, and Carithers, 2006). This was up a bit from the 2001 survey (244,000 positive dogs), and it is believed that the survey underestimated the actual prevalence of infection. There are 50 million or so dogs in the United States, and this would mean that about 0.5% of the dogs each year (one in 200) are being diagnosed as infected. This is a preventable disease.

Diagnosis

Infections in dogs with heartworms can be diagnosed with various antigen detection tests or by finding microfilariae in the blood. Antigen will appear in the blood about 5 months after the inoculation of third-stage larvae. In the normal course of events, microfilariae of *D. immitis* first appear in the circulation about 6½ months after exposure of the dog to the bites of infected mosquitoes. Thus during the rather long prepatent period, no microfilariae can be detected in blood samples from an infected dog.

In the young dog, even in areas with a very high background prevalence in dogs not on prevention, there is very little to be gained by an examination for heartworm infection before it is 6 or so months of age. Thus dogs younger than 6 months old should just be started on monthly prevention, and if there is concern that a dog may have been infected before beginning prevention, it can be checked after 6 months of preventive therapy rather than waiting a year.

For adult dogs that have not been on preventive therapy, they should be examined first to verify that they are heartworm negative. This can be done with an antigen test. I and others have seen the occasional dog that is antigen-negative with very high microfilarial counts (50,000 to 100,000 per milliliter). Thus, if an adult dog is from an area with a very high background prevalence or if its background is unknown, it would probably be wise to also examine a drop of blood under a microscope to look for microfilariae. In this case there is no need to perform a concentration method, because one is looking for the dog that is antigen-negative and has very high microfilarial counts to ensure that it does not react to the death of the microfilariae when the preventive is administered. If microfilariae are found in the blood of a North American dog, they most likely belong to either *D. immitis* or *Dipetalonema reconditum;* dogs infected with *D. reconditum* will be antigen-negative and typically have fairly low microfilarial counts. (Differentiation of microfilariae of these two species is discussed in Chapter 7.)

If a dog is on a preventive regimen year-round, testing should be performed yearly. With year-round prevention, there is no reason why testing cannot be performed any time during the year, and in these cases and with puppies that started year-round prevention soon after birth, heartworm testing can just become part of the annual examination. It must be remembered that macrocyclic lactone products are anthelmintics, and there is always the potential for resistance. Because of the relatively long life cycle of *D. immitis*, it seems unlikely that resistance will occur, but the threat remains.

Only by the regular checking of dogs on a preventive program can a vigilance be guaranteed that would identify and prevent the spread of a resistant form of the parasite if one ever did appear.

For a dog receiving monthly preventives only part of the year, it must be retested before the initiation of therapy each year. Unfortunately, in the case of all tests, there is a greater chance of a false-positive result when the population tested is nearly certain to be all negative (Peregrine, 2005). In this context, it must be remembered when performing an antigen test on a large population of uninfected dogs (by definition, all dogs on preventive regimens should be without infection) that there are going to be false-positive results no matter how good the test is (sensitivity and specificity of 99.9% translate to one false-positive test result in every 1000 tests performed). Thus if a dog on a preventive regimen tests positive for heartworm, it should be retested, and if still testing positive, carefully examined for clinical signs that support the diagnosis of heartworm infection. The treated dog is going to receive a large dose of arsenic, so there is a fairly good reason to proceed toward treatment with a bit of trepidation.

Treatment

Different anthelmintics are used to attack three different parasitic stages of *D. immitis:* adult worms in pulmonary arteries and the right side of the heart, microfilariae in the circulating blood, and larvae from mosquitoes migrating through the tissues on their way to the heart. Treatment of a dog with patent heartworm infection consists

of first removing the adult parasites with an arsenical and then eliminating the circulating microfilariae with ivermectin or milbemycin oxime later. Drugs targeting the larvae migrating through the tissues are used for prevention.

Melarsomine dihydrochloride has been approved for the treatment of dogs infected with adult heartworms. In dogs with mild-to-moderate clinical signs, the treatment consists of two intramuscular injections (2.5 mg/kg) given 24 hours apart. This treatment can be repeated 4 months later if necessary. Dogs with more severe disease should receive a single intramuscular injection of 2.5 mg/kg followed 1 month later by two such treatments 24 hours apart. Melarsomine dihydrochloride treatment seems to be more effective than the older intravenously administered thiacetarsemide without any increase in the severity of posttreatment hypertension and thromboembolism (Rawlings et al, 1993).

After arsenical therapy has been used, heartworms die slowly over a period of days or weeks and are carried by the pulmonary arteries to the lungs, where they lodge and obstruct the circulation temporarily. Eventually the dead worms are removed by phagocytosis. Probably, if the worms were killed rapidly and simultaneously, treatment would prove more lethal than the heartworms. However, even with the slow kill, the lungs are gravely insulted during the 4 to 6 weeks after arsenical therapy, and the dog must not be subjected to stress during this period. Occasionally a

dog vomits or has fever and respiratory distress after treatment. If these reactions are more than transitory, arsenical medication should be discontinued and supportive therapy, administration of steroids, and enforced rest initiated.

For the removal of microfilariae from the circulation after adulticide therapy, dogs can be given either a microfilaricidal dose of ivermectin (0.05 mg/kg body weight), ivermectin at the preventative dose of 0.006 mg/kg, or milbemycin oxime at the prophylactic dose of 0.5 mg/kg body weight. These products are not labeled for this use, but because of the lack of drugs approved for the removal of circulating microfilariae, the American Heartworm Society has included these treatments in its recommendations.

There are those who recommend that adult heartworms be removed by placing infected dogs on year-round ivermectin therapy for a number of years (*2005 Guidelines For the Diagnosis, Prevention and Management of Heartworm* [Dirofilaria immitis] *Infection in Dogs,* American Heartworm Society). I am of the opinion that in this context the FDA's label claims for the monthly products should be followed, and dogs should be started on monthly therapy only after having been cleared of their infection with adult worms. If dogs with patent heartworm infections are started on monthly prophylaxis with an avermectin, some 10% to 20% or more of dogs, depending on the product chosen, will continue to have circulating microfilariae in their blood for up to a year, or perhaps longer (Bowman et al, 1992; Bowman and Torre, 2006a, 2006b). If one wanted to create a scenario in which one was selecting for resistant

microfilariae, one would take a dog with a high microfilarial count and give it an avermectin for months so that the majority of microfilariae in circulation would be “resistant.” The conservative approach is to place only dogs that are heartworm free on avermectin preventive therapy.

Heartworms and many other filarioids are host to endosymbiotic bacteria of the genus *Wolbachia*. The bacterium is passed transovarially from the female to her offspring (Kozek, 1977). These bacteria are also present in *D. immitis,* in *Onchocerca volvulus*, and in the species that causes lymphatic filariasis in humans. It has been suspected that if these endosymbionts are required for survival or if their breakdown products are toxic for the nematode host, they might be used as targets for chemotherapy. Cattle infected with the related filarioid *Onchocerca ochengi* were cleared of their adult worms in nodules by treatment with ocytetracycline (Langworthy et al, 2000). Unfortunately, the results of trials with *D. immitis* have not been as dramatic. However, it has been shown in one long-term trial that treating dogs with doxycycline prevented the development in mosquitoes of the few microfilariae available for transmission studies (McCall, 2007). It is possible that the doxycycline may be having a direct effect on the worms rather than through the *Wolbachia* (Smith and Rajan, 2000), but whatever the cause, this seems an excellent reason to provide doxycycline therapy to dogs undergoing adulticide therapy, preventing potential secondary infections in the lungs around dying worms, and preventing

transmission of any residual microfilariae until they are removed with an avermectin.

Prevention

Prevention of heartworm infection currently involves the monthly oral or topical administration of a macrocyclic lactone or the injection every 6 months of a slow-release formulation of a macrocyclic lactone (moxidectin) to all dogs exposed to attacks of infectious mosquitoes. The vast majority of dogs on preventive therapy are receiving products that are administered once per month. The prolonged injectable heartworm preventive with moxidectin in a slow-release carrier is currently unavailable in the United States.

There is a spectrum of avermectin/macrocyclic lactone products available that when regularly given monthly to dogs will kill any heartworms that are less than 30 days old. These include ivermectin, milbemycin oxime, selamectin, and moxidectin. Although some of the molecules themselves at heartworm preventive doses have activity against internal parasites, many of the products have been combined with agents that provide additional internal parasite control or have activity against ectoparasites, mainly fleas. Thus, practitioners can now choose from several different products that will provide dogs with protection against heartworms that will also treat or control internal and external parasites, making it fairly easy to develop a useful program

for a pet within any given geographic area or with a specific lifestyle.

A commonly asked question is whether dogs should undergo a heartworm prevention program year-round, for 6 months, or for even shorter periods in regions where the potential transmission cycle may be less than 6 months. Dr. Slocombe and colleagues (Slocombe et al, 1995) and Drs. Knight and Lok (1995) presented isolines for the mean start and end dates of heartworm transmission in Canada and the United States. These isolines are based on a model that includes the average life of a mosquito, the times when mosquitoes are likely to take their first and last blood meals each year, the amount of time required at different temperatures for an ingested microfilaria to become an infectious third-stage larva, and temperature data collected at different national weather collection stations. Thus by examination of the maps presented, the period of transmission for the locale in which they practice can be determined. The model proposed by Knight and Lok (1995) indicates that there are probably no parts of the continental United States where transmission occurs throughout the year. Thus treatment might be given for 3 months in parts of Canada and 10 months in parts of Florida, with different starting and stopping dates in various locations from south to north. This model has received support recently by work done in Florida and Louisiana, where mosquitoes (a total of 109,597) were examined year-round with a PCR assay for *D. immitis* DNA (Watts et al, 2001). No infected mosquito heads were detected in Gainesville, Florida, or Baton

Rouge, Louisiana, in the months of December, January, February, and March.

The practical advantage of applying this model is a reduction in the prescriptions for unnecessary preventive treatment in areas where it is not required. If the model is to be applied, other factors must be taken into consideration. First, there are likely to be microclimatic fluctuations (large bodies of water that stabilize temperatures, decaying manure or vegetable matter that raises temperatures, heated industrial effluents, or heat-absorbing natural and artificial surfaces) that allow mosquitoes to feed longer, perhaps much longer, in certain areas within given isolines. Also, there are several species of mosquito that overwinter as adults in some very cold places in North America, and the contained infective-stage larvae may overwinter within diapausing adult females mosquitoes. Second, it is likely that many dogs will travel with their owners, with the effect that isolines will be crossed by many pets during the course of a year. It also is unlikely that most patients will see their veterinarian often enough for the discovery and initiation of preventive therapy to work in all cases. Third, the availability of products that control infections or have been combined with anthelmintics active against intestinal helminths complicates the desire to stop therapy for the pets of some clients during periods when there may be no heartworm transmission. *Toxocara canis, T. leonina,* and *T. vulpis* are all capable of being transmitted even in the coldest months of the year if soil containing infective eggs is disturbed, and *A. caninum* larvae in sequestered sites in the body are

known to migrate periodically back to the intestine, where they develop. Finally, the addition of a flea-control product to the heartworm preventive adds another reason for considering year-round prevention. In a household, it is highly possible that the temperatures will remain such that fleas can continue to cycle throughout the year, even if they are worse in the summer.

With the currently available products, there is no good reason why any dog under the care of a veterinarian should become infected with heartworm. Thus it is imperative that the practitioner carefully consider the area in which the practice is located, the individual client, and the stated and suspected behavior of the pet when formulating a plan for each individual going on a preventive program. However, in the design of specific programs for individuals, it is important to remember that clients do converse with one another, and difficulties will arise when all clients and pets are not treated equally if the reasons behind the specific recommendations are not made very clear.

Feline heartworm

Infection with *D. immitis* in cats has received increasing awareness; in 1995, the American Heartworm Society first published *Guidelines for the Diagnosis, Treatment, and Prevention of Heartworm* (Dirofilaria immitis) *Infection in Cats,* and current guidelines can be obtained at the Society's website (www.heartwormsociety.org). The cat differs from the dog in several major respects relative to heartworm infection. First, cats tend to harbor very few adult worms and to

remain amicrofilaremic. Thus examination of blood with concentration methods usually is not a reliable detection method, and there may not be sufficient circulating antigen for detection by the different antigen detection assays. There are antigen and antibody tests that are available for use in cats. Antibodies will simply show exposure, and antigen may be negative if cats are infected with few worms. Second, cats can develop severe disease owing to the migration of young adult heartworms in their lungs even if they do not develop patent infection; this syndrome is called HARD for heartworm-associated respiratory disease (Blagburn and Dillon, 2007). Third, cats can have heartworms migrate to ectopic sites and can die suddenly as a result of aberrantly migrating heartworms. Fourth, adulticide therapy in cats usually is reserved for animals in stable condition that nevertheless continue to have clinical signs not controlled by empiric therapy. Fifth, surgical removal of the worms is considered a potential option in cats. There are now several products that can be topically or orally administered to cats monthly that will prevent heartworm and other internal parasites, including ivermectin, milbemycin oxime, selamectin, and moxidectin with imidacloprid. As with similar products for use in dogs, these products all have slightly different spectra of activity, giving the veterinarian an opportunity to pick a product that best fits the practice.

Setaria

Setaria labiatopapillosa (Figure 4-142) and *Setaria equina* (Figure 4-143) are large white parasites of the serous membranes of cattle and horses, respectively. The infection is transmitted between hosts by mosquitoes. Microfilariae of *Setaria* species show up on blood smears (see Figure 7-73), and the adult parasites are likely to be encountered during abdominal surgery or on the killing floor or necropsy table (Figure 4-144). Migrating *Setaria* larvae occasionally invade the central nervous system and cause serious neurologic disease, especially when they find themselves in other than their normal host species.

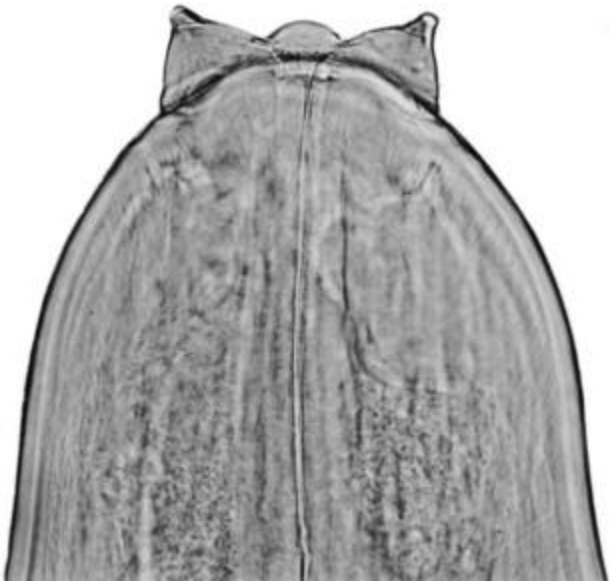

FIGURE 4-142 *Setaria labiatopapillosa,* stomal end.

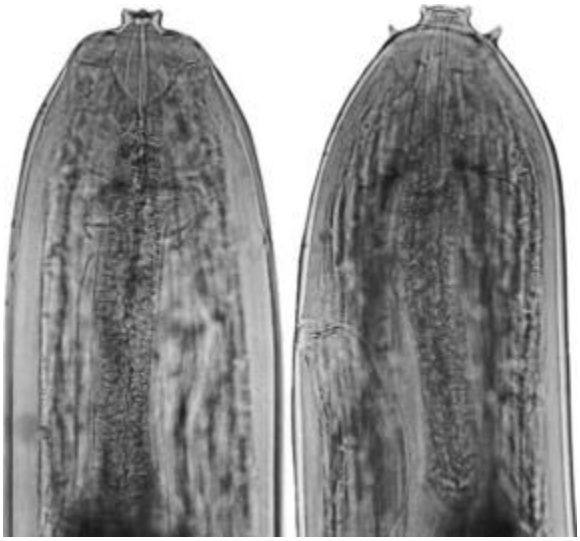

FIGURE 4-143 *Setaria equina*, dorsoventral *(left)* and lateral *(right)* aspects of the stomal end.

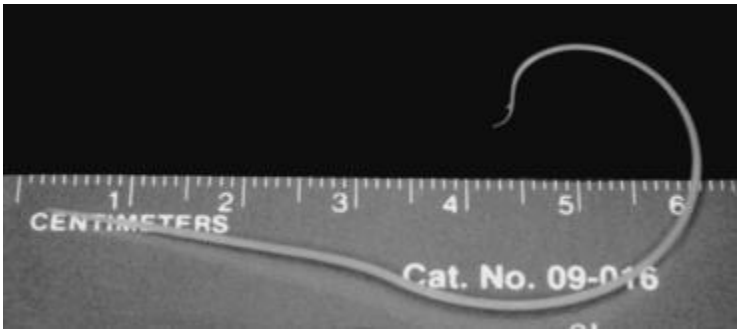

FIGURE 4-144 *Setaria labiatopapillosa,* complete worm, recovered at surgery from a cow.

Actively motile *Setaria* adult worms are occasionally observed in the anterior eye chamber of horses. Jemelka (1976) described surgical removal of a 4.38-cm–long *Setaria digitata* adult from the anterior eye chamber of a horse suffering from corneal opacity and hypopion.

Onchocerca

Onchocerca adults, although large, are likely to escape notice because they are intricately woven into the deep connective tissues. Once found, they are virtually impossible to isolate intact, so specimen bottles tend to contain many fragments of midsection and very few ends.

Onchocerca cervicalis adults are found in the nuchal ligament of the horse (see Figures 8-111 and 8-112Figure 8-111Figure 8-112), and the microfilariae (see Figure 7-73) are widely distributed in the dermis and other connective tissues including those of the ocular conjunctivae. Infection is transmitted between horses by species of *Culicoides*. In a random survey of pastured horses in Tompkins County, New York, eight of 12 horses yielded from 1 to 3000 *O. cervicalis* microfilariae per biopsy specimen, a piece of skin weighing about 15 mg (Georgi, 1976b). Microfilarial pityriasis, summer mange, equine dhobie itch, and plica polonica are colloquial names for an intensely pruritic dermatitis conventionally ascribed to microfilariae of *O. cervicalis*.

In North American cattle, *Onchocerca gutturosa* adults are found in connective tissues about the nuchal ligament, and *Onchocerca lienalis* are found in the connective tissue between the spleen and rumen. Both species also may be found in other connective tissue locations on occasion. Microfilariae of both species are found in the dermis (see Figure 7-73). The intermediate hosts of bovine *Onchocerca* species are species of *Simulium* and *Culicoides*.

Microfilaricidal treatment

Herd and Donham (1983) successfully treated 40 horses with dermatitis, alopecia, and pruritus in association with microfilariae of *O. cervicalis* with a single intramuscular injection of 0.2 mg ivermectin per kilogram body weight. Twenty-four hours after medication, the ventral abdomens of four of the horses became edematous. However, this reaction to dead microfilariae subsided over the next few days, and marked clinical improvement followed in all horses 2 to 3 weeks after treatment. Moxidectin at 0.3 to 0.5 mg/kg also will eliminate these microfilariae from the blood of infected horses (Monahan et al, 1995).

Parafilaria

Parafilariosis ("summer bleeding") occurs only outside of North America and is caused by *Parafilaria multipapillosa* in horses and *Parafilaria bovicola* in cattle. These parasites live in the subcutaneous and intermuscular connective tissues and, when sexually mature, produce crops of pea-sized nodules that bleed through a tiny pore. The blood escapes in fine drops, runs off in streaks along the hairs, and dries in brown crusts. Eggs and microfilariae of *Parafilaria* species may be demonstrated in this material but never in samples from the circulation. Active bleeding occurs only during daylight hours and especially when horses are exposed to direct sunshine. Baumann (1946) reported that bleeding in affected horses would, as a rule, immediately stop when they were brought into the stable, only to start again when they were led back out into the sunshine. He rarely observed bleeding during cool weather. The activity of the

lesions observed by Baumann suggests an adaptation on the part of *Parafilaria* to the habits of flies that feed on blood; they are active in warm weather and avoid shade. It has been shown that *P. multipapillosa* develops in the fat body of *Haematobia atripalpis* (Gnedina and Osipov, 1960).

P. bovicola causes dermal bleeding and subcutaneous bruiselike lesions in cattle in the Philippines, India, Tunisia, Morocco, the former Soviet Union, Rwanda, Burundi, Romania, Bulgaria, South Africa, and Sweden (Bech-Nielsen, Sjogren, and Lundquist, 1982). The subcutaneous lesions result in substantial trim losses at slaughter. In South Africa, three vectors have been identified: *Musca lusoria*, *Musca fasciata*, and a third as yet undescribed species. Transmission probably occurs there throughout the year (Nevill, 1975, 1985). These dung-breeding *Musca* species ingest the first-stage larvae in the bloody discharge from skin perforations made by the adult *P. bovicola* female worms lying in the subcutaneous tissues. The larvae develop to the infective third stage in the body of the fly and are probably deposited in the eyes of cattle when the infected fly feeds on the lachrymal secretions (Nevill, 1975).

Dipetalonema

Adult specimens of *Dipetalonema* species are most likely to be encountered as parasites of the peritoneal cavity of monkeys, in which they are very common (Figure 4-145).

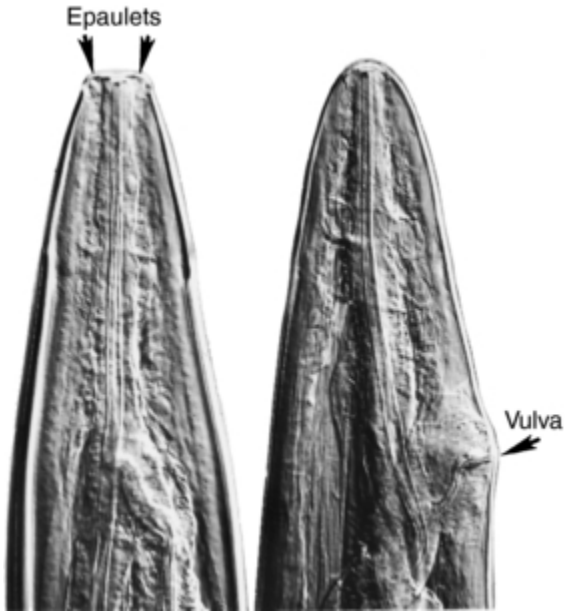

FIGURE 4-145 *Dipetalonema* sp. from the peritoneal cavity of a monkey. *Left,* The dorsoventral aspect of the stomal end. *Right,* The lateral aspect of the stomal end.

The canine parasite *D. reconditum* has, as its species name suggests, been viewed by few humans because it is small, it is usually few in number, and it lies inconspicuously in the connective tissues. *D. reconditum* is placed by some within a genus named *Acanthocheilonema,* whereas others continue to consider this a subgenus within the larger genus *Dipetalonema*. The microfilariae, on the other hand, are rather commonly seen (see Figure 7-38) and are easy to confuse with those of *D. immitis*. *D. reconditum* is nonpathogenic to dogs. Its clinical importance attaches only to confusion of its microfilariae with those of *D. immitis* (Lindemann, Evans, and McCall, 1983).

Life history

D. reconditum develops to the infective stage in the flea *Ctenocephalides felis* and in the amblyceran louse *Heterodoxus spiniger*. Microfilariae taken in with the blood meal develop into infective third-stage larvae in 7 to 14 days. When injected into a dog, these third-stage larvae develop into adult worms in 2 to 3 months (Farnell and Faulkner, 1978; Lindemann and McCall, 1984).

Diagnosis

The small adults of *D. reconditum* cause no pathologic changes to betray their presence but may be seen in a sufficiently lean cadaver by scanning the loose subcutaneous fascia of the limbs and back with a stereoscopic microscope (Nelson, 1962). About 90% of the adults are located in subcutaneous tissues, but a small percentage can be found in the peritoneal cavity (Mello, Maia, and Mello, 1994). The microfilariae circulate in the blood, usually at low densities. However, substantial microfilaremias are occasionally observed. It is not safe to assume that because many microfilariae are present, it must necessarily follow that their parents are heartworms. The microfilariae of *D. reconditum* are distinguished from those of *D. immitis* by the more slender body, lack of taper at the anterior extremity, and presence of a very much larger cephalic hook in the former species. (Differentiation of these two species of microfilaria is considered in detail in Chapter 7.)

Patton and Faulkner (1992) found that the microfilariae in about 50% of 805 microfilarial-positive dogs in eastern Tennessee were the microfilariae of *D. reconditum*, and these authors warn

practitioners concerning the need for making an accurate diagnosis before initiating heartworm adulticide therapy. Most of the antigen detection tests used for diagnosing *D. immitis* infections are capable of distinguishing between infections with these two parasites.

Elaeophora

Microfilariae of *Elaeophora schneideri*, the arterial worm of deer, elk, and domestic sheep, produce patches of moist, exudative dermatitis with crust formation on the polls and faces of sheep sent to summer range above 6000 feet (1828 m) in New Mexico, Arizona, and Colorado. Adults up to 120 mm long are found in the carotid, iliac, and mesenteric arteries. Tabanids are cyclodevelopmental intermediate hosts.

Stephanofilaria

Adults and microfilariae of *Stephanofilaria stilesi*, a very small (less than 6 mm long) filarioid, are found in dermatitic lesions on the ventral abdomen of cattle. The infective larvae of *S. stilesi* develop in the horn fly *Haematobia irritans*.

In India, *Stephanofilaria assamensis* causes a serious dermatitis called humpsore in cattle *(Bos indicus)*. Lesions may occur on other parts of the body, but the major sites are the hump, neck, and legs.

Order Enoplida

The nematodes in the order Enoplida differ markedly from all the other nematodes discussed up to this point. Older classifications consider the Enoplida part of a different class within the phylum

Nematoda called the Adenophorea. All the other orders discussed up to here, the Strongylida, Rhabditida, Oxyurida, Ascaridida, and Spirurida, would be placed within the Class Secernentea. The Enoplida, discussed here, differ from the Secernentea in two major respects. They do not have tails, i.e., the anus is terminal, so the posterior end of the worm looks like a snipped-off piece of tubing; and if present, there is only a single spicule. Also, the first-stage larva of all these genera have a little stylet called an *onchiostyle*. For the Secernentea, the final host is almost invariably infected by a third-stage infective larva, whether on pasture, in an egg, or coming out of a mosquito. For the Trichinelloidea, the final host is always infected by eating a first-stage larva, even if there is a paratenic host involved. In the case of the Dioctophymatoidea, infections of the final host is similar to the Secernentea at least in the most familiar example in that the infective stage is the third stage. In the newer classifications, Adenophorea would be replaced with Enoplea, and Secernentea with Chromadorea; also, there would be potential changes in how the words would end. Twenty years ago the Secernentea were the Phasmidia, and the Adenophorea were the Aphasmidia.

One other worm is included in this section, *Haycocknema perplexum*. These are members of the family Robertdollfusidae, which is a family of parasites related to the Trichinelloidea with a few species in mammals.

Superfamily Dioctophymatoidea

Dioctophyme

Dioctophyme renale, the giant kidney worm of carnivorans, swine, and sometimes humans, is one of the largest species of nematodes (Figure 4-146). Mink are the principal definitive hosts. The female *D. renale*, which may reach 1 m in length and 1 cm in diameter, produces brownish, thick-shelled eggs (68 × 44 μm) with bipolar plugs. Males are somewhat smaller (less than 400 mm) and have a terminal bell-shaped copulatory bursa and one spicule. The eggs are passed in the urine in the one- or two-cell stage and develop, in water, to the first larval stage in a month or longer. Larvated eggs are infective to oligochaete annelid worms in which they develop to the infective third larval stage. If infected oligochaetes are ingested by fish or frogs, the larvae invade the tissues of these paratenic hosts but do not undergo development. However, if the infected oligochaete (or paratenic host) is ingested by a dog, the *D. renale* larvae mature and complete the cycle (Karmanova, 1968). In the dog, *D. renale* may be found in the pelvis of the right kidney or free in the abdominal cavity. The latter type of infection is nonpatent.

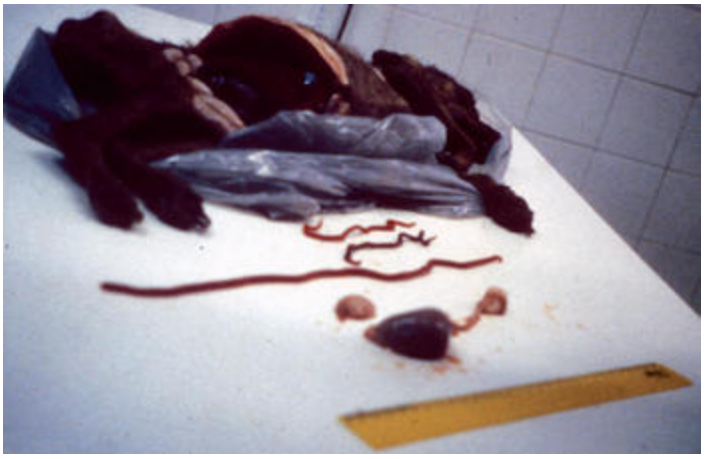

FIGURE 4-146 Three specimens of *Dioctophyme renale* recovered at necropsy from the abdominal cavity of a dog in Brazil. The ruler in the figure is 30 cm long.

Courtesy Dr. Suzanne Wolfson.

Superfamily Trichinelloidea

The superfamily Trichinelloidea contains some very common parasites of domestic animals. Members of this superfamily are distinguished by their stichosome esophagus, which consists of a capillary tube surrounded by the bodies of a single-file column of gland cells called stichocytes (Figure 4-147). There are five genera of interest: *Trichinella*, *Trichuris*, *Capillaria*, *Trichosomoides*, and *Anatrichosoma*. Of these five genera, all lay eggs but *Trichinella*, and the laid eggs have bipolar plugs. Also, the males of the genera in the superfamily, other than adult male *Trichinella*, have a single spicule or at least a spicular sheath, which is often spinate.

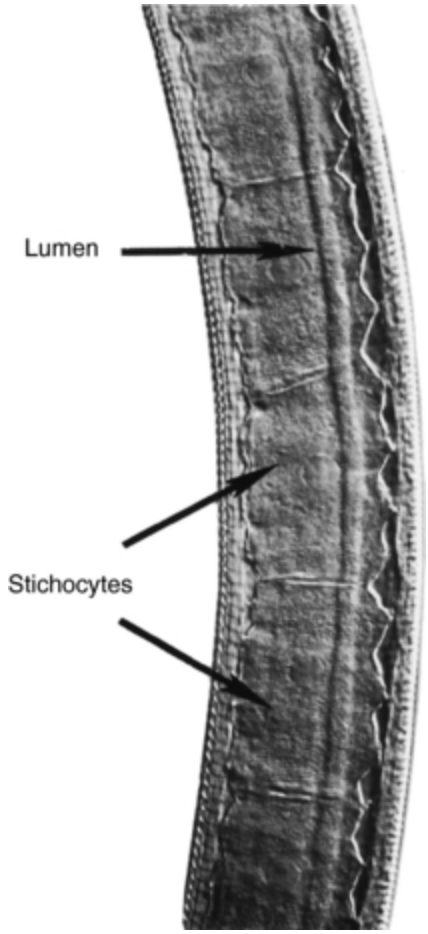

FIGURE 4-147 A portion of the stichosome esophagus of *Trichuris giraffae*.

Trichinella

Identification

The tiny adults of *Trichinella spiralis* are found embedded in the mucosa of the small intestine of swine, carnivorans, and man (see Figure 8-115). The male is 1.4 to 1.6 mm long, lacks spicule or spicular sheath, and presents two small knobs over the cloaca. The female is 3 to 4 mm long, with vulva in the midesophageal region and anus terminal. She deposits prelarvae directly into the host's intestinal mucosa (Figure 4-148).

FIGURE 4-148 *Trichinella spiralis* adult male *(left)* and female *(right)* from the small intestine of an experimentally infected rat; a prelarva is exiting the vulva of the female.

Courtesy Dr. Judy Appleton.

Life history

Predation has provided an efficient channel for the evolutionary development of many parasites. In most instances the larval parasite lies encysted in the tissues of the prey, and the reproductive adults inhabit the alimentary tract of the predator. Thus in most systems the predator becomes infected by eating the prey, and the prey becomes infected by ingesting eggs passed in the feces of the predator. However, in the unique life history of *T. spiralis*, both adult and larval stages occur in sequence in the same host, the tiny adults lying among the villi of the small intestine and the larvae they produce becoming curled up in cysts in the striated muscle (see Figure 8-116). In this sense, for the *Trichinella* life cycle to work, the predator has to become prey.

First-stage larvae of *T. spiralis*, liberated from their cysts by digestive enzymes of the host (see Figure 7-93), invade the intestinal mucosa. Both sexes reach maturity about 2 days after the infected meat is eaten. At 5 days after infection, the viviparous females are giving birth to prelarvae (Figure 4-149), which enter the lymphatics and later the bloodstream to be transported to the muscles (Ali Kahn, 1966). After these prelarvae invade striated muscle cells, they at first lie parallel to the long axes of the fibers and are quite easily overlooked. After 2 or 3 weeks they have developed into first-stage larvae and roll up in spirals, or like pretzels become enveloped in cysts and are then infective (Figure 4-150; see also Figures 7-93 and 8-116Figure 7-93Figure 8-116). Old cysts containing defunct larvae calcify.

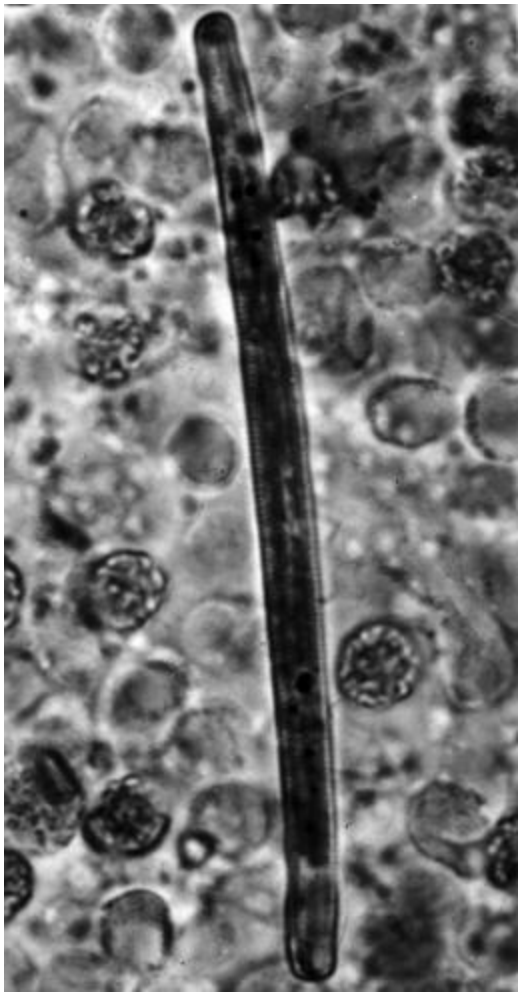

FIGURE 4-149 *Trichinella spiralis* prelarva demonstrated in the blood of a cat by the Knott technique.

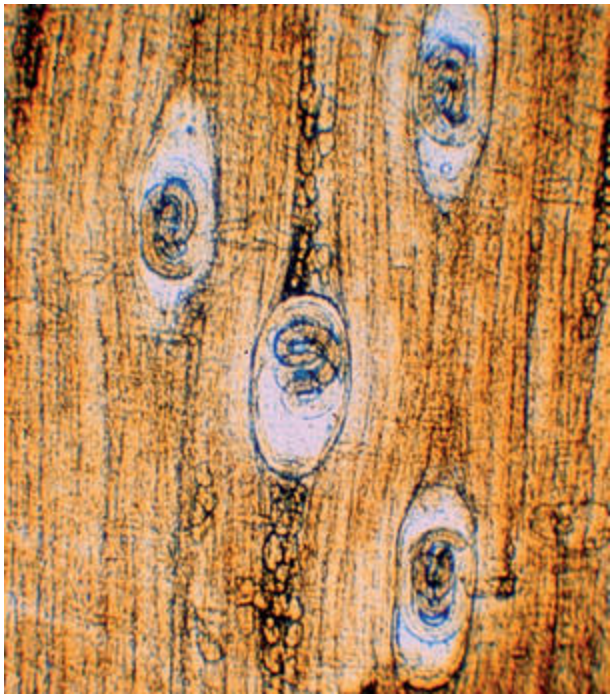

FIGURE 4-150 *Trichinella spiralis* larvae in muscle press.

The intestinal (adult) phase of *T. spiralis* infection varies in duration from a little more than a week in dogs to 3 or 4 months in humans. Immunosuppressant therapy, often instituted to ameliorate the tissue reaction to invading larvae, may prolong the lives of the adult female worms. Fortunately, these are accessible to anthelmintic attack. Almost all mammals can be experimentally infected with *T. spiralis*, but carnivores and omnivores are more likely to become naturally infected. Infection occurs through predation, cannibalism, and carrion feeding. The larvae encysted in muscles are exceptionally resistant to external conditions, including extreme putrefaction.

Importance

Human trichinosis usually results from eating raw or undercooked pork or bear. In the United States, outbreaks of human clinical trichinosis most often involve small groups of people who have shared uncooked sausage, an undercooked roast from a locally slaughtered pig, or undercooked bear meat. However, in one Illinois outbreak, in which 23 of 50 members of an extended Dutch-German family became ill, the source of the *T. spiralis* larvae in the homemade sausage was USDA-inspected pork (Potter et al, 1976). Occasionally, individuals eat completely raw ground meat ("cannibal sandwich"), a habit more prevalent among beef lovers than pork lovers. However, hamburger often contains a considerable amount of ground pork whether it is supposed to or not. Outbreaks of trichinellosis in France and other European countries have been traced to consumption of horsemeat. It seems that horses are more willing to eat meat scraps than people expected and that they are fed table scraps more commonly than expected (Murrell et al, 2004).

It has been estimated that for humans, ingestion of five trichina larvae per gram of body weight is fatal, for hogs, 10, and for rats, 30 (Chandler and Read, 1961). Human trichinosis sufferers may display periorbital edema, myalgia, fever, gastroenteritis, conjunctivitis, pruritus, and skin eruption. Eosinophilia usually exceeds 20%.

Clinical trichinosis in domestic animals may result from both insult inflicted on the intestinal mucosa by the adult worms and the host's reaction to invasion of skeletal muscles by the larvae. A case

of trichinosis in a rural Massachusetts cat caused transient hemorrhagic enteritis, during which adult *T. spiralis* worms were found in the feces, and prelarvae were identified in the blood (see Figure 4-149). The phase of muscle invasion was without clinical signs, but eosinophilia persisted for 3 months (Holzworth and Georgi, 1974). A second case in a 3-month-old kitten is typical of the phase of muscle invasion: The kitten was lying helplessly on its side with limbs extended, showed pain on handling, salivated, breathed superficially, and cried constantly (Hemmert-Halswick and Bugge, 1934). Case reports of trichinosis in dogs and cats are few, but it is a question how often it may be overlooked or misdiagnosed.

Treatment

T. spiralis infection is infrequently diagnosed in cats and dogs, but because both of these hosts frequently consume uncooked meat in the form of scraps and prey and because the dog displays such a predilection for eating carrion, it stands to reason that canine and feline *Trichinella* infection must in fact be rather common. Treatment is experimental. Cats and dogs experimentally infected with *T. spiralis* have been found to have reduced numbers of muscle-stage larvae after treatment with albendazole, 50 mg/kg body weight twice daily for 7 days (Bowman et al, 1993).

Control

Properly cooked trichinae are quite harmless, but a sojourn in the oven does not guarantee that the parasites in the center of a large

roast will be made more than uncomfortable unless raised to a uniform internal temperature of 77° C. The cut surface of cooked fresh pork should be “white”; any trace of pink demands its return to the oven or frying pan. Some methods of rapid cooking in microwave ovens do not kill all of the encysted *T. spiralis* at 77° C or even at 82° C, apparently because the meat does not heat uniformly (Kotula et al, 1983); even roasts appearing well done may contain live larvae when prepared in a microwave oven (Zimmermann, 1983).

Freezing of pork products for several weeks (e.g., at −15° C for 20 days) has long been considered adequate to kill *T. spiralis*. However, this cannot safely be applied to the sylvatic sibling species, *Trichinella nativa*, found in bears and other holarctic wildlife, which can withstand storage at −20° C for 6 months (Pozio et al, 1992). In certain countries (e.g., Germany) where the public demands uncooked pork products, meat inspection includes microscopic examination for trichinae in diaphragm muscle squash preparations of every carcass. In the United States the traditional policy has been instead to persuade the public to cook fresh pork thoroughly and to require manufacturers of “ready-to-eat” products to cook or freeze them according to specifications that ensure the destruction of trichinae.

Trichuris

Identification

Adult capillarids are found in mammals and other vertebrates, but the adults of the genus *Trichuris* are only found in mammals. The adult body is whip-shaped; the anterior end fine, hairlike, and embedded in the wall of the large intestine (see Figure 8-113); and the posterior end stout and lying free in the lumen (Figure 4-151; see also Figures 7-47 and 8-114Figure 7-86Figure 8-114). The egg is lemon-shaped with a distinct plug at each pole and contains a single cell when passed in the feces (Figures 4-152; see also Figures 7-25, 7-52, 7-58, and 7-91Figure 7-25Figure 7-52Figure 7-58Figure 7-91); the male has a spinate, spicular sheath (Figure 4-153).

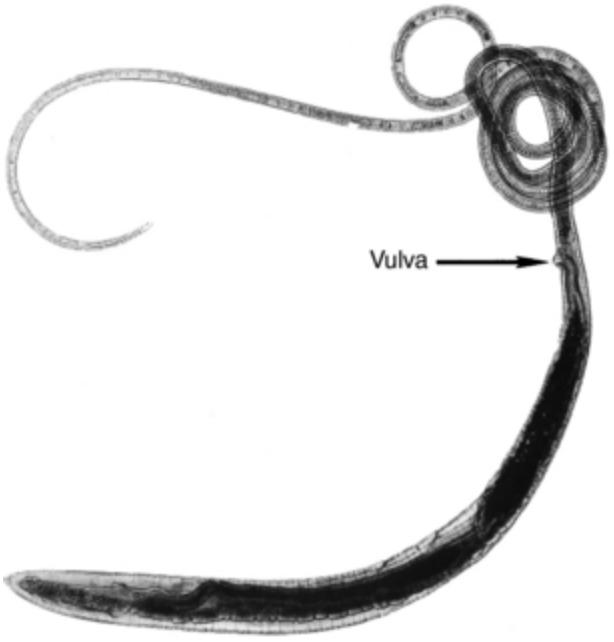

FIGURE 4-151 *Trichuris* sp. from a cat from Puerto Rico.

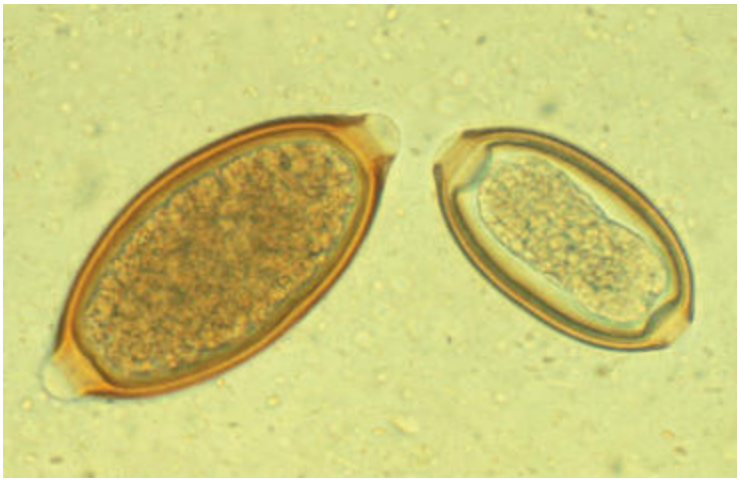

FIGURE 4-152 *Trichuris vulpis* and *Eucoleus boehmi* eggs in a fecal preparation from a dog.

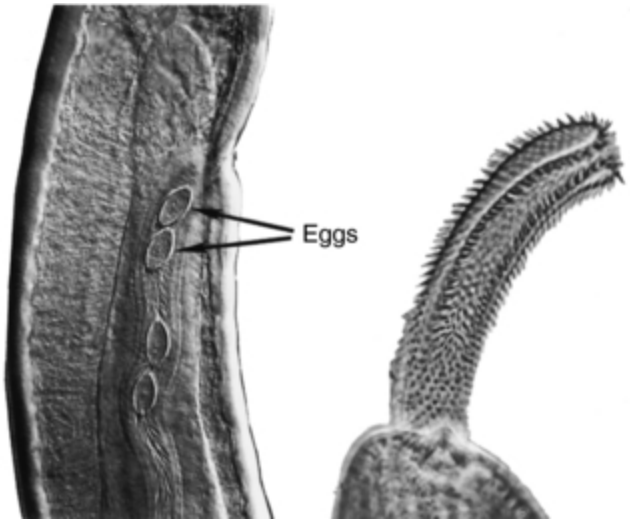

FIGURE 4-153 *Trichuris discolor*. *Left,* Four eggs are seen in the vagina of a female. *Right,* The spinate spicular sheath of the male is protruded.

Life history

Eggs passed in the feces contain only a single cell and are not infective. An infective first-stage larva develops inside the egg in about 1 month but does not hatch unless swallowed by a suitable host. The infective egg is very resistant, so animals confined in

contaminated environments tend to become reinfected after treatment. Once eggs are ingested, all development occurs within the epithelium of the intestine (i.e., there is no extraintestinal migration). The prepatent period of *Trichuris vulpis* in the dog is slightly less than 3 months, in cattle about 3 months, and in swine about 45 days.

Importance

Most canine whipworm infections are symptom-free, but heavy infections cause bouts of diarrhea alternating with periods during which normal stools are passed. The diarrheal feces often contain much mucus and may be flecked with blood. *Trichuris* infection is rare and unimportant in North American cats but interesting for its novelty (see Figures 4-151 and 7-52).

Ruminants are frequently infected but only occasionally made ill by their respective species of *Trichuris*. Individual young cattle with extraordinarily heavy *Trichuris discolor* infections may suffer massive, sometimes fatal hemorrhages into the lumen of the cecum (Georgi, Whitlock, and Flinton, 1972). Such cases tend to be isolated and rare. When a bona fide case of bovine whipworm disease is diagnosed, all other members of the herd may be free of clinical signs. Possibly, clinically affected individuals are those that practice peculiar habits favoring ingestion of soil containing *T. discolor* eggs, or perhaps they are afflicted with a hemorrhagic diathesis that magnifies the cost of the minor trauma inflicted on the cecal wall by the parasites.

Very severe *Trichuris suis* infections in young swine cause catarrhal enteritis with clinical signs of diarrhea, dehydration, anorexia, and retardation of growth (Batte et al, 1977). It has been shown that pigs experimentally infected by the feeding of *T. suis* eggs in the presence of antibiotics will have significantly reduced lesions compared with pigs that are simply infected with the whipworms (Mansfield and Urban, 1996). The authors suggest that the complex pathogenesis of necrotic proliferative colitis in pigs may be linked to worm-induced suppression of mucosal immunity to resident bacteria. The control of *T. suis* infection depends on separating swine from the source of infective eggs, which usually is contaminated soil or filthy housing.

Treatment and control

Trichuris infections in beef cattle can be treated with ivermectin, eprinomectin, or doramectin pour-on with 5 mg/10 kg body weight or with injectable doramectin with 0.2 mg/kg body weight. Ivermectin can be used as a drench in sheep for treatment of *Trichuris ovis* at 0.2 mg/kg body weight.

T. suis infections in swine are susceptible to dichlorvos (Atgard) fed in meal-type feed at 11.2 to 21.6 mg/kg body weight. *T. suis* infections are also susceptible to fenbendazole (9 mg/kg for 3 to 12 days).

Infective *T. vulpis* eggs survive in soil for a long time, and dogs kept in contact with contaminated soils tend to become reinfected after treatment. Lasting success in removing these parasites depends

on separating the patient from these eggs. However, in the emphasis for the need for sanitation, an important possibility may be overlooked. Assuming that the developing parasitic larvae are more resistant to anthelmintic action than are the adult worms, it follows that patent infection is almost certain to recur through maturation of immature forms that have survived a dose of anthelmintic. Most common canine intestinal nematode parasites require only a few weeks to mature, so a second dose of anthelmintic administered 2 or 3 weeks after the first theoretically rids the host of the worms that were unaffected by the first treatment. *T. vulpis* differs from the others in requiring about 3 months to mature, so medication should be routinely repeated three times at monthly intervals to destroy the worms as they mature and prevent them from contaminating the environment.

In the United States, the preferred drugs for treatment of *T. vulpis* infection are fenbendazole (Panacur), milbemycin oxime (Interceptor or Sentinel), febantel (with praziquantel and pyrantel pamoate in Drontal Plus), and moxidectin (with imidacloprid in Advantage Multi). The rare case of *Trichuris* infection in the cat must be handled on an experimental basis because no drug has been cleared specifically for this purpose, although fenbendazole or febantel are probably suitable.

Capillarids

The genus *Capillaria* has been divided by taxonomists into a number of genera on several occasions (Moravec, 1982; Moravec, Prokopic,

and Shlikas, 1987). The capillarids comprise a very large group of worms parasitic in all classes of vertebrates, and it would seem that differences in morphology and life cycles would warrant such a division of the group, although not all systematists working in the field agree with some or all the divisions that have been made. Because it is such a large group, the genus *Capillaria* has been divided into quite a large number of smaller genera with names unfamiliar to most (e.g., *Eucoleus*, *Hepaticola*, *Skrjabinocapillaria*, *Thominx*, and upward of a dozen others), and most of us would be incapable of distinguishing the adults of the different genera.

The adult worms typically are associated with certain epithelial surfaces of their hosts. The veterinary practitioner almost never sees the worms themselves, that is, unless the worms are associated with visible epithelia allowing their tracts to be observed, as when the worms are in the skin of the African clawed frog (Wade, 1982) or the frontal sinuses of the fox (Supperer, 1953). Thus in most cases the practitioner sees only eggs passed in the feces. The species found in the dog and cat have been placed in three genera: (1) *Eucoleus* for those found in the airways, (2) *Aonchotheca* for the worms found in the intestinal tract, and (3) *Pearsonema* for those that occur in the bladder. The worms found in the liver of rats and a few other hosts have been placed in the genus *Calodium*. It is possible to differentiate these few capillarid eggs with relative ease, and it seems that this division, at least, is workable.

Identification

The adult body is small and, although not whip-shaped, otherwise somewhat resembles that of *Trichuris* species and lies partially embedded in mucous membranes (e.g., bronchial, alimentary, vesical) or buried in tissue (e.g., liver; see Figure 8-117). The eggs differ from those of *Trichuris* species only in detail and are described well by Campbell (1991).

Nasal capillariasis

Eucoleus (*Capillaria*) *boehmi* was described as a parasite of the frontal sinus mucosae of the fox (Supperer, 1953). This report was largely overlooked and for a long time it was assumed that capillarids found in the nasal and paranasal sinuses were the same as those found in the bronchi (i.e., *Eucoleus aerophilus*). The eggs of *E. boehmi* can be distinguished from those of *E. aerophilus* by careful microscopic inspection of their surfaces. The surface of *E. boehmi* is covered with tiny pits like those of a thimble, whereas the surface of *E. aerophilus* is a network of branching and anastomosing ridges (Supperer, 1953). Also, the eggs of E. *boehmi* when passed in the feces have undergone a number of cell divisions (see Figure 4-152), whereas the eggs of *E. aerophilus* are passed containing a single cell. A fecal specimen from a dog that had been treated repeatedly over a period of a year for purported intractable whipworm infection was found to contain the eggs of *E. boehmi*, not *T. vulpis*, and the reason for the repeated therapeutic failures became clear.

Bronchial capillariasis

The life history of *E. (Capillaria) aerophilus* may be direct or it may involve earthworms as facultative intermediate hosts. Infection of dogs and cats is rarely responsible for more than a slight cough, but foxes on fur farms may harbor pathogenic burdens. Hanson (1933) described the disease in foxes as insidious and chronic, characterized by a rattling and wheezy respiration with spells of coughing and weakness, and by poor growth, unthrifty fur, failure to shed properly, and death due to bronchopneumonia in heavy infections. Low-grade *E. aerophilus* infection is common in cats and dogs. Diagnosis is based on identifying the rather plump, often asymmetric bipolar eggs in the feces or tracheal mucus (see Figures 7-25, 7-52, and 7-58Figure 7-25Figure 7-52Figure 7-58). However, cats and dogs infrequently develop the severe degree of infection observed in captive foxes confined to earthen runs.

Intestinal capillariasis

Aonchotheca (Capillaria) putorii, a parasite of the small intestine of bears, hedgehogs, raccoons, swine, bobcats, and various mustelids, is occasionally found in the domestic cat, in which it causes little if any harm. However, the eggs present a differential diagnostic problem with respect to those of other capillarid species found in cats (Greve and Kung, 1983).

Ruminants also host several species of capillarids that fall within the genus *Aonchotheca* (Pisanu and Bain, 1999), none of which are of importance in producing disease in these hosts.

Hepatic capillariasis

Adult *Calodium (Capillaria) hepaticum* worms live in the livers of rats, muskrats, woodchucks, other rodents, and a wide range of occasional hosts, including humans. Eggs deposited by the female worms are trapped in the hepatic tissues (see Figure 8-117) where, for lack of sufficient oxygen, they remain undeveloped until the host is eaten or otherwise dies and disintegrates. Only then do the eggs develop to the infective first larval stage.

Urinary capillariasis

Pearsonema (Capillaria) plica adults weave the anterior portions of their bodies into the mucous membrane of the urinary bladder and other parts of the urinary tract of dogs, cats, foxes, and wolves. The eggs contain one cell when passed in the urine. The first-stage larva develops in a little more than a month but does not hatch unless ingested by an earthworm, which serves as paratenic host. The definitive host becomes infected by eating earthworms with first-stage larvae in their tissues, and eggs first appear in the urine about 2 months later. Enigk (1950a) claimed that *P. plica* infection caused growth impairment in young foxes, but dogs and cats appear to bear their usually modest worm burdens without inconvenience. *Pearsonema (Capillaria) feliscati* is a parasite of the urinary bladder of the cat and resembles *P. plica* in its biologic properties (see Figure 7-52).

Treatment

Capillariasis, whether nasal, bronchial, urinary, or intestinal, is usually asymptomatic. Nevertheless, having identified *Capillaria* eggs in the feces or urine sediment or on a bronchial swab, the veterinarian usually feels compelled to medicate. There is no known specific drug for the treatment of these infections. Evinger, Kazacos, and Cantwell (1985) reported success in treating nasal capillariasis with a single oral dose of ivermectin, 0.2 mg/kg. Kirkpatrick and Nelson (1987) reported apparent success in treating a case of symptomatic urinary capillariasis in a border terrier with a single dose of ivermectin, 0.2 mg/kg, injected subcutaneously.

Trichosomoides

Trichosomoides crassicauda is a parasite of the urinary bladder of rats. The tiny male *T. crassicauda* lives inside the uterus of its mate (Figure 4-154; see also Figure 8-120). Infection usually is transmitted from mother rats to their offspring before weaning. *T. crassicauda* has been treated in laboratory rats with ivermectin subcutaneously at 0.2 mg/kg or orally at 3 mg/kg (Findon and Miller, 1987; Summa et al, 1992) and in pet hooded rats (Bowman, Pare, and Pinckney, 2004).

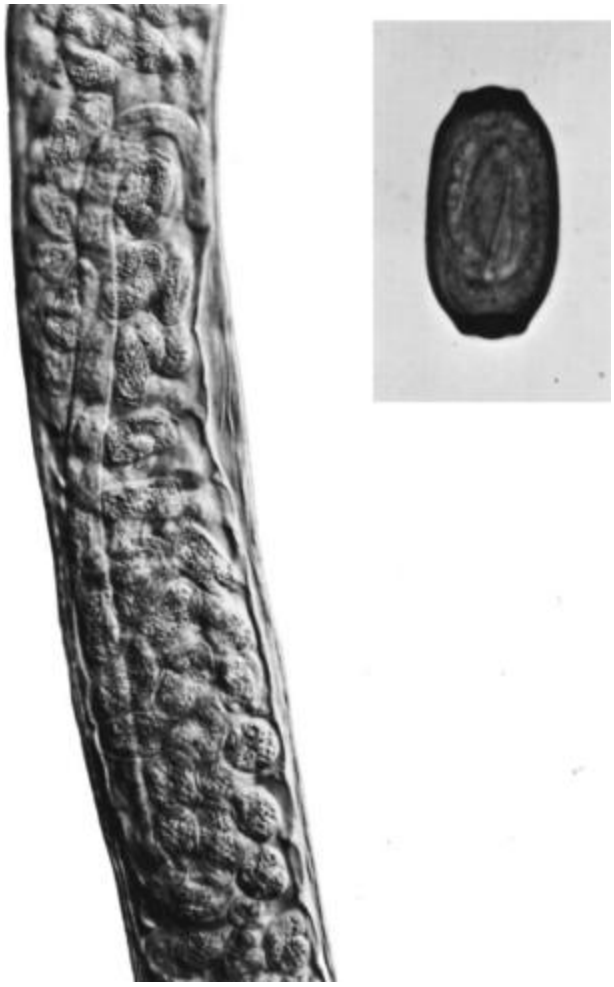

FIGURE 4-154 *Trichosomoides crassicauda* male in the uterus of a female *T. crassicauda (left)*. S. H. Weisbroth, who provided this specimen, has described a Millipore filtration procedure for demonstrating the eggs of *T. crassicauda (right)* in rat urine.

Anatrichosoma

Anatrichosoma species are 25 × 0.2 mm long capillarid-like worms that burrow within the stratified squamous epithelium of the nasal passages of African monkeys and the buccal mucosa of the American opossum, *Didelphis virginiana*. The female worms deposit 76 × 58 μm bipolar eggs in these burrows. The fully embryonated eggs reach the surface in the normal course of regeneration and desquamation.

Antemortem diagnosis is based on demonstrating the eggs on nasal swabs or in skin biopsies (see Figures 7-104, 8-118, and 8-119Figure 7-104Figure 8-118Figure 8-119). *Anatrichosoma cutaneum* gives rise to subcutaneous nodules and edema about the joints of the extremities and serpiginous blisters of the palms and soles of monkeys.

Haycocknema perplexum

H. perplexum is a nematode that has been seen in three people in or from Tasmania who become seriously ill with a worm that has adults and larvae within muscle fibers (Spratt, 2005). It was described as a member of the superfamily Muspiceoidea in the family Robertdollfusidae. This group of worms has poorly known species in the subcutaneous tissues of mice and bats, the anterior chamber of the eye of cervids, the brain of falconids, the portal and intracardiac veins and epicardial lymphatics of kangaroos and wallabies, the pulmonary arteries of koalas and brushtail possums, and the subcutaneous capillaries of the ears of reindeer (Spratt et al, 1999).

A 14-year-old horse imported from Ireland to Switzerland had masseter atrophy and severe chronic myositis caused by numerous immature and mature female nematodes (Eckert and Ossent, 2006). The authors felt that the infection was due to something that appeared *Haycocknema*-like, but they could not rule out the possibility of *H. gingivalis* because of the degeneration of many of

the worms. Attempts were made to compare isolated DNA with that of *Trichinella* and *Halicephalobus*, but there was no amplification.

MISCELLANEOUS WORMS

Thorny-headed worms and leeches are not related to the nematodes, nor are they related to one another. They are lumped together here for want of a logical and convenient alternative.

Phylum Acanthocephala

The Acanthocephala, or thorny-headed worms, are a small phylum of highly specialized parasites of the vertebrate digestive tract (Figures 4-155 to 4-157). There are separate sexes. The body is normally white and flattened in situ but becomes more or less cylindric when placed in water, which is the indispensable first step in preparing specimens for identification. The resulting osmotic turgor forces the retractable, spiny attachment organ or proboscis out of the body so that the shape and number of spines can be ascertained and the specimen thereby identified (see Figure 4-156). Once the proboscis (and male copulatory bursa) is well protracted, the specimen can be fixed in hot alcohol-formaldehyde-acetic acid (AFA) solution (85 parts of 85% ethanol, 10 parts of stock formalin, 5 parts of glacial acetic acid). These technical details are stressed here because unless specimens are properly prepared, even a specialist may not be able to identify them.

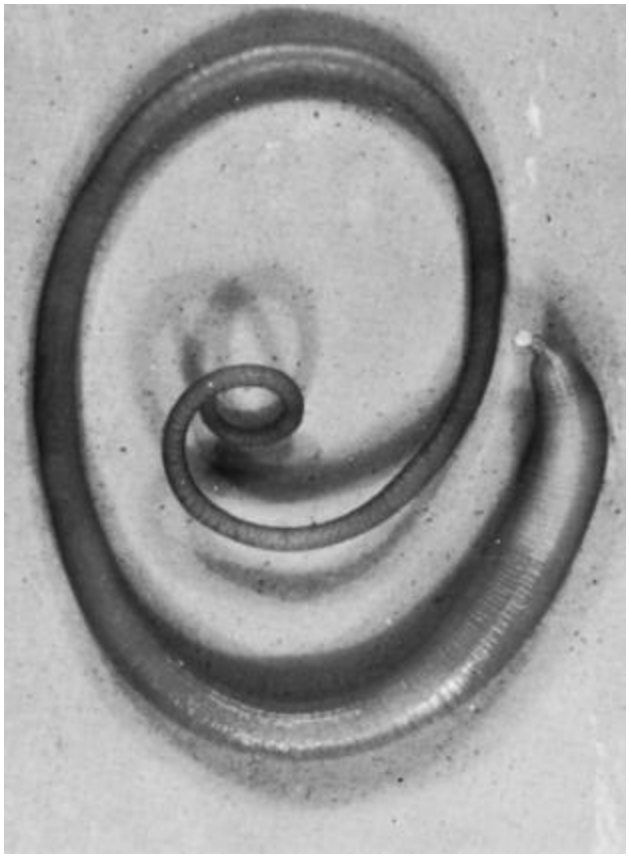

FIGURE 4-155 *Macracanthorhynchus hirudinaceus* (three fourths natural size). This worm typically is white but with fixation appears dark in this photograph.

FIGURE 4-156 *Macracanthorhynchus ingens* proboscis.

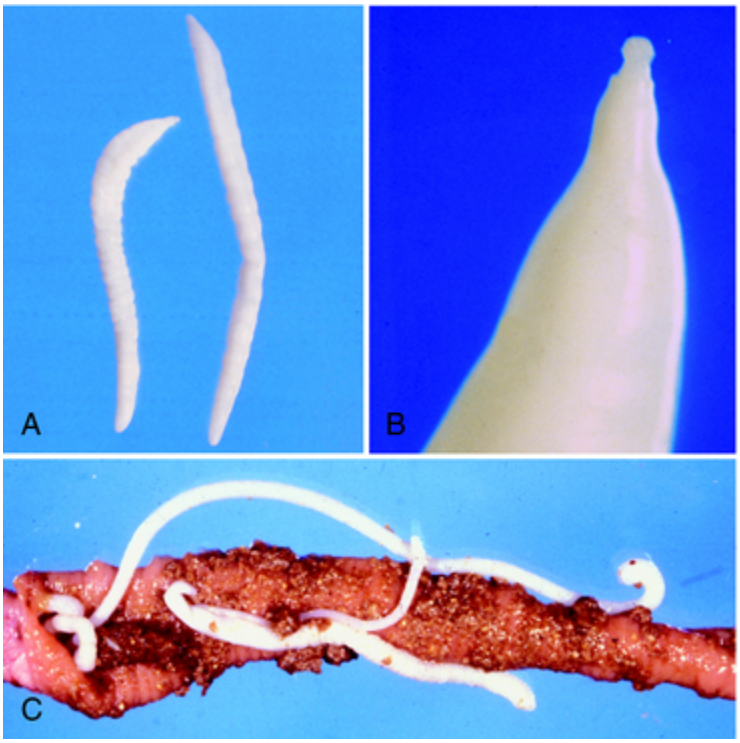

FIGURE 4-157 Adult *Macracanthorhynchus ingens*. Two adults *(left),* anterior end with proboscis *(right),* adult worms in situ in dog intestine *(bottom)*.

Identification

Acanthocephalans consist of a body and a retractable spiny proboscis by which the parasite attaches itself to the intestinal wall of its host. There is no digestive tract. Nutrients are absorbed through the tegument.

Life History

When the egg is laid, it contains a fully developed larva called an *acanthor* (Figure 4-158). If the egg is ingested by a suitable arthropod intermediate host, the acanthor develops through an acanthella stage (Figure 4-159) into an encysted infective larva called a *cystacanth* (Figure 4-160). The cystacanth is capable of

reencysting in a range of vertebrate paratenic hosts should they ingest the infected arthropod. Frequently the cystacanth even reencysts in its normal definitive host instead of developing to maturity. For example, *Prosthenorchis elegans* adults may be found in the intestinal lumen of a monkey, and cystacanths of the same parasite may be found encysted in the peritoneal membranes.

FIGURE 4-158 *Macracanthorhynchus ingens* egg containing acanthor larva.

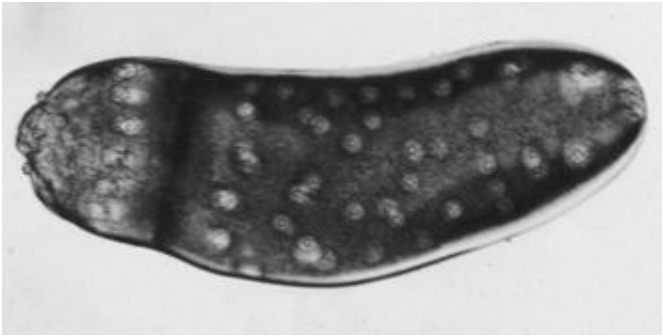

FIGURE 4-159 *Macracanthorhynchus ingens* acanthella from a *Narceus* millipede.

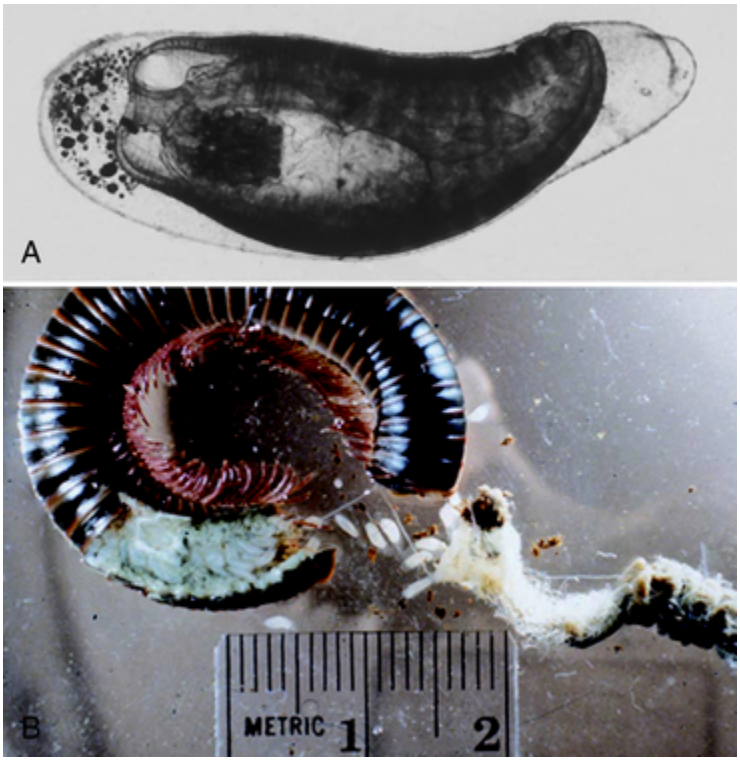

FIGURE 4-160 *Macracanthorhynchus ingens* cystacanth infective larvae above and as they appear when recovered from a broken *Narceus* millipede.

Macracanthorhynchus

Macracanthorhynchus hirudinaceus is a parasite of the small intestine of swine (see Figure 4-155). The body is white, flattened, and transversely wrinkled, which occasionally causes this parasite to be mistaken for a tapeworm. The males are about 10 cm long, whereas the females can be 35 cm long. Development to the cystacanth stage infective for pigs occurs in May beetles, dung beetles, or water beetles in about 3 months. Pigs acquire *M. hirudinaceus* infection when rooting for beetle grubs, but the infected adult beetle is also a source of cystacanths. The prepatent period is 2 or 3 months. Pigs may display no outward sign of M. hirudinaceus infection, or there may be diarrhea and emaciation with evidence of acute abdominal

pain, depending on how deeply the proboscis is embedded in the intestinal wall.

Treatment

There is no approved treatment for *M. hirudinaceus* infection. Benzimidazole anthelmintics may be tried. An in-feed formulation of ivermectin (0.1 or 0.2 mg/kg body weight for 7 days) resulted in 100% removal of adult *M. hirudinaceus* from pigs (Alva-Valdes et al, 1989). Doramectin at 0.3 mg/kg also proved very good in removing *M. hirudinaceus* from pigs (Yazwinski et al, 1997).

Macracanthorhynchus ingens (see Figure 4-157), even larger than *M. hirudinaceus*, is a parasite of the raccoon *(P. lotor)* and black bear *(Ursus americanus)* and uses millipedes of the genus *Narceus* as intermediate hosts. These parasites occasionally infect dogs that eat the infected millipedes. To eat a millipede requires extraordinary cunning, frightful taste, great excitement, or utter boredom on the part of the dog because the millipedes give off a potent defensive secretion. The raccoon gets around the problem by rolling the millipede about in the dust to exhaust its supply of defensive secretion, but few dogs have learned that trick. Cases in dogs have been treated with ivermectin (Pearce et al, 2001).

Prosthenorchis

Prosthenorchis species are up to 55 mm long, pink acanthocephalan parasites of primates. *Prosthenorchis* organisms propagate very successfully in monkey colonies by using cockroaches and certain

beetles as intermediate hosts. Monkeys become infected when they eat a cockroach containing the cystacanth larvae of *Prosthenorchis* species.

Both chronic and acute disease syndromes have been described for *Prosthenorchis* infection. The chronic course is marked by watery diarrhea of several months' duration, with weakness and progressive emaciation. The appetite remains normal until a day or so before death. The acute course is of less than 1 day's duration and is caused by acute bacterial peritonitis resulting from perforation of the intestinal wall by the proboscis.

Treatment of caged marmosets *(Saguinus mystax)* infected with *P. elegans* has shown that fenbendazole (20 mg/kg body weight for 7 days) was effective in removing these parasites (Demidov et al, 1988).

Moniliformis

Common parasites of wild rodents, *Moniliformis* species use cockroaches as intermediate hosts. The great length (up to 32 cm) and pseudosegmentation of the body invite misidentification of this acanthocephalan as a tapeworm.

Oncicola

Oncicola canis (Figure 4-161), less than 14 mm long, is a parasite of the dog, coyote, and other canids. It uses the armadillo as paratenic host for cystacanths.

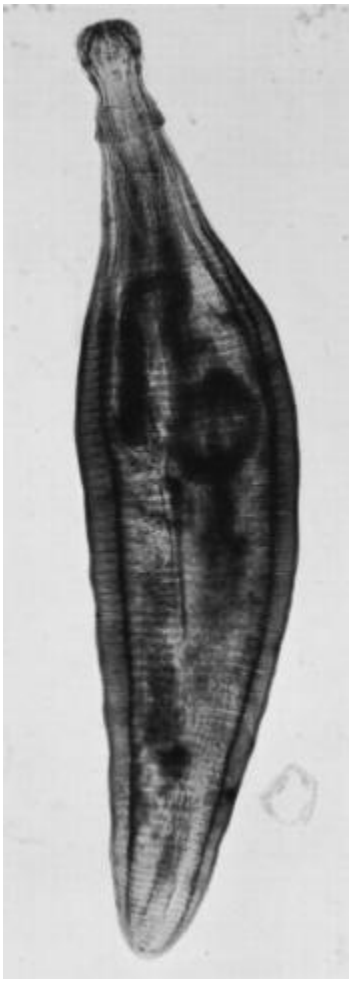

FIGURE 4-161 *Oncicola* sp. from an Arizona coyote *Canis latrans*.

Courtesy Dr. Frances Phillips.

Phylum Annelida

Class Hirudinea

Leeches are predatory or parasitic worms of the phylum Annelida, which includes the free-living earthworms. Leeches have terminal suckers for locomotion and attachment and move by looping movements like those of an inchworm. They usually are dark or black in color. Bloodsucking species fasten to the skin or oropharyngeal mucous membrane by means of their powerful

suckers, pierce the epidermis, and suck blood. A salivary enzyme, hirudin, acts as an anticoagulant and ensures a copious flow of blood. In some localities, surface waters abound with bloodsucking leeches that attach to the oropharyngeal or laryngeal mucous membrane when imbibed by the unwary person or animal. Their presence in these locations may cause severe bouts of coughing and choking, during which blood is ejected by the victim. Infection may last several weeks and occasionally causes death. Treatment consists of mechanically removing the leech.

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CHAPTER 5

Vector-Borne Diseases

Susan E. Little

The term *vector-borne disease* refers to any of a broad array of infectious diseases caused by pathogens that are transmitted by arthropods or other biologic intermediaries. Although transmission usually occurs on blood feeding by an infected insect or acarine parasite, infection can also result when a vertebrate host ingests a vector or on contamination of a wound by infectious organisms in the feces of the arthropod intermediary. Regardless of the means of transmission, the vector, a critical component in disease transmission, engages in a lifestyle that is at least partially parasitic and that somehow contributes to its ability to both acquire and serve as a source of infection to animals.

Diseases transmitted by arthropods have held a central role in veterinary medicine in general, and veterinary parasitology in particular, for over a century. In 1889, Drs. Theobald Smith, Frederick Kilborne, and Cooper Curtice completed their description of transmission of *Babesia bigemina*, causative agent of Texas cattle fever, by *Rhipicephalus* (*Boophilus*) spp. ticks, and then used that knowledge to design and implement a successful eradication program in the United States (Logue, 1995). Their discovery was the first recognition of arthropod transmission of an infectious agent, and it paved the way for the elucidation of numerous other vector-

pathogen relationships. In recent years, knowledge about the relative importance and diversity of vector-borne diseases in both veterinary medicine and public health has dramatically expanded, particularly in North America, where a number of new disease agents have been described.

The apparent increase in the frequency with which veterinarians and physicians encounter vector-borne diseases has been attributed to several factors, including increasing vector populations as a result of spread to new areas or point introductions of new species of vectors, expanding habitat and increasing wildlife reservoir host populations, and relatively recent biogeographic and climate changes that favor vector populations (Gratz, 1999). However, another likely explanation for the increased awareness of vector-borne disease agents is the increased recognition of these organisms owing to improved detection methods that use molecular rather than purely classic microbiologic approaches. Indeed, several of the organisms discussed in this chapter have been described only by nucleic acid sequence and have yet to be isolated in culture.

Arthropod vectors transmit disease agents from almost every major class of pathogens, including viruses, rickettsia and other bacteria, protozoa, and helminths. Many of these organisms gain entry to the host via blood feeding, but vector-borne disease agents are by no means limited to the circulation and on initial infection may go on to establish and cause disease in virtually any organ system. Arthropods may serve as **mechanical** transmitters of pathogens, in which the vector harbors a transient infection on, for example, contaminated mouthparts, or the arthropod may be a true **biologic** vector of the disease agent, remaining infected with the

organism long term, and in many instances even may be a required part of the life cycle of a given pathogen. When there is a long-standing evolutionary relationship, biologic vectors may become intimately associated with the pathogen and may maintain the infection **transstadially** as they molt from an immature to a mature form, or they may **transovarially** pass the organisms from the female to the offspring. In addition, some disease agents can be transmitted horizontally within vector populations through sexual contact between arthropods or via simultaneous cofeeding on a vertebrate host.

Classically, arthropod vectors acquire infections via feeding on an infected vertebrate **reservoir host.** Therefore the disease agent requires both an active vector population and an infected reservoir host system to persist in nature. In some systems, vertebrates may become only transiently infected and the disease agent instead is maintained in chronically infected arthropods and/or is passed transovarially to the next arthropod generation. In these systems, the infected arthropods may infect a vertebrate **amplifying host,** which can develop a short-lived infection capable of infecting the rest of the vector population. In other systems, infection in the vertebrate reservoir hosts may be maintained by transmission by a species of arthropod that does not feed on domestic animals or people. In these instances, a distinct, often related species of arthropod is required to serve as a **bridge vector** to actually bring the infection from the wildlife reservoir host to companion animals, livestock, or people.

Vectors and the organisms they transmit develop intimate associations over evolutionary time. The species of arthropod that

can effectively serve as a biologic intermediary for a given pathogen is often limited to one or a few closely related organisms that serve as the **primary vector** for that disease agent. However, in some cases other **secondary vectors** that have the ability to transmit at least some strains of the same species of pathogen are also found. Although these secondary vectors may have a somewhat reduced competency for transmission, they can be regionally important and may facilitate the spread of a given disease agent or allow the persistence of an organism on introduction into a new area. Similarly, a given arthropod species may be infected with and capable of transmitting several distinct agents. Exposure to a vector population that harbors several different pathogens creates a risk of **co-infection,** which may exacerbate the disease state in the animal (Thomas et al, 2001).

The **transmission rate** of a pathogen is defined as the number of new infections that occur per unit time. For vector-borne diseases, characteristics of the vector, the reservoir host, and the pathogen itself all influence the transmission rate. In addition to direct variables such as longevity and home range of vector species and longevity and persistence of infection in the reservoir host, the interactions among vector, reservoir, and pathogen will affect the ultimate transmission rate of a given vector-borne disease agent. For example, the **extrinsic incubation period** required for the pathogen to develop in the vector to the infectious stage will directly influence how rapidly the vector can transmit the organism after acquisition; the length of this extrinsic incubation period may be influenced by ambient temperature. Similarly, the **intrinsic incubation period** required for a vertebrate reservoir to develop a

patent infection that can go on to infect subsequent vectors will affect prevalence of infection in the vector population (Reisen, 2002).

To effectively serve as a reservoir host, a given vertebrate species not only must be susceptible to infection and able to infect vectors that are likewise competent to go on to transmit the infection, but it also must share a common niche with the competent vector that allows frequent interactions. For example, the reservoir and vector must be active in the same habitat, at the same time of day, and at the same time of year for acquisition and transmission to occur. Without frequent ecologic interactions, vector-borne diseases are unlikely to persist even when ample vertebrate reservoir hosts, arthropod vectors, and pathogens are present in a given area.

VIRAL PATHOGENS TRANSMITTED BY ARTHROPODS

A number of important viral pathogens are transmitted by arthropods (Table 5-1). Viral disease agents transmitted by arthropod biologic vectors are commonly referred to as **arboviruses** and include members of the Togaviridae, Flaviviridae, Bunyaviridae, and Reoviridae. Mosquitoes are by far the most common vectors of arboviruses. The majority of known arboviruses are zoonotic, with wild birds, wild rodents, and, in some cases, domestic animals serving as reservoir hosts and amplifying hosts to infect mosquitoes and create the risk of infection to both animals and people. Other arboviruses of both veterinary and public health importance are transmitted via biting midges (*Culicoides* species) or mechanically by fleas, mosquitoes, or blackflies.

TABLE 5-1 Vector-Borne Viral Diseases of Veterinary Importance

Disease	Cause	Virus Family	Vector	Reservoir Host	Species Affected
Equine encephalitides	Eastern equine encephalitis virus (EEEV)	Togaviridae	Mosquitoes	Passerine birds	Horses, birds, dogs, pigs, people
	Western equine encephalitis virus (WEEV)	Togaviridae	Mosquitoes	Passerine birds	Horses, people
	Enzootic Venezuelan equine encephalitis virus (enVEEV)	Togaviridae	Mosquitoes	Rodents primarily; also birds, opossums, bats	Horses, people
	Epizootic Venezuelan equine encephalitis virus (epVEEV)	Togaviridae	Mosquitoes	Birds, horses	Horses, people
West Nile	West Nile virus (WNV)	Flaviviridae	Mosquitoes	Birds	Horses, people, dogs
Japanese encephalitis	Japanese encephalitis virus (JEV)	Flaviviridae	Mosquitoes	Birds, horses, pigs	Horses, pigs, people
Rift valley fever	Rift valley fever virus (RVFV)	Bunyaviridae	Mosquitoes	Ruminants	Cattle, goats, sheep, people
Bluetongue, epizootic hemorrhagic disease (BT, EHD)	Reoviridae virus Epizootic hemorrhagic disease virus	Reoviridae	*Culicoides*	Ruminants	Sheep, goats, deer
African horse sickness (AHS)	African horse sickness virus	Reoviridae	*Culicoides*	Wild equids, horses	Horses, mules, donkeys
Colorado tick fever	Colorado tick fever virus	Reoviridae	*Dermacentor*	Rodents	People
Tick-borne encephalitis complex (louping ill, Powassan encephalitis, Russian spring-summer encephalitis, Omsk hemorrhagic fever)	Tick-borne encephalitis viruses	Flaviviridae	*Ixodes, Dermacentor, Haemaphysalis*	Various	People, sheep, cattle, horses, dogs, pigs, and others
African swine fever	African swine fever virus	Asfarviridae	*Ornithodorus* species, *Stomaxys calcitrans*	Ticks, wild suids, pigs	Pigs
Myxomatosis	Myxoma virus	Poxviridae	Fleas, mosquitoes, *Simulium* species	Rabbits, hares	European rabbits
Equine infectious anemia	Equine infectious anemia virus	Retroviridae	*Stomaxys, Chrysops*	Horses	Horses, other equids
Fowlpox	Fowlpox, canarypox, pigeonpox virus	Poxviridae	Mosquitoes, fleas	Birds	Birds

Equine Encephalitides

The equine encephalitides are perhaps the best known of the veterinary mosquito-borne viral disease agents. This complex within the Togaviridae is composed of a large group of related serovars of Eastern, Western, and Venezuelan equine encephalitis virus, which are commonly referred to as EEE, WEE, and VEE virus, respectively. The serovars of VEE virus are further subdivided into either endemic or epizootic types. EEE virus and WEE virus are maintained in passerine bird reservoir hosts and strictly ornithophilic mosquitoes. However, outbreaks can occur when bridge vectors emerge to carry virus from birds to horses and people. Enzootic VEE virus is maintained largely in rodent reservoir hosts and is transmitted by culicine mosquitoes. The maintenance cycle of epizootic VEE virus is less well understood but appears to involve avian reservoir hosts,

a large number of mosquito vectors, and equine amplifying hosts; horses develop high viremia on infection, providing a ready source of virus to infect mosquitoes during outbreaks. Vaccines are available to protect horses from infection with the equine encephalitis viruses (Tabamo and Donahue, 1999; Weaver et al, 2004).

Flaviviruses

Other important mosquito-borne veterinary viral diseases include those caused by flaviviruses, such as West Nile and Japanese encephalitis. Both West Nile and Japanese encephalitis viruses are maintained in cycles involving bird reservoir hosts and mosquito vectors. Infection of horses, people, and rarely dogs with West Nile virus can lead to development of a febrile disease that in severe cases can progress to encephalitis and death. The virus, which was originally described in Africa, was introduced to North America in 1999 and is now well established across the United States. Horses do not serve as a source of mosquito infection with West Nile virus. A vaccine is available to protect horses from the severe disease associated with infection with West Nile virus (Dauphin and Zientara, 2006). Outbreaks of Japanese encephalitis in Asia usually involve pigs as well as horses and people, and pigs have been shown to serve as an amplifying host for this virus (Wu, Huang, and Chien, 1999).

Bunyaviruses

Diseases caused by bunyaviruses, like Rift Valley fever, are also arboviral diseases. Rift Valley fever is endemic in areas of Africa and is maintained in a cycle between mosquito vectors and ruminant

reservoir hosts. Huge epidemics involving hundreds of thousands of cases in ruminants and people have occurred. Although Rift Valley fever virus is zoonotic, with people becoming infected via direct contact with infected animals as well as through mosquito bites, human disease is usually characterized by high morbidity but low mortality (Gerdes, 2004).

Reoviruses

Bluetongue and **epizootic hemorrhagic disease** (EHD) are caused by closely related members of the Reoviridae and are transmitted to ruminants via biting midges (*Culicoides* species). *Culicoides variipennis* is considered the principal vector of both bluetongue virus and EHD virus in North America; *Culicoides brevitarsis* is more important in Australia, and *Culicoides imicola* is the major vector in southern Europe, Africa, and the Middle East. There are more than 25 serotypes of bluetongue worldwide and at least 10 serotypes of EHD. Although many ruminants are susceptible, disease caused by bluetongue virus is most common in sheep, is occasionally seen in goats, and is considered rare in cattle (Barratt-Boyes and MacLachlan, 1995). Disease is characterized by ulcerative lesions in the mouth, around the muzzle, on the coronary band, and between the toes. In severe cases, respiratory compromise due to pleural effusion and hemorrhage is manifested as cyanosis, which gives a bluish cast to the tongue. Hemorrhage is also a prominent finding in EHD, which in North America most commonly infects and causes disease in deer. Cattle and sheep are susceptible to EHD virus, but most infections in domestic ruminants appear to result in subclinical disease. The **Ibaraki virus,** which is considered to be a member of

the EHD virus group, does cause a febrile disease in cattle that results in both oral ulceration and striated and skeletal muscle degeneration (Inaba, 1975).

African horse sickness (AHS) virus is another *Culicoides*-borne member of the Reoviridae and is transmitted between equids by *C. imicola* and *Culicoides bolitinos*. This virus causes a severe, often fatal disease of horses and other equids in sub-Saharan Africa; outbreaks have also been reported in the Middle East and southern Europe. During epidemics, which occur after periods of drought followed by heavy rains, mechanical transmission by other biting flies may also occur. Dogs can become infected with AHS virus but do not play a role in the epidemiology of disease. Infected horses develop a fever that may be followed by respiratory distress and/or pronounced facial edema. In susceptible populations of horses, mortality rates from AHS virus infection range from 50% to 95%. Mules and donkeys develop less severe disease with lower mortality, and death is rarely seen in zebras (Mellor and Hamblin, 2004).

Tick-Transmitted Viruses

Viruses may also be transmitted by ticks. For example, Coltivirus, which causes Colorado tick fever in people, is transmitted from rodent reservoir hosts to people via *Dermacentor andersoni*. Disease is most commonly seen in the western United States and Canada and develops as soon as 4 to 5 days after a tick bite, when affected individuals develop a nonspecific febrile flulike illness; the fever is often biphasic. Similar diseases of people and animals include those caused by flaviviruses in the tick-borne encephalitis (TBE) complex, such as louping ill, Powassan encephalitis, TBE, Russian spring-

summer encephalitis, and Omsk hemorrhagic fever; all are transmitted via hard ticks, including members of the genera *Ixodes*, *Dermacentor*, and *Haemaphysalis* (Dumpis, Crook, and Oksi, 1999; Emmons, 1988). Some authors suspect that members of the TBE complex may also be transmitted by fleas, but these relationships are not well defined. Louping ill is primarily a disease of sheep, although cattle, horses, pigs, and humans may also be affected; infected individuals develop a febrile illness followed by progressively worsening neurologic disease that in sheep is often characterized by gait abnormalities (Gritsun, Nuttall, and Gould, 2003). Powassan encephalitis is reported primarily from people in the western United States, western Canada, and the former Soviet Union, whereas TBE, Russian spring-summer encephalitis, and Omsk hemorrhagic fever are more commonly seen in people in Europe and northern Asia (Gritsun, Nuttall, and Gould, 2003). All mammals are susceptible to infection with TBE viruses; human disease can follow ingestion of unpasteurized dairy products, particularly those prepared from goat milk (Dumpis, Crook, and Oksi, 1999).

African swine fever (ASF) virus, currently classified with other ASF-like viruses as an Asfarviridae, is directly or indirectly transmissible between pigs but can also be maintained in *Ornithodoros* species soft ticks transstadially, transovarially, and sexually for years, being transmitted to pigs whenever the opportunity arises for feeding to occur (Plowright, 1981). Biting flies, including *Stomoxys calcitrans*, are also able to transmit ASF virus mechanically between pigs (Mellor, Kitching, and Wilkinson, 1987). Infection of pigs results in high fever, anorexia, hemorrhage, and rapid death; with the most virulent strains, mortality

approaches 100% (Mebus, 1988). Less virulent strains produce chronic ASF and may result in weight loss, respiratory disease, and enlarged lymph nodes in infected pigs (Mebus, 1988). Treatment and vaccines for ASF are not available.

Mechanical Transmission of Viruses by Arthropods

Mechanical transmission of viruses by arthropod vectors also occurs. Although **iatrogenic transmission** via needle inoculation can allow transmission, for some of these disease agents the presence of arthropod vectors greatly facilitates transfer within a population. For example, myxoma virus of rabbits is mechanically transmitted between rabbits by a number of blood-feeding arthropods, including mosquitoes and fleas; the organisms may survive and remain infectious in a flea for several months. Native rabbits in the Americas develop only mild fibromas when infected, but when the virus is transmitted to European rabbits, a severe and usually fatal infection characterized by high viremia and progressively enlarging skin lesions ensues, characteristics that led this virus to be used in attempts at biologic control of rabbits in both Australia and Europe. However, over time, populations of European rabbits develop resistance to strains of myxoma virus, making control efforts largely ineffective (Kerr and Best, 1998).

Equine infectious anemia virus is another example of a virus that is transmitted mechanically by arthropods. Infection is readily spread between horses in relatively close proximity by blood-feeding flies, particularly horseflies and deerflies. These large biting flies deliver irritating, painful bites, and defensive activity by the horses results in frequent interrupted feeding. The flies quickly return,

however, to complete their blood meal on the same horse or another horse in the same vicinity, resulting in mechanical transmission (Issel et al, 1988). Most infected horses do not develop clinical disease. However, in some horses, acute infection can result in high fever and death within 2 to 3 weeks. Others may develop chronic disease associated with intermittent fever, depression, anemia, and petechial hemorrhages. Regardless of the presence of clinical disease, almost all infected horses remain so for life, serving as a reservoir of infection (Coggins, 1984). An agar immunodiffusion test (Coggins test) is widely used to identify these carriers so they can be segregated from noninfected horses and thus transmission can be prevented.

Fowlpox of birds, including poultry, canaries, pigeons, and a variety of wild birds, is caused by a variety of avian pox viruses that can be transmitted mechanically by mosquitoes or through direct contact between infected and naive birds. Infections have also been associated with the presence of the sticktight flea, *Echidnophaga gallinarum*, on poultry (Gustafson et al, 1997). The viral infection induces the development of hyperplastic cutaneous lesions on the unfeathered regions of the skin (beak, cere, legs) that often become hemorrhagic. Occasionally, perhaps owing to infection after inhalation or ingestion of contaminated material, lesions form in the oral cavity or respiratory tract. Infection results in decreased growth and production, but most affected animals survive. Mortality, when it occurs, is associated with severe oral or respiratory tract lesions or, in the case of wild birds, large lesions on the legs, feet, or periocular region that impair mobility or vision, resulting in predation or starvation. There is no treatment once lesions have

developed. However, vaccines are available to prevent disease in poultry.

RICKETTSIAL PATHOGENS TRANSMITTED BY VECTORS

The term *rickettsia* refers to any of a large number of obligate intracellular gram-negative bacteria within the order Rickettsiales. Two major families are currently defined: the **Rickettsiaceae,** which include the genera *Rickettsia*, *Orientia*, and *Coxiella*, and the **Anaplasmataceae,** which include the genera *Anaplasma*, *Ehrlichia*, *Wolbachia*, and *Neorickettsia;* phylogenetic reorganization of the latter group in 2001 resulted in a number of taxonomic changes, particularly at the genus level (Dumler et al, 2001). Survival of these organisms and transmission between animals are dependent on invertebrate vectors. Ticks are by far the most common vector of rickettsial agents, but some rickettsial organisms, including members of the genera *Wolbachia* and *Neorickettsia*, use helminth vectors (Table 5-2).

TABLE 5-2 Vector-Borne Rickettsial Diseases of Veterinary Importance

Disease	Cause	Primary Vector	Reservoir Host
Rocky Mountain spotted fever	*Rickettsia rickettsii*	*Dermacentor* spp.	Rodents
Epidemic typhus	*Rickettsia prowazekii*	*Pediculus humanus*	Humans, flying squirrels
Endemic typhus; murine typhus	*Rickettsia typhi*	*Xenopsylla cheopis*; other fleas	Rodents, other mammals
Murine typhus–like disease	*Rickettsia felis*	*Ctenocephalides felis*	Opossums
Rickettsialpox	*Rickettsia akari*	*Liponyssoides* mites	Rodents
Q fever	*Coxiella burnetii*	*Amblyomma* spp., other ticks	Various mammals
Scrub typhus	*Orientia tsutsugamushi*	*Leptotrombidium* mites	Rodents
Bovine anaplasmosis	*Anaplasma marginale*	*Dermacentor* spp.	Cattle
Canine anaplasmosis	*Anaplasma phagocytophilum*	*Ixodes* spp.	Rodents, ruminants
	Anaplasma platys	*Rhipicephalus sanguineus**	Dogs
Canine ehrlichiosis	*Ehrlichia canis*	*Rhipicephalus sanguineus*	Dogs
	Ehrlichia ewingii	*Amblyomma americanum*	Dogs, white-tailed deer
	Ehrlichia chaffeensis	*Amblyomma americanum*	White-tailed deer
Heartwater	*Ehrlichia ruminantium*	*Amblyomma* spp.	Ruminants
Salmon poisoning	*Neorickettsia helminthoeca*	*Nanophyetus salmincola*	Salmonid fish
Potomac horse fever	*Neorickettsia risticii*	*Acanthatrium oregonense*	Bats, caddisflies

*Transmission by *Rhipicephalus sanguineus* is suspected but has not yet been fully confirmed.

Many rickettsial organisms have long been recognized as agents of veterinary and human disease. In recent years, evidence continues to amass that underscores the significance and importance of rickettsia as pathogens (see Table 5-2). Species of rickettsia differ in the primary vector responsible for transmitting infection, the reservoir host(s) important for maintaining a source of infection in nature, and the cell type infected, but all are susceptible to tetracycline antibiotics. Because of this shared susceptibility, tetracycline, specifically doxycycline, is considered the treatment of choice for rickettsial infections in both veterinary and human medicine (Raoult and Drancourt, 1991). To date, with the exception of Potomac horse fever, there are no widely available commercial vaccines that reliably protect against infection with rickettsial agents; accordingly, stringent attention to control and avoidance of ticks and other vectors remains the best means of preventing disease.

The Rickettsiaceae

Rocky Mountain Spotted Fever

The best known member of the family Rickettsiaceae in the Americas is *Rickettsia rickettsii*, causative agent of Rocky Mountain spotted fever. The organism is transmitted between rodent reservoir and amplifying hosts and to dogs and people via ticks. *Dermacentor* species are the most important vectors of *R. rickettsii* in North America and maintain the infection within the tick population transovarially as well as transstadially, thus serving as a reservoir of the organism as well (McDade and Newhouse, 1986). *Rhipicephalus sanguineus* has long been established, along with *Amblyomma cajennense*, as an important vector of *R. rickettsii* in Mexico, Central America, and South America and was recently was implicated in an outbreak of Rocky Mountain spotted fever in humans and dogs in the southwestern United States (Demma et al, 2005).

Rodents are widely considered the most important vertebrate reservoir amplifying hosts in nature for *R. rickettsii;* however, the involvement of *R. sanguineus*, which prefers to feed on dogs in all life stages, in transmitting infection to dogs and people in some regions suggests other vertebrate hosts may also play a role in maintaining a source of infection. The full role of other ticks historically implicated as vectors of *R. rickettsii*, including *Amblyomma americanum* or *Haemaphysalis leporispalustris*, warrants further investigation. Understanding the epidemiology of *R. rickettsii* is complicated by the presence of a variety of closely related *Rickettsia* species, such as *Rickettsia conorii* or *Rickettsia japonica*, which may cross-react on serologic assays (Brouqui et al, 2007).

Infection with *R. rickettsii* causes a febrile illness that may be severe. Disease is most commonly seen in dogs and people, although

Rocky Mountain spotted fever has also been reported in cats. The organisms infect and damage endothelial cells, resulting in a progressive necrotic vasculitis; thrombocytopenia is also commonly seen. People with Rocky Mountain spotted fever often develop a nonpruritic rash ("spots") that characteristically appears first on the forearms, wrists, and ankles 3 to 4 days after initiation of fever (Thorner et al, 1998). Petechial and/or ecchymotic hemorrhages may develop in some dogs, but a rash is not evident. In Europe and Africa, ticks transmit *R. conorii,* which causes the relatively milder disease of Boutonneuse fever. A number of tick-transmitted spotted fever rickettsia with potential public health importance, including *Rickettsia parkeri* and *Rickettsia amblyommii*, continue to be described (Azad and Beard, 1998).

Other *Rickettsia*

Other *Rickettsia* species of public health importance include *Rickettsia typhi*, a flea-transmitted organism that causes **endemic or murine typhus,** and *Rickettsia prowazekii*, causative agent of **epidemic typhus** in people and primarily transmitted between people by body lice. Both of these organisms cause a disease in people similar to spotted fever. Another rickettsial agent, *Coxiella burnetii*, causes **Q fever** in people and a variety of animals. Transmission of *C. burnetii* by ticks can occur, but most cases in people are thought to be acquired by inhalation of organisms in contaminated dust (Terheggen and Leggat, 2007). Mites transmit some rickettsial pathogens as well, including *Rickettsia akari*, causative agent of **rickettsialpox,** a nonfatal febrile disease of people that is predominantly seen in urban areas, and *Orientia*

tsutsugamushi, the causative agent of **scrub typhus** in Asia and Australia (Boyd, 1997; Chattopadhyay and Richards, 2007).

The Anaplasmataceae

The family Anaplasmataceae includes a wide variety of pathogens, including organisms such as *Anaplasma marginale* and *Ehrlichia canis*, which have been known to be important in veterinary medicine for many decades, as well as a number of recently recognized important zoonotic and veterinary pathogens. Although the different species tend to infect different cell types and to cycle in nature using distinct reservoir hosts and tick vectors, all respond to therapy with doxycycline, and, with the exception of the *Neorickettsia* and *Wolbachia* species, all are primarily transmitted by ixodid ticks. Direct mechanical transmission of some blood-borne rickettsia by biting flies or via intentional or accidental blood subinoculation has also been shown to occur.

Anaplasma species

A. marginale, which causes anemia and fever in cattle, is transmitted between cows by *Dermacentor* and *Rhipicephalus (Boophilus)* species ticks; *A. marginale* may also be transmitted mechanically between cattle via biting flies (e.g., *Tabanus* species) (Ewing, 1981; Hawkins, Love, and Hidalgo, 1982). Morulae of *A. marginale* are readily found in erythrocytes of acutely affected cattle (Figure 5-1). *Anaplasma (Ehrlichia) platys*, on the other hand, infects platelets of dogs. Although not yet definitely shown, this organism is thought to be transmitted to dogs by *R. sanguineus* and can cause a mild febrile disease characterized by cyclic thrombocytopenia in some dogs, which may be exacerbated on co-infection. Neither *A. marginale* nor

A. platys have been shown to be zoonotic. However, *Anaplasma phagocytophilum,* which is transmitted from rodent reservoir hosts by *Ixodes* ticks, is able to infect a wide variety of vertebrates including people. This organism was originally referred to as *Ehrlichia equi* and the human granulocytic ehrlichiosis (HGE) agent in North America and *Ehrlichia phagocytophila* in Europe; various strains of *A. phagocytophilum* have been shown to cause an acute febrile disease in people, horses, dogs, and ruminants (Dumler et al, 2005). The disease produced is referred to as *granulocytic anaplasmosis*, or, in the case of ruminants in Europe, *tick-borne fever*.

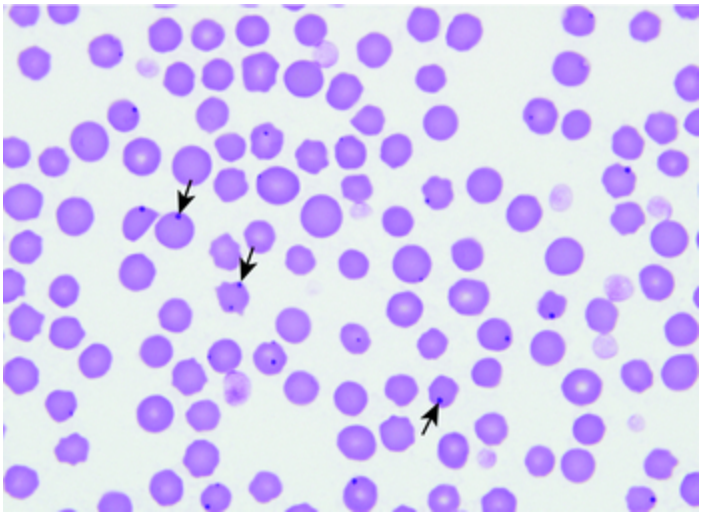

FIGURE 5-1 *Anaplasma maginale (arrows)* in bovine erythrocytes.

Courtesy K. Kocan, Oklahoma State University.

Ehrlichia species

The species important in veterinary medicine and public health include *E. canis*, causative agent of canine monocytic ehrlichiosis (Figure 5-2), *Ehrlichia ewingii*, which primarily infects neutrophils (Figure 5-3), and *Ehrlichia chaffeensis*, the causative agent of human

monocytic ehrlichiosis, which has also been reported from dogs. All three of these organisms are now known to be zoonotic, with people becoming infected after a tick bite (Parola, Davoust, and Raoult, 2005).

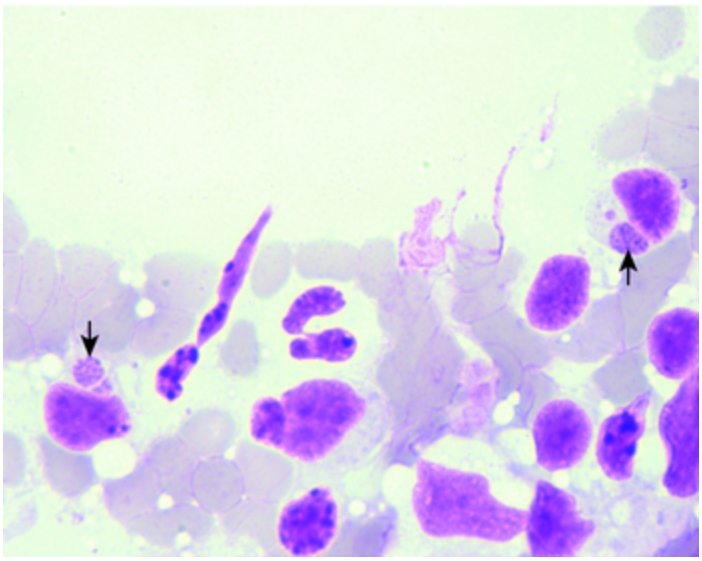

FIGURE 5-2 Morulae *(arrows)* of *Ehrlichia canis* within a circulating monocyte.

Courtesy E. Johnson, Oklahoma State University.

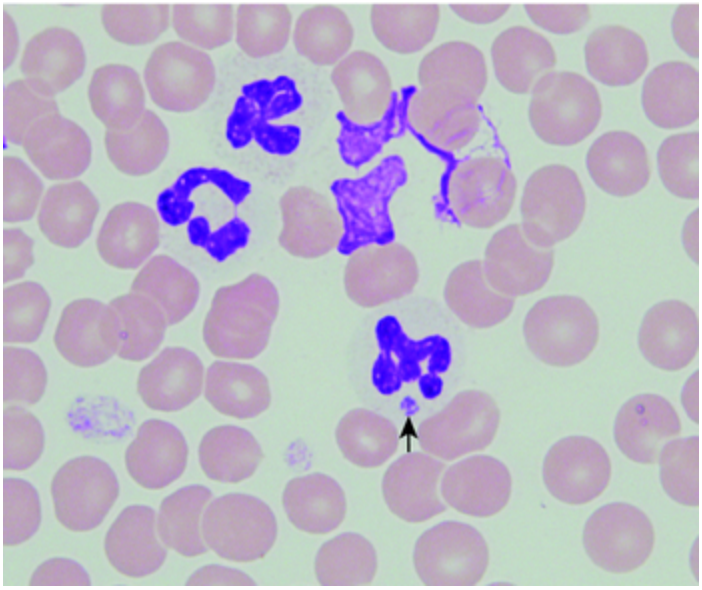

FIGURE 5-3 Morula *(arrow)* of *Ehrlichia ewingii* inside a neutrophil.

E. canis causes a severe febrile disease in dogs characterized by thrombocytopenia, lymphadenomegaly, ocular signs, and bleeding diatheses. Chronic infections may result in emaciation and hypoplastic bone marrow leading to pancytopenia. The organism is maintained in dog populations and is transmitted between dogs by *R. sanguineus; Dermacentor variabilis* has also been shown capable of transmitting *E. canis* (Johnson et al, 1998).

Infection with *E. ewingii* appears to result in less severe disease in dogs; however, in some areas of the southern United States, *E. ewingii* infection is more common in dogs than that caused by *E. canis* (Liddell et al, 2003). Although other ticks may be involved, *E. ewingii* is known to be transmitted by *A. americanum*, and both dogs and deer may be able to serve as a source of infection to vector ticks (Anziani, Ewing, and Barker, 1990; Yabsley et al, 2002).

E. chaffeensis infection in dogs also occurs but appears to only rarely result in overt clinical disease. However, human monocytic ehrlichiosis caused by *E. chaffeensis* is considered the most common tick-borne disease of people in many areas of the southern United States. *E. chaffeensis* is maintained in nature in a cycle involving *A. americanum* as vector tick and white-tailed deer as primary reservoir host (Lockhart et al, 1997).

Heartwater disease

Another ehrlichial agent, *Ehrlichia ruminantium* (formerly *Cowdria ruminantium*), causes heartwater, or cowdriosis, in ruminants in Africa as well as in areas of the Caribbean where the organism and vector ticks have been introduced and established. This organism, which is transmitted by a variety of *Amblyomma* ticks, may also

cause disease in dogs and people (Allsopp and Allsopp, 2001; Allsopp, Louw, and Meyer, 2005). A variety of wild ruminants, including blesbok and wildebeest, serve as reservoir hosts for *E. ruminantium*. On introduction by a feeding tick, the organisms invade and multiply in endothelial cells, resulting in a febrile disease characterized by vasculitis; the common name of the disease refers to the development of pericardial effusion in acute cases. Although an endemic cycle of heartwater is not known to have been established in the continental Americas, occasional introductions occur, and native ticks and wildlife have been shown to be competent vectors and reservoir hosts, respectively (Burridge et al, 2002; Uilenberg, 1982). Recently an *E. ruminantium*–like organism from *A. americanum* collected from the southern United States was reported to cause disease in a goat; this agent has also been implicated in a human infection (Loftis et al, 2006).

Neorickettsia species

Members of the genus *Neorickettsia* are unusual among the rickettsial pathogens in that they are transmitted by trematodes rather than arthropod vectors; accordingly, infection is associated with consumption of fish or other intermediate hosts rather than infestations with ticks or other ectoparasites.

Neorickettsia helminthoeca is vectored by *Nanophyetus salmincola*, a trematode of dogs and other carnivores and causes **salmon poisoning disease.** The rickettsiae invade the tissues of the fluke and are passed along with the offspring through snails to salmonid fish intermediate hosts. When a dog ingests the fish it becomes infected with both the trematodes and the rickettsia. A highly fatal

disease, commonly referred to as *salmon poisoning*, ensues and is characterized by severe gastroenteritis, enlarged lymph nodes, and a very high fever that decreases to hypothermia shortly before death. Affected dogs are anorexic and rapidly lose weight. Although many vertebrates, including humans, may develop infections with *N. salmincola,* salmon poisoning caused by *N. helminthoeca* appears to occur only in dogs and wild canids. Salmon poisoning in dogs is largely limited to areas of the Pacific Northwest where the vector trematode cycles in nature, although canine disease caused by *N. helminthoeca* has been reported from Brazil (Headley et al, 2006).

Neorickettsia risticii is a related rickettsia that causes **Potomac horse fever,** also referred to as **equine monocytic ehrlichiosis,** sporadically in many areas of North America; this disease has also been reported from Europe. Horses acquire the infection on ingestion of caddisflies parasitized with metacercaria of *Acanthatrium oregonense*, a trematode of bats (Pusterla et al, 2003). Infection results in an acute, febrile disease that can be severe; depression, anorexia, dehydration, abortion, diarrhea, and laminitis also occur. The organisms are primarily found in monocytes. Although *N. risticii* has not been reported to infect people, a related organism, *Neorickettsia sennetsu*, is well established as the causative agent of Sennetsu fever in Japan and Malaysia. The life history and maintenance cycle for *N. sennetsu* are unknown (Rikihisa, 2006).

Wolbachia species

Members of the genus *Wolbachia* have been reported as endosymbionts from a variety of helminths and arthropods (Fenn et al, 2006). *Wolbachia* species are found in close association with

several filarid worms, including *Dirofilaria immitis*, the causative agent of heartworm disease (Sironi et al, 1995). There is some evidence that *Wolbachia* species play a role in inflammation during heartworm infections, and removing these rickettsia appears to decrease worm fecundity and survival (Genchi et al, 1998; Kramer et al, 2005). Understanding the role of *Wolbachia* species in filarid worm survival and pathogenesis is an area of ongoing research.

OTHER BACTERIAL PATHOGENS TRANSMITTED BY VECTORS

Several other bacterial pathogens, in addition to rickettsia, are also transmitted by arthropod vectors. Some of these diseases are of considerable consequence and concern to pet and livestock owners. Some of the important genera of bacteria involved include *Borrelia, Bartonella*, *Mycoplasma*, and *Yersinia* (Table 5-3).

TABLE 5-3 Other Bacterial Vector-Borne Diseases of Veterinary Importance

Disease	Etiology	Primary Vector	Reservoir Host
Lyme borreliosis	*Borrelia burgdorferi*; also *Borrelia afzelii* and *Borrelia garinii* in Europe	*Ixodes scapularis*, other *Ixodes* species	Mice, other rodents
Avian spirochetosis	*Borrelia anserina*	*Argas persicus*	*Argas persicus*
Tick-borne relapsing fever	Various *Borrelia* species	*Ornithodorus* species	Rodents
Louse-borne relapsing	*Borrelia recurrentis*	*Pediculus humanus*	People
Bovine borreliosis	*Borrelia theileri*	*Rhipicephalus* species	Cattle
Trench fever	*Bartonella quintana*	*Pediculus humanus*	People
Cat scratch disease	*Bartonella henselae, Bartonella clarridgeiae*	Fleas *(Ctenocephalides felis)*	Cats
Canine bartonellosis	Various *Bartonella* species	Ticks suspected	Unknown
Feline hemoplasmosis	*Mycoplasma haemofelis, Mycoplasma haemominutum*	Fleas suspected	Cats
Canine hemoplasmosis	*Mycoplasma haemocanis*	*Rhipicephalus sanguineus*	Dogs
Tularemia	*Francisella tularensis*	Various ticks, mosquitoes	Rabbits, other mammals
Plague	*Yersinia pestis*	*Xenopsylla cheopis*; other fleas	Rodents
Infectious bovine keratoconjunctivitis	*Moraxella bovis*	*Musca autumnalis*	Cattle

Borrelia species

The best known and most commonly diagnosed arthropod-transmitted bacterial disease in the United States is *Borrelia burgdorferi*, the causative agent of **Lyme borreliosis** or **Lyme disease** in North America. Over 20,000 cases of Lyme borreliosis are reported each year in the United States alone. In Europe, borreliosis in people and dogs may be caused by *B. burgdorferi*, *Borrelia garinii*, or *Borrelia afzelii*. *Borrelia burgdorferi* is maintained in nature in a cycle involving rodent reservoir hosts and *Ixodes* species vectors. The most important vector of *B. burgdorferi* in the eastern United States is *Ixodes scapularis*, whereas *Ixodes pacificus* is responsible for the majority of infections seen on the West Coast. Other *Ixodes* species can transmit *B. burgdorferi* in nature but rarely feed on humans or dogs (Oliver et al, 2003). Deer are important as a host for the adult ticks and thus serve to maintain large tick populations in an area, but deer are not considered a competent reservoir host for *B. burgdorferi* (Telford et al, 1988).

Endemic transmission of Lyme borreliosis in North America appears to be largely limited to areas of the northeastern, upper midwestern, and West Coast states. A laboratory confirmed case of **autochthonous infection** (an infection transmitted locally or indigenously, as opposed to imported) with *B. burgdorferi* in any eastern state south of Maryland or Virginia has not been documented, and Lyme disease is considered rare, if it occurs at all, in the southern United States (Wormser et al, 2006). Infection in dogs parallels that in humans. In published surveys, most dogs that test positive for *B. burgdorferi* in nonendemic areas have a history of travel to an area where disease is endemic (Duncan et al, 2004).

Nonetheless, large numbers of dogs in nonendemic areas will test positive for antibodies to *B. burgdorferi*.

Dogs with Lyme borreliosis most commonly have fever, anorexia, polyarthritis, and lymphadenopathy; although uncommon, protein-losing nephropathy associated with infection may result in edema, weight loss, vomiting, and diarrhea. In people, acute Lyme borreliosis is characterized by headache, fever, muscle and joint pain, and, in approximately 70% of patients, an expanding circular rash (>5 cm diameter), termed *erythema migrans*, that develops at the primary tick bite or as a secondary lesion; erythema migrans is not recognized in dogs. If not treated in the acute phase, people may experience chronic, disseminated disease that can result in arthritis, carditis, or neurologic disease; it is not clear if cardiac and neurologic disease is associated with *B. burgdorferi* infection in dogs (Littman et al, 2006).

Other Diseases Caused by *Borrelia* species

Other diseases caused by *Borrelia* species include avian spirochetosis, relapsing fever, and bovine borreliosis.

Avian spirochetosis due to infection with *Borrelia anserina* causes disease in turkeys, chickens, geese, pheasants, and other birds. Affected birds become febrile and cyanotic. Infection is transmitted to birds via the feces of the soft-tick vectors, *Argas persicus* and related species; infection can also be maintained long term in soft-tick populations through transovarial transmission (Zaher, Soliman, and Diab, 1977).

Tick-borne relapsing fever is caused by a large number of soft-tick–transmitted *Borrelia* species, such as *Borrelia hermsii*, *Borrelia*

turicata, and *B. parkeri*, each of which is transmitted by a corresponding *Ornithodoros* soft tick (Barbour and Hayes, 1986). Tick-borne relapsing fever borreliosis is present in Asia, Europe, Africa, and the Americas; in North America, disease is most commonly seen in people in the western United States (Dworkin, Schwan, and Anderson, 2002).

Louse-borne relapsing fever is caused by *Borrelia recurrentis* and is transmitted by the human body louse, *Pediculus humanus*. Infection with *B. recurrentis* occurs only in people, with epidemics developing in times of famine, war, or mass migration; animals are not involved as reservoir hosts (Raoult and Roux, 1999).

Bovine borreliosis caused by *Borrelia theileri* induces a relatively mild disease in cattle, sheep, and horses; infection is transmitted by *Rhipicephalus* ticks, including *Boophilus* subspecies. Also referred to as *tick spirochetosis,* bovine borreliosis caused by *B. theileri* has been reported from Africa, Australia, and central and southern North America (Smith et al, 1985).

Other related *Borrelia* species include *Borrelia miyamotoi* and *Borrelia lonestari* (Figure 5-4), both of which are also hard-tick–transmitted spirochetes that infect both ticks and mammals (Fukunaga et al, 1995; Moyer et al, 2006).

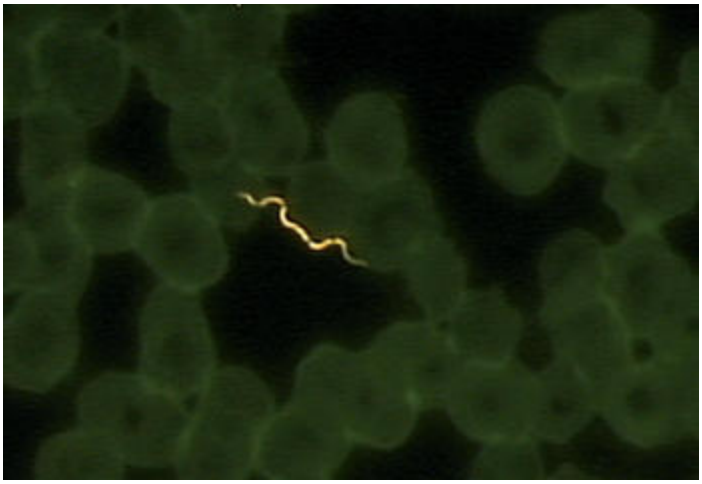

FIGURE 5-4 Relapsing-fever–like *Borrelia* species *(Borrelia lonestari)* on a blood smear from a white-tailed deer.

Bartonella species

Several vector-borne *Bartonella* species also infect and cause disease in people, dogs, and cats. **Trench fever**, a moderate to severe febrile disease of people characterized by marked splenic enlargement, is caused by *Bartonella quintana* and is transmitted to people via infected body lice, *P. humanus*. Trench fever, so named because of the widespread illness recognized in soldiers during the First World War, is not a zoonotic disease, and people rather than animals serve as reservoir hosts (Maurin and Raoult, 1996). In contrast, **cat scratch disease** caused by *Bartonella henselae* and *Bartonella clarridgeiae* is directly zoonotic, with people most often infected when bitten or scratched by a bacteremic cat that harbors infectious *B. henselae* or *B. clarridgeiae* on teeth or claws. Infection of immunocompetent people usually results in a self-limiting, mild febrile disease characterized by regional lymphadenopathy. The agents of cat scratch disease are not known to be transmitted to people by arthropod vectors; however, *B. henselae* can be

transmitted from infected to naive cats, particularly kittens, through fleas as well as through direct contact, and controlling flea infestation is considered important to limit bacteremia in cats (Foil et al, 1998; Foley et al, 1998). In addition to the characteristic febrile diseases caused by bartonellosis in immunocompetent people, infection with both *B. quintana* and *B. henselae* can induce potentially fatal bacillary angiomatosis in immunocompromised patients (Koehler et al, 1997).

B. quintana and *B. henselae*, along with other *Bartonella* species such as *Bartonella vinsonii* subsp. *berkhoffii* and *Bartonella elizabethae,* have also become increasingly recognized as canine pathogens in recent years. These organisms have been associated with endocarditis, myocarditis, and granulomatous lymphadenitis in dogs (Kelly et al, 2006; Morales et al, 2007). Although the arthropod(s) responsible for transmitting these *Bartonella* infections to dogs, if any, have not yet been confirmed, ticks are strongly suspected to play a role, and these agents are likely to increase in importance as canine vector-borne pathogens in the future. Human infection and associated disease has been reported with some of the canine-associated *Bartonella* species (e.g., *B. vinsonii* subsp. *berkhoffii*); transmission routes to people are not clear, but direct transmission from an infected dog to a person via a bite or scratch is suspected to be a potential route for exposure (Chomel et al, 2006).

Mycoplasma species

Other important vector-associated bacterial infections include the hemoplasma species of *Mycoplasma* (formerly *Haemobartonella*), which appear as small pleomorphic bacteria attached to the surface

of erythrocytes on stained blood smears. *Mycoplasma haemofelis* is widely thought to be transmitted to cats by fleas, although this route of infection has yet to be experimentally confirmed (Woods, Wisnewski, and Lappin, 2006). *Mycoplasma haemocanis* is known to be transmitted to dogs by ticks *(R. sanguineus)*, and infections with *M. haemocanis* are maintained in tick populations both transstadially and transovarially (Seneviratna et al, 1973). In cats, infections with *M. haemofelis* and the related *Mycoplasma haemominutum* may be clinically inapparent. However, *M. haemofelis* can cause mild to severe clinically apparent anemia, splenomegaly, enlarged lymph nodes, icterus, and respiratory distress. Disease is more common in cats immunocompromised by concurrent immunosuppressive viral infections such as with feline leukemia virus (FeLV) but can also be seen in cats without concurrent FeLV infection (Harrus et al, 2002). Disease due to infection with *M. haemocanis* is considered rare in spleen-intact dogs.

Tularemia

Arthropod vectors can also be important in the transmission of disease agents considered to have a potential role in bioterrorism, including the causative agents of tularemia and plague. In North America, infections with *Francisella tularensis*, the causative agent of tularemia, are acquired directly from contact with infected carcasses, particularly rabbits. However, transmission by ticks and transmission by biting flies are also considered important routes of infection, and a number of tick species in the genera *Dermacentor*, *Amblyomma*, *Ixodes*, and *Haemaphysalis* may be responsible for transmitting infection between animals in nature. Mosquitoes are

also involved in transmission of some biovars of *F. tularensis* (Petersen and Schriefer, 2005). Clinical disease in animals is most commonly seen in cats, presumably after ingestion of infected prey (Woods et al, 1998). Transmission of *F. tularensis* to people directly via bites or scratches of infected cats, although possible, is considered rare.

Plague

Plague caused by *Yersinia pestis* is transmitted between animals and to people via fleas; infection with *Y. pestis* is rare in North America, but a natural focus of transmission is maintained in a cycle involving fleas and prairie dogs in the western United States (Anderson and Williams, 1997). Animals infected with *Y. pestis* may develop fever and enlarged lymph nodes; cats appear particularly susceptible to the disease (Gage et al, 2000). Infected cats can serve as a source of infection directly through bites and scratches or through aerosolization of bacteria; cats also may support populations of fleas, which are then able to transmit the infection to people. Both flea control and prevention of ingestion of prey species are critical to preventing infections with *Y. pestis* in cats and dogs.

Mechanical Transmission of Bacteria by Arthropods

In addition to their role in biologic maintenance and transmission of disease agents, arthropods can also serve as important mechanical transmitters of bacteria. For example, transmission of *Moraxella bovis*, the causative agent of infectious bovine keratoconjunctivitis (pink eye) in cattle, is facilitated by the presence of the face fly, *Musca autumnalis*, which efficiently moves the organism between animals housed together on pasture (Gerhardt et al, 1982). Disease

is more commonly seen in pastured cattle in summer and early fall, when face fly populations are well established and exposure to ultraviolet light, another risk factor for infection, is at its peak (Lepper and Barton, 1987). Vaccines and effective antibiotic treatments are available, but face fly control remains a critical component of preventing infection with *M. bovis* in cattle.

VECTOR-BORNE PROTOZOA AND HELMINTHS

In addition to viral and bacterial pathogens, a number of protozoal and helminth parasites are transmitted via vectors (Tables 5-4 and 5-5). Biting flies transmit several important protozoan and metazoan parasites, including the *Leishmania* species (Figure 5-5) that cause visceral and cutaneous leishmaniasis, *Trypanosoma cruzi* and other trypanosomiasis-inducing agents, and *Dirofilaria immitis,* the causative agent of heartworm. Similarly, ticks are centrally important in the transmission of protozoal infections that cause serious, at times fatal, disease in the host including those caused by *Babesia* species (Figure 5-6), *Cytauxzoon felis* (Figure 5-7), *Theileria parva*, and *Hepatozoon* species (Figure 5-8). Fleas or chewing lice are required to transmit *Dipylidium caninum* to dogs and cats. Although infection with all of these parasites may be reduced by efforts to control vector populations, vector control alone is not considered an effective means of preventing infection or disease in animals. These pathogens and the diseases they cause are described in Chapters 3 and 4.

TABLE 5-4 Representative Vector-Borne Protozoal Diseases of Veterinary Importance

Disease	Cause	Primary Vector	Reservoir Host
Trypanosomiasis (nagana; sleeping sickness; surra; mal de Caderas)	Various *Trypanosoma* species	Tsetse flies	Various mammals, including humans
Chagas disease	*Trypanosoma cruzi*	Triatomine bugs	Rodents; other small and medium-sized mammals; domestic dogs
Leishmaniasis (visceral leishmaniasis; cutaneous leishmaniasis; mucocutaneous leishmaniasis)	*Leishmania* species	Sand flies	Rodents; other small mammals; domestic dogs
Histomoniasis	*Histomonas meleagridis*	*Heterakis gallinarum*	Various birds, especially inapparent carriers such as pheasants, chickens
Hepatozoonosis	*Hepatozoon canis*	*Rhipicephalus sanguineus*	Domestic dogs
	Hepatozoon americanum	*Amblyomma maculatum*	Domestic dogs, other wildlife?
Babesiosis (Texas cattle fever; bovine babesiosis; equine piroplasmosis; canine babesiosis)	Various *Babesia* species	*Rhipicephalus, Dermacentor, Ixodes*	Various mammals for each of the different species
East Coast fever	*Theileria parva*	*Rhipicephalus* species	African buffalo
Cytauxzoonosis	*Cytauxzoon felis*	*Dermacentor variabilis*	Bobcats

TABLE 5-5 Representative Vector-Borne Helminth Diseases of Veterinary Importance

Disease	Cause	Primary Vector	Reservoir Host
Dipylidiasis	*Dipylidium caninum*	*Ctenocephalides felis*; also chewing lice	Dogs, cats
Eyeworm	*Thelazia* species	Muscid flies	Various mammals
Habronemiasis; swamp cancer; summer sores	*Habronema* species, *Draschia* species	Muscid flies	Horses
Heartworm	*Dirofilaria immitis*	Mosquitoes	Dogs, wild canids
Onchocerciasis	*Onchocerca* species.	*Culicoides* species; *Simulium* species	Horses, cattle
Setariasis	*Setaria* species	Mosquitoes	Cattle, horses
Parafiliariasis; summer bleeding	*Parafilaria multipapillosa*	*Haematobia* species	Horses
	Parafilaria bovicola	Muscid flies	Cattle
Elaeophorosis; sorehead	*Elaeophora schneideri*	Tabanid flies	Mule deer
Bovine stephanofilariasis; hump sore	*Stephanofilaria stilesi, Stephanofilaria assamensis*	*Haematobia irritans, Musca conducens*	Cattle

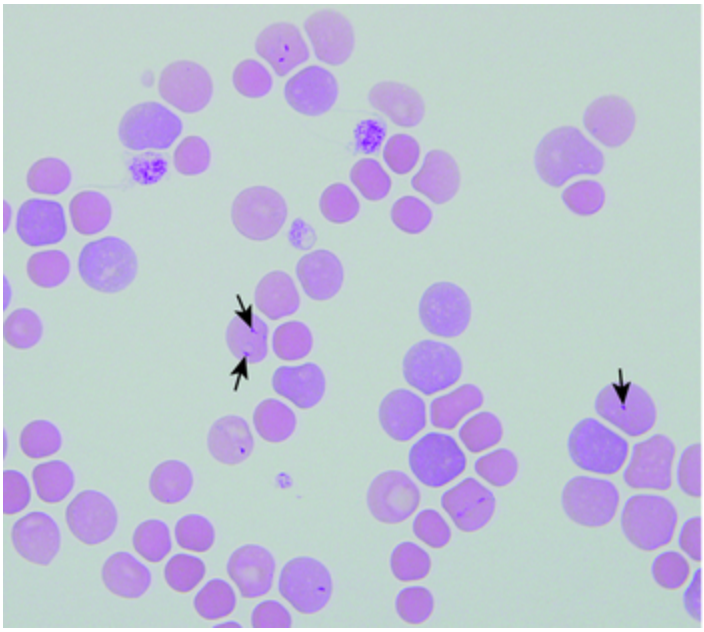

FIGURE 5-5 *Babesia gibsoni (arrows)* within canine erythrocytes.

Courtesy R. Allison, Oklahoma State University.

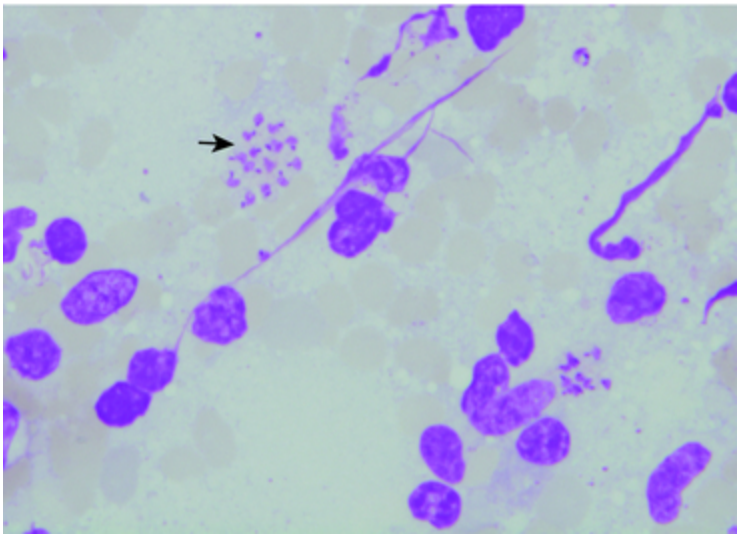

FIGURE 5-6 *Leishmania* amastigotes *(arrow)* within macrophages.

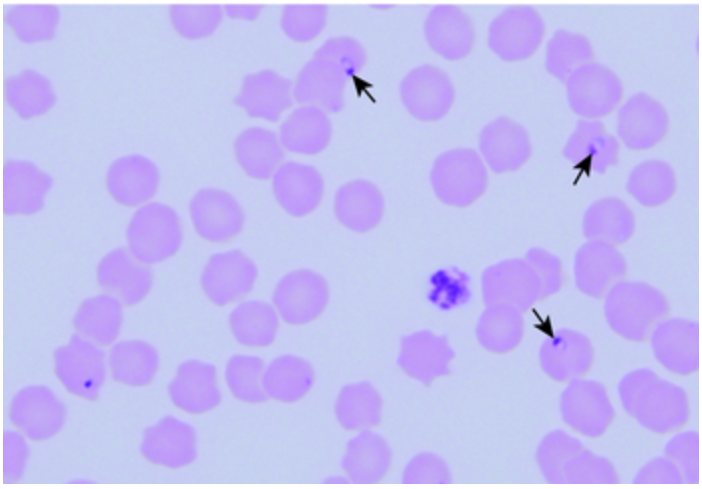

FIGURE 5-7 *Cytauxzoon felis* merozoites *(arrows)* within feline erythrocytes.

Courtesy M. Reichard, Oklahoma State University.

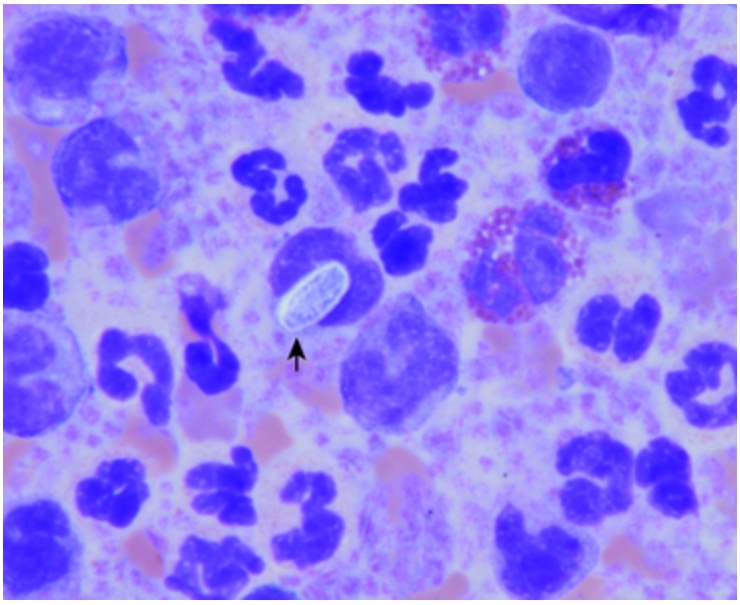

FIGURE 5-8 *Hepatozoon americanum* gamont *(arrow)* within a canine leukocyte.

Courtesy E. Johnson, Oklahoma State University.

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CHAPTER 6

Antiparasitic Drugs

Randy C. Lynn

A parasiticide is a poison that is more toxic to parasites than to their hosts. The degree of discrimination is sometimes small, sometimes considerable, but never complete, so that application of parasiticides always entails some hazard to the host. As a matter of fact, it is sometimes easier to explain the deleterious effects that parasiticides frequently exert on the host than to explain how they kill parasites.

DEVELOPMENT

Stages in the development of a typical insecticide or anthelmintic proceed approximately as follows. First, many thousands of compounds must be screened before one is found that shows promise. The screening procedure, in the case of an anthelmintic, could require the demonstration of in vivo activity against some convenient parasite (e.g., *Nematospiroides dubius, Nippostrongylus brasiliensis, Syphacia obvelata*, or *Hymenolepis nana* of laboratory rodents; *Ascaridia galli* or *Heterakis gallinarum* of chickens). In vitro assays have been developed that allow rapid screening of large numbers of potential agents (Londershausen, 1996). A preliminary estimate of mammalian toxicity is also obtained from experiments on rats and mice.

The activity screening tests and preliminary toxicity studies greatly reduce the list of suitable candidates but are of little value in predicting the effect of a particular drug either on a particular species of domestic animal or on its customary assemblage of parasites. Responses of various species and strains of parasites and their hosts to antiparasitic agents are sometimes quite selective. Thus ascarids are very sensitive to piperazines, whereas hookworms are quite refractory. Most breeds of cattle and dogs tolerate judicious applications of organophosphate insecticides, whereas Brahman cattle, greyhounds, and whippet dogs are likely to be fatally intoxicated by such treatment. The necessary information can be obtained only through experiments on domestic animals and the parasites for which the anthelmintic is intended.

When a manufacturing firm files a New Animal Drug Application with the Food and Drug Administration (FDA), it must submit complete information on its chemistry, process of manufacture, and quantitative assay methods. Results of all experiments conducted to establish the safety and efficacy of the new product and all relevant published reports must also be submitted. Drugs intended for food animals must be accompanied by data on tissue residues and the route and rate of excretion of the parent compound and its major metabolites. The amount and the structures of the longest-lasting tissue residue also must be determined, and if the substance has similarities to known carcinogenic chemicals, a 2-year toxicity experiment is then required in rats and mice.

The Environmental Protection Agency (EPA) requires an environmental impact analysis of the new compound. Phytotoxicity and the effects on fish and other lower animals also must be

vigorously studied. A thorough analysis must be conducted to establish any potential effects on workers who apply the product. Worker safety must also be addressed, so that the appropriate safety measures (e.g., gloves, safety glasses) can be written into the instructions.

Before a new anthelmintic or any new parasiticide can be approved, well-controlled experiments must be carried out involving sacrifice of the test animals and determination of residual worm burdens after treatment. Confirmation experiments must be conducted by several independent laboratories as a series of field tests in different geographic regions of the United States.

The package label is required by law to bear all the necessary cautions and to notify the user about all adverse reactions that have been discovered. Six months after a product enters the market and at regular intervals thereafter, the manufacturer is required to report to the FDA any adverse reactions that have come to light and to add appropriate notices to the label or withdraw the product from the marketplace. As a result, the label (or package insert) has become one of the most objective and current sources of information on parasiticides.

In the early phases of new product development, the molecule is usually identified by only a code number, S-147 for example. This is to keep the hundreds of thousands of potential products separate and to avoid the trouble of naming each one. Once the product clears the early hurdles of activity and safety, it is given a nonproprietary (generic) name. The nonproprietary name is used in the scientific literature worldwide to identify the molecule. Thus S-147 now becomes milbemycin oxime. As product development

proceeds, the marketing staff develops a trade name. This name will be trademarked and applied to a specific formulation. At this point milbemycin oxime becomes Interceptor.

One molecule may have several different trade names that correspond to different formulations or to different countries. For example, milbemycin oxime is marketed and sold as Interceptor for internal parasite control, sold as MilbeMite for treatment of ear mites, and sold in combination with lufenuron as Sentinel. These trade names will be used in the advertising and promotion of the product. In this text the nonproprietary names are used to identify the products, and some of the trade names are mentioned.

Resistance to Parasiticides

Regular application of antiparasitic drugs to populations of parasites inevitably results in the development of resistant parasite populations through selection of resistant phenotypes. Eventually the once-effective drug ceases to work and must be replaced by another.

Unfortunately, the replacement also may fail against the resistant strain, especially if it is a chemical congener of the original. This has happened often enough to serve us warning. We need to develop better ways of controlling parasites than to lash away at them crudely and blindly with one chemical after another.

The literature on antiparasitic drugs is enormous. In the interests of both economy and readability, we have tried to list the few references that will guide the veterinarian who needs more specific information about these agents.

It is important to note here whom one calls when potential adverse reactions or problems arise. The American Society for the Prevention of Cruelty to Animals (ASPCA) National Animal Poison Control Center is exquisitely staffed and has the largest database available for consultation. They charge a small consultation fee for each case and can be reached at 800-548-2423. The manufacturer of the product also can be consulted and is required by law to notify federal authorities concerning all adverse reactions. The manufacturer may also be prepared to provide assistance in investigating and treating any adverse event.

INSECTICIDES

The United States Federal Environmental Pesticide Control Act (FEPCA) of 1972 is administered by the EPA, which controls the distribution, sale, and use of pesticides within each state and between states. This act even specifies what penalties may be imposed for the misuse of pesticides. State governments may establish even stricter standards than those set by FEPCA.

Users of pesticides bear a legal responsibility in the United States for knowing which chemicals they are currently permitted to use and for using these chemicals only in strict accordance with the indications and directions on the package labels. Current information on pesticides should be sought from the pesticide coordinator, extension entomologist with livestock responsibility, or extension veterinarian appointed by the state agricultural extension services and land grant colleges.

The diversity of structure, biologic activity, and toxicity among insecticides is exceeded only by the number and variety of insects,

mites, and ticks that need to be controlled. The label of every insecticide container must be read carefully and understood before the contents are applied to the animal. The label is the most up-to-date and authoritative source of information available (Bayley, 2007). In addition, there are several good review texts that discuss the chemistry, mode of action, and toxicity of insecticides (Coats, 1982; Fest and Schmidt, 1982; Hassall, 1982; Hayes and Laws, 1991; Plapp, 1991; Ware, 1983; Ware, 1986). The Insecticide Resistance Action Committee (IRAC) recently organized all known insecticides by their mode of action (IRAC, 2007).

The treatment of insecticidal overdose or toxicity is a complex subject that lies outside the scope of this chapter. A few general comments, however, are included about treatment of affected patients. For more specific up-to-date information, the veterinarian should consult the ASPCA National Animal Poison Control Center at 800-548-2423. They maintain a 24-hour service staffed with veterinary toxicologists to consult about animal poisoning of any type.

Botanic Agents

The botanic insecticides are derived from plant materials. Ground plant parts (e.g., flowers, leaves, stems, roots) or their extracts may be combined in a variety of formulations. Essential oils from plants are often used as insect attractants or repellents. Botanic insecticides, particularly pyrethrins, have excellent toxic effects against a variety of crop and animal insect pests, very short persistence in the environment, and relatively low toxicity to

animals. Pyrethroids are synthetic pyrethrum-like compounds with superior potency and knockdown activity.

Rotenone

Rotenone is an insecticidal product obtained from the roots of several plants. Rotenone was first used by natives in South America to paralyze fish, causing them to surface so that they could easily be caught. In the 1800s it was first used to control leaf-eating caterpillars. Rotenone is the insecticidal component of derris root, cube root, and several other leguminous shrubs. It acts as an inhibitor of mitochondrial respiratory enzymes. Rotenone is insoluble in water but very soluble in alcohols, acetone, carbon tetrachloride, chloroform, and many other organic solvents. It decomposes on exposure to light and air. The oral median lethal dose (LD_{50}) of rotenone for rats is 133 mg/kg and for white mice, 350 mg/kg, but it is toxic to fish. Rotenone, alone or synergized, is the main insecticidal ingredient in Goodwinol Ointment and several ear mite solutions. It may be applied to cats and dogs as an ointment, solution, or shampoo for the control of a variety of arthropod parasites including localized demodicosis in dogs and ear mites, *Otodectes cynotis*, in cats, dogs, and rabbits.

Warning: Kittens younger than 4 weeks old and suckling puppies should not be treated with rotenone products. Rotenone is toxic to swine, fish, and snakes and should not be applied to these animals. Cats and dogs may vomit after licking rotenone from their coats. It may be carcinogenic in rats.

Pyrethrins

The flower head of the pyrethrum plant *Chrysanthemum cinerariaefolium* contains six closely related insecticidal substances (pyrethrin I and II, cinerin I and II, jasmolin I and II) that are known as pyrethrins. Pyrethrins are rapidly degradable in the presence of moisture, air, and light and are also rapidly biodegradable. They are very soluble in kerosene but insoluble in water. The oral LD_{50} of pyrethrin for rats is 200 to 1500 mg/kg, depending on the purity of the product, and the dermal LD_{50} for rats is greater than 1800 mg/kg. Pyrethrins may produce some inhalation problems in rats, but regular aerosol applications should not produce any adverse reactions in domestic animals. Because they are toxic to fish, pyrethrin aerosols should not be used near fish tanks, but regular use has little impact on game fish and other wildlife.

Pyrethrins rapidly knock down, paralyze, and kill arthropods by disrupting sodium and potassium ion transport in nerve membranes, thus poisoning neurotransmission along the axon and at the synapse (Kahn, 2005). Residues of pyrethrins are sometimes repellent. Pyrethrins are usually combined with a synergist such as piperonyl butoxide or *N*-octyl bicycloheptene dicarboximide. Synergists increase the insecticidal activity 10 to 20 times (Plapp, 1991). Synergists poison the mixed function oxidases, which detoxify insecticides in the insect (Kahn, 2005).

Because of the safety and rapid knockdown effect of natural pyrethrins, they enjoy widespread use in the home and in agriculture. Natural pyrethrins have more uses approved by the EPA than any other insecticide. Many commercially available insecticides formulated as aerosols, fogs, shampoos, and mists contain a mixture

of pyrethrins and a synergist (e.g., Aurimite, Mita-Clear, Mycodex Pet Shampoo, Synerkyl).

Pyrethrin aerosols, fogs, sprays, and powders control face flies, horseflies, houseflies, stable flies, mosquitoes, fleas, lice, and ticks. Pyrethrins are registered for application to beef and lactating dairy cattle and in dairy barns and milk houses. They are not persistent insecticides, so regular and repeated application is necessary. Resistance to pyrethrins has been reported in houseflies and in some cattle ticks.

Warning: Pyrethrins should not be applied to kittens younger than 4 weeks old or to suckling puppies. In case of ingestion, the most toxic component is usually the solvent. Therefore vomiting is contraindicated. Administer activated charcoal and supportive therapy. In case of dermal exposure, the animal should be bathed with a good detergent.

Pyrethroids

Pyrethroids are synthetic pyrethrin-like substances. These new chemicals are more potent and possess a greater knockdown effect than do the plant pyrethrins. Pyrethroids are biodegradable but sufficiently stable when exposed to air and light so that weekly or biweekly applications provide excellent control of insects.

Pyrethroids have a greater insecticidal effect when the temperature is lowered. In chemist's language, they have a negative temperature coefficient. Pyrethroids initially stimulate and then depress nerve cell function and eventually cause paralysis. The fast knockdown of flying insects is the result of rapid muscular paralysis.

Pyrethroids have low mammalian toxicity, but some pyrethroids provoke sensation of the skin or mucosa. They are toxic to fish.

Research into pyrethroid chemistry has resulted in many new products. For one to make some sense of this profusion of new products, it is best to divide them by generation. The first generation was represented by D-trans-allethrin, which was a synthetic duplicate of cinerin I, a component of natural pyrethrin. The second-generation pyrethroids include tetramethrin, resmethrin, and phenothrin. They are more potent than pyrethrin in knockdown potency but decompose rapidly on exposure to air and sunlight. The third-generation pyrethroids are appreciably more potent than earlier generations and are photostable for several days in full sun. They are represented by fenvalerate and permethrin. The fourth-generation pyrethroids are represented by cypermethrin and fluvalinate.

The fifth-generation pyrethroids are the newest available and are represented by beta-cyfluthrin, an isomer subset of cyfluthrin. They are more photostable and more potent than the previous generation. The disadvantage of increased potency, and especially increased persistence in the environment, is the development of insect resistance. In fact, insect resistance to synthetic pyrethroids has been documented (Plapp, 1991). Synthetic pyrethroid products commonly used on domestic animals are listed in the following discussion according to generation.

First-Generation Pyrethroids

The first-generation synthetic pyrethroid (D-trans-allethrin) is a synthetic duplicate of the natural pyrethrin, cinerin I. No more

potent or stable than natural pyrethrin, it is rapidly degraded by light and air. D-Trans-allethrin, the first-generation pyrethroid, is a mixture of several optical isomers. It has low mammalian toxicity. The LD_{50} of allethrin for rats is greater than 920 mg/kg. D-Trans-allethrin is formulated into a flea shampoo (Hartz Advanced Care 2 in 1) for removing fleas from dogs and cats.

Second-Generation Pyrethroids

The second-generation synthetic pyrethroids were the first step forward from the natural pyrethrins. They increased the knockdown potency 10 to 50 times more than the natural products but were not much more stable in sunlight than the natural pyrethrins.

Phenothrin

Phenothrin is a second-generation pyrethroid that recently appeared on the scene for flea control in pets. The acute oral LD_{50} of phenothrin in rats is 5000 mg/kg, and the LD_{50} for dermal exposure in rats is greater than 10,000 mg/kg. Phenothrin is formulated into an array of over-the-counter spot-on products for control of fleas (Hartz Advanced Care 3 in 1) for use on dogs and cats. The product is applied as a spot-on every 30 days to treat and control fleas and ticks. It is also formulated in combination with an insect growth regulator (IGR), methoprene, to more effectively break the flea life cycle (Hartz Advanced Care 4 in 1) in dogs and cats. The label states that the product is waterproof after application.

Resmethrin

Resmethrin, a second-generation synthetic pyrethroid, is not synergized to any appreciable extent by pyrethrum synergists. Of

great significance is resmethrin's low mammalian toxicity. Its acute oral LD_{50} for rats is 4240 mg/kg. Resmethrin shows excellent knockdown effect and is available for use in a fly repellant, and for premises foggers (Formula F-500) for the control of flies, mosquitoes, gnats, and other insects.

Tetramethrin

Tetramethrin is a second-generation synthetic pyrethroid originally developed in Japan. Its acute oral LD_{50} in rats is greater than 2500 mg/kg. Tetramethrin is available in a total release fogger in combination with etofenprox (a pyrethroid ether insecticide) to kill flying and crawling insects in the outside environment (Vet-Kem Siphotrol Outdoor Fogger). As with all foggers, be certain to follow the directions including covering food, avoiding contact with pilot lights and open flames, leaving the area, and airing out the premises thoroughly after treatment. Tetramethrin is also available as an inverted aerosol for control of fleas, ticks, and carpet beetles (Virbac KnockOut).

Third-Generation Pyrethroids

The third-generation synthetic pyrethroids became available in the 1970s. Photostability is the hallmark of this class. For the first time, increased potency and photostability were fixed in the same molecule.

Fenvalerate

Fenvalerate, the first of the third-generation pyrethroids to be commercially successful, is very photostable and potent. Its acute oral LD_{50} for rats is 451 mg/kg, and its acute dermal LD_{50} in rabbits

is 2500 mg/kg. Fenvalerate is highly toxic to fish. It is formulated for long residual insecticide activity. Ectrin cattle ear tags are used in dairy and beef cattle for control of horn flies, face flies, Gulf Coast ticks, and spinose ear ticks and as an aid in the control of lice, stable flies, and houseflies.

Permethrin

Permethrin, a third-generation pyrethroid, is an extremely active insecticide with a rapid knockdown effect against a variety of insects. Its acute oral LD_{50} for rats is greater than 4000 mg/kg. Like fenvalerate, permethrin is very toxic to fish. It is photostable, with effective residues lasting 4 to 7 days on crop foliage. Permethrin is registered in a wide variety of formulations as a treatment for residual animal quarters (dairy barns, feedlots, stables, poultry houses, swine, and other animal housing) to control houseflies, stable flies, and other manure-breeding flies.

Permethrin is the most ubiquitous of the pyrethroids approved for use on or around animals. It is available in on-animal sprays, dips, shampoo, ear tags, pour-on formulas, and dust, for use on dogs, cats, horses, cattle, and swine. It is also available in concentrated form for direct application to dogs (Proticall). Permethrin is also available in combination with imidacloprid and methoprene for flea control (see discussion of combination products, later). It then acts systemically to control adult fleas. Permethrin is widely used as a premises spray (Defend, Ectrin, Expar) for use around livestock and pets to control fleas, ticks, and flies.

Fourth-Generation Pyrethroids

The fourth-generation pyrethroids are more potent and longer lasting than earlier generations. The class is represented by cyfluthrin, cypermethrin, deltamethrin, and lambdacyalothrin in an increasing variety of formulations.

Cyfluthrin

Cyfluthrin is a fourth-generation pyrethroid with an acute oral LD_{50} for rats of 500 mg/kg. The product is formulated into a pour-on (CyLence) for beef and dairy cattle (including lactating cows) to control horn flies, face flies, biting lice, and sucking lice. It is approved in a 1% dust and wettable powder (Tempo) for use in and around livestock housing and for food-handling locations for a long list of flying and crawling insects.

Cypermethrin

Cypermethrin is a potent fourth-generation synthetic pyrethroid. Its acute oral LD_{50} for rats is 4150 mg/kg. It is approved for use in fly lotion (Repel-X), and fly spray (Endure) for use on horses.

Deltamethrin

Deltamethrin is a fourth-generation pyrethroid. The acute oral LD_{50} in rats is 31 to 139 mg/kg for deltamethrin, and the acute dermal LD_{50} in rabbits is greater than 2000 mg/kg. It is formulated into a premise spray (Annihilator), wettable powder, for control of pest species in pet housing and residential areas. It is also available as a flea collar for dogs (Novation).

Lambdacyalothrin

Lambdacyalothrin is a fourth-generation synthetic pyrethroid. Its acute oral LD_{50} for male rats is only 79 mg/kg. The product is available as a pour-on (Saber) for use on beef cattle and calves. It is labeled for use against lice and horn flies. It is formulated into a premises spray (Grenade) to control insects in and around livestock housing structures. Lambdacyalothrin is also formulated in combination with the organophosphate pirimiphos to form ear tags (Double Barrel VP) labeled for up to 5 months' control of horn flies and up to 4 months' control of face flies. The ear tags are approved for use on beef cattle and nonlactating dairy cattle and calves.

Fifth-Generation Pyrethroids

The fifth-generation pyrethroids are at the cutting edge of pyrethroid development. They are the most potent and the longest lasting. Currently they are available only in insecticidal ear tags.

Beta-cyfluthrin

Beta-cyfluthrin is one of the isomers found in cyfluthrin. It is designated by the manufacturer as a fifth-generation pyrethroid. The insecticide is formulated into ear tags (CyLence Ultra) approved for use on beef cattle to control face flies, horn flies, Gulf Coast ticks, and spinose ear ticks. The ear tags remain effective for up to 5 months. Like other insecticide ear tags, continuous use of one agent can lead to insect resistance. To help delay resistance, one should rotate the class of insecticide from season to season. The cyfluthrin ear tags should be removed at the end of fly season and before slaughter.

Carbamates and Organophosphates

Carbamates and organophosphates are commonly used insecticides. One should be aware of their toxic effects on animals (Hayes and Laws, 1991). These insecticides exert their toxic action by inhibiting acetylcholinesterase (AChE), an important enzyme of the nervous system. The carbamate and organophosphate insecticides bind and inactivate AChE, with the result that acetylcholine accumulates at the neural synapse. They thus function as synaptic poisons (Ware, 1983).

The accumulation of acetylcholine produces signs of acute poisoning, which are principally the result of acetylcholine's muscarinic effects at autonomic effector organs (miosis, lacrimation, salivation, vomiting, diarrhea, frequent urination, dyspnea, bradycardia, and hypotension) and its nicotinic effects at the neuromuscular junction (rapid involuntary muscle twitching and scattered fasciculations followed by severe weakness and paralysis) (Brunton, 2006). Death is usually due to respiratory failure.

Many organophosphorus insecticides show a chronic neurotoxicity with degeneration of long axons in the spinal cord and peripheral nerves (e.g., sciatic nerve). Atropine administered parenterally is the preferred antidote for carbamate and organophosphate poisoning. Organophosphate poisoning also may be reversed with pralidoxime (2-PAM), but this drug is contraindicated in carbamate poisoning.

The principal action of pralidoxime chloride is to reactivate AChE, which in turn destroys the accumulated acetylcholine so that the synapses and neuromuscular junctions can regain normal function. Pralidoxime chloride is relatively short acting, so repeated administration is usually required (Buck, 1991). Artificial

respiration may be required in severe cases of carbamate and organophosphate poisoning.

Carbamates, and particularly organophosphates, should not be used in conjunction with other cholinesterase inhibitors or other insecticides because the effect of these chemicals on cholinesterase reserves is cumulative. Organophosphates should not be applied to sighthounds (e.g., greyhounds and whippet dogs) or to certain breeds of cattle (e.g., Chianina, Charolais, Gelbvieh, Simmental, Brahman) because these breeds have idiosyncratic reactions to this class of compound. Application of organophosphates to cattle infested with *Hypoderma* larvae may lead to host-parasite reaction.

Carbamates

Carbamates inactivate AChE in a two-step process: first a reversible carbamate-AChE complex is formed, then the AChE is carbamylated and inactive. Later the carbamate is cleaved away, which frees the original AChE, but the carbamate is unable to bind another AChE molecule (Hayes and Laws, 1991). The antidote of choice is atropine; 2-PAM is contraindicated for carbamate toxicity.

Carbaryl

Carbaryl, also known by the trade name Sevin, is the most commonly used carbamate. Introduced in 1956, it was the first commercially successful carbamate. The mammalian toxicity of carbaryl is low; its oral LD_{50} for female rats is 500 mg/kg. Carbaryl is highly toxic to honeybees. The product is most commonly used to control fleas and ticks on small animals.

Dogs and cats

Carbaryl is used alone or in combination with synergists. Adult dogs and cats infested with fleas, lice, or ticks may be washed with products containing 0.5% to 1% carbaryl (Mycodex with carbaryl). A free-flowing dust formulation containing 2% to 5% carbaryl (Adams flea and tick dust) also may be used. The dust is sprinkled over the animal then thoroughly rubbed into the coat. Unfortunately, fleas and ticks in many areas have developed resistance to carbaryl.

WARNING: Do not use other cholinesterase-inhibiting chemicals with products containing carbaryl. Puppies and kittens younger than 4 weeks should not be treated with carbaryl preparations. Read the label for other specific product restrictions. If animals show signs of poisoning, administer atropine. Use of 2-PAM is contraindicated in carbaryl poisoning.

Methomyl

Methomyl, introduced in 1966, is more potent than carbaryl and very toxic to mammals. Its oral LD_{50} for rats is 17 mg/kg. Methomyl has demonstrated a broad spectrum of activity against a wide range of insects infesting vegetables and field crops. It has a very rapid action. Flies are killed when they come into contact with or ingest methomyl. Methomyl is the insecticidal ingredient in Blue Streak Fly Bait.

WARNING: Methomyl is toxic to fish and honeybees. It should be kept away from domestic animals. In case of poisoning, administer atropine.

Propoxur

Propoxur is an older carbamate that was introduced in 1959. It has a quick knockdown action and affords residual effects for several weeks. Propoxur is toxic to birds and honeybees but can be used safely on and around domestic animals. The oral LD_{50} of propoxur for rats is 100 mg/kg. Propoxur is the active ingredient in foam control topical insecticides. It is also commonly used in flea collars for dogs and cats (Bansect, Scratchex). It is an ingredient in several formulations that combine propoxur with methoprene, an IGR (Sergeant's Double Duty, Vet-Kem Breakaway).

Organophosphates

The organophosphates are synaptic poisons that work by inactivating AChE. The inactivation process occurs in two steps. First the organophosphate reversibly binds to the active site of AChE. Later the phosphate becomes irreversibly bound to the AChE enzyme. Once irreversibly bound, the enzyme cannot be regenerated, so the tissue must synthesize new enzyme. 2-PAM is effective in reversing the first reaction and regenerating the enzyme. It is most effective when given soon after exposure (Buck, 1991).

A long list of organophosphates is available for use on and around animals. For the list to be less imposing, it will be divided into three groups by chemical structure: aliphatic derivatives, phenyl derivatives, and heterocyclic derivatives. The aliphatic derivatives were the first to be developed. They have a simple linear structure, without complex rings. Because their structure is simple, they are rapidly broken down in the animal and the environment. The phenyl derivatives, the second group, have a benzene ring in their structure. The phenyl derivatives were the second class of

organophosphates to be developed. They are longer lasting than the aliphatic derivatives. The last group to be developed, the heterocyclic derivatives, has ring structures in which at least one carbon atom is replaced by oxygen, nitrogen, or sulfur. The members of this group are the longest lasting of the organophosphates.

Toxicity from organophosphate insecticides is usually a medical emergency requiring treatment with activated charcoal and bathing to decrease absorption, 2-PAM to reverse binding to AChE, and atropine to decrease the clinical signs of acetylcholine excess (Kahn, 2005).

Many of the organophosphates available in the past have disappeared from the scene, either from losing market share to newer products or from reregistration issues with the EPA. The current list is shorter than that found in the earlier editions of this volume.

Aliphatic derivatives

The aliphatic derivatives were the very first organophosphate products to be commercially available. Dichlorvos and ethion are the only aliphatic derivatives still used on animals. Because of their simple straight-chain structures, they are readily broken down.

Dichlorvos

Dichlorvos (DDVP) is an aliphatic organophosphate developed in the early 1960s. Its acute oral LD_{50} for rats is approximately 50 mg/kg. A unique property of dichlorvos is its high vapor pressure, which makes it an excellent agent for killing insects in a closed

space. It was also the first product to be incorporated into an effective flea collar. Dichlorvos has quick knockdown insecticidal action as a contact, systemic, and fumigant agent, but it has little residual effect. Its half-life in neutral aqueous media is about 8 hours. Rapid hydrolysis also is noted in the mammalian body. In slow-release pharmaceutical forms, dichlorvos demonstrates a high degree of activity against the economically important nematodes of swine (see discussion of anthelmintics).

Cattle

Dichlorvos Vapona Concentrate is diluted to a concentration of 1% in water or diesel oil. The product is sprayed on beef and dairy cattle at the rate of 30 to 60 mL per head for the control of face flies, horn flies, stable flies, houseflies, gnats, and mosquitoes. It can also be used as a premise spray.

Food animals should not be treated within 1 day of slaughter. For standard precautions to be followed in dealing with organophosphorus insecticides, see earlier discussion.

Phenyl derivatives

The phenyl derivatives are structurally more complex organophosphates than the aliphatic derivatives because they have a benzene ring in their structure. They were the second major class of organophosphate to be developed. Because of their structural differences from the aliphatic derivatives, they are longer lasting in the environment. The phenyl derivatives are represented by tetrachlorvinphos.

Tetrachlorvinphos

Tetrachlorvinphos is a phenyl derivative organophosphate with low mammalian toxicity. The oral LD_{50} of tetrachlorvinphos for rats is 4000 to 5000 mg/kg. Tetrachlorvinphos is available as a spray, powder and collar for control of fleas on dogs and cats and a feed-through for horses.

Dogs and cats

Tetrachlorvinphos is available in an array of sprays, powders, and collars (Hartz Advanced Care 2 in 1) for control of fleas and ticks on dogs and cats and in their environment. It is also formulated into combination with an IGR, methoprene, for more effective control of the flea life cycle (Hartz Advanced Care 3 in 1).

Horses

This product is formulated into a feed-through fly control for control of stable flies and houseflies (Equitrol). For best results all horses in the stable should be fed the product. Begin treatment before flies emerge in the spring, and continue feeding until fly season is over.

Heterocyclic derivatives

The heterocyclic derivatives were the last group of organophosphates to be developed. Chemically they all have a ring structure in which at least one of the atoms in the ring is oxygen, nitrogen, or sulfur. The heterocyclic ring may consist of three, five, or six atoms. The heterocyclic derivatives are the longest lasting of all the organophosphates. They are used widely on animals and are represented by chlorpyrifos, coumaphos, diazinon, phosmet, and pirimiphos.

Chlorpyrifos

Chlorpyrifos (Dursban) is moderately persistent in the environment and serves well for the control of mosquito larvae, fly larvae, fire ants, and termites. Its acute oral LD_{50} in rats is 163 mg/kg, and its acute dermal LD_{50} in rabbits is 2000 mg/kg.

Chlorpyrifos is formulated as a dip and a shampoo that are indicated for the control of fleas and ticks on dogs only. It is claimed that one application will kill fleas and protect against reinfestation for up to 1 month. For more effective control of fleas, bedding and resting areas should also be sprayed. It is suggested that pregnant bitches and pups younger than 10 weeks old should not be treated with chlorpyrifos.

Coumaphos

Coumaphos is a heterocyclic derivative organophosphate of relatively low toxicity for mammals. Mice are very sensitive to coumaphos. Their oral LD_{50} is 55 mg/kg, whereas the oral LD_{50} for rats is 90 to 110 mg/kg. Coumaphos hydrolyzes slowly under alkaline conditions, but rapid degradation occurs in the liver of cattle. Coumaphos is available as an emulsifiable concentrate (Co-Ral) or dust for use on animals and premises to control a wide range of parasitic arthropods.

Cattle

For the control of cattle lice, horn flies, face flies, and ticks, coumaphos is sprayed on, dusted, or applied with a backrubber. Coumaphos may be used on beef and lactating dairy cattle without limitations for slaughter.

Coumaphos is also formulated in an ear tag in combination with diazinon (Co-Ral Plus). It is approved for control of horn flies, Gulf Coast ticks, and spinose ear ticks and as an aid to control of face flies. These ear tags are approved for use on beef and nonlactating dairy cattle.

Swine

Coumaphos spray (Co-Ral) is applied directly to pigs for the control of lice by spray or dust.

Horses

Coumaphos is sprayed on horses for the control of external parasites, including flies, lice, and ticks.

Diazinon

Diazinon is a relatively safe heterocyclic organophosphate with a good record of safety. Over several decades it has been used to kill a wide spectrum of insect pests. Its oral LD_{50} for rats is 300 to 400 mg/kg, and its acute dermal LD_{50} in rabbits is 4000 mg/kg.

Diazinon is currently available in a flea collar (Preventef) for use on dogs and cats against fleas and ticks. It is also available in ear tags (Patriot) for use on beef and nonlactating dairy cattle to control horn flies, Gulf Coast ticks, and spinose ear ticks and as an aid in the control of face flies, stable flies, houseflies, and lice. These ear tags can also be used in winter to control lice.

Phosmet

Phosmet is a time-tested heterocyclic organophosphate insecticide registered for use on many insect pests. Its oral LD_{50} for male rats is

147 to 316 mg/kg, and its acute dermal LD_{50} for rabbits is 3160 mg/kg.

Cattle

Phosmet is formulated (Del-Phos Emulsifiable Liquid) for the control of lice, winter ticks, Lone Star ticks, Gulf Coast ear ticks, horn flies, and sarcoptic mange on beef and nonlactating dairy cattle. The product may be applied by spray or backrubber. Cattle treated with the spray may be slaughtered 3 days after treatment. Do not apply to sick, diseased animals or calves younger than 3 months old. Do not treat dairy animals within 28 days of freshening.

Swine

Phosmet is registered (Del-Phos Emulsifiable Liquid) as a spray for the control of lice, and sarcoptic mange in swine. Swine treated with the spray may be slaughtered 1 day after treatment. Do not apply to sick pigs or directly to nursing pigs.

Pirimiphos

Pirimiphos is a heterocyclic organophosphate. Its acute oral LD_{50} for female rats is 2050 mg/kg. It is formulated into a 20% cattle ear tag (Dominator) that is approved for use on beef cattle, calves, and nonlactating dairy cattle. Pirimiphos protects against horn flies and aids in control of face flies for 5 months.

Pirimiphos is also formulated in combination with the synthetic pyrethroid lambdacyalothrin to form ear tags (Double Barrel VP) labeled for up to 5 months' control of horn flies and up to 4 months' control of face flies. The ear tags are approved for use on beef cattle and nonlactating dairy cattle and calves.

Formamidines

The formamidines are a promising new group of acaricidal compounds effective against cattle ticks and mange mites of swine and dogs. Formamidines work as octopaminergic agonists (IRAC, 2007; Salgado, 2007). In the United States, amitraz is approved for use in dogs, cattle, and swine.

Amitraz

Amitraz is the only formamidine approved for use on animals in the United States. Its acute oral LD_{50} for rats is 800 mg/kg, and its dermal LD_{50} for rabbits is greater than 200 mg/kg. When applied to the skin of dogs as a 0.025% solution, amitraz produced transient sedation, depression of the rectal temperature, and elevation of blood glucose. Amitraz was well tolerated by dogs when administered orally at 0.25 mg/kg daily for 90 days, but at 1 to 4 mg/kg hyperglycemia was consistently observed. In clinical studies, transient sedation was the most frequently observed untoward effect.

Dogs

Mitaban liquid contains 19.9% amitraz and is diluted to a 0.025% solution for the treatment of generalized demodicosis in dogs. The contents of one 10.6-mL vial are mixed with 2 gallons of warm water for each of three to six treatments spaced 14 days apart. It is suggested that treatment be continued until no viable mites are found in skin scrapings made at two successive treatments, or until six treatments have been applied. The Mitaban package insert states that amitraz should not be used for treatment of localized

demodicosis or scabies. The safety of amitraz has not been evaluated in pregnant bitches or in dogs younger than 4 months old. Mitaban concentrate is flammable. Wear rubber gloves when preparing dilutions and applying these to dogs.

Amitraz is also available in a collar for dogs. The product Preventic kills ticks on dogs for 3 months. The collar contains enough amitraz to cause illness if ingested. The collar must be fitted properly to prevent it from coming loose and being ingested. The amitraz collar must not be used on sick, convalescing animals or puppies less than 12 weeks of age. It has no effect on fleas, so other means of insect control must be applied. A recently approved combination product (ProMeris for dogs) contains amitraz plus metaflumizone for treatment of ticks and fleas in dogs. For more information on the combination product, see the section on metaflumizone.

Cattle and swine

Amitraz is available in a 12.5% emulsifiable concentrate (Taktic EC) for use against ticks, mange mites, and lice on beef cattle, dairy cattle, and swine. For use against cattle ticks and lice, the product is diluted 760 mL/100 gallons of water and applied as a spray or dip. For lice a second treatment in 10 to 14 days is required For use against cattle scabies and mange and lice in swine, the product is diluted 760 mL/50 gallons of water and used as a spray or dip. For scabies, a second treatment must be applied in 7 to 10 days.

No slaughter withdrawal is required for cattle, and no milk withdrawal is required for dairy cattle. Swine must not be treated within 3 days of slaughter.

WARNING: Horses must not be treated with amitraz, or fatal colon impaction may result.

Neonicotinoids

The neonicotinoids represent a heterogenous class of insecticides that are just now coming the veterinary marketplace in the United States. Insecticides in this class work by binding to the nicotinic AChE receptors. They represent the newest and most exciting chemistry to be applied to arthropod pests of domestic animals (Tomizawa and Casida, 2005).

Dinotefuran

Dinotefuran is a new nicotinoid insecticide that has excellent activity against fleas (Wakita et al, 2005). It is formulated as a topical spot-on combination product containing 4.95% dinotefuran, 0.44% pyriproxyfen, and 36.08% permethrin (Vectra 3D). The dinotefuran provides knockdown against fleas, the pyriproxyfen interrupts the flea life cycle, and the permethrin provides activity against ticks (deer tick, *Ixodes scapularis;* brown dog tick, *Rhipicephalus sanguineus;* American dog tick, *Dermacentor variabilis;* and Gulf Coast tick, *Amblyomma maculatum*) and mosquitoes *(Culex pipiens, Ochlerotatus triseriatus*, and *Aedes aegypti)*. A single topical dose kills 96% of fleas within 6 hours and provides effective control of fleas, ticks, and mosquitoes for at least 30 days. *Do not* use this product on cats.

Imidacloprid

Imidacloprid is a chloronicotinyl insecticide. It binds irreversibly at nicotinic acetylcholine receptor sites. This receptor is a subtype that

is apparently essential for insect neurofunction but that is different in pharmacology and tissue distribution from all known mammalian nicotinic receptors (Griffin, Krieger, and Liege, 1997; Liu and Weller, 1996; Londershausen, 1996). Its acute oral LD_{50} in rats is 450 mg/kg. Imidacloprid is available in a 9.1% topical spot-on formulation (Advantage) for use in dogs, cats, puppies, and kittens for control of fleas. The product is very effective in laboratory and field use to control fleas (Arther et al, 1997; Cruthers and Bock, 1997; Cunningham and Everett, 1997; Hopkins, 1997; Hopkins et al, 1997). It is also effective after shampooing (Cunningham et al, 1997a), although the label recommends reapplication after bathing. Safety testing has revealed no concerns when the product is used according to the label (Griffin, Hopkins, and Kerwick, 1997). Do not use it in puppies 7 weeks or younger or kittens 8 weeks or younger or in sick or debilitated animals.

Imidacloprid is also formulated in combination with permethrin, a synthetic pyrethroid. The combination product (K9 Advantix) is registered for use against fleas, ticks, and mosquitoes in dogs. The spot-on formulation is applied once every 30 days. Do not use on puppies less than 7 weeks old. Do not use on cats.

The newest imidacloprid combination product (Advantage Multi) contains imidacloprid for external parasites and moxidectin for internal parasites, including heartworm. It is approved for use in dogs and cats. For more information, see combination products at the end of the chapter.

Nitenpyram

Nitenpyram is a neonicotinoid insecticide. It has the unique action of rapid oral absorption and low toxicity to dogs and cats. As a result of this action, a single oral dose provides extremely rapid knockdown of flea populations (Schenker et al, 2003). Studies have shown activity against fleas within 30 minutes after oral administration. Efficacy was greater than 90% within 4 hours in dogs and within 6 hours in cats. Nitenpyram has a short half-life and is quickly cleared from th body. Daily administration in dogs and cats will not result in bioaccumulation.

Nitenpyram is available in tablet form (Capstar). The small tablet contains 11.4 mg and is labeled for use in cats and dogs up to 25 pounds in body weight. The large tablet contains 57 mg and is for use in dogs weighing 25.1 to 125 pounds. The wide dosage range is a testament to the favorable margin of safety.

Nitenpyram should not be used in dogs and cats less than 2 pounds in body weight or less than 4 weeks of age. Pets that are heavily infested with fleas may begin scratching after treatment with nitenpyram; this is usually an effect from the dying fleas and not an adverse effect from the product (Chatellier, 2001; Dobson et al, 2000; Dryden et al, 2001; Schenker, 2000; Schenker, Luempert, and Barnett, 2000; Schenker, Luempert, and Barnett, 2001; Schenker et al, 2000; Schenker et al, 2001; Witte and Luempert, 2001; Witte et al, 2000a; Witte et al, 2000b).

Spinosad

Spinosad is structurally classed as a spinosyn, which is a nonbacterial tetracyclic macrolide. Although it is not a true neonicotinoid insecticide, this molecule works by activating

nicotinic acetylcholine receptors in the insect (IRAC, 2007; Salgado, 2007). The receptor binding site for spinosad is separate and distinct from other neonicotinoids, fiproles, milbemycins, avermectins, and cyclodienes. Spinosad-treated insects show involuntary muscle contractions and tremors from activation of the motor neurons. Prolonged exposure results in paralysis and death of the flea. Selective toxicity in the flea versus the vertebrate host is conferred by the differential sensitivity of the nicotinic receptors between the flea and the host (Snyder et al, 2007). Spinosad had a wide safety margin when tested in laboratory and clinical studies. Spinosad is thought to be secreted in the milk of lactating bitches. Safety studies in nursing bitches showed increased lethargy, weakness, and dehydration in the litters of bitches given a high dose (4.4×) of spinosad.

Spinosad has been employed in Australia to control blowflies and lice on sheep (Kirst et al, 2002). In dogs it demonstrates rapid oral absorption and low toxicity. Studies in dogs have shown 53% activity against fleas within 30 minutes after oral administration, and efficacy was 100% within 4 hours. Spinosad also confers long-lasting protection against fleas that provides 100% efficacy at 21 days and 96% efficacy at 30 days after a single oral dose (Snyder et al, 2007).

Spinosad is available in a chewable, beef-flavored tablet form (Comfortis). There are five different chewable tablet sizes; all are formulated to deliver the minimum target dose of 30 mg/kg of body weight. The product is approved for redosing every 30 days in dogs for the prevention and control of flea infestations. In 2008, the FDA issued a safety warning about concurrent use of Comfortis in

combination with high doses of ivermectin to treat nonresponsive demodectic mange. Some dogs treated in this manner have developed ivermectin toxicity. The manufacturer recommends that dogs given high doses of ivermectin should not be given Comfortis.

Novel Insecticides

Benzyl Benzoate

Benzyl benzoate is an insecticide with an unknown mode of action. It is effective against most ectoparasites but is used only on dogs infested with sarcoptic mange. Benzyl benzoate is marketed as a 36% lotion (Mange Treatment) for treatment of *Sarcoptes scabiei*. For spot treatment of localized infestations, apply every 7 days. It is also available in a 29% preparation (Happy Jack Sardex II) for sarcoptic mange. For the treatment of generalized forms of sarcoptic and demodectic mange, the hair is first clipped from the entire body, and the dog is bathed to remove all crusty materials. Mange lotion is then applied while the dog is still wet. Benzyl benzoate has no residual effect. Therefore repeated applications are required every 7 days until the condition clears up These products should not be applied to dogs under 12 weeks old, or to pregnant or nursing bitches. Benzyl benzoate–containing drugs should not be used on cats. If application is carried out by dipping, protect the patient's eyes with a bland ointment.

Fipronil

Fipronil is a phenylpyrazole insecticide. It is a potent antagonist of the GABA-gated chloride channel (Gant et al, 1996; IRAC, 2007; Tomlin, 2000). The acute oral LD_{50} of fipronil for rats is 100 mg/kg.

A large volume of literature is available to show the mechanism of action, clinical efficacy, and safety when fipronil is used against fleas in dogs and cats. It is approved in a 0.29% spray (Frontline Spray) for use on dogs, cats, puppies, and kittens. This spray is effective against fleas even after bathing (Jeannin et al, 1994; Postal et al, 1994; Tanner et al, 1996). It is also effective against ticks and sarcoptic mange mites (Curtis, 1996; Hunter, Keister, and Jeannin, 1996a; LeNain et al, 1996). The spray should not be used in puppies and kittens younger than 8 weeks old.

Fipronil is available in convenient spot-on formulations for dogs and for cats (Frontline Top Spot). These formulations are effective in spreading the product through the sebum covering the hair and skin with minimal systemic absorption (Birckel et al, 1996; Weil et al, 1997). The cat product is effective against ticks for 30 days and fleas for as long as 45 days. The dog product is effective against ticks for at least 30 days and fleas for as long as 90 days. (Hunter, Keister, and Jeannin, 1996b; Cunningham et al, 1997b; Cunningham et al, 1997c; Postal et al, 1996a; Postal et al, 1996b). It is effective against chewing lice in cats. It is also effective after exposure to rain or bathing (Everett et al, 1997). Laboratory and field safety studies reveal no concerns when the product is used according to the label (Arnaud and Consalvi, 1997a; Arnaud and Consalvi, 1997b; Consalvi et al, 1996). Do not use it in puppies younger than 10 weeks old or in kittens younger than 8 weeks old. Wear rubber gloves when applying the product. Some reports indicate that fipronil is effective against ear mites (Vincenzi and Genchi, 1997).

Fipronil is now available in combination with methoprene, an IGR, in a convenient spot-on formulation. The combination product is

sold under the trade name Frontline Plus. For dogs and cats it is effective against fleas, ticks, and chewing lice for 30 days. The combination of an adulticide and an IGR provides activity against the immature and adult life stages of the flea, thus breaking the life cycle of the pest. Do not use in puppies or kittens younger than 8 weeks old.

Metaflumizone

Metaflumizone is a semicarbazone insecticide that binds to voltage-dependent sodium channels in the axon and dendrite and blocks the flow of sodium across the neuronal membrane (IRAC, 2007; Salgado and Hayashi, 2007; Takagi et al, 2007). The molecule has extremely low mammalian toxicity in rats with an oral LD_{50} greater than 5000 mg/kg (Hempel et al, 2007). It is approved as an 18.53% topical for cats (ProMeris for cats), should be given before flea exposure, and may be given every month for control of flea populations. The active ingredient is distributed throughout the skin and hair of the cat and works by direct contact with the flea (DeLay et al, 2007a; Dryden et al, 2007). A single dose is effective against adult fleas and prevents flea egg production for up to 7 weeks (Holzmer et al, 2007). Repeated use at five times the approved dose was safe in cats and kittens as young as 8 weeks old (Heaney and Lindahl, 2007). When administered to cats and kittens every 30 days, the product was highly effective against fleas in a large scale European clinical study (Hellmann et al, 2007a).

Metaflumizone is also approved as a topical for use in dogs (ProMeris for dogs). The dog product contains 14.24% metaflumizone and 14.24% amitraz. The metaflumizone molecule

knocks out fleas, and amitraz provides activity against ticks. The product should be given before flea exposure and may be given every month for control of flea and tick populations (deer ticks, *I. scapularis;* brown dog ticks, *R. sanguineus;* American dog ticks, *D. variabilis;* and lone star ticks, *Amblyomma americanum*) (Rugg and Hair, 2007; Sabnis, Zupan, and Gliddon, 2007). Metaflumizone is distributed throughout the skin and hair of the dog and works by direct contact with the flea (DeLay et al, 2007b). A single dose is effective against adult fleas and prevents flea egg production for up to 6 weeks and against ticks for up to 4 weeks (Rugg et al, 2007). Repeated use at three to five times the approved dose produced mild transient effects on blood urea nitrogen (BUN), blood glucose, leukocyte, neutrophil, and monocyte numbers and was safe at the recommended dose in dogs and puppies as young as 8 weeks old. When administered to dogs and puppies every 30 days, the product was highly effective against fleas and ticks in a large scale European clinical study (Hellmann et al, 2007b). Although the drug is not approved for use against mange mites *(Demodex canis* and *S. scabiei)*, there are published reports that the dog product has efficacy in that regard (Fourie et al, 2007a; Fourie et al, 2007b).

Repellents

Repellents are compounds that prevent or discourage pests from approaching a treated area or that induce them to leave soon after approaching. The most intensive research in this area has been to protect humans from flying insects. In general these products are rather volatile and regarded as having little toxicity to the host animal (Hayes and Laws, 1991).

DEET

DEET is the official nonproprietary name for *N,N*-diethyl-3-methylbenzamide or *N,N*-diethyl-*m*-toluamide. Its oral LD_{50} for rats is 2000 mg/kg. DEET is used as a repellent for mosquitoes, gnats, flies, fleas, ticks, and chiggers. For continuing protection, frequent applications are necessary.

Di-*N*-propyl isocinchomeronate

Di-*N*-propyl isocinchomeronate is a relatively safe insect repellent, with an oral LD_{50} for rats of 5200 to 7200 mg/kg. The chemical is best known by its proprietary name, MGK Repellent 326. It is usually formulated with other insect repellents, insecticides, or synergists for use on pets and livestock.

Insect Growth Regulators

An exciting area of recent advance in the struggle against insects is the advent of insect growth regulators (IGRs). The sheer number of insecticides covered in this chapter would suggest that insect problems are no longer a threat to the health and welfare of our domestic animals, but anyone who works in the field knows that this is far from the case. The central problem with most insecticides is that they are effective against and directed toward only the adult insect, the one that bites and annoys.

Adulticidal products need to be applied thoroughly and often to control adult insect populations, but this is often unworkable. The applicator trying to stem the flow of adult insects often feels like the Dutch boy with his finger in the dike. The IGRs provide relief from this approach by killing immature insects where they grow and

develop, thus breaking the life cycle and providing true relief from insect annoyance. The IGRs typically are juvenile hormone mimics that bind to juvenile hormone receptors in the immature insect and prevent survival to the next stage of development. Methoprene and pyriproxyfen are the best-known juvenile hormone mimics.

IGR products are the safest and most effective products available. Their safety lies in the fact that mammalian hosts have no juvenile hormones or juvenile hormone receptors (Londershausen, 1996). Therefore IGR products cannot have any biologic effect on the host. These products have an important side effect on safety. When used properly, they dramatically decrease the use of more toxic adulticides. It follows then that insect control programs with IGRs are often safer to the host and the environment than programs with adulticides alone.

Cyromazine

Cyromazine is a unique product that has IGR properties limited to the filth flies (e.g., houseflies, lesser houseflies, stable flies, soldier flies). It has no effect on most of the other orders of beneficial insects. Cyromazine works by blocking the formation of new cuticle in the fly larvae. It is a molting disruptor; the fly larva molts from the first to the second instar stage, but it does not survive the molt (IRAC, 2007).

Horses

Cyromazine is formulated into a 2.12% feed additive pellet (Solitude IGR) for use in horses. The product should be fed as part of the daily ration to contain 300 mg per horse per day. It is registered for use against houseflies and stable flies in and around horses, barns,

stables, paddocks and race tracks. Do not contaminate water, food, or feed with this product. Do not apply directly to water.

Poultry

The product is formulated as a feed premix (Larvadex 1% Premix) and a liquid concentrate (Larvadex 2 SL). The premix is approved for feeding to caged layers and broiler breeders at 1 pound of premix per ton of final feed. Cyromazine passes through the bird and is deposited in the manure, where it controls filth flies developing there. The surface spray is used to control fly larvae in other breeding places such as feed spills, dead bird piles, and manure storage areas.

Diflubenzuron

Diflubenzuron is not a true IGR but is included here for simplicity. It does not bind to juvenile hormone receptors. Diflubenzuron is an inhibitor of chitin biosynthesis. It interferes with chitin deposition and thus prevents the shedding of the old skin, leading to the death of larvae or pupae. It also prevents hatching of eggs. In both acute and chronic studies in laboratory animals, diflubenzuron was well tolerated.

Horses

Diflubenzuron is formulated into 0.24% feed additive (SimpliFly, Equitrol II) for use against stable flies and houseflies in horses. The product is fed to horses daily to control filth fly larvae in the manure. The daily dose is 6.8 mg of diflubenzuron per 100 pounds of body weight. Do not use in horses intended for slaughter.

Cattle

Diflubenzuron is also formulated into a 5% pour-on product in combination with permethrin, a synthetic pyrethroid. The product is applied directly to beef and dairy cattle at a rate of 3 mL per 100 pounds body weight for control of lice. Cattle treated with the approved rate can be slaughtered or milked immediately. This product is toxic to aquatic invertebrates; do not contaminate water sources.

Lufenuron

Lufenuron is an IGR that works by inhibiting chitin biosynthesis (IRAC, 2007). Lufenuron is approved for use in dogs and cats for control of fleas (Program) and is approved for use in pets who are at least 4 weeks old. It is given orally to dogs and cats every 30 days. Lufenuron is also available in an injectable formulation (Program 6-Month Injectable for Cats) that is designed to allow application every 6 months for control of fleas. The drug is very lipophilic, so it resides in the fat tissues of the pet, where it redistributes into the bloodstream for at least 30 days. Adult fleas ingest lufenuron when they feed, and the drug is passed transovarially to the flea egg. Most flea eggs exposed to lufenuron fail to hatch, and the few flea larvae that do successfully hatch die during their first molt. The action on the immature flea is thought to be due to disruption of chitin synthesis and deposition. Lufenuron is a convenient and effective agent for flea control in pets. It is known to be safe in pets of all ages, as well as in breeding dogs and cats. Lufenuron is also available in a two-way combination with milbemycin oxime (Sentinel) for control of fleas and internal parasites in dogs; see the combination products at the end of this chapter for more information.

Methoprene

Methoprene is an IGR with low toxicity in mammals. Its oral LD_{50} for rats is 34,600 mg/kg. Methoprene is a true IGR, acting as a juvenile growth hormone mimic that arrests larval development, which in turn results in the death of the larva (IRAC, 2007). Methoprene is sensitive to degradation by ultraviolet (UV) light.

Methoprene has had wide commercial success against fleas. It is available in a wide variety of products formulated with methoprene alone or in combination with adult insecticides for control of fleas and other pests. Methoprene is ovicidal and larvicidal against fleas. Products with methoprene alone will be covered in this portion of the chapter. Combination products are covered later under headings with the adulticides.

Methoprene is formulated into feed premix and a salt block (Altosid) that delivers the IGR orally to cattle. These products are registered for control of horn flies in cattle. These products may be used in beef cattle and both dry and lactating dairy cattle during the horn fly season. No withdrawal period is required before slaughter or milking. Do not allow this product to contaminate surface water.

Pyriproxyfen

Pyriproxyfen is an IGR and a juvenile hormone mimic (IRAC, 2007). The secretion of juvenile hormone in the immature insect causes it to molt into the next life stage, but the absence of juvenile hormone at the time of the molt allows maturation to occur. The net effect of the juvenile hormone mimic is to interfere with the larval-to-pupal and pupal-to-adult molts (*Nylar Technical Bulletin,* 1997). The acute oral LD_{50} of pyriproxyfen in rats is greater than 5000 mg/kg, which

demonstrates the very wide margin of safety. The product is 100% effective against flea reproduction in carpets for more than 6 months after application (*Nylar Technical Bulletin,* 1997). It represents another important addition to the insecticide arsenal.

Pyriproxyfen is available in a wide variety of products formulated alone or in combination with adult insecticides for control of fleas and other pests. Products with pyriproxyfen alone are covered in this portion of the chapter. Combination products are covered under headings with the adulticides.

This IGR is registered as a 1.3% concentrate (EctoKyl IGR, OmniTrol IGR) to be sprayed in residential locations and pet premises to kill flea larvae and eggs. A single application lasts for 7 months. Pyriproxyfen is also formulated into a 0.01% ready to use spray (HouseSaver). It is labeled to spray in the indoor environment to control flea larvae and eggs.

Pyriproxyfen is formulated into a 5.3% stripe-on formulation (Bio Spot) that is labeled for direct application to cats for control of flea eggs. A single application controls flea eggs for 3 months. Do not use in kittens less than 12 weeks old.

This IGR is also incorporated into a wide range of products that contain adult insecticides and synergists for application to dogs, cats, and premises to control fleas and other animal parasites.

Synergists

The synergists are not considered toxic in their own right and have no direct effect in killing insects. They are used with insecticides to enhance insecticidal activity. They are most often used with

pyrethrins, in which they can increase the potency tenfold to twentyfold (Plapp, 1991). The mode of action is to inhibit mixed-function oxidases—enzymes in the insect that metabolize foreign compounds. When the insect is inhibited from destroying the insecticide, the agent can kill the pest. The synergists are most commonly listed on the label by their chemical name, which is not designed to be user friendly.

N-Octyl Bicycloheptene Dicarboximide

N-Octyl bicycloheptene dicarboximide inhibits the microsomal detoxification of insecticides, thus maximizing their toxicity. It is also known by the designation MGK 264. The drug is registered for application to beef and dairy cattle, sheep, goats, horses, swine, dogs, and cats and to agricultural buildings and animal quarters for the control of annoying insects. It is often formulated with piperonyl butoxide and insecticides as aerosols, pressurized sprays, and free-flowing dusts.

Piperonyl Butoxide

Piperonyl butoxide is a pale yellowish liquid, soluble in alcohols, benzene, freons, and other organic solvents.

It is very safe for animals, with an oral LD_{50} for rats of about 7500 mg/kg. Chlorinated hydrocarbons, carbamates, organophosphates, and particularly pyrethrins and rotenone are synergized by piperonyl butoxide. The insecticidal activity of these compounds is enhanced because piperonyl butoxide inhibits degradation of the insecticide by the insect's microsomal enzymes (IRAC, 2007). Numerous products contain piperonyl butoxide as a synergist with pyrethrins, permethrin, carbaryl, or diazinon.

ANTIPROTOZOALS

We have tried in this discussion to characterize briefly the biologic activities of a few approved and some nonapproved but legally obtainable antiprotozoal drugs. As with any drug, the information on the label or package insert must always be read and directions followed before antiprotozoal agents are administered. For more detailed information, the reader should consult detailed review articles (Barr, 2006; Campbell and Rew, 1985; Lindsay and Blagburn, 2001; Schillhorn van Veen, 1986; Snyder, Floyd, and DiPietro, 1991; Speer, 1999).

Nonsulfonamides

Albendazole

Albendazole is more completely described later in the section on benzimidazole anthelmintics. It is included in this section for a discussion of its activity against *Giardia* organisms. Evidence in one study suggests that albendazole is 100% effective in treating giardiasis in dogs (Barr et al, 1993). The dosage given in that study was 25 mg/kg twice a day for four doses. Unfortunately, recent evidence has shown that albendazole can cause significant adverse reactions in dogs and cats.

Albendazole, like other benzimidazoles, is well absorbed (about 50% bioavailable) and converted in the liver to its active metabolites, albendazole sulfoxide and albendazole sulfone. These active metabolites are thought to bind to tubulin molecules, which prohibits the formation of microtubules and disrupts cell division. There is also evidence that benzimidazoles can inhibit fumarate

reductase, which blocks mitochondrial function, thus depriving the parasite of energy and resulting in death. In *Giardia* organisms, albendazole causes structural changes in the trophozoite stage, including damage to the adhesive disk and the internal microtubule cytoskeleton, but not the flagella (Lindsay and Blagburn, 2001). The parent drug and its metabolites are excreted primarily in the urine.

Albendazole has proved to be teratogenic, thus limiting its use in pregnant animals. Dogs treated with 50 mg/kg twice daily may have anorexia, and cats treated with 100 mg/kg/day for 14 to 21 days showed weight loss, neutropenia, and mental dullness (Plumb, 2005). The drug is known to be toxic in dogs and cats in clinical use (Meyer, 1998; Stokol et al, 1997). Reported toxicities included myelosuppression (anemia, leukopenia, and/or thrombocytopenia), abortion, teratogenicity, anorexia, depression, ataxia, vomiting, and diarrhea. Veterinarians are advised to use caution with this product in dogs and cats. Albendazole is available in an oral suspension and paste (Valbazen) containing 113.6 mg/mL.

Amprolium

The coccidiostatic activity of amprolium is related to its mimicry of thiamine and competition for absorption of thiamine by the parasite. The activity occurs because of the structural similarity between thiamin and amprolium (United States Pharmacopeia [USP], 1998). The anticoccidial effect may by reversed by the feeding of excess thiamine. Amprolium is most effective against the first-generation schizont stage and thus is more effective as a preventative than as a treatment.

Broilers, layers, and turkeys

Amprolium (Amprol) is fed in poultry rations or drinking water to prevent or treat coccidiosis. Amprolium is given in the water for 2 weeks at 0.0125% (0.025% for severe outbreaks), then given at 0.006% for another 2 weeks.

Cattle

For treatment of active coccidia, *Eimeria bovis*, and *Eimeria zuernii*, infections in cattle, amprolium is formulated as a 9.6% drench solution (Corid Oral Solution), 20% soluble powder (Corid Soluble Powder), or feed additive (Corid 25%). Administration of amprolium is by drench or drinking water, or it is mixed into a complete feed at the approximate dosage of 10 mg/kg for 5 consecutive days. For prevention of coccidiosis caused by coccidia, *E. bovis*, and *E. zuernii*, during periods of exposure a dosage of 5 mg/kg daily for 21 days is recommended. Other species of *Eimeria* are also susceptible to amprolium, but the drug label claims efficacy against only *E. bovis* and *E. zuernii*. Cattle treated with 50 mg of amprolium per kilogram per day did not have adverse reactions. Animals should not be medicated within 24 hours of slaughter.

Sheep and goats

Amprolium may protect lambs against coccidia when given orally at 55 mg/kg twice daily for 19 days (USP, 1998).

Pigs

Coccidiosis caused by *Isospora suis* is occasionally a problem in swine. Pigs aged 5 to 10 days die without passing oocysts. Although not approved, amprolium therapy may be beneficial in preventing the disease (USP, 1998).

Dogs

Treatment of dogs requires adapting the approved formulations to small animal use. The target dose for treatment of dogs is 100 to 200 mg/kg by mouth daily in food and water (Plumb, 2005). Dogs may be treated by mixing 30 mL of 9.6% amprolium and 1 gallon (3.8 L) of drinking water and offering it as the sole source of drinking water (Smart, 1971). Alternatively, 1.25 g of 20% amprolium powder can be mixed with enough daily ration for four puppies (USP, 1998). Amprolium should be provided in either the food or water but not both for a period of 7 days. It may be given as a treatment for coccidia or as a preventative for 7 days before shipping puppies or to bitches just before whelping.

Cats

Amprolium may be used against coccidia at a dose of 60 to 100 mg/kg by mouth, which may be accomplished by direct oral administration (Dubey and Greene, 2006). Medication in food or water may be more unreliable in cats than in dogs because of their finicky tastes.

Clindamycin

Clindamycin is currently considered the drug of choice for treating clinical toxoplasmosis in dogs and cats (Dubey and Lappin, 2006). Structurally, clindamycin is a congener of lincomycin. The drug is well absorbed (90%) after oral administration and widely distributed in most tissues, except the central nervous system. It readily crosses the placenta and is extensively bound to plasma proteins. Clindamycin is metabolized in the liver and excreted primarily in the urine and bile. It acts by binding to the 50S subunit

of the bacterial (or parasitic) ribosome and blocking the transpeptidation reaction (Brunton, 2006). Gastrointestinal upset is sometimes reported in animals receiving clindamycin. Severe, even fatal, pseudomembranous enterocolitis has been reported in people, caused by overgrowth of *Clostridium difficile*.

Treatment of systemic toxoplasma infection in dogs can be accomplished with oral or intramuscular clindamycin at 15 to 22 mg/kg twice daily for 4 to 8 weeks (Dubey and Lappin, 2006; Greene, Cook, and Mahaffey, 1985). Cats can be treated for systemic infections with oral or parenteral clindamycin at 12.5 to 25 mg/kg twice daily for 2 to 4 weeks. This regimen is also useful to control the shedding of oocysts (Lappin et al, 1989). The drug should be given with caution in cats with pulmonic toxoplasmosis; parenteral administration to experimentally infected cats resulted in several deaths (Plumb, 2005).

Clindamycin is available in several veterinary formulations (Antirobe): tablets containing 25, 75, or 150 mg and an oral solution containing 25 mg/mL. Similar clindamycin formulations are available for use in people (Cleocin): 75- and 150-mg oral capsules, 15 mg/mL oral pediatric suspension, and an injectable solution containing 150 mg/mL.

Clopidol

Clopidol is a pyridinol coccidiostat that has some activity against ionophore-resistant strains of coccidia. It acts against the sporozoite stage, allowing host cell penetration without development. It is insoluble in water but is available as a feed additive (Coyden 25). The product is fed to chickens at 0.0125% or 0.025%. It should not

be fed to laying hens, to chickens older than 16 weeks of age, or within 5 days of slaughter (Lindsay and Blagburn, 2001).

Decoquinate

Decoquinate is an approved coccidiostatic drug for the control of coccidial *(Eimeria)* infections in chickens, cattle, sheep, and goats. This quinolone product kills the sporozoite stage of the life cycle. It disrupts the electron transport in the mitochondrial cytochrome system of the parasite (Plumb, 2005). Decoquinate is primarily indicated for prevention rather than treatment of coccidiosis.

Decoquinate is indicated for prevention of coccidiosis caused by *E. bovis* and *E. zuernii* in ruminating calves and older cattle. It is fed (Deccox) at 0.5 mg/kg body weight per day for at least 28 days during periods of exposure to infective oocysts. In young sheep and goats, decoquinate is used at the same rate for the prevention of infections caused by *Eimeria* species.

Warning: Decoquinate should not be fed to laying hens, breeding animals, or lactating cows, sheep, or goats. Complete feeds containing decoquinate should be consumed within 7 days of manufacture. Bentonite should not be used in decoquinate feeds.

Imidocarb

Imidocarb is an aromatic diamidine antiprotozoal agent. It works by inhibiting nucleic acid metabolism in susceptible organisms. It is particularly effective in treating infections with intracellular arthropod-borne organisms, including *Babesia, Haemobartonella, Ehrlichia, Hepatozoon,* and *Cytauxzoon* (Plumb, 2005). The approved product (Imizol) is a 12% sterile injectable solution that is approved

for treatment of babesiosis in dogs. The product should be injected at a dose of 6.6 mg/kg, and injections should be given 14 days apart. Do not give by intravenous injection. The safety of this product has not been established in puppies or breeding, pregnant, or lactating dogs.

Lasalocid

Lasalocid, an ionophore closely related to monensin, is produced by a streptomycete. Like other ionophores, it forms complexes with sodium and potassium ions. This action renders the parasite membranes permeable to ions, and mitochondrial functions are inhibited. The trophozoite stage is most susceptible to lasalocid (Guyonnet, Johnson, and Long, 1990). Lasalocid is the least toxic of the ionophores. It is approved for use in cattle, sheep, rabbits, and poultry for the control of coccidia and improvement of feed efficiency. Do not feed to horses, or fatal reactions may result.

Cattle

Lasalocid is available in dry or liquid feed additives (Bovatec). The product may be mixed into a complete feed for confined cattle or a feed supplement for pasture cattle to deliver a target dose of 1 mg/kg body weight per day (360 mg/head maximum dose). It is effective against *E. bovis* and *E. zuernii* in cattle. Feed continuously during exposure to coccidia. Do not feed to calves to be processed for veal.

Sheep

Lasalocid may be mixed into a complete feed for sheep fed in confinement. The feed should be mixed to provide a final

concentration of 20 to 30 g of lasalocid per ton of complete feed, to deliver a dose of 15 to 70 mg/head/day. This dose is effective against *Eimeria ovina, Eimeria crandallis, Eimeria ovinoidalis (Eimeria ninakholyakimovi), Eimeria parva,* and *Eimeria intricata* in sheep. Feed continuously during exposure to coccidia.

Rabbits

Lasalocid is approved for use in rabbits for the prevention of coccidiosis caused by *Eimeria stiedae*. The product is formulated in a complete ration at a concentration of 113 g per ton.

Poultry

Lasalocid is approved in broilers, turkeys, and chukar partridges to prevent coccidiosis caused by *Eimeria tenella, Eimeria necatrix, Eimeria acervulina, Eimeria brunetti, Eimeria mivati, Eimeria maxima, Eimeria meleagrimitis, Eimeria gallopavonis, Eimeria adenoeides,* and *Eimeria legionensis*. It is also approved for use in chukar partridges for prevention of *E. legionensis*. The product (Avatec) is mixed into a complete ration for broilers and turkeys at a rate of 68 to 113 g/ton. Chukar partridges should be fed lasalocid at a dose rate of 113 g/ton. Withdraw product at least 3 days before slaughter.

Metronidazole

The nitroimidazoles represent a very useful class of antibiotics that have broad-spectrum activity against trichomonads, amebas, and *Giardia* organisms, as well as anaerobic cocci and bacillus species. The prototypical nitroimidazole is metronidazole, which has become the drug of choice for treatment of infection with *Giardia* organisms. Other drugs in the class (ipronidazole, tinidazole, nimorazole,

ornidazole, and benznidazole) have been used to control *Giardia* organisms. Only metronidazole and tinidazole are currently available in the United States. None of the nitroimidazole drugs are approved for use in animals. The FDA strongly warns against their use in food-producing animals because this class of drug has been shown to produce tumors in laboratory rodents.

Metronidazole (Flagyl) is well absorbed from the gastrointestinal tract. It has low protein binding and is well distributed in the body. After entering the target cell, metronidazole interacts with the protozoal DNA, in which it causes a loss of helical structure and strand breakage (USP, 1998). The liver extensively metabolizes the drug, and in humans hepatic transformation is responsible for 50% of the total elimination. Patients receiving cimetidine or phenobarbital may require adjustment in the dosage because of drug interaction. Metronidazole toxicity may be seen with high doses. Neurologic toxicity includes ataxia, nystagmus, seizures, tremors, or weakness (Dow et al, 1989; USP, 1998).

Numerous studies have demonstrated that metronidazole is an effective treatment for giardiasis (Barr, 2006; Boreham, Phillips, and Shepherd, 1984; Kirkpatrick and Farrell, 1984; Watson, 1980; Zimmer, 1987; Zimmer and Burrington, 1986), although efficacy is rarely 100%. Dogs may be treated orally with 15 to 30 mg/kg once or twice daily, and therapy should be continued for 5 to 7 days (Barr, 2006). Cats may be treated orally with 10 to 25 mg/kg once or twice daily, and therapy should be continued for 5 to 7 days (Barr, 2006). The commercially available product (Flagyl) is formulated in 250- and 500-mg tablets. Parenteral formulations are also available, but their usefulness would seem questionable

considering that the giardial trophozoites live in the lumen of the gastrointestinal tract.

Monensin

Monensin is an antibiotic produced as a fermentation product of *Streptomyces cinnamonensis*. It is used in cattle, goats, poultry, and quail for its coccidiostatic activities. It forms ionophores with sodium and potassium in the host and in the parasite. When the parasite mitochondrial membrane is affected, it is rendered permeable to potassium and sodium ions. Feeding monensin to horses or guinea fowl can be fatal.

Cattle

Monensin is available as a feed additive (Rumensin) for cattle for growth promotion and for prevention and control of coccidiosis. For control of coccidiosis due to *E. bovis* and *E. zuernii*, the product should be fed at a rate of 10 to 30 g/ton, up to 360 mg/head/day. It should be fed continuously during periods of exposure to coccidia or when coccidia are likely to be a hazard. The product is not for use in veal calves.

Goats and sheep

Monensin is approved for use in goats (Rumensin) for the prevention of *E. crandallis, Eimeria christenseni,* and *E. ninakholyakimovi* infection in confined goats. It should be fed at a rate of 20 g/ton of complete ration. Do not feed to lactating goats. Monensin is not approved for use in sheep, but some authorities indicate that it is useful when fed at a rate of 1 mg/kg of body

weight per day (McDougald and Roberson, 1988; Schillhorn van Veen, 1986).

Poultry

Monensin (Coban) is used in broilers and pullets to prevent coccidiosis caused by *E. necatrix, E. tenella, E. acervulina, E. brunetti, E. mivati*, and *E. maxima*. It is fed at a rate of 90 to 110 g/ton of complete feed. It is also approved for use in turkeys to prevent infection with *E. adenoeides, E. meleagrimitis*, and *E. gallopavonis* when fed at 54 to 90 g/ton. Bobwhite quail can be fed monensin at 73 g/ton to prevent coccidiosis caused by *Eimeria dispersa* and *Eimeria lettyae*.

Narasin

Narasin is an ionophore coccidiostat produced by *Streptomyces aureofaciens*. Similar in structure to salinomycin (Lindsay and Blagburn, 2001), it is available as a feed additive (Monteban) for use only in broilers. The product is fed at a rate of 54 to 72 g/ton of feed for prevention of coccidiosis caused by *E. necatrix, E. tenella, E. acervulina, E. brunetti, E. mivati,* and *E. maxima.* No withdrawal period is required before slaughter. It should not be fed to laying hens. Ingestion by adult turkeys, horses, or ponies may be fatal.

Nicarbazin

Nicarbazin is a synthetic coccidiostat effective in preventing cecal and intestinal coccidiosis caused by *E. tenella, E. acervulina, E. maxima, E. necatrix,* and *E. brunetti*. The mechanism of action is unknown (Lindsay and Blagburn, 2001). It is available as a 25% feed additive (Nicarb) and is approved for use at 0.0125% in the

feed of broilers. The product should not be fed within 4 days of slaughter or to laying hens. It is not effective for treatment of coccidiosis, and it may depress growth in young birds (Lindsay and Blagburn, 2001).

Nitazoxanide

Nitazoxanide is an thiazolide antiprotozoal agent with broad spectrum activity against internal parasites, protozoa, and viral diseases (Craig et al, 2003; Fox and Saravolatz, 2005). In people it is approved (Alinia) for treatment of *Giardia* and *Cryptosporidium* infection in young children and adults. In horses it is effective in treatment of *Sarcocystis neurona*, the cause of equine protozoal myeloencephalitis (EPM) (Gargala, Delaunay, and Pitel, 2001). It is formulated into a ready-to-use oral paste (Navigator) that is administered daily for 28 days. The product is given at 25 mg/kg for 5 days, then given at 50 mg/kg for 23 days. Because this product has broad-spectrum activity, oral administration can disrupt the normal microbial flora of the gastrointestinal tract. The incidence of this effect is not different from that after the administration of oral antibiotics to horses. Navigator has an EPM relapse rate of less than 1%, because the active ingredient produces a lethal effect on the parasite.

The dosage of Navigator should be determined using an accurate body weight. Navigator may cause a spike in body temperature, temporary anorexia, or a temporary worsening of neurologic status. These effects are believed to be due to the death of the parasites in the central nervous system. It should not be used in horses less than 1 year of age or in horses that are sick or debilitated.

A recent study suggests that administration of nitazoxanide is effective in preventing EPM in young horses that are at increased risk for EPM owing to intensive training. The dose tested in this study was 11.36 mg/kg body weight 2 days per week (Easter, 2007).

Ponazuril

Ponazuril is an antiprotozoal product (Marquis) that is approved for treatment of EPM, which is caused by *S. neurona* (*Freedom of information summary for Marquis, 2001*; Lech, 2002).

The product has been tested at 5 mg/kg and 10 mg/kg. The approved dose is 5 mg/kg orally per day for 28 days. In the pivotal clinical study 54% of the horses with EPM improved at least one grade as judged by the attending veterinarian, and 58% of the horses treated with 10 mg/kg improved at least one grade. In a smaller field study with seven horses, all seven improved when treated with 5 mg/kg. Safety studies demonstrated that administration at doses of 10 mg/kg or greater produced transient episodes of loose feces (Furr and Kennedy, 2001; Furr et al, 2001; Furr et al, 2006; Kennedy, Campbell, and Seizer, 2001).

Robenidine

Robenidine is a synthetic coccidiostat chemically similar to guanidine. It is an older drug with a history of developing resistant strains of coccidia but is now used to treat ionophore-resistant strains. Robenidine is available in a feed additive (Robenz) for use in broilers only. The product is fed at 30 g/ton of feed for prevention of coccidiosis caused by *E. mivati, E. brunetti, E. tenella, E. acervulina, E. maxima,* and *E. necatrix*. It should not be fed to laying

hens or within 5 days of slaughter. Meat and eggs from treated birds have an unpleasant taste if the withdrawal period is not followed (Lindsay and Blagburn, 2001).

Salinomycin

Salinomycin was the third ionophore coccidiostat to enter the market in the United States. A fermentation product of *Streptomyces albus*, it is most active against the sporozoite stage. Salinomycin is available as a feed additive (Bio-Cox) for use in broilers, pullets, and quail. It is fed at 40 to 60 g/ton (50 g/ton for quail) for prevention of coccidiosis caused by *E. tenella, E. necatrix, E. acervulina, E. maxima, E brunetti,* and *E. mivati* in chickens and coccidiosis caused by *E. dispersa* and *E. lettyae* in quail. Do not feed salinomycin to laying hens. No withdrawal period is required before slaughter. The product may be fatal if fed to adult turkeys or horses.

Semduramicin

Semduramicin is an ionophore coccidiostat produced by *Actinomadura roseorufa*. It is available as a feed additive (Aviax) for use in broiler chickens only. The product is fed at 22.7 g/ton for prevention of coccidiosis caused by *E. tenella, E. acervulina, E. maxima, E. brunetti, E. necatrix,* and *E. mivati*. It should not be fed to egg-laying chickens or to broilers within 5 days of slaughter.

Sulfonamides

Sulfonamides are the treatments of choice for small-animal coccidia and very useful for the treatment of large-animal coccidiosis. Unfortunately there is a paucity of research information to support their efficacy. Two pivotal studies with sulfamethoxine and

sulfaguanidine against coccidia support their use. However, these two agents are no longer available in the United States (Boch et al, 1981; Correa et al, 1983). Clinicians have empirically substituted more readily available sulfonamides and have had apparent clinical success (Dubey, 1993). Several simple sulfas and potentiated sulfas are commonly used in the United States: sulfachlorpyridazine (Vetisulid), sulfadimethoxine (Albon), sulfadimethoxine with ormetoprim (Primor), sulfadiazine with pyrimethamine (ReBalance), sulfadiazine with trimethoprim (Tribrissen), sulfamethazine, sulfamethoxazole with trimethoprim (Bactrim, Septra), and sulfaquinoxaline.

The sulfonamides are structural analogues of para-aminobenzoic acid (PABA) that competitively inhibit the dihydropterate synthetase step in the synthesis of folic acid, which is required for synthesis of RNA and DNA. Inhibition by sulfas impairs protein synthesis, metabolism, and growth of the pathogen. A vast array of sulfa agents has been created and described, but most have been lost in the sands of time. The important differences among these agents are their solubility, duration of action, and activity against key pathogens. Fortunately, the sulfas included in this discussion demonstrate acceptable performance in all three categories: solubility is adequate; they are given once or twice daily or in the feed; and they have a reasonably broad spectrum of action. The sulfa drugs are primarily effective against the schizont stages of the coccidia; therefore prolonged treatment may be required for the drug effectively to block the life cycle (USP, 1998).

The diaminopyrimidine potentiators (trimethoprim, ormetoprim, pyrimethamine) act in concert with sulfonamides by blocking the

next step (dihydrofolate reductase) in folic acid synthesis. These agents are highly selective inhibitors of dihydrofolate reductase. This sequential blockade of folic acid synthesis produces significant potentiation of activity and is a classic case of drug potentiation.

The sulfonamides are weak acids that are well absorbed from the gastrointestinal tract (except for sulfaquinoxaline) and are widely distributed in the body. Sulfadimethoxine and sulfamethoxazole have high serum protein binding, which provides decreased body clearance and long half-lives. They undergo metabolic alteration in the liver and subsequent renal clearance. Trimethoprim, ormetoprim, and pyrimethamine are also well absorbed from the gut, widely distributed, then hydroxylated and excreted through the urinary tract.

The long history of sulfa use in veterinary medicine has resulted in a wide array of toxic and idiosyncratic reactions in animals. Historically, the most common and most avoidable reactions result from crystallization in the urinary tract, with secondary crystalluria, hematuria, and urinary obstruction. Recent reviews in human medicine indicate that the improved solubility of the modern preparations has greatly decreased the risk of crystalluria. Nevertheless, it is still prudent to ensure adequate water intake and proper hydration during sulfa therapy (Cribb et al, 1996). The human literature also suggests that the sulfonamides may be directly nephrotoxic (Cribb et al, 1996). Hematopoietic disorders (thrombocytopenia and leukopenia) have also been reported as a result of sulfa therapy. Sulfaquinoxaline especially has been associated with hypothrombinemia, hemorrhage, and death in puppies receiving therapy for coccidia (Patterson and Grenn, 1975).

Idiosyncratic reactions in animals and people often include immune-mediated phenomena, including hypersensitivity reactions, drug fever, urticaria, nonseptic polyarthritis, focal retinitis, and hepatitis. Fortunately, these reactions occur at very low rates when sulfonamides are used at recommended dose rates and for less than 2 weeks (USP, 1998).

Four sulfa products are currently available for use in small-animal medicine: sulfadimethoxine, sulfadimethoxine with ormetoprim, sulfadiazine with trimethoprim, and sulfamethoxazole with trimethoprim. Sulfamethazine and sulfaquinoxaline are used in livestock, and sulfadiazine plus pyrimethamine (ReBalance) is approved for use in horses for treatment of EPM.

Sulfadimethoxine

Sulfadimethoxine is a rapidly absorbed, long-acting sulfonamide. It is not acetylated in the dog and is excreted unchanged in the urine. The drug is approved for treatment of coccidiosis in dogs, cats, cattle, chickens, and turkeys and for treatment of strangles in horses. It has a wide margin of safety. Dogs given multiple oral doses of 160 mg/kg by mouth daily for 13 weeks showed no signs of toxicity. Diarrhea was the only reaction seen in dogs given single oral doses of 16 g/kg (Bayley, 2007).

It is important that all treated animals receive adequate water intake to prevent dehydration and crystalluria, as well as proper nutrition during therapy for coccidiosis. Sulfadimethoxine is available as a 40% injection (Albon), in 125-, 250-, and 500-mg tablets (Albon), and as a pleasant-tasting 5% suspension (Albon), a

12.5% oral solution (Albon), an oral bolus (Albon), and a sustained-release bolus (Albon SR).

Dogs and cats

The recommended dosage is an initial dose of 55 mg/kg orally or by subcutaneous or intravenous injection for the first day and subsequent doses of 27.5 mg/kg orally once per day for 12 to 21 days. It seems reasonable that because coccidia are enteric pathogens, the oral route would be most effective.

Cattle and horses

The recommended dosage is an initial dose of 55 mg/kg orally or by subcutaneous or intravenous injection for the first day and subsequent doses of 27.5 mg/kg orally once per day for 4 days. For the sustained-release bolus, give cattle one 12.5-g bolus orally per 200 pounds' body weight. Discard milk for 60 hours (five milkings) after the last treatment. Do not administer drug within 7 days of slaughter. Consult the approved label for accurate dosage and withdrawal information, because there are differences according to dosage form.

Poultry

Coccidiosis in broilers, pullets, and turkeys can be treated with oral sulfadimethoxine mixed into the drinking water. The usual dosage is 0.05% for chickens and 0.025% for turkeys for 5 days. Do not use drug in chickens older than 16 weeks or in turkeys older than 24 weeks. Do not administer drug within 5 days of slaughter.

Sulfadimethoxine with Ormetoprim

Sulfadimethoxine with ormetoprim constitutes a rational combination that potentiates the action of both drugs by blocking two sequential steps in the synthesis of folic acid. Ormetoprim is a diaminopyrimidine potentiator with very low mammalian toxicity. The available tablets contain 100/20, 200/40, 500/100, or 1000/200 mg of sulfadimethoxine/ormetoprim (Primor). The tablets are designated by the total weight of active ingredient in each tablet. Thus the Primor 120 contains 100 mg of sulfadimethoxine and 20 mg of ormetoprim. The approved starting dosage for dogs is 55 mg/kg orally on the first day of treatment, then 27.5 mg/kg orally once per day for 14 to 21 days. Do not treat beyond 21 days (Bayley, 2007).

It is interesting to note that the only recent controlled study of coccidiosis therapy in dogs was conducted with this drug combination. In that study, 32.5 mg/kg or 66 mg/kg was given continuously in the food for 23 days, subsequent to experimental oocyst infection. The higher dose of 66 mg/kg provided better results and did not produce any adverse reactions (Dunbar and Foreyt, 1985).

Poultry can be treated with the combination in a feed additive (RofenAid 40). Chickens are fed at 0.0125% sulfa and 0.0075% ormetoprim. Turkeys are treated with 0.00625% sulfa and 0.00375% ormetoprim, ducks with 0.05% and 0.03%, and chukar partridge with 0.0125% and 0.0075%, respectively. Do not feed drug within 5 days of slaughter. Do not feed to birds producing eggs for human consumption.

Sulfadiazine with Pyrimethamine

Sulfadiazine with pyrimethamine (ReBalance) is a rational drug combination that is approved for the treatment of horses with EPM caused by *S. neurona*. It is provided in an oral suspension containing 250 mg of sulfadiazine per milliliter and 12.5 mg of pyrimethamine per milliliter. The approved oral dose is 4 mL/50 kg body weight, once daily. The duration of treatment is dependent on clinical response to treatment, but the usual course of therapy is from 90 to 270 days.

Horses undergoing treatment should be watched closely for worsening neurologic function (treatment crisis), which may occur during the first 5 weeks of treatment. Anemia, leukopenia, or bone marrow suppression may occur in some horses. Interruption of treatment or administration of dietary supplements with folinic acid may be indicated.

Sulfadiazine with Trimethoprim

Sulfadiazine with trimethoprim is the potentiated sulfa with the most years of actual use in veterinary medicine. For many years it was the only potentiated sulfa approved for use in animals. Trimethoprim is a diaminopyrimidine potentiator with very low mammalian toxicity.

The manufacturer recommends that animals with marked hepatic parenchymal damage, blood dyscrasias, or previous sulfonamide sensitivity should not be given this product (Bayley, 2007; Plumb, 2005). Horses may be treated with an oral paste formulation (Tribrissen), which contains 333 mg sulfadiazine and 67 mg trimethoprim per gram. The approved dosage is 5 g of paste per 150 pounds of body weight once daily for 5 to 7 days. The equine

injectable formulation contains 400 mg of sulfadiazine per milliliter and 80 mg of trimethoprim per milliliter (Tribrissen 48% injection).

Sulfamethazine

The sodium salt of sulfamethazine may be administered in water (Sulmet) or by oral bolus (Sulfa-Max, Sulmet) to cattle, swine, chickens, and turkeys, for the control of coccidiosis. The usual dose is 237 mg sulfamethazine per kilogram, which may be administered orally on the first day and followed by 123 mg/kg every day for 4 days (5 days total treatment). A sustained-release bolus (Sustain III) is available for cattle, which delivers 32.1 g of sulfamethazine over 3 days. One bolus is given per 200 pounds of body weight. Animals should be provided with plenty of water when they are on sulfonamide medication. Withdrawal recommendations should be followed for food-producing animals.

Sulfamethoxazole with Trimethoprim

Sulfamethoxazole with trimethoprim is a readily available product approved for use in people (Bactrim, Septra). It is not currently approved for use in animals. Because of its similarity to veterinary potentiated sulfonamides and because low-cost generics are available, this drug is widely used in veterinary medicine. There is some controversy about the appropriate dosage regimen for this human-labeled product in animals, but many clinicians gain acceptable clinical results using the same dosage as for sulfadiazine.

A 5/1 fixed combination of sulfamethoxazole/trimethoprim is available as tablets and a pediatric suspension. The available single-strength tablets contain 400 mg and 80 mg, and the double-strength tablets contain 800 mg and 160 mg, of sulfamethoxazole and

trimethoprim, respectively. The pediatric oral suspension contains 40 mg of sulfamethoxazole per milliliter and 8 mg of trimethoprim per milliliter. The dosage for bacterial infections and coccidiosis in dogs and cats is 30 mg/kg once or twice daily for 14 to 21 days and may be indicated in severe coccidial infections.

Sulfaquinoxaline

Sulfaquinoxaline is a sulfonamide approved for use in chickens, turkeys, and cattle for control and treatment of coccidia. It is not well absorbed from the gastrointestinal tract. Sulfaquinoxaline is available as a water medication (Sul-Q-Nox). It should be mixed according to the label, which provides cattle with a target dose of 6 mg/lb/day. Chickens should receive 10 to 45 mg/pound/day. Turkeys should be given 3.5 to 55 mg/pound/day. Treatment should be administered for 3 to 5 days in cattle and for 2 to 3 days in chickens and turkeys. Make a fresh solution every day. Do not give sulfaquinoxaline to lactating dairy cattle or to veal calves. It should not be used within 10 days of slaughter.

ANTHELMINTICS

Several changes have occurred since the last edition of this volume was published (Bowman, 2003), most notably the more widespread use of ivermectin and the emergence of other macrocyclic lactones. Drug manufacturers have discontinued production of many tried and true anthelmintics such as Task Capsules (dichlorvos) and Filaribits (diethylcarbamazine). For simplicity, these drugs do not appear in the current edition. Earlier editions of this text should be consulted for information about discontinued products.

An exhaustive review of the pharmacology, mechanism of action, pharmacokinetics, and efficacy of anthelmintics is outside the scope of this book. We have included a few key references in the text to help the veterinarian understand the mechanism of action (Martin, 1997). For more exhaustive information on anthelmintics, two excellent works should be consulted (Arundel et al, 1985; Campbell and Rew, 1985). A compendium of products approved by the FDA and commercially available can be found in the *Compendium of Veterinary Products* (Bayley, 2008).

Gastrointestinal parasites are among the most common infectious agents that veterinarians must manage (Blagburn et al, 1996). In the landmark parasite prevalence study, Blagburn and colleagues evaluated more than 6000 canine fecal specimens from all 50 states and the District of Columbia. The results indicate that internal parasites remain common in dogs. Nationwide, 36% of the samples tested were positive for roundworm, *Toxocara canis;* hookworm, *Ancylostoma caninum;* or whipworm, *Trichuris vulpis*. Even more surprising, 52% of the samples from the southwestern United States were positive for at least one of the important nematodes. Although these parasites affect the health of dogs, several are also zoonotic pathogens.

Much research has focused on defining the mechanism of action for anthelmintics. It is hoped that this information will lead eventually to new therapeutic agents. Several reviews discuss this exciting research (Londershausen, 1996; Martin, 1993; Martin, 1997). The current information has shed new light on mechanisms of drug action and in many cases has changed our opinion on how these drugs work.

Anthelmintics approved by the FDA and still commercially available are grouped together by class according to their generic names.

Macrocyclic Lactones

Macrocyclic lactones (or macrolides) have revolutionized the control of parasites in both man and animal. Ivermectin is the best-known agent in this class, which includes avermectins and milbemycins. They are generally regarded as the most effective and least toxic parasiticides yet developed. These products are all similar in that they are antibiotics produced by streptomycete microorganisms, and they have large macrocyclic structures. Although originally thought to act by disturbing GABA-mediated neurotransmission, it is now known that they all bind with high affinity to a glutamate-gated chloride channel (Arena et al, 1991; Martin, 1993; Martin, 1997; Shoop, Mrozik, and Fisher, 1995; Vercruysse and Rew, 2002; Wolstenholme and Rogers, 2005). The macrocyclic lactones bind to glutamate receptors that trigger chloride influx, which hyperpolarizes the parasite neuron and prevents initiation or propagation of normal action potentials. The net effect is paralysis and death of the target parasite.

The macrocyclic lactones have revolutionized treatment of parasitic disease. In general, they are highly effective at low doses, are very safe, and provide true broad-spectrum activity against nematodes and arthropods. Commercially they have crushed the competition. Many conventional drugs that are direct competitors of this class were soon retired from common use and eventually

discontinued by the manufacturer. Many of the old drugs are casualties of the "macrocyclic revolution."

Despite their beneficial activities, macrocyclic lactones have several flaws. They are ineffective against cestodes and trematodes and they are sometimes expensive. The U.S. patent on ivermectin has now expired; this has allowed generic competitors to enter the market, which is now changing cost of treatment with ivermectin.

The literature surrounding these products is overwhelming, but there are several good reviews that pare the literature down to comprehendible levels (Bennett, 1986; Campbell, 1989; Shoop, Mrozik, and Fisher, 1995; Vercruysse and Rew, 2002).

Doramectin

Doramectin is a fermentation product from a mutant strain of *Streptomyces avermitilis*, and its spectrum of action is similar to that of avermectin B_1, although it has an elimination half-life about twice that of ivermectin (Shoop, Mrozik, and Fisher, 1995; Friis and Bjoern, 1997).

Cattle

Doramectin (Dectomax, Dectomax Pour-On) provides broad-spectrum activity against bovine parasites. When injected subcutaneously in cattle at a dose of 0.2 mg/kg or applied topically at a dose of 0.5 mg/kg, it is effective against brown stomach worm, *Ostertagia ostertagi, Ostertagia lyrata;* barber pole worm, *Haemonchus placei;* small stomach worm, *Trichostrongylus axei, Trichostrongylus longispicularis;* bankrupt worm, *Trichostrongylus colubriformis;* small intestinal worm, *Cooperia oncophora, Cooperia punctata, Cooperia*

pectinata, Cooperia surnabada; hookworm, *Bunostomum phlebotomum;* intestinal threadworm, *Strongyloides papillosus;* nodular worm, *Oesophagostomum radiatum;* whipworm, *Trichuris* species; lungworm, *Dictyocaulus viviparus;* eyeworm, *Thelazia* species; cattle grub, *Hypoderma bovis, Hypoderma lineatum;* mange mite, *Psoroptes bovis, S. scabiei;* sucking lice, *Haematopinus eurysternus, Linognathus vituli,* and *Solenopotes capillatus* (Eddi et al, 1993; Gonzales et al, 1993; Goudie et al, 1993; Hendrickx et al, 1993; Jones et al, 1993; Kennedy and Phillips, 1993; Logan et al, 1993; Moya-Borja et al, 1993a; Reinemeyer and Courtney, 2001a; Vercruysse et al, 1993; Weatherley et al, 1993; Wicks et al, 1993). Rather surprising is doramectin's activity against the screwworm *Cochliomyia hominivorax*, which is missing from other macrocyclic agents (Moya-Borja et al, 1993b). The injection should not be used within 35 days of slaughter. The pour-on product also has activity against biting lice *Damalinia bovis* and the mange mite *Chorioptes bovis*. The injectable solution should not be used in cattle within 30 days of slaughter, and the pour-on product should not be used in cattle within 45 days of slaughter.

Swine

Doramectin injection (Dectomax) is also approved for use in swine. Injections of 0.3 mg/kg are effective against large roundworm, *Ascaris suum;* nodular worm, *Oesophagostomum dentatum, Oesophagostomum quadrispinulatum;* small stomach worm, *Hyostrongylus rubidus;* threadworm, *Strongyloides ransomi;* kidney worm, *Stephanurus dentatus;* lungworm, *Metastrongylus* species; mange mite, *S. scabiei* var. *suis;* and sucking lice, *Haematopinus suis* (Arends, Skogerboe, and Ritzhaupt, 1997a; Arends, Skogerboe, and

Ritzhaupt, 1997b; Lichtensteiger et al, 1997; Logan, Weatherley, and Jones, 1997; Saeki et al, 1995; Stewart, Fox, and Wiles, 1996a; Stewart, Fox, and Wiles, 1996b). It should not be used in swine within 24 days of slaughter.

Eprinomectin

Eprinomectin is a second-generation macrocyclic lactone. It was synthesized from avermectin B_1 by the same group that discovered ivermectin. The paper that describes the effort to find eprinomectin is a beautiful description of targeted research and should be read by any scientist interested in understanding the pharmaceutical research process (Shoop et al, 1996a). Eprinomectin is synthesized from a fermentation product of *S. avermitilis*. It has extremely broad-spectrum activity, is formulated in an easy-to-apply pour-on formulation, and, most surprisingly, has zero time withdrawal for meat and milk. It is the only macrocyclic that can be used in lactating dairy cattle because it partitions away from milk (Shoop et al, 1996b).

Cattle

Eprinomectin (Eprinex) is approved in a topical formulation, which is applied at 0.5 mg/kg. It is effective against all common cattle nematodes, including barber pole worm, *H. placei;* brown stomach worm, *O. ostertagi, O. lyrata, Ostertagia leptospicularis;* small intestinal worm, *C. oncophora, C. punctata, C. surnabada;* small stomach worm, *T. axei, T. longispicularis;* bankrupt worm, *T. colubriformis;* thread-necked intestinal worm, *Nematodirus helvetianus;* nodular worm, *O. radiatum;* hookworm, *B. phlebotomum;* intestinal threadworm, *S. papillosus;* lungworm, *D. viviparus;* and

whipworm, *Trichuris* species (Cramer, Eagleson, and Farrington, 1997; Gogolewski et al, 1997b; Reid, Eagleson, and Langholff, 1997; Yazwinski et al, 1997). The efficacy is not affected by coat length or by rain or weather (Gogolewski et al, 1997a). Not surprisingly, eprinomectin is also effective against many arthropod ectoparasites, including cattle grubs, *H. lineatum, H. bovis;* sucking lice, *L. vituli, H. eurysternus, S. capillatus;* biting lice, *Damalinia (Bovicola) bovis;* mange mite, *C. bovis, S. scabiei;* and horn fly, *Haematobia irritans* (Eagleson, Holste, and Pollmeier, 1997; Eagleson et al, 1997; Thompson et al, 1997).

Ivermectin

Ivermectin was the first commercially available macrolide. The avermectins were isolated from the fermentation broth of *S. avermitilis*. The discovery of the anthelmintic activity was made by administering the actinomycetic broth to mice infected with the nematode *N. dubius*. Ivermectin is effective against many nematodes and arthropods. It is very effective against immature heartworm, *D. immitis*, but has minimal effect on adult heartworms. The thick-necked intestinal worm, *N. helvetianus*, in cattle is one of the least sensitive worms; about 85% efficacy was reported in the literature. The suggested dose levels are 0.2 mg/kg for cattle, sheep, and horses and 0.3 mg/kg for swine. The current literature contains reports of use against more that 300 species of parasites in a very long list of hosts.

Administration of ivermectin to pregnant rats, mice, and rabbits produced teratism in fetuses only at or near maternotoxic doses. There was no teratogenesis in cattle, sheep, and dogs when

ivermectin was administered to pregnant animals at four times the recommended dose. Although toxicity for aquatic animals is high, the binding of ivermectin in soil reduces its concentration to levels that have no impact on the quality of the environment. The acute oral LD_{50} of ivermectin in mice varied from 11.6 to 87.2 mg/kg, and the LD_{50} for rats was 42.8 to 52.8 mg/kg. In a 14-week study with rats, the “no-effect” level was 0.4 mg/kg.

Although originally believed to act by disturbing GABA-mediated neurotransmission, it is now known that ivermectin binds with high affinity to a glutamate-gated chloride channel (Martin, 1993; Shoop, Mrozik, and Fisher, 1995). Ivermectin binds to the glutamate receptor, which triggers chloride influx, which hyperpolarizes the parasite neuron and prevents initiation or propagation of normal action potentials. The net effect is paralysis and death of the target parasite. In arthropods, ivermectin inhibits transmission of signals at the neuromuscular junctions by the same mechanism. Death results from paralysis in both nematodes and arthropods.

Horses

Ivermectin (Eqvalan paste or liquid) has a broad spectrum of activity against nematodes and arthropod parasites of horses and is administered orally at 0.2 mg/kg of body weight. It is used for the treatment and control of large strongyles: adult *Strongylus equinus;* adult, arterial, and migrating larval stages of *Strongylus vulgaris;* adult and migrating tissue stages of *Strongylus edentatus;* adult *Triodontophorus* species (including *Triodontophorus brevicauda, Triodontophorus serratus,* and *Craterostomum acuticaudatum*); and small strongyles, including those resistant to some benzimidazole

class compounds: *Coronocyclus* species (including *Coronocyclus coronatus, Coronocyclus labiatus,* and *Coronocyclus labratus*); adult and fourth-stage larvae of *Cyathostomum* species (including *Cyathostomum catinatum* and *Cyathostomum pateratum*); *Cylicocyclus* species (including *Cylicocyclus insigne, Cylicocyclus leptostomum, Cylicocyclus nassatus,* and *Cylicocyclus brevicapsulatus*); *Cylicodontophorus* species; *Cylicostephanus* species (including *Cylicostephanus calicatus, Cylicostephanus goldi, Cylicostephanus longibursatus,* and *Cylicostephanus minutus*); *Petrovinema poculatum;* adult and fourth-stage larvae of pinworm *Oxyuris equi;* adult and larval stages of ascarid *Parascaris equorum;* adult hairworm, *T. axei;* adult stomach worm, *Habronema muscae;* botfly larvae, *Gasterophilus intestinalis* and *Gasterophilus nasalis;* adult and fourth-stage larvae of lungworm, *Dictyocaulus arnfieldi;* threadworm, *Strongyloides westeri;* summer sore caused by *Habronema* and *Draschia* species; and dermatitis caused by microfilariae of neck threadworm *Onchocerca cervicalis*. On occasion, treated horses exhibit edematous reactions caused by a massive release of parasitic antigens.

Oral administration of three times the recommended dose of ivermectin was well tolerated by horses. Pregnant mares treated orally with 0.6 mg of ivermectin per kilogram throughout the organogenesis period gave birth to normal, healthy foals. Treatment with 0.6 mg of ivermectin per kilogram did not affect the sexual behavior of stallions, and the quality of semen was not affected. Ivermectin may be used in horses of all ages, including mares at any stage of pregnancy, and breeding stallions.

Cattle

Ivermectin (Ivomec) is formulated as a 1% (10 mg/mL) liquid for subcutaneous injection at a dose level of 0.2 mg/kg of body weight. The subcutaneous administration of ivermectin affords excellent efficacy against adult and larval stages of brown stomach worm, *O. ostertagi* (including inhibited forms), *O. lyrata;* barber pole worm, *H. placei;* small stomach worm, *T. axei;* bankrupt worm, *T. colubriformis;* small intestinal worm, *C. oncophora, C. punctata, C. pectinata;* nodular worm, *O. radiatum;* hookworm, *B. phlebotomum;* adult thread-necked intestinal worm, *N. helvetianus*, *Nematodirus spathiger;* adult intestinal threadworm, *S. papillosus;* and lungworm, *D. viviparus*. Ivermectin injection is highly active against cattle grubs (first, second, and third instars) *H. bovis* and *H. lineatum;* sucking lice, *L. vituli, H. eurysternus, S. capillatus;* and mange mite, *Psorptes ovis,* and *S. scabiei* var. *bovis*. Injectable ivermectin affords consistently good efficacy against sucking lice and mites. The efficacy of ivermectin against biting lice is erratic. Ivermectin is also active against adult *Parafilaria bovicola,* which causes summer bleeding, and adult and immature eyeworm, *Thelazia rhodesi*. The drug is absorbed, widely distributed in the tissues, and excreted in the feces as unaltered ivermectin that may prevent the development of coprophilic larvae. Ivermectin is slowly eliminated from the body.

Ivermectin up to 1.2 mg/kg was well tolerated by cattle. Higher doses resulted in transient localized swellings at the injection site. Cattle injected with 8 mg/kg became recumbent within 24 hours after treatment, and three animals died. Ivermectin at a dose of 0.4 mg/kg was administered to pregnant cows 7 to 56 days after insemination. There were no adverse effects on the cows and no teratogenic effects in the calves that were delivered. No adverse

effects were observed in the breeding performance or semen quality of bulls treated with ivermectin at 0.4 mg/kg. The withdrawal time for cattle given the injectable ivermectin is 35 days. Do not use in female dairy cattle of breeding age, and do not use in lactating dairy cattle. Do not use in veal calves. The rapid death of cattle grubs after administration of ivermectin may result in acute esophagitis and posterior paresis as a consequence of spinal cord hemorrhages.

Ivermectin is also available in a pour-on formulation for application to cattle. It contains 5 mg of ivermectin per milliliter and is applied at a rate of 1 mL/10 kg. The pour-on formulation is approved for the removal of brown stomach worm, *O. ostertagi;* barber pole worm, *H. placei;* small stomach worm, *T. axei;* bankrupt worm, *T. colubriformis;* small intestinal worm, *C. oncophora, C. punctata, C. surnabada;* adult intestinal threadworm, *S. papillosus;* nodular worm, *O. radiatum;* whipworm, *Trichuris* species; lungworm, *D. viviparus;* cattle grub, *H. bovis, H. lineatum;* mange mites, *S. scabiei* var. *bovis;* sucking lice, *L. vituli, H. eurysternus, S. capillatus;* biting lice, *D. bovis,* and horn fly *H. irritans*. Cattle must not be treated with topical ivermectin within 48 days of slaughter for human consumption. Because a withdrawal time in milk has not been established, do not use ivermectin in female dairy cattle of breeding age. Do not use in veal calves.

Sheep

Ivermectin (Ivomec) drench at a dose level of 0.2 mg/kg is approved for the treatment and control of the adult and fourth-stage larvae of barber pole worm, *Haemonchus contortus, H. placei* (adults only); brown stomach worm, *Telodorsagia (Ostertagia) circumcincta;* small

stomach worm, *T. axei;* bankrupt worm, *T. colubriformis;* Cooper's worm, *C. oncophora* (adults only), *Cooperia curticei;* nodular worm, *Oesophagostomum columbianum, Oesophagostomum venulosum* (adults only); thread-necked intestinal worm, *Nematodirus battus, N. spathiger;* intestinal threadworm, *S. papillosus* (adults only); large-mouth bowel worm, *Chabertia ovina* (adults only); whipworm, *Trichuris ovis* (adults only); lungworm, *Dictyocaulus filaria*, and all the larval stages of the nasal bot *Oestrus ovis*. There is a label limitation stating that sheep should not be treated within 11 days of slaughter.

Overseas, injectable ivermectin is used for the treatment of psoroptic mange. Numerous reports indicate that ivermectin is highly active against benzimidazole-resistant populations of *Haemonchus, Trichostrongylus*, and *Ostertagia* organisms, although recent evidence suggests that ivermectin-resistant strains are now developing in sheep and goats. The USP monograph cautions against the routine use of ivermectin oral solution in goats in order to delay the onset of parasite resistance (USP, 2006). The unapproved parenteral dose in sheep and goats is 0.2 mg/kg by subcutaneous injection.

Swine

Ivermectin 1% injection (Ivomec) is administered subcutaneously in the neck area at a dose level of 0.3 mg/kg. It is indicated for the treatment and control of adult and fourth-stage larvae of large roundworm, *A. suum;* small stomach worm, *H. rubidus;* nodular worm, *Oesophagostomum* species; threadworm, *S. ransomi* (including the somatic larvae); adult lungworm *Metastrongylus* species; sucking

lice, *H. suis;* and mange mites, *S. scabiei* var. *suis.* The colostral transmission of *S. ransomi* can be prevented by injecting ivermectin into sows 7 to 14 days before farrowing. Ivermectin was shown to be highly active against the adult and fourth-stage larvae of the swine kidney worm *S. dentatus.* Swine should not be treated within 18 days of slaughter. In short-term studies, ivermectin was injected into swine at up to 30 mg/kg without fatal sequelae, but lethargy, ataxia, labored breathing, and other toxicity signs were noted. No toxic effects were observed in sows treated with 0.6 mg/kg during the first month of gestation, and no teratogenic effects were observed in the litters. Also, no adverse effects were observed in the breeding performance or semen quality of boars treated with 0.6 mg of ivermectin per kilogram.

Ivermectin is also available in a premix for administration in feed (Ivomec Premix for Swine). It is formulated to provide 0.1 mg of ivermectin per kilogram of body weight daily for a maximum of 7 consecutive days. The drug is approved for the treatment of large roundworm, *A. suum;* thick stomach worm, *Ascarops strongylina;* small stomach worm, *H. rubidus;* nodular worm, *Oesophagostomum* species; kidney worm, *S. dentatus;* threadworm, *S. ransomi;* lungworm, *Metastrongylus* species; sucking lice, *H. suis;* and mange mites, *S. scabiei* var. *suis*. Medicated feed should be withdrawn 5 days before slaughter.

American bison and reindeer

Ivermectin (Ivomec) 1% injection is approved by the FDA for the treatment and control of grubs, *H. bovis*, in American bison *(Bison bison)* and for warbles, *Oedemagena tarandi,* in reindeer *(Rangifer*

tarandus). The effective dose is 0.2 mg/kg injected subcutaneously. Do not treat these animals within 8 weeks of slaughter.

Dogs

Ivermectin (Heartgard) tablets and chewable tablets are administered orally at a dose level of 0.006 mg (6 mcg) per kilogram at monthly intervals to prevent the establishment of heartworm, *Dirofilaria immitis*. The initial dose should be given within a month after the first exposure to mosquitoes and throughout the year when mosquitoes are active. The last treatment must be given to dogs within a month after the last exposure to mosquitoes. Ivermectin has minimal activity against the adult heartworm. It is active only against the third and fourth-stage larvae and the circulating microfilariae. Heartgard should not be given to dogs younger than 6 weeks of age.

A single oral dose of ivermectin administered within 2 months after infection prevents the establishment of the worms in the heart. A single dose of 0.05 mg/kg is adequate to clear the circulating microfilariae when given to dogs 4 weeks after the administration of an adulticide. Ivermectin is not approved as a microfilaricide. When ivermectin (6 mg/kg) is given to heartworm-positive dogs over several months, the circulating microfilariae are eliminated, resulting in an occult infection. Thus dogs on monthly ivermectin should be tested with an occult heartworm test (Bowman, 1992; Courtney, Zeng, and Maler, 1998; Lok and Knight, 1995).

Ivermectin as a single subcutaneous injection at 0.2 mg/kg demonstrated high efficacy against immature and adult roundworm, *T. canis;* hookworm, *A. caninum, Ancylostoma braziliense, Uncinaria*

stenocephala; and parasitic threadworm, *Strongyloides stercoralis*. Ivermectin activity against roundworm, *Toxascaris leonina*, and whipworm, *T. vulpis*, is erratic (USP, 2006).

Ivermectin is safe in collies at the approved dose of 0.006 mg (6 mcg) per kilogram. When ivermectin is given at a dose of 200 mg/kg (32 times the label dose), some genetic lines of collies exhibit severe adverse reactions: mydriasis, ataxia, tremors, drooling, paresis, recumbency, excitability, stupor, and coma. A single oral dose of 2 mg/kg and repeated oral doses of 0.5 mg/kg/day for 14 weeks were well tolerated by dogs of other breeds. Mydriasis, depression, tremors, ataxia, coma, and death have been observed after doses in excess of 20 mg/kg in laboratory dogs (Pulliam et al, 1985). No teratism was observed in fetuses when pregnant bitches received repeated oral doses of ivermectin at 0.5 mg/kg.

Ivermectin has been used in the treatment of mange, *D. canis*, at a dosage of 0.4 to 0.6 mg/kg orally daily for 2 to 4 months (Mueller, 2004; Plumb, 2005); this use is not approved and should be applied with caution in collies and other herding breeds.

Several combination products containing ivermectin are available. For more information, see the section on combination products.

Cats

Ivermectin is approved as a heartworm preventive for cats (Heartgard Chewables for Cats). Monthly doses of 0.024 mg (24 mcg) per kilogram are effective in preventing the development of heartworm, *D. immitis* (McTier et al, 1992; Paul et al, 1992). It is also approved for use against hookworm, *Ancylostoma braziliense* and *Ancylostoma tubaeforme* (Nolan et al, 1992; Roberson et al,

1992). A dose of 0.3 mg/kg is required to eliminate roundworm, *Toxocara cati* (Blagburn et al, 1987; Kirkpatrick and Megella, 1987).

Ivermectin is approved in a liposomal formulation (Acarexx). It is approved for the treatment of ear mites, *O. cynotis*, in cats and kittens 4 weeks of age or older. Recent studies have demonstrated activity against the eggs and immature stages of the ear mite (Bowman, Kato, and Fogarty, 2001; Wexler-Mitchell, 2001).

Milbemycin Oxime

Milbemycin oxime was the second macrocyclic lactone to achieve approval by the FDA. It is a fermentation product of *Streptomyces hygroscopicus* subsp. *aureolacrimosis*. The drug has structural similarities to ivermectin and works by the same mechanism of action.

Dogs

Milbemycin oxime tablets (Interceptor) are formulated to deliver 0.5 mg/kg of body weight. When given every 30 days, they are effective in preventing heartworms, *D. immitis* (Bater, 1989; Bradley, 1989; Grieve et al, 1991). The product also kills hookworms, *A. caninum,* and removes and controls roundworm, *T. canis* and *T. leonina,* and whipworm, *T. vulpis* (Blagburn et al, 1992b; Bowman, Johnson, and Hepler, 1990; Bowman et al, 1988; Bowman et al, 1991; USP, 2006). Milbemycin oxime has been extensively tested with regard to safety. It is nontoxic to collies at up to 20 times the recommended dose (Blagburn et al, 1989; Sasaki et al, 1990) and can safely be given to pregnant and nursing animals. Although an LD_{50} was never determined in dogs, the drug was well tolerated when given at 200 mg/kg in a single oral dose.

Milbemycin oxime, like ivermectin, is known to kill heartworm microfilariae and inhibit the release of new microfilariae, so all dogs on routine monthly heartworm prophylaxis should be tested with adult antigen tests (Blagburn et al, 1992a; Bowman, 1992; Courtney, Zeng, and Maler, 1998; Lok and Knight, 1995; Lok et al, 1992).

Some work (Garfield and Reedy, 1992; Miller et al, 1993; Miller et al, 1995b; Mueller, 2004) has shown that milbemycin oxime is effective in curing amitraz-resistant mange mite *D. canis* when given at a dosage of 1 to 2 mg/kg daily for 60 to 90 days. It is also highly effective against mange mite *S. scabiei* when given orally at 1 mg/kg every other day for 10 to 14 days (Bourdeau, Blumstein, and Ibisch, 1997). It is interesting that milbemycin oxime is effective against the nasal mite *Pneumonyssoides caninum* when given at 0.5 to 1 mg/kg once a week for 3 weeks (Gunnarsson et al, 1997). Use of milbemycin against nasal mites is not approved by the FDA.

Cats

Approved for use in cats (Interceptor), milbemycin oxime is effective against heartworm, *D. immitis*, at a dose of 0.5 mg/kg every 30 days (Stewart, Hepler, and Grieve, 1992) and against hookworm, *A. tubaeforme;* it is also effective against roundworm, *T. cati*, when given at a dose of 1.5 mg/kg (Blagburn et al, 1992c; USP, 2006).

Milbemite Otic Solution is a 0.1% solution of milbemycin oxime approved for the treatment of ear mite, *O. cynotis,* infestations in cats and kittens 8 weeks of age or older. It is effective against all life stages of the ear mite (*Milbemite Otic Solution*, 2000).

Turtles

It is interesting to note that milbemycin oxime is apparently nontoxic in turtles and proved somewhat effective in a small study conducted on red-eared sliders *(Chrysemys scripta elegans)* and Gulf Coast box turtles *(Terrapene carolina major)* (Bodri, Nolan, and Skeeba, 1993). It is not approved for this use.

Moxidectin

Moxidectin is a chemically altered product of *Streptomyces cyaneogriseus noncyanogenus*. It has a similar range of activity and safety margin as ivermectin.

Horses

Moxidectin 2% gel (Quest Gel) can be given by oral administration (0.3 mg/kg) against large strongyles, *S. vulgaris* (adult L4/L5), *S. edentatus* (adult, tissue stages), *T. brevicauda* (adult), *T. serratus* (adult); small strongyles, *Cyathostomum* species (including *C. catinatum* and *C. pateratum*), *Cylicostephanus* species (including *C. calicatus, C. goldi, C. longibursatus,* and *C. minutus*), *Cylicocyclus* species (including *C. insigne, C. leptostomum, C. nassatus, and C. radiatus*), *Coronocyclus* species (including *C. coronatus, C. labiatus, C. labratus, Gyalocephalus capitatus*, and *P. petrolatu*); ascarid *P. equorum* (adults and L4); pinworm, *O. equi;* hairworm, *T. axei* (adult); stomach worm, *H. muscae;* and botfly larva, *G. intestinalis* and *G. nasalis* (Bello and Laningham, 1994; Lyons et al, 1992; New Quest Gel dewormer and boticide, Anon, 1997a; Slocombe and Lake, 1997; Taylor and Kenny, 1995; Vercruysse et al, 1997b). It seems to be particularly effective against encysted small strongyles. Moxidectin is safe for use in mares during breeding, gestation, and lactation, and for foals older than 6 months.

Cattle

Moxidectin (Cydectin) 1% injectable solution is approved by the FDA for use in beef cattle and nonlactating dairy cattle. It is injected subcutaneously at a dose of 0.2 mg/kg for treatment and control of brown stomach worm, *O. ostertagi* (adult and L4); barber pole worm, *H. placei* (adult); small stomach worm, *T. axei* (adult); bankrupt worm, *T. colubriformis* (L4); small intestinal worm, *C. oncophora* (adult and L4), *C. punctata* (adult and L4), *C. surnabada* (adult and L4); nodular worm, *O. radiatum* (adult and L4); whipworm, *Trichuris* species (adult); lungworm, *D. viviparus;* cattle grub, *H. bovis, H. lineatum;* mange mite, *P. ovis;* sucking lice, *L. vituli,* and *S. capillatus* (Eysker and Boersema, 1992; Ranjan et al, 1992; Scholl, Guillot, and Wang, 1992; Williams, Barras, and Wang, 1992; Williams et al, 1992; Zimmerman, Hoberg, and Pankavich, 1992). Moxidectin injection should not be given to cattle less than 8 weeks old and not within 21 days of slaughter. The product should not be given to veal calves or lactating dairy cattle.

A 0.5% pour-on formulation of moxidectin (Cydectin) is approved in the United States at a dose of 0.5 mg/kg to control all the parasites previously mentioned along with additional species of small intestinal worm, *C. pectinata* (adult), *Cooperia spatulata* (adult); hookworm, *B. phlebotomum* (adult); thread-necked intestinal worm, *N. helvetianus* (adult and L4); mange mite, *Chorioptes bovis;* sucking lice, *H. eurysternus;* biting lice, *Bovicola (Damalinia) bovis;* and horn fly, *H irritans* (Morin et al, 1996; Vercruysse et al, 1997a).

Moxidectin pour-on, is approved for use in beef and dairy cattle; there is neither a preslaughter withdrawal period or milk discard time. Meat and milk may used at any time after treatment. Do not use in veal calves or preruminating calves.

Sheep

Moxidectin is approved in a 1% oral drench (Cydectin) for use in sheep. When given orally at a dose of 0.2 mg/kg, it is effective in removing adult and L4 stages of barber pole worm, *H. contortus;* brown stomach worm, *Teladorsagia (Ostertagia) circumcincta, Teladorsagia (Ostertagia) trifurcata;* small stomach worm, *T. axei, T. colubriformis, Trichostrongylus vitrinus;* Cooper's worm, *C. curticei, C. oncophora;* nodular worm, *O. columbianum, O. venulosum;* thread-necked intestinal worm, *N. battus, Nematodirus filicollis,* and *N. spathiger* (Craig et al, 1992). Sheep treated with moxidectin oral solution should not be slaughtered within 7 days of treatment. Moxidectin should not be used in sheep that are producing milk for human consumption. The USP monograph cautions against the routine use of moxidectin oral solution in goats in order to delay the onset of parasite resistance (USP, 2006).

Dogs

Moxidectin is known to be very active against heartworms *(D. immitis)* and gastrointestinal nematodes. Proheart 6 is a sustained-release formulation that provides therapeutic levels of moxidectin for 6 months after injection. In 2001, Proheart 6 was approved in

the United States for prevention of heartworm *(D. immitis)* and for the treatment of existing larvae and adult hookworm *(A. caninum)* infection (Blagburn, Paul et al, 2001; Lok, Knight et al, 2001; McCall, Supakorndej et al, 2001).

In 2004, the manufacturer voluntarily recalled Proheart 6 at the request of the FDA, which was concerned about the incidence of adverse reactions. These reactions included reports of anaphylaxis, liver disease, autoimmune hemolytic disease, convulsions, and death. The incidence approached 5.2 cases per 10,000 doses given in 2002 (FDAH, 2008). Extensive studies conducted by the manufacturer showed that a mixture of residual solvents were to blame for the adverse reactions. Product marketed outside the United States with low levels of residual solvent demonstrated improved safety over the original production batches. In addition, the manufacturer and the FDA have formulated a "Risk Minimization Action Plan (RiskMAP)" that permitted the product to be reintroduced to the United States market in 2008 (FDAH, 2008). The RiskMAP requires that practicing veterinarians complete web-based training before using the product. Key components of the training are to make veterinarians aware of which patients are suitable candidates for treatment and to require pretreatment bloodwork, complete record keeping, and a commitment to report adverse reactions promptly. The RiskMAP also requires that pet owners sign a consent form before injection of the product. The

RiskMAP program is similar to other programs applied in human medicine for important life-saving drugs.

The manufacturer states that Proheart 6 is generally well tolerated. The product is not to be used in sick, debilitated, or underweight animals; animals with a history of weight loss; or within a month of vaccination. Proheart 6 is to be used with caution in dogs with preexisting allergic disease. A small percentage of dogs show mild, transient swelling or itching at the injection site. Although rare, allergic, digestive, hematologic, or neurologic reactions may occur.

Time will tell if the reintroduction of this important heartworm preventative under the RiskMAP will be embraced by practicing veterinarians and their patients.

Selamectin

Selamectin is a novel endectocide that is prepared by semisynthetic modification of doramectin (Bishop et al, 2000). It is the first macrocyclic lactone to provide activity against internal and external parasites of dogs without toxicity in collies.

Dogs and cats

Selamectin topical solution (Revolution) is formulated for topical application in dogs and cats. It is approved for use in dogs that are at least 6 weeks old and cats that are at least 8 weeks old. The stated dose is a minimum of 6 mg/kg every 30 days. Selamectin topical solution is approved for control of external parasites including the elimination and control of fleas, *Ctenocephalides felis,*

and ear mites, *O. cynotis* (Boy et al, 2000; McTier et al, 2000a; McTier et al, 2000b; Shanks et al, 2000a; Shanks et al, 2000b; Six et al, 2000a). In dogs it is approved for the treatment and control of sarcoptic mange, *S. scabiei*, and the American dog tick, *D. variabilis* (Jernigan et al, 2000; Shanks et al, 2000c). It is especially known for the prevention of heartworm, *D. immitis,* in both dogs and cats (Boy et al, 2000). It is not effective in clearing microfilariae. Although unapproved, selamectin is also effective against the roundworm, *T. canis* (USP, 2006). In cats it is also effective in the treatment and control of hookworm, *A. tubaeforme,* and roundworm, *T. cati* (McTier et al, 2000b; Six et al, 2000b). All this activity is provided in a convenient topical product that demonstrates a good margin of safety in both dogs and cats (Krautmann et al, 2000; Novotny et al, 2000).

Benzimidazoles

The benzimidazoles represent a large family of broad-spectrum agents that have been used widely for many years in a broad array of animal species. Excellent review articles (Campbell, 1990; Lacey, 1990; Loukas and Hotez, 2006; Martin, 1997; McKellar and Scott, 1990) discuss the history, mode of action, and spectrum of activity of this useful class of anthelmintics.

Thiabendazole was the first benzimidazole discovered, and it represented a major step forward when it became available more than 30 years ago. At the time of its introduction, thiabendazole was a true broad-spectrum product that was very safe to the host animal.

Since that time, parasite resistance to the benzimidazoles has been discovered in several species.

Considerable effort has been devoted to determining the mechanism by which the benzimidazoles act on parasites. Conventional wisdom holds that benzimidazoles bind to tubulin molecules, which inhibits the formation of microtubules and disrupts cell division (Frayha et al, 1997; Martin, 1997; Reinemeyer and Courtney, 2001a). It has a much higher affinity for nematode tubulin versus mammalian tubulin, thus providing selective activity against parasites. Evidence also indicates that the benzimidazoles can inhibit fumarate reductase, which blocks mitochondrial function, depriving the parasite of energy and thus resulting in death.

The benzimidazoles are poorly soluble and therefore are generally given by mouth. In general, they are more effective in horses and ruminants because of their slow transit through the cecum and rumen. The dose is usually more effective when divided, thus prolonging the contact time with the parasite. Two members of the benzimidazole group (albendazole and oxfendazole) have been found to be teratogenic, which limits their use in pregnant animals.

For simplicity the probenzimidazole drug febantel is included in this section. It is a nonbenzimidazole drug that is metabolized to a benzimidazole. It therefore shares a similar efficacy and mechanism of action with the other benzimidazoles.

Albendazole

Albendazole, the newest benzimidazole, has potent broad-spectrum anthelmintic activity. It offers a wide margin of safety in cattle when used according to the label specifications.

Albendazole has demonstrated a broad spectrum of anthelmintic activity against gastrointestinal nematodes; lung nematodes, including inhibited larval forms; cestodes; and lung and liver trematodes in farm animals, companion animals, and humans. Albendazole (Zentel) is used overseas for the treatment of intestinal helminth infections, hydatid disease, and cysticercoses of humans.

Cattle

Albendazole is available in oral paste and oral suspension for cattle (Valbazen). It is administered orally at a dose level of 10 mg/kg for the removal and control of adult and larval stages of internal parasites including barber pole worm, *H. contortus, H. placei;* brown stomach worm, *O. ostertagi*; adult and fourth-stage inhibited larvae of small stomach worm, *T. axei;* bankrupt worm, *T. colubriformis,* thread-necked intestinal worm, *N. spathiger, N. helvetianus;* small intestinal worm, *C. punctata, C. oncophora;* hookworm, *B. phlebotomum;* nodular worm, *O. radiatum;* lungworm, *D. viviparus;* tapeworm, *Moniezia benedeni, Moniezia expansa;* and adult liver fluke, *Fasciola hepatica* (Bogan and Armour, 1987; Prichard, 1986; Prichard, 1987).

The safety of albendazole in single and repeated treatments was evaluated in healthy and parasitized cattle. A single dose of 75 mg/kg of body weight was well tolerated. Albendazole was

embryotoxic when administered to cows at a dosage rate of 25 mg/kg during the first 7 to 17 days of gestation. The conception rate of cows treated after the twenty-first day of gestation was comparable to that in controls, and all cows gave birth to normal calves.

In the United States, cattle must not be slaughtered within 27 days after treatment. Also, albendazole should not be used in female dairy cattle of breeding age, and the label cautions that the drug should not be given to pregnant cows during the first 45 days of gestation.

Sheep

Albendazole 11.36% suspension (Valbazen) is FDA approved as an oral drench for sheep. The product is administered orally at 7.5 mg/kg for the removal and control of adult liver fluke, *F. hepatica, Fasciola magna;* common tapeworm, *M. expansa;* fringed tapeworm, *Thysanoma actinioides;* brown stomach worm, *Telodorsagia (Ostertagia) circumcincta, Marshallagia marshalli;* barber pole worm, *H. contortus;* small stomach worm, *T. axei;* thread-necked worm, *N. spathiger, N. filicollis;* Cooper's worm, *C. oncophora;* bankrupt worm, *T. colubriformis;* nodular worm, *O. columbianum;* large-mouth bowel worm; *C. ovina;* and lungworm, *D. filaria* (McKellar and Scott, 1990). Albendazole at 15 mg/kg is used overseas for the treatment of small liver fluke *Dicrocoelium dendriticum*. The maximum tolerated dose in sheep is reported to be about 37.5 mg/kg.

Albendazole may induce fetal skeletal abnormalities when administered at a dose level of 11 mg/kg or more to ewes during the first 10 to 17 days of pregnancy. No untoward effects have been reported after its use in many thousands of sheep, however.

Warning: Care should be taken to adhere to recommended dosages, particularly when treating ewes during the first month of pregnancy. Do not give to ewes during the first 30 days of pregnancy or for 30 days after removal of rams. Sheep should not be treated within 7 days of slaughter.

Dogs and cats

Albendazole is not approved for use in dogs and cats. Dogs treated with 50 mg/kg twice daily may have anorexia, and cats treated with 100 mg/kg daily for 14 to 21 days showed weight loss, neutropenia, and mental dullness (Plumb, 2005). Dogs can be treated for lungworm, *Filaroides hirthi*, at a dosage of 25 to 50 mg/kg twice daily for 5 days (Georgi, Slauson, and Theorides, 1978). Bladder worm, *Capillaria plica*, can be treated at a dosage of 50 mg/kg twice daily for 10 to 14 days (Brown and Barsanti, 1989) and lung fluke, *Paragonimus kellicotti,* can be treated at a dosage of 25 mg/kg twice daily for 21 days. The same dosage is effective for *Paragonimus* organisms in cats (Plumb, 2005). Although albendazole is effective against these uncommon parasites, ivermectin and praziquantel are more convenient therapies and likely to be just as effective. More interesting is the use of albendazole against *Giardia* organisms in dogs at 25 mg/kg twice daily for 2 days (Barr et al, 1993). Recent

evidence suggests that this product may cause aplastic anemia in dogs and cats, so it should be used with caution (Plumb, 2005).

Febantel

Febantel is a prodrug that is metabolized to fenbendazole and oxfendazole, which are undoubtedly the active parasiticide molecules (McKellar and Scott, 1990). The oral acute toxic dose in mice, rats, and dogs is more than 10,000 mg/kg. At oral doses above 150 mg/kg daily for 6 days, transient salivation, diarrhea, vomiting, and anorexia may be seen in dogs and cats.

Febantel is not available in a single entity formulation, but combination products of febantel with praziquantel and pyrantel are discussed in the section on combination products.

Fenbendazole

Fenbendazole is a commercially successful benzimidazole that is widely used in domestic animals. The oral LD_{50} for rats and mice is higher than 10,000 mg/kg. Fenbendazole does not have embryotoxic or teratogenic effects in rats, sheep, and cattle. In the rabbit, fenbendazole was fetotoxic but not teratogenic, and no carcinogenesis was observed in lifetime studies in rats and mice. In a 6-month toxicity study in dogs, no effect was observed at 4 mg/kg or less.

Absorbed fenbendazole is metabolized to at least two active metabolites, oxfendazole sulfoxide and oxfendazole sulfone. In

ruminants it is known to undergo enterohepatic cycling, which serves to prolong effective blood levels (USP, 1998).

Fenbendazole is a broad-spectrum anthelmintic with activity against gastrointestinal nematodes and cestodes and lung nematodes in cattle, sheep, goats, and horses. Activity against a variety of helminth parasites in dogs, cats, and many zoo animals also has been reported. In the United States, fenbendazole is approved for control of helminth parasites in horses, cattle, dogs, and zoo animals.

Cattle

Fenbendazole is available in a wide range of formulated products including suspension, premix pellets, granules, paste, and deworming block, and a free-choice mineral supplement (Panacur, Safe-Guard) is administered orally or fed to dairy and beef cattle at 5 mg/kg for the removal and control of adult and larval stages of barber pole worm, *H. contortus, H. placei;* brown stomach worm, *O. ostertagi;* small stomach worm, *T. axei;* hookworm, *B. phlebotomum;* thread-necked worm, *N. helvetianus;* small intestinal worm, *C. punctata, C. oncophora;* bankrupt worm, *T. colubriformis;* nodular worm, *O. radiatum,* and lungworm, *D. viviparous* (Yazwinski et al, 1985; Yazwinski et al, 1989). For the removal of tapeworms, *M. benedeni,* and the inhibited fourth-stage larvae of brown stomach worm, *O. ostertagi*, fenbendazole is used in beef cattle at 10 mg/kg; this dose is not approved for use in dairy cattle. Overseas, the recommended dose level is 7.5 mg/kg, with additional claims of

efficacy against *Trichuris, Strongyloides,* and *Capillaria* species and nematode eggs. The maximum tolerated dose is about 2000 mg/kg. In cattle, fenbendazole is not embryotoxic or teratogenic and does not impair the fertility of bulls (Muser and Paul, 1984). Fenbendazole has been shown to be effective against *Giardia* organisms in calves when given as a single oral dose of 10 mg/kg (O'Handley et al, 1997).

WARNING: Cattle must not be slaughtered within 8 days of medication with fenbendazole, and dairy cattle of breeding age should not be treated with the 10 mg/kg dose. No milk discard is required for dairy cattle treated with the 5 mg/kg dose. Do not use in veal calves.

Horses

Fenbendazole suspension, granules, or paste (Panacur) is administered orally to horses at 5 mg/kg for the control of large strongyles, *S. vulgaris, S. edentatus, S. equinus, Triodontophorus* species; small strongyles, *Cyathostomum, Cylicocyclus, Cylicostephanus,* and *Cylicodontophorus* species; and pinworm, *O. equi*. For the removal of ascarids, *P. equorum*, a dose of 10 mg/kg is recommended. Pregnant mares, stallions, and foals may be treated safely with fenbendazole at the recommended dosages. For the control of fourth-stage larvae of *S. vulgaris*, the unapproved dosage is 10 mg/kg daily for 5 days (Lyons, Tolliver, and Drudge, 1983; Leneau, Haig, and Ho, 1985).

Swine

Fenbendazole is approved as a feed additive (Safe-Guard) for swine. A total dose of 9 mg/kg is divided and fed over a 3- to 12-day period. This dosage removes the adult and immature forms of large roundworm, *A. suum;* small stomach worm, *H. rubidus;* nodular worm, *O. dentatum, O. quadrispinulatum;* whipworm, *Trichuris suis;* kidney worm, *S. dentatus;* and lungworm, *Metastrongylus apri, Metastrongylus pudendotectus* (Biehl, 1986). There is no withdrawal time restriction when pigs are treated at the approved dose.

Dogs

Fenbendazole granules (Panacur) at a dose level of 50 mg/kg are mixed in the feed and given to dogs for 3 consecutive days for the removal of roundworm, *T. canis, T. leonina;* hookworm, *A. caninum, U. stenocephala;* whipworm, *T. vulpis;* and tapeworm, *Taenia pisiformis* (Bowman, 1992; Burke and Roberson, 1978; Burke and Roberson, 1979; Roberson and Burke, 1982; Reinemeyer, 2000). Fenbendazole is approved for use in dogs only at least 6 weeks of age.

Prolonged therapy at 50 mg/kg for several weeks demonstrated excellent activity against the lung fluke, *P. kellicotti* (Dubey et al, 1979). Fenbendazole is safe, and there are no known contraindications for its use in dogs with *Giardia* organisms at a dose of 50 mg/kg (Barr, 2006).

Cats

Fenbendazole is not currently approved for use in cats. When given at an oral dose of 50 mg/kg for 3 consecutive days, it is effective against adult roundworm, *T. cati*, and hookworm, *A. tubaeforme*. Treatment of lungworm, *Aelurostrongylus abstrusus,* and lung fluke, *P. kellicotti,* may require 14 days of therapy (Bowman, 1992; Plumb, 2005; Roberson and Burke, 1980).

Goats

Fenbendazole 10% suspension (Safe-Guard) is approved for use in goats. A single oral dose of 5 mg/kg is recommended for removal of barber pole worm, *H. contortus*, and brown stomach worm, *Telodorsagia (Ostertagia) circumcincta*. Some *Haemonchus* populations apparently have developed resistance to fenbendazole. Do not use in dairy goats producing milk for human consumption. Do not treat goats within 6 days of slaughter.

Sheep

Overseas, oral administration of fenbendazole at 5 mg/kg is recommended for removal of adult and immature stages of gastrointestinal nematodes, cestodes, and lung nematodes. Some *Haemonchus* populations apparently have developed resistance to fenbendazole. The FDA has approved the use of fenbendazole for the treatment of lungworm, *Protostrongylus* species, in Rocky Mountain bighorn sheep.

Zoo animals

Fenbendazole granules (Panacur) are among the few commercial products actually approved by the FDA for use in zoo animals. The label allows use in lions, *Panthera leo;* tigers, *Panthera tigris;* cheetahs, *Acinonyx jubatus;* pumas, *Felis concolor;* jaguars, *Panthera onca;* leopards, *Panthera pardus;* panthers, *Panthera* species; grizzly bears, *Ursus horribilis;* polar bears, *Ursus maritimus;* and black bears, *Ursus americanus.* The label recommends 10 mg/kg orally for 3 consecutive days. It is used to remove ascarids, hookworms, and tapeworms from these species. The actual list of approved parasite indications is rather complex owing to the large number of host species involved and the common parasites found in each. In summary, the following parasites may be controlled in these zoo animals: roundworm, *T. cati, T. leonina, Baylisascaris transfuga;* hookworm, *Ancylostoma* species, *A. caninum;* and tapeworm, *Taenia hydatigena, Taenia krabbei,* and *Taenia taeniaeformis*. The label requires that the drug not be given to game animals 14 days before or during hunting season (Bayley, 2007).

Safety trials in zoo animals dosed at 100 mg/kg (use rate $\times 10$) showed mild signs of anorexia and loose stool. There was no effect on reproduction at this dose.

Fenbendazole (Safe-guard) is also approved by the FDA for use in large wildlife and game animals, including feral swine, *Sus scrofa*; bighorn sheep, *Ovis canadensis canadensis;* and ruminants of the subfamily Antilopinae, gazelles and impala; Hippotraginae, addax and oryx; and Caprinae, mouflon and saiga. These animals are

treated in the feed with 2.5 mg/kg (ruminants), 3 mg/kg (swine), or 10 mg/kg (bighorn sheep) for 3 consecutive days. The label requires that the drug not be given to game animals 14 days before or during hunting season (Bayley, 2007).

Oxfendazole

Oxfendazole is a broad-spectrum benzimidazole approved in the United States for use in cattle. Oxfendazole is metabolized in ruminants to oxfendazole sulfone and fenbendazole, but the primary anthelmintic action is caused by the parent drug (Marriner and Bogan, 1981). Its oral LD_{50} is more than 1600 mg/kg for Beagle dogs and exceeds 6400 mg/kg for rats and mice.

Cattle

Oxfendazole suspension (Synathic) is administered at 2.5 mg/kg by oral dosing syringe. The drug is approved for use in beef and nonlactating dairy cattle. It is effective against lungworm, *D. viviparus;* barber pole worm, *H. contortus, H. placei;* small stomach worm, *T. axei;* brown stomach worm, *O. ostertagi;* nodular worm, *O. radiatum;* hookworm, *B. phlebotomum;* small intestinal worm, *C. punctata, C. oncophora, Cooperia mcmasteri;* and tapeworm, *Moniezia benedeni* (Todd and Mansfield, 1979).

Cattle must not be slaughtered within 7 days of treatment. Because no milk withdrawal time has been established, do not use oxfendazole in female dairy cattle of breeding age.

Oxibendazole

Oxibendazole, a broad-spectrum benzimidazole, is apparently effective against benzimidazole-resistant small strongyles (Drudge, Lyons, and Tolliver, 1979). Its acute oral LD_{50} is greater than 10,000 mg/kg in guinea pigs, hamsters, and rabbits and greater than 32,000 mg/kg in mice. A single dose of 600 mg/kg was well tolerated by cattle, sheep, and ponies, and no adverse reactions were observed in rats and dogs treated with up to 30 mg/kg daily for 3 months. No evidence of teratogenicity or embryotoxicity was observed in rats, mice, sheep, cattle, or horses.

Horses

Oxibendazole paste or suspension (Anthelcide EQ) is administered orally to horses at 10 mg/kg for the removal and control of large strongyles, *S. vulgaris, S. edentatus, S. equinus, Triodontophorus* species; small strongyles, *Cyathostomum, Cylicocyclus, Cylicostephanus, Cylicodontophorus, Gyalocephalus* species; ascarid, *P. equorum;* and pinworms, *O. equi* (Drudge et al, 1981a; Drudge et al, 1981b; Drudge et al, 1985). The dose must be increased to 15 mg/kg for treatment of threadworm, *S. westeri* (DiPetro and Todd, 1987). Oxibendazole is not effective against botfly larvae, but it is highly effective against benzimidazole-resistant cyathostomes (Drudge et al, 1981a; Drudge et al, 1981b; Drudge et al, 1985)

Thiabendazole

The discovery of thiabendazole in 1961 marked the beginning of truly broad-spectrum anthelmintics. The first of the benzimidazoles, thiabendazole is a very safe compound. Its acute oral LD_{50} for rats is

3100 mg/kg. Thiabendazole was used as an anthelmintic in sheep, goats, cattle, horses, swine, and other animals in which it is active against the adults and some immature forms of nematodes, and it inhibited embryonation of nematode eggs. It was also active against fungi and mites. Owing to its wide margin of safety, thiabendazole was used in animals of all ages and in pregnant and debilitated animals. Thiabendazole was available in a variety of pharmaceutical forms (suspension, bolus, paste, feed block, and top-dressing pellets) under various proprietary names. All but one dosage form have left the market in the United States. Thiabendazole is still available in a combination product for use in ears (Tresaderm), which has activity against ear mites, *O. cynotis*, in dogs and cats.

Imidazothiazoles

Tetramisole, discovered in 1966, was the first in the development of the imidazothiazoles. Tetramisole was actually a racemic mixture of two optical isomers. Only the L-isomer (levamisole) has anthelmintic activity. The active isomer was subsequently developed as levamisole. In this class of anthelmintic, only levamisole is still commercially available.

The imidazothiazoles act as nicotinic agonists that disturb the neuromuscular system, thus causing contraction and subsequent tonic paralysis (Coles, 1977; Coles et al, 1975; Martin, 1993). It seems that the nicotinic acetylcholine receptors of invertebrate parasites are essential for neurofunction but differ in physiology and distribution in mammals (Londershausen, 1996). The

imidazothiazoles also are known to interfere with the fumarate reduction system, which plays a key role in mitochondrial energy production (Arundel et al, 1985; Behm and Bryant, 1979).

Levamisole

Levamisole (Levasole) is administered orally as a bolus, oral drench, or injectable solution to cattle, sheep, and swine for the control of gastrointestinal and lung nematodes. An aqueous solution of levamisole phosphate (13.6% or 18.2%) is for subcutaneous injection in cattle.

The oral LD_{50} of levamisole for rats is 480 mg/kg and for mice, 210 mg/kg. Some sheep treated orally with tetramisole at 80 mg/kg died. Subcutaneous injection is more toxic than oral administration. Signs of cholinergic toxicity such as lip licking, salivation, lacrimation, head shaking, ataxia, and muscle tremors may occur at lower dosage levels. At the recommended dosage level, an occasional animal may show transitory muzzle foam and licking of the lips. At twice the therapeutic dosage level, calves may show increased alertness, salivation, head shaking, and muscle tremors.

Cattle

Levamisole hydrochloride administered orally as a drench, bolus, or injectable solution (Levasole) is highly effective against barber pole worm, *H. placei;* brown stomach worm, *O. ostertagi*; small stomach worm, *T. axei, T. longispicularis;* small intestinal worms, *C. oncophora, C. punctata*; thread-necked intestinal worm, *N. spathiger;*

hookworm, *B. phlebotomum;* nodular worm, *O. radiatum;* and lungworm, *D. viviparous* (Baker and Fisk, 1972; Curr, 1977; Lyons et al, 1972; Lyons et al, 1975; Seibert et al, 1986). Arrested early fourth-stage larvae of *Ostertagia* species are refractory to levamisole. The dose for cattle is 8 mg/kg orally and 6 mg/kg by subcutaneous injection of the phosphate salt.

Warning: A slight nonpersistent reaction may occur at the site of levamisole phosphate injection. Cattle should not be slaughtered within 7 days of injection or 2 days of oral medication. Levamisole is not to be used in dairy animals of breeding age to avoid drug residues in milk.

Sheep

Orally administered levamisole drench or bolus (Levasole) removes barber pole worm, *H. contortus;* small stomach worm, *T. axei;* brown stomach worm, *Teladorsagia (Ostertagia) circumcincta;* bankrupt worm, *T. colubriformis;* Cooper's worm, *C. curticei;* thread-necked intestinal worm, *N. spathiger;* hookworm, *Bunostomum trigonocephalum;* nodular worm, *O. columbianum;* large-mouth bowel worm, *C. ovina;* and lungworm, *D. filaria,* at an oral dose of 8 mg/kg (Callinan and Barton, 1979; Craig and Shepherd, 1980). Levamisole is also efficacious against the immature stages of *Haemonchus, Nematodirus, Bunostomum, Oesophagostomum, Chabertia,* and *Dictyocaulus* species.

Warning: Levamisole has an ample therapeutic margin, but an occasional sheep will show side effects (e.g., lip licking, salivation,

increased alertness, muscle tremors), even at the recommended dose. Debilitated sheep appear to be more susceptible to toxicity. Sheep should not be slaughtered within 72 hours of treatment.

Swine

Levamisole administered to swine in water (Levasol) removes large roundworm, *A. suum;* nodular worm, *Oesophagostomum* species; intestinal threadworm, *S. ransomi;* and lungworm *Metastrongylus* species.

Warning: Levamisole should be administered to pigs of weanling to market age after an overnight fast. Breeding pigs do not need to be fasted before treatment. Pigs should not be treated within 3 days of slaughter. Salivation or muzzle foam is occasionally observed after treatment. Pigs infected with adult lungworms may vomit or cough. These reactions may be caused by the expulsion of paralyzed lungworms from the bronchi.

Opossum

Levamisole is unapproved for use in opossums *(Didelphis virginiana)* but is the drug of choice for controlling internal parasites according to the National Opossum Society (NOS). The NOS advocates subcutaneous injection of levamisole at a dose of 6 mg/kg for animals over 200 g body weight (NOS, 2007).

Tetrahydropyrimidines

The tetrahydropyrimidines include the numerous salts of pyrantel, morantel, and the investigational compound oxantel, which is

available outside the United States. They all act as nicotinic agonists, which disturb the neuromuscular system, causing contraction and subsequent tonic paralysis (Aubry et al, 1970; Eyre, 1970; Martin, 1993; Martin, 1997). In vitro experiments indicate that pyrantel is 100 times more powerful than acetylcholine. It seems that the nicotinic acetylcholine receptors of invertebrate parasites are essential for neurofunction but different in physiology and distribution in mammals (Londershausen, 1996).

In ruminants these products are rapidly metabolized to inactive metabolites. Therefore ruminants require higher doses than monogastric animals (Campbell and Rew, 1985).

Pyrantel

Pyrantel is the most widely used of all the tetrahydropyrimidine anthelmintics. The tartrate salt is a white powder, soluble in water, which is used as a powder and pellets in horses and swine. Pyrantel tartrate is well absorbed after oral administration in the rat, dog, and pig. Plasma levels peak within 2 to 3 hours, and the drug is rapidly metabolized and eliminated in the urine.

Pyrantel pamoate is a yellow powder, insoluble in water, which is available as a ready-to-use suspension for dogs and horses and as tablets for dogs. Pyrantel salts are stable in solid form but photodegrade when dissolved or suspended in water, resulting in reduction of potency. Pyrantel pamoate is poorly absorbed from the intestine.

Dogs

Pyrantel pamoate, as a palatable suspension, chewable tablets, or plain tablets (Nemex), is indicated for the removal of roundworm, *T. canis* and *T. leonina,* and hookworm, *A. caninum*, and *U. stenocephala*, from dogs and puppies (Bradley and Conway, 1978; Clark et al, 1991; Jacobs, 1987a; Klein, Bradley, and Conway, 1978; Linquist, 1975; Todd et al, 1975). The recommended dose of 5 mg/kg is administered orally or mixed with a small amount of feed. For animals weighing 2.25 kg or less, the dose is increased to 10 mg/kg. Pyrantel pamoate has been shown to be safe in nursing and weanling pups, pregnant bitches, males used for breeding, and dogs infected with heartworm, *D. immitis*. Its oral LD_{50} is greater than 690 mg/kg in dogs. No significant morphologic changes were induced in dogs given 94 mg/kg daily for 90 days. Pyrantel pamoate is compatible with organophosphates and other antiparasitic and antimicrobial agents.

Horses

Pyrantel pamoate, available for horses as a paste or caramel-flavored suspension (Strongid Paste, Strongid T), administered at 6.6 mg of pyrantel base per kilogram eliminates large strongyles, *S. vulgaris, S. edentatus, S. equinus;* pinworm, *O. equi;* ascarid, *P. equorum*, and several species of the subfamily Cyathostominae, including populations resistant to benzimidazoles (Lyons, Drudge, and Tolliver, 1974). A single oral dose of 13.2 mg of pyrantel base per kilogram was 98% effective against tapeworm, *Anoplocephala*

perfoliata, but this is not an approved dose level (Craig et al, 2003; Lyons et al, 1986).

Pyrantel tartrate (Strongid C) is fed continuously at a dose of 2.6 mg/kg of body weight daily for the prevention of *S. vulgaris* larval migration and the control of adult large strongyles, *S. vulgaris, S. edentatus, Triodontophorus* species; adult and larval small strongyles, *Cyathostomum, Cylicodontophorus, Cylicocyclus, Cylicostephanus,* and *Poteriostomum* species; adult and larval pinworm, *O. equi;* and adult and larval ascarid, *P. equorum* (Cornwell and Jones, 1968; Drudge et al, 1982; Lyons, Drudge, and Tolliver, 1975). Pyrantel is safe for use in horses and ponies of all ages, including sucklings, weanlings, and pregnant mares. It can be used concurrently with insecticides, tranquilizers, muscle relaxants, and central nervous system depressants.

Swine

Pyrantel tartrate (Banminth 48), when fed once at 96 g/ton of complete feed as the sole ration, prevents the migration and establishment of large roundworm, *A. suum;* and nodular worm, *Oesophagostomum* species. When fed to pigs for 3 consecutive days, this medicated feed removes the adults and fourth-stage larvae of *A. suum*. Pyrantel tartrate is also mixed with feed at the rate of 800 g/ton of complete feed and fed to pigs for the treatment of *A. suum* and *Oesophagostomum* species infection for 1 day at the rate of 1 kg feed per 40 kg body weight (1 pound of feed per 40 pounds body weight) up to 2.3 kg of feed for pigs 91 kg and heavier. Pyrantel is

the only approved anthelmintic that will prevent the appearance of "milk spots" on the livers of pigs when administered continuously. It does so by killing the larvae of *A. suum* in the lumen of the gut as they hatch from eggs (Biehl, 1986).

WARNING: Pyrantel should not be given to pigs within 24 hours of slaughter. Because the drug is photodegradable, it should be used immediately after the package is opened. Pyrantel tartrate should not be mixed with rations containing bentonite. Because pyrantel and piperazine appear to be pharmacologic antagonists, they probably should not be used concurrently.

Cattle, sheep, and goats

Pyrantel tartrate is not approved by the FDA for use in cattle, sheep, and goats but is effective at 25 mg/kg against barber pole worm, *H. contortus;* brown stomach worm, *O. ostertagi, Teladorsagia (Ostertagia) circumcincta;* small stomach worm, *T. axei;* bankrupt worm, *T. colubriformis;* thread-necked worm, *N. battus, N. spathiger;* small intestinal worm, *Cooperia* species; and hookworm, *Bunostomum* species (Arundel et al, 1985; Campbell and Rew, 1985; Reinemeyer and Courtney, 2001a).

Morantel Tartrate

Morantel is the 3-methyl analogue of pyrantel. Morantel tartrate is used for the control of gastrointestinal nematodes in cattle and goats. Its acute oral LD_{50} is 437 mg/kg in male mice and 926 mg/kg in male rats.

Cattle

Morantel tartrate (Rumatel) is mixed in a complete feed or top dressed to deliver 9.7 mg/kg of body weight for the removal of adult barber pole worm, *Haemonchus* species; brown stomach worm, *Ostertagia* species; small stomach worm, *Trichostrongylus* species; small intestinal worm, *Cooperia* species; thread-necked intestinal worm, *Nematodirus* species; and nodular worm, *O. radiatum* in cattle (Anderson and Marais, 1975; Conway et al, 1973; Ciordia and McCampbell, 1973). Activity against larval stages of these nematodes appears to be variable. Morantel may be administered to lactating dairy cows without requiring milk withdrawal. Cattle should not be slaughtered within 14 days after treatment. It may be given simultaneously with vaccines, injectable drugs, and external parasiticides without concern.

Goats

Morantel tartrate (Goat Care-2X) is mixed in a complete feed or top dressed to deliver 9.7 mg/kg of body weight for the removal of adult barber pole worm, *H. contortus;* brown stomach worm, *Teladorsagia (Ostertagia) circumcincta;* and small stomach worm, *T. axei* in goats. Goats should not be slaughtered within 30 days of treatment.

Cyclic Depsipeptides

Emodepside

Emodepside is the first cyclic depsipeptide to be approved for use against animal parasites in the United States. The product binds to a presynaptic latrophilin receptor in parasitic nematodes, which results in flaccid paralysis and death (Harder et al, 2005). It has low to moderate acute toxicity in mammalian species; the oral LD_{50} in rats is greater than 500 mg/kg and is more than 2000 mg/kg when applied to the skin. Studies in rats and rabbits suggest that emodepside may interfere with fetal development. Women who are pregnant or who may become pregnant should avoid direct contact with emodepside by wearing disposable gloves when handling the product. It is formulated in a topical spot-on product that contains 1.98% emodepside and 7.94% praziquantel for use in cats (Profender). The prefilled applicators deliver the minimum dose of 3 mg of emodepside per kilogram and 12 mg of praziquantel per kilogram. The active ingredients are readily absorbed through the skin, enter systemic circulation, and act on target parasites in the gastrointestinal tract. The product is effective in removing roundworm, *T. cati* (adult and L4); hookworm, *A. tubaeforme* (adult, immature adult and L4); and tapeworm, *Dipylidium caninum* and *T. taeniaeformis* (Altreuther et al, 2005a; Charles et al, 2005; Reinemeyer et al, 2005). Profender was very effective when used in large scale clinical studies (Altreuther et al, 2005b).

Piperazine

Piperazine produces a neuromuscular blockade through disruption of GABA neurotransmission. Most data suggest that the receptors in

nematodes and insects resemble the mammalian GABA subtype, but they are clearly different from their vertebrate counterparts (Londershausen, 1996; Martin, 1997). Piperazine is quite safe to use in all species, but it has a narrow spectrum of action (Reinemeyer and Courtney, 2001a).

Various salts of piperazine (e.g., adipate, hydrochloride, sulfate, monohydrate, citrate, dihydrochloride) are used as anthelmintics in swine, poultry, horses, dogs, and cats. The amount of piperazine base in each salt varies widely. The adipate, citrate, phosphate, and dihydrochloride salts contain a 37%, 35%, 42%, and 50% piperazine base, respectively (USP, 1998). Anthelmintic activity depends on freeing piperazine base in the gastrointestinal tract. Piperazine is rapidly absorbed from the gastrointestinal tract and quickly cleared by urinary excretion. Elimination is virtually complete within 24 hours. Piperazine should be used with caution in animals with hepatic or renal dysfunction. The drug may not be effective in animals with intestinal hypomotility because the paralyzed worms may recover from the effects of the drug before they are passed in the stool. Occasional adverse reactions observed include ataxia, diarrhea, and vomiting.

Piperazine is available as tablets, solution, and soluble powder under many proprietary names (Pipa-Tabs, Tasty Paste). The drug is practically nontoxic. Its oral LD_{50} for rats is 4.9 g/kg and for chickens, 8 g/kg. Piperazine can be administered to animals of all ages.

Dogs and cats

Piperazine is administered orally at 45 to 65 mg of piperazine base per kilogram (USP, 1998), although higher doses (100 to 250 mg/kg) have been reported in the literature (English and Sprent, 1965; Jacobs, 1987a; Jacobs, 1987b; Sharp, Sepesi, and Collins, 1973). It is effective against adult roundworm, *T. canis, T. cati,* and *T. leonina*.

Horses

Piperazine is effective against ascarid, *P. equorum*, at an oral dose of 110 mg of piperazine base per kilogram. Reasonable efficacy was also observed against large strongyle, *S. vulgaris;* pinworm, *O. equi;* and many species of small strongyles at 220 to 275 mg/kg (Downey, 1977; Gibson, 1957; Poynter, 1955a; Poynter, 1955b; Poynter, 1956). Foals should first be treated when they are 8 weeks old. The treatment may be repeated every 4 weeks if necessary.

Cattle, goats, and sheep

Piperazine is given at 110 mg of base per kilogram orally in a single dose for control of nodular worms (*Oesophagostomum* species) and roundworm *(Toxocara [Neoascaris] vitulorum)* (Reinemeyer and Courtney, 2001a; USP, 1998). It is not often used in ruminants because of its narrow spectrum of action.

Swine

Piperazine in drinking water is offered to pigs at 110 mg/kg for the removal of large roundworm *(A. suum)* and nodular worm

(*Oesophagostomum* species) (Biehl, 1986).

Chickens and turkeys

Piperazine is administered in feed or water for 2 days at 32 mg of base per kilogram. It is very effective against roundworm, *A. galli*, but not against the cecal worm, *H. gallinarum* (Reinemeyer and Courtney, 2001a; USP, 1998).

Organophosphates

Dichlorvos

Dichlorvos is an organophosphate taken internally to kill parasites. It phosphorylates the AChE enzyme. Normal AChE eliminates acetylcholine when it is released at the postsynaptic junction. When AChE is inactivated, acetylcholine accumulates at the postsynaptic junction, which results in continued depolarization. The end result is paralysis (Fest and Schmidt, 1982; Hart and Lee, 1966; Lee and Hodsden, 1963). The toxicity of organophosphates is generally related to their ability to inactivate the AChE of the host. Such toxicity is best treated with pralidoxime (2-PAM) and atropine (Nelson, Allen, and Mozier, 1967; Smith, 1986; Woodard, 1957).

Dichlorvos is an organophosphate that is effective against many internal and external parasites. It is rapidly degraded in mammals. The acute oral LD_{50} of dichlorvos for rats is 80 mg/kg. In dogs, the oral LD_{50} of unformulated dichlorvos is 28 to 45 mg/kg, whereas formulated (resinated) dichlorvos is of low toxicity, with an oral LD_{50} of 387 to 1262 mg/kg. No untoward reactions were observed

in pregnant mice, rats, rabbits, sows, mares, bitches, and queens medicated with dichlorvos.

Swine

Dichlorvos is formulated for pigs in polyvinyl chloride resin pellets (Atgard). It is mixed into a complete meal type feed (not unground grain or pelleted meal) to deliver 12.5 to 21.6 mg/kg of body weight for the removal of adults and fourth-stage larvae of large roundworm, *A. suum;* whipworm, *T. suis;* nodular worm, *Oesophagostomum* species; and adult thick stomach worms, *A. strongylina* in boars, weaners, fatteners, gilts, and sows (Arundel et al, 1985; Biehl, 1986). For best results, sows and gilts should be medicated shortly before farrowing and again at weaning. It is best to administer the medicated feed to small lots of compatibly sized pigs (e.g., single litters) at one time so they can be watched while feeding to ensure that all eat their share. Preliminary fasting is unnecessary, but alternative sources of feed should be excluded during the medication period. When administered immediately before parturition at 8.8 times the recommended dose, resinated dichlorvos produced no adverse reactions in sows. There is no preslaughter withdrawal period when the drug is used at the recommended dosage level.

Warning: Dichlorvos should not be used with other cholinesterase-inhibiting chemicals, taeniacides, antifilarials, muscle relaxants, phenothiazine tranquilizers, or central nervous system

depressants. Atropine and pralidoxime (2-PAM) are the recommended antidotes for organophosphate poisoning.

Isoquinolones

The isoquinolones are represented by two closely related cestocides: praziquantel and epsiprantel. This class of cestocide is the safest and most effective yet approved in the United States. These drugs attack the neuromuscular junction and the tegument. The first effect causes an instantaneous contraction and paralysis of the parasite (Andrews et al, 1983). The second effect is a devastating vacuolization and destruction of the protective tegument (Arundel et al, 1985; Frayha et al, 1997). The combined effects of paralysis and tegmental destruction provide excellent activity against cestodes.

Praziquantel

Praziquantel was the first isoquinolone cestocide approved in the United States. It displays marked anthelmintic activity against a wide range of adult and larval cestodes and trematodes of the genus *Schistosoma*. Praziquantel is a very safe anthelmintic. Rats tolerated daily administration of up to 1000 mg/kg for 4 weeks, and dogs tolerated up to 180 mg/kg daily for 13 weeks. Adverse reactions in dogs and cats include transient anorexia, diarrhea, incoordination, and lethargy. Vomiting and salivation are typically observed at high dosage rates. The drug has high oral bioavailability, high protein binding, and a marked first-pass effect. It is rapidly metabolized in the kidney and liver, and the half-life for elimination is about 2 hours. About 80% of the dose is eliminated through the urine. The

remainder is cleared through the bile and stool. Praziquantel did not induce embryotoxicity, teratogenesis, mutagenesis, or carcinogenesis, nor did it affect the reproductive performance of test animals.

Dogs and cats

Praziquantel (Droncit) is administered orally or injected subcutaneously at 2.5 to 7.5 mg/kg for the removal of the following tapeworms: *D. caninum, T. taeniaeformis, T. pisiformis, T. hydatigena, T. ovis, Mesocestoides corti, Echinococcus granulosus, Echinococcus multilocularis, Spirometra* species, *Diphyllobothrium latum, Diphyllobothrium erinacei*, and *Joyeuxiella pasqualei* (Andersen, Conder, and Marsland, 1978; Andersen, Conder, and Marsland, 1979; Gemmell, Johnstone, and Oudemans, 1977; Gemmell, Johnstone, and Oudemans, 1980; Kruckenberg, Meyer, and Eastman, 1981; Thakur et al, 1978; Thomas and Gonnert, 1978; USP, 1998). A higher dosage is also highly active when injected subcutaneously or intramuscularly. Praziquantel is not intended for use in puppies or kittens younger than 4 weeks old.

Sheep, goats, and chickens

Although not approved for use in these species, praziquantel may be used for tapeworm infections from *Avitellina* species, *Stilesia* species, *Moniezia* species, *Choanotaenia infundibulum, Davainea proglottina*, and *Raillietina cesticellus*. Sheep and goats may be treated with a

dose of 10 to 15 mg/kg, and chickens with a dose of 10 mg/kg (Reinemeyer and Courtney, 2001b).

Horses

Although not approved alone for use in horses, praziquantel may be used for tapeworm infections from *A. perfoliata.* Horses may be treated with a single dose of 1.25 mg/kg (Craig et al, 2003). Praziquantel is approved in combination with macrocyclic lactones for use in horses. Combination products containing praziquantel and other anthelmintics such as febantel, pyrantel or ivermectin are also available. See the section on combination products for more information.

Epsiprantel

Epsiprantel (Cestex) was the second isoquinolone cestocide to be approved in the United States. Acute toxicity studies in mice and rats showed the oral minimum lethal dose of epsiprantel to be more than 5000 mg/kg. Epsiprantel at an oral dosage level of 2.75 mg/kg for cats or 5.5 mg/kg for dogs, as a single oral film-coated tablet, effectively removes the following tapeworms: *D. caninum, T. taeniaeformis, T. pisiformis,* and *T. hydatigena* (Corwin et al, 1989; Manger and Brewer, 1989). Doses as high as 100 mg/kg and 200 mg/kg in cats and dogs were well tolerated. Epsiprantel was given concurrently with antiinflammatory drugs, insecticides, and other anthelmintic drugs with no incompatibilities observed. Epsiprantel is only slightly absorbed through the digestive tract of cats and dogs. It is eliminated in the feces unchanged.

WARNING: The safety of using epsiprantel in pregnant dogs and cats has not been determined, and it should not be used in puppies and kittens younger than 7 weeks of age.

Arsenicals

Heavy metals such as arsenic and antimony are well represented in the history of anthelmintics. Today they have been replaced largely by safer and more effective drugs for the most common parasites. Their use in domestic animals is now limited to one product that is used to remove adult heartworm *(D. immitis)*. The therapeutic effect depends on a reaction between the arsenic salt and sulfhydryl-containing enzymes (Ledbetter, 1984; Gilman et al, 1990). Inactivation of parasite enzyme systems results in death. Arsenic is widely known as a toxin in humans and animals. Due caution is required when using arsenical products.

Melarsomine

Melarsomine dihydrochloride (Immiticide) is the only arsenical anthelmintic that is commercially available in the United States for veterinary use. Melarsomine has an efficacy of 92% to 98% for adult *D. immitis* (Dzimianski et al, 1992; Keister, Tanner, and Meo, 1995; Keister et al, 1992; Miller et al, 1995a; Rawlings et al, 1993). The product is administered intramuscularly at a dose of 2.5 mg/kg for two injections given 3 or 24 hours apart. The drug is rapidly absorbed from the injection site, with a mean absorption half-life after intramuscular administration of 2.6 minutes and peak blood concentration occurs at 8 minutes after injection. The drug is

rapidly distributed to most tissues. The parent drug and the arsenoxide metabolite are rapidly eliminated in the feces, probably by biliary excretion. The arsenic acid metabolite is rapidly eliminated in the urine, so there is no significant bioaccumulation (Keister, Tanner, and Meo, 1995).

Clinical studies indicate that the treatment is well tolerated even in dogs that have clinical signs of heartworm disease (Case et al, 1995; Miller et al, 1995a; Vezzoni, Genchi, and Raynaud, 1992).

Miscellaneous Anthelmintics

The miscellaneous anthelmintics include an assortment of many different classes of drug. Some of these anthelmintics are older chemicals that have not yet outlived their usefulness. Some have unique attributes that keep them in use and commercially available.

Clorsulon

Clorsulon, a benzene sulfonamide compound, is very effective in cattle against the immature and mature liver fluke *Fasciola hepatica*. The formulated product (Curatrem) is given in a drench to cattle and sheep at a dose of 7 mg/kg. A single dose is more than 99% effective in removing *F. hepatica* (Campbell and Rew, 1985; Kilgore et al, 1985; Wallace et al, 1985). The drug should not be given to lactating dairy cattle because no milk withdrawal time has been established. Cattle should not be treated within 7 days before slaughter. Timing for retreatment should be based on risk patterns where the cattle are pastured.

Clorsulon is also available in combination with ivermectin. For more information, see the section on combination drugs.

Dichlorophene

Dichlorophene (Happy Jack Tapeworm Tablets) is a chlorinated analogue of diphenylmethane. It has low toxicity in mammals. The oral LD_{50} of dichlorophene for rats is 2690 mg/kg, and the acute oral LD_{50} for dogs is 1000 mg/kg. Dichlorophene has bacteriostatic, fungicidal, and cesticidal properties. It uncouples electron-transport–linked phosphorylation in the parasite mitochondria. The drug is relatively safe in the host because of its low gastrointestinal absorption (Arundel et al, 1985; Lovell et al, 1990).

Dichlorophene may be given orally as an "aid in the removal" of *D. caninum* and *T. pisiformis* tapeworms from dogs (Reinemeyer and Courtney, 2001b). The drug may be administered orally in tablet or capsule form at 220 mg/kg after an overnight fast. The tapeworms are killed, digested, and eliminated in an unrecognizable form. An occasional animal may vomit or have diarrhea after treatment with dichlorophene.

Broad-Spectrum Combinations

The veterinary practitioner is always looking for anthelmintic products that cover ever-increasing spectra of parasites. Broad-spectrum products have two important advantages. First, they obviate dosing with several different products at once when a patient has a mixed parasite infection, which makes administration

easier. Second, they provide peace of mind that a parasitized animal will be cleared of parasites missed perhaps in diagnosis. For instance, a puppy from the animal shelter will be better served with a product that is effective in removing both roundworms and hookworms than with a product that is effective only against roundworms.

There are two ways to get broad-spectrum products: either discover a single chemical that has a broad spectrum (not an easy task) or combine several compatible products to build the desired spectrum of activity.

In this section the combination products are discussed. In most cases the formulation may have changed, and the dosing regimen is different from that of the single-entity drugs discussed in the preceding sections. The toxicity and mechanism of action are covered in the preceding sections of the chapter.

Ivermectin and Clorsulon

An injectable product (Ivomec Plus) containing clorsulon and ivermectin is approved for use in cattle. The addition of clorsulon extends the parasitic spectrum of ivermectin to include liver fluke *F. hepatica*. The product is injected subcutaneously behind the shoulder at a dose of 1 mL/50 kg of body weight. This dose volume delivers 0.2 mg ivermectin and 2 mg clorsulon per kilogram of body weight. It is effective against brown stomach worm, *O. ostertagi, O. lyrata;* barber pole worm, *H. placei;* small stomach worm, *T. axei;* bankrupt worm, *T. colubriformis;* small intestinal worm, *C. oncophora, C.*

punctata, C. pectinata; hookworm, *B. phlebotomum;* thread-necked intestinal worm, *N. helvetianus, N. spathiger;* nodular worm, *O. radiatum;* lungworm, *D. viviparus;* liver fluke, *F. hepatica;* cattle grub, *H. bovis, H. lineatum;* sucking lice, *L. vituli, H. eurysternus, S. capillatus;* and mange mites, *P. ovis,* and *S. scabiei* var. *bovis*. Do not treat cattle within 49 days before slaughter. Do not use product in female dairy cattle of breeding age, because no milk withholding time has been established. Do not use in veal calves.

Ivermectin and Praziquantel

Two oral paste products (Equimax, Zimectrin Gold) containing ivermectin and praziquantel are approved for use in horses. The addition of praziquantel extends the parasitic spectrum of ivermectin to include the tapeworm *A. perfoliata*. Equimax paste is given orally at a dose of 0.2 mg/kg body weight for ivermectin and 1.5 mg/kg body weight for praziquantel. Zimectrin Gold is given orally at a dose of 0.2 mg/kg body weight for ivermectin and 1 mg/kg body weight for praziquantel.

Both combination products are approved for the treatment and control of tapeworms, *A. perfoliata;* large strongyles, adult *S. equinus*; adult, arterial, and migrating larval stages *of S. vulgaris*, adult and migrating tissue stages *of S. edentatus*, adult *Triodontophorus* species (including *T. brevicauda, T. serratus,* and *Craterostomum acuticaudatum*); small strongyles, including those resistant to some benzimidazole class compounds, *Coronocyclus* species (including *C. coronatus, C. labiatus,* and *C. labratus*), adult

and fourth-stage larvae of *Cyathostomum* species (including *C. catinatum* and *C. pateratum*), *Cylicocyclus* species (including *C. insigne, C. leptostomum, C. nassatus,* and *C. brevicapsulatus*), *Cylicodontophorus* species, *Cylicostephanus* species, (including *C. calicatus, C. goldi, C. longibursatus,* and *C. minutus*), *P. poculatum*; adult and fourth-stage larvae of pinworms, *O. equi;* adult and larval stages of roundworms, *P. equorum;* adult hairworms, *T. axei;* adult stomach worms, *H. muscae;* botfly larvae, *G. intestinalis* and *G. nasalis;* adult and fourth-stage larvae of lungworms *D. arnfieldi;* intestinal threadworms, *S. westeri;* summer sores caused by cutaneous third-stage larvae of *Habronema* and *Draschia* species; and dermatitis caused by microfilariae of neck threadworm *O. cervicalis*. On occasion, treated horses exhibit edematous reactions caused by a massive release of parasitic antigens.

Oral administration of 10 times the recommended dose of Zimectrin Gold was well tolerated in 5-month-old foals. Zimectrin Gold has not been tested in pregnant mares, in breeding stallions, or in foals less than 5 months of age. On the other hand, Equimax paste is approved for use in horses as young as 4 weeks of age, breeding stallions, and breeding, pregnant, or lactating mares. Do not use either product in horses intended for food.

Ivermectin and Pyrantel Pamoate

Ivermectin combined with pyrantel pamoate is available in flavored chunks or tablets (Heartgard-30 Plus, Iverhart Plus, Tri-Heart Plus) for dogs. Because the heartworm preventative dose of ivermectin is

not effective against gastrointestinal parasites, pyrantel pamoate is added to provide action against these important parasite species. The product is formulated to deliver a target dose of 0.006 mg (6 mcg) of ivermectin and 5 mg of pyrantel pamoate per kilogram of body weight. The product is given orally to dogs every 30 days to prevent heartworm, *D. immitis*, and for the treatment and control of roundworm, *T. canis and T. leonina,* and hookworms, *A. caninum, A. braziliense,* and *U. stenocephala* (Clark et al, 1992a). The product should be given at monthly intervals during the heartworm season. Recent studies have shown that adult heartworms are not able to maintain detectable levels of microfilariae when exposed to ivermectin, so an antigen test should be used to reveal the presence of adult heartworms (Bowman et al, 1992). Safety tests have revealed that the ivermectin-pyrantel combination is well tolerated (Clark, Pulliam, and Daurio, 1992). Do not give this medication to dogs younger than 6 weeks of age or to those with existing heartworm infections.

Ivermectin, Pyrantel Pamoate, and Praziquantel

Ivermectin combined with pyrantel pamoate and praziquantel is available in flavored tablets (Iverhart Max) for dogs. Adding praziquantel to the two-way combination product mentioned earlier extends the parasite spectrum to include the tapeworms. The product is formulated to deliver a target dose of 0.006 mg (6 mcg) of ivermectin, 5 mg of pyrantel pamoate, and 5 mg of praziquantel per kilogram of body weight. The product is given orally to dogs

every 30 days to prevent heartworm, *D. immitis*, and for the treatment and control of roundworm, *T. canis* and *T. leonina;* hookworms, *A. caninum, A. braziliense, U. stenocephala;* and tapeworm, *D. caninum, T. pisiformis*. The product should be given at monthly intervals during the heartworm season. Recent studies have shown that adult heartworms are not able to maintain detectable levels of microfilariae when exposed to ivermectin, so an antigen test should be used to reveal the presence of adult heartworms (Bowman et al, 1992). Do not give this medication to dogs younger than 8 weeks of age or to those with existing heartworm infections.

Milbemycin Oxime and Lufenuron

A two-way combination of milbemycin oxime and lufenuron (Sentinel) is approved for use in dogs. It is formulated to deliver a minimum dose of 0.5 mg of milbemycin oxime and 10 mg of lufenuron per kilogram of body weight. When given every 30 days, it is effective in preventing heartworms *(D. immitis)*. The product also kills hookworms, *A. caninum;* removes and controls roundworm *(T. canis, T. leonina)* and whipworm *(Trichuris vulpis),* and controls flea populations. Do not use in puppies less than 4 weeks of age or weighing less than 2 pounds. This product is approved for concurrent administration with nitenpyram (Capstar) for quick knockdown of preexisting flea populations.

Moxidectin and Imidacloprid

A new combination product (Advantage Multi) contains imidacloprid for external parasites and moxidectin for internal

parasites. It is approved for use in dogs and cats.

Advantage Multi is a topical product designed to deliver 10 mg/kg of imidacloprid and 2.5 mg/kg moxidectin for dogs or 1 mg/kg moxidectin for cats. In dogs the product is approved for the prevention of heartworm, *D. immitis*, and for the treatment and control of adult and larval hookworm, *A. caninum, U. stenocephala*; adult and larval roundworm, *T. canis, T. leonina;* and whipworm, *T. vulpis* (Arther et al, 2005). The cat product is approved for the prevention of heartworm, *D. immitis*, and for the treatment and control of adult and larval hookworm, *A. tubaeforme*, and adult and larval roundworm, *T. cati.* The product is also effective in killing adult fleas and in treating flea infestations due to *C. felis* and for the removal and control of ear mites, *O. cynotis*.

Do not use the dog product on cats. The dog product has not been tested in dogs less than 7 weeks old or under 3 pounds (1.36 kg) body weight. It has not been tested in breeding, pregnant, or lactating dogs. Dogs should be tested for the presence of heartworm before administration. The dog product is not effective against adult heartworm or for clearing microfilariae. The dog product was well tolerated when given at five times the approved dose. Ensure that dogs cannot lick the product from the application site. Ingestion of the product by dogs may cause serious reactions including depression, salivation, dilated pupils, incoordination, panting, and generalized tremors.

The cat product should not be used on cats less than 9 weeks of age or under 2 pounds (0.9 kg) body weight. The product was well tolerated when given at five times the approved dose in 9-week-old kittens. Cats treated with a single 10× dose exhibited mild, transient hypersalivation. Avoid oral ingestion. Cats may experience hypersalivation, tremors, vomiting, and decreased appetite if the product is given orally or licked from the application site.

Moxidectin and Praziquantel

Two oral paste products (ComboCare, Quest Plus) containing moxidectin and praziquantel are approved for use in horses. The addition of praziquantel extends the parasitic spectrum of ivermectin to include the tapeworm *A. perfoliata*. The combination products are given orally at a dose of 0.4 mg/kg body weight for moxidectin and 2.5 mg/kg body weight for praziquantel.

Both combination products are approved for the treatment and control of tapeworm, *A. perfoliata*; large strongyles, adult and migrating larval stages of *S. vulgaris*, adult and migrating tissue stages *S. edentatus*, adult *T. brevicauda*, adult *T. serratus*; adult small strongyles, *Cyathostomum* species (*C. catinatum* and *C. pateratum)*, *Cylicostephanus* species (*C. calicatus, C. goldi, C. longibursatus,* and *C. minutus), Cylicocyclus* species, (*C. insigne, C. leptostomum,* and *C. nassatus), Coronocyclus* species (*C. coronatus, C. labiatus, C. labratus,* and *Gyalocephalus capitatus);* adult and larval ascarids, *P. equorum*; adult and larval pinworms, *O. equi;* adult hairworms, *T. axei;* stomach worms, *H. muscae;* and botfly larvae, *G. intestinalis,* and *G.*

nasalis. It seems to be particularly effective against encysted small strongyles. The moxidectin combination products are safe for use in horses older than 6 months of age; they have not been tested in mares during breeding, gestation, and lactation or in breeding stallions.

Pyrantel and Praziquantel

Two-way combinations of praziquantel and pyrantel are approved for use in dogs (Virbantel) and for cats and kittens (Drontal). The dog product is formulated to deliver 5 mg of praziquantel and 5 mg of pyrantel pamoate per kilogram of body weight. A single dose is given to dogs to remove tapeworm, *D. caninum, T. pisiformis;* hookworm, *A. caninum, A. braziliense, U. stenocephala;* and roundworm, *T. canis, T. leonina*.

The cat product is formulated to deliver 5 mg of praziquantel and 20 mg of pyrantel pamoate per kilogram. A single dose is given to cats and kittens to remove tapeworms, *D. caninum, T. taeniaeformis;* hookworm, *A. tubaeforme;* and roundworm, *T. cati*. This combination product should not be used in kittens under 1.5 pounds in body weight or younger than 4 weeks of age.

Pyrantel, Praziquantel, and Febantel

A three-way combination of febantel, praziquantel, and pyrantel (Drontal Plus) is available in the United States. This product is formulated to deliver 25 to 35 mg of febantel, 5 to 7 mg of praziquantel, and 5 to 7 mg of pyrantel pamoate per kilogram. A

single dose is given to dogs to remove tapeworm, *D. caninum, T. pisiformis, E. granulosus;* hookworm, *A. caninum, U. stenocephala;* roundworm, *T. canis, T. leonina;* and whipworm, *T. vulpis* (Bowman and Arthur, 1993; Cruthers, Slone, and Arthur, 1993). This combination is effective against the nematodes when given in a single oral dose. Febantel alone requires three daily doses to be effective in monogastric animals. This combination should not be used in pregnant dogs, in dogs less than 2 pounds in body weight, or in puppies younger than 3 weeks of age.

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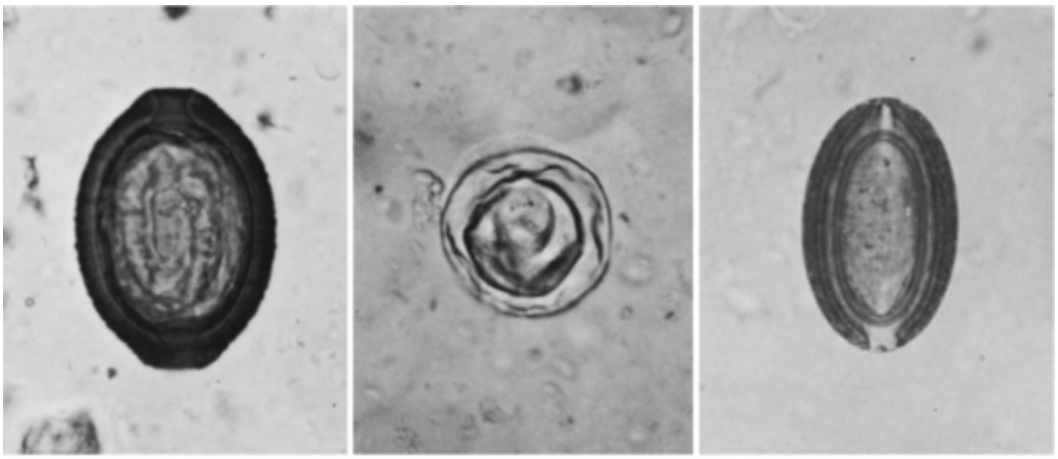

Figure 7-104 Three parasites of primates. For a more complete listing of simian parasites by host and organ, see text. *Anatrichosoma cynomolgi* adult worms tunnel in the nasal mucosa. Anoplocephalid eggs have a pear-shaped embryophore surrounding the oncosphere. *Prosthenorchis elegans* (Acanthocephala) eggs have a thick outer shell and thin inner shells enclosing the embryo (acanthor).

CHAPTER 7

Diagnostic Parasitology

For busy veterinarians it is necessary to achieve fairly accurate identification of parasites with a reasonable expenditure of effort. The conventional system is to take advantage of the site and host specificities of parasites and list them according to their customary locations in or on their customary hosts. With the use of this system, it is good to recognize that it must fail in abnormal cases. Whenever doubt arises or the exact identity of a parasite is essential (e.g., as for publication), recourse must be had to detailed morphologic study, preferably by a recognized expert.

The diagnostic categories used in the following discussion do not adhere consistently to any particular level of taxonomic nomenclature. This is because the goals of typologic taxonomy differ from those of applied parasitology. Taxonomists strive to arrange living organisms into ranks and files in a way that, to their tastes at least, best displays the phylogenetic relationships among them. However, the needs of clinicians and clinical parasitologists are best served by diagnostic categories that do not happen to coincide consistently with any particular level of the taxonomist's classification scheme. Therefore we identify an egg from one of several dozens of species of canine tapeworms as a taeniid egg rather than as a *Taenia pisiformis* egg because it is practically impossible to carry the identification of such eggs below the family level. Fortunately, all members of this particular family except *Echinococcus* respond in about the same way to anthelmintic therapy, and the infective larvae of all develop in vertebrate intermediate hosts. Therefore the diagnostic category "taeniid" is adequate to the needs of effective treatment and control. In another instance, the recognition of a worm as a member of its particular phylum may suffice. For example, an acanthocephalan from a pig is almost certain to be *Macracanthorhynchus hirudinaceus*. In still other instances, however, species identification is necessary. For example, the distinction between *Toxocara canis* and *Toxascaris leonina* is important from the standpoints of both animal parasite control and public health.

Unfortunately there are many important practical distinctions that transcend even the lowest levels of conventional systematics. There exist infraspecific races of many nematodes that may differ

remarkably in pathogenicity, antigenicity, and response to pharmacologic agents yet, on morphologic grounds, fall into the same species. Here we must make our way with whatever criterion proves helpful.

FECAL EXAMINATION

Qualitative Fecal Examination

Direct Smear

The direct smear made by breaking up a very small particle of feces in a drop of saline is a simple, quick method. When examining outpatients, many small animal practitioners routinely smear the feces adhering to the rectal thermometer directly on a microscope slide. Use of a coverslip improves the optics, subdues eddy currents, and helps prevent soiling of the objective lens of the microscope. The use of saline rather than water prevents the lysis of fragile trophozoites of protozoa that are subject to distortion by osmotic changes. Because the resulting suspension must be thin enough to read through, only a small particle of feces can be examined, but limited efficiency is the only shortcoming of this technique. Negative findings are inconclusive, but positive results are just as valid as those obtained with the more efficient concentration techniques. In fact, the smear presents advantages over concentration techniques in dealing with delicate forms such as nematode larvae and protozoan trophozoites, which may be distorted or destroyed by concentration media, and with particularly heavy eggs that fail to float in them. Direct smears of fresh fecal material also allow us to observe motility of amebas, flagellates,

nematode larvae, and the like. As a rule, the concentration techniques should supplement rather than supplant the smear, but in practice one or the other technique is adopted as a matter of routine.

Detecting Parasite Antigens in Feces

The detection of antigens in feces **(coproantigens)** by various antigen-capture immunoassays is becoming more and more routine. Methods have existed for some time for the laboratory detection of parasite antigens in feces, particularly those of *Giardia* and *Cryptosporidium*. Now the method exists for the routine in-house detection of the cyst wall antigen of *Giardia* in the feces of dogs and cats using the IDEXX SNAP *Giardia* Test, and many labs now run similar plate tests for submitted veterinary samples.

The need to be able to distinguish the eggs of taeniid tapeworms in dogs for the purpose of distinguishing the dangerous eggs of *Echinococcus granulosus* and *Echinococcus multilocularis* from the eggs of *T. pisiformis* and other *Taenia* species has led to the development of coproantigen detection enzyme-linked immunosorbent assays (ELISAs) for these parasites. Thus it is possible to detect the antigens of this parasite in certain laboratories and to distinguish those of *E. granulosus* and *E. multilocularis*, as well as to distinguish them from those of *Taenia* species and other intestinal parasites and pathogens (Deplazes et al, 1999). It has also been shown that these types of antigen assays can be used to follow experimental infections with echinococcosis in dogs and to monitor treatment efficacy (Jenkins et al, 2000). It appears that these assays are now good enough to begin to be used routinely in surveys of canine populations for the

presence of these parasites and perhaps to monitor the success of control programs.

Coproantigens are being examined as to their usefulness in the diagnosis of bovine trichostrongylids. This could prove highly useful for prescreening cattle and other ruminants for various drug-testing protocols. In cattle experimentally infected with *Ostertagia ostertagi*, a coproantigen capture ELISA gave very good results in experimentally infected cattle, showing a rise over the course of the infection (Agneessens, Claerebout, and Vercruysse, 2001); unfortunately, in this early stage, ELISA values were not very well correlated with worm numbers at necropsy, but some correlation was evident. More recently promise has also been found using an ELISA to look for *Teladorsagia circumcincta* in sheep in which cross-reactivity could be minimized by the heat treating of the fecal sample (Johnson, Behnke, and Coles, 2004). There is every reason to believe that such tests are going to become more and more common, and perhaps routine, as they have become for *Giardia*.

Polymerase Chain Reaction

The detection of various genetic markers for different parasites found in feces is now being routinely done in the case of several protozoa. The most commonly used are currently various assays for *Cryptosporidium* and *Giardia* (e.g., O'Handley et al, 2000; Xiao et al, 2001). This is being driven mainly by the desire to determine the source of parasites that may have caused zoonotic infections in different waterborne outbreaks. More recently, work has begun on the detection of different trichostrongylid species (Schnieder, Heise, and Epe, 1999; Zarlenga et al, 2001). Once such work is

incorporated into a quantitative assay, it may be possible to determine, with DNA extracted from feces, the relative abundance of different worms within the ruminant host. The recent use of the reverse line blot hybridization method for the identification of horse strongyles, if applied to feces of hosts and their respective helminths, would be a very powerful tool to aid in the diagnosis of infections in most domestic animals (Traversa et al, 2007).

Flotation Concentration of Eggs and Cysts

All flotation techniques take advantage of a difference in the buoyancy of parasites relative to food residues. If some feces are suspended in water, the eggs and solid fecal particles will settle out, allowing the supernatant fats and dissolved pigments to be decanted. If the sediment is then resuspended in a solution intermediate in density between the eggs and fecal debris, the former will float, whereas the latter will sink. In general, techniques based on the flotation principle work well for nematode and cestode eggs and some protozoan cysts but fail to float some trematode eggs and distort protozoan trophozoites and certain nematode larvae and protozoan cysts beyond recognition. Zinc sulfate (specific gravity 1.18) is superior to sucrose of equal density for floating protozoan cysts and nematode larvae because it is slower to shrink and distort them.

Feces puddling is by no means an exact science. The actual procedure followed is less important than a show of respect for the basic principles involved. A workable procedure is outlined as follows:

1. Mix a teaspoonful or so of feces with enough water to make a semisolid suspension. Use a tongue depressor and a paper cup.

2. Place two layers of single-sheet gauze over a second paper cup, and empty the fecal suspension into it. Return the gauze with the solid waste to the first cup and discard.

3. Pinch the rim of the second paper cup to form a pouring spout, and transfer contents to 15-mL centrifuge tubes.

4. Centrifuge for 3 minutes, and decant the supernatant containing fats and dissolved pigments.

5. Add concentrated sucrose solution (specific gravity 1.33) to 1 cm from the top of the tube, and resuspend the sediment with an applicator stick. Insert stopper, and mix by four or more inversions. The viscosity of the sugar solution impedes mixing, but the solution must nevertheless be thoroughly mixed with the sediment.

6. Centrifuge for 5 minutes. Without removing the tube from the centrifuge, pick up the surface film containing eggs and cysts by touching it gently with a “glass nail” or wire loop. Transfer the surface film to a microscope slide, and add a coverslip. Variant: Alternatively, after step 5 has been completed, the centrifuge tube may be filled to the brim with saturated sucrose solution and a coverslip applied to the top. After centrifuging, remove the coverslip by lifting it straight up and place it and its adherent film of sugar solution on a glass slide. This variant will not work with fixed angle-head centrifuges.

7. Scan the slide under ×100 magnification. To avoid omission or overlap of fields, start by scanning along one edge of the coverslip from one corner to the other. Then shift one field width and continue scanning. The shift can be executed precisely by concentrating attention on any object that happens to lie at or near the edge of the field and moving that object to the other edge with the mechanical stage adjustment. As skill in identification is acquired, the scanning may be done under ×50 magnification with considerable saving of time. Very small objects such as *Giardia* cysts and *Cryptosporidium* oocysts must, of course, be hunted with the high dry lens and perhaps studied further under oil immersion.

Gravitational force may be used in lieu of centrifugal force, but it is weaker and therefore takes longer. Several commercially available, disposable fecal analysis kits that work by gravity afford satisfactory results. If sodium nitrate solution (specific gravity 1.20) is used as flotation medium, the preparation is ready for microscopic examination in 10 minutes. Saturated sucrose solution, because of its greater viscosity, requires 15 to 20 minutes to yield equivalent results. A disadvantage of sodium nitrate is that the slide must be examined promptly. Otherwise, osmotic distortion may have rendered the parasites difficult to identify, or crystallization of the medium may have totally obscured the microscopic field.

Fecal Sedimentation Techniques

Sedimentation techniques, like direct fecal smears, demonstrate objects that are too heavy or too delicate to concentrate by the techniques just described. Sedimentation is more sensitive than the direct smear in terms of the number of organisms demonstrated, and the slide is easier to read because much of the fecal debris has been

removed. Sedimentation is particularly appropriate for trematode and acanthocephalan eggs, amebas, ciliates, and formalin-fixed *Giardia* cysts. However, sedimentation is far less sensitive than flotation in concentrated sucrose for most nematode eggs and coccidian oocysts including *Cryptosporidium*, less sensitive than flotation in zinc sulfate (specific gravity 1.18) for fresh *Giardia* cysts and *Filaroides* larvae, and less sensitive than the Baermann technique described later for larvae of *Strongyloides, Aelurostrongylus*, and *Dictyocaulus* and other active nematode larvae. It is unfortunate that there is not one best technique that serves all purposes equally well. However, considering the extreme diversity of the organisms with which we deal, our techniques are remarkably few and simple.

The formalin-ether method should be avoided at all costs because ethyl ether has blown up enough people already. The formalin-ethyl acetate method is safer and probably just as good. Formalin preserves the feces, stops or slows development of most parasites, and reduces the odor of the sample. Ethyl acetate removes fats, pigments, and other substances that interfere with microscopic study. The following outline is freely adapted from Faler and Faler (1984):

1. Mix a teaspoonful or so of feces with 10 mL of water or 10% neutral buffered formalin.

2. Strain the mixture through a tea strainer or two layers of cheesecloth.

3. Transfer strained mixture to a 15-mL centrifuge tube.

4. Centrifuge for 1 to 2 minutes at 1500 to 2000 rpm.

5. Discard the supernatant.

6. Resuspend the sediment in 10 mL of water or formalin, and repeat steps 4 and 5 until the supernatant is clear.

7. Resuspend the sediment in 10 mL of water or formalin, and add 3 mL reagent grade ethyl acetate.

8. Insert stopper and shake the preparation vigorously for 30 seconds.

9. Remove stopper and centrifuge for 1 minute at 2000 rpm.

10. Decant supernatant, transfer a portion of the sediment to a microscope slide, and examine.

Note: To duplicate the sensitivity of flotation techniques in detecting most nematode eggs and coccidian oocysts, examine at least half of the sediment microscopically.

Concentration of Nematode Larvae by the Baermann Technique

In the Baermann technique, advantage is taken of the inability of most nematode larvae to swim against gravity. The vertical migrations of nematode larvae on vegetation occur in moisture films where surface tension translates their sinusoidal body movements into effective locomotion. By contrast, nematode larvae tend to sink gradually in an appreciable body of water within which there is no surface tension. A typical Baermann apparatus is illustrated in Figure 7-1. Break up a fairly large fecal specimen (5 to 15 g); place it in a tea strainer or wrap it in cheesecloth; and place it in

lukewarm water in the funnel. The warmth stimulates larval motility, and many larvae will come to the surface of the fecal mass, fall off, and descend to the pinch clamp. In heavy infections, larvae can be drawn off in a drop of water after an hour or so, but when few larvae are present, it may be necessary to leave the “Baermann” set up overnight. If more than a single drop of water is drawn for examination, it will be necessary to centrifuge, decant, and pipette a drop of sediment. There are many refinements and modifications of this technique, but the same simple principle underlies them all.

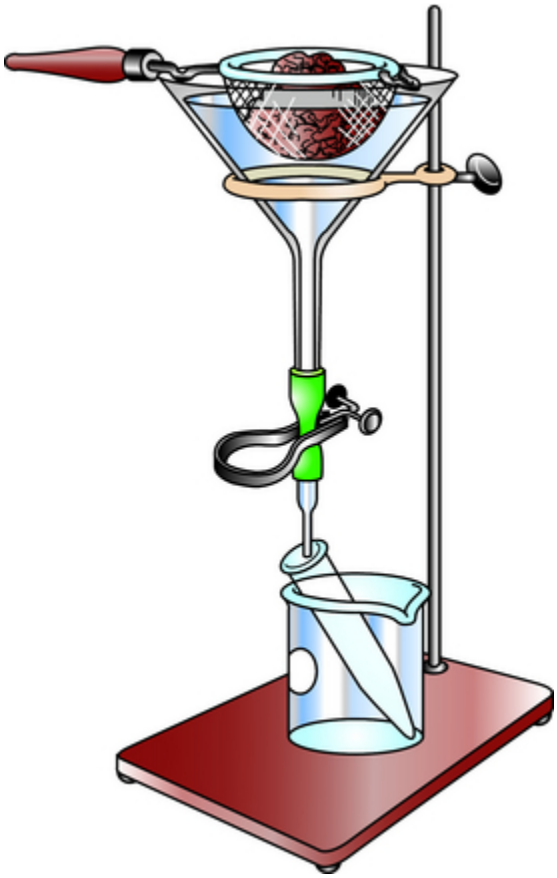

Figure 7-1 Baermann apparatus for separating and concentrating nematode larvae from feces, minced tissues, and soil samples. The specimen is placed in the basket of a tea strainer or wrapped in cheesecloth and immersed in lukewarm water in the funnel. Nematode larvae unable to swim against gravity descend to the pinch clamp and may

then be recovered in a small volume of water. A few minutes to several hours may be required, depending on the kind of larvae and the degree of infection.

The infective first-stage larvae of *Filaroides osleri* and *Filaroides hirthi* are lethargic and do not migrate out of the fecal mass. The Baermann technique is therefore an utter failure with respect to *Filaroides* larvae, and it is necessary to resort to the flotation concentration technique with zinc sulfate (specific gravity 1.18) as flotation medium.

Culture of Nematode Larvae

Generic identification of strongylid eggs usually requires rearing infective-stage larvae. Well-formed horse and sheep feces contain just the right amount of water and can usually be successfully cultured merely by placing a few pellets in a covered jar that has been rinsed with 0.1% sodium carbonate solution to inhibit mold growth and by storing the jar in a drawer or dark shelf at room temperature for a week to 10 days. The walls of the jar should always be covered with droplets of condensed moisture. If the culture appears to be drying out, add a few drops of water or sodium carbonate solution. When the jar is returned to the light after incubation, larvae will soon be found squirming about in the condensation droplets on the walls of the jar.

Cattle feces of similar consistency can also be cultured without further preparation, but usually cattle feces are more fluid and require the addition of vermiculite or sand to produce a damp but not wet culture.

All fecal cultural techniques are essentially qualitative because various species of nematodes have differing optimum conditions for

hatching, development, and survival. As a result, the relative abundance of species of third-stage larvae harvested from cultures is not a simple function of the relative abundances of species of strongylid eggs that were present at the start. *Haemonchus contortus* or *Strongyloides papillosus* larvae tend to predominate in culture whenever eggs of either of these species are present in the feces, and the possible clinical importance of *Trichostrongylus* or *Cooperia* should not be discounted because they are represented by only a small number of larvae.

Culture of dog feces for the demonstration of *Strongyloides stercoralis* filariform larvae consists of merely storing the specimen in a jar at room temperature. Filariform larvae of the homogonic generation appear by 24 to 48 hours, but if the isolate under study is principally or entirely heterogonic, substantial numbers of filariform larvae will not appear in less than 96 hours.

When larvae can be seen swimming in droplets of condensed moisture on the walls of the culture jar, rinse the walls of the jar with a small volume of water, collect the rinsings, and concentrate the larvae by centrifugation. Few larvae will be lost with the supernatant if the decanting is done by simply inverting the centrifuge tube in a single motion. Sediment containing the larvae can then be taken up in the small volume of water retained by cohesion and transferred with a bulb pipette to a microscope slide.

Nutrient agar plates provide excellent growing conditions for certain nematode eggs or larvae that have been separated from feces and concentrated by the techniques already described. For example, rhabditiform larvae that have been concentrated from dog feces by the Baermann technique are deposited on the surface of the agar in

a small volume of water and incubated at room temperature. If these are *Strongyloides* larvae, the culture will be found teeming with infective filariform larvae and/or rhabditiform adult worms in less than 2 days.

Identification of larvae often requires that they be killed in an extended posture. This is easily accomplished by judiciously warming the droplet of water before applying the coverslip. Hold a lighted match below the slide and view the cessation of motion and extension of larvae from above. “Relaxation” is the customary euphemism applied to the thermal death of nematodes. Because *Strongyloides* tend to revive, it may be necessary to heat them up again. Avoid overheating the larvae because this distorts them. As an alternative to heating, a drop of Lugol’s solution may be added at the edge of the coverslip. This both relaxes and stains the larvae.

Whenever measurements are critical, the coverslip must be supported, or it will press on the larvae and distort them. Ring the coverslip with petroleum jelly to avoid this effect and to retard evaporation. The coverslip may be ringed quickly and conveniently as follows: Spread some petroleum jelly in a thin film on the heel of the left hand. Then, holding a coverslip edgeways between the thumb and forefinger of the right hand, draw each edge of the coverslip in turn through the film to obtain a uniform dam of petroleum jelly all around the perimeter.

Culture of Coccidian Oocysts for Sporulation

Mix a small amount of feces or concentrated suspension of oocysts with 1% potassium dichromate solution, and make a shallow pool of this mixture in a Petri dish. Sporulating oocysts need a lot of air, so

the pool must be shallow to favor diffusion of oxygen, but do not let the culture dry out; add more dichromate solution if necessary. Sporulation is usually complete after 2 to 4 days' incubation at room temperature, but some species require weeks.

Micrometry

Measuring the lengths of parasites with a microscope equipped with a calibrated eyepiece micrometer sometimes provides the most efficient means of reaching a diagnosis. An object micrometer is a glass microscope slide etched with a linear scale 1 or 2 mm long and subdivided in units of 10 μm (0.01 mm). An eyepiece micrometer is a glass disc etched with a scale of arbitrary units. The disc is inserted into the microscope eyepiece, and the scale may be used to compare linear dimensions of objects in the microscopic field. For example, the ratio of length to width of a particular kind of egg may be determined. To measure absolute lengths, however, one must first calibrate the eyepiece micrometer for each objective magnification against the scale of the object micrometer.

1. Focus the ×10 objective on the scale of the object micrometer.

2. Rotate the eyepiece until the eyepiece scale and objective scale are parallel.

3. Align their zero marks by adjusting the mechanical stage (Figure 7-2).

4. Locate any point past the halfway mark at which the two scales are in perfect register. The ratio of the object length to the number of eyepiece scale divisions up to this point provides a factor for converting all subsequent eyepiece micrometer measurements made

with the ×10 objective to absolute units. In Figure 7-2, 40 eyepiece scale divisions correspond exactly to 170 mm of the object micrometer scale, yielding a ratio of 4.25 mm per scale division.

5. Repeat the calibration procedure for all objective magnifications.

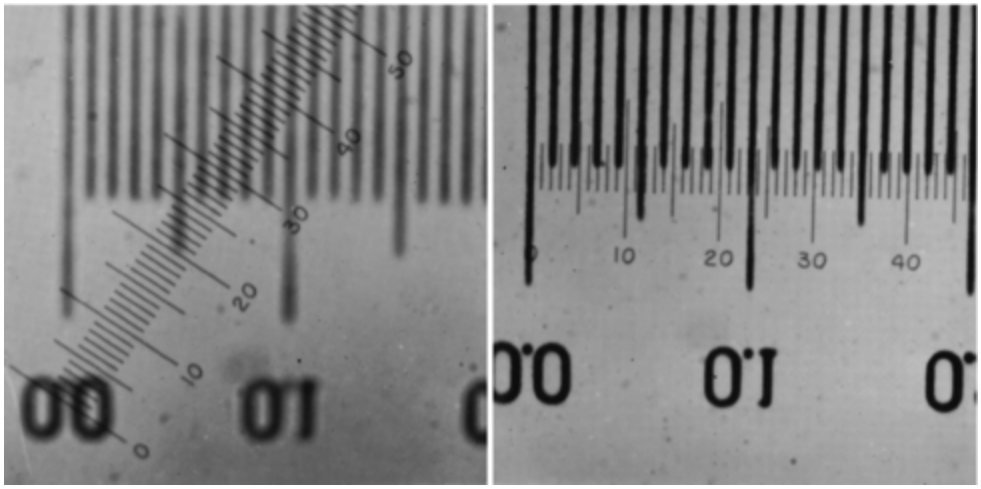

Figure 7-2 Eyepiece micrometer calibration. *Left,* The object micrometer scale is out of focus, and the eyepiece micrometer scale is about one-eighth turn out of alignment. *Right,* The scales have been made parallel by rotating the eyepiece; the object scale has been brought into focus, and the zero line (0.0) of the object scale has been aligned with the zero (0) line of the eyepiece scale by adjustment of the mechanical stage. Notice that 0.17 mm (170 mm) equals 40 eyepiece divisions (measuring consistently from the right edges of the rather thick object scale lines) so that at this magnification each ocular division equals 4.25 mm. An oocyst measuring 9 by 5.5 divisions would therefore be 38.2 mm long by 23.4 mm wide.

Note: Microscopes with variable tube lengths and other sources of variation in secondary magnification must be brought into the same state of adjustment each time measurements are taken or else they must be recalibrated anew. Any variation of the interpupillary distance of certain binocular microscopes alters the tube length and is easily overlooked as a source of error.

Quantitative Fecal Examination

Dilution Egg Counts

The Cornell-McMaster dilution egg counting technique as described in the following paragraphs is based on the work of Stoll (1923 and 1930), Gordon and Whitlock (1939), Whitlock (1941), and Kauzal and Gordon (1941).

Briefly, a sample of feces is weighed and vigorously mixed with water in the proportion of 1 g/15 mL. Aliquots of 0.3 mL are drawn from this suspension and mixed with equal parts of saturated sucrose solution in a counting chamber. The parasite eggs float in this medium and come to rest at the undersurface of the chamber cover. In this way, all the eggs in a 0.02-g subsample are brought into the same focal plane of a microscopic field that is relatively free of fecal debris. The number of eggs counted in this aliquot is multiplied by 50 to yield an estimate of the number of eggs per gram of feces.

Materials required

1. Balance sensitive enough to indicate a change of as little as 0.1 g in sample weight.

2. Mixing apparatus (Figure 7-3) consisting of a 250- to 300-mL graduated cylinder with a height-to-diameter ratio of about 2 to 1 (the cylinder in Figure 7-3 was made by sawing off a 500-mL plastic cylinder at the 300-mL mark) and an electric hand drill with a special beater. The beater may be easily fabricated with a brass rod for the shank and a strip of old inner tube for the beater. The beater

shank should glide freely through a hole in a rubber stopper that fits the graduated cylinder.

3. Counting chamber (Figure 7-4). Two microscope slides separated by two thicknesses of slide cut into narrow strips and cemented together with aquarium cement. The upper and lower slides should be offset slightly to facilitate filling the chamber. To clean the chamber, rinse under a stream of cold water.

4. Avian tuberculin syringe, 1 mL. The needle hub may be ground off to avoid plugging by coarse debris.

5. Saturated sucrose solution. Add granulated table sugar to boiling water, stirring continuously until no more will dissolve. Cool. Add a few phenol crystals to inhibit mold growth. The specific gravity at room temperature should be at least 1.31.

6. Paper cups, tongue depressors, and dissecting needles.

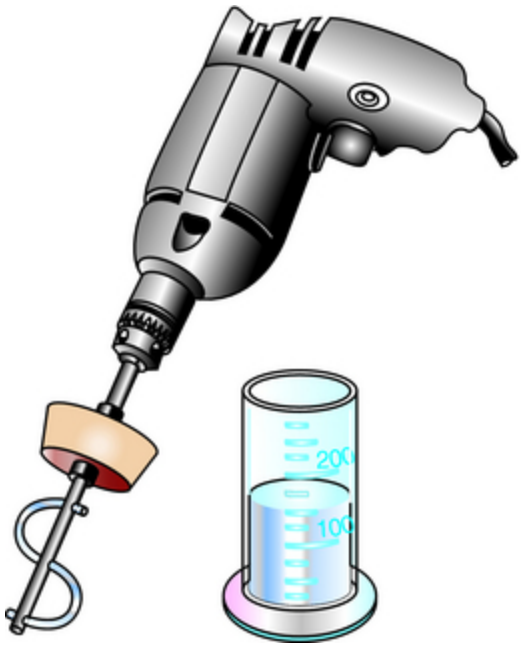

Figure 7-3 Mixing apparatus for preparing fecal suspensions.

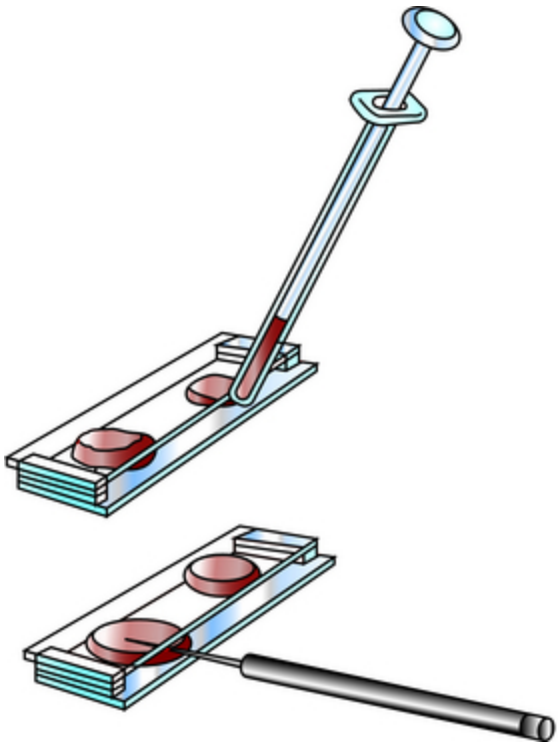

Figure 7-4 Loading the counting chamber. Two 0.3-mL volumes of saturated sucrose solution are placed in the counting chamber. Then a 0.3-mL aliquot of fecal suspension is added to each volume of sucrose solution and thoroughly mixed with a dissecting needle.

Procedure

1. Weigh out 10 g of feces in a paper cup (correct for tare) and add to 150 mL water in the graduated cylinder. If less than 10 g of feces is available, reduce the volume of water to preserve the 1:15 proportion.

2. Mix feces and water thoroughly. With the hand drill mixer, only a few seconds are required.

3. (Optional) The suspension may be passed through a tea strainer to remove coarse debris that might interfere with microscopic

examination. This is often necessary when examining horse manure but should be avoided if possible because it may yield lower counts.

4. Place 0.3 mL saturated sucrose solution in each half of the counting chamber (see Figure 7-4).

5. Stir the fecal suspension, withdraw two 0.3-mL aliquots, and add one to each pool of sucrose solution in the counting chamber.

6. Mix each aliquot-sucrose pool thoroughly with a dissecting needle, and allow the preparation to stand for about 15 minutes.

7. Count all the eggs in each pool while scanning with the low power of the microscope. The focal plane containing the eggs may be quickly located by the presence of air bubbles. Take care to include eggs lying in the optically darkened borders of the pools.

Variations of this technique with the use of calibrated chambers overcome the difficulty of counting eggs in the optically darkened borders of the pools. Unfortunately such chambers often prove difficult to obtain commercially.

An alternative method with an electric stir plate, a magnetic stir bar, a 100-mL beaker, and magnesium sulfate (Epsom salts) of a specific gravity of 1.2 as the flotation medium is described in the following procedure with a precalibrated counting chamber (Advanced Equine Products, 5004 228th Ave. SE, Issaquah, WA 98029).

1. Place beaker on balance, tare it, and weigh out 4 g of feces into the beaker.

2. Add approximately 10 mL of the magnesium sulfate solution, and mix well using applicator sticks or a tongue depressor to break up the fecal matter as much as possible.

3. Bring the volume to 60 mL with additional flotation medium, and add a stir bar. Stir for 5 minutes at moderate speed.

4. Using a glass slide to make a score mark, score a pasture pipette halfway between the tip and the barrel and break off the tip to produce a wider bore. (Caution: Pasteur pipettes have caused numerous laboratory accidents; use with care).

5. Load the pipette with the fecal material from the stirring beaker, and fill both chambers on the precalibrated counting chamber.

6. Let the preparation stand 5 minutes to allow the eggs to float to the surface, and then count all eggs within the grids of both chambers using the $\times 10$ objective.

7. Calculate eggs per gram of feces by multiplying the total number of eggs counted in the two chambers by 50.

Concentration Egg Counts

Dilution egg count procedures are less reliable for quantifying low levels of parasitic infection than are concentration egg counts (see Statistical Considerations, later). Of course, there is a limit to the number of eggs that can be counted conveniently, so one must choose the procedure best suited to the level of infection. A practical solution is proposed as follows:

1. Weigh out 10 g of feces in a paper cup (correct for tare), and add to 150 mL water in the graduated cylinder. If less than 10 g of feces

is available, reduce the volume of water to preserve the 1:15 proportion.

2. Mix feces and water thoroughly. With the hand drill mixer, only a few seconds are required.

3. (Optional) The suspension may be passed through a tea strainer to remove coarse debris that might interfere with microscopic examination. This step is often necessary when examining horse manure but should be avoided if possible because it may yield lower counts. *Note:* So far, the procedure is identical to the dilution egg count procedure described before.

4. Draw a 15-mL (1-g solids equivalent) aliquot of well-mixed fecal suspension, and transfer it to a 15-mL centrifuge tube.

5. Centrifuge for 3 minutes, and decant the supernatant containing fats and dissolved pigments.

6. Add concentrated sucrose solution (specific gravity 1.3) to 1 cm from the top of the tube, and resuspend the sediment with an applicator stick. Insert stopper and mix by four or more inversions.

7. Add concentrated sucrose solution to the brim, and place a coverslip on top.

8. Centrifuge for 10 minutes. Do not use a fixed-angle centrifuge. The cups must be horizontal during centrifugation.

9. After centrifuging, remove the coverslip by lifting it straight up and place it and its adherent film of sugar solution on a glass slide.

10. Scan the slide under ×50 to ×100 magnification, counting eggs as you go. To avoid omission or overlap of fields, start by scanning along one edge of the coverslip from one corner to the other. Then shift one field width and continue scanning. The shift can be executed precisely by concentrating attention on any object that happens to lie at or near the edge of the field and moving that object to the other edge with the mechanical stage adjustment.

The number of eggs counted by this procedure provides a minimum estimate of the number of eggs per gram of feces. The estimate can be improved by adding another drop of concentrated sucrose solution to the centrifuge tube, placing a second coverslip on top, and repeating steps 7 through 10. If there are too many eggs on the first coverslip to count conveniently, either repeat the procedure with a smaller aliquot or resort to dilution egg counting. Perhaps because the sucrose solution used is twice as concentrated, the concentration procedure is more efficient in detecting *Eimeria* oocysts than is the dilution procedure.

Interpretation of Egg Count Data

Statistical considerations

If it were possible to obtain a uniform distribution of parasite eggs in the fecal suspension, we could expect to find the same number of eggs in all aliquots. However, as we mix the suspension, the distribution of eggs does not become uniform but instead becomes a random distribution and stays random as long as we continue mixing. Aliquots from a thoroughly mixed suspension thus represent fair samples drawn from a random distribution, and the numbers of eggs counted in replicate aliquots vary in a predictable fashion.

When relatively rare objects are distributed at random in space (or relatively infrequent events are distributed at random in time), the number of objects to be found in each sample volume (or the number of occurrences in each sample time interval) follows a Poisson distribution. In a 150-mL fecal suspension there is room for well over a billion eggs, yet even in acute haemonchosis, there rarely will be more than a half million present. This means that for every 2000 volumes the size of one *Haemonchus* egg, no more than one volume will actually contain an egg. Therefore eggs counted in aliquots drawn from a well-mixed fecal suspension meet the specifications for "relatively rare objects distributed at random in space," and we can expect the number counted in each sample volume to follow a Poisson distribution.

The mean and variance of a Poisson distribution are equal. This fact can be turned to practical advantage because it provides a criterion by which we can assess the adequacy of our technique. If the variance of a series of aliquot counts turns out to be much greater than the mean, we may conclude that the mixing, sampling, or counting has been carelessly done. If, on the other hand, the sample variance turns out to be much smaller than the mean, we may conclude that someone has "fudged" the data. Chi-square analysis provides an objective numeric method for testing how well replicate egg counts fit the Poisson distribution (Hunter and Quenouille, 1952), but few practitioners would be tempted to bother with the necessary calculations. A simple alternative is provided by the graph in Figure 7-5. The diagonal lines drawn on this graph enclose a zone within which 95% of all points representing duplicate egg counts should fall, on the average,

provided the sampling and counting are adequate. The tolerance bounds on the graph are nearly parallel instead of divergent, as might be expected considering the equality of means and variances inherent in the Poisson distribution, because the axes have square root scales. Square root transformation of a Poisson variate converts the variance to a constant for all but very small values of the variate. In Figure 7-5, of 151 pairs of egg counts, 19 (13%) lie on or outside the boundaries of the 95% zone. This is almost three times too many, and we may conclude that technical performance could be improved.

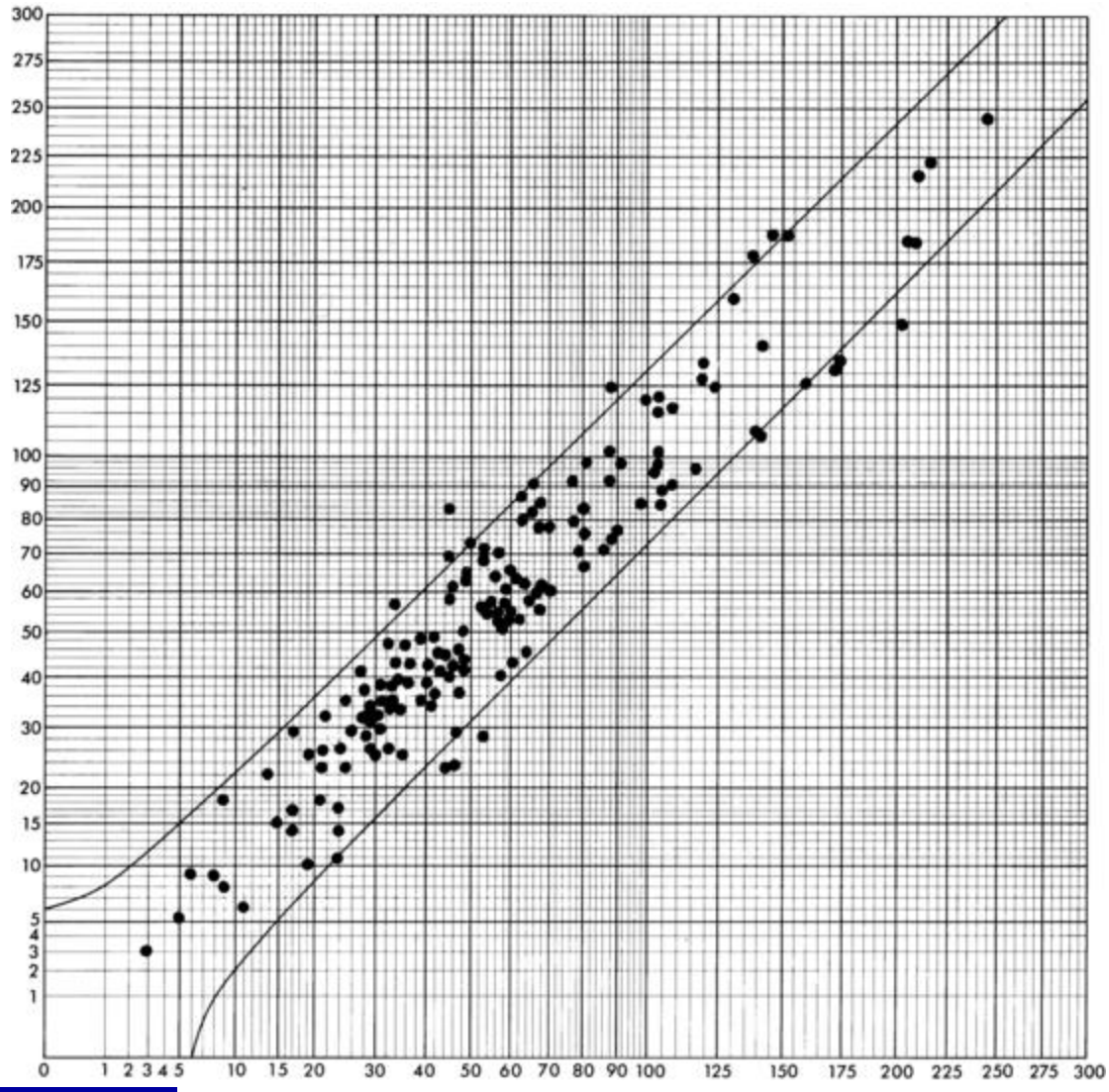

Figure 7-5 Plot of 151 duplicate egg counts. According to theory, no more than eight points should have fallen outside the diagonal boundary lines. More careful mixing, sampling, and counting could improve the picture.

Applications

Egg-counting techniques may be applied, in principle, to any patent parasitic infection of any host. For practical purposes, however, they find their greatest utility in estimating levels of strongyle infections in ruminants and horses. Under conditions of ordinary husbandry, these species of domestic animals always shed strongyle eggs in

their feces except when they have recently been treated with an effective anthelmintic drug. Therefore the question is not whether these animals are infected with strongyles but, instead, what level of infection is present.

Determining Rates of Environmental Contamination

Most contemporary methods for controlling strongyles in grazing livestock depend heavily on periodic medication with anthelmintic drugs to suppress the production of eggs and thereby curtail contamination of the pastures. Unfortunately, when populations of parasites are repeatedly exposed to anthelmintics for several years, they develop resistance to these anthelmintics and their chemical congeners. The more frequently anthelmintic medication is applied, the more rapidly does resistance to them develop. To slow or stop the development of resistance, one should administer anthelmintics only when they are actually needed to reduce a significant rate of pasture contamination. This can be accomplished by performing periodic fecal egg counts on a representative sample of the herd. When egg output is low, treatment may be delayed until it has reached a point deemed significant in relationship to the extent and productivity of pasture, the stocking rate, the species and susceptibility of hosts, and the objectives of the husbandry operation. The critical number of eggs per gram at which the herd ought to be treated cannot be specified without taking all of these factors into consideration. For example, 1000 eggs per gram might supposedly be an appropriate critical number for clinically normal sheep grazing at low stocking rate under weather conditions favorable to *H. contortus*. However, it would be best not to exceed 100 eggs per gram for brood mares with foals at their sides grazing

a small paddock. In both of these cases the critical number would be subject to revision according to the results achieved and any significant modifications of management practices.

Diagnosing Clinical Illness

High egg counts (e.g., more than 5000 eggs/g for sheep and goats or more than 500 eggs/g for cattle) are easy to interpret. They indicate that these animals are infected with many reproductively active parasites. However, high counts do not necessarily indicate that the host is suffering from clinical parasitic disease because healthy, well-nourished hosts can often support and compensate for very impressive populations of parasites. Negative egg counts indicate that the host either is uninfected or is infected with nonreproductive worms (e.g., developing or arrested larvae, infertile adults). Negative egg counts are typical of the early stages of winter ostertagiosis in cattle and peracute hookworm disease in newborn pups. Such facts tend to discredit quantitative fecal analysis in the minds of those who require short lists of simple, plausible rules. However, when interpreted by minds familiar with the biology of both host and parasite, egg counts provide one valuable insight into the interactions taking place between them.

GENERAL IDENTIFICATION OF EGGS, CYSTS, AND LARVAE

Parasite vs. Pseudoparasite

One must first learn to distinguish between parasites and superficially similar but unrelated objects such as air bubbles, pollen grains, hair, plant fibers, fat droplets, and corn smut spores.

Identification of **pseudoparasites** may occasionally shed light on the host's recent dietary adventures. Suppose, for example, that we find *Moniezia expansa* eggs in a specimen of dog feces. We know then that the dog has recently eaten sheep feces because *M. expansa* is a parasite of sheep and never of dogs. Actually, because *M. expansa* is a true parasite when it is in a sheep, its egg should be called a **spurious parasite** rather than a pseudoparasite when it is found in dog feces, but perhaps that distinction is a bit too pedantic. For practical purposes, if a dog or cat is passing an unidentifiable object in its feces, give the animal an enema, confine it for 24 to 36 hours, and do another fecal examination. If the unidentifiable object is still there, chances are it is a parasite, whereas if it is gone, it was probably a pseudoparasite. It is probably more efficient to learn to identify the bona fide parasites and to ignore the irrelevant rubbish scattered about them rather than trying to identify all objects in the microscopic field. However, some objects are commonly observed that have regular shapes. Examples of these more common pseudoparasites are shown in Figure 7-6.

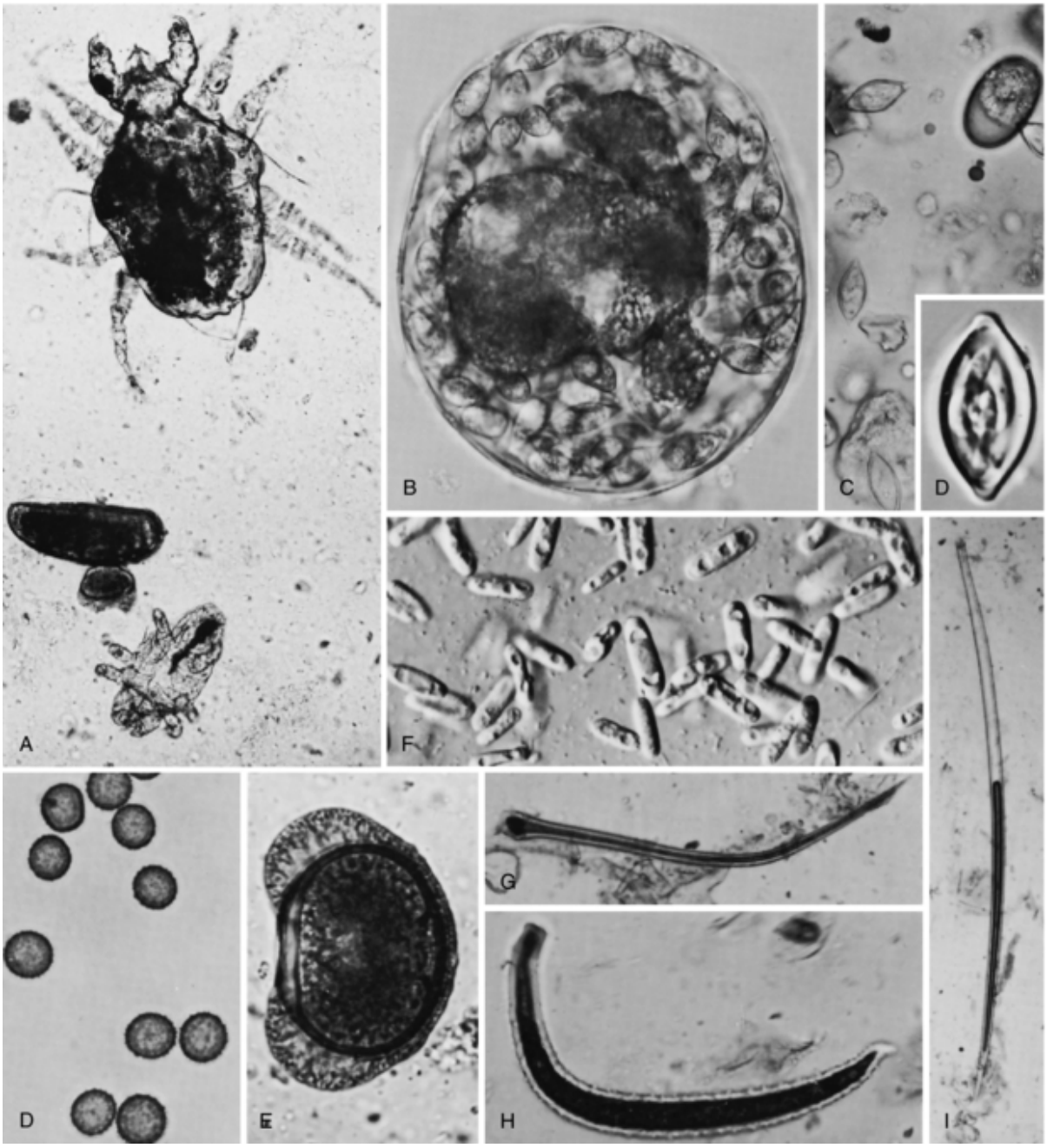

Figure 7-6 Pseudoparasites. **A,** *Cheyletiella blakei*, an arachnid parasite of the cat (×108). **B,** *Monocystis*, a protozoan parasite of the earthworm. **C,** *Monocystis* and ruminant *Eimeria* cysts in dog feces (×425). *Inset:* Sporulated *Monocystis* (×1000). **D,** Corn smut spores (×630). **E,** Pine pollen (×425). **F,** *Saccharomycopsis guttulatus*, normal alimentary yeast of rabbits (×425). **G,** Plant hair (×168). **H,** Plant hair (×63). **I,** Plant hair (×63).

Fecal specimens for parasitologic examination should be fresh and not contaminated with soil or bedding. If feces are allowed to stand, single cells develop into morulae, larvae hatch, and oocysts begin to sporulate. Identification of developmental stages other than those usually encountered is possible but requires greater skill. Contamination with soil or bedding will likely lead to confusion because the specimen may be invaded by free-living nematodes and arthropods. Starting, however, with a fresh, uncontaminated specimen may frequently allow a more specific identification by observation of the subsequent development in fecal culture.

Nematode Eggs

Nematodes have eggs. An egg contains a fertilized zygote, with the fertilization of the ovum by the amoeboid sperm having occurred within the oviduct and seminal receptacle before the eggs enter the uterus. The shell proper of the nematode egg is a smooth, homogeneous, transparent capsule of chitin. An internal lipid layer (vitelline membrane) and a narrow fluid-filled space separate the capsule from its contained embryo. Depending on the parasite, the egg may be passed with the zygote in a single-cell stage, having undergone a number of divisions, or already developed to contain a fully formed first-stage larva. In some cases, first-stage larvae hatch from the eggs within the host and are passed in the feces.

Nematode eggs representative of the different orders and superfamilies of these parasites have characteristics that typify the group. Thus an egg can usually be identified as that of an oxyurid, ascaridid, spirurid, rhabditoid, strongylid, or trichinelloid. In general, nematode eggs vary in size from 30 μm to 100 μm in

greatest diameter, although a few examples such as *Nematodirus* may be up to 200 μm in length.

The Oxyurid Egg

The eggs of the oxyurid parasites of ruminants, horses, and primates tend to have a rather thick, colorless shell and to contain a larva when observed. Most of the eggs also appear flattened on one side. The large pinworm of the horse, *Oxyuris equi*, has an egg that appears to have an operculum on one end. Dogs and cats are not hosts to pinworms, so the presence of these eggs in their feces should be considered a spurious finding unless proven otherwise (Figure 7-7).

Figure 7-7 Oxyurid (pinworm) eggs from a bearded dragon, *Pogona vitticeps*.

The Ascaridoid Egg

The eggs of the ascaridoid parasites of domestic animals are typically thick shelled and oblong to spheric in appearance. In some ascaridoid eggs there is an apparent operculum as in some eggs such as those of *Porrocaecum* from hawks (Figure 7-8). When passed in

the feces, these eggs tend to contain a single cell. Some eggs, such as those of *Toxocara*, *Parascaris*, and *Ascaris*, are covered with an albuminous coat applied by the female over the chitinous eggshell; this layer of protein may be smooth as in *Toxascaris* (Figure 7-9), rough as in *Parascaris* (see Figure 7-71), or uniformly and distinctively patterned as in *Toxocara* (Figure 7-10). The material may be tanned in the fecal stream, giving it a dark-brown color as in *Ascaris* and *Parascaris*. This material may sometimes break off from the eggshell, and the egg will then appear with a clear smooth shell. The eggs of infertile ascaridoids are sometimes found in the feces, and their shape is often less regular than that of the fertilized egg. The eggs of ascaridoids tend to be large overall, around 80 to 100 μm in diameter.

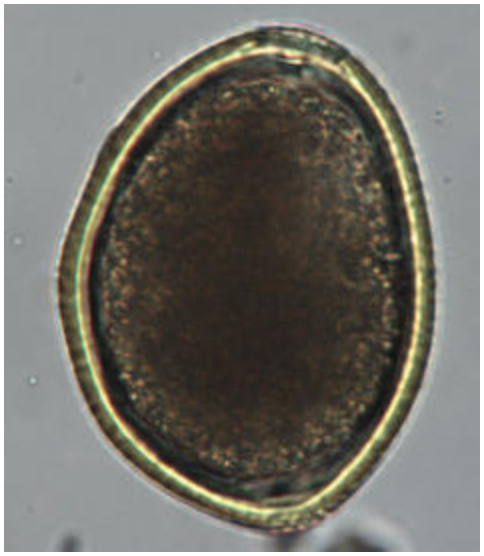

Figure 7-8 Ascaridoid, *Porrocaecum*, egg from a red-tailed hawk, *Buteo jamaicensis*.

Figure 7-9 Development of *Toxascaris leonina* eggs. **A,** One-cell stage typically found in fresh fecal specimens, with shell layers indicated by opposed arrowheads, **B,** Two-celled stage. **C,** Morula stage. **D,** Infective larva in eggshell. **E,** Infective larva artificially hatched in vitro. Hatching of ascarid eggs does not normally occur until they have been ingested by a host (×425).

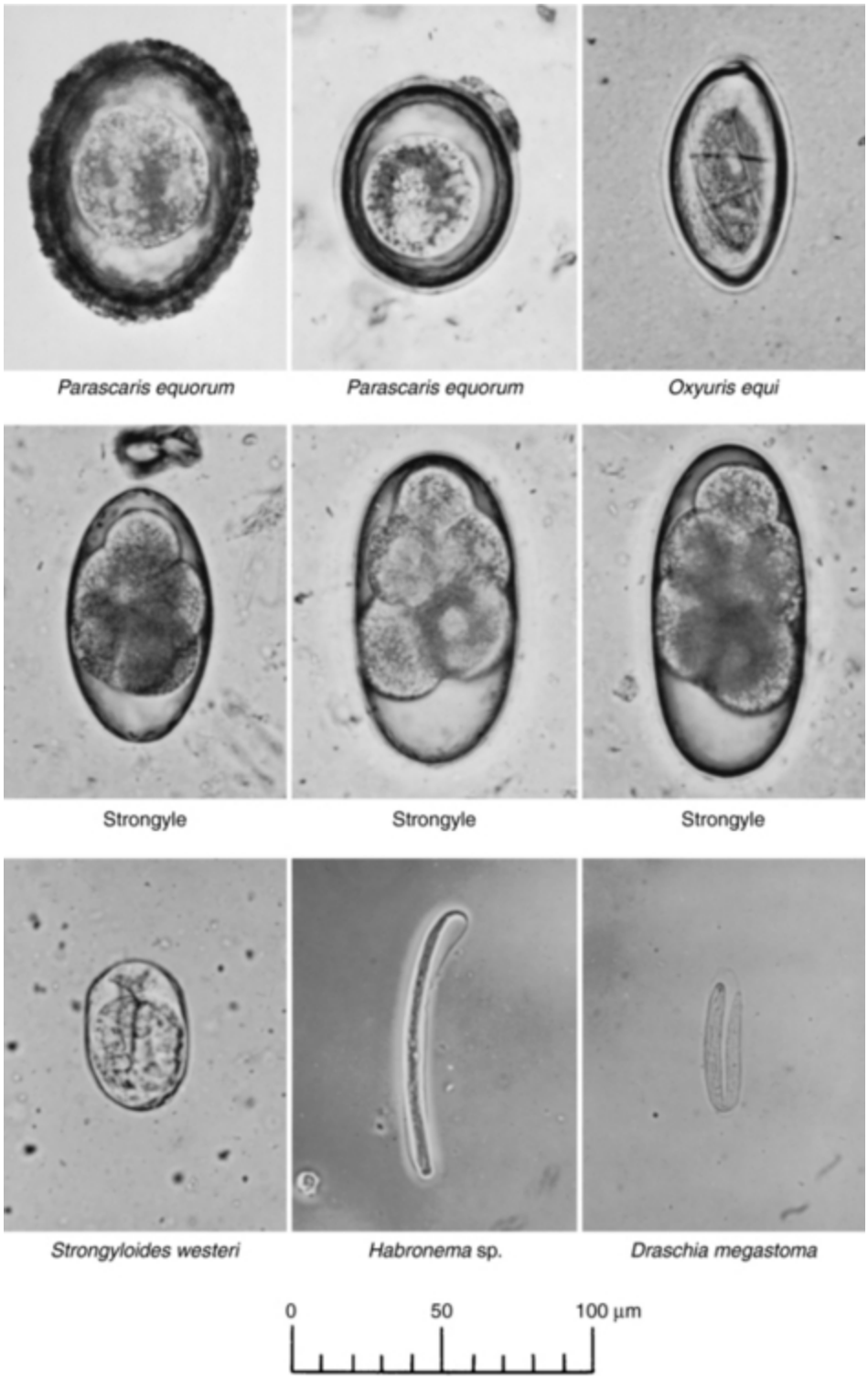

Figure 7-71 Eggs of some nematode parasites of horses.

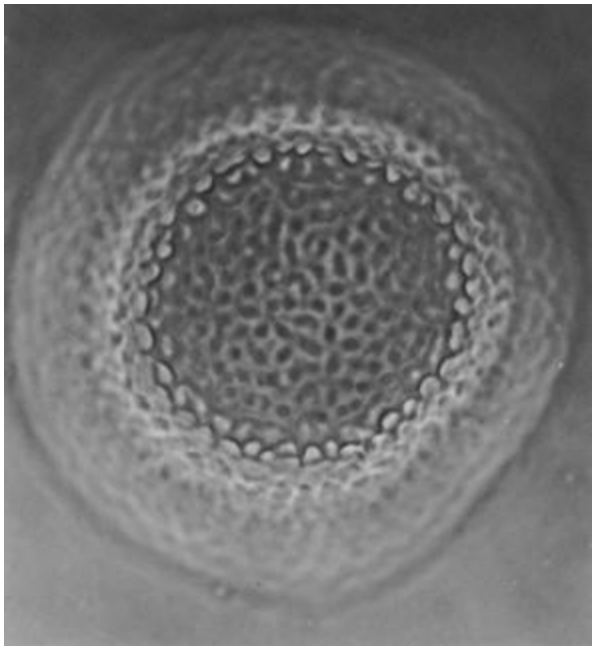

Figure 7-10 Surface of a *Toxocara canis* egg cleared in Berlese solution to show the distinctive dimpled pattern of the protein layer (phase contrast ×660).

The Spirurid Egg

The eggs of the spirurid nematodes found in feces are of at least two basic types. One type of egg, represented by those of *Physaloptera* and *Spirocerca*, is about 30 μm long, covered by a thick colorless shell, and contains an embryo. These eggs are typical of those spirurids transmitted by terrestrial coprophagous insects (Figure 7-11). The other spirurids, such as *Habronema* and *Draschia*, have very thin eggshells that may be distorted by the contained larva. These eggs and the contained larva are typical of those spirurids transmitted by flying insects that obtain their infection through the feeding of maggots on fecal material. Filariids are an ovoviviparous form of spirurid that produce microfilariae rather than eggs.

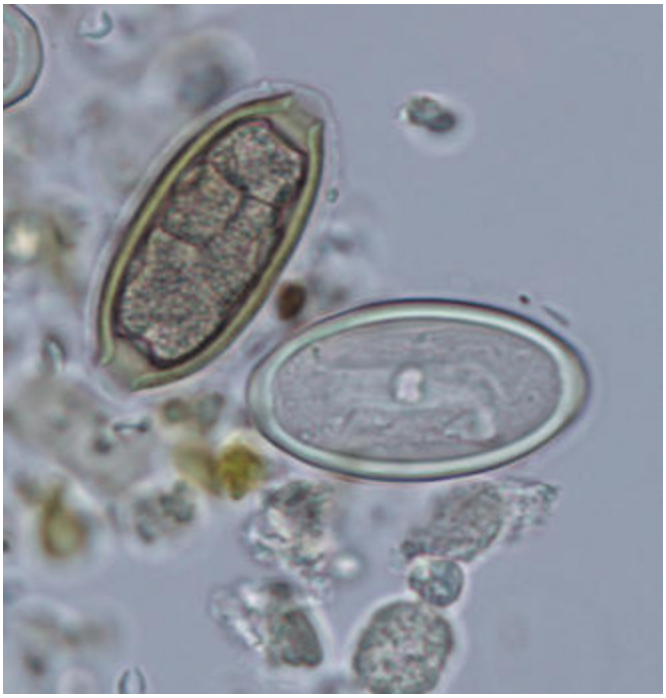

Figure 7-11 Eggs of a spirurid *(Tetrameres)* and a trichinelloid (capillarid) from a duck.

The Rhabditoid Egg

The rhabditoid eggs found in the feces of domestic animals are of two types. One type represents the spurious eggs of soil nematodes that have been ingested by a host or even laid by free-living coprophagous nematodes that have invaded a fecal pat. The second type of rhabditoid egg represents the eggs of those parthenogenetic females of the *Strongyloides* species that produce eggs (Figure 7-12). In domestic animals in North America, only *S. stercoralis* of the dog and human typically produces larvae. Other *Strongyloides* species, such as *Strongyloides felis* of cats in Australia and Southeast Asia and various species in wildlife hosts, also shed larval stages in the feces. The eggs of the *Strongyloides* species shed by horses, swine, and ruminants are typically small, with a thin colorless shell, and contain a larva. In feces that are not fresh, the small size of these

eggs, less than 50 μm, will be one of the best criteria for separating these eggs from those of developed strongylid eggs.

Figure 7-12 Rhabditoid egg *(Strongyloides papillosus)* from a goat.

The Strongyle Egg

Females of the superfamilies Strongyloidea, Trichostrongyloidea, and Ancylostomatoidea lay rather thin-walled ellipsoidal eggs containing an embryo in the morula stage of development, and this same stage is found in the host's feces (Figures 7-13, 7-14, and 7-15). In this text, such eggs are collectively referred to as "strongyle" eggs because that is what most clinicians and diagnostic parasitologists call them. The eggs of Metastrongyloidea are also thin walled and ellipsoidal, but the developmental stage deposited in the host's tissues by different species of female metastrongyloids varies from a single cell (e.g., *Muellerius*) to a first-stage larva that is ready to hatch (e.g., *Filaroides*). Even those laid in the single-cell stage develop to the first larval stage and may have hatched by the time they appear in the feces. Therefore either larvated eggs (e.g., *Metastrongylus*) or first-stage larvae are found in the feces of hosts with patent metastrongyloid infections.

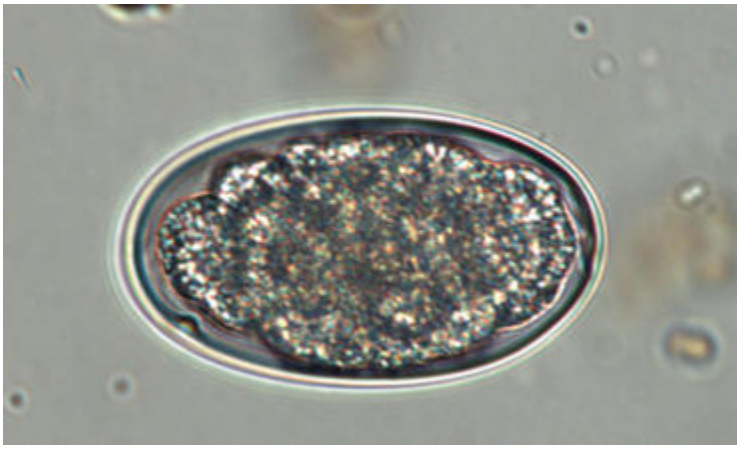

Figure 7-13 Strongylid egg *(Obeliscoides cuniculi*, Trichostrongyloidea) from a rabbit.

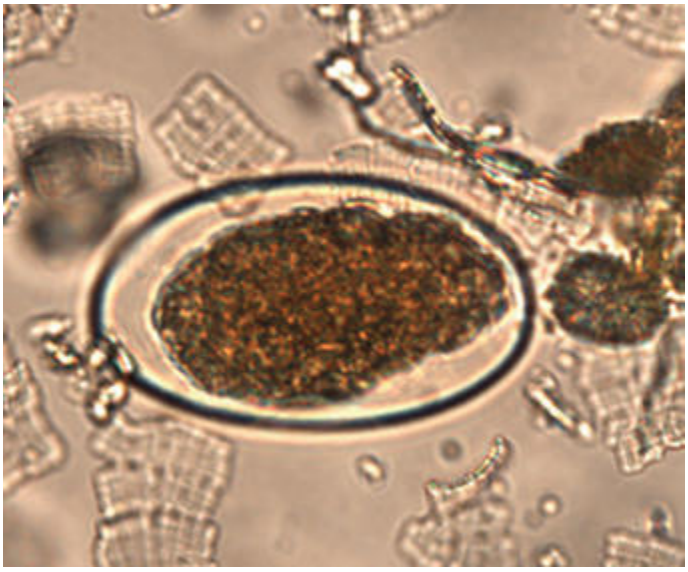

Figure 7-14 Strongylid egg *(Oesophagostomum* sp., Strongyloidea) from a gorilla; this egg was fixed with formalin, and the morula appears somewhat contracted.

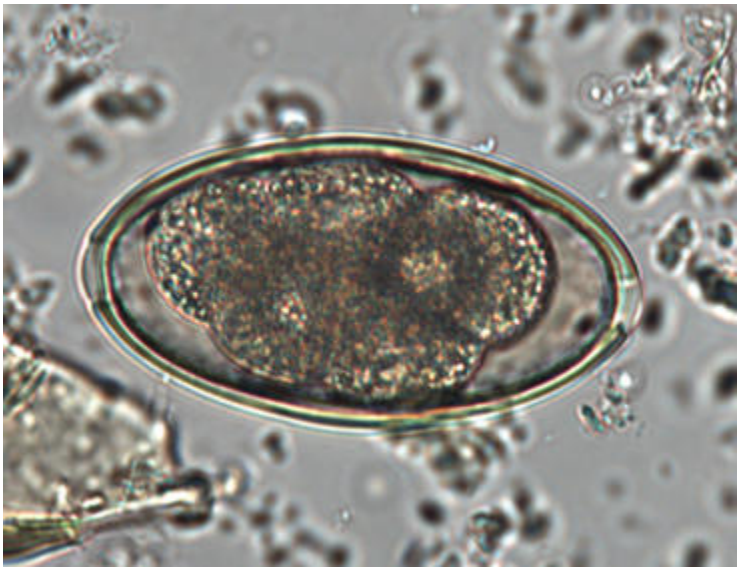

Figure 7-15 Strongylid egg (*Syngamus* sp., Strongyloidea) from a crow, *Corvus brachyrhynchos*.

A diagnostic dilemma

With few exceptions, the generic identity of individual strongyle eggs cannot be established reliably by microscopic inspection or micrometry (see Figure 7-58). *Nematodirus* eggs stand out because of their large size, and *Bunostomum phlebotomum* eggs have sticky surfaces that accumulate debris, but the rest look very much alike. Necropsy of a few animals to establish an accurate diagnosis is justifiable if the unit value of the animal is sufficiently low or the herd sufficiently large. Owners of valuable animals are understandably reluctant to sacrifice them, however, and recourse must be had to larval identification (see discussion of identification of strongyle infective larvae). Whenever the situation is too urgent to afford the necessary delay of culturing, the clinical signs should be clear enough to suggest a reasonably accurate diagnosis.

Figure 7-58 Eggs of common ruminant parasites. Strongyle eggs are ellipsoidal, are smooth-walled, and contain a morula. Although *Nematodirus* species eggs are very large, some species are considerably smaller than the one shown here. *Marshallagia marshalli* eggs (not shown) are also very large but differ from *Nematodirus* eggs in having more parallel sides and less pointed poles. *S. papillosus* eggs are slightly smaller than strongyle eggs and contain a rhabditiform larva in fresh fecal specimens. On incubation, the larvae soon hatch and develop into infective filariform larvae (see Figure 3-62) or free-living adult males and females, predominantly the latter. *Trichuris* eggs of ruminants are more than 60 mm long; those of *Capillaria* are less than 60 mm long. *Moniezia* eggs contain a

pear-shaped embryophore containing an oncosphere. *Thysanosoma* eggs (not shown here) are grouped in uterine capsules.

The Trichinelloid Egg

The eggs of *Trichuris* and capillarids are typically brown shelled with polar plugs and tend to be elongate or barrel-shaped. *Trichuris* is confined to mammalian hosts. Therefore when these eggs are found in other vertebrates, the first thought should be that they are capillarid eggs. The eggs of the *Trichuris* species tend to have smooth shells, whereas those of capillarids tend to have various forms of delicate surface ornamentation (e.g., pits, roughened areas, small wavy lines). Capillarid eggs, unlike those of *Trichuris* species, may have polar plugs that are not on the same straight-line axis (Figure 7-16). However, the eggs of *Trichuris* may become highly distorted after drug therapy that has not removed all female worms. Both *Trichuris* and capillarids tend to have eggs that are single celled or in the early stages of division when passed in the feces. The eggs of *Anatrichosoma* and *Trichosomoides* are different in that they contain a fully formed larva. In the dog, the eggs of the capillarids are smaller than the egg of *Trichuris vulpis*, which is about 80 μm long. Unfortunately, this is not necessarily true for other mammalian hosts.

Figure 7-16 Trichinelloid egg (capillarid) from a duck.

Nematode Larvae

The larvae of nematodes shed in the feces are most readily identified with reference to the host parasitized and therefore are discussed for each host as appropriate. The initial goal must be to identify them for what they are and not to confuse them with hairs, threads, or plant fibers. The more common problem is finding an artifact and thinking it a nematode larva. Most individuals will recognize a larva when they see one (Figure 7-17). The important thing is not to forget to look for them. The nematode larvae found in the feces of domestic animals all tend to be around 300 μm in length. Special attention must be paid to the relative lengths of the buccal capsule and esophagus, the structure of the tail, and the size and position of the genital primordium. If feces are old or collected from the soil, there may be many nematode larvae present that have hatched from eggs of developed parasitic forms or from soil or

coprophagous nematodes that have invaded the fecal matter. The process of identification is much more difficult in these situations.

Figure 7-17 *Didelphostrongylus* larva (Metastrongyloidea) from the feces of an opossum, *Didelphis virginiana*.

Trematode Eggs

The eggs of trematode parasites of vertebrates tend to have a golden- to dark-brown color and to have an operculum on one end (Figure 7-18). The eggs can vary in size from 20 to 200 μm in maximum length. Some of these eggs contain a fully formed miracidium when passed in the feces, whereas others contain a number of developing cells. In the identification of trematode eggs, attention must be given to the size and shape of the eggs, as well as to whether they contain an embryo, whether the operculum appears

as a simple cap or a cap in an indented seat or rim on the eggshell, and whether there are any structures on the shell such as bumps or spines opposite the operculum. The eggs of the schistosomes are not operculate, contain fully developed miracidia when passed with the feces, and often have different types of spines on one end of the eggshell depending on the species involved. Trematode eggs tend to be denser and not to float as well as those of nematodes in many of the lighter flotation media, and in sugar the eggs often rupture and appear as empty brown shells that may be collapsed on one side. When dealing with the schistosomes, one must take care to wash the feces with saline rather than water because the water induces the miracidium to hatch, making the eggs harder to find and identify.

Figure 7-18 Trematode egg (Strigeidae) from a great horned owl, *Bubo virginianus*.

Cestode Eggs

Some tapeworms commonly shed eggs into the fecal stream (e.g., *Diphyllobothrium*), whereas others more typically shed segments,

(e.g., *Taenia*). However, it is not uncommon to find eggs or egg capsules of the latter type in fecal matter from which the segments may have crawled away before collection. The larva that develops in these eggs will have six hooklets (three pairs) (Figures 7-19 and 7-20), but those in the eggs of the pseudophyllidean tapeworms *Diphyllobothrium* and *Spirometra* will not have developed by the time the eggs are passed in the feces. The eggs of these two species are also operculate and may initially be confused with the egg of a trematode. The confusion may persist even after a good deal of study of the actual eggs and pictures of them. The eggs of the cyclophyllidean tapeworms contain six hooklets when passed, which will help to identify the eggs as tapeworm eggs (see Figure 7-20). The "shells" of cyclophyllidean tapeworms can vary markedly (e.g., the thick, brown surface of a taeniid egg, the thin shells on the individual eggs of *Dipylidium*, and the odd-shaped square to round eggs of the various anoplocephalid genera (see Figure 7-19). Tapeworm eggs appear to behave erratically in different flotation media and can be hard to demonstrate even when present. Sugar solution works well for taeniid eggs, but not for many of the other egg types that may be encountered.

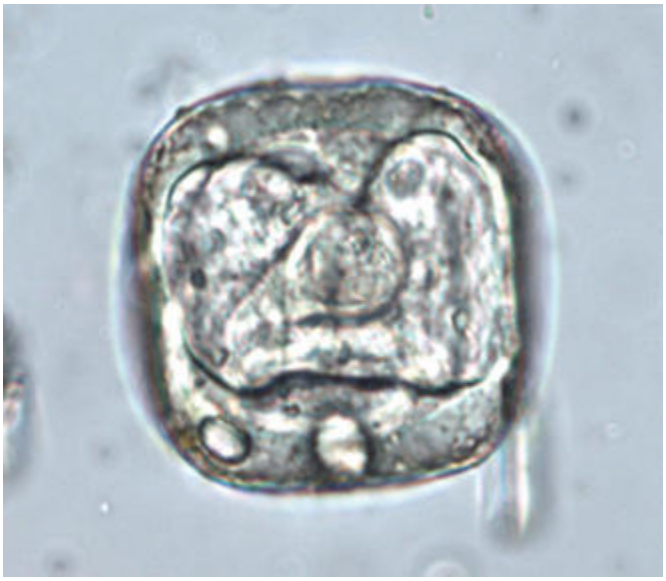

Figure 7-19 Tapeworm egg (Anoplocephalidae) from a gorilla, *Gorilla gorilla berengi*.

Figure 7-20 Tapeworm egg (Cyclophyllidean) from a chicken. Note the hooklets in the embryo (oncosphere) within the egg. Underneath the egg is a *Monocystis* sporocyst that was probably ingested in an earthworm.

Acanthocephala Eggs

The eggs of Acanthocephala tend to be elongated and have shells composed of three layers (Figure 7-21). If the larva inside can be

seen, the spines present on one end of the larva can often be identified, which clinches the diagnosis. The eggs of some Acanthocephala often appear dark brown in the feces (e.g., *Macracanthorhynchus* species) and are probably tanned in a manner similar to ascaridoid eggs because the eggshells are clear when the eggs leave the female worm. Not all acanthocephalan eggs are brown, and the very clear ones may be difficult to observe, particularly if one is not expecting to find them. There are numerous Acanthocephala present in wildlife hosts, and it is there that skill has to be developed in diagnosing infections with different species.

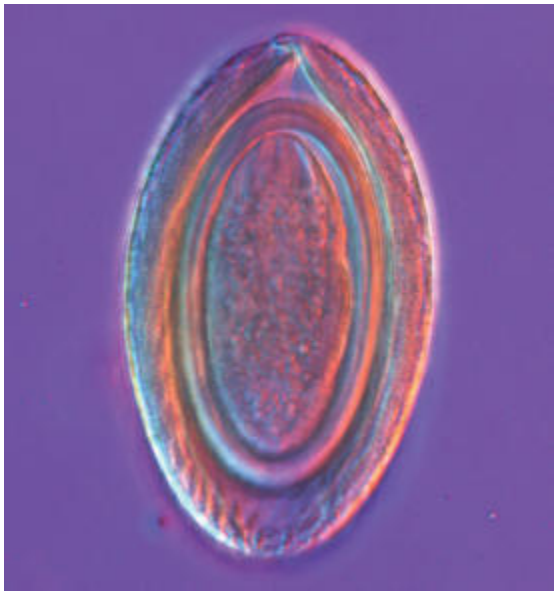

Figure 7-21 Acanthocephalan egg *(Macracanthorhynchus ingens)* from a raccoon; note the several layers to the eggshell and the contained acanthor larva.

Pentastomid Eggs

In the United States the eggs of pentastomids will most typically be observed in the feces of snakes or gulls. Elsewhere in the world they can be observed in the feces of dogs and other hosts. Pentastomid

eggs are typically quite large, 100 to 200 μm in diameter, with a thin external shell that surrounds what looks like a developing mite. The developing larva is often separated from the eggshell by a rather large area of empty space. The difficulty is in determining whether what is observed is the egg of a pentastomid or the egg of a mite that has been ingested. It is not uncommon to find in feces the eggs of free-living mites and parasitic mites ingested while an animal is grooming. The pentastomid developing within the egg will typically have four or six small claws, which might help distinguish the mite from the pentastomid (see Figures 2-124 and 8-10Figure 2-124Figure 8-13).

Protozoan Cysts and Oocysts

The cysts and oocysts of protozoa will range from 4 to 30 μm in greatest diameter, with the odd large cysts of *Balantidium* and *Buxtonella* (Figure 7-22) reaching sizes of 40 to 60 μm and the thick-walled oocysts of *Eimeria leuckarti* and *Eimeria macusaniensis* (Figure 7-23) reaching 80 μm in length. The cysts of *Giardia* appear rather clear in both zinc-sulfate and sugar preparations, and their overall appearance is similar to that of amebas that are more round in outline. In many flotation media, cysts of *Giardia* will appear collapsed internally with the ovoid cyst wall remaining intact, whereas collapsed cysts of amebas may appear much like Ping-Pong balls that have been indented various amounts on one side. The oocysts of *Cryptosporidium* are very small and can be found near the surface of the coverslip. They are much easier to see in a sugar flotation, where they will appear as a hyaline pink body, than in zinc-sulfate, where they appear to be clearer. The oocysts of *Isospora*

and *Eimeria* do very well in sugar flotation media and present a crisp, clear image of a shell and a central sporoblast. On many species of *Eimeria*, the micropyle and micropylar cap, when present, can be easily discerned. On some *Eimeria* species it may be difficult to make out the micropyle on all specimens. The oocysts of *Toxoplasma* are similar in size to the cysts of *Giardia*. If the aperture on the condenser diaphragm is not closed and the light coming through the scope is too bright, many of the smaller protozoa will disappear into the background.

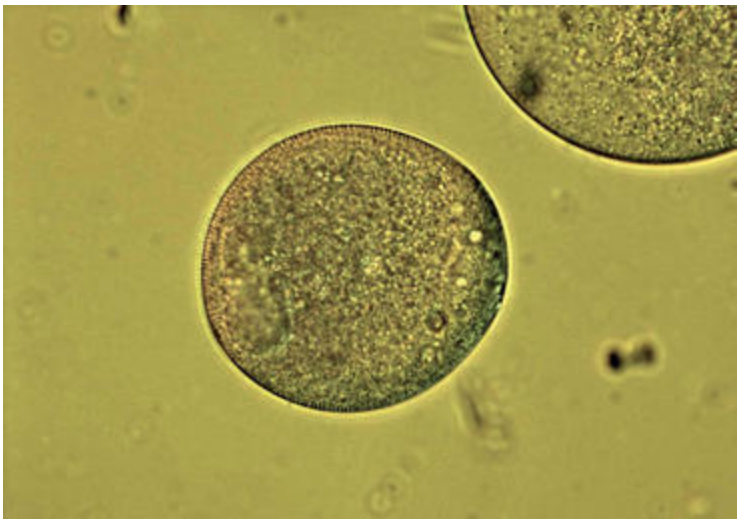

Figure 7-22 Ciliate cyst *(Buxtonella sulcata)* from the feces of a cow.

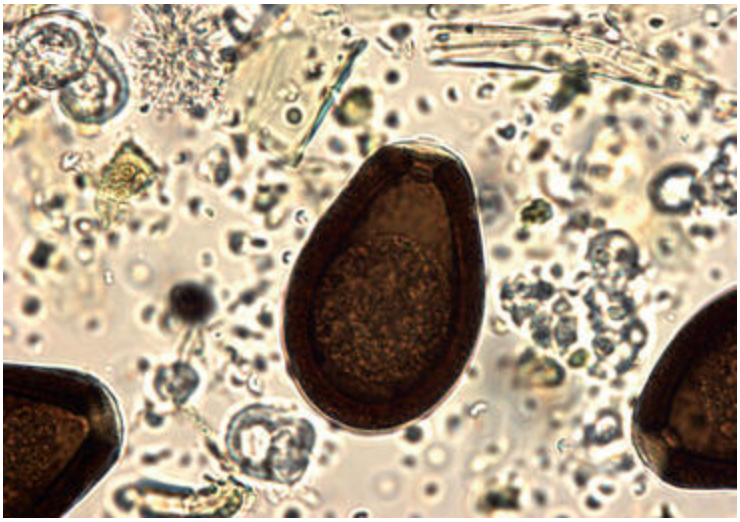

Figure 7-23 Coccidian oocyst *(Eimeria macusaniensis)* from a llama.

SKIN SCRAPINGS FOR MANGE DIAGNOSIS

Skin scrapings for mange diagnosis must be obtained in a manner that takes into account both the nature of the lesion and the location of the mite in question (Figure 7-24).

Figure 7-24 *Orthohalarachne attenuata* (mite, Halarachnidae) from a northern fur seal, *Callorhinus ursinus*.

For lesions with minimal epidermal hyperplasia and lesions caused by deeply burrowing mites (e.g., *Sarcoptes*, *Demodex*), dip a scalpel blade in mineral oil, pinch a fold of skin firmly between the thumb and forefinger and, holding the blade at right angles to the skin, scrape until blood begins to seep from the abrasion. Most animals do not object to deep scraping, although local anesthesia may occasionally be required. Much of the detritus will adhere to the layer of mineral oil on the scalpel blade and may be transferred to a microscope slide and searched for mites.

For lesions with marked epidermal hyperplasia and exfoliation and lesions caused by lice and superficially dwelling mites (e.g., *Chorioptes*), scrape the detritus into an ointment tin using the cover as a scraper. Examine scrapings under a stereoscopic microscope or with a hand lens to find the lice and mites crawling about. Dip fine-tipped thumb forceps or a dissecting needle into Berlese solution, and use this sticky mounting medium to pick up mites and transfer them to a slide for closer study under the compound microscope. Berlese solution is made by mixing 200 g chloral hydrate, 30 g gum arabic, 20 g glycerin, and 50 mL distilled water; boiling this mixture for 5 to 15 minutes; and filtering it through cheesecloth. Berlese solution clears the specimen and hardens to produce a permanent preparation. Unfortunately, chloral hydrate is now regulated as a narcotic, and different lots of gum arabic vary considerably in quality so that good Berlese solution is getting hard to come by. Glycerin is a reasonably satisfactory temporary mounting medium. Five percent sodium or potassium hydroxide solution also may be used as a temporary mounting medium that digests epidermis and hair, thus helping to clear the microscopic field of debris.

If the scraping contains much debris, and no lice or mites have been found by inspection with the stereoscopic microscope or hand lens, proceed as follows:

1. Add 10 volumes of 5% KOH to 1 volume of skin scrapings in a large (500- to 1000-volume capacity) beaker, cover with a watch glass or funnel to return condensate, and heat until hair and epidermal scales dissolve. It may be necessary to boil the mixture, but do not allow it to boil dry. Beware of spattering lye!

2. Allow to cool.

3. Transfer to a centrifuge tube, centrifuge, decant supernatant, resuspend sediment in water, and centrifuge again. These steps dispose of interfering soaps. Decant the supernatant.

4. Transfer sediment to a Petri dish and search for mites and eggs with a stereomicroscope or ×10 pocket lens, or proceed with step 5.

5. Add saturated sucrose solution to the tube, and centrifuge again. Pick mites off the top of the sucrose solution with a wire loop or glass nail and transfer them to a microscope slide for study under the compound microscope.

Ear mites may be removed from the external ear canal with a cotton swab. If the swab is placed on a dark background in sunlight or near an incandescent lamp, white *Otodectes* mites may be seen crawling about within a few minutes.

NECROPSY PROCEDURES

Occasionally, severe or fatal parasitosis may escape antemortem diagnosis. For example, pups with peracute hookworm disease may bleed to death before shedding an egg. When disease breaks out in a flock of sheep, postmortem examination of a few sick animals often provides the most efficient and economical means of arriving at a diagnosis. In strongylid infections of sheep, various combinations of primary and secondary pathogens often yield a confusing array of clinical signs that may be resolved by identification and enumeration of the worms.

Necropsy findings must be correlated with the case history and clinical signs to arrive at a definitive diagnosis. This is especially true of parasitic diseases. For example, a diagnosis of acute haemonchosis must rest not only on the demonstration of a sufficient number of *H. contortus* worms in the abomasum, but also on the existence of clinical anemia. If there is no anemia, then there is no haemonchosis. In fact, *H. contortus* worms sometimes desert a moribund host so that, on necropsy examination, pallor and edema of the tissues is found, but no worms. The correct diagnosis is still haemonchosis.

Opening the Cadaver

Arrange a ruminant cadaver on its left side to get the rumen out of the way. Cadavers of other species are about equally accessible from either side, but you should adopt a consistent approach to develop a mental image of the normal appearance and location of the various organs so that any abnormal relationship will be quickly noticed. Incise the skin along the midline from the submaxillary space to the perineum. Reflect the skin from one side, including the superficial

thoracic muscles and the pectoral limb with it so as to lay bare the rib cage. Cut the ribs close to the axial muscles and the costal cartilages close to the sternum. Lift away the rib cage, severing attachments to the diaphragm in the process. Incise the abdominal wall along the midline, taking pains to avoid puncturing the viscera. Carry the incision across the brim of the pubis and reflect the abdominal wall. Split the pubic symphysis or incise the ligaments of the hip joint and reflect the pelvic limb.

Thoracic Viscera

Incise the intermandibular muscles, hyoid apparatus, and other attachments, and dissect the tongue, larynx, trachea, and esophagus. Removal of the heart and lungs is facilitated by traction on the trachea and esophagus. The points of attachment (aorta, cavae, azygous vein, various ligaments) are easily found and severed. Remove the thoracic viscera from the carcass. Lay open the tracheobronchial tree, heart chambers, cavae, aortic trunk, and ramifications of the pulmonary arteries, and inspect the contents and linings for macroscopic parasites. Very small metastrongylid nematodes (e.g., *Muellerius capillaris*, *Aelurostrongylus abstrusus*, *F. hirthi*) are practically invisible grossly. These may be demonstrated in squash preparations of their grayish subpleural nodules. The Baermann technique is useful for demonstrating larvae of lung nematodes (e.g., *Muellerius*, *Aelurostrongylus*), but usually fails in the case of *F. hirthi* because the larvae of this parasite are too lethargic to migrate out of the lung tissues.

Abdominal Viscera

Examine the peritoneum for cysticerci, tetrathyridia, encysted pentastomids, and acanthocephalan nymphs. *Strongylus edentatus* larvae may often be observed immediately beneath the parietal peritoneum of horses. Examine the surface of the liver for migration racks of ascarid, taeniid, and *Fasciola* larvae, and the kidneys for encysted *Toxocara* larvae. The equine pancreas is a favorite location for *Strongylus equinus* larvae. Place double ligatures around the cardia (or omasoabomasal junction), pylorus, and ileocecal junction, thus isolating the stomach, small intestine, and large intestine. These regions provide differing environments for distinct sets of parasites, and valuable diagnostic information is lost by pooling the collection from the entire gut. Open one region at a time, carefully poking through the ingesta and scanning the mucosa for the smaller forms. Many parasites of dogs, cats, horses, and pigs are large enough to see with the unaided eye, but there are a few very small ones that are important (e.g., *Strongyloides*, *Trichinella*). Scrape the mucosa of the small intestine and examine the scrapings for small nematodes, coccidia, and the like.

Most of the important nematode parasites of ruminants are very small, and great care must be taken not to overlook them. The population of nematodes sufficient to kill a heifer may pass the notice of a careless prosector completely. The following technique accomplishes the concentration and separation of these worms from much of the ingesta and mucosal debris and, with a bit of extra effort, provides an estimate of the number of worms present.

1. Transfer all ingesta from a particular organ (the abomasum is an easy one with which to begin) to a bucket; scrub or lightly scrape the mucosal surface to ensure complete transfer of worms.

2. Add several quarts of tepid water, mix, and allow to stand for about 5 minutes so that the worms and heavy debris can settle to the bottom; then decant the supernatant. Repeat this process until the sediment consists principally of worms and coarse ingesta.

3. Transfer a small amount of sediment to a Petri dish and examine with transillumination, preferably under a magnifying glass or stereoscopic microscope. If the worms have been taken from the cadaver of a recently dead animal, they will become very active in the tepid water and can be easily detected and fished out with forceps for closer examination.

The small intestine is long, and life is short. Most of the important nematode parasites of the ruminant small intestine can be collected by flushing a liter of water through its first 6 meters. Insert a funnel into the pyloric end of 6 meters of unopened small intestine and pour a beaker of water into it. Massage the water along the length of gut and collect it at the other end; then proceed with steps 2 and 3 above.

A popular alternative to step 2 is to rinse sediment vigorously over a sieve with openings small enough to retain the parasites but large enough to pass water and fine debris. The sieve may then be inverted and back-rinsed to transfer the parasites and coarse debris to a collecting vessel. If time or facilities to examine sediment for parasites are lacking, the sediment can be preserved in 10% formalin and attended to later. Be sure to sieve preserved sediments once again to remove the formalin before attempting to isolate and study the parasites; this may save you a big headache.

Because we are almost certain to find parasites in sheep, young cattle, and horses, it follows that the evaluation of the necropsy findings must rest on the abundance of the parasites as well as on their identity. To obtain an estimate of worm numbers, substitute step 3a for step 3 and proceed as follows:

3a. Transfer the washed sediment to a graduated cylinder, and fill with water to 1 liter. We now have all the worms from some particular organ suspended in 1 liter.

4. Stir the suspension thoroughly, and withdraw a 50-mL aliquot.

5. Pour a small portion of the 50-mL aliquot into a Petri dish, and count all of the worms. Continue until the 50 mL is used up. The number of worms counted times 20 provides an estimate of the total number of worms in the particular organ.

The worm count must be interpreted in the light of other necropsy findings, especially the nutritional status of the cadaver and lesions specifically related to the parasites found. Etiologic significance should be attached to *Trichostrongylus* or *Cooperia* only if it is apparent that the animal has suffered severe and protracted diarrhea. The presence of even 10,000 *Trichostrongylus* worms in a well-nourished lamb carcass with formed fecal pellets in the rectum suggests only that we should search further for the cause of death. Etiologic significance should be attached to *Haemonchus* only if the carcass shows signs of anemia. Cattle with ostertagiosis can become emaciated on full feed. These animals do not even lose their appetites but develop malabsorption that causes them to starve to death in the midst of plenty. It is just as well not to accuse the

farmer of starving the animal to death when in fact *Ostertagia* is the culprit.

PARASITES OF DOGS

Stages in Feces

The common internal parasitisms of dogs can usually be diagnosed on the basis of the microscopic appearance of eggs, cysts, or larvae found in the feces. Micrometry or fecal culture may be necessary when more specific identification is required than can be accomplished on the basis of microscopic appearance alone.

Nematode Eggs

Eggs of some nematode parasites of dogs are shown in Figures 7-25 and 7-26.

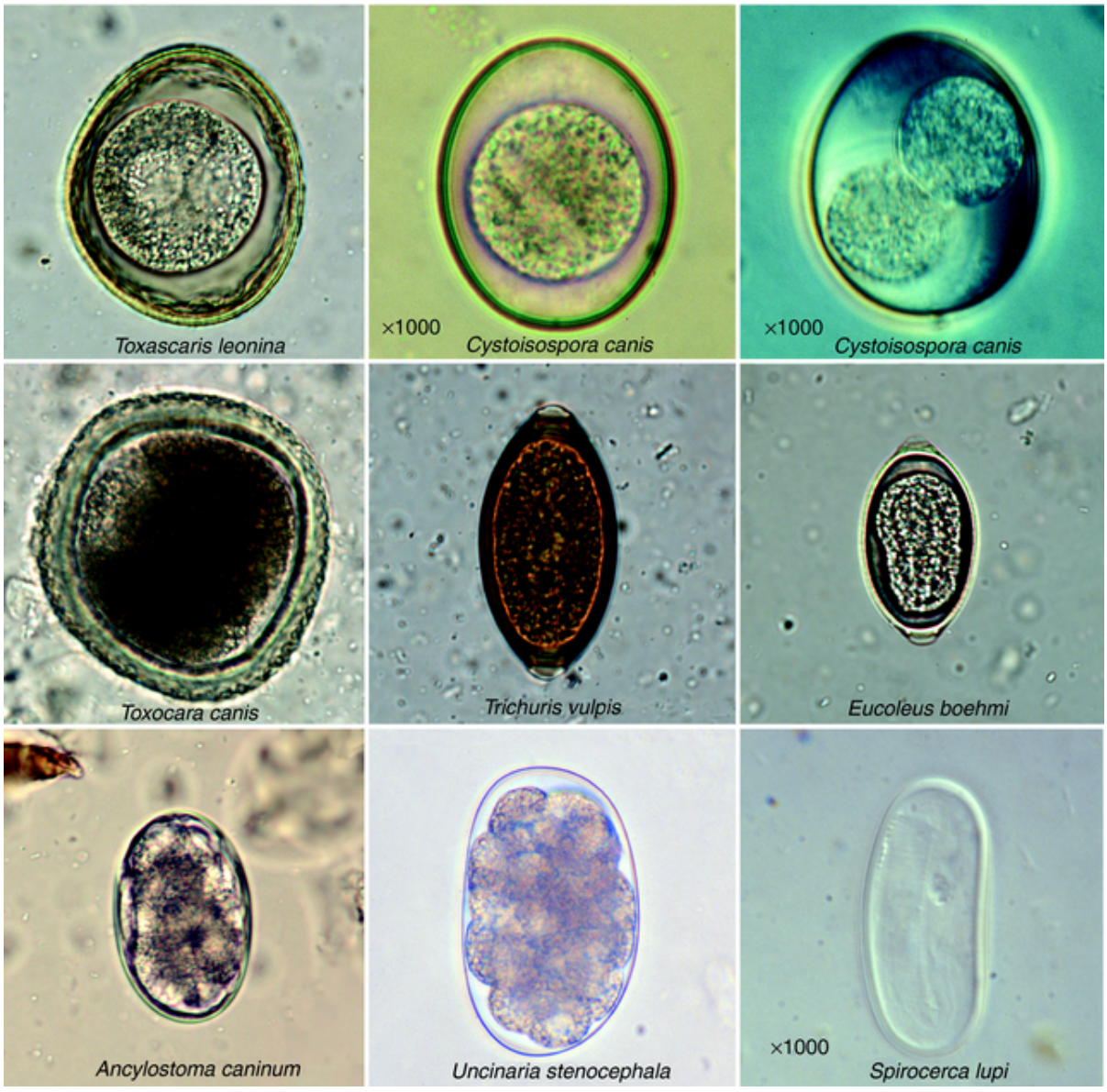

Figure 7-25 Eggs of some nematode parasites of dogs (×400, except for *Cystoisospora canis* and *Spirocerca lupi;* bar represents 100 μm divided into 10-μm units). *Toxascaris leonina* produces a colorless, subspheric to ellipsoidal egg shell with a smooth shell surface and a prominent lipid layer containing one or sometimes two cells in fresh specimens. *Cystoisospora canis*, a coccidian oocyst and not a nematode egg, is portrayed here ×1000 to illustrate how easily it might be confused with *T. leonina* unless the difference in size or the absence of a lipid layer is noticed. *Toxocara canis* produces a yellowish brown, subspheric egg with a uniformly pitted shell surrounding a single cell in fresh specimens. *Trichuris vulpis* and capillarid eggs are lemon-shaped and have bipolar plugs. *T. vulpis* eggs average more than 75 μm, whereas those of capillarids average less than 75 μm in length.

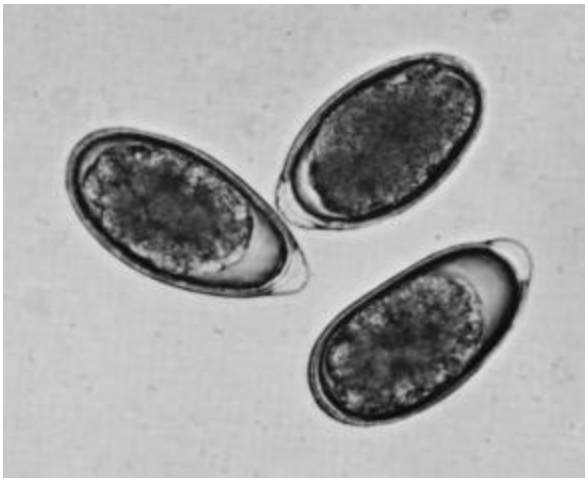

Figure 7-26 *Gnathostoma spinigerum* from a dog (×400). This dog belonged to a pet shop owner who occasionally fed it defunct tropical fish. Infection with this exotic parasite probably was acquired by eating one of these fishes.

The stage of embryonic development of eggs found in fresh fecal specimens varies among nematode species and thus provides us with diagnostic criteria. In fresh fecal specimens, *Toxocara*, *Toxascaris*, *Trichuris*, and the capillarid eggs of *Eucoleus aerophilus* and *Aonchotheca putorii* contain a single cell. The *Ancylostoma* or *Uncinaria* embryo has already segmented to produce a morula, as has the capillarid egg of *Eucoleus boehmi*. Many spirurid eggs contain first-stage larvae, and *Strongyloides* and *Filaroides* have already hatched and appear in the feces as first-stage larvae. The development of a typical nematode egg is portrayed in Figure 7-9.

Recovery of *E. aerophilus* eggs from respiratory mucus by tracheal swab requires general anesthesia. The presence of *Pearsonema plica* eggs in fresh fecal specimens represents contamination with urine. Urine specimens may also contain eggs of *Dioctophyme renale*, but these have much larger and rougher shells than do the eggs of *P. plica*, and the eggs of *D. renale* are typically in a two-cell stage when

passed. *Ancylostoma* and *Uncinaria* eggs have a smooth, clear, colorless, ellipsoidal shell and contain an embryo in the morula stage of development. *Ancylostoma caninum* eggs average less than 65 μm, whereas *Uncinaria stenocephala* eggs average more than 70 μm in length. Mixed infection with these two common species is easily recognized by the simultaneous presence of eggs of disparate size. Gomes de Faria (1910), who first described *Ancylostoma braziliense*, gave the dimensions of that egg as 65 by 32 μm. *Caution:* The eggs of strongyle parasites of domestic herbivores frequently find their way into dog feces through coprophagy and may be confused with hookworm eggs. Eggs of the order Spirurida are usually smooth walled and contain a larva. The most important of these, *Spirocerca lupi*, produces very small (30 by 12 μm), cylindric eggs with rounded ends.

Nematode Larvae

If the canine fecal sample is fresh and not contaminated with soil or extraneous organic material, larvae found swimming about the microscopic field may be either *S. stercoralis* or one of the following metastrongyloids: *F. osleri*, *F. hirthi*, *Crenosoma* sp., or *Angiostrongylus vasorum*. The esophagus of metastrongyloid larvae is longer than the rhabditiform esophagus of the first-stage *Strongyloides* larva, and the tail may have a slight kink as in *Filaroides* or a dorsal spine as in *Angiostrongylus*, whereas the tail of the *Strongyloides* and *Crenosoma* first-stage larva tapers smoothly to a point (Figure 7-27).

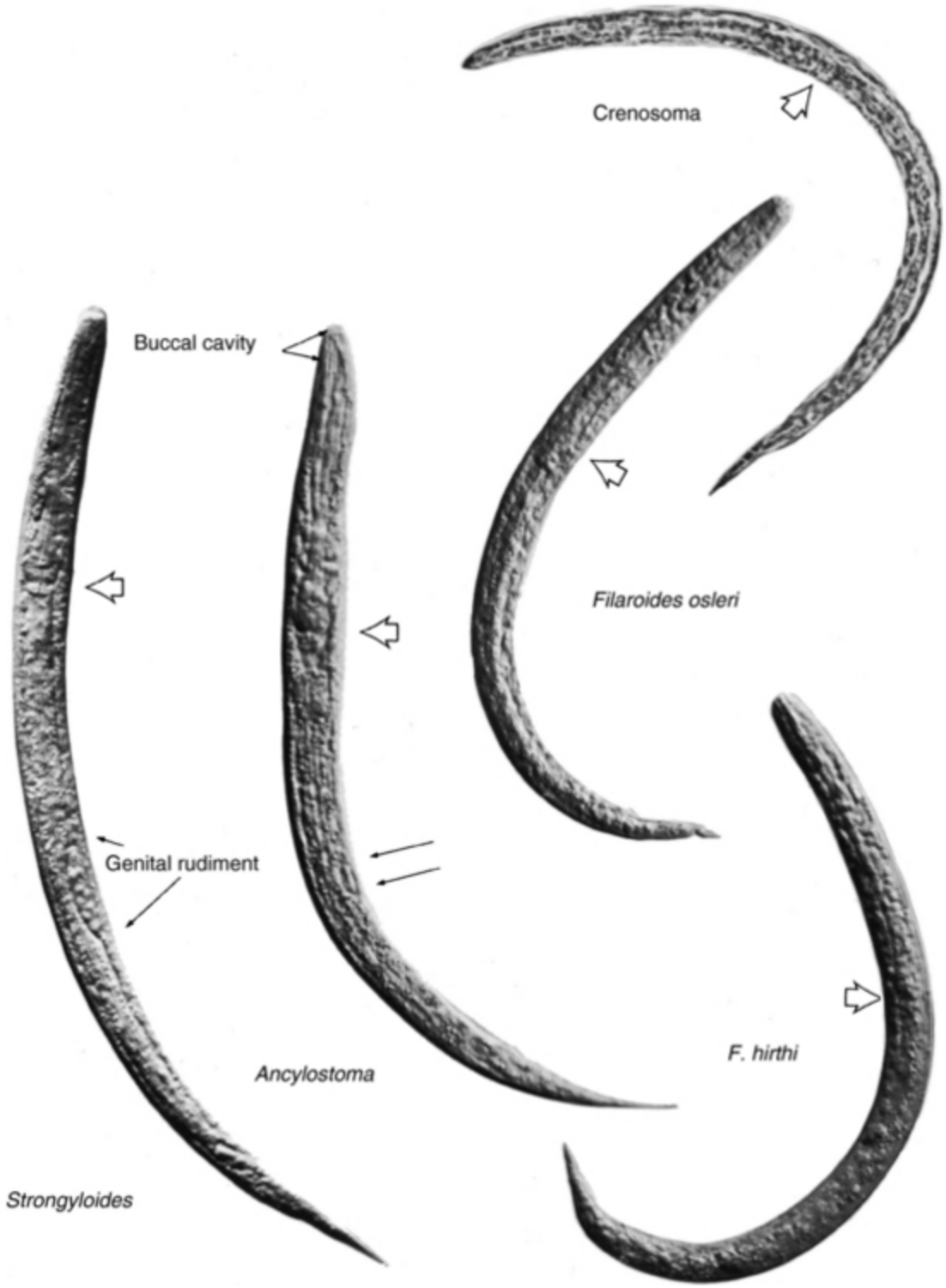

Figure 7-27 First-stage larvae of some nematode parasites of dogs. *Crenosoma* and *Filaroides* species are metastrongyloid lungworms and usually undergo no development in fecal cultures. *Strongyloides* and *Ancylostoma* first-stage larvae can be distinguished by differences in the relative sizes of their genital rudiments and relative lengths of their

buccal cavities. In fecal cultures, both *Strongyloides* and *Ancylostoma* develop to the infective stage (see Figure 7-28).

If the sample is stale, hookworm larvae may have developed and hatched. These somewhat resemble *Strongyloides* rhabditiform larvae but have a longer buccal capsule and smaller genital rudiment (see Figure 7-27). Should doubt remain, culture the feces for the development of infective stages. The infective sheathed third-stage larvae of hookworms do not begin to appear until after 5 to 7 days of incubation at room temperature, whereas homogonic *Strongyloides* filariform larvae appear as early as 24 to 36 hours, and heterogonic filariform larvae appear in about 4 days. *Strongyloides* filariform larvae are slender, with a very long esophagus, and the tip of their tail appears notched or truncated (Figure 7-28). If the specimen is contaminated with soil or extraneous organic material, free-living nematodes and their larvae may confuse the issue. Under such circumstances, the best course is to obtain a fresh sample directly from the dog's rectum.

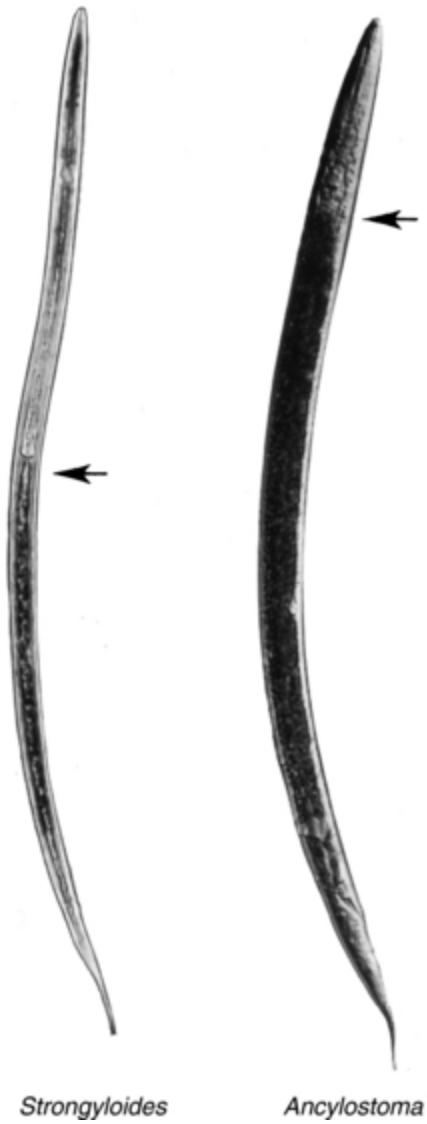

Figure 7-28 Third-stage infective larvae of *Strongyloides* and *Ancylostoma*. *Strongyloides* infective larvae have a very long esophagus, and the tip of the tail appears to be notched. (Actually, it is composed of four small projections of the double lateral alae.) *Ancylostoma* infective larvae are usually enclosed in the uncast cuticle (sheath) of the second stage, here seen extending slightly beyond the tail of the third stage. The arrows point to the esophageal-intestinal junctions.

Tapeworm Segments

Detached segments of cyclophyllidean tapeworms are often found crawling about on the perineum or fresh feces of infected dogs (and cats). Hand lens inspection permits identification for practical

purposes. Owners sometimes submit for identification shriveled objects that are actually dehydrated tapeworm segments (Figure 7-29, *A*). If these are soaked in water, they will usually regain their familiar appearance (Figure 7-29, *B*). Should doubt remain, the "reconstituted" segment may be squashed between two microscope slides bound together with adhesive tape. The segment may then be identified by the microscopic appearance of its eggs and such organs (e.g., genital pore, uterine diverticula or capsules, parauterine organ) as may persist in gravid segments of various species (Figures 7-30 to 7-33; see also Figure 7-29). Taeniid segments are roughly rectangular with a single, lateral genital pore and contain taeniid eggs (see Figures 7-29, 7-30, and 7-33, *A*). *Dipylidium* segments are shaped somewhat like cucumber seeds, have a genital pore on each lateral margin, and contain eggs clustered in packets (uterine capsules) (see Figures 7-31 and 7-33, *D*). *Mesocestoides* segments have a dorsal genital pore and eggs massed in a central, thick-walled parauterine organ (Figure 7-32), and fresh segments are said by some to resemble sesame seeds.

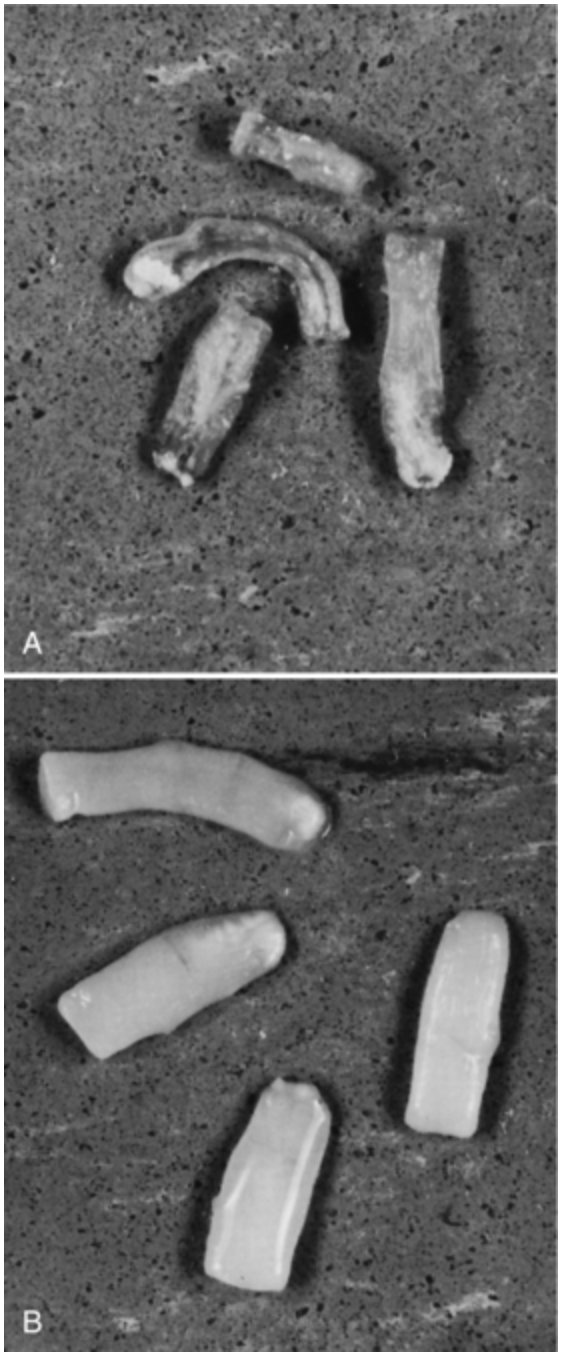

Figure 7-29 **A,** Dehydrated taeniid segments. **B,** Same segments after an overnight soaking in water.

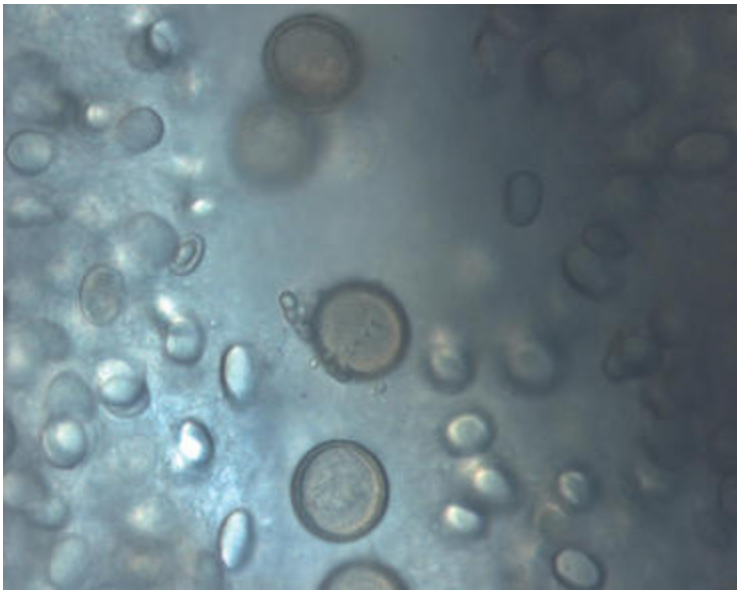

Figure 7-30 Taeniid segment in squash preparation.

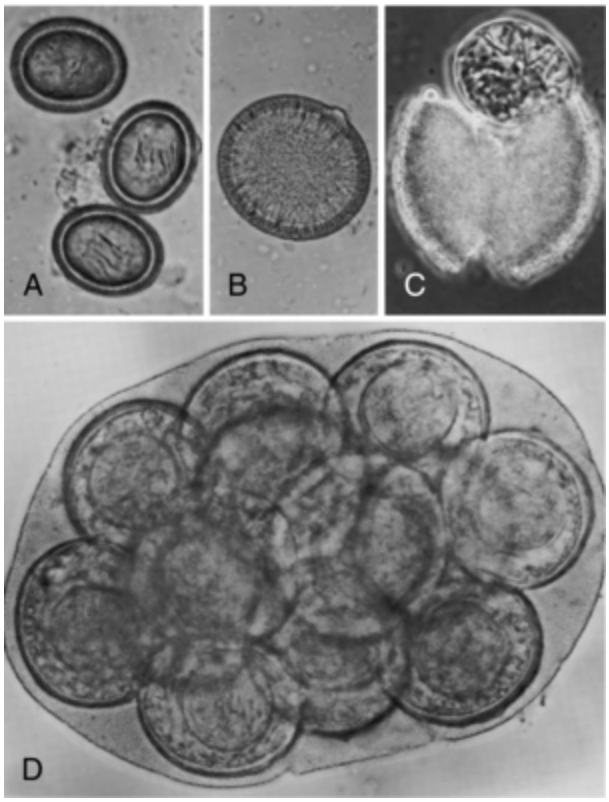

Figure 7-33 Tapeworm eggs. **A,** Three taeniid eggs. **B,** Taeniid egg, hooks not visible. **C,** Oncosphere emerging from the broken embryophore of the taeniid egg at left. **D,** *Dipylidium* egg capsule (×400).

Figure 7-31 *Dipylidium caninum* segments.

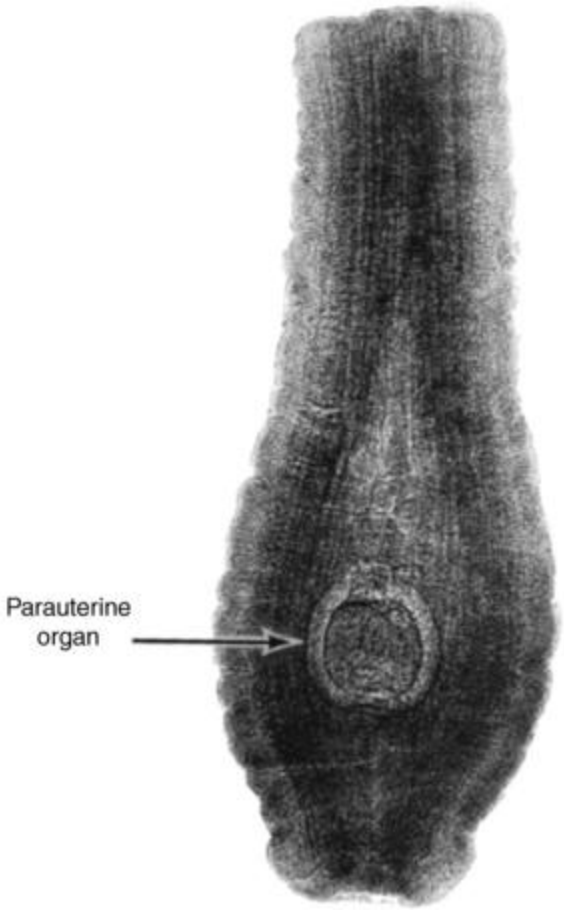

Figure 7-32 *Mesocestoides* sp. gravid segment; fresh, unrelaxed, and viewed with transmitted light.

Tapeworm Eggs

In the majority of tapeworms, the segmentation, gastrulation, and embryogeny of the egg takes place within the uterus of the adult worm. This is the case in the common cyclophyllidean tapeworm eggs. In the case of the pseudophyllidean eggs, the egg, surrounded by yolk cells, does not begin to embryonate until it leaves the uterus and enters the environment.

Cyclophyllidean Eggs

Taeniid eggs are spheric or subglobular with a radially striated embryophore (a shell-like covering) and contain an embryo (oncosphere or hexacanth embryo) with three pairs of hooks (see Figures 4-36 and 7-33, A). If the hooks are not clearly visible, they may sometimes be demonstrated by pressing a needlepoint on the coverslip to break the embryophore (see Figures 7-33, B and 7-33, C). The eggs of *Echinococcus* are a serious menace to human health and cannot be distinguished from those of *Taenia*. In *Echinococcus* endemic areas, therefore, the discovery of taeniid eggs in canine fecal samples demands prompt anthelmintic therapy and caution in the handling and disposal of feces. The eggs of Dipylidiidae are spheric or subspheric with an unstriated embryophore, contain an oncosphere, and are enveloped in a uterine capsule. In *Dipylidium* there may be up to 29 eggs per capsule (see Figure 7-33, *D*). In *Joyeuxiella* and *Diplopylidium* there is only one egg per uterine capsule. The eggs of *Mesocestoides* are oval and thin shelled and contain an oncosphere.

Diphyllobothriid Eggs

Diphyllobothriid eggs are discharged continuously through the uterine pores of many segments along the body of the worm and hence are passed independently of any detached segment. *Diphyllobothrium* and *Spirometra* eggs are oval with an operculum at one pole and a small button at the other (Figure 7-34, *A*) which often makes them difficult to distinguish from certain trematode eggs (Figure 7-34).

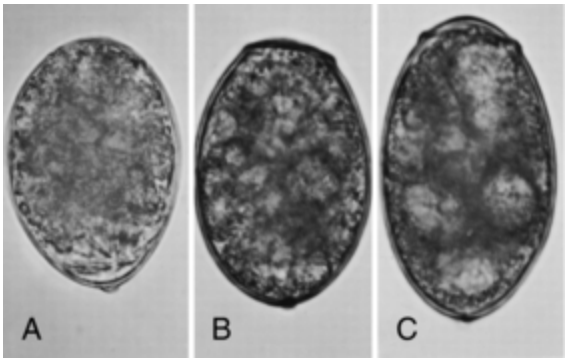

Figure 7-34 Operculate eggs (×400). **A,** *Diphyllobothrium* egg. **B** and **C,** Unidentified eggs; their prominent opercula suggest that, except for their small size, these might be *Paragonimus* eggs (see Figure 7-36, *B*). This figure illustrates the difficulty of distinguishing *Diphyllobothrium* eggs from those of certain trematodes.

Acanthocephalan Eggs

Acanthocephalan eggs have a thick outer and thinner inner shell enclosing an embryo called an *acanthor*. The external surface of the egg of *Macracanthorhynchus* is elegantly patterned (Figure 7-35).

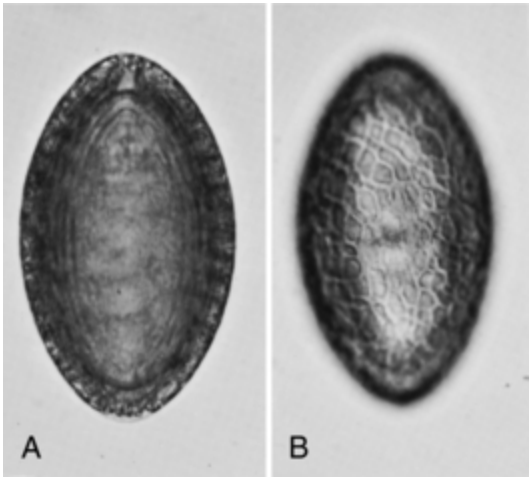

Figure 7-35 *Macracanthorhynchus ingens* (Acanthocephala) egg (×400). **A,** Acanthor in focus. **B,** Surface of shell in focus.

Trematode Eggs

Eggs of most digenetic trematodes have an operculum at one pole and contain an embryo whose stage of development varies with the species in question (Figure 7-36). Schistosome eggs, on the other hand, lack an operculum and contain a fully developed miracidium that hatches shortly after the egg comes in contact with water. Many, but not all, schistosome eggs have a sharp spine. If a dog has fed recently on trematode-infected tissues such as sheep liver infected with *Dicrocoelium* or *Fasciola* or rabbit entrails infected with *Hasstilesia*, the presence of myriad trematode eggs in its fecal specimen may lead to misdiagnosis.

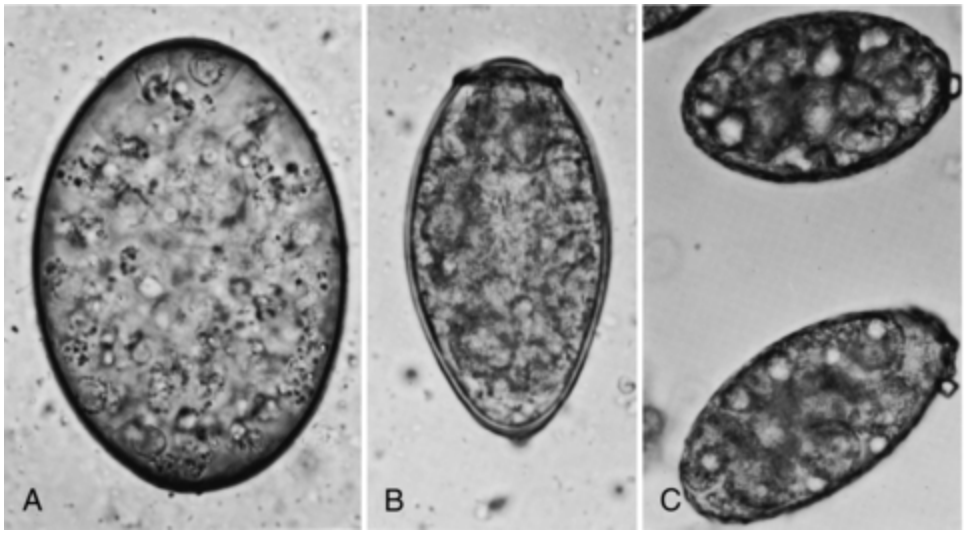

Figure 7-36 Trematode eggs (×400). **A,** *Alaria* sp. **B,** *Paragonimus kellicotti.* **C,** *Nanophyetus salmincola.*

Coccidian Oocysts and Sporocysts

Cystoisospora

Cystoisospora, Hammondia, and *Neospora* oocysts have colorless, ovoid or ellipsoidal, smooth-surfaced walls without micropyle or polar cap and contain a single sporont when passed in the feces of

the host (see Figure 7-25). Sporulation occurs in 2 to 4 days at room temperature. The fully sporulated *Cystoisospora* oocyst then contains two sporocysts, each of which contains four sporozoites (Figure 7-37, *A*). Because dogs tend to be coprophagic, oocysts of various other coccidia, especially *Eimeria* species of herbivores, are very common pseudoparasites in dog feces. If the *Eimeria* species in question have micropyles, polar caps, or other distinguishing features, they present no diagnostic problem (Figure 7-37, *B*), but many species are difficult to differentiate from *Cystoisospora* species. Differentiation of *Eimeria* and *Cystoisospora* may be accomplished by fecal culture for oocyst sporulation. Sporulated *Eimeria* oocysts contain four sporocysts, each of which contains two sporozoites (Figure 7-37, *C*).

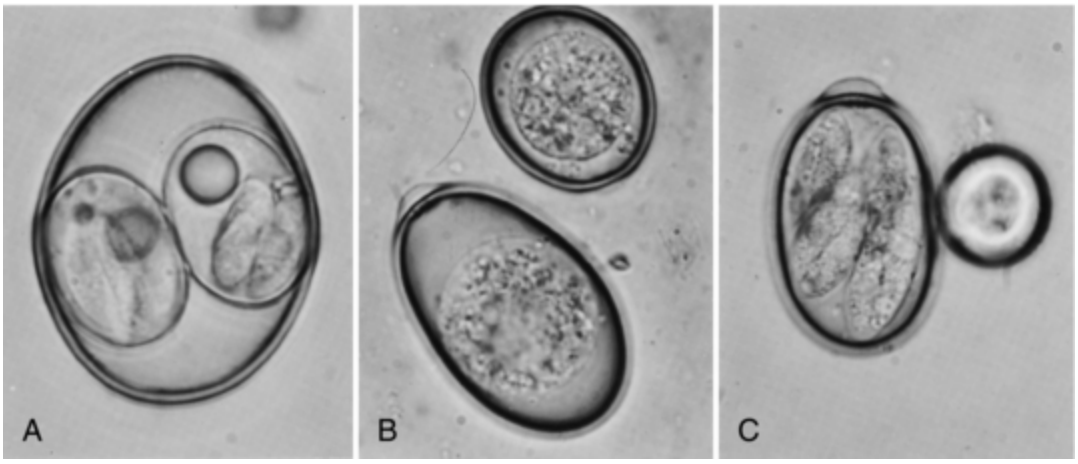

Figure 7-37 Coccidian oocysts (×1000). **A,** *Cystoisospora canis*, sporulated. **B,** *Eimeria* spp., one-cell stage. **C,** *Eimeria* sp., sporulated. *Cystoisospora* species sporulated oocysts contain two sporocysts, each of which contains four sporozoites. *Eimeria* species sporulated oocysts contain four sporocysts, each of which contains two sporozoites. See Figure 7-25 for *Cystoisospora canis* one-cell stage.

Identification of species of *Cystoisospora*, *Hammondia*, and *Neospora* requires micrometry. Oocyst dimensions in micrometers

for species infecting dogs are as follows: *Cystoisospora canis*, 32 to 42 × 27 to 33; *Cystoisospora ohioensis*, 19 to 27 × 18 to 23; *Cystoisospora burrowsi*, 17 to 22 × 16 to 19; *Hammondia heydorni*, 10 to 13 × 10 to 13 (Trayser and Todd, 1978); and *Neospora caninum*, 11.7 × 11.3 (Lindsay, Upton, and Dubey, 1999).

Sarcocystis

Sarcocystis species sporulate within the host, and the fragile oocyst wall often breaks so that the sporocyst containing four sporozoites is the form usually found in the feces (see Figure 7-54, *D*). Sporocysts measure 11 to 28 × 7 to 13 μm, but it is not possible to distinguish species of *Sarcocystis* by micrometry of sporocysts (Dubey, 1976). The host relationships of common species of *Sarcocystis* are presented in Table 3-1.

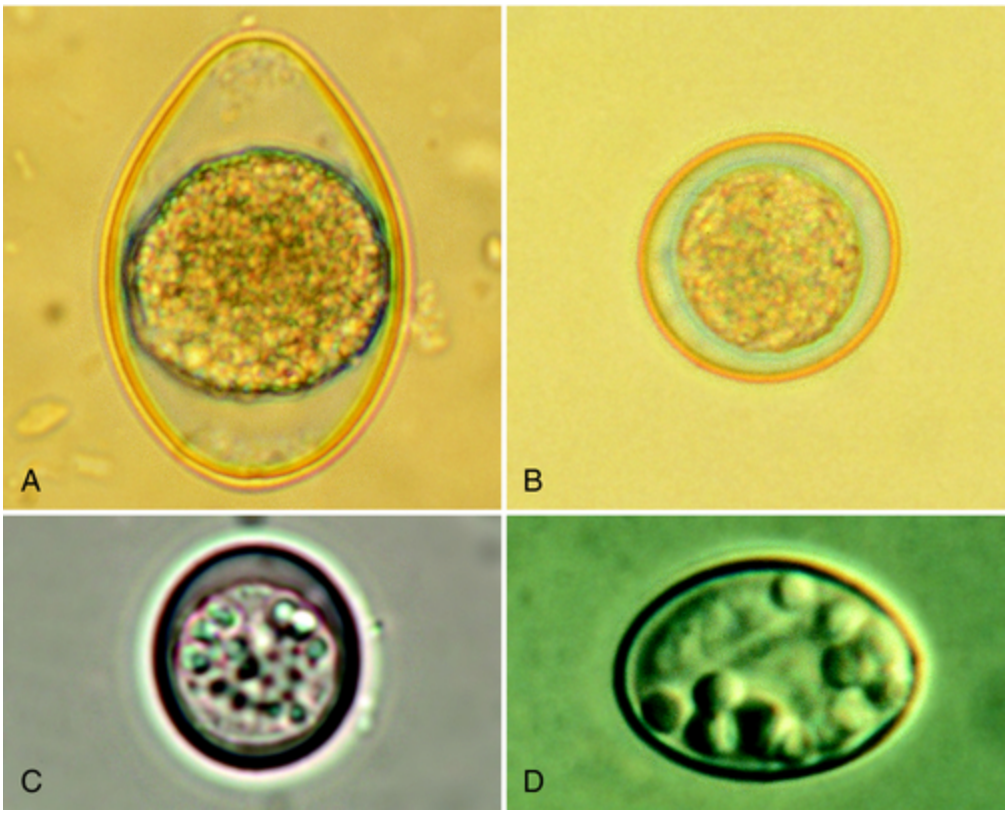

Figure 7-54 Coccidian cysts of cats. **A,** *Cystoisospora felis* (×1000). **B,** *Cystoisospora rivolta* (×2000). **C,** *Toxoplasma gondii* (×2000). **D,** *Sarcocystis* sp (×2000). *Sarcocystis* sporocysts released by rupture of the oocyst wall are only slightly larger than *T. gondii* but are ovoid rather than subspheric and contain four sporozoites.

Amebas

Entamoeba histolytica, a serious human pathogen, may appear in canine fecal specimens as either trophozoite or cyst. The trophozoites are more likely to be encountered in diarrheal feces and the cysts in formed fecal specimens. Trophozoites of the *E. histolytica* are 10 to 30 μm across, and their nuclei have marginated chromatin and a small central endosome. *E. histolytica* trophozoites display ameboid movement and often ingest erythrocytes. The mature cysts are 10 to 20 μm in diameter and contain four nuclei.

Entamoeba coli trophozoites are 20 to 30 μm in diameter. Their nuclei have a relatively large eccentric endosome. Erythrocytes are not found in *E. coli* trophozoites. As many as eight nuclei may be counted in *E. coli* cysts.

Entamoeba gingivalis, a parasite of the oral cavity, infects both man and dog. Only trophozoites, ranging in size from 5 to 35 μm, are found in oral scrapings.

Flagellates

Giardia trophozoites are less than 21 μm long, bilaterally symmetric, and pear-shaped. Two nuclei with large central endosomes look like a pair of eyes (see Figure 7-94). *Giardia* cysts are less than 12 μm long, are ellipsoidal, and contain four nuclei.

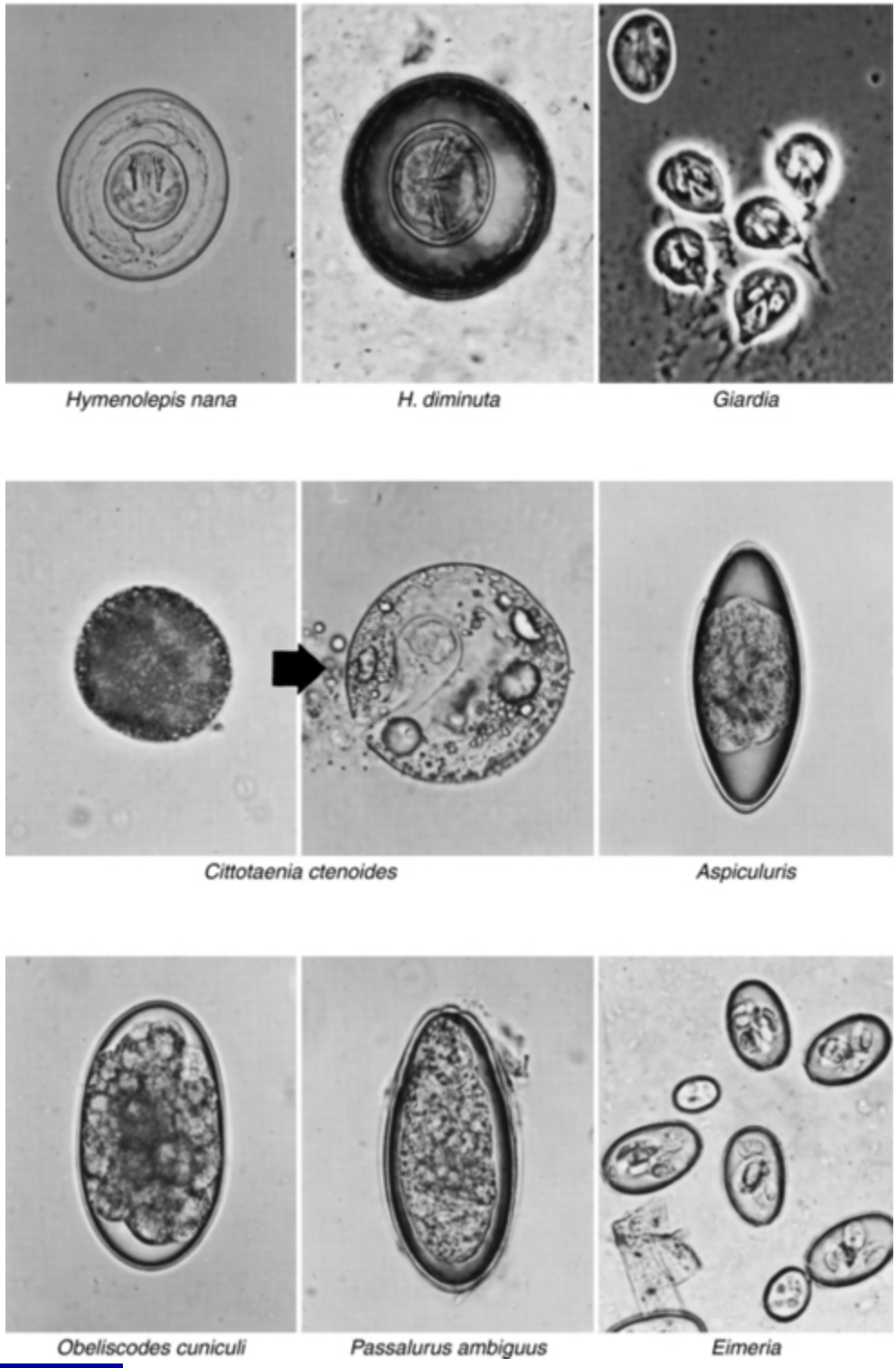

Figure 7-94 Common parasites of laboratory mice, rats, and rabbits. For a more comprehensive listing of laboratory animal parasites by host and organ, see text. *Mouse and rat: Hymenolepis nana* and *Hymenolepis diminuta* (Hymenolepididae) are also parasites of humans. *H. nana* infection in rodent colonies is directly infective to human beings; no

intermediate host is required by this tapeworm. Various beetles and cockroaches serve as intermediate hosts for *H. diminuta* and, facultatively, for *H. nana*. *Giardia* (Mastigophora) trophozoites *(group of five, center)* and cysts *(inset, upper left)* are common parasites of mice. *Rabbit: Cittotaenia ctenoides* (Anoplocephalidae) eggs appear as amorphous spheres *(left of arrow)* until crushed by pressure on the coverslip *(right of arrow)*, whereupon the oncosphere and pear-shaped embryophore become visible. *Obeliscoides cuniculi* eggs are typical strongyle eggs. *Passalurus ambiguus* (Oxyuridae) are somewhat asymmetric and have a cap at one end. *Eimeria*, sporulated oocysts. Avoid mistaking *Saccharomycopsis guttulatus* (see Figure 7-6) for a bona fide parasite of the rabbit. All ×425 except *Giardia* (×1000).

Trichomonas and related genera do not form cysts and occur in feces (usually diarrheal) only as mononucleated trophozoites.

Ciliates

Balantidium coli trophozoites are ovoid with a cytostome at one end; measure 25 to 150 μm in diameter; contain one macronucleus and one micronucleus, two contractile vacuoles, and inclusions; and are covered with rows of cilia (see Figure 3-8). Cysts are spheric or ovoid, measure 40 to 60 μm in diameter, and have a wall consisting of two membranes (see Figure 3-8).

Fixation and Identification of Microfilariae in Blood

The simplest procedure for diagnosing the presence of microfilariae in the blood of dogs is to place a drop of heparinized venous blood on a slide, add a coverslip, and examine the preparation under low and high dry magnification. Microfilariae reveal their presence by agitating the erythrocytes in their immediate vicinity. In general, if more than 5 or 10 microfilariae are observed per drop of blood, they are probably *Dirofilaria immitis*. If fewer than that are observed, they may represent either heartworm or another filariid parasite

infection. In North America the only other filariid recognized in dogs is *Dipetalonema reconditum* (Newton and Wright, 1956, 1957), but in certain other parts of the world, there are also other species that need to be dealt with. The following procedure is about 15 times as sensitive as the direct smear and permits more accurate differentiation of microfilariae of *D. immitis* and *D. reconditum*.

Technique of Knott (1939) Modified

1. Draw a sample of venous blood into a syringe containing a suitable anticoagulant such as ethylene-diaminetetraacetic acid (EDTA) or heparin.

2. Draw 1 to 2 mL of air into the syringe, and mix the blood and anticoagulant by rocking the syringe so as to run the air bubble back and forth along the length of the barrel. Prolonged delay and thermal extremes are to be avoided. Remix blood immediately before proceeding with step 3.

3. Place 1 mL of blood in a 15-mL centrifuge tube. Add 10 mL of 2% formalin, stopper, and mix by inversion and shaking. *Note:* When submitting blood samples to a laboratory for identification of microfilariae, complete only steps 1, 2, and 3 to prepare them for shipment.

4. Wait 2 or 3 minutes.

5. Centrifuge for about 5 minutes, and pour off the supernatant by inverting the centrifuge tube only once. Remove the drop that clings to the rim of the tube with absorbent paper.

6. Add one drop of 0.1% methylene blue to the sediment, mix, and transfer some stained sediment to a slide for microscopic examination.

There are other microfilarial concentration techniques, but the Knott test is preferred because it is standard, it is inexpensive, and it includes the best preparative technique for specimens submitted to the laboratory. The quality and concentration of the formalin solution are critical. Two percent formalin is 2 mL of stock 37% formaldehyde solution (i.e., formalin) and 98 mL of distilled water. This reagent tends to deteriorate in storage and should be made up fresh periodically.

Differentiation of Microfilariae

Microfilariae of *D. immitis* are 6.0 to 7.0 μm wide, whereas those of *D. reconditum* are less than 5.6 μm wide. Length measurement is a more tedious and less reliable differential criterion. When fixed by the preceding technique, the tails of *D. reconditum* microfilariae tend to be curved like an ovariectomy hook. The anterior end of the *D. immitis* microfilaria tapers gently, whereas that of *D. reconditum* maintains about the same diameter throughout. The cephalic hook of *D. reconditum* (Figure 7-38) is demonstrable with the ×40 objective of any modern, standard, compound microscope in samples prepared by the Knott technique described earlier. It is not necessary to resort to thick smears or special stains to demonstrate the cephalic hook. Patience is required at first, but with practice the cephalic hook proves the quickest, easiest, and most reliable differential criterion.

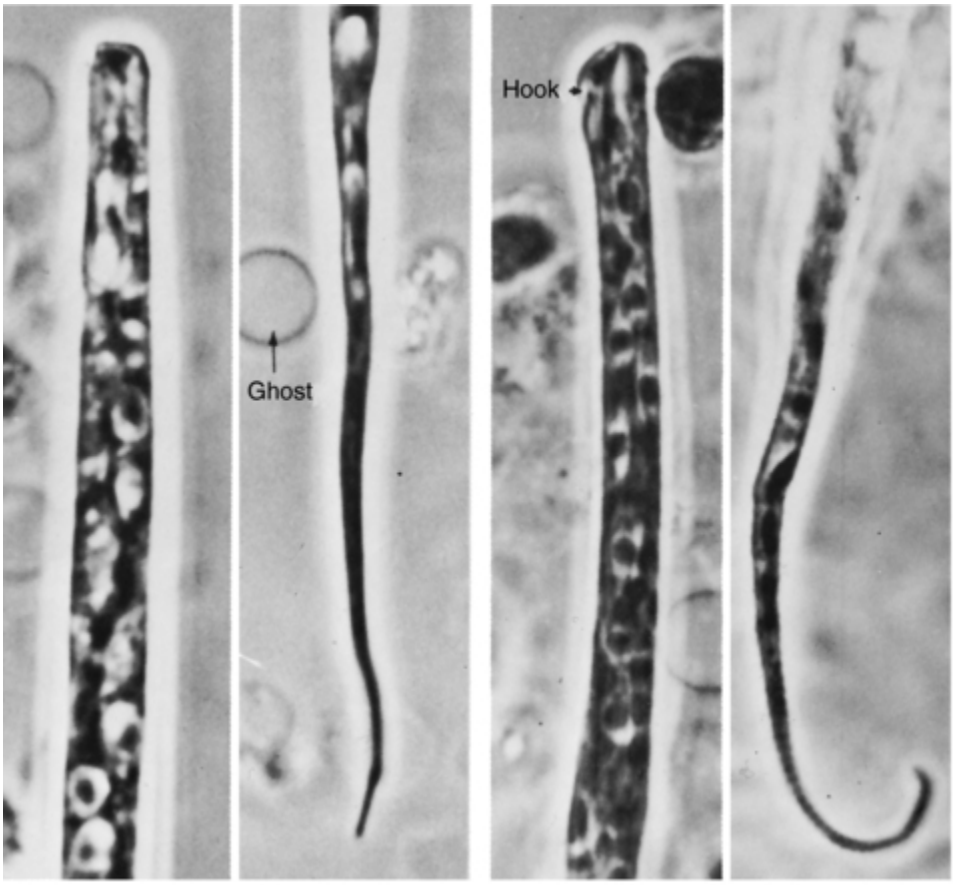

Figure 7-38 Microfilariae of *Dirofilaria immitis* and *Dipetalonema reconditum* (×2000). See text for exposition of differential characters.

Annotated Host-Organ Listing of Parasites of Dogs

Toxoplasma gondii may occur in any tissue of any host as extracellular or intracellular tachyzoites or as bradyzoites in cysts (see Figure 8-35). *N. caninum* may occur in similar locations (see Figures 3-22 and 8-36Figure 3-22Figure 8-36).

Alimentary System

Mouth

Protozoa

Trichomonas canistomae (Mastigophora). Found around gum margins; nonpathogenic.

Esophagus and stomach

Nematodes

Spirocerca lupi (Spirurida). Found in fibrous nodules in the wall of the esophagus and sometimes the stomach (see Figures 8-103 to 105Figure 8-103Figure 8-104Figure 8-105). Larvae migrate through the adventitia of the arteries and aorta to the walls of the stomach or esophagus. Adults encyst in nodules that communicate with the lumen of these two organs. Cysts may be found in other locations as well. Chronic infection is associated with dysphagia, vomiting, esophageal osteosarcoma, aortic aneurysm (rupture rare), and pulmonary osteoarthropathy.

Physaloptera rara and *Physaloptera praeputialis* (Spirurida). Adult worms (see Figures 4-130 and 4-131Figure 4-130Figure 4-131) are found with their anterior end embedded into the gastric mucosa. Infection can be asymptomatic or may be associated with vomiting and anorexia.

Gnathostoma spinigerum (Spirurida). Relatively rare in North America (see Figure 4-129). Adults encyst in nodules in the stomach wall. Larval migration through the liver and other organs is destructive. Rupture of nodules containing adult worms into the peritoneal cavity can cause a medical emergency.

Small intestine

Nematodes

Toxocara canis and *T. leonina* (Ascaridoidea). *Toxocara* has a ventriculus intercalated between the esophagus and the intestine (Figure 7-39), whereas *Toxascaris* has none (Figure 7-40). The ventriculus is visible in transilluminated fresh specimens under the stereoscopic microscope and in fixed, cleared specimens under the compound microscope. Large, fixed specimens may be dissected to determine the presence or absence of a ventriculus. The tail of male *Toxocara* is fingerlike (Figure 7-41), whereas the tail of male *Toxascaris* tapers to a point (Figure 7-42). Female *Toxocara* and *Toxascaris* may be distinguished by comparing their eggs (see Figure 7-25). In acquiring diagnostic skill, one must not be content with merely comparing general impressions of the microscopic image with a set of pictures in a book. Persons basing their diagnoses on superficial appearances often confuse *Toxascaris* eggs with *Cystoisospora canis* oocysts less than half as large. In Figure 7-25, a *T. leonina* egg $\times 425$ and a *Cystoisospora canis* oocyst $\times 1000$ have been placed side by side to show how easily this mistake could be made. The matter may be resolved with an ocular micrometer or, more simply, through observation of whether a distinct lipid layer is present *(Toxascaris)* or absent *(Cystoisospora)*. Ascarids in the small intestine may cause bloating and can interfere with intestinal motility and digestion (Figure 7-43). Mucoid diarrhea, vomiting, abdominal distension, emaciation, and a failure to thrive may all be noted as clinical signs. Infection with *T. leonina* is less pathogenic and usually only results in the worst cases with diarrhea and vomiting.

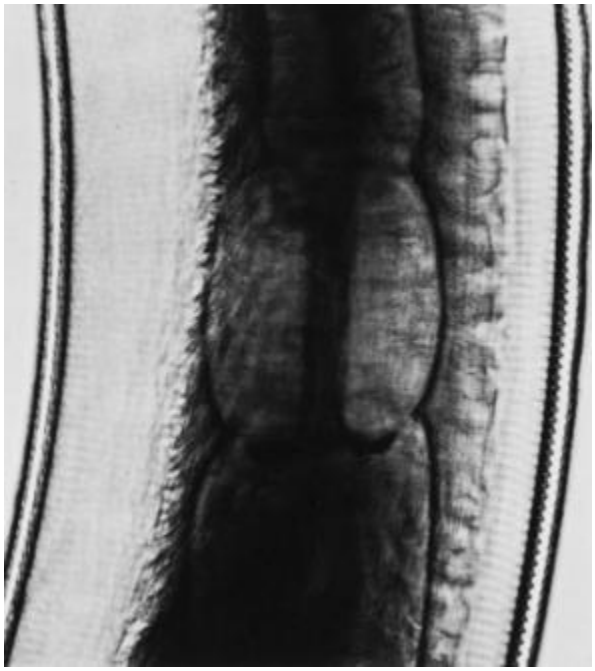

Figure 7-39 *Toxocara*. A ventriculus is intercalated between the esophagus and the intestine (×108).

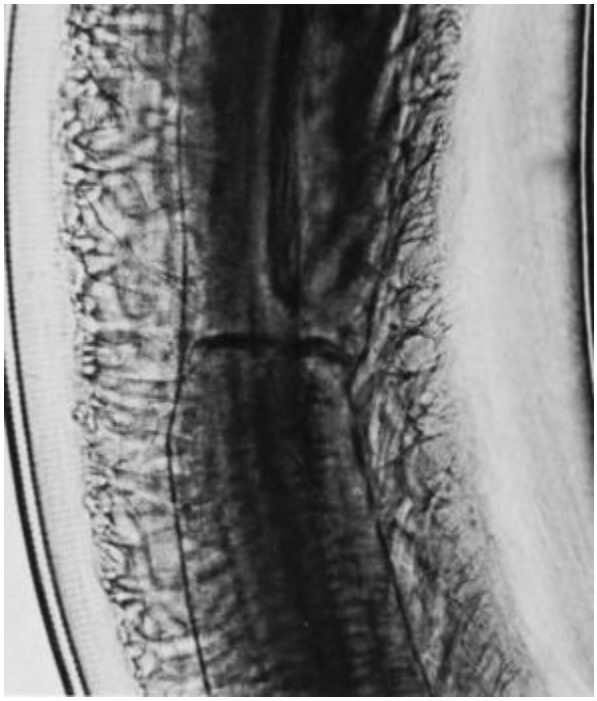

Figure 7-40 *Toxascaris*. There is no ventriculus between the esophagus and the intestine (×108).

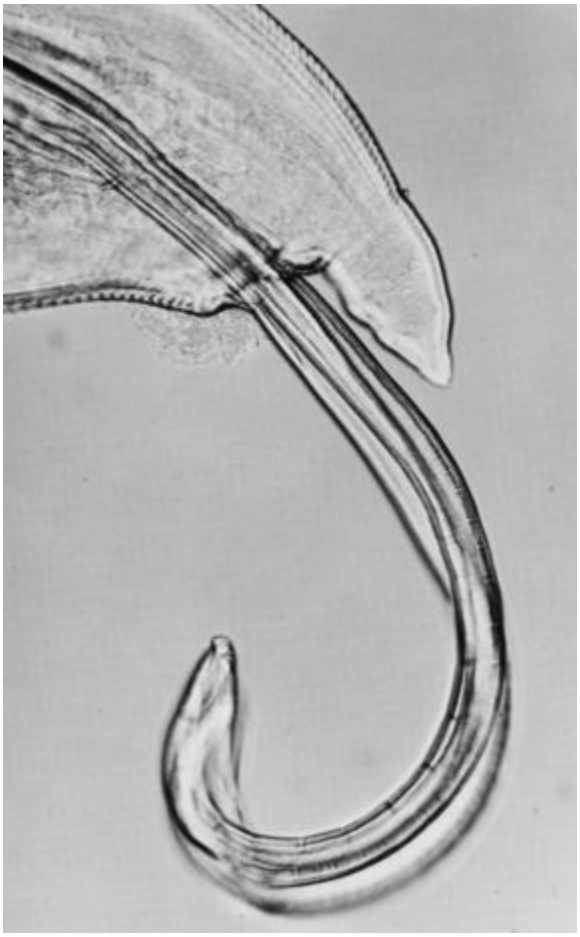

Figure 7-41 *Toxocara*. The tail of the male is fingerlike (×108).

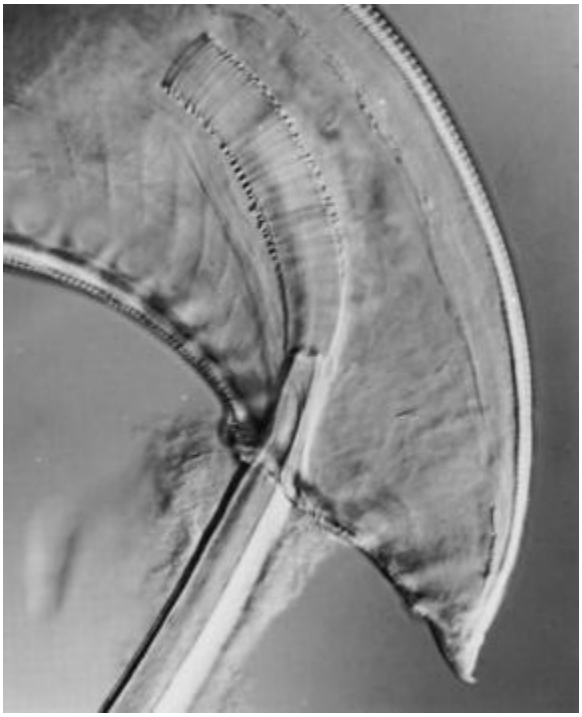

Figure 7-42 *Toxascaris*. The tail of the male tapers gradually (×168).

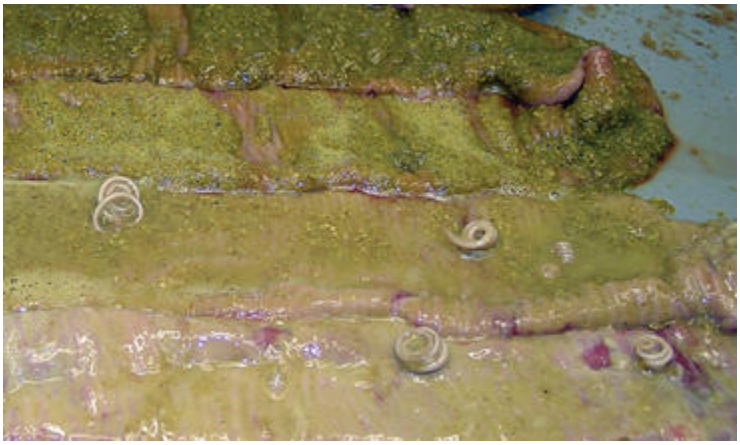

Figure 7-43 *Toxocara canis* worms in the intestine of a dog at necropsy.

Baylisascaris procyonis, the raccoon roundworm, is showing up in dogs as adult worms. This is a dangerous parasite because the zoonotic disease produced by the ingestion of embryonated eggs can be devastating and life threatening. Although a rather rare condition, cases are regularly occurring. When fully mature, the

worms tend to be larger than *Toxocara canis* or *T. leonina*, and the eggs can be differentiated by the facts that they are smaller, have a rough external shell (see Figure 4-125), and appear browner than the eggs of the two common dog ascaridoids. Infected dogs are typically without any clinical signs.

Ancylostoma caninum, *A. braziliense*, and *U. stenocephala* (Ancylostomatoidea). Mature hookworms are found anchored to the mucosa by their buccal capsules unless the cadaver has cooled out or the host has died of an overdose of barbiturate, in which case many specimens will be found unattached. Preadult *A. caninum* burrow deeply and destructively in the mucosa (Figure 7-44), and the mesenteric lymph nodes may be hemorrhagic as a result during the prepatent phase of severe infections. An adult *A. caninum* is colored red, whereas *A. braziliense* and *U. stenocephala* are grayish white. The red color of *A. caninum* quickly fades on fixation, however. Specimens may be differentiated by microscopic examination of their buccal structures: *A. caninum* has three pairs of pointed teeth on the ventral border of the buccal capsule; *A. braziliense* has one pair of pointed teeth; and *U. stenocephala* has a pair of rounded plates instead of teeth (see Figure 4-95). *A. caninum* sucks much more blood than either of the other hookworm species affecting dogs. Suckling pups experience peracute infections owing to transmammary transmission of larvae; infection may be fatal. Affected pups will have pale mucous membranes, and they can pass soft liquid stools containing partially digested blood.

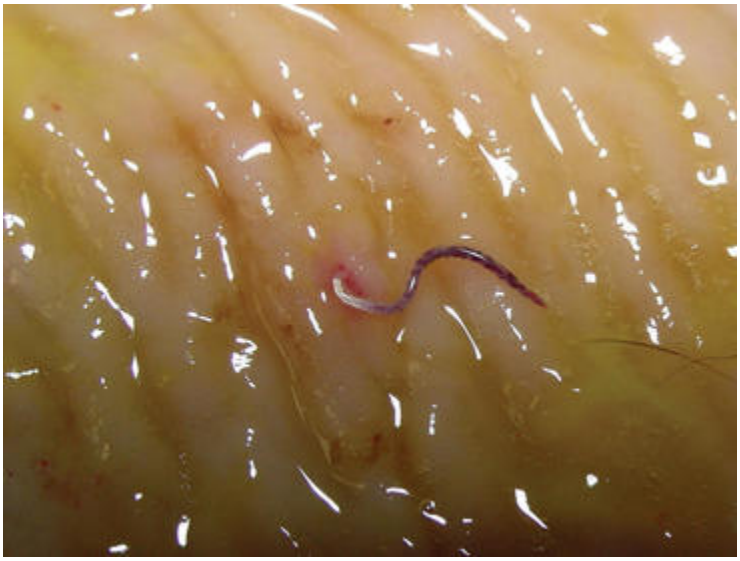

Figure 7-44 *Ancylostoma caninum* female attached to the intestinal mucosa at a feeding site.

S. stercoralis (Rhabditoidea). The tiny (2.2 mm) parthenogenetic parasitic female worms (see Figure 4-108) may be found in scrapings of the mucous membrane. Clinical signs vary from none to watery diarrhea.

Trichinella spiralis (Trichinelloidea). The small adults are found threaded through the mucosa of the duodenum and produce "prelarvae" that enter the intestinal mucosa (see Figure 4-148). Vomiting or mild diarrhea may result.

Cestodes

T. pisiformis, *Taenia hydatigena*, *Taenia ovis*, *Taenia multiceps*, and *Taenia serialis* (Taeniidae). Adult tapeworms typically (Figure 7-45; see also Figures 4-33 to 4-35 and 4-37Figure 4-33Figure 4-34Figure 4-35Figure 4-37), cause no significant signs.

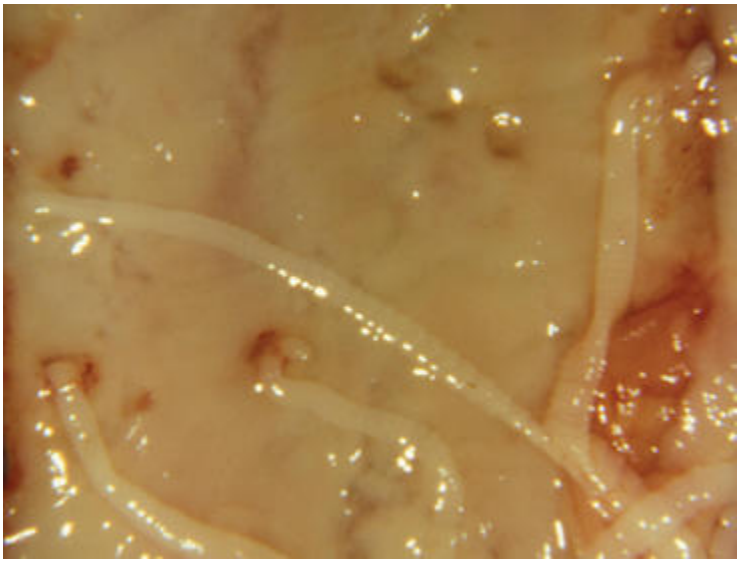

Figure 7-45 Anterior ends of *Taenia pisiformis* with the attachment sites from three scolices.

E. granulosus and *E. multilocularis* (Taeniidae). Adult tapeworms typically (see Figure 4-43), cause no significant signs.

Dipylidium caninum, *Diplopylidium*, and *Joyeuxiella* (Dipylidiidae). Typically without clinical signs (Figure 7-46; see also Figures 4-55, 7-31, and 7-33), infection can result in impaction in young puppies.

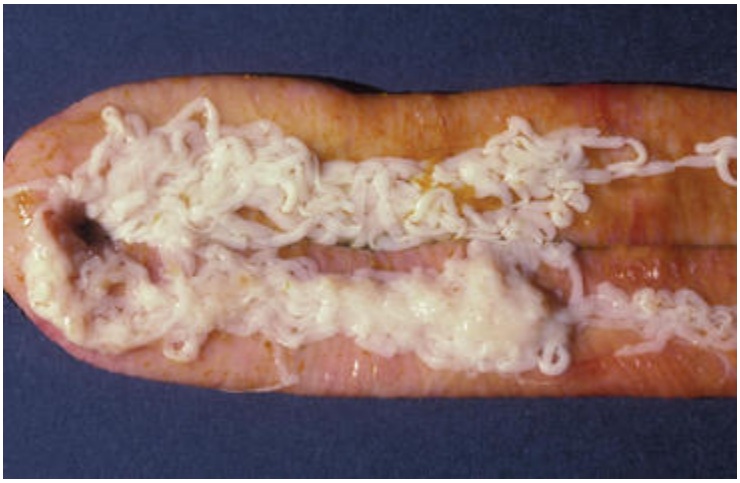

Figure 7-46 *Dipylidium caninum* in the intestine of a dog at necropsy.

Mesocestoides species (Mesocestoididae). Typically, infection is without clinical signs (see Figures 4-58 and 7-32).

Diphyllobothrium latum (Diphyllobothriidae). Typically, infection is without any signs (see Figures 4-25, 4-26Figure 4-25Figure 4-26, and 7-34, A).

Trematodes

Alaria americana (5 mm), *Alaria arisaemoides* (10 mm), *Alaria canis* (3.2 mm), and *Alaria michiganensis* (1.9 mm) (Diplostomatidae) (see Figure 4-22).

Mesostephanus appendiculatum (1.8 mm) and *Mesostephanus longisaccus* (1 mm) (Cyathocotylidae). These cyathocotylids resemble *Alaria* in having a bulbous tribocytic organ but differ in not being divided into distinct fore- and hind-body regions.

Echinochasmus schwartzi (2.1 mm) (Echinostomatidae) is a slender echinostomatid with a collar of spines surrounding the oral sucker.

Apophallus venustus (1.4 mm), *Cryptocotyle lingua* (2.2 mm), and *Phagicola longa* (1.2 mm) (Heterophyidae). Dogs ingesting fish and acquiring *C. lingua* can have severe enteritis.

Plagiorchis species. This small (1.2 mm) plagiorchiid has a spindle-shaped, spinous body with well-developed suckers; the genital pore is anterior to the ventral sucker.

Nanophyetus salmincola (1.1 mm, see Figure 4-13) and *Sellacotyle mustelae* (0.4 mm) (Troglotrematidae) are ovoid and pear-shaped, respectively, and have spinous bodies and well-developed suckers. *N. salmincola* is host to *Neorickettsia helminthoeca*, which causes

salmon poisoning in dogs. Signs include hemorrhagic enteritis and lymphadenopathy.

Acanthocephala

Oncicola canis is small (14 mm) and spindle-shaped (see Figure 4-161). *Macracanthorhynchus ingens* is very large (see Figures 4-155 and 7-35); dogs acquire infection by ingesting millipedes, with diarrhea as the main clinical sign.

Protozoa

Flagellates

Giardia canis (see Figure 7-94) trophozoites on mucosa of the small intestine can be visualized in scrapings examined by microscopy. Diarrhea and vomiting may occur, typically in younger animals. Other infected dogs may or may not have signs but may have periodically soft feces with a foul odor. Cysts are often excreted without clinical signs.

Coccidia

Cystoisospora canis, *C. ohioensis, C. burrowsi*, *H. heydorni*, and *N. caninum* (Apicomplexa) oocysts contain a single sporont when shed in the feces (see Figure 7-25). Schizonts, gamonts, and oocysts may also be found in histologic sections or mucosal scrapings. These coccidia cause damage to host enterocytes. Young animals and immunocompromised animals are most often affected. The main clinical sign is diarrhea, which is usually watery but may also contain mucus or blood.

Sarcocystis cruzi, Sarcocystis ovicanis, Sarcocystis miescheriana, Sarcocystis bertrami, Sarcocystis fayeri, and Sarcocystis hemionilatrantis (see Table 2-1 and Figure 7-54) (Apicomplexa) have sexual stages in the mucosa, usually with no clinical signs.

Cryptosporidium canis (Apicomplexa) has minute stages on the apical margins of the enterocytes that would be difficult to see without histologic sections. Most infections occur in dogs less than 6 months old or in dogs that are immunocompromised.

Cecum and colon

Nematodes

T. vulpis (Trichuroidea) (Figure 7-47; see also Figures 4-151, 4-153Figure 4-151Figure 4-153, 7-25, 8-113, and 8-114). In small numbers, worms are found in the cecum; in heavier infections, worms also are found with their anterior end embedded in the mucosa of the colon and rectum. Most dogs are without clinical signs. Dogs can have large bowel diarrhea characterized by hematochezia; mucus and straining are the main clinical signs. Diarrhea may lead to dehydration or pseudohypoadrenocorticism in middle-aged and older dogs as a result of isotonic fluid loss causing hyponatremia, metabolic acidosis, and hyperkalemia.

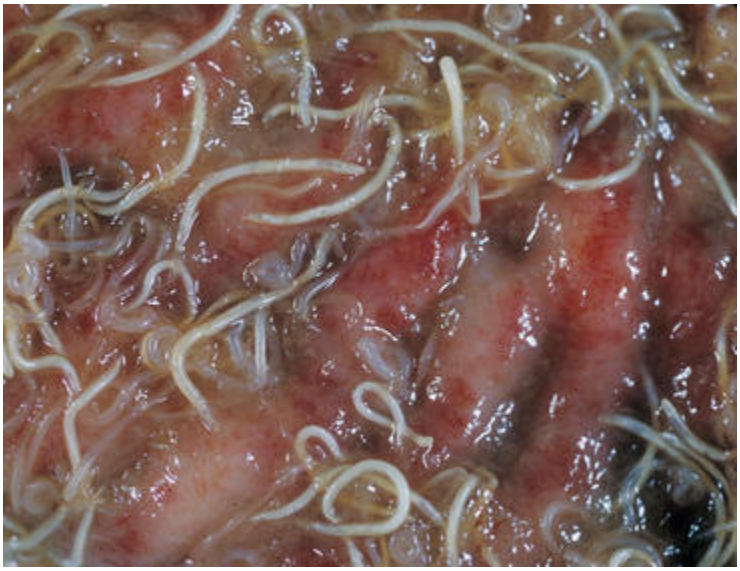

Figure 7-47 *Trichuris vulpis* posterior ends of worms on the mucosa of the cecum; the anterior portions of the worms are embedded in the mucosa.

Protozoa

E. histolytica and *E. coli* are cyst-forming amebas. Trophozoites of *E. histolytica* may contain phagocytosed erythrocytes. Infection with these organisms seems very rare in dogs in the United States.

Trichomonas species and *Pentatrichomonas hominis* are non–cyst-forming mucosoflagellates. They can be found by examination of mucus and will lyse in water, so saline preparations are required.

B. coli (ciliate) (see Figure 3-8) has caused colitis in dogs on very rare occasions.

Liver and pancreas

Nematodes

Toxocara canis and *T. leonina* (Ascaridoidea) sometimes erratically invade the common bile duct or pancreatic duct causing obstruction or rupture.

Calodium (Capillaria) hepaticum (Trichinelloidea) (see Figure 8-117) is found in the liver of dogs usually as an incidental necropsy finding.

Nematode larvae

Toxocara canis (Ascaridoidea) can have encapsulated larvae widely distributed in adult animals, especially in skeletal muscle and the kidneys, but also the liver.

Filaroides species.

Trematodes

Opisthorchis tenuicollis, *Opisthorchis viverrini*, *Clonorchis sinensis*, *Metorchis albidus*, and *Metorchis conjunctus* (Opisthorchiidae) in bile ducts (see Figure 4-10); infections are usually asymptomatic unless a large worm burden is present, in which case severe hepatic dysfunction can result.

Eggs of *Heterobilharzia americana* (Schistosomatidae) in tissues are surrounded by granulomatous reaction; granulomatous lesions in the liver may be associated with an elevation of hepatic enzymes. Flushing the vascular system of the liver with saline may produce large numbers of paired flukes. Clinical signs are nonspecific and may include anorexia, lethargy, weight loss, and diarrhea.

Peritoneum and peritoneal cavity

Cestode larvae

Mesocestoides tetrathyridia (see Figures 8-65 to 8-67Figure 8-65Figure 8-66Figure 8-67) can be associated with massive infections

owing to asexual multiplication that may be associated with diarrhea, abdominal distension, pain, and weakness.

Nematode

D. renale is a giant red worm (up to 1 m, Trichinelloidea) in the peritoneal cavity or renal pelvis (see Figure 4-146). Besides the occasional free adult in the peritoneal cavity, the third-stage larvae cross through the peritoneal cavity on their way to the liver, where they molt to the fourth stage. Fourth-stage larvae again traverse the peritoneal cavity before entering the renal capsule. A serofibrinous to chronic fibrinous peritonitis can result.

Respiratory System

Nasal passages

Nematodes

Eucoleus (Capillaria) boehmi (Trichinelloidea) may cause sneezing.

Arthropods

Pneumonyssoides caninum (Mesostigmata) (Figure 7-48; see also Figure 8-8). Clinical signs include reverse sneezing, chronic nasal discharge, nasal irritation, and epistaxis. Inflammation of the nasal cavity may result in the loss of the sense of smell.

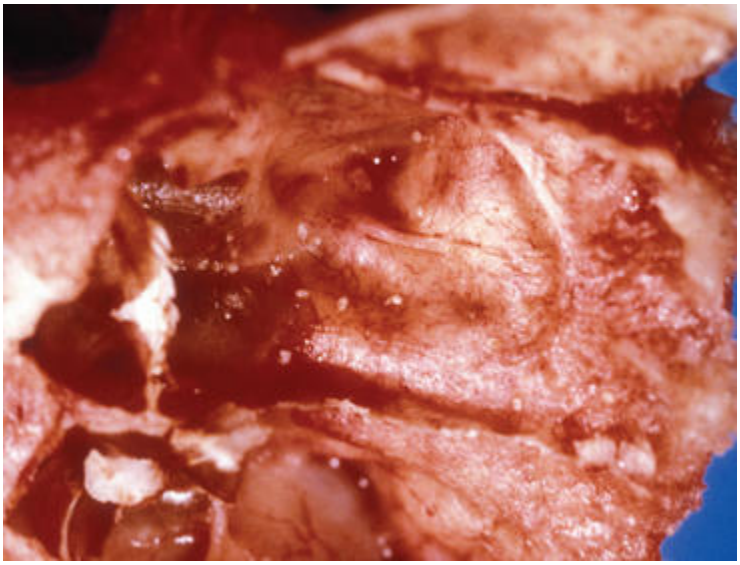

Figure 7-48 *Pneumonyssoides caninum* mites (Mesostigmata, Halarachnidae) in the nasal sinuses of a dog at necropsy.

Courtesy Dr. John M. King.

Linguatula serrata (130 mm, Pentastomida). These organisms are bloodsucking, wormlike parasites of the nasal cavity and paranasal sinuses. They can cause epistaxis, inflammation, and respiratory distress.

Trachea and bronchi

Nematodes

F. osleri (Metastrongyloidea) (see Figures 4-105 and 7-27). *F. osleri* occurs in nodules near the bifurcation of the trachea with clinical signs of respiratory distress.

Crenosoma vulpis (Metastrongyloidea) (see Figures 4-102 and 7-27) are small worms (16 mm) found on bronchial and bronchiolar mucosa, causing most typically signs of chronic cough, dyspnea, and exercise intolerance.

Eucoleus (Capillaria) aerophilus (Trichinelloidea) is associated with signs of coughing.

Lung parenchyma

Nematodes

F. hirthi and *Filaroides milksi (Andersonstrongylus milksi)* (Metastrongyloidea) (Georgi, 1975, and see Figures 4-69, 7-27, 8-89, and 8-90). Most dogs are asymptomatic, but immunocompromised dogs may show signs of severe pneumonia that can be fatal.

D. immitis (Filarioidea) (see Figures 4-137 and 7-38) organisms are large (30 cm) worms that occur in pulmonary infarcts.

Nematode larvae

Petechial hemorrhages, areas of focal necrosis, and nodular inflammation of lung tissue may be caused by migrating nematode larvae. Such lesions should be investigated by preparing squashes and by the Baermann technique. Identification of nematode larvae in histologic preparations is considered in Chapter 8.

A. vasorum (Metastrongyloidea) eggs and larvae cause respiratory lesions, and clinical signs are varied. Dogs may experience exercise intolerance, weight loss, subcutaneous edema due to congestive heart failure and lung damage, or coagulation abnormalities.

S. stercoralis (Rhabditoidea) filariform larvae (see Figure 7-28) are migrating larvae that can also cause areas of ecchymotic and petechial hemorrhage throughout the lung parenchyma.

A. caninum, A. braziliense, and *U. stenocephala* (Ancylostomatoidea) (see Figure 7-28).

Toxocara canis (Ascaridoidea) (Figure 7-51) migrating larvae can cause pneumonia.

Figure 7-51 *Toxocara* larva from a rabbit's liver (×250).

Microfilariae of *D. immitis* (Onchocercidae).

Trematodes

Paragonimus kellicotti (Troglotrematidae) (see Figures 4-14, 4-15Figure 4-14Figure 4-15, and 7-36, B) live in fluke-filled cysts that

are surrounded by large areas of granulation tissue around the escaping eggs. These organisms can cause severe loss of lung function.

Vascular System

Pulmonary artery, right side of the heart, and venae cavae

Protozoa

T. gondii, cardiac muscle (Apicomplexa).

Trypanosoma cruzi (hemoflagellate) amastigotes in heart muscle cause acute myocarditis by myocardial invasion and cycles of multiplication and cell rupture. Weakness, exercise intolerance, syncope, lymphadenopathy, pale mucous membranes, neurologic signs, and signs of right- or left-sided heart failure manifested on the electrocardiogram (ECG) as decreased QRS complexes and heart block can be seen clinically. Chronic infection can progress to dilated cardiomyopathy, and dogs can show signs of weakness, exercise intolerance, syncope, ventricular tachycardia, and sudden death.

Nematodes

D. immitis (300 mm, Filarioidea) occurs in right ventricle, right atrium, pulmonary arteries, and rarely venae cavae (see Figures 4-137 and 7-38). Adult worms live in the pulmonary arteries and cause clinical signs indicative of cardiac, pulmonary, hepatic, and renal involvement. In heavy infections, worms can invade the right side of the heart and cause congestive heart failure and ascites. Clinical signs can include coughing, exercise intolerance, dyspnea, syncope, hepatomegaly, and abnormal heart and lung sounds on

auscultation. Vena cava syndrome can also result owing to obstruction by adult worms.

A. vasorum (25 mm, Metastrongyloidea) is much smaller than *D. immitis* and located in the pulmonary arterial branches. First-stage larvae resembling those of *Aelurostrongylus* (see Figure 7-52) are shed in the host's feces. Dogs may experience exercise intolerance, weight loss, subcutaneous edema due to congestive heart failure and lung damage, or coagulation abnormalities.

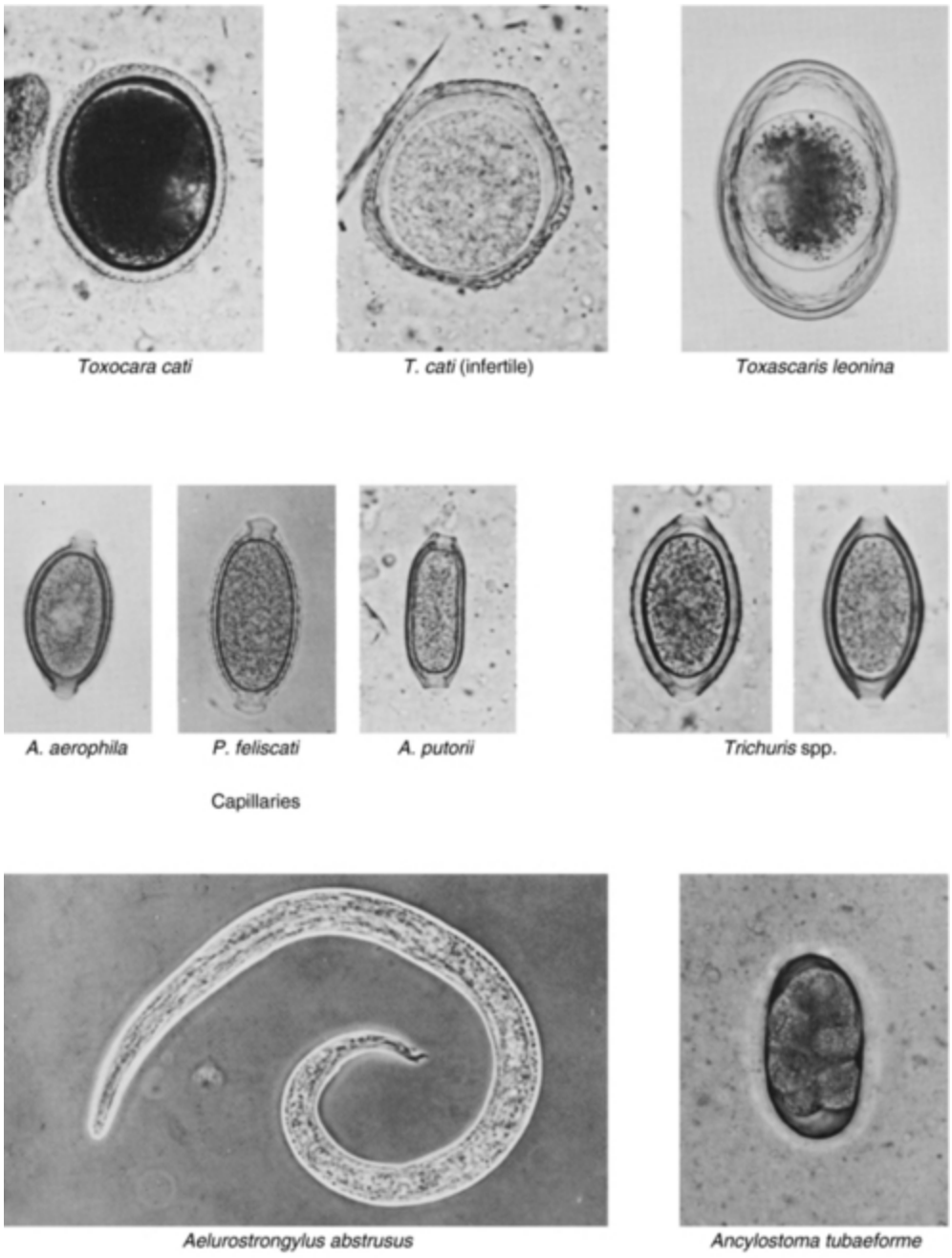

Figure 7-52 Nematode parasites of cats. *Toxocara cati* eggs are smaller and more delicate than *Toxocara canis* eggs (see Figure 7-25). *Toxascaris leonina* is a parasite of both cats and dogs. The egg in this figure came from a tiger. *Trichuris* species are rare parasites of North American cats. The *Trichuris* egg at left was observed in the feces of a cat from

Puerto Rico that was found during necropsy to contain three female *Trichuris* sp. worms. The egg at right, from a New York State cat, was presumptively identified as *Trichuris* sp. because of its close resemblance (except for smaller size) to *Trichuris vulpis* (see Figure 7-25). *Aelurostrongylus abstrusus* larvae may be identified by their curiously shaped tail.

Toxocara canis (Ascaridoidea) larvae in cardiac muscle.

Mesenteric and portal veins

Trematodes

Heterobilharzia americana (Schistosomatidae) (see Figures 4-24 and 8-50Figure 4-24Figure 8-50) causes disease by the eggs that erode their way through the intestinal mucosa and cause granulomatous reactions in the liver.

Blood

Nematode microfilariae

D. immitis and *D. reconditum* (Filarioidea) (see Figure 7-38).

Protozoa

Babesia canis (Apicomplexa) (see Figure 3-28) will be seen only at necropsy if blood films are made. Clinical signs of canine babesiosis include pale mucous membranes, icterus, hemoglobinemia and hemoglobinuria, depression, weakness, fever, anorexia, and splenomegaly

T. cruzi (hemoflagellate) trypomastigotes may be scarce in blood films. Examine heart muscle histologically for amastigotes (see Figure 8-17).

Skeletal Muscles

Protozoa

N. caninum (see Figure 2-20, Apicomplexa) causes disease mainly in dogs less than 6 months of age, which will show signs of paralysis. The pelvic limbs are more severely affected than the thoracic, and signs of progressive muscle atrophy are present.

Nematode larvae

T. spiralis (Trichinelloidea) (see Figures 4-150, 7-92, and 8-116) usually does not cause clinical signs in dogs.

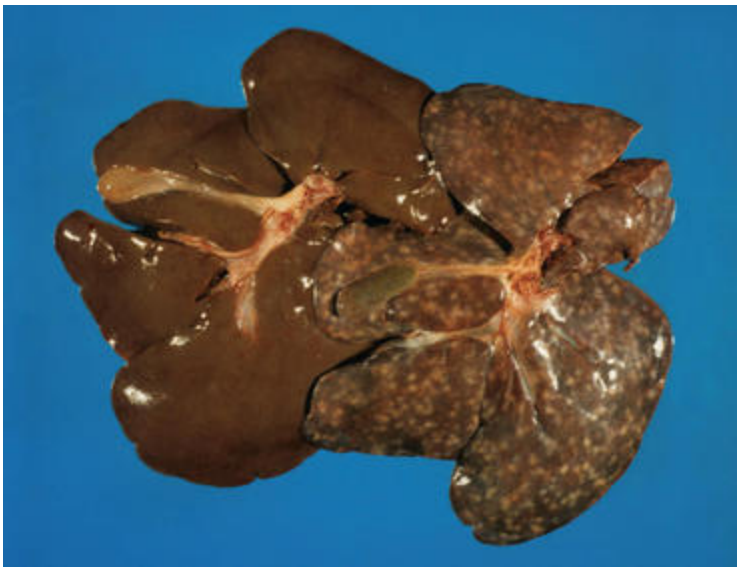

Figure 7-92 *Trichinella spiralis* cyst in a fresh digest preparation of rat muscle.

A. caninum (Ancylostomatoidea) larvae are present in vacuoles in muscle fibers with little or no evidence of host reaction (see Figure 8-86).

Connective Tissues

Protozoa

Hepatozoon americana (Apicomplexa) can cause myositis and periosteal bone proliferation with changes that might be evident on radiographs. The organisms can form large cysts in the muscles, and muscle atrophy, hyperesthesia, and reluctance to move can result.

Nematodes

D. reconditum (32 mm, Filarioidea) (see Figure 4-145) without clinical signs.

D. immitis (300 mm, Filarioidea) (see Figure 4-135) migratory stages and ectopically migrating adults.

Dracunculus insignis (360 mm, Spirurida) (Figure 7-49, and see Figures 4-127, 4-128, and 8-108Figure 4-127Figure 4-128Figure 8-108) causes subcutaneous nodules with associated pyoderma and focal erythema. Larvae with very long tails may be expressed from the nodules.

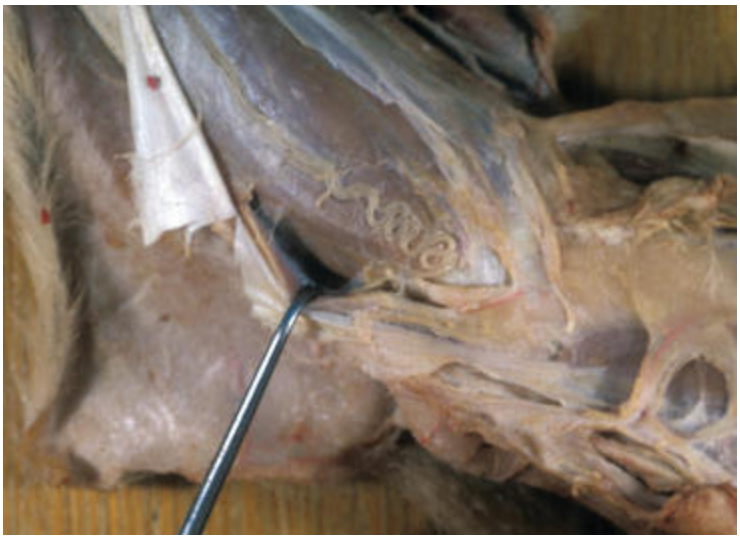

Figure 7-49 *Dracunculus insignis* discovered in canine dissection as part of anatomy class in 1966.

Insect larvae

Cuterebra (30 mm, Cuterebridae) (see Figures 2-31, 2-32, 8-1, and 8-2Figure 2-31Figure 2-32Figure 8-1Figure 8-2) larvae migrate to the skin to create a warble. The skin can be sensitive in this area, and a draining tract may be present. The spiracles of the larvae may be seen protruding from the fistula, and the larvae can be extracted from the opening.

Cochliomyia hominivorax (17 mm, Calliphoridae) (see Figures 2-12 and 2-19Figure 2-12Figure 2-19).

Phaenicia sericata, Phormia regina, and *Protophormia terraenovae* (17 mm, Calliphoridae) (see Figures 2-12 and 2-19Figure 2-12Figure 2-19).

Wohlfahrtia vigil and *Wohlfahrtia opaca* (Sarcophagidae) (see Figure 2-19).

Urogenital System

Kidney

Nematodes

D. renale (up to 1 meter, Trichinelloidea). A giant red worm in the renal pelvis or peritoneal cavity (see Figure 4-146). The right kidney is most often affected. Clinical signs include enlargement of the right kidney, hematuria, urinary tract infections, and rarely renal failure if both kidneys are affected.

Nematode larvae

Toxocara canis (Ascaridoidea) (Figures 7-50 and 7-51) larvae can cause nodular lesions to form in the kidneys but typically do not cause clinical signs.

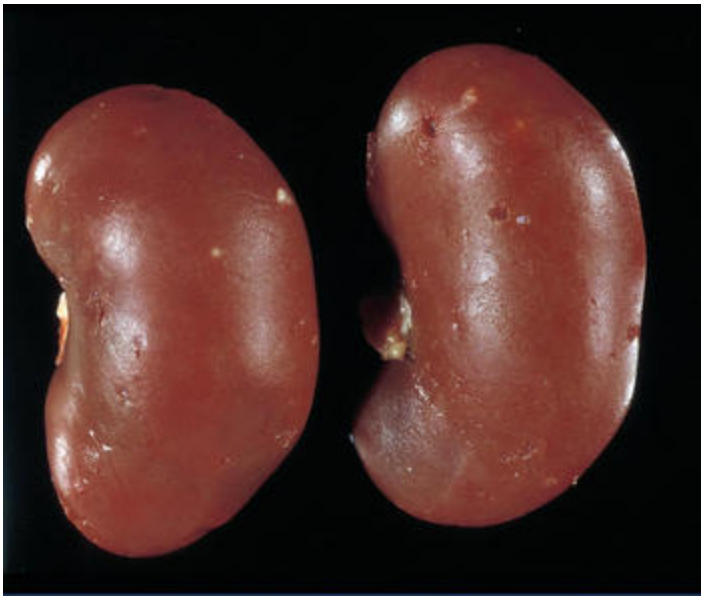

Figure 7-50 *Toxocara canis* lesions in canine kidneys.

A. caninum (Ancylostomatoidea) larvae will enter muscle cells of dogs.

Urinary bladder

Nematodes

Pearsonema (Capillaria) plica (60 mm, Trichinelloidea) organisms can be found in the epithelium of the urinary bladder and usually do not cause signs. If large numbers are present, dogs can have pollakiuria, dysuria, hematuria, and stranguria.

Nervous System

Brain and spinal cord

Protozoa

N. caninum (Apicomplexa) (see Figure 3-22) can appear in older dogs, causing signs of central nervous system involvement that

include seizures and tremors, whereas cerebellar involvement will result in postural deficits

Nematodes

Baylisascaris species (Ascaridoidea) larvae have on rare occasions caused neurologic disease in dogs (Thomas, 1988).

Eye

Nematodes

Toxocara canis (Ascaridoidea) has on rare occasion been found in the retina (Hughes, Dubielzig, and Kazacos, 1987).

D. immitis (Filarioidea) (see Figures 4-137 and 7-38) can occur erratically in the anterior chamber of the eye or the epidural space.

Thelazia californiensis (19 mm, Spirurida) (see Figure 4-132) can on occasion be found in the conjunctival sac and ducts of the lacrimal gland.

Skin and Hair

Insects

Adult dipterans.

L. setosus (Anoplura) (see Figure 2-39).

Trichodectes canis (Mallophaga) (see Figure 2-47).

Heterodoxus spiniger (Mallophaga) has club-shaped antennae that lie in cephalic grooves, and the anterior margin of the head is pointed; the organism is restricted to warm climates.

Ctenocephalides canis, Ctenocephalides felis, Pulex irritans, and *Echidnophaga gallinacea* (Siphonaptera) (see Figures 2-52, 2-53, 2-

54, and 2-56Figure 2-52Figure 2-53Figure 2-54Figure 2-56).

Arachnids

Rhipicephalus sanguineus, Dermacentor variabilis, Dermacentor andersoni, Amblyomma americanum, Amblyomma maculatum, Ixodes species, and others (Ixodidae) (see Figures 2-69, 2-70, and 2-74 to 2-90Figure 69Figure 70Figure 74Figure 75Figure 76Figure 77Figure 78Figure 79Figure 80Figure 81Figure 82Figure 83Figure 84Figure 85Figure 86Figure 87Figure 88Figure 89Figure 90).

Sarcoptes scabiei (Sarcoptidae) (see Figures 2-102 and 8-3Figure 2-102Figure 8-3) mites cause alopecia that usually spares the dorsum. Skin lesions are reddish and covered with yellowish crusty material. Severe self-trauma to the skin may result owing to intense pruritus.

Otodectes cynotis (Psoroptidae) (see Figure 2-111) causes otitis with predisposition to secondary infections.

Demodex canis (Demodicidae) (see Figures 2-115 and 8-6Figure 2-115Figure 8-6) can normally be found on dogs in low numbers, and usually they do not cause disease. Demodicosis can be a localized problem, usually affecting the face and presenting as alopecia and scales surrounding the eyes and the mouth. Generalized demodicosis causes large reddened scaly alopecic coalescing patches on the head, legs, and trunk. Folliculitis and furunculosis can be present, and generalized lymphadenopathy is typical. Secondary bacterial infections cause inflammation and exudation.

Cheyletiella yasguri (Cheyletidae) (see Figure 2-116) is not generally associated with signs; may cause mild dermatitis.

Nematode larvae

Rhabditis strongyloides (Rhabditida) (see Figures 4-107 and 8-72Figure 4-107Figure 8-72) larvae cause a pruritic hyperemic dermatitis. The larvae are usually free living on decaying organic matter, and therefore the lesions are typically distributed on areas of the body that come in contact with the ground such as the feet and the ventral thorax and abdomen.

PARASITES OF CATS

Stages in Feces

Cats share a few parasites (e.g., *T. leonina*, *Eucoleus* [*Capillaria*] *aerophilus*, *D. caninum*, *P. kellicotti*) with dogs, and cross-infections with others may occur on rare occasions. In other parts of the world, cats and dogs may share numerous trematodes acquired from the ingestion of fish. However, the most common cat parasites (Figures 7-52 to 7-54) are different species of the genera found in dogs (e.g., *Toxocara cati, Ancylostoma tubaeforme*, *Cystoisospora felis*).

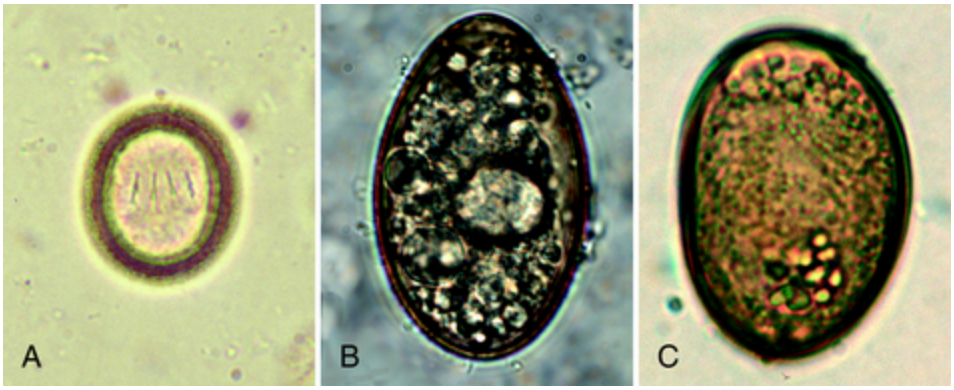

Figure 7-53 Eggs of cat platyhelminths. **A,** *Taenia taeniaeformis*. This taeniid cestode egg has a radially striated embryophore and contains a fully developed oncosphere. **B,** *Spirometra mansonoides*. This diphyllobothriid cestode egg has an operculate capsule and contains an undeveloped embryo. **C,** *Platynosomum fastosum*. This dicrocoeliid trematode egg also has an operculate capsule but contains a fully developed miracidium.

Nematode Eggs and Larvae

The most common nematodes of the cat are *T. cati* and *A. tubaeforme;* in the southeastern United States, a good percentage of the hookworm eggs might also be those of *A. braziliense*. Cats can harbor *T. leonina*, but this seem to be more uncommon now than it once was. Pseudoparasitism in cats is usually the result of predation rather than coprophagy. For example, the eggs of *Calodium (Capillaria) hepaticum* accumulate in infected rodent livers and may be found in the feces of a cat that has eaten such a rodent (see Figure 8-117). Feline *Trichuris* infection often excites lively debate because its rare appearances in cats in North American violate a time-honored belief that it does not exist at all. In any case, it is certainly of little practical importance aside from its tendency to complicate the differential diagnosis of pulmonary and vesical capillariasis. Cats are host to capillarids, typically *E. aerophilus* from the respiratory system and *A. putorii* from the stomach and small intestine.

Cestode Eggs and Segments

Cats most commonly are host to one of four tapeworms, although they can be infected with *D. latum* and a few other unusual species. The four tapeworms most commonly found in cats in North America are *Spirometra mansonoides*, *Taenia taeniaeformis*, *D. caninum*, and *Mesocestoides* species. The eggs of *Spirometra* species are brown, fairly elongate, and operculate. The eggs of *T. taeniaeformis* are nearly spheroid. In the case of cats that use litter pans, people are often aware of the segments passed by cats: rectangular segments are taeniid segments, cucumber-seed–shaped segments are those of

D. caninum, and the small sesame-seed–shaped segments are those of *Mesocestoides* species. Cats can be infected with species of *Echinococcus* but are less likely to be infected than dogs.

Trematode Eggs

Cats around the world are host to nearly 100, or perhaps more, species of trematodes (Bowman et al, 2002). The trematodes live in the mouth, intestinal tract, pancreatic and bile ducts, nasal fossae, lungs, and blood vessels. In all cases the eggs make their way into the feces. The eggs of most of these trematodes are operculate, but the eggs of the Schistosomatidae are not. Some of the eggs are embryonated when passed (e.g., those of *Platynosomum fastosum*) whereas others (e.g., *P. kellicotti*) contain the zygote surrounded by yolk. Some eggs can be quite large, such as those of *Alaria* species, whereas others are very small, such as those of *Metagonimus* species.

Cystoisospora, Hammondia, Besnoitia, and *Toxoplasma*

The species of *Cystoisospora* infecting cats are entirely distinct from those infecting dogs. The largest oocyst is that of *Cystoisospora felis*. A midsize oocyst is *Cystoisospora rivolta*. There are several species and genera producing smaller oocysts, including *Besnoitia darlingi*, *Besnoitia wallacei*, and *Besnoitia jellisoni*, along with *T. gondii* and *Hammondia hammondi*. Careful micrometry affords differentiation of the larger species of oocysts, but, unfortunately, the most important species, *Toxoplasma*, remains confounded with *Hammondia*. Until this dilemma is resolved, oocysts smaller than 14 μm should be regarded as *Toxoplasma*, just to be on the safe side (see Figure 7-54 and Table 7-1).

TABLE 7-1 Oocyst Dimensions in Cat Parasites

Species	Oocyst Dimensions (μm)
C. felis	38-51 × 27-39
Cystoisospora rivolta	21-28 × 18-23
Besnoitia darlingi	11-13 × 11-13
Besnoitia wallacei	16-19 × 10-13
Toxoplasma gondii	11-13 × 9-11
Hammondia hammondi	11-13 × 10-12

Sarcocystis

Sarcocystis sporulates within the host, and the fragile oocyst wall often breaks. Therefore the sporocyst measuring 9 to 12 × 7 to 12 μm and containing four sporozoites is the form usually found in the feces (see Figure 7-54). It is not possible to easily distinguish species of *Sarcocystis* by micrometry.

Cryptosporidium

The oocysts of *Cryptosporidium felis* are best floated in saturated sucrose solution. Because the oocysts are a mere 5 μm in diameter, slides must be scanned at high dry magnification. *Cryptosporidium* oocysts tend to lie in the focal plane immediately below the coverslip (i.e., at the top of the air bubbles) (see Figure 3-16).

Annotated Host-Organ Listing of Parasites of Cats

T. gondii may occur in any tissue of any host as extracellular or intracellular tachyzoites or as bradyzoites in cysts (see Figures 3-21 and 8-35Figure 3-21Figure 8-35). Sexual reproduction with formation of oocysts (see Figure 7-54) occurs only in the intestinal mucosae of members of the cat family (Felidae).

Alimentary System

Mouth

Protozoa

Trichomonas felistomae (flagellate) is found around the gum margins and is mainly observed in cats infected with feline

immunodeficiency virus (FIV), feline leukemia virus (FeLV), or feline infectious peritonitis (FIP) or cats suffering from gingivitis; it is nonpathogenic.

Stomach and esophagus

Nematodes

G. spinigerum (Spirurida) (see Figure 4-129), with head attached to stomach mucosa, may cause gastric wall perforation.

P. praeputialis and *P. rara* (Spirurida) (Figure 7-55; see also Figures 4-130 and 4-131Figure 4-130Figure 4-131), with the anterior end attached to the gastric mucosa, may be diagnosed endoscopically and may cause vomiting.

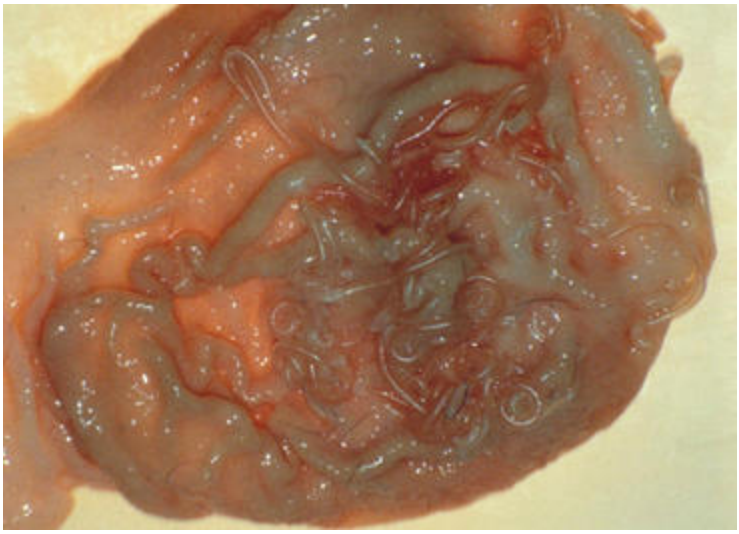

Figure 7-55 *Physaloptera praeputialis* in the stomach of a cat.

Ollulanus tricuspis (1 mm, Trichostrongyloidea) (see Figure 4-80) living in the stomach wall of infected cats causes chronic gastritis that results in vomiting, anorexia, weight loss, and possibly death.

Aonchotheca (Capillaria) putorii (Trichinelloidea) (see Figure 7-52) usually causes no clinical signs; it has been reported to cause perforation at the caudal aspect of the pylorus.

Small intestine

Nematodes

T. cati (Ascaridoidea) (Figure 7-56; see also Figures 4-123, 7-39 to 7-42, and 7-52) infection is usually without clinical signs except in very heavy infections.

Figure 7-56 *Toxocara cati* in the intestine of a cat at necropsy.

T. leonina (Ascaridoidea) (see Figures 4-123, 7-39 to 7-42, and 7-52) infection is typically without signs.

A. tubaeforme (Ancylostomatoidea) (see Figures 4-95, 4-96, 4-98Figure 4-95Figure 4-96Figure 4-98, and 7-52) usually causes no clinical signs, but cats may have weight loss, regenerative anemia, and loose, tarry stools, and infection has resulted in death owing to significant blood loss from the intestinal mucosa.

A. braziliense (Ancylostomatoidea) (see Figures 4-95, 4-96, 4-98Figure 4-95Figure 4-96Figure 4-98, and 7-52) causes less blood loss than *A. tubaeforme*, and experimentally infected kittens have maintained unaffected red blood cell parameters.

U. stenocephala (Ancylostomatoidea) (see Figures 4-95, 4-96, 4-98Figure 4-95Figure 4-96Figure 4-98, and 7-52) infections in cats in the United States are very rare.

Strongyloides felis (common in Australia; Speare and Tinsley, 1987) (5 mm, Rhabditida).

T. spiralis (Trichinelloidea) (see Figure 4-148) causes signs referable to mild gastrointestinal upset, such as vomiting and diarrhea, maybe bloody diarrhea.

Aonchotheca (Capillaria) putorii (Trichinelloidea) (see Figures 7-52) is present in the small intestine as well as the stomach.

Cestodes

T. taeniaeformis (Taeniidae) (see Figures 4-34 and 4-36Figure 4-34Figure 4-36) occurs typically without signs.

E. multilocularis (Taeniidae) (see Figure 4-43) occurs typically without signs.

D. caninum (Dipylidiidae) (see Figures 4-53, 7-5, and 7-33) occurs typically without signs.

Mesocestoides lineatus (Mesocestoididae) (see Figures 4-58 and 7-32) occurs typically without signs.

S. mansonoides (Diphyllobothriidae) (see Figures 4-27 and 4-29Figure 4-27Figure 4-29) may be associated with diarrhea,

emaciation, or vomiting.

Trematodes

Alaria marcianae (5 mm, Diplostomatidae) (see Figures 4-20 and 4-22Figure 4-20Figure 4-22) occurs typically without signs.

A. venustus (1.4 mm, Heterophyidae) occurs typically without signs.

P. longa (1.2 mm, Heterophyidae) occurs typically without signs.

Mesostephanus milvi (1.8 mm, Cyathocotylidae) occurs typically without signs.

Acanthocephala

Oncicola species (see Figure 4-161) occurs typically without signs.

Protozoa

Cystoisospora felis, *C. rivolta*, *Besnoitia* species, *H. hammondi*, and *T. gondii* (Coccidia) (see Figure 7-54) stages occur in the intestinal epithelium, where they might cause enteritis and perhaps mild diarrhea.

Sarcocystis hirsuta, *Sarcocystis tenella*, *Sarcocystis porcifelis*, and *Sarcocystis leporum* (Coccidia) (see Table 2-1 and Figure 7-54) occur with sexual stages in the intestinal epithelium.

Giardia felis (see Figure 3-6) trophozoites present on intestinal epithelium may be detected in mucosal scrapings. *G. felis* infection usually occurs without signs, but diarrhea may occur.

Cryptosporidium felis (see Figure 3-16; Apicomplexa) asexual and sexual stages occur in the apical portion of the epithelial cells; they are probably visible only via histologic sections. Infection is usually without signs, although occasionally it is accompanied by severe diarrhea.

Large intestine

Nematodes

Strongyloides tumefaciens (5 mm, Rhabditida) forms large tumorlike nodules in the large intestine, which are detected on abdominal palpation as a firm, fibrotic colon.

Trichuris campanula and *Trichuris serrata* (exotic, South America: Trichinelloidea) (see Figures 4-151 and 7-52).

Liver, bile ducts, and gallbladder; pancreatic duct

Nematodes

Calodium (Capillaria) hepaticum (Trichinelloidea) (see Figure 8-117).

Toxocara canis (Ascaridoidea) larvae, granulomas (Figure 8-99) (Parsons et al, 1988).

Trematodes

O. tenuicollis and *Opisthorchis felineus* (30 mm, Opisthorchiidae) in gall bladder and bile ducts is likely to induce cirrhosis, cholecystitis, and the development of edema and ascites owing to continuing periportal fibrosis.

M. albidus (4.6 mm) and *M. conjunctus* (6.6 mm) (Opisthorchiidae) in bile ducts are associated with icterus and cholangiohepatitis, ascites, jaundice, and emaciation.

Amphimerus pseudofelineus (22 mm, Opisthorchiidae) occurs in gallbladder and bile ducts with anorexia, weight loss, diarrhea, vomiting, and icterus.

Parametorchis complexus (10 mm, Opisthorchiidae) occurs in bile ducts.

C. sinensis (Asia) (Opisthorchiidae) (see Figures 4-10 and 4-17Figure 4-10Figure 4-17) occurs in gallbladder and bile ducts with occasional pancreatic duct involvement causing progressive liver cirrhosis.

P. fastosum (Platynosomum concinnum?) (8 mm, Dicrocoeliidae) occurs in tropical climates in gallbladder and bile ducts, causing anorexia, weight loss, vomiting, depression, mucoid diarrhea, jaundice, and hepatomegaly.

Eurytrema procyonis (3.3 mm) (Dicrocoeliidae) (Figures 4-19 and 7-53) occurs in pancreatic duct, bile ducts, and gallbladder, causing cirrhosis and pancreatic atrophy and fibrosis.

Respiratory System

Nasal cavity, trachea, and bronchi

Nematodes

Eucoleus (Capillaria) aerophilus (Trichinelloidea) (see Figure 7-52).

Mammomonogamus species (Syngamidae) (Figure 7-57) occurs in nares and nasopharynx; species seen in the middle ear.

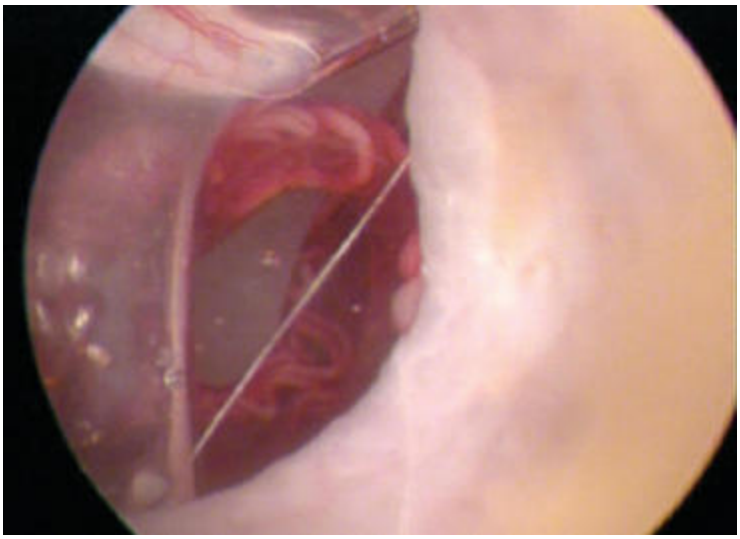

Figure 7-57 *Mammomonogamus auris* in the middle ear of a cat as viewed through an otoscope.

Courtesy Dr. Edgar Tudor, Paradise Animal Hospital, Saipan, USA.

Lung parenchyma

Nematodes

A. abstrusus (9 mm, Metastrongyloidea) (see Figures 7-52 and 8-85) occurs in terminal respiratory bronchioles and alveolar ducts, with the majority of signs being related to developing eggs lodged in the tissues; cats harboring large worm burdens may experience bronchopneumonia and show signs of open mouthed abdominal breathing.

Trematodes

P. kellicotti and other *Paragonimus* species outside United States (Troglotrematidae) (see Figures 4-14, 4-15Figure 4-14Figure 4-15, and 7-36, *B*) occur in nodules, typically in pairs or in greater numbers within the cysts; animals are generally without signs, but respiratory distress or even death may be associated with the infection.

Vascular System

Heart

Nematodes

D. immitis (Filarioidea) (see Figures 4-137, 4-138, and 8-109Figure 4-137Figure 4-138Figure 8-109) occurs in arteries; cats very typically have few worms and signs of infection from migrating developmental forms.

Toxocara canis (Ascaridoidea) larvae, granulomas (Parsons et al, 1988).

Mesenteric veins

Trematodes

Schistosoma japonicum (Schistosomatidae) in cats in southeast Asian countries.

Blood

Protozoa

Cytauxzoon felis (piroplasm) (see Figure 3-29) occurs with merozoites in erythrocytes and schizonts in macrophages in lumen of vessels in most organs. Cats may show signs of anemia, depression, anorexia, dehydration, fever, icterus, and enlargement of the liver and spleen.

Nematode microfilariae

D. immitis (Filarioidea) (see Figure 7-38) rarely produces microfilariae in cats; other filarids infect cats in other parts of the world.

Skeletal Muscles

Nematode larvae

T. spiralis (Trichinelloidea) (see Figures 4-150, 7-92, and 8-116).

Connective Tissues

Insect larvae

Cuterebra species (Diptera) (30 mm) (see Figures 2-32, 8-1, and 8-2Figure 2-32Figure 8-1Figure 8-2) occur as migrating forms.

Urogenital System

Kidneys

Nematodes

Toxocara canis (Ascaridoidea) larvae, granulomas (Parsons et al, 1988).

Urinary bladder

Nematodes

Pearsonema (Capillaria) plica (60 mm), and *Pearsonema feliscati* (32 mm) (Trichinelloidea) (see Figure 7-52).

Nervous System

Nematodes

D. immitis (Filarioidea) adults migrate erratically in meninges and ventricles (see Figures 4-137 and 4-138Figure 4-137Figure 4-138).

Insect larvae

Cuterebra species (Diptera) (30 mm) (see Figures 2-32, 8-1, and 8-2Figure 2-32Figure 8-1Figure 8-2) larvae can migrate through spinal cord and brain with clinical signs largely dependent on the path taken; seizures, vestibular signs, blindness, dementia, circling, disorientation, and death have all been noted.

Eye

Protozoa

T. gondii (Coccidia) can cause iritis, uveitis, detached retina, iridocyclitis, keratic precipitates, mydriasis, anisocoria, and delayed pupillary reflex.

Skin and Hair

Insects

Adult dipterans.

Felicola subrostratus (Mallophaga) (see Figure 2-48).

Ctenocephalides felis, Ctenocephalides canis, and *E. gallinacea* (Siphonaptera) (see Figures 2-53 and 2-54Figure 2-53Figure 2-54).

Insect larvae

Cuterebra species (Diptera) (30 mm) (see Figures 2-32, 8-1, and 8-2Figure 2-32Figure 8-1Figure 8-2) larvae penetrate the skin of the cat after internal migrations and form a subcutaneous warble. The third stage larvae and its spiracles can often be seen through the pore of the warble.

Arachnids

Dermacentor species, *Haemaphysalis leporispalustris,* and *Ixodes* species (Ixodidae) (see Figures 2-75 to 2-79, 2-82, and 2-86 to 2-88Figure 2-75Figure 2-76Figure 2-77Figure 2-78Figure 2-79Figure 2-82Figure 2-86Figure 2-87Figure 2-88).

Notoedres cati and *S. scabiei* (Sarcoptidae) (see Figures 2-100, *A* and 2-102 to 2-105Figure 2-100, *A*Figure 2-102Figure 2-105).

O. cynotis (Psoroptidae) (see Figure 2-101, *A* and 2-111Figure 2-101, *A*Figure 2-111).

Lynxacarus radovskyi (Listrophoroidea) (see Figure 2-114).

Cheyletiella blakei (Cheyletidae) (see Figure 2-116).

Demodex cati (Demodicidae) (see Figure 2-115).

Neotrombicula whartoni and *Walchia americana* (Trombiculidae) (see Figures 2-119 and 2-120Figure 2-119Figure 2-120). *N. whartoni*,

a bright red chigger, has been found in the external ear canal of cats. *W. americana*, normally a parasite of the gray squirrel *Sciurus carolinensis*, is capable of causing a severe and generalized dermatitis in cats (Lowenstine, Carpenter, and O'Connor, 1979).

PARASITES OF RUMINANTS

Stages in Feces

Nematode Eggs

Other than the numerous eggs of various strongylid parasites that will be present in the feces, one commonly finds the eggs of *Strongyloides*, *Trichuris*, and capillarids (Figure 7-58). The strongylid eggs present in ruminant feces cannot be readily identified to genus or species with the exception of certain types (e.g., *Nematodirus battus*). When a more specific diagnosis is required, it is necessary to culture the stages present in the feces to the infective stage.

Eggs of the following ruminant nematodes are not illustrated in Figure 7-58. *Toxocara vitulorum* (parasite of cattle) eggs look a lot like *Toxocara canis* eggs, are subglobular with a uniformly pitted surface, and contain a single cell when passed. *Note:* Patent *Ascaris suum* infections are occasionally reported from sheep and cattle. *A. suum* eggs (see Figure 7-64) are easy to distinguish from those of *T. vitulorum*. *Gongylonema* eggs are thick walled, have bipolar opercula, and contain vermiform embryos. *Skrjabinema ovis* eggs are typical pinworm eggs, with one side slightly flattened (see Figure 7-67).

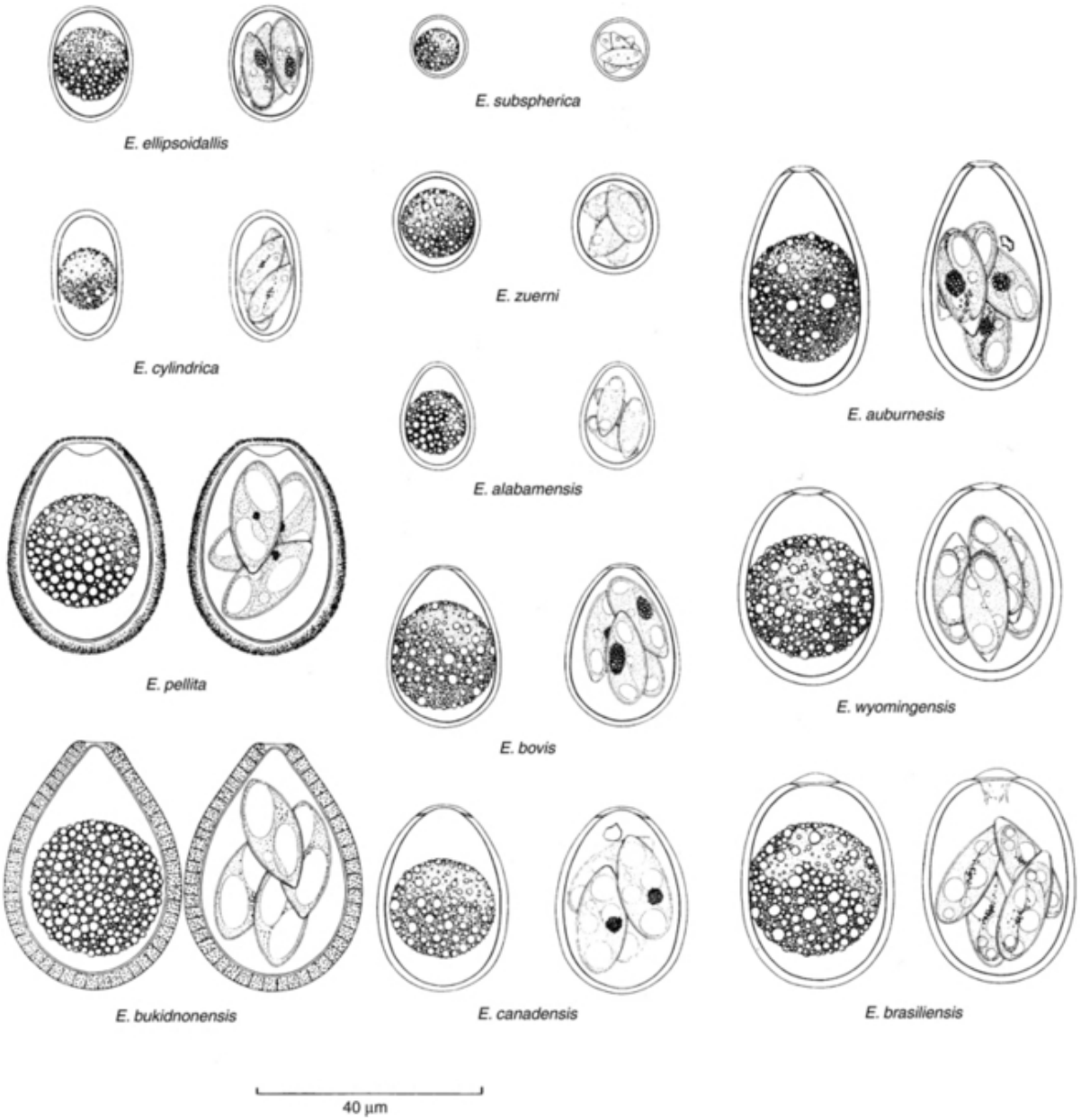

Figure 7-64 Unsporulated and sporulated oocysts of 12 species of *Eimeria* of cattle (×1000).

From Joyner LP, Norton CC, Davies SFM, Watkins CV: The species of coccidia occuring in cattle and sheep in the southwest of England, Parasitology 56:536, 1966. Crown copyright. Reproduced with permission from the Controller of Her Britannic Majesty's Stationery Office.

Figure 7-67 *Skrjabinema caprae* egg and an *Eimeria* oocyst in the feces of a goat (×400).

Identification of Strongyle Infective Larvae

Identification of third-stage infective larvae in cultured ruminant feces is challenging but not formidable. Usually two or more genera are present, and one can best determine just how many there are by scanning the slide at low power and mentally grouping those of similar appearance. Certain species stand out from the crowd. For example, *Strongyloides* larvae are more slender than any of the others, lack a sheath, and have a long cylindric esophagus and truncated tail. Two sizes, of which the larger is "standard," are portrayed in Figure 7-59. Dr. Georgi has encountered both sizes in a single culture. Similarly, *Bunostomum* species are distinguished from other sheathed strongyle larvae by their smaller size. Other genera of sheathed larvae may be grouped according to the length of their caudal sheath extension (the extension of the sheath beyond the tip of the larva's tail): short, *Trichostrongylus* and *Ostertagia;* medium,

Haemonchus and *Cooperia;* and long, *Oesophagostomum* and *Chabertia*, as illustrated in Figures 7-59 and 7-60. Within these groupings, further identification depends on micrometry and observation of such morphologic details as the caudal tubercles of *Trichostrongylus*, the "oval bodies" of *Cooperia*, and the number and shape of the intestinal cells of *Oesophagostomum* and *Chabertia*. The odd larva may defy identification, but accurate diagnosis of the predominating genera in a culture is not a difficult task. Proceed as follows:

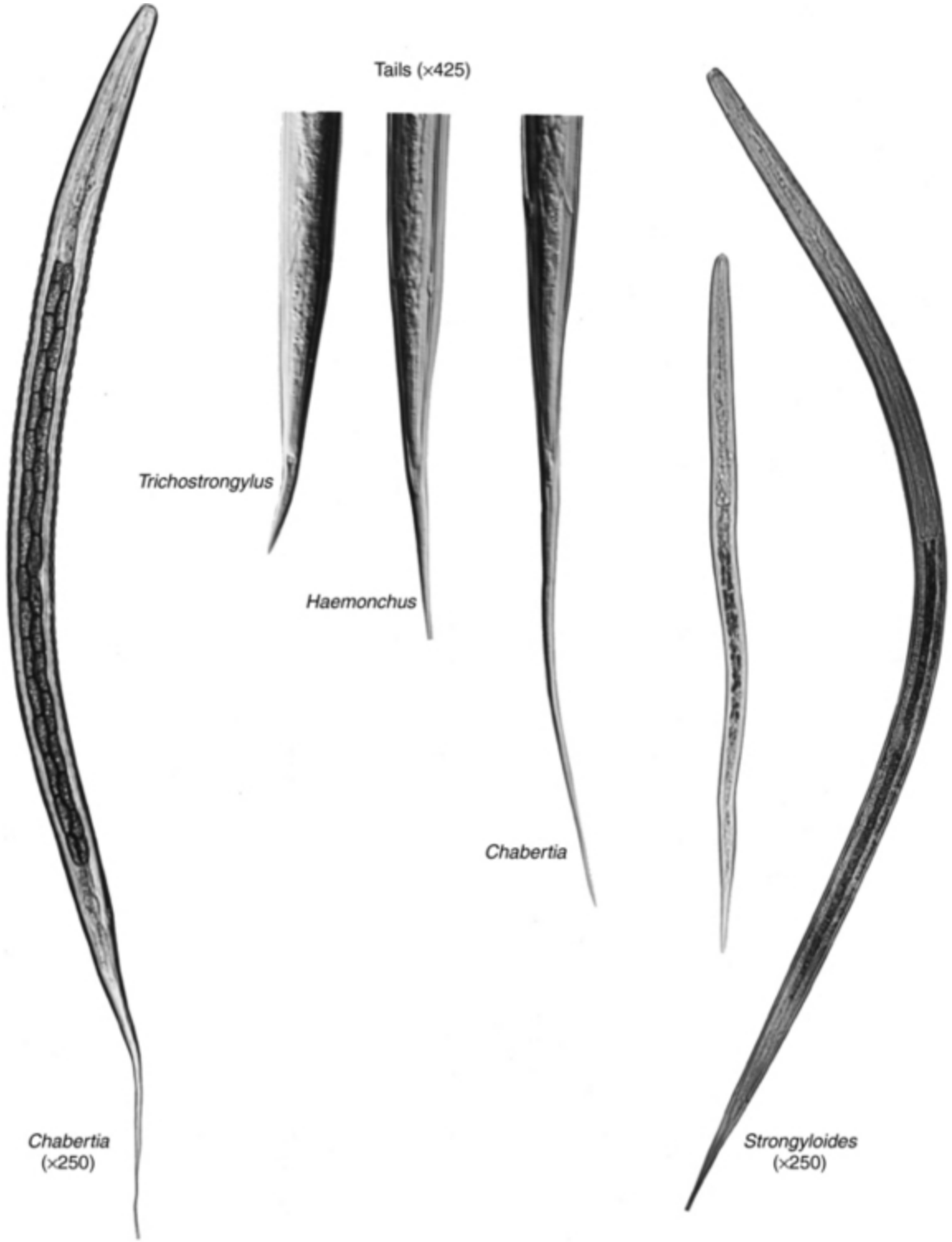

Figure 7-59 Infective third-stage larvae of nematode parasites of sheep. Both large and small *Strongyloides* infective larvae are represented at the same magnification.

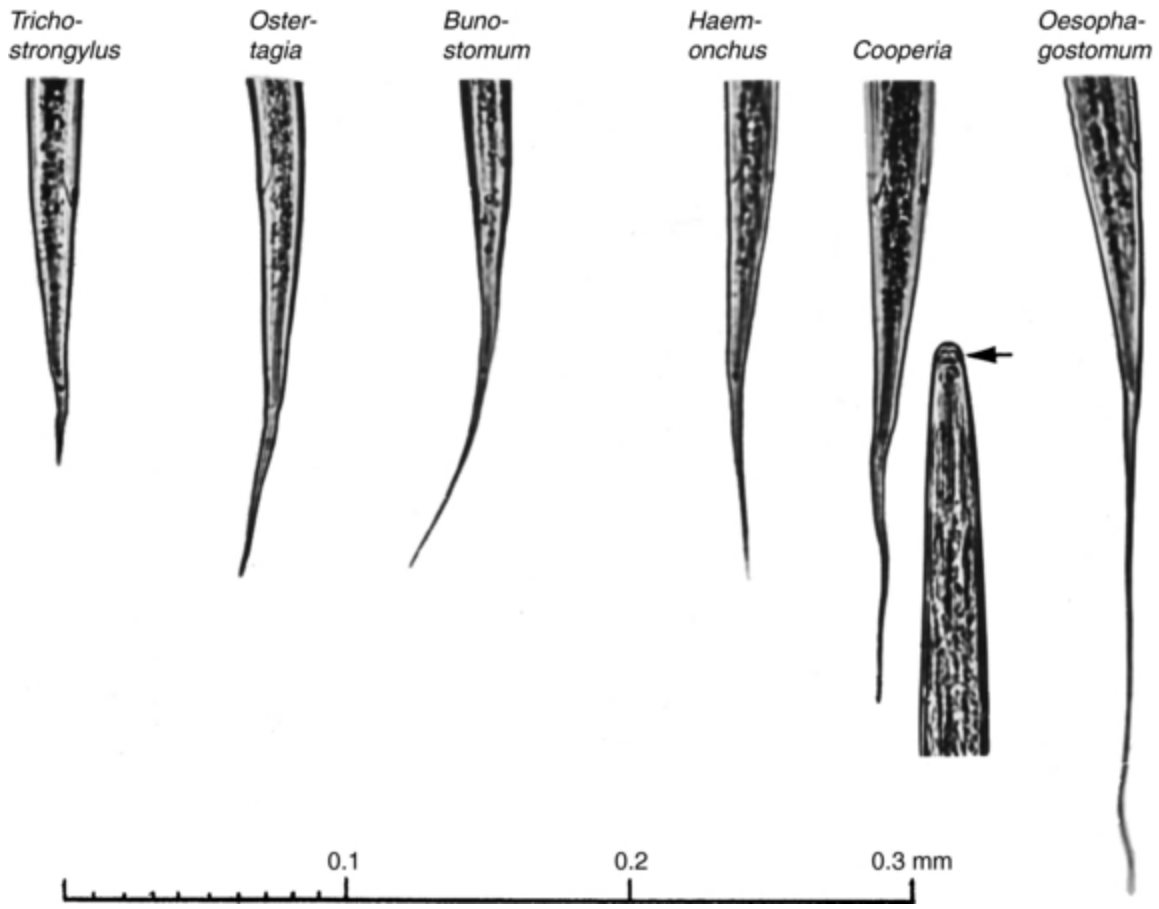

Figure 7-60 Tails of infective third-stage larvae of nematode parasites of cattle and the anterior end of a *Cooperia* larva showing the conspicuous oval bodies *(arrow)*, which represent optical cross-sections of a bundle of fibers surrounding the buccal capsule (×350).

From Whitlock JH: The diagnosis of veterinary parasitisms, Philadelphia, 1960, Lea & Febiger.

Place a drop of the larval suspension on a microscope slide. Relax the larvae by gentle warming or by adding a drop of Lugol's solution (5 g iodine crystals and 10 g potassium iodide in 100 mL distilled water). Ring the coverslip with petroleum jelly for support and thus prevent distortion of the larvae. Avoid higher magnifications at first but instead scan the slide under low power to get an impression of how many different kinds of larvae are present.

Then seek representatives of each kind; examine these under higher power; and take whatever measurements may be necessary for generic or specific diagnosis. The data in Table 7-2 are taken from the works of Dikmans and Andrews (1933, sheep) and Keith (1953, cattle). The number of intestinal cells is 16, except as otherwise noted. Taxa grouped with braces are similar in appearance and require more care for their differentiation than comparisons among other groups.

TABLE 7-2 Table of Measurements of Infective Third-Stage Larvae of Strongyles Infecting Sheep and Cattle

Lungworm Larvae

D. viviparus is the only lung nematode of cattle. *Dictyocaulus filaria*, *Protostrongylus rufescens*, and *M.capillaris* are common lung nematodes of sheep and goats in North America. Differential diagnosis is based on morphologic features of the first-stage larvae found in the host's feces (Figure 7-61). *Dictyocaulus* species larvae are tough enough to be countable by the Cornell-McMaster egg-counting technique, but the counting should be done promptly to avoid osmotic shriveling of the larvae. For sensitive qualitative diagnosis of lungworm infections, the Baermann is the technique of choice.

Figure 7-61 First-stage larvae of ruminant lungworms. *Dictyocaulus viviparus* is the only lungworm of cattle, and *D. viviparus* first-stage larvae are the only larvae of parasitic nematodes found in fresh cattle dung. Notice the prominent granules. *Dictyocaulus filaria* first-stage larvae from sheep are large and have bluntly rounded tails and a "button" at

the mouth, and likewise have prominent granules. *Protostrongylus rufescens* larvae are rather stout and have conically tapering tails without spines. *Muellerius capillaris* larvae have a curiously shaped tail with a dorsal spine *(inset)*.

Cestode Eggs

The eggs found in the feces of cattle are all from tapeworms within the family Anoplocephalidae (see Figures 4-50 and 7-19). The egg of *Moniezia benedeni* has a fairly thick shell and seems to be cuboidal in shape. The other species of anoplocephalid tapeworms for the most part seem to have fairly thin shells that distort in various flotation media (and also clear to some extent). In almost all cases, careful inspection of the egg will allow the visualization of the pyriform apparatus containing the larva with its six hooklets.

Trematode Eggs

Trematode eggs may fail to float in the concentrations of sugar solutions ordinarily used. They are best concentrated by washing feces through sieves to remove coarse debris, then centrifuging the washings. The eggs will be found in the sediment. The formalin-ethyl acetate sedimentation technique is also appropriate. The operculum of trematode eggs is sometimes difficult to see. When in doubt, press the coverslip with a pencil point. Usually, the type of operculum found on trematode eggs will pop open under such pressure (Figure 7-62, *B*).

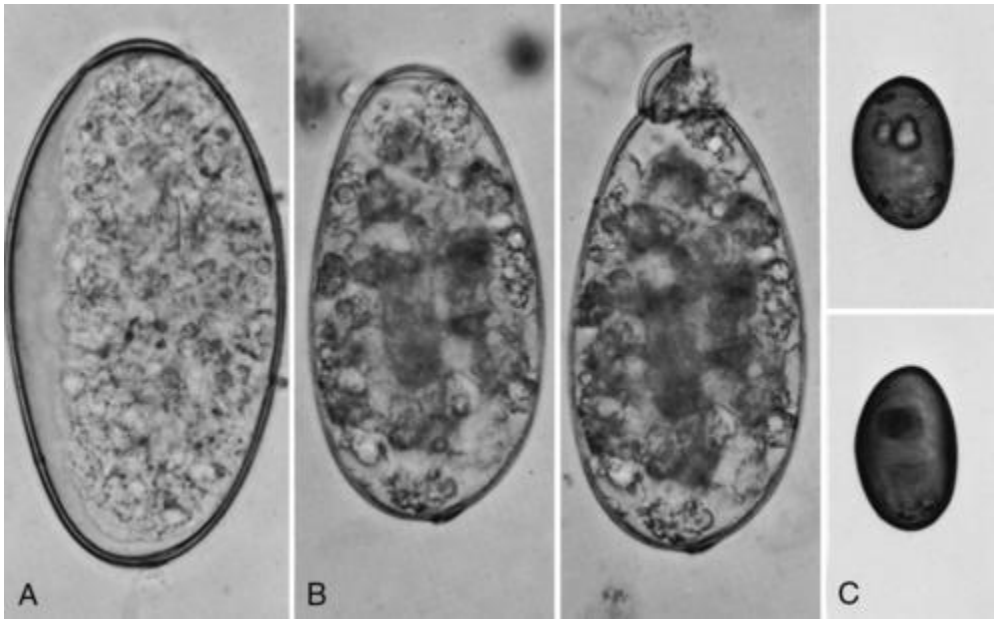

Figure 7-62 Eggs of some trematode parasites of ruminants (×425). **A,** *Fasciola hepatica*. **B,** (*Right* and *Left*), Paramphistominae. **C,** (*Top* and *Bottom*), *Dicrocoelium dendriticum*.

Fasciola hepatica eggs are large (up to 150 μm) and operculate and contain a cluster of yolk cells (Figure 7-62, *A*). *Fasciola gigantica* (Africa, Hawaii, Philippines, and India) eggs are like those of *F. hepatica* but larger (more than 150 μm). Eggs of *Fascioloides magna*, normally a parasite of deer, resemble those of *F. hepatica* but are infrequently found in the feces of infected domestic ruminants because the eggs are trapped in the hepatic cysts containing the adult worms in cattle and because the flukes fail to mature in sheep and goats. Paramphistomatid (rumen fluke) eggs are large and easily confused with those of *Fasciola* species (Figure 7-62). *Dicrocoelium dendriticum* eggs are small (50 μm), lopsided, and yellowish brown and contain a miracidium (Figure 7-62, *C*). *Eurytrema pancreaticum* (Far East) eggs resemble those of *D. dendriticum*. Schistosome eggs

lack an operculum, contain a fully developed miracidium, and are armed with a spine.

Coccidia of Ruminants

Oocysts of *Eimeria* species are often found in considerable numbers in the feces of healthy ruminants. Even experimental lambs raised on wire become infected with coccidia. Despite their frequent occurrence in healthy animals, coccidia are quite capable of causing serious disease in cattle, sheep, and goats. At times, severe disease signs appear before oocysts are shed in the feces. Diagnosis of clinical coccidiosis must be based not only on identification of the oocysts in the feces (Figures 7-63 and 7-64), but also on consideration of the case history and clinical signs.

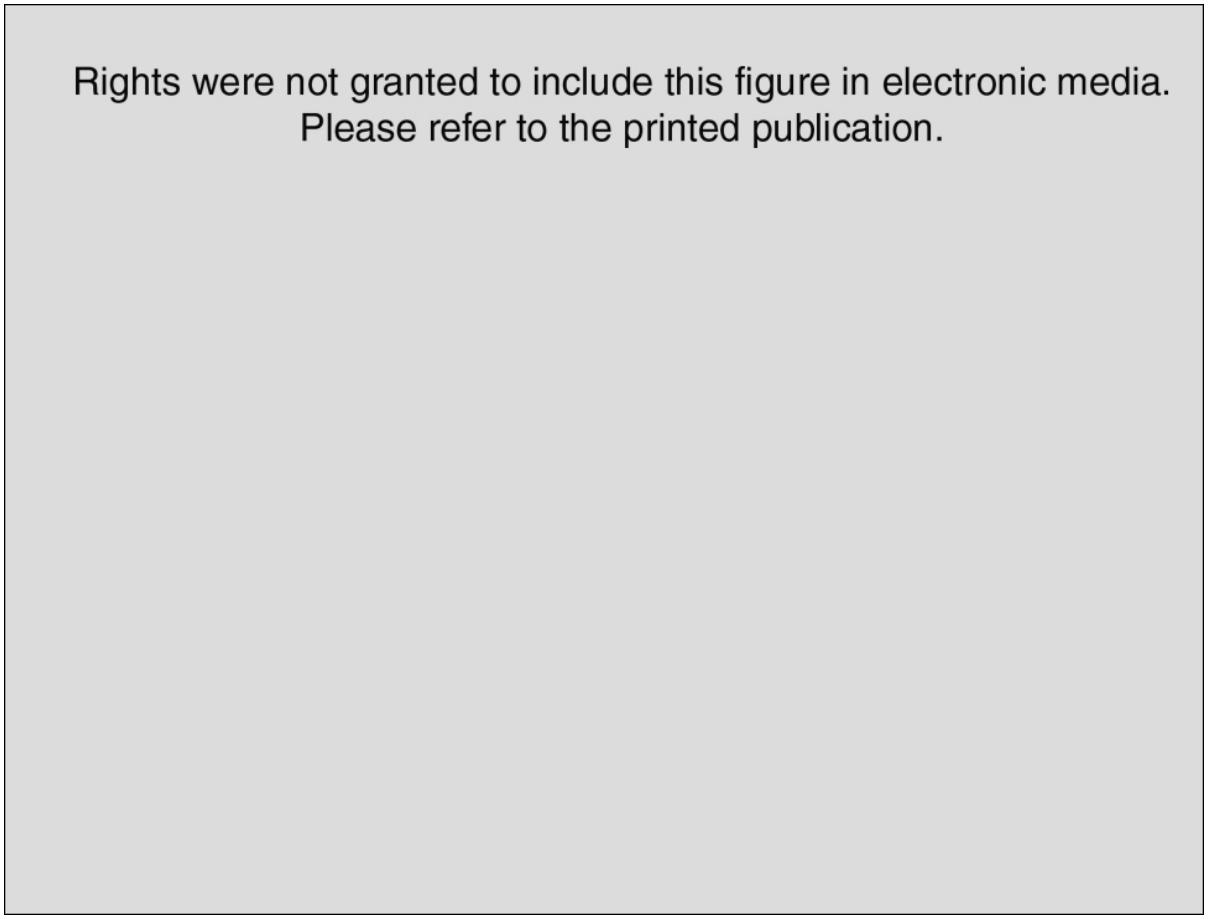

Figure 7-63 Unsporulated and sporulated oocysts of nine species of *Eimeria* of sheep (×1000).

From Joyner LP, Norton CC, Davies SFM, Watkins CV: The species of coccidia occurring in cattle and sheep in the southwest of England, Parasitology 56:533, 1966. Crown copyright. Reproduced with permission from the Controller of Her Britannic Majesty's Stationery Office.

Figure 7-63 presents the unsporulated and sporulated oocysts of nine species of *Eimeria* from sheep. Goats have a closely similar set, which do not, however, cross-infect and are probably all distinct species. Corresponding species of *Eimeria* of sheep and goats are listed in Table 7-3. The species listed for sheep are those illustrated in Figure 7-63. *Eimeria ahsata*, *Eimeria bakuensis*, and *Eimeria crandallis* differ mainly in size, and the ranges overlap, so

differentiating these three species is problematic. Therefore these three species are listed in Table 7-3 under "*Ahsata* group," and their counterpart goat parasites are listed under "*Arloingi* group." Oocysts of *Eimeria caprovina*, *Eimeria absheronae*, and *Eimeria caprina* resemble those of *Eimeria faurei* very closely, so we have also assigned these species to an unofficial composite group. (In the table, asterisks indicate those species most likely to be responsible for clinical signs of coccidiosis.)

TABLE 7-3 Corresponding Species of *Eimeria* of Sheep and of Goats

Ahsata Group	Arloingi Group	Faurei Group	Absheronae Group
Eimeria ahsata, Eimeria bakuensis,** and *Eimeria crandallis*	*Eimeria arloingi,* Eimeria hirci,* and *Eimeria christenseni**	*Eimeria faurei* and *Eimeria caprovina*	*Eimeria absheronae,* Eimeria caprina,* and *Eimeria caprovina*
Eimeria intricata	*Eimeria kocharii**	*Eimeria ovinoidalis*	*Eimeria ninakohlyakimovae*
Eimeria granulosa	*Eimeria jolchijevi*	*Eimeria parva*	*Eimeria alijevi**
		Eimeria pallida	*Eimeria pallida*

*Those species most likely to be responsible for clinical signs of coccidiosis.

Cryptosporidium

The oocysts are best concentrated by flotation in saturated sucrose solution. Because the oocysts of *Cryptosporidium parvum* and *Cryptosporidium bovis* are a mere 5 μm in diameter, the slide must be scanned under high dry magnification. *Cryptosporidium* oocysts tend to lie in the focal plane immediately below the coverslip (i.e., at the top of the air bubbles) (see Figure 3-16). Cattle are hosts of three species of *Cryptosporidium: C. parvum* and *C. bovis* of the small intestine and *Cryptosporidium andersoni* of the abomasum. The

oocysts of *C. andersoni* are larger than those of *C. parvum*, being about 7 μm in diameter, and are ellipsoidal (see Figure 3-17).

Other Protozoa

Cattle, sheep, and other ruminants can also be host to other protozoa. Among the most common groups of protozoa seen in the feces of cattle, sheep, and other ruminants are ameba cysts, considered in these hosts to be commensals. Also, *Giardia* can sometimes be found in the feces of ruminants, some having signs of infection and some without. Cattle are also host to a commensal protozoan, *Buxtonella sulcata*, which has cysts in the feces that look very similar to those of *B. coli* of pigs.

Annotated Host-Organ Listing of Parasites of Ruminants

T. gondii may occur in any tissue of any host as extracellular or intracellular tachyzoites or as bradyzoites in cysts (see Figure 8-35).

Alimentary System

Mouth, esophagus, and forestomachs

Protozoa

Sarcocystis (Apicomplexa) sarcocysts occur in muscles of tongue and esophagus (see Figures 8-32 and 8-33Figure 8-32Figure 8-33).

Cestode larvae

Taenia species (Taeniidae) cysticerci occur in muscles of tongue (see Figures 4-38 and 8-60Figure 4-38Figure 8-60).

Insect larvae

Hypoderma lineatum (Diptera: Hypodermatidae) in wall of esophagus.

Nematodes

Gongylonema pulchrum (150 mm), and *Gongylonema verrucosum* (100 mm) (Spirurida) (see Figures 4-133, 4-134Figure 4-133Figure 4-134, and 7-105) occur woven in a neat, sinusoidal pattern in the esophageal *(G. pulchrum)* or ruminal *(G. verrucosum)* mucosa.

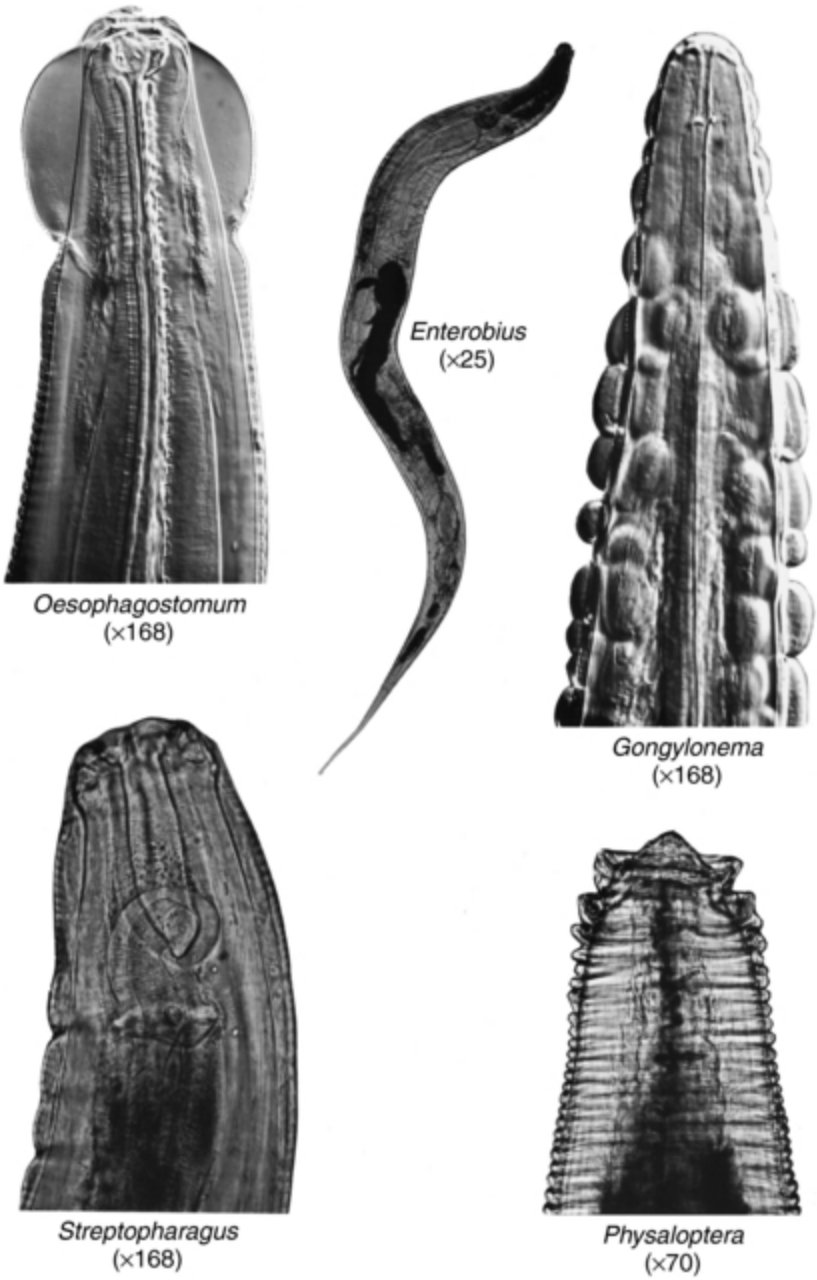

Figure 7-105 Some nematode parasites of monkeys and apes.

Courtesy Dr. M.M. Rabstein.

Trematodes

Cotylophoron cotylophoron, Paramphistomum cervi, Paramphistomum liorchis, and *Paramphistomum microbothroides (Paramphistomatidae)*

(see Figure 4-12).

Abomasum

Protozoan

Eimeria gilruthi (Coccidia) megaschizonts (see Figure 8-27).

C. andersoni (Apicomplexa) occurs usually without clinical signs.

Nematodes

H. contortus, Haemonchus placei, Haemonchus similis, Mecistocirrus digitatus, Ostertagia ostertagi, Ostertagia bisonis, Ostertagia (Teladorsagia) circumcincta, Ostertagia orloffi, Ostertagia trifurcata, Ostertagia (Grosspiculagia) lyrata, Ostertagia (Grosspiculagia) occidentalis, Ostertagia (Telodorsagia) davtiani, Ostertagia (Pseudostertagia) bullosa, M. marshalli, and *Trichostrongylus axei* (Strongylida: Trichostrongyloidea) (Figure 7-65, Table 7-4). These parasites, depending on the species, cause anemia, diarrhea, abomasitis, and so on.

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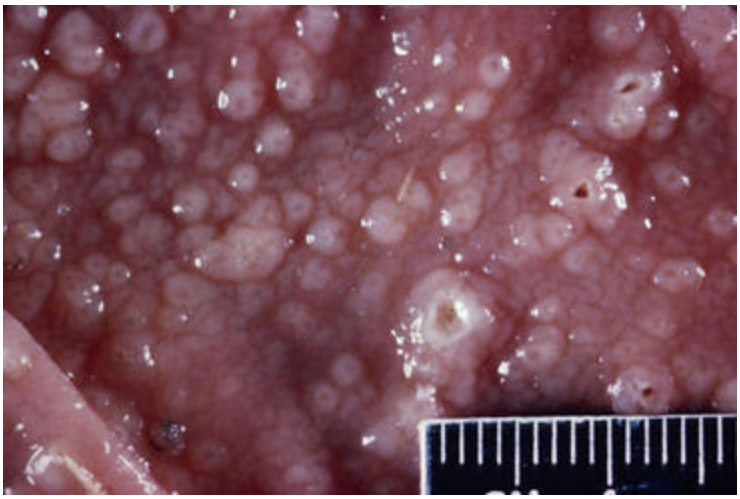

Figure 7-65 Lesions in the abomasum of a cow caused by larvae of *Ostertagia ostertagi*.

TABLE 7-4 Nematodes in the Abomasum and Small Intestine

Genus	Length (mm)	Figure(s)
Abomasum		
Haemonchus	14-30	4-72, 4-75
Mecistocirrus	43	4-77
Ostertagia	7-9	4-66, 4-72
Trichostrongylus axei	7	4-70, 4-72
Small Intestine		
Cooperia	6-16	4-72, 4-78
Trichostrongylus	6-7	4-70, 4-72
Nematodirus	20-25	4-72, 4-76

Small intestine

Nematodes

T. vitulorum (30 cm, Ascaridoidea) is only rarely seen in the United States, although it can be common in the developing world. It has an esophageal ventriculus and produces subspheric eggs with a pitted *T. canis*–like shell surface. *A. suum*, a very occasional parasite of ruminants, lacks a ventriculus and produces ellipsoidal eggs with a mammillated shell surface.

Cooperia curticei, Cooperia bisonis, Cooperia oncophora, Cooperia pectinata, Cooperia punctata, Cooperia spatulata, Cooperia occidentalis, Trichostrongylus colubriformis, Trichostrongylus longispicularis, Trichostrongylus capricola, Trichostrongylus vitrinus, Nematodirus helvetianus, Nematodirus spathiger, Nematodirus filicollis, Nematodirus abnormalis, Nematodirus lanceolatus, and *N. battus* (Strongylida:

Trichostrongyloidea) occur, with the typical associated signs in heavy infections being diarrhea (see Table 7-4).

B. phlebotomum (cattle) and *Bunostomum trigonocephalum* (sheep) (25 mm, Ancylostomatoidea) (see Figure 4-93) are capable of causing anemia in younger animals with heavy infections.

S. papillosus (6 mm, Rhabditida) (see Figure 4-109) can cause diarrhea and anemia when present in large numbers.

Aonchotheca (Capillaria) bovis and *Aonchotheca (Capillaria) brevipes* (Trichinelloidea) (see Figure 7-58).

Oesophagostomum species third- and fourth-stage larvae (Strongyloidea) (see Figure 4-90).

Cestodes

M. expansa and *M. benedeni* (Anoplocephalidae) (Figure 7-66; see also Figures 4-49, 4-50Figure 4-49Figure 4-50, and 7-58) typically occur with no clinical signs.

Figure 7-66 *Moniezia benedeni* in the intestine of a cow at necropsy.

Thysanosoma actinoides, *Wyominia tetoni* (Anoplocephalidae) typically occur with no clinical signs.

Thysaniezia, *Stilesia*, *Avitellina* (Anoplocephalidae) are exotic anoplocephalids of ruminants.

Protozoa

Eimeria species (Coccidia) (see Figures 7-63, 7-64, and 8-20 to 8-24Figure 8-20Figure 8-21Figure 8-22Figure 8-23Figure 8-24), depending on the species involved, can cause severe enteritis with bloody diarrhea; stages may be visible in wet mount scrapings of the intestinal mucosa.

C. parvum, *C. bovis*, and *C. andersoni* (Apicomplexa) occur, with the *C. parvum* being a cause of diarrhea in calves less than 30 days of age (see Figures 3-16 and 3-17Figure 3-16Figure 3-17).

Giardia species (flagellate) (see Figure 7-94) can cause diarrhea in young animals and sometimes adults.

Cecum and colon

Nematodes

Oesophagostomum radiatum (cattle), *Oesophagostomum columbianum* (sheep and goats), *Oesophagostomum venulosum* (sheep and goats), and *Chabertia ovina* (sheep and goats) (18 to 22 mm, Strongyloidea) (see Figures 4-86 to 4-90Figure 4-86Figure 4-87Figure 4-88Figure 4-89Figure 4-90). The fourth-stage larvae of *O. radiatum* in cattle and *O. columbianum* in sheep may be found in abscesses in the gut wall (see Figure 4-90).

Trichuris discolor (52 mm, cattle) and *Trichuris ovis* (70 mm, sheep and goats) (Trichinelloidea) (see Figure 7-58) can be associated with clinical diarrhea.

S. ovis and *Skrjabinema caprae* (8 to 10 mm, Oxyurida) infections are usually without clinical signs (Figure 7-67).

Protozoa

Eimeria species (Coccidia) (see Figures 7-63, 7-64, and 8-20 to 8-24Figure 8-20Figure 8-21Figure 8-22Figure 8-23Figure 8-24).

Entamoeba bovis and other species of amebas are considered nonpathogenic parasites or commensals of the large bowel of ruminants.

B. sulcata (ciliate) is a commensal of the large bowel of cattle (see Figure 7-22).

Liver

Nematodes

A. suum (Ascaridida) of swine will on rare occasions sometimes appear in the bile ducts of sheep and cattle.

Stephanurus dentatus (Strongyloidea) (see Figure 4-91) has immature larvae that can migrate through the bovine liver and cause severe trauma.

Cestodes

T. actinoides and *Wyominia tetoni* (Anoplocephalidae) can sometimes be found in the bile ducts of ruminants into which they have

migrated soon after the animal's death; with rapid ligation of the duct, the worms will be found in the small intestine.

Cestode larvae

E. granulosus and *E. multilocularis* hydatids (Taeniidae) (see Figures 4-44 to 4-48, 8-57, 8-58, and 8-64Figure 4-44Figure 4-45Figure 4-46Figure 4-47Figure 4-48Figure 8-57Figure 8-58Figure 8-68) cause signs that may be severe depending on the location of the cysts produced.

T. hydatigena cysticerci (Taeniidae) (see Figure 4-38).

Trematodes

Fasciola hepatica, F. gigantica, and *F. magna* (Fasciolidae) (Figure 7-68; see also Figures 4-1 to 4-9Figure 4-1Figure 4-2Figure 4-3Figure 4-4Figure 4-5Figure 4-6Figure 4-7Figure 4-8Figure 4-9 and 7-62, *A*). *F. hepatica* (30 mm) is endemic in western and Gulf states of the United States and in Hawaii, Puerto Rico, British Columbia, and eastern provinces of Canada. *F. gigantica* (75 mm) is endemic in Hawaii and Africa. *F. magna* (100 mm) occurs in foci throughout North America; remember that the final host is typically the white-tailed deer. The migratory tracts and lesions produced by *F. magna* can be marked in ruminants with large deposits of black "fluke pigment," often fatal in smaller ruminants.

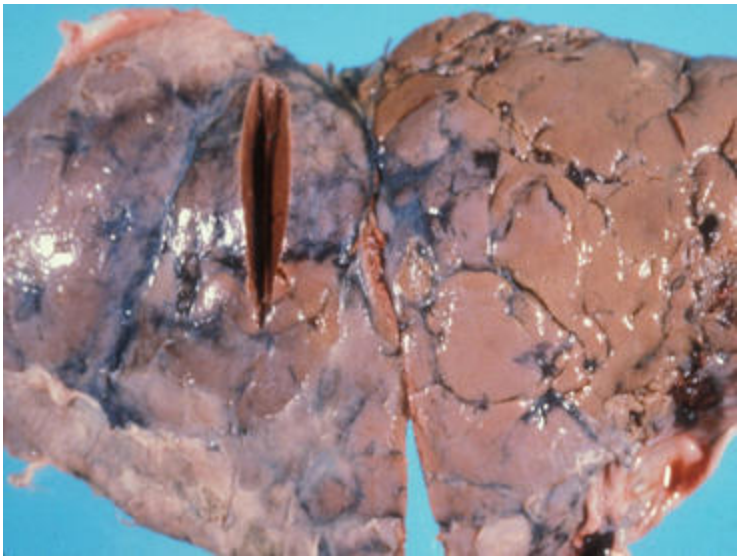

Figure 7-68 Liver of a sheep that has been fatally infected with *Fascioloides magna* showing the typical lesions and deposits of black "fluke pigment."

D. dendriticum (Europe, Asia, Africa, South America) has been introduced into North America, and it occurs in central New York State and the Pacific northwest; it causes chronic hepatic fibrosis.

E. pancreaticum (Asia and Brazil) (Dicrocoeliidae) (see Figures 4-18 and 7-62, C).

Peritoneum and peritoneal cavity

Nematode

Setaria labiatopapillosa (Filarioidea) (see Figure 4-142) are large white filarids that are sometimes found as incidental findings in the abdominal cavity of cattle.

Cestode larvae

T. hydatigena larvae (Taeniidae) (see Figure 4-48) are cysticerci that often have a long “neck” anterior to the scolex.

Pentastomid nymphs

L. serrata (Pentastomida) (see Figure 2-123) larvae can be found in the abdominal cavity of viscera of ruminants, most commonly in Africa.

Respiratory System

Nasal cavity and paranasal sinuses

Insect larvae

Oestrus ovis larvae in sheep and goats (Oestridae) (see Figure 2-22) are found in the nasal sinuses; they may be rather small or quite large (10 to 20 mm) depending on their developmental age.

Trachea and bronchi

Nematodes

Dictyocaulus viviparus (80 mm, cattle) (Trichostrongyloidea) is the only lung-dwelling nematode found in cattle; these can cause severe respiratory distress when present in large numbers.

D. filaria (100 mm, sheep and goats) (Trichostrongyloidea) (see Figures 4-72, 4-81Figure 4-72Figure 4-81, and 7-61) can cause respiratory distress in the infected host.

P. rufescens (50 mm; sheep) (Metastrongyloidea) (see Figures 4-68 and 7-61).

Mammomonogamus laryngeus (Syngamidae) (see Figure 3-91). Male and female worms are fused in copula; they are endemic in

Puerto Rico and various Caribbean islands. These worms have a large strongylid buccal capsule.

Lung parenchyma

Nematodes

M. capillaris (Metastrongyloidea) (see Figures 3-100 and 5-35).

O. columbianum larvae (erratic migration) (see Figure 4-90).

Cestode larvae

E. granulosus (Taeniidae) (see Figures 4-44, 4-45, and 8-64Figure 4-44Figure 4-45Figure 8-64) has cysts that can become quite large when present in lung tissue.

Vascular System

Heart

Cestode larvae

Taenia saginata (Taeniidae) cysticerci are found in the muscles of cattle in the United States.

T. ovis (Taeniidae) cysticerci are found in the various muscles of sheep but are considered exotic now in the United States.

Arteries

Nematodes

Elaeophora schneideri (sheep; Filarioidea) occurs in the western United States.

Elaeophora poeli (cattle; Filarioidea) is an exotic infection in Africa and Asia.

Onchocerca armillata (cattle; Filarioidea) is an exotic infection in Africa and Asia.

Veins

Trematodes

Schistosoma species (Schistosomatidae) (see Figure 4-24) are all exotic. *S. japonicum* is found in Asia with a wide mammalian host range. Species in cattle, sheep, and goats include *Schistosoma bovis* (Africa, Asia, southern Europe) and *Schistosoma nasalis*, *Schistosoma matthei, Schistosoma indicum, Schistosoma spindale*, and *Schistosoma turkestanica* (Asia).

Lymph nodes

Pentastomids

Linguatula serrata (see Figure 2-123).

Blood

Nematode microfilariae

S. labiatopapillosa (Filarioidea).

Protozoa

Babesia bigemina, *Babesia bovis, Babesia divergens*, *Babesia argentina*, *Theileria parva*, *Theileria annulata*, and *Theileria mutans* (piroplasms)

(see Figure 3-29) are all basically exotic at this time in the United States.

Trypanosoma theileri (cattle) and *Trypanosoma melophagium* (sheep) (hemoflagellates) (see Figure 3-2). Rarely seen in blood films, these organisms are readily demonstrable by blood culture.

Rickettsia

Anaplasma marginale, Mycoplasma wenyonii, and *Mycoplasma ovis.*

Skeletal Muscles and Connective Tissues

Cestode larvae

T. saginata (Taeniidae) cysticerci are found most frequently in the muscles of mastication, tongue, heart, and muscular portion of the diaphragm of cattle; scolex with four suckers but no hooks.

T. hydatigena (Taeniidae) (see Figure 3-29) cysticerci are sometimes found in skeletal muscles but more commonly in liver or on peritoneal membranes.

T. ovis (Taeniidae) cysticerci are pea-sized vesicles found in the heart and esophagus and beneath the epicardium and diaphragmatic pleura of sheep and goats; exotic in the United States.

Insect larvae

Hypoderma bovis and *H. lineatum* (Hypodermatidae) (see Figure 2-22) larvae overwinter in the northern climates within cattle, with *H. bovis* being in the spinal canal and *H. lineatum* being in tissues around the esophagus.

Nematodes

Onchocerca gutturosa, *Onchocerca lienalis*, *Onchocerca bovis,* and *Onchocerca gibsoni* (Filarioidea). Adult *Onchocerca* worms are found in deep connective tissues, microfilariae in the dermis. In Australian cattle, *O. gibsoni* produces nodules in the brisket that require extensive trimming. We have seen *O. gibsoni* in corned beef purchased in a local supermarket.

Protozoa

Sarcocystis species (Apicomplexa) sarcocysts in muscles (see Table 2-1 and Figure 8-32).

Urogenital System

Protozoans

Tritrichomonas foetus (Flagellate) (see Figures 3-4 and 3-5Figure 3-4Figure 3-5).

T. gondii (Apicomplexa) placentas of aborting sheep.

N. caninum (Apicomplexa) placentas of aborting cattle.

Nervous System

Brain, spinal cord, and meninges

Protozoa

Sarcocystis-like organism (Apicomplexa) in brain of cattle (Dubey, Perry, and Kennedy, 1987).

Nematode

Parelaphostrongylus tenuis (Metastrongylidae) (see Figures 8-93 and 8-94Figure 8-93Figure 8-94). Adults are typically found in white-tailed deer. Larvae and young adults that find their way into sheep and goats migrate through the spinal cord and brain, causing paralysis. Infections in cattle are rare but are reported.

Cestode larvae

T. multiceps (Taeniidae) occurs in the brain of sheep and goats causing "gid" (see Figures 4-42 and 8-62Figure 4-42Figure 8-62); the organism is exotic and supposedly no longer in North America.

Insect larva

H. bovis (Hypodermatidae) larvae in the spinal canal of cattle.

Eye

Nematodes

T. californiensis (sheep), *Thelazia gulosa* (cattle), and *Thelazia skrjabini* (cattle) (Spirurida), in conjunctival sac and lachrymal duct (see Figure 4-132) may be associated with conjunctivitis and development of granulation tissue.

Skin and Hair

Insects

Dipteran adults

Musca autumnalis, *Stomoxys calcitrans,* and *Haematobia irritans* (Muscidae) (see Figures 2-13, 2-14, and 2-15Figure 2-13Figure 2-

14Figure 2-15) adults spend a good deal of time on cattle; *S. calcitrans* is more likely to rest off of cattle when not feeding.

Glossina species (Africa) (see Figure 2-16).

Melophagus ovinus (Hippoboscidae) (see Figure 2-17) pupae and adults of the ked are found on the fleece.

H. bovis and *H. lineatum* (Hypodermatidae), the gadflies, are rarely seen as they hover about cattle gluing their eggs to hairs on the animals.

Tabanidae (see Figures 2-10 and 2-11Figure 2-10Figure 2-11) land on cattle typically only long enough to feed.

Dipteran larvae

H. bovis and *H. lineatum* (30 mm, Hypodermatidae) (see Figure 2-22) bots mature in warbles in the skin of cattle typically along the back of the animal.

Calliphoridae and Sarcophagidae (see Figures 2-12, 2-18, and 2-19Figure 2-12Figure 2-18Figure 2-19) maggots can be serious pests of ruminant, newborns, and animals that are wounded or down and soiled for an extended period.

Anoplurans

Haematopinus eurysternus, Haematopinus quadripertusus, Haematopinus tuberculatus, Linognathus vituli, Solenopotes capillatus (cattle), *Linognathus ovillus, Linognathus pedalis, Linognathus oviformis* (sheep), *Linognathus oviformis,* and *Linognathus stenopsis* (goat) (see Figures 2-36, 2-38, and 2-40Figure 2-36Figure 2-38Figure 2-40).

Mallophagans

Damalinia (Bovicola) bovis (cattle), *Damalinia ovis* (sheep), *Damalinia caprae, Damalinia limbatus, Damalinia (Holokartikos) crassipes* (goats) (see Figure 2-45).

Siphonaptera

Echidnophaga gallinacea (see Figure 2-54).

Ctenocephalides felis can cause severe distress in calves and has even been reported to cause the death of calves, lambs, and sheep, although mainly in tropical settings overseas (see Figure 2-53).

Arachnids

Metastigmata: ixodidae

A. americanum, Amblyomma cajennense, A. maculatum, Amblyomma inornatum (Mexico), *Amblyomma oblongoguttatum* (Central and South America), and *Amblyomma variegatum* (imported to Caribbean from Africa, eradication from area in process) (see Figure 2-69).

Boophilus annulatus and *Boophilus microplus* (see Figure 2-84); *B. annulatus* is considered exotic and should be reported if found on cattle.

D. andersoni, Dermacentor albipictus, Dermacentor occidentalis, Dermacentor nigrolineatus, D. variabilis, and *Dermacentor (Otocentor) nitens* (see Figures 2-86 to 2-88Figure 2-86Figure 2-87Figure 2-88).

Ixodes cookei, Ixodes pacificus, Ixodes scapularis (see Figures 2-70, 2-75, and 2-78Figure 2-70Figure 2-75Figure 2-78).

Metastigmata: argasidae

Otobius megnini (spinose ear tick) (see Figure 2-73), with larvae and nymphs in the ears.

Ornithodoros coriaceus and *Ornithodoros turicata* (see Figure 2-72) will get on the hosts only long enough to feed.

Astigmata

S. scabiei (see Figures 2-100 and 2-102Figure 2-100Figure 2-102) can cause severe dermatitis, especially in cattle.

Chorioptes bovis (see Figures 2-101, 2-109, and 2-110Figure 2-101Figure 2-109Figure 2-110).

Psoroptes ovis (see Figure 2-100, 2-107, and 2-108Figure 2-100Figure 2-107Figure 2-108) is considered eradicated for the most part from the United States, but this or other very similar mites turn up in the ears of llamas and other American camelids, various wild sheep, and cattle in the southern and western parts of the United States.

Prostigmata

Demodex bovis, *Demodex ovis*, and *Demodex caprae* (see Figures 2-115 and 8-7Figure 2-115Figure 8-7) can cause very large lesions in the skin of goats and cattle, each containing thousands of mites.

Psorobia bos (cattle) and *Psorergates ovis* (sheep and goats) (Psorergatidae) are the ruminant itch mites.

Trombiculidae (see Figures 2-118 to 2-120Figure 2-118Figure 2-119Figure 2-120), chiggers, are larvae of free-living adult mites and can cause severe pruritus often localizing within the ears.

Mesostigmata

Raillietia auris (cattle) and *Raillietia caprae* (goats). Ear mites (see Figure 2-96).

Protozoan

Besnoitia besnoiti (Coccidia), exotic.

Nematodes

Stephanofilaria stilesi (6 mm, Filarioidea). Very small adult filariids in skin of ventral abdomen, exotic.

Parafilaria bovicola (Filarioidea). Adults in subcutaneous tissues cause “summer bleeding” in cattle, exotic.

O. gutturosa, *O. lienalis*, and *O. bovis* (Filarioidea). Microfilariae found in dermis of cattle.

E. schneideri (Filarioidea) microfilariae can be found in the skin, usually in the head region.

Rhabditis strongyloides (Rhabditida) (see Figures 4-107 and 8-72Figure 4-107Figure 8-72) larvae will enter the hair follicles of animals on occasion if they are resting on damp hay or other bedding.

PARASITES OF HORSES

Stages in Feces

The intestinal parasites of horses form a unique group. Horses host only two coccidian species, *C. parvum* and *E. leuckarti* (Apicomplexa) (Figure 7-69), and only three species of tapeworms (*Anoplocephala magna*, *Anoplocephala perfoliata*, and *Paranoplocephala mamillana*), all of which belong to the family Anoplocephalidae (Figure 7-70). Nematodes form the largest group (Figure 7-71), which includes one ascarid *(Parascaris equorum)*, two pinworms (*O. equi* and *Probstmayria vivipara*), one rhabditoid nematode, *Strongyloides westeri*, three habronematid spirurids (*Habronema muscae*, *Habronema microstoma*, and *Draschia megastoma*), and many strongylids that are all members of the Strongyloidea except one, *T. axei* in the Trichostrongyloidea. Although the horse hosts no hookworms or whipworm, 54 species of strongylids more than make up for these deficiencies. The strongylids are cosmopolitan in distribution, and naturally infected horses tend to harbor a dozen or more species simultaneously. The diagnostic dilemma associated with strongylid eggs is thus accentuated in the case of the horse. However, the major diagnostic categories can be identified by fecal culture (Figure 7-72).

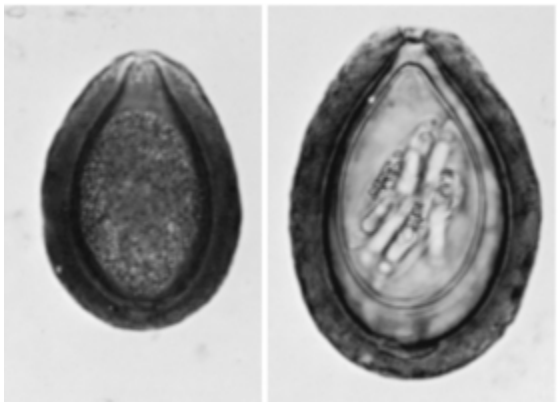

Figure 7-69 *Eimeria leuckarti* unsporulated *(left)* and sporulated *(right)* oocysts (×425).

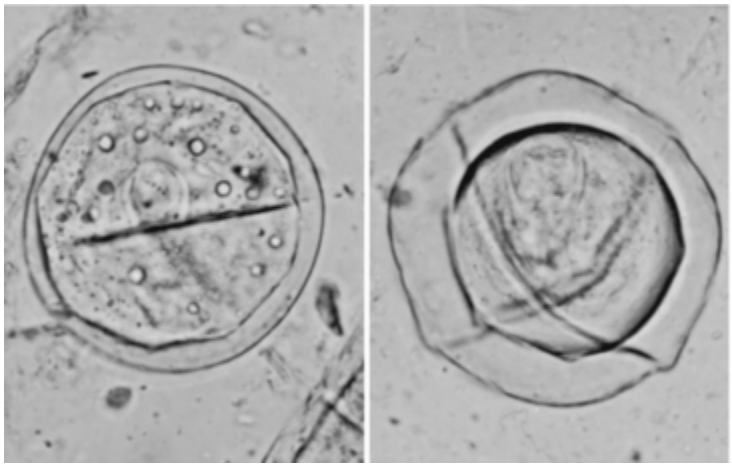

Figure 7-70 *Anoplocephala magna (left)* and *Anoplocephala perfoliata (right)* eggs (×425). The oncospheres are enclosed by pear-shaped embryophores. The egg of *Paranoplocephala mamillana* is only three fourths as large as these.

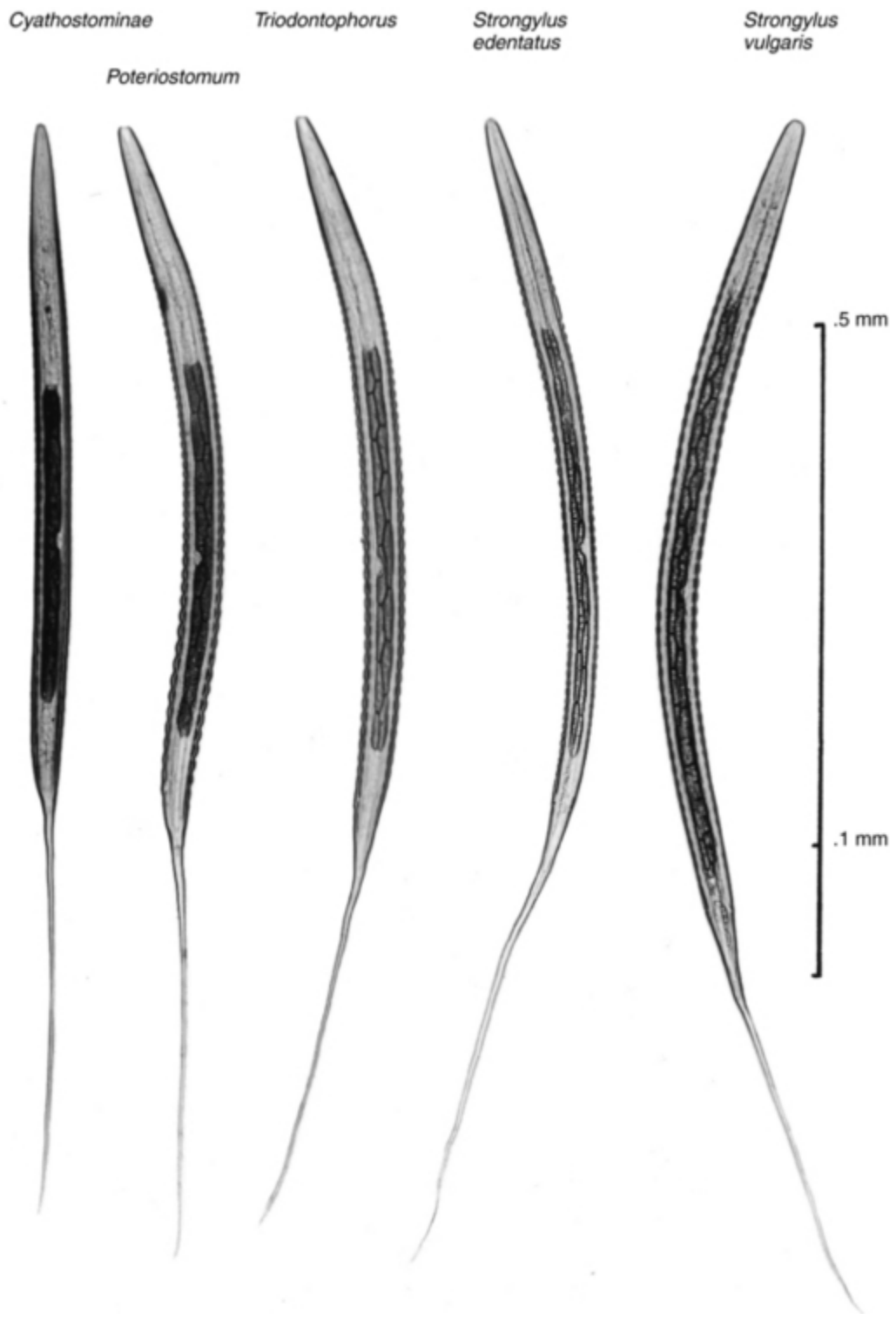

Figure 7-72 Infective third-stage larvae of some horse strongylids. Larvae of the subfamily Cyathostominae, represented here by *Cyathostomum catinatum*, have eight intestinal cells. *Gyalocephalus capitatus* (not shown) has 12, *Poteriostomum* has 16, *Triodontophorus* has 18 (but the *Triodontophorus serratus* larvae shown here have only 16),

Strongylus edentatus has 18 to 20, and *Strongylus vulgaris* has 32 intestinal cells. *S. vulgaris* is easily distinguished from all the rest by its large size and long column of intestinal cells.

The majority of parasite stages that float in a sugar flotation of equine feces are relatively easy to recognize. *P. equorum* eggs are yellowish brown with thick, subspheric, rough-surfaced shell walls and contain one cell. Eggs are often found with their external protein layer partially or completely detached. The exposed portions of such shells are smooth and clear. Strongyle eggs present the usual differential diagnostic problem. Recourse may be had to fecal culture and identification of infective third-stage larvae (see Figure 7-72). *S. westeri* eggs are smaller than strongyle eggs and contain a rhabditiform larva in fresh specimens. *O. equi* eggs are more likely to be recovered from anal scrapings than from fecal specimens. The egg shown here was collected by momentarily pressing the adhesive side of a piece of cellophane tape against a horse's anus and then was mounted by sticking the tape to a microscope slide (see Figure 7-71).

The eggs of *Draschia*, *Habronema*, and the equine tapeworms tend not to float very well in various solutions because they are fairly fragile and hard to float in common flotation media. They can actually even be very hard to find when its seems that they should be present in large numbers such as when the adults are present in the same animal on the necropsy table. *Draschia* and *Habronema* eggs are cigar-shaped and contain a vermiform embryo. Such eggs are difficult to demonstrate in feces. If a technique for antemortem

diagnosis of gastric habronemiasis is essential, resort to xenodiagnosis using *Musca domestica* larvae for *D. megastoma* and *H. muscae*, and *S. calcitrans* larvae for *H. microstoma*.

Identification of Equine Microfilariae

Equine microfilariae as drawn by Dr. Jay Georgi are shown diagrammatically in Figure 7-73. The reality is that after the approval of ivermectin and the other avermectins for use in horses, it is hard to find microfilariae commonly in horses any more; the routine ivermectin administration to horses may be reducing transmission or suppressing microfilariae.

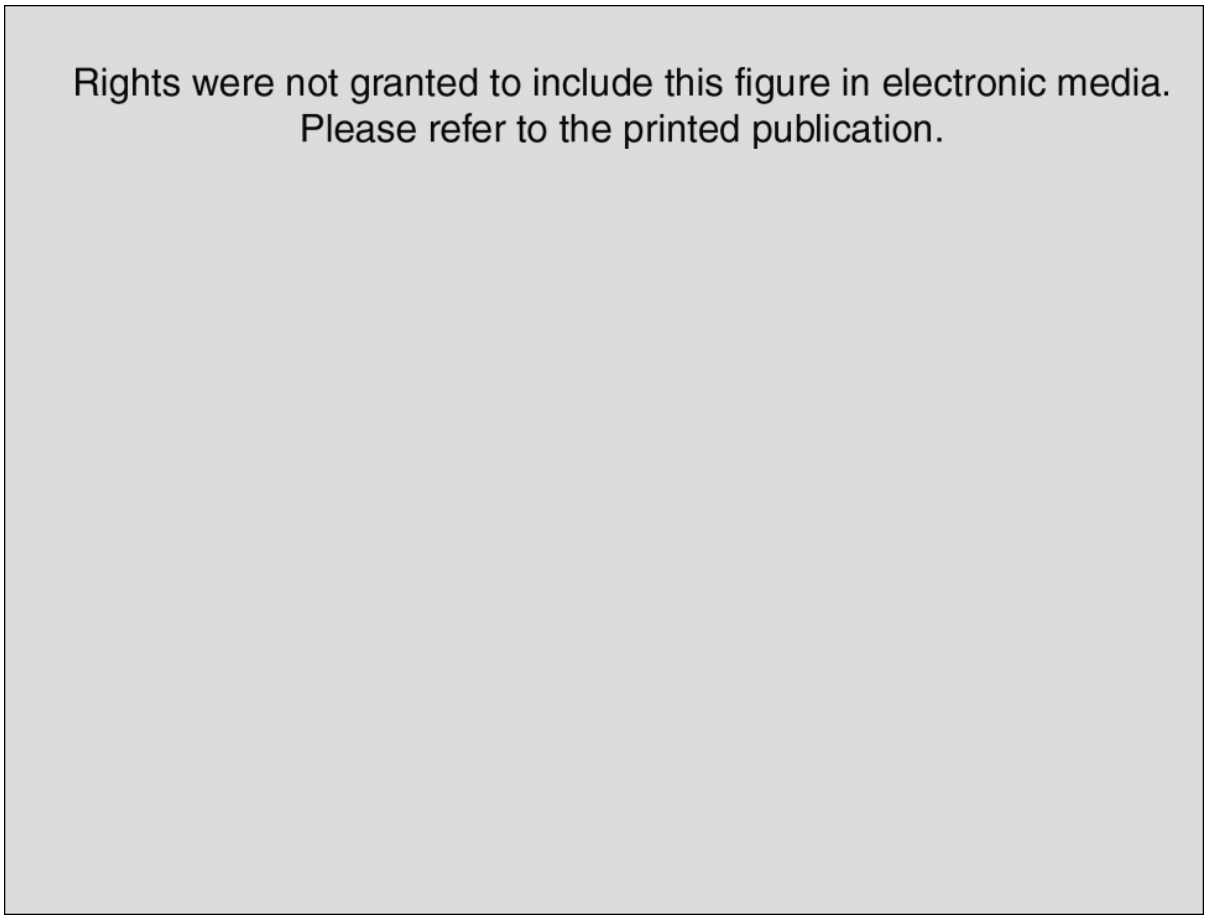

Figure 7-73 Microfilariae of filariid parasites of horses.

With kind permission from Springer Sciences+Business Media: Parasitology research, Capillaria Böhmi spec. nov., eine neue Haarwurmart aus den Stirnhöhlen des Fuchses, Vol 16, No 1, January 1953, Supperer R.

The sheathed microfilariae of *Setaria equina* may be demonstrated in blood samples by the techniques described for detecting the microfilariae of the canine heartworm.

Parafilaria multipapillosa microfilariae may be found in blood discharged from "summer bleeding" nodules caused by the adult female worms. They are less than 200 μm long, are unsheathed, and have a rounded posterior extremity (Supperer, 1953).

Microfilariae of *Onchocerca cervicalis*, *Onchocerca reticulata*, and *Elaeophora böhmi* may be demonstrated by excising a small piece of skin from near the linea alba and placing it in physiologic saline solution. The microfilariae of these three species will soon be observed migrating out of the dermis into the saline solution. Leave the preparation set up overnight to detect low levels of microfiladerma.

O. cervicalis microfilariae are slender, delicate, and 207 to 240 μm long.

O. reticulata microfilariae are 330 to 370 μm long and have a long, whiplike tail ending in a fine point.

E. böhmi microfilariae are 300 to 330 μm long and may be distinguished from *O. reticulata* by a difference in the distance from the genital cell to the tip of the tail, which is greater than 140 μm for *O. reticulata* and less than 120 μm for *E. böhmi*.

Annotated Host-Organ Listing of Parasites of Horses

Alimentary System

Mouth

Insect larvae

Gasterophilus intestinalis, *Gasterophilus nasalis* and *Gasterophilus haemorrhoidalis* (Diptera: Gasterophilidae) (Figure 7-74; see also Figures 2-22 and 2-26 to 2-30Figure 2-22Figure 2-26Figure 2-27Figure 2-28Figure 2-29Figure 2-30) larvae can be found in the tongue, in the interdental pockets, or at the base of the tongue.

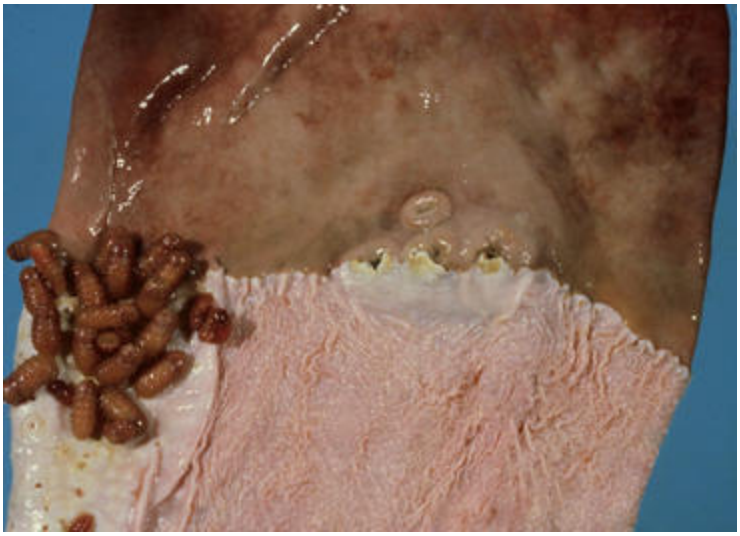

Figure 7-74 Stomach of a horse showing the attachment of bots, *Gasterophilus intestinalis*, and a lesion produced at the margo plicatus by an infection with the spirurid *Draschia megastoma*.

Protozoan

Trichomonas equibuccalis (mucosoflagellate) is found around gum margins of cheek teeth.

Stomach

Nematodes

D. megastoma, *H. muscae*, and *H. microstoma* (Spirurida) (see Figure 4-136) are found in the stomach, with *H. muscae* and *H. microstoma* being on the mucosa and *D. megastoma* in nodules at the margo plicatus (see Figure 7-74).

Trichostrongylus axei (Trichostrongyloidea) (see Figures 4-70 and 4-72Figure 4-70Figure 4-72) infections may cause hypertrophic gastritis with mucosal proliferations and are often associated with shared pasturage with cattle.

Insect larvae

G. intestinalis (Diptera: Gasterophilidae) (see Figures 2-22, 2-26 to 2-30Figure 2-22Figure 2-26Figure 2-27Figure 2-28Figure 2-29Figure 2-30, and 7-74), even with their specific designation, are found in the stomach.

Small intestine

Nematodes

P. equorum (Ascaridoidea) (see Figure 7-71) can be anywhere in length from 1 inch to 2 feet; often with regular deworming only small worms are found at necropsy.

S. westeri (Rhabditida) (see Figures 4-109, 7-71, and 8-74) is very small and threaded through the intestinal mucosa.

Cestodes

A. magna, P. mamillana (Anoplocephalidae) (see Figures 4-51, 4-52Figure 4-51Figure 4-52, and 7-70).

Protozoa

Cryptosporidium species (Apicomplexa) can cause serious diarrhea in neonatal foals.

E. leuckarti (Coccidia) (see Figures 7-69 and 8-25) has large schizonts and oocysts that may be demonstrated in mucosal scrapings.

Giardia species (flagellate) (see Figure 7-94) can be found as trophozoites in light scrapings of the mucosal surface of the anterior small intestine.

Insects

G. nasalis and *G. haemorrhoidalis* (Diptera: Gasterophilidae) larvae are found in the in duodenum.

Large intestine

Nematodes

O. equi (150 mm) and *P. vivipara* (3 mm) (Oxyurida) (see Figures 4-111 to 4-113Figure 4-111Figure 4-112Figure 4-113, and 7-71). *O. equi* (Figure 7-75) is commonly seen because the females crawl out of the anus, causing tail rubbing; *P. vivipara* is almost never seen.

Figure 7-75 *Oxyuris equi* adults recovered from a horse at necropsy.

Family Strongylidae

The horse is host to about 60 species belonging to the family Strongylidae, and as many as 20 different species are often found in the same horse.

Subfamily Strongylinae

Strongylus vulgaris, S. edentatus, S. equinus, Triodontophorus serratus, Triodontophorus brevicauda, Triodontophorus tenuicollis, Triodontophorus nipponicus, Oesophagodontus robustus, and *Craterostomum acuticaudatum* (Figure 7-76; see also Figures 4-63, 7-79 [bottom row], 7-78, and 7-79).

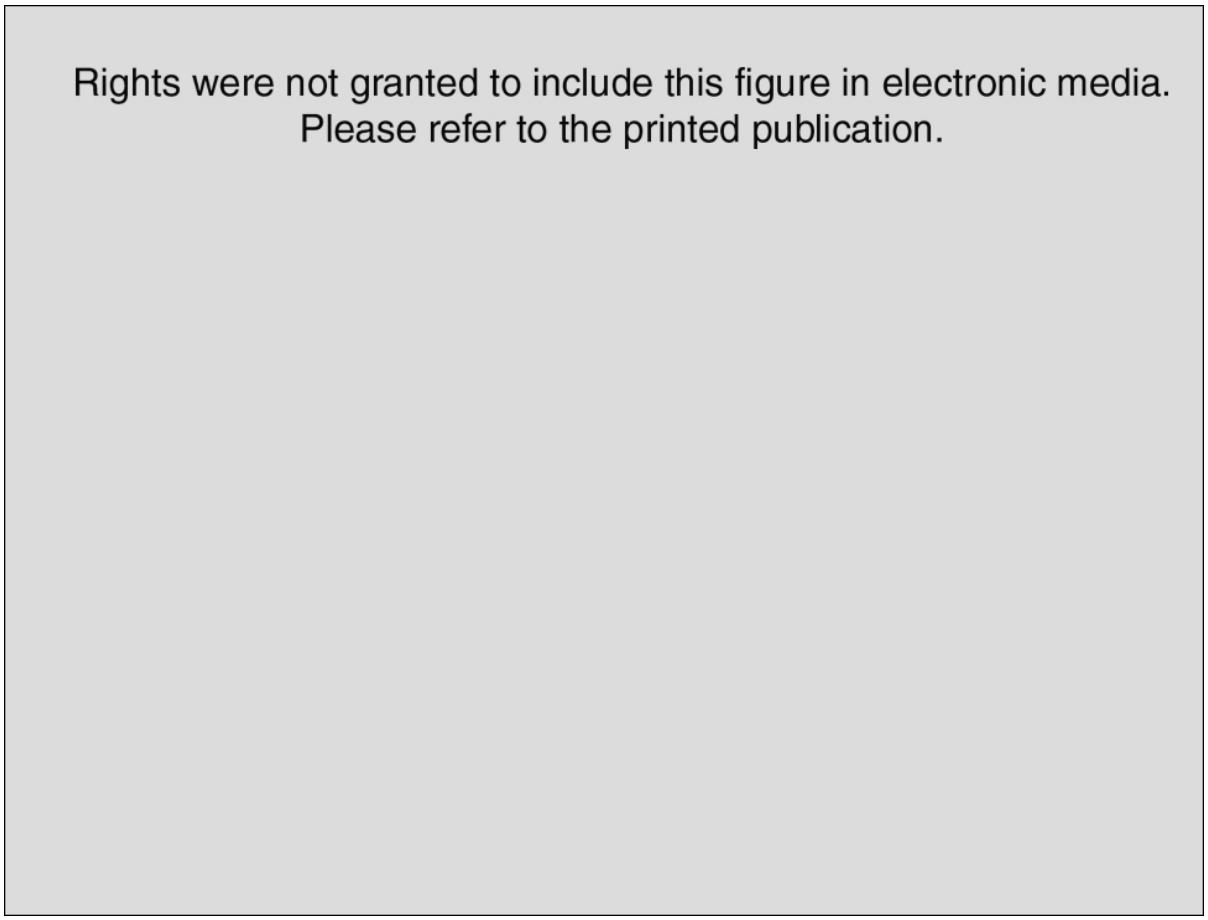

Figure 7-76 Members of the subfamily Strongylinae (large strongyles) and *Gyalocephalus capitatus* (subfamily Cyathostominae). *Strongylus vulgaris* and *Oesophagodontus robustus* (×72); *Strongylus equinus* (×40); *Strongylus edentatus* (×33); *Triodontophorus* spp. and *Gyalocephalus capitatus* (×112).

Strongylus species cleared and mounted by the glycol methacrylate method of Pijanowski et al: Cornell Vet 62:333, 1972.

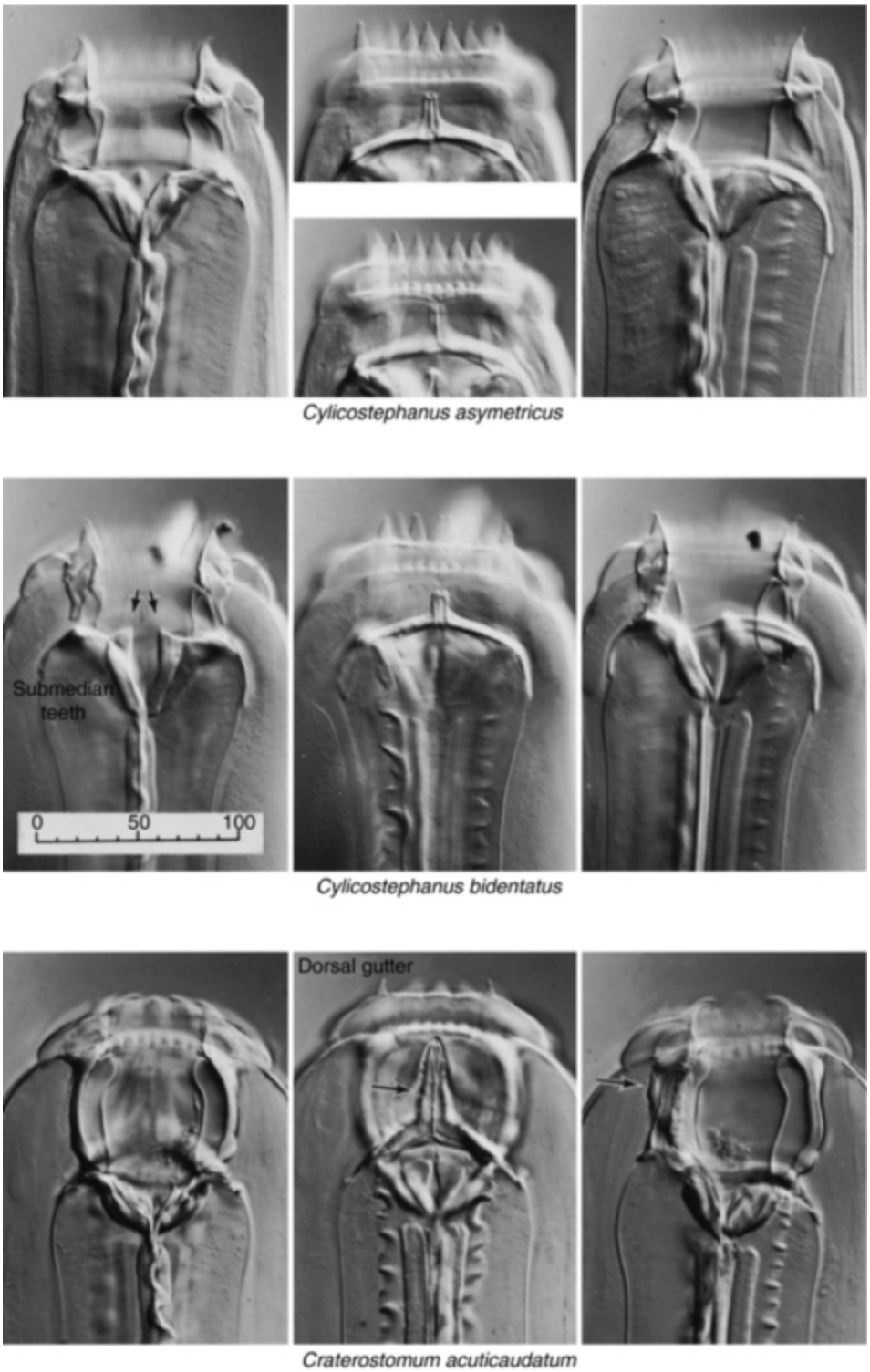

Figure 7-79 Members of the subfamily Cyathostominae and *Craterostomum acuticaudatum* (subfamily Strongylinae). Dorsoventral *(left)*, dorsal surface *(center)*, and lateral *(right)* views of the heads of *Cylicostephanus asymetricus (top row)*, *Cylicostephanus bidentatus (middle row)*, and *Craterostomum acuticaudatum (bottom row)*. (All ×283.)

Subfamily Cyathostominae

Genera: *Cyathostomum, Cylicocyclus, Cylicostephanus, Cylicodontophorus, Poteriostomum, Paraposteriostomum, Petrovinema, Coronocyclus,* and *Gyalocephalus* (Figures 7-77 to 7-87).

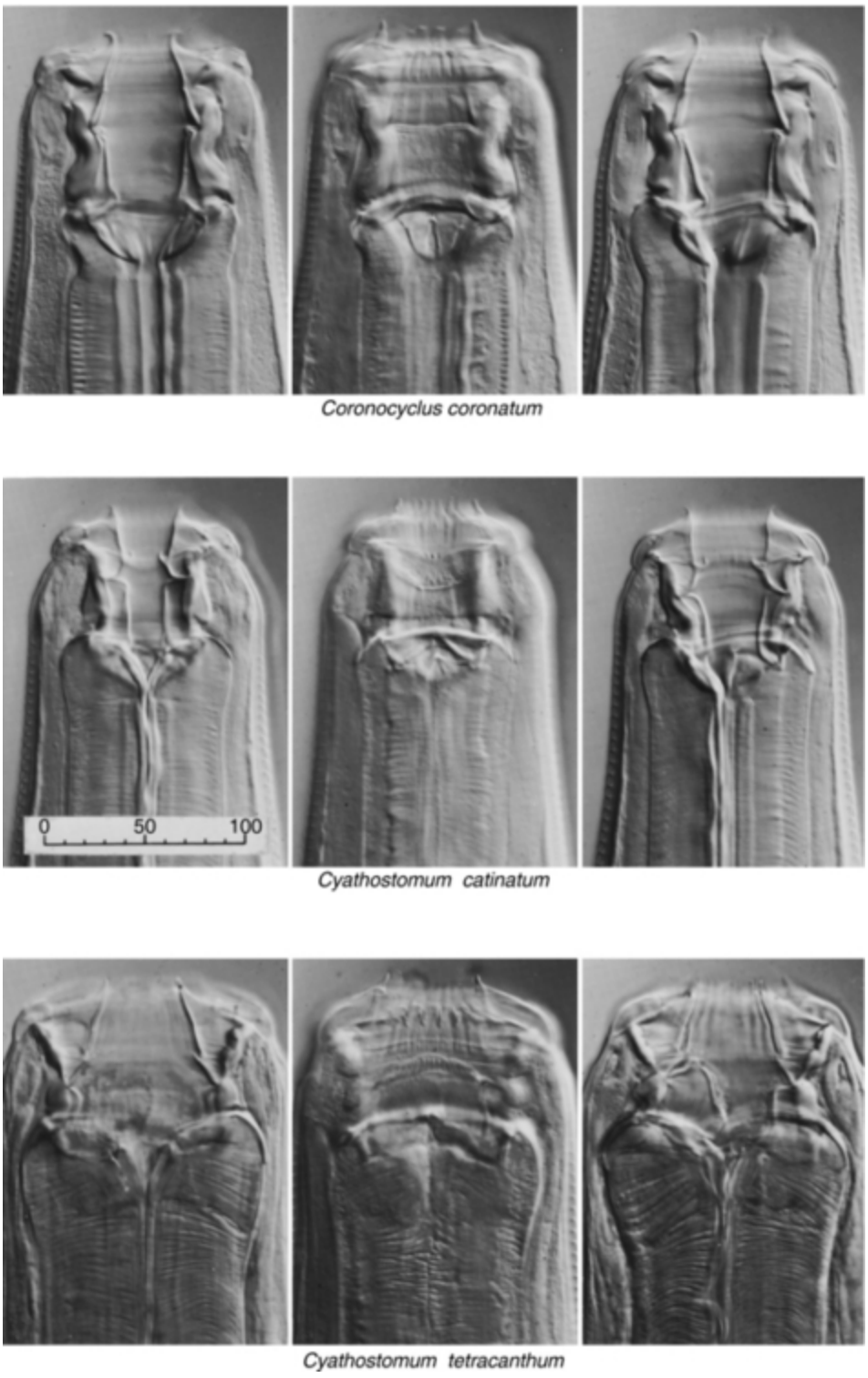

Figure 7-77 Members of the subfamily Cyathostominae. Dorsoventral *(left)*, dorsal surface *(center)*, and lateral *(right)* views of the heads of *Coronocyclus coronatus (top row)*, *Coronocyclus catinatum (middle row)*, and *Cyathostomum tetracanthum (bottom row)*. (All ×283.)

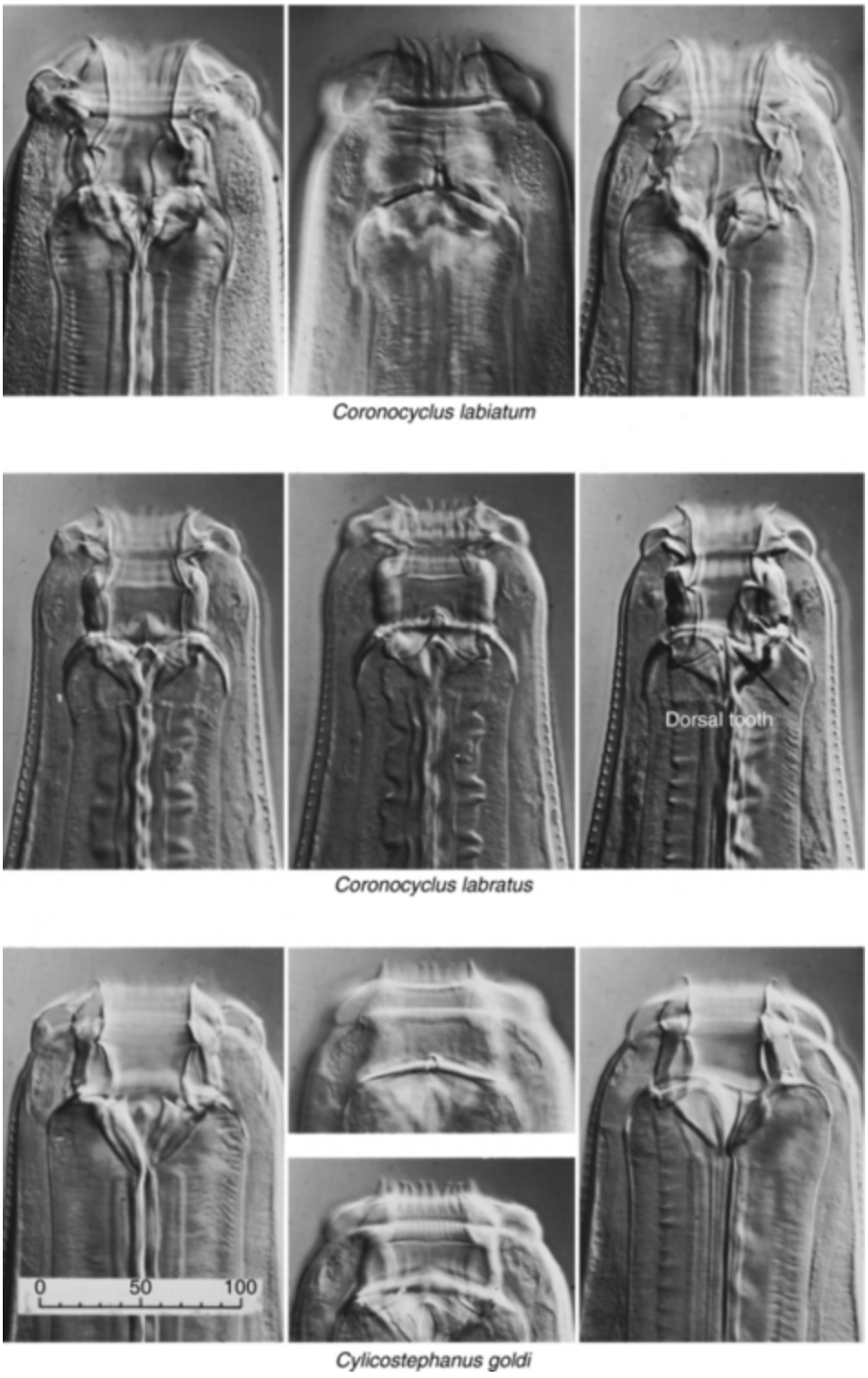

Figure 7-78 Members of the subfamily Cyathostominae. Dorsoventral *(left)*, dorsal surface *(center)*, and lateral *(right)* of the heads of *Coronocyclus labiatus (top row), Coronocyclus labratus (middle row)*, and *Cylicostephanus goldi (bottom row)*. (All ×283.)

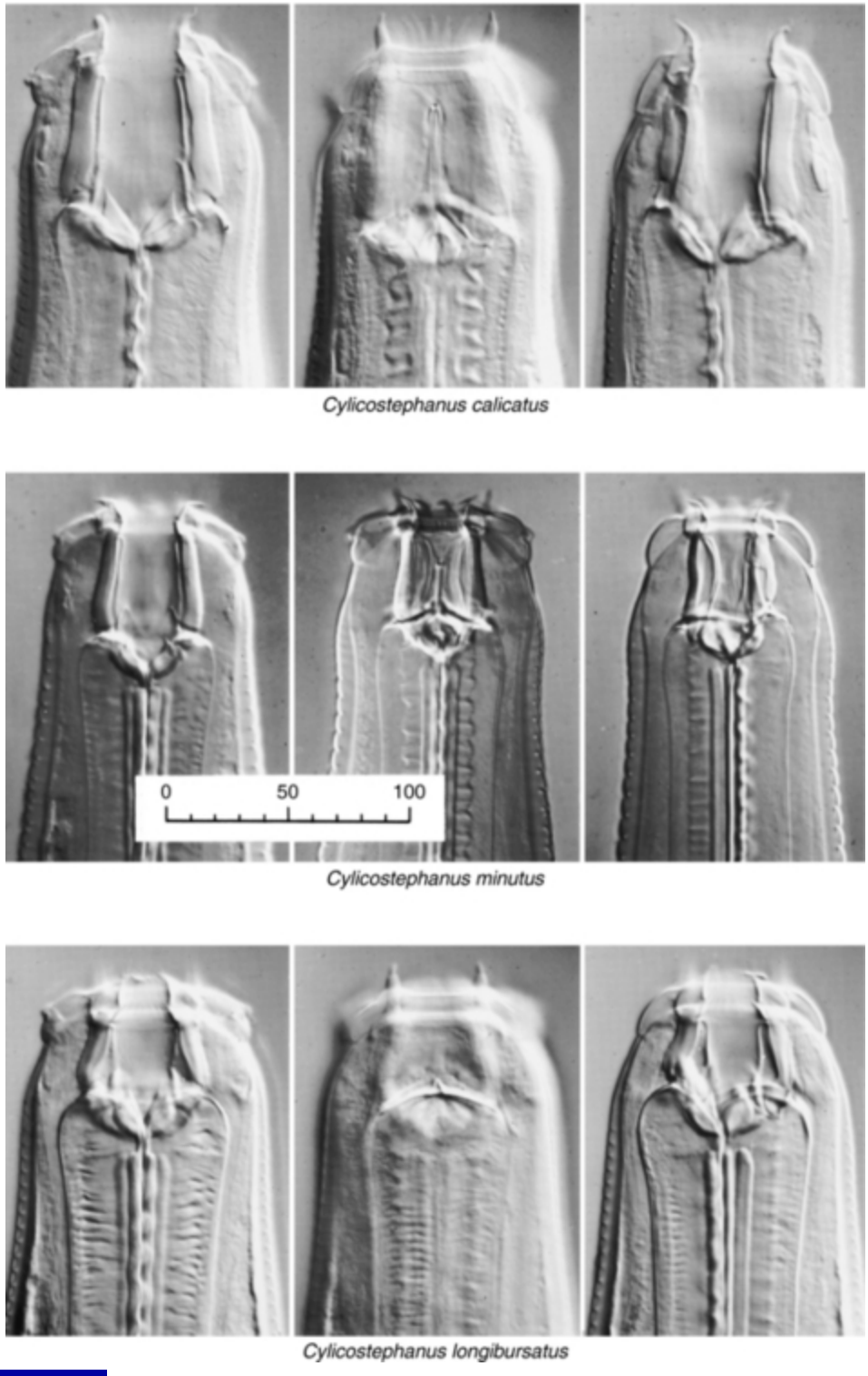

Figure 7-80 Members of the subfamily Cyathostominae. Dorsoventral *(left)*, dorsal surface *(center)*, and lateral *(right)* views of the heads of *Cylicostephanus calicatus (top row), Cylicostephanus minutus (middle row)*, and *C. longibursatus (bottom row)*. (All $\times$425.)

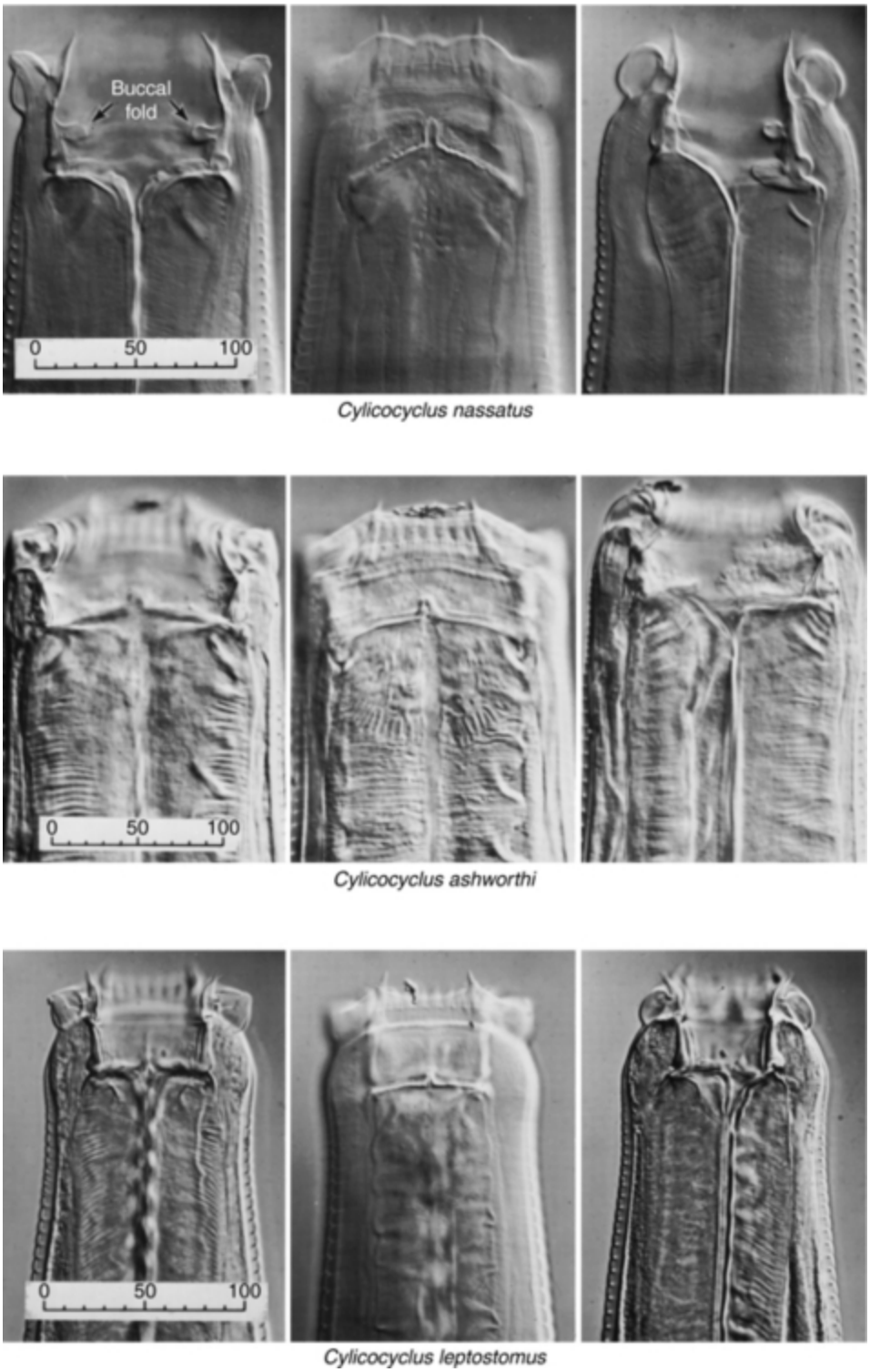

Figure 7-81 Members of the subfamily Cyathostominae. Dorsoventral *(left)*, dorsal surface *(center)*, and lateral *(right)* views of the heads of *Cylicocyclus nassatus (top row)*, *Cylicocyclus ashworthi (middle row)*, and *Cylicocyclus leptostomus (bottom row)*. *(C. nassatus* and *C. leptostomus* ×283, *C. ashworthi* ×242.)

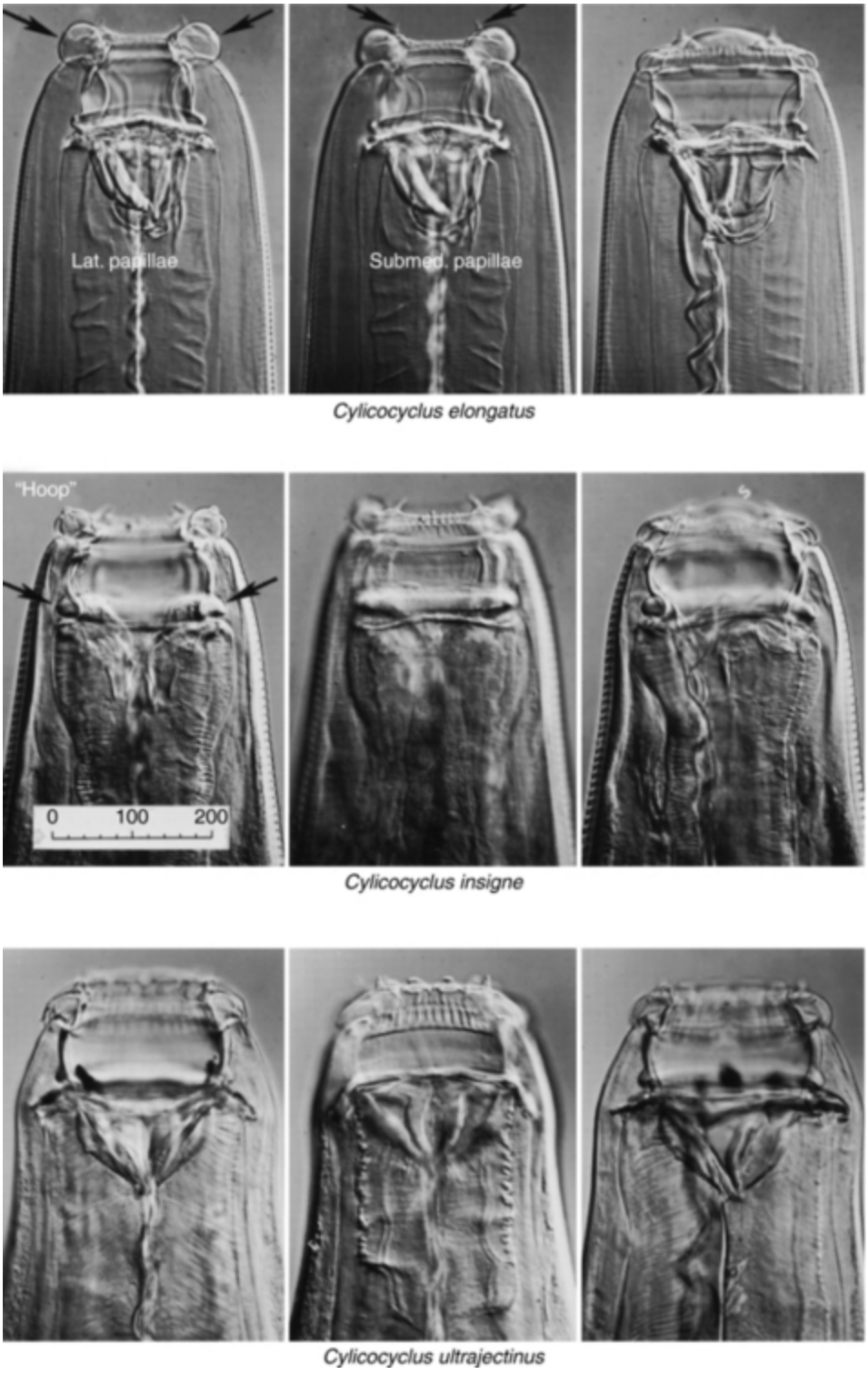

Figure 7-82 Members of the subfamily Cyathostominae. Dorsoventral *(left)*, dorsal surface *(center)*, and lateral *(right)* views of the heads of *Cylicocyclus elongatus (top row), Cylicocyclus insigne (middle row)*, and *Cylicocyclus ultrajectinus (bottom row)*. (All ×112.)

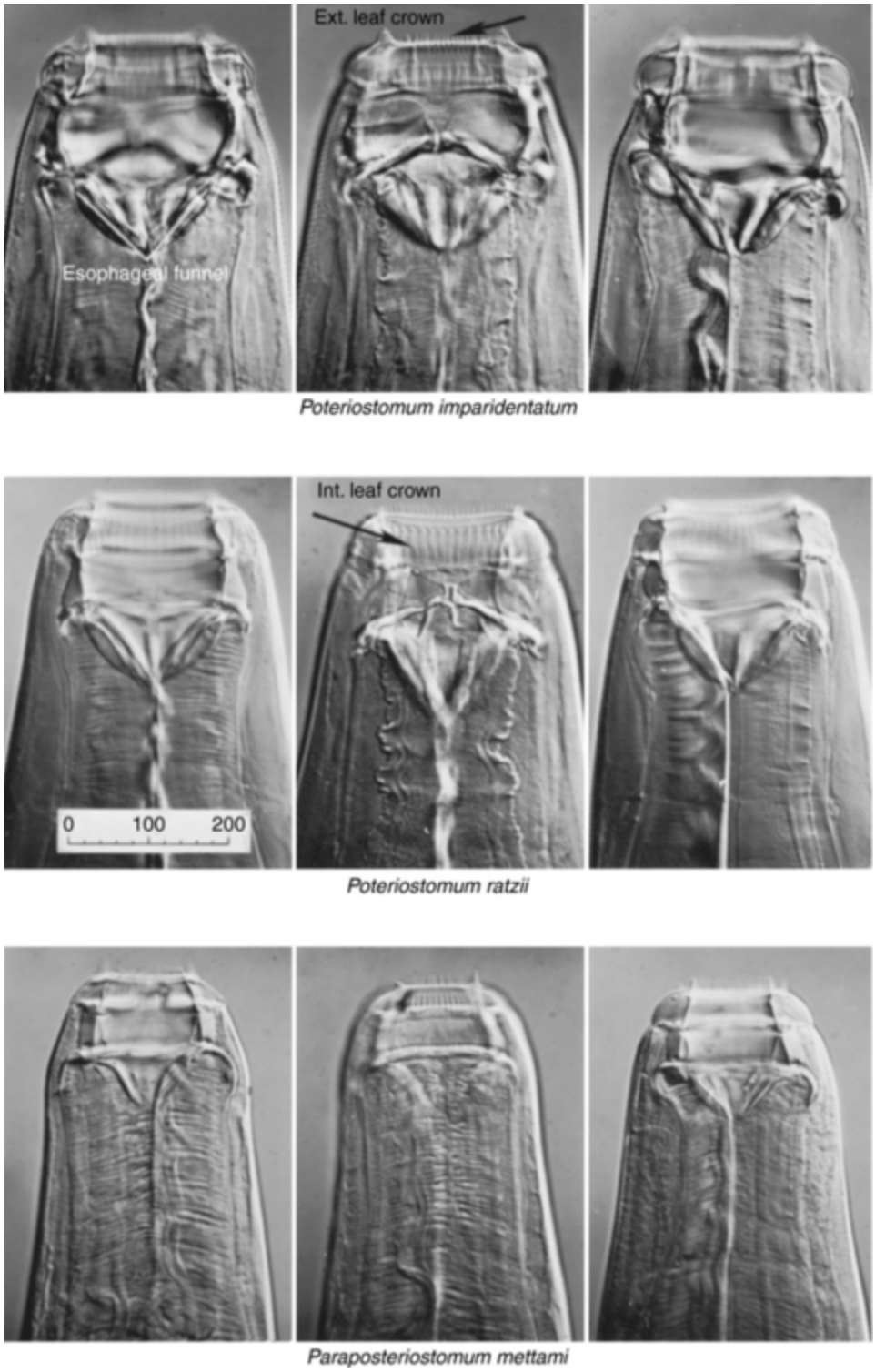

Figure 7-83 Members of the subfamily Cyathostominae. Dorsoventral *(left)*, dorsal surface *(center)*, and lateral *(right)* views of the heads of *Poteriostomum imparidentatum (top row), Poteriostomum ratzii (middle row)*, and *Paraposteriostomum mettami (bottom row)*. (All ×112.)

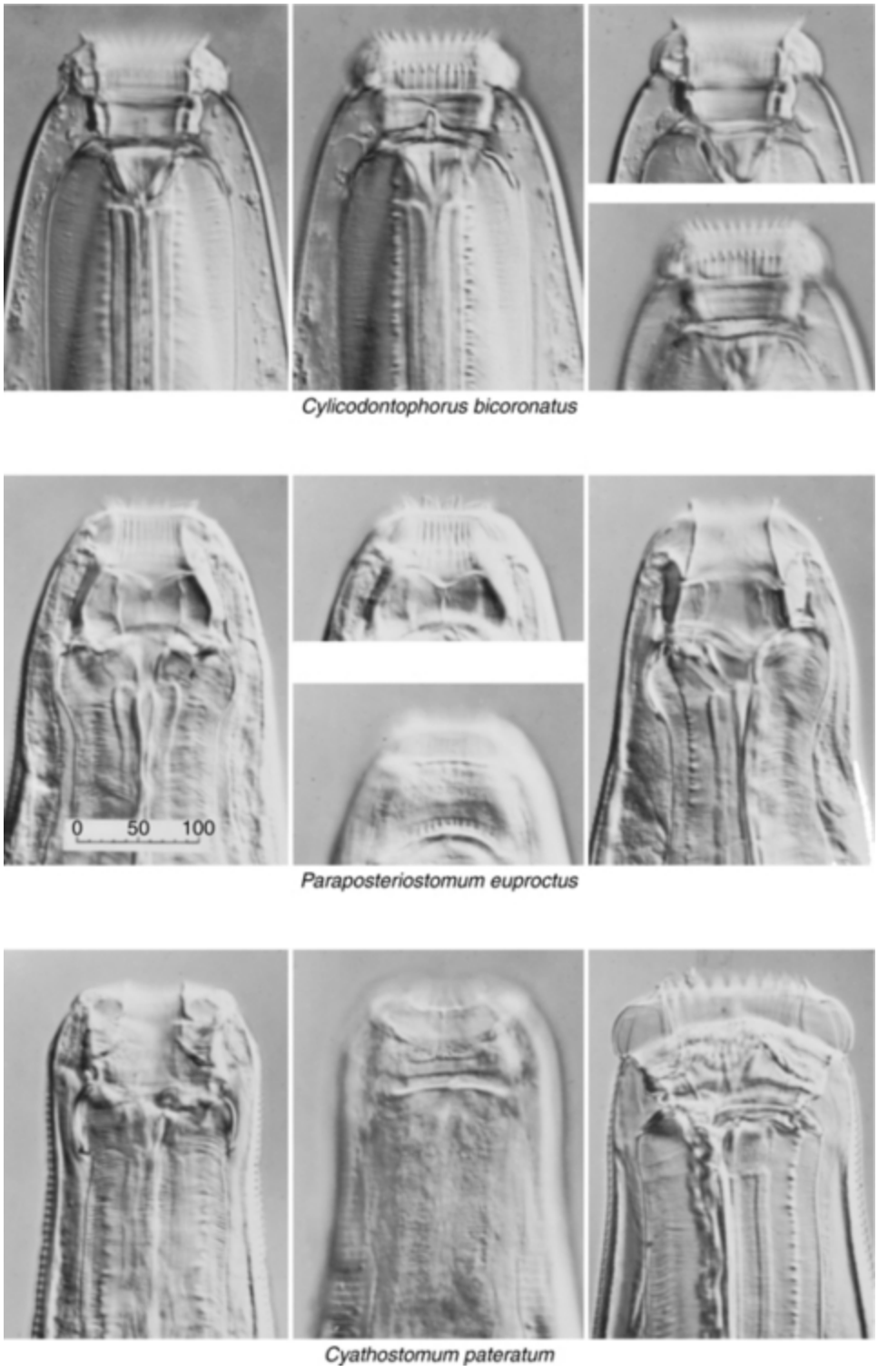

Figure 7-84 Members of the subfamily Cyathostominae. Dorsoventral *(left)*, dorsal surface *(center)*, and lateral *(right)* views of the heads of *Cylicodontophorus bicoronatus (top row)*, *Paraposteriostomum euproctus (middle row)*, and *Cyathostomum pateratum (bottom row)*. (All ×170.)

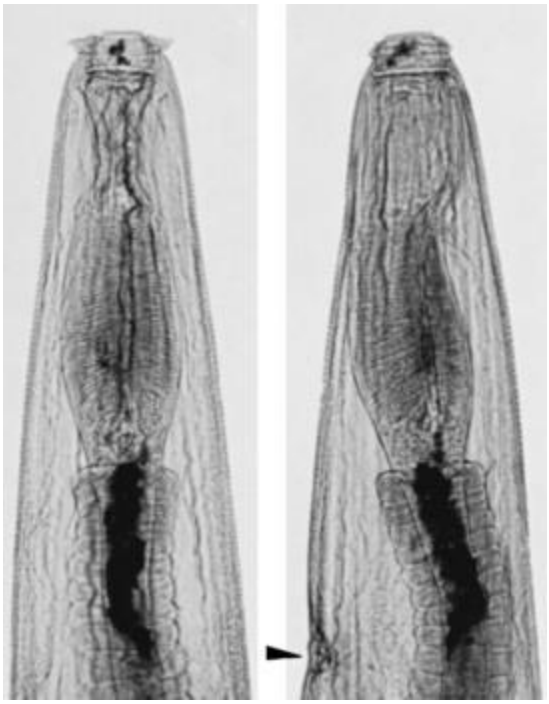

Figure 7-85 *Cylicocyclus auriculatus* (subfamily Cyathostominae) (×50). Note prominent lateral head papillae. Arrow indicates position of excretory pore.

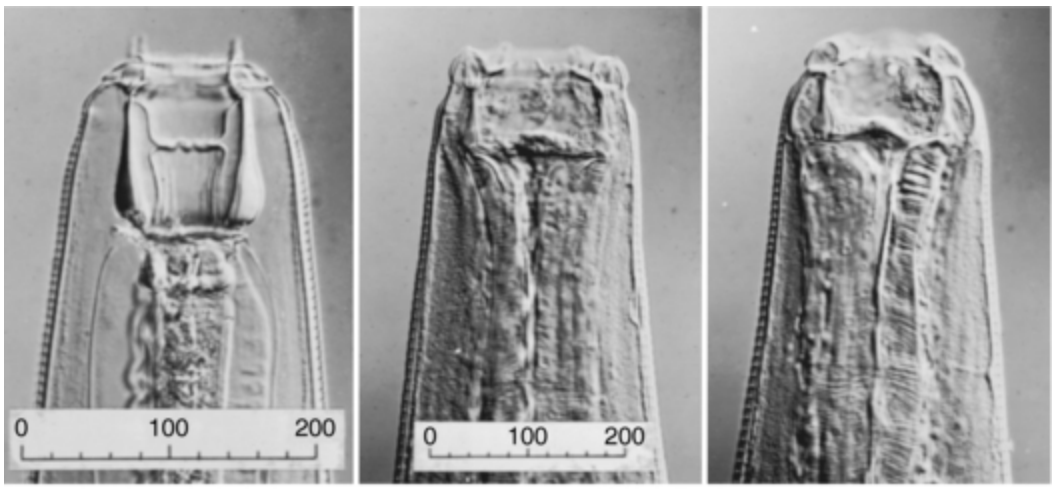

Figure 7-86 Members of the subfamily Cyathostominae.

Figure 7-87 *Cylicocyclus brevicapsulatus*, the only homely member of the subfamily Cyathostominae (×168).

Each series can be identified by careful study of the stomal region alone. With fresh specimens, detail sufficient for identification can be seen without recourse to clearing agents. Simply mount the specimen under a coverslip in a drop of water. With this simple preparation it is usually possible to roll the specimen so that both dorsal and lateral aspects may be studied. Even preserved specimens may be studied in this manner but tend to be considerably less transparent than fresh specimens. For comparisons to be made easily, illustrations of the species that bear the greatest resemblance to one another have been grouped together. The nomenclature of J. Ralph Lichtenfels's excellent monograph *Helminths of Domestic Equids* (*Proc Helminthol Soc Wash*,

42, 1975) along with an update on the taxonomy of the group (Lichtenfels et al, 1998) is the system that has been applied in the following pictorial key.

Cestode

A. perfoliata (Anoplocephalidae) (see Figures 4-52 and 7-70) is found mainly in the cecum; this tapeworm tends also to cluster in the ileum near the ileocecal valve, where it is associated with ulceration and chronic inflammation of the ileal wall.

Insect

G. haemorrhoidalis (Diptera: Gasterophilidae) larvae sometime attach briefly as they make their way out of the intestinal tract into the environment.

Liver

Nematode larvae

P. equorum (Ascaridoidea) passes through the liver on its way to the lung after the infective-stage eggs are ingested.

S. edentatus and *S. equinus* (see Figures 8-79 to 8-82Figure 8-79Figure 8-80Figure 8-81Figure 8-82) will wander through the liver for a period of time before patency.

Cestode larvae

E. granulosus (Taeniidae) (see Figures 4-44 to 4-46 and 8-64Figure 4-44Figure 4-45Figure 4-46Figure 8-64) hydatid cysts are very rare in

horses in most of the world and especially so in the United States.

Pancreas

Nematode

S. equinus (Strongylinae) (see Figure 8-82) larvae migrate sometimes into the pancreas before patency.

Peritoneum and peritoneal cavity

Nematodes

S. equina (150 mm; Filarioidea) (see Figures 4-143 and 7-73) adults live in the peritoneal cavity.

S. edentatus (44 mm; Strongylinae) (see Figures 8-78 to 8-81Figure 8-78Figure 8-79Figure 8-80Figure 8-81) larvae migrate.

Respiratory System

Paranasal sinuses

Insect larva

Rhinoestrus purpureus (Oestridae) is an exotic nasal bot.

Bronchi and bronchioles

Nematode

Dictyocaulus arnfieldi (65 mm; Trichostrongyloidea) (see Figures 4-143 and 7-73) is found in horses; donkeys are thought to help maintain the infection among equines.

Lung parenchyma

Nematode

S. edentatus (aberrant migration) (see Figures 8-78 and 8-80Figure 8-78Figure 8-80).

P. equorum (Ascaridoidea) has larvae that routinely make a liver-to-lung migration in the horse before returning to the intestinal tract. There is reason to believe that many of the larvae that do not develop to the adult stage in horses still make it to the lungs and cause eosinophil-associated pathology.

Vascular System

Arteries

Nematodes

S. vulgaris (Figures 7-88 and 7-89) larvae migrating through the walls of the mesenteric arteries produce remarkably severe lesions in the walls of these vessels.

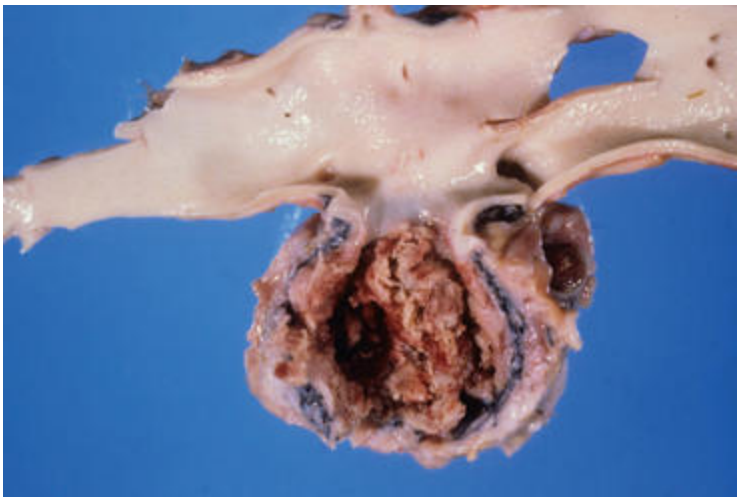

Figure 7-88 *Strongylus vulgaris* verminous arteritis and aneurysm in a pony aorta discovered during junior surgery.

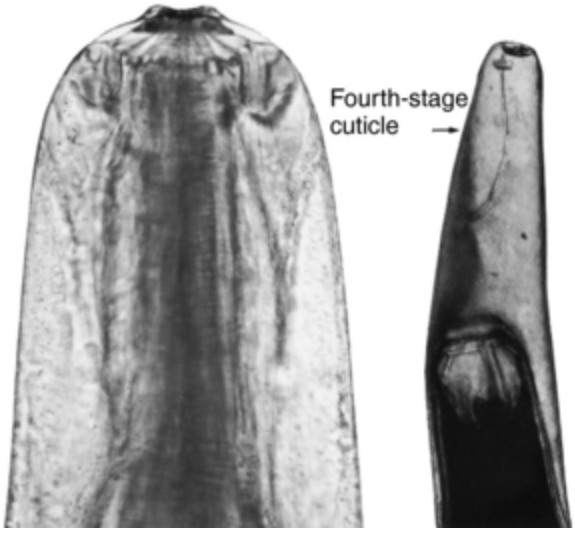

Figure 7-89 *Strongylus vulgaris* fourth stage (*left,* ×108) and immature fifth stage (*right,* ×38) from a mural thrombus of the cranial mesenteric artery of a horse.

E. böhmi (Filarioidea) (see Figure 7-73) is found in intimal nodules of the wall of the aorta and other vessels. It is exotic.

Blood

Nematode microfilaria

S. equina (Filarioidea) (see Figure 7-73).

Protozoan

Babesia caballi (piroplasm) (see Figure 3-29) could be seen in fixed red blood cells.

Skeletal Muscles and Connective Tissues

Nematodes

T. spiralis (Trichinelloidea) first-stage larvae has been found in Europe in horses fattened for human consumption.

O. cervicalis (Filarioidea) adults are found in nuchal ligament.

Protozoa

S. bertrami and *S. fayeri* (coccidians) (see Table 2-1 and Figures 8-32 and 8-33Figure 8-32Figure 8-33) occur as sarcocysts within muscle fibers.

Insect Larvae

H. bovis and *H. lineatum* (Diptera: Hypodermatidae) (see Figure 2-22) will on occasion migrate erratically into the subcutaneous dorsal tissues of horses.

Nematode microfilariae

O. cervicalis and *O. reticulata* (Filarioidea) (see Figures 8-111 and 8-112Figure 8-111Figure 8-112) microfilariae are found in the dermis.

Urogenital System

Kidneys

Nematode

Halicephalobus gingivalis (Rhabditida) can be found in various viscera of the horse as adult females and larvae, with one site of infection often being the kidney.

Protozoan

Klossiella equi (coccidian) (Figure 8-30).

Testes

Nematode

S. edentatus (Strongylinae) (see Figures 8-78 to 8-81Figure 8-78Figure 8-79Figure 8-80Figure 8-81) sometimes has immature adults in vaginal tunics.

Nervous System

Brain and spinal cord

Nematodes

S. vulgaris (Strongylinae) (see Figures 7-76 and 7-89) may have fourth-stage larvae or young adults migrating erratically; even one worm can cause fatal neurologic disease.

Setaria species (Filarioidea) (see Figures 4-32, 4-33Figure 4-32Figure 4-33, and 7-73) can undergo erratic migration with neurologic disease; this seems to happen most often in Asia.

H. gingivalis (Rhabditoidea) causes neurologic disease that can be fatal.

D. megastoma (Spirurida) (Mayhew et al, 1983).

Insects

H. bovis and *H. lineatum* (Diptera: Hypodermatidae) may have larvae undergoing erratic migration in the atypical equine host; one larva can cause fatal neurologic disease.

Protozoa

Equine protozoan myelitis (EPM) organism (Apicomplexa) *Sarcocystis neurona*.

Eye

Nematodes

Thelazia lacrymalis (Spirurida) (see Figure 4-132) is found in the conjunctival sac and lachrymal ducts.

D. megastoma and *Habronema* species (Spirurida) larvae may cause habronemic conjunctivitis.

Onchocerca species microfilariae (see Figure 7-73).

Skin and Hair

Insects

M. autumnalis and *S. calcitrans* (Diptera: Muscidae) (see Figures 2-13 and 2-14Figure 2-13Figure 2-14).

Hippobosca equina and *Lipoptena cervi* (Diptera: Hippoboscidae) (see Figure 2-17) are the keds of horses. *H. equina* tends to be rare in the United States; *L. cervi* of deer is common but fortunately only rarely gets on horses.

G. intestinalis, *G. nasalis*, and *G. haemorrhoidalis* (Diptera: Gasterophilidae) females will hover around horses while they lay their eggs glued to hairs.

Tabanus and *Chrysops* species (Diptera: Tabanidae) (see Figures 2-10 and 2-11Figure 2-10Figure 2-11) will attack in bright sun long

enough to inflict a painful bite.

Haematopinus asini (Anoplura).

Damalinia equi (Mallophaga: Ischnocera).

E. gallinacea (Siphonaptera) (see Figure 2-54).

Triatoma sanguisuga (Hemiptera: Triatominae) (see Figure 2-63).

Insect larvae

H. bovis and *H. lineatum* (Diptera) (see Figure 2-22) larvae are found in the subcutis of the saddle area.

Arachnids

Amblyomma, Anocentor, Boophilus, Dermacentor, Haemaphysalis, Hyalomma, Ixodes, and *Rhipicephalus* (Metastigmata: Ixodidae) (see Figures 2-74, 2-91Figure 2-74Figure 2-91).

S. scabiei (Sarcoptidae; Astigmata) (see Figures 2-100 and 2-102Figure 2-100Figure 2-102).

P. ovis and *C. bovis* (Psoroptidae; Astigmata) (see Figures 2-100, 2-101, and 2-107 to 2-110Figure 2-100Figure 2-101Figure 2-107Figure 2-108Figure 2-109Figure 2-110).

Trombiculidae (Prostigmata) (see Figures 2-118 to 2-120Figure 2-118Figure 2-119Figure 2-120).

Demodex equi (Prostigmata) (see Figure 2-115).

Nematode microfilariae and larvae

P. multipapillosa (Filarioidea) (see Figure 7-73) has microfilariae in serosanguineous discharge from ulcerated nodules.

O. cervicalis and *O. reticulata* (Filarioidea) (see Figures 7-71, 8-111, and 8-112Figure 8-111Figure 8-112) have microfilariae almost universally present in the dermis of horses, especially the dermis of the ventrum, if they have not been on routine avermectin therapy.

R. strongyloides (Rhabditida) (see Figure 4-107) can cause dermatitis in horses if they are down, as, for example, on straw for a day or two after surgery.

D. megastoma, *H. muscae*, and *H. microstoma* (Spirurida) have larvae that excite exuberant granulomatous reactions in skin wounds, areas of skin subject to frequent wetting, and ocular conjunctiva.

PARASITES OF SWINE

Stages in Feces

Intestinal protozoa include eight species of *Eimeria* and *Cystoisospora suis* (Figure 7-90), *Cryptosporidium suis, Entamoeba polecki*, *Iodamoeba buetschlii*, *Endolimax nana*, *Giardia* species, other flagellates, and the very common ciliate *B. coli* (see Figure 3-8). Other than the species of *Eimeria*, *Cystoisospora*, and *Cryptosporidium*, most of these parasites will not be seen in sugar flotations owing to distortion.

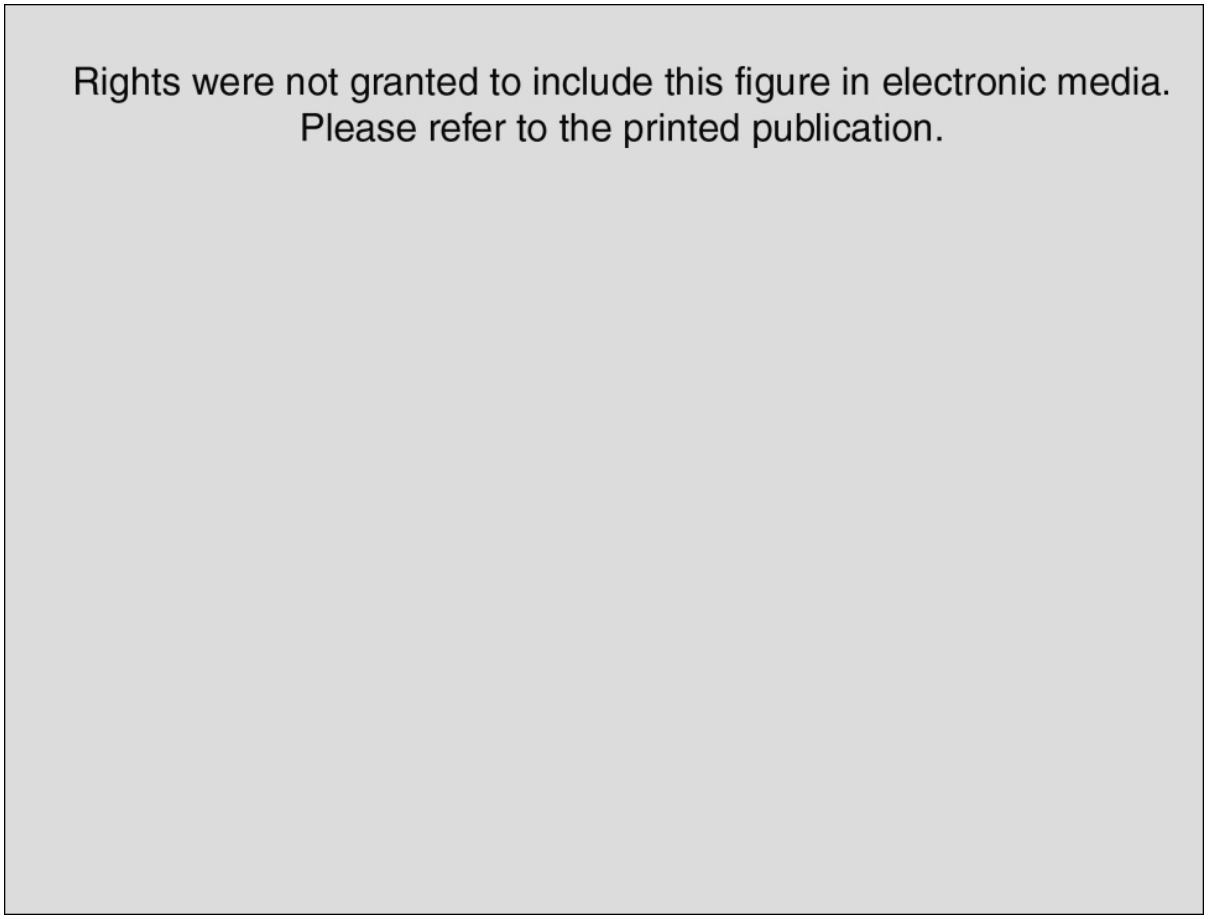

Figure 7-90 Sporulated oocysts of eight species of *Eimeria* and one species of *Cystoisospora* from swine.

From Vetterling JM: J Parasitol 51:909, 1965.

There are a number of common eggs found in pig feces that include nematodes and an acanthocephalan (Figure 7-91). The fertile eggs of the ascaridoid *A. suum* have a rough, bile-stained, external protein layer. Infertile *A. suum* eggs can be common and appear a little longer and thinner than the fertilized eggs; the middle wall of the shell tends to be thinner, and the central portion looks disorganized. The spirurids *Ascarops* and *Physocephalus* produce thick-walled, larvated eggs. *Strongyloides ransomi*

(Rhabditida) eggs resemble those of *S. papillosus* (Rhabditida) and are thin-shelled and larvated (see Figure 7-58). Strongyle eggs in pig feces may represent infection with *Hyostrongylus rubidus* (Trichostrongyloidea), *Oesophagostomum* species (Strongyloidea), or *Globocephalus urosubulatus* or *Necator americanus* (Ancylostomatoidea), but most commonly with only the first two. The Metastrongyloidea parasitic organism in swine is unusual compared with many in that it has an earthworm rather than a molluscan intermediate host, and unlike most metastrongyloids of domestic animals, *Metastrongylus apri*, *Metastrongylus salmi*, and *Metastrongylus pudendotectus* eggs are small and subglobular and contain a larva. *Trichuris suis* (Trichinelloidea) living in the mucosa of the cecum and colon are typical of the genus, are almost identical to the *Trichuris trichiura* of humans, and are smaller than the eggs of the dog whipworm, *T. vulpis*. *M. hirudinaceus* (Acanthocephala) eggs have three concentric, ellipsoidal shells surrounding the acanthor embryo.

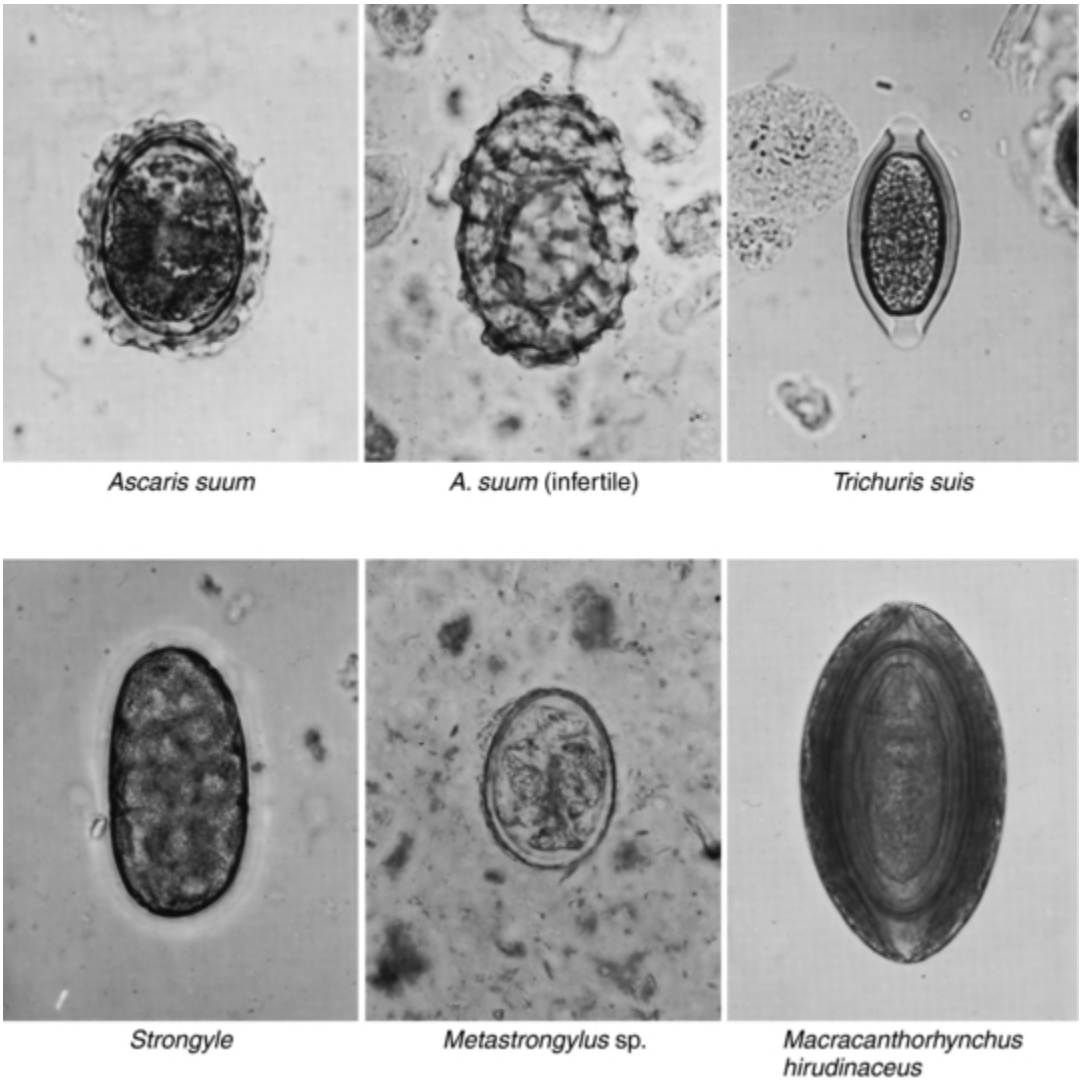

Figure 7-91 Eggs of some parasites of swine (×425).

Stages in Urine

The eggs of *S. dentatus* (Strongyloidea) are large and morulated and are found in urine specimens from infected swine. The last urine voided contains the highest concentration of eggs.

Examination for Trichinae

Squash Preparation

Moderate to heavy *T. spiralis* infections can be diagnosed by simply squashing bits of muscle tissue between two glass slides and scanning under low power. The diaphragm and masseter muscles are especially likely to yield positive findings.

1. Detach a small scrap of meat and place it on a microscope slide.

2. Cover with a second microscope slide, and press the two slides together with the thumb and forefinger, thus squashing the scrap of meat.

3. While maintaining pressure, bind the slides firmly together by wrapping each end with adhesive tape.

4. Trim off any meat protruding from between the slides to avoid contaminating the microscope stage.

5. Scan the entire field under low power. Larvae, if present, are easily visible (Figure 7-92). *Note:* This procedure is also applicable to the other tissue-dwelling parasites such as the smaller lungworms of sheep and carnivorans, encysted *Toxocara* larvae, and the like.

Tissue Digestion

Peptic digestion is used to detect light infection with *T. spiralis* and other nematodes in tissues. Gastric juice digests the muscle tissue but not the larvae of *T. spiralis*. Pepsin-acid solution consists of 0.2 g granular pepsin and 1.0 mL concentrated hydrochloric acid in 100 mL distilled water.

1. Weigh out 4 g of tissue and mince it with a scalpel.

2. Add 100 mL of pepsin-acid solution, and allow to stand for about 1 to 6 hours at 37° C.

3. Decant excess supernatant carefully, suspend sediment, and transfer to a Petri plate.

4. Count larvae under a dissecting microscope. Larvae may be retrieved with a Pasteur pipette for closer study under the compound microscope.

Annotated Host-Organ List of Parasites of Swine

Alimentary System

Mouth and esophagus

Nematodes

G. pulchrum (150 mm; Spirurida) (see Figures 4-133, 4-134Figure 4-133Figure 4-134, and 7-105).

Eucoleus (Capillaria) garfiai (Trichinelloidea) is found in the epithelia of the tongue of wild pigs.

Stomach

Nematodes

Physocephalus sexalatus (see Figure 4-135), *Ascarops strongylina, Gnathostoma hispidum* (see Figure 4-129), and *Simondsia paradoxa* (Spirurida).

H. rubidus (9 mm) and *O. tricuspis* (1 mm) (Trichostrongyloidea) (see Figures 4-78 and 4-79Figure 4-78Figure 4-79).

Aonchotheca (Capillaria) gastrosuis (Trichinelloidea) (see Figure 7-52).

Small intestine

Nematodes

A. suum (410 mm; Ascaridoidea) (Figure 7-93; see also Figures 4-114 to 4-116Figure 4-114Figure 4-115Figure 4-116 and 7-52).

Figure 7-93 Lesions induced in the liver of a pig exposed to the infective eggs of *Ascaris suum (right);* normal liver on left.

G. urosubulatus (6 mm; Ancylostomatoidea) (see Figure 4-94).

S. ransomi (5 mm; Rhabditida) (see Figures 4-108 and 4-109Figure 4-108Figure 4-109).

T. spiralis (4 mm; Trichinelloidea) (see Figures 4-148 to 4-150Figure 4-148Figure 4-149Figure 4-150, and 7-92).

Acanthocephala

M. hirudinaceus (470 mm) (see Figure 4-155).

Protozoa

Eimeria debliecki and about 10 other species of *Eimeria* (coccidians); usually infection is without clinical signs.

Cystoisospora suis (coccidian) causes enteritis in the small intestine of young animals.

Cryptosporidium suis (Apicomplexa)

Giardia species (mucosoflagellate) (Figure 7-94; see also Figure 3-6); infection is usually without signs.

Cecum and colon

Nematodes

Oesophagostomum dentatum, Oesophagostomum brevicaudum, Oesophagostomum georgianum, and *Oesophagostomum quadrispinulatum* (Strongyloidea) (see Figures 4-86 and 4-87Figure 4-86Figure 4-87).

T. suis (Trichinelloidea) (see Figures 4-151 to 4-153Figure 4-151Figure 4-152Figure 4-153, and 7-91).

Protozoans

E. polecki, E. nana, I. buetschlii, and others (amebas) are considered for the most part to be commensals.

Chilomastix mesnili, Tetratrichomonas buttreyi, Trichomitus rotunda, and *Tritrichomonas suis* (mucosoflagellates) are considered for the most part to be commensals.

B. coli (ciliate) (see Figure 3-8) is a commensal organism that can on occasion cause colitis.

Liver, pancreas, and peritoneal cavity

Nematode larvae

A. suum (Ascaridoidea) (see Figure 4-116) has migrating larvae that cause "milk spot" lesions on the liver surface.

S. dentatus (Strongyloidea) migrating larvae in liver and pancreas (see Figure 4-91).

Trematodes

F. hepatica and *F. gigantica* (Fasciolidae) (see Figures 4-2 and 4-11Figure 4-2Figure 4-11).

Cestode larvae

E. granulosus (Taeniidae) (see Figures 4-44 to 4-46 and 8-64Figure 4-44Figure 4-45Figure 4-46Figure 8-64) hydatids are very rare in the United States.

T. hydatigena (Taeniidae) (see Figure 4-48) cysticerci can be found on rare occasions, mainly in wild pigs.

Respiratory System

Bronchi and bronchioles

Nematodes

M. apri, *M. salmi*, and *M. pudendotectus* (Metastrongyloidea) (see Figure 4-99) can cause signs of respiratory distress in pigs.

Lung parenchyma

Nematode larva

A. suum (Ascaridoidea) (see Figure 4-116) organisms migrate through after the liver and cause disease in reaction to their passage.

Cestode larva

E. granulosus (Taeniidae) (see Figures 4-44 to 4-46 and 8-64Figure 4-44Figure 4-45Figure 4-46Figure 8-64) hydatids in pigs in the United States seem to be very rare.

Trematode

Paragonimus kellicotti (Troglotrematidae) (see Figures 4-14, 4-15Figure 4-14Figure 4-15, and 7-36, *B*) would be an excellent parasite of wild pigs and is liable to do very well in pigs fed crayfish.

Skeletal Muscles and Connective Tissues

Nematode larva

T. spiralis (Trichinelloidea) (see Figures 7-92 and 8-116) larvae can be present in very large numbers per gram of pig muscle without the pig showing signs of disease.

Cestode larvae

Taenia solium (Taeniidae) (see Figure 8-60) cysticerci in muscle are a potential problem in areas where humans who might be infected with adults, especially those from certain developing countries, are working around pigs as animal handlers; cysts cause carcass condemnations.

S. mansonoides (Diphyllobothriidae) (see Figures 4-31 and 8-68Figure 4-31Figure 8-68) spargana can occur in pigs, which serve as paratenic hosts.

Trematode larvae

Alaria (mesocercariae, Diplostomatidae).

Protozoa

S. miescheriana, *S. porcifelis*, and *Sarcocystis suihominis* (coccidians) (see Table 2-1 and Figures 8-32 and 8-33Figure 8-32Figure 8-33) sarcocysts occur in the muscles of pigs.

Urogenital System

Nematode

S. dentatus (45 mm; Strongylida) (see Figure 4-91). Stout, white worms occur in the kidneys, ureters, urinary bladder, perirenal fat, pork chops, spinal canal, and elsewhere as a result of erratic migrations.

Skin and Hair

Insects

Musca and *Stomoxys* (Diptera) (see Figures 2-13 and 2-14Figure 2-13Figure 2-14).

Haematopinus suis (Anoplura) (see Figure 2-37).

P. irritans, *E. gallinacea*, and *Tunga penetrans* (Siphonaptera) (see Figures 12-54, 2-56, and 2-62Figure 12-54 Figure 2-56 Figure 2-62).

Arachnids

Metastigmata (ticks) (see Figures 2-74 and 2-91Figure 2-74Figure 2-91).

S. scabiei (Astigmata) (see Figures 2-100 and 2-102Figure 2-100Figure 2-102) continues to be a problem in pigs.

Demodex phylloides (Prostigmata) (see Figure 2-115) causes pimples on pigs full of huge numbers of mites.

PARASITES OF LABORATORY RABBITS AND RODENTS

Many parasites lose all opportunity to complete their life histories the day their host becomes a member of a laboratory animal colony. Although they may limit the usefulness of their immediate hosts as experimental subjects, such parasites present no continuing problem of control. Heartworm infection, for example, renders a dog unfit for experiments involving the circulatory or respiratory system but, in the absence of mosquitoes, must remain confined to the host in which it arrived. On the other hand, a surprising variety of arthropod, protozoan, and helminth parasites do succeed in maintaining impressive populations even in reasonably hygienic

laboratory animal colonies. Hair-clasping mites, mucosoflagellates, coccidians, *Hymenolepis* tapeworms, and pinworms are particularly common. The following incomplete outline includes only the common parasites of laboratory rabbits, rats, mice, guinea pigs, monkeys, and apes.

A few of the more common parasites of rodents and rabbits are represented in Figure 7-94.

Annotated Host-Organ Listing of Common Parasites of Rabbits

Alimentary System

Stomach

Nematodes

Obeliscoides cuniculi and *Graphidium strigosum* (18 to 20 mm; Trichostrongyloidea) (Figure 7-95). Spicules of *O. cuniculi* are 0.54 mm; of *G. strigosum*, 2.4 mm.

Figure 7-95 *Obeliscoides cuniculi*, stomal end *(left)* and bursa and spicules of male *(right)* (×120).

Intestine

Nematodes

Trichostrongylus retortaeformis and *Nematodirus leporis* (Trichostrongyloidea) (see Figures 4-70 and 4-72Figure 4-70Figure 4-72).

S. papillosus (6 mm; Rhabditida).

Passalurus ambiguus (11 mm; Oxyurida) (see Figure 4-110).

Trichuris leporis (Trichinelloidea).

Cestode

Cittotaenia ctenoides (Anoplocephalidae) (see Figure 7-94).

Protozoa

Eimeria species (coccidian) (see Figure 7-94). Ten species of *Eimeria* parasitize the intestinal epithelium and cause diarrhea and emaciation.

Entamoeba cuniculi (ameba). Nonpathogenic.

Liver and peritoneal cavity

Protozoa

Eimeria stiedae (Coccidia) causes biliary coccidiosis (see Figure 8-28).

Cestode larvae

T. pisiformis (Taeniidae) (Figure 7-96) cysticerci initially migrate through the liver but ultimately settle down to mature in the peritoneal cavity.

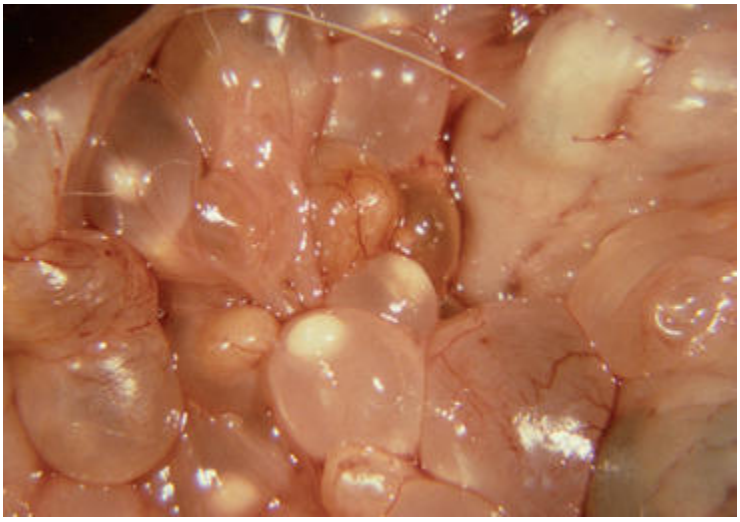

Figure 7-96 Cysticerci of *Taenia pisiformis* in the abdominal cavity of an experimentally infected domestic rabbit.

Skin and Hair

Arachnids

Psoroptes cuniculi (Astigmata) (Figure 7-97; see also Figures 2-100, 2-107, and 2-108Figure 2-100Figure 2-107Figure 2-108) can cause severe ear canker in rabbits.

Figure 7-97 Ear of a rabbit infested with *Psoroptes cuniculi*.

Sarcoptes and *Chorioptes* (Astigmata) (see Figures 2-100, 2-101, 2-102, and 2-109Figure 2-100Figure 2-101Figure 2-102Figure 2-109).

Leporacarus gibbus (Listrophoridae) (Figure 7-98).

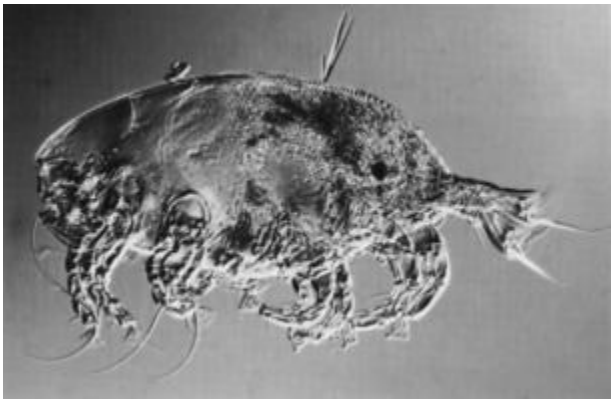

Figure 7-98 *Leporacarus gibbus*, a hair-clasping mite of rabbits (×100).

Courtesy Dr. Stephen Weisbroth.

Cheyletiella parasitovorax (Prostigmata) (see Figure 2-116).

Annotated Host-Organ Listing of Common Parasites of Rats

Alimentary System

Stomach and intestines

Nematodes

Nippostrongylus brasiliensis (6 mm; Trichostrongyloidea) (Figure 7-99).

Figure 7-99 *Nippostrongylus brasiliensis*. **A,** Bursa and spicules of male (×125). **B,** Caudal end of female (×150). **C,** Esophageal region (×150).

Strongyloides ratti (Rhabditida) (see Figure 4-109).

Gongylonema neoplasticum (Spirurida) (see Figure 7-105).

Syphacia muris and *Aspiculuris ratti* (Oxyurida).

Heterakis spumosa (16 mm; Ascaridida).

T. spiralis (Trichinelloidea) (see Figure 4-148).

Trichuris muris (Trichinelloidea).

Cestode

Hymenolepis diminuta (Hymenolepididae) (see Figure 7-94). Scolex without hooks.

Protozoans

Eimeria nieschultzi and other species (coccidians) (see Figure 7-94).

Giardia (mucosoflagellate) (see Figure 7-94).

Liver

Nematode

Calodium (*Capillaria*) *hepaticum* (Trichinelloidea) (see Figure 8-117).

Cestode larvae

T. taeniaeformis (Taeniidae) (see Figure 8-61).

Protozoa

Hepatozoon muris (plasmodium) has schizogony occurring in the hepatic cells; gamonts are found in the monocytes of the circulating blood. The vector is a mesostigmatid mite, *Echinolaelaps echidninus*.

Urogenital System

Nematodes

Trichosomoides crassicauda (Trichinelloidea) (see Figures 3-142 and 8-120Figure 3-142Figure 8-120) lives threaded through the bladder epithelium; the male lives in the reproductive system of the female worm.

Skin and Hair

Insects

Polyplax spinulosa (Anoplura) (Figure 7-101).

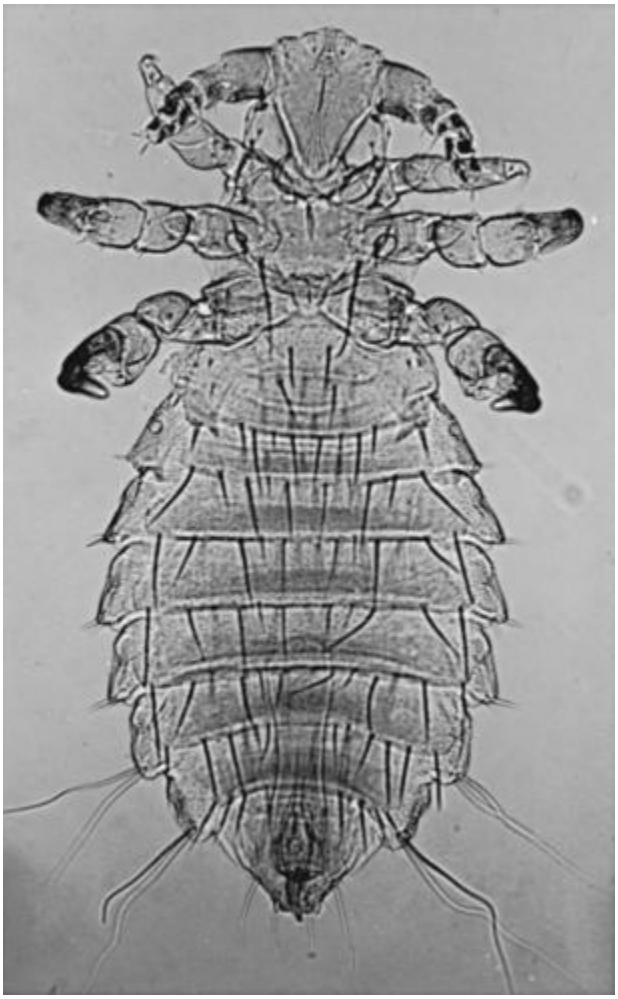

Figure 7-101 *Polyplax spinulosa* male (×108).

Xenopsylla cheopis (Siphonaptera) (see Figure 2-55).

Arachnids

Ornithonyssus bacoti (Mesostigmata).

Radfordia ensifera (Prostigmata).

Notoedres muris (Astigmata) (see Figures 2-103 and 2-104Figure 2-103Figure 2-104).

Annotated Host-Organ Listing of Common Parasites of Mice

Alimentary System

Stomach and intestines

Protozoa

Cryptosporidium muris (stomach) and *C. parvum* (small intestine) (see Figures 3-17, *C. andersoni;* 3-18, *C. parvum*Figure 3-17Figure 3-18).

Nematodes

Heligmosomoides polygyrus (syn. *Nematospiroides dubius;* Trichostrongyloidea) organisms are reddish and tightly coiled.

N. brasiliensis (6 mm; Trichostrongyloidea) (see Figure 7-99).

Syphacia obvelata and *Aspiculuris tetraptera* (Oxyuroidea) (see Figure 7-100).

Figure 7-100 Pinworms of mice: *Syphacia obvelata* male *(left)* and *Aspiculuris tetraptera* anterior end *(right)* (×80).

H. spumosa (Ascaridida).

T. muris (Trichinelloidea).

Cestodes

Hymenolepis nana and *H. diminuta* (Hymenolepididae) (see Figure 7-94). The scolex of *H. nana* is armed with hooks; that of *H. diminuta* is unarmed.

Urogenital System

Kidneys

Protozoa

Klossiella muris (coccidian) usually seen on histosections.

Skin and hair

Insects

Polyplax serrata (Anoplura) (see Figure 2-41).

Arachnids

Myobia musculi and *Radfordia affinis* (Prostigmata) (see Figure 2-117). Myobiids do not migrate away from a dead host; the carcass must be scanned carefully with a stereoscopic microscope to find them.

Myocoptes musculinus (Astigmata) (see Figure 2-113).

O. bacoti and *Allodermanyssus sanguineus* (Mesostigmata) (see Figure 2-92, *Ornithonyssus sylviarum)*.

Annotated Host-Organ Listing of Common Parasites of Guinea Pigs

Alimentary System

Nematode

Paraspidodera uncinata (Oxyurida).

Cestode

H. nana (see Figure 7-94).

Protozoa

Eimeria caviae (coccidian).

Balantidium species (ciliate) (Figure 7-102, and see Figure 3-8).

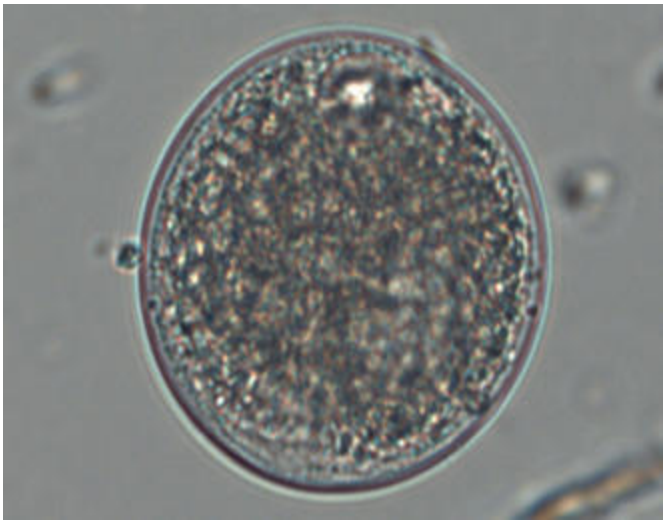

Figure 7-102 *Balantidium coli* cyst in the feces of a guinea pig.

Cryptosporidium wrairi (see 3-18, *C. parvum*).

Skin and Hair

Insects

Gliricola porcelli, *Gyropus ovalis*, and *Trimenopon hispidum* (Mallophaga) (Figure 7-103, and see Figure 2-50).

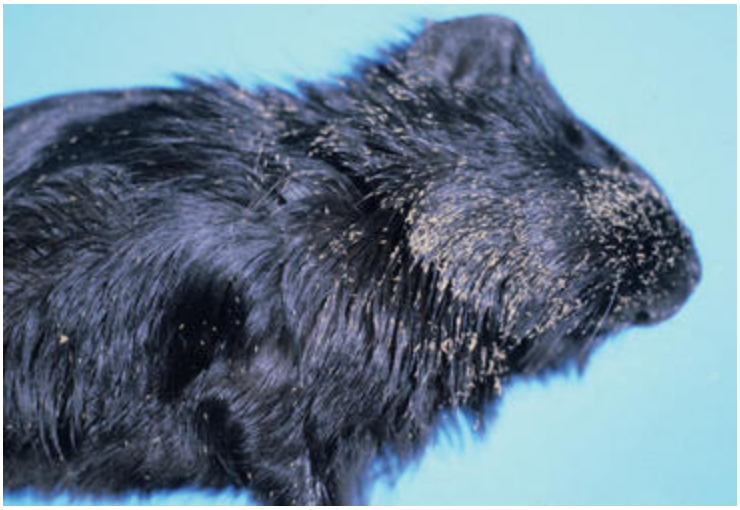

Figure 7-103 Guinea pig infested with the louse *Gliricola porcelli*.

Arachnids

Chirodiscoides caviae (Astigmata) (see Figure 2-112).

Trixacarus caviae (Astigmata) can cause severe mange in guinea pigs that can be fatal.

PARASITES OF MONKEYS AND APES

The kinds of parasites to be found depend on the species and geographic origin of the monkey and on the duration and environmental conditions of its captivity. Certain parasites (e.g., *Strongyloides* and *Oesophagostomum*) flourish in captive monkeys. Others, especially those whose natural intermediate hosts are no longer available, tend to fade away. In mixed colonies, parasites that are not discriminating in their selection of hosts may spread to species of monkeys that, for geographic or ecologic reasons, rarely or never infect in the wild. Such cross-infections are more likely to cause disease because of the lack of mutual adaptation of host and parasite. The following therefore represents a composite listing of the more common parasites of monkeys and apes without particular regard to natural host species' preferences or geographic origins.

Stages in Feces

Some eggs of primate parasites are shown in Figure 7-105. Many of the parasites are shared with humans, and a text such as *Atlas of Human Parasitology* (Ash and Orihel, 1990) can be consulted for the identification of the many shared parasites.

Alimentary System

Nematodes

Cephalobus parasiticus (Rhabditida). These harmless parasites of the stomach and intestines of *Macaca iris mordax* (and probably others) resemble the free-living generation of *Strongyloides*. Their rhabditiform larvae may be confused with those of *Strongyloides* on fecal examination. They do not, however, develop into filariform larvae, so the dilemma may be resolved by culturing the fecal specimen.

Strongyloides fuelleborni and *S. stercoralis* (Rhabditida) (see Figure 4-109). Simian strongyloidosis is a human health hazard.

Nochtia nochti (Trichostrongyloidea). Bright red worms lie within or protrude from gastric papillomata in the prepyloric region of the stomach. Cross-sections of *N. nochti* in histologic preparations display 16 distinct longitudinal cuticular ridges and channeled lateral alae.

Trichostrongylus, Molineus and *Nematodirus* (Trichostrongyloidea) (see Figure 4-72).

Oesophagostomum (*Conoweberia*) *apiostomum*, *Oesophagostomum stephanostomum*, and *Ternidens deminutus* (Strongyloidea) (see Figures 4-63 and 7-105). Stout-bodied “nodular worms” with leaf crowns and transverse ventral cervical groove.

Necator, *Ancylostoma*, and *Globocephalus* (Ancylostomatoidea) (see Figures 4-94 and 4-95Figure 4-94Figure 4-95).

Ascaris lumbricoides (Ascaridoidea) (Figure 4-114).

Trichuris species (Trichinelloidea) (4-151).

Enterobius species (Oxyurida) (see Figure 7-105). Pinworms are quite host-specific. Generally speaking, a species of pinworm infects a genus of monkeys. *Enterobius vermicularis* and *Enterobius anthropopitheci* occur in chimpanzees. *Enterobius* species are usually considered nonpathogenic, but sometimes they invade the wall of the intestine and produce serious or even fatal disease.

Streptopharagus, *Gongylonema*, *Protospirura,* *Physocephalus*, and *Rictularia*, *Physaloptera* (Spirurida) (see Figures 4-130, 4-131, 4-133, 4-134Figure 4-130Figure 4-131Figure 4-133Figure 4-134, and 7-105). *Protospirura muricola*, a parasite of rodents that uses the cockroach *Leucophaea maderae* as intermediate host, has been observed to cause perforation of the stomach in captive monkeys (Foster and Johnson, 1939).

Cestodes

Bertiella studeri (Anoplocephalidae) is large and has four suckers and no hooks.

H. nana (Hymenolepididae) (see Figure 7-94) is very small, has four suckers, and has hooks.

Acanthocephalans

Prosthenorchis and *Moniliformis* (see Figure 7-95).

Trematode

Gastrodiscoides hominis (Paramphistomatidae).

Protozoans

B. coli (ciliate) (see Figure 3-8) causes acute enteritis (Teare and Loomis, 1982).

E. histolytica (ameba) is pathogenic as in humans.

Giardia lamblia (flagellate) (see Figure 7-94).

Liver and Pancreas

Protozoans

Hepatocystis kochi schizonts.

E. histolytica (ameba) can cause hepatic abscess.

Nematodes

Calodium (Capillaria) hepaticum (Trichinelloidea) (see Figure 8-117) occurs with worms and eggs in hepatic parenchyma.

Trichospirura leptostoma (Spirurida) is a 10- to 20-mm worm with a long capillary pharynx; associated with varying degrees of fibrosing pancreatitis. Found in pancreatic duct of American primates.

Respiratory System

Nose and throat

Nematode

Anatrichosoma (Trichinelloidea) (see Figures 8-118 and 8-119Figure 8-118Figure 8-119).

Annelids

The leeches that attack the pharyngeal mucosa of monkeys are large, black annelids with a large cup-shaped caudal sucker. The presence of this bloodsucking parasite is suggested by chronic epistaxis in a recently captured monkey. When the host drinks infested water, the young leeches enter the mouth, nose, pharynx, or larynx and attach to the mucous membrane. They remain in these locations for several weeks unless removed.

Arachnid

Rhinophaga species.

Lungs

Nematodes

Filaroides (Metastrongyloidea).

Metathelazia (Spirurida).

Cestode larva

E. granulosus (Taeniidae) (see Figures 4-44 to 4-46 and 8-64Figure 4-44Figure 4-45Figure 4-46Figure 8-64).

Arachnid

Pneumonyssus simicola (Mesostigmata) (Figure 8-8).

Serous cavities

Nematode

Dipetalonema species (Filarioidea) (see Figure 4-145).

Cestode larvae

T. hydatigena (cysticercus) (see Figure 4-48).

Mesocestoides (tetrathyridium) (see Figures 8-65 to 8-67Figure 8-65Figure 8-66Figure 8-67).

S. mansonoides (plerocercoid) (see Figures 4-31 and 8-68Figure 4-31Figure 8-68).

Pentastomid nymphs

Porocephalus, Armillifer, and *Linguatula.*

Acanthocephalans

Prosthenorchis species.

Blood

Nematode microfilariae

Dirofilaria, *Dipetalonema*, *Tetrapetalonema*, *Loa*, and *Brugia* (Filarioidea). Differentiation of the many kinds of microfilariae found in monkeys from all parts of the tropics is a task for the specialist. Many species remain to be described.

Protozoans

Simian malaria organisms, *Plasmodium* and *Hepatocystis*.

Muscles and Connective Tissues

Nematodes

Onchocerca, *Dirofilaria*, *Dipetalonema*, *Tetrapetalonema*, *Loa*, and *Brugia* (Filarioidea) (see Figures 4-137 and 4-145Figure 4-137Figure 4-145). *Onchocerca* microfilariae are found in the dermis.

Cestode larvae

Taenia (cysticercus).

Mesocestoides (tetrathyridium) (see Figures 8-65 to 8-67Figure 8-65Figure 8-66Figure 8-67).

Spirometra (plerocercoid) (see Figures 4-31 and 8-68Figure 4-31Figure 8-68).

Skin and Hair

Insects

Pedicinus and *Pthirus* (Anoplura) (see Figure 2-43).

Nematodes

Anatrichosoma cutaneum (Trichinelloidea). Very slender (25 by 0.2 mm) worms give rise to subcutaneous nodules, edema about the joints, and elongated, serpiginous blisters of the palms and soles. Adult females burrow in the epidermis of the palms and soles.

Onchocerca microfilariae.

Dracunculus (Spirurida) (see Figures 4-127 and 4-128Figure 4-127Figure 4-128).

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CHAPTER 8

Histopathologic Diagnosis

Mark L. Eberhard

The microscopic identification of parasites in tissue sections is an interesting challenge. Often a diagnostician is provided with a single slide that shows only pieces of the parasite. In an attempt to identify an object believed to be a parasite, one should gather as much information about the patient as possible, including life history and clinical signs. It is also important to be familiar with the kind of parasites most likely to be found in the particular host and tissue under study, as well as in the specific geographic area. The host-organ listing of parasites in the preceding chapter should be considered as a checklist of possibilities. The main objective of this section is to emphasize some of the major microscopic anatomic features of parasites that can be helpful in their identification in histologic sections. For the arthropods and metazoan parasites, several defining characteristics can be listed for each group of parasites, but the presence or absence of a body cavity and digestive tract, and the type and distribution of muscle fibers are important criteria to be considered in making an initial placement into a major group.

For further reading and assistance with diagnosis of parasites in tissues, the following sources are helpful. A report dealing with the present subject is “Identification of Parasitic Metazoa in Tissue

Sections" by MayBelle Chitwood and J. Ralph Lichtenfels, first published in *Experimental Parasitology*, volume 32, pages 407 to 519, 1972, and later reprinted as a monograph by the U.S. Department of Agriculture. Texts dealing with the subject include *Pathology of Tropical and Extraordinary Diseases*, volumes 1 and 2, edited by C.H. Binford and D.H. Connor, Washington, DC, 1976, Armed Forces Institute of Pathology (AFIP); *Pathology of Infectious Diseases*, volumes 1 and 2, by D.H. Connor, F.W. Chandler, D.A. Schwartz, H.J. Manz, and E.E. Lack, Stamford, Connecticut, 1997, Appleton & Lange; *An Atlas of Protozoan Parasites in Animal Tissues*, by C.H. Gardiner, R. Fayer, and J.P. Dubey, USDA Agriculture Handbook No. 651, U.S. Government Printing Office, Washington, DC, 1988 and edition 2, published by AFIP, American Registry of Pathology, Washington, DC; *Diagnostic Pathology of Parasitic Infections with Clinical Correlations*, edition 2, by Y. Gutierrez, Philadelphia, 1990, Lea & Febiger; *Parasites in Human Tissues* by T.C. Orihel and L.R. Ash, Chicago, 1995, American Society of Clinical Pathology (ASCP) Press; *Parasitic Diseases,* by J. Toft and M.L. Eberhard, in *Nonhuman Primates in Biomedical Research: Diseases,* edited by B.T. Taylor, C.R. Abee, and R. Henrickson, San Diego, 1998, Academic; and *Pathology of Infectious Diseases,* volume 1, *Helminthiases,* by W.M. Meyers, R.C. Neafie, A.M. Marty, and D.J. Wear, AFIP, 2000, American Registry of Pathology, Washington, DC.

ARTHROPODS

Arthropods, composed of hundreds of thousands of species, have such diverse features that attempting to describe them succinctly is nearly impossible. Arthropods do have some shared features—e.g.,

they have a segmented body, chitinous exoskeleton, coelom, and jointed appendages. The chitinous exoskeleton, the cuticle, in histologic sections usually appears thick and dark, but usually the exoskeleton itself does not take up stain. Over some parts of the body, especially in areas between segments or joints in an appendage, the cuticle can be very thin. The striated muscle of arthropods is diagnostic for this group of pathogens if they can be found in the sections. The larger arthropods also have a respiratory system that is composed of a racemose tracheal system that in section appears as variously sized tubes coursing throughout the body. The larger of the tracheal branches have chitinous reinforcing rings. Arthropods also can contain fat bodies that often appear darkly stained in sections. Smaller parasitic arthropods often have rounded to elongate bodies that are apparent in tissue sections, and sometimes one is fortunate enough to observe sections through paired, jointed legs. All together these features are fairly complete in defining an arthropod in section.

There are three major groups of arthropods that are likely to appear in histologic section. The insects (subphylum Mandibulata, class Insecta) contain the maggots of various myiasis-producing flies, and these commonly appear in histologic sections. The mites are in the class Arachnida of the subphylum Chelicerata, and these creatures because of their small size and ability to colonize various mainly superficial body surfaces, e.g., skin and respiratory mucosae, also appear in sections of lesions. Ticks tend to remain superficial to the host, attaching only long enough to feed, so typically, unless there is a strange clinical presentation or an interested researcher, they do not appear in histologic sections. The Pentastomids are a

group of parasitic crustaceans that have larval stages that parasitize vertebrates.

Maggots

Maggots in tissue are the larvae of dipteran flies and may represent species that require a living host or species, causing secondary myiasis such as caused by various *Calliphora* and *Sarcophaga*. Both types of maggots will display similar features, and the difficult part is making a generic diagnosis based strictly on morphology. The spiracular plate is important in identification of fly larvae and may need to be retrieved from the wet tissues or paraffin block (see Figure 2-22).

Sections of maggots will display the typical features of an arthropod, i.e., body cavity (Figure 8-1), segmentation, striated muscles attached at various points to the chitinous exoskeleton, and tracheae, often with cuticular rings (Figure 8-2). Some species have prominent spines (see Figure 8-2). *Cuterebra* larvae are obligate endoparasites of rodents and lagomorphs, and these larvae may invade dogs, cats, and occasionally humans. Typically, they are found in the cervical subcutaneous tissues, but in dogs and cats they migrate into the central nervous system with disastrous results (see Figures 8-1 and 8-2). First-stage *Hypoderma* larvae migrate extensively in cattle, and erratic migration through the brain of horses has been reported.

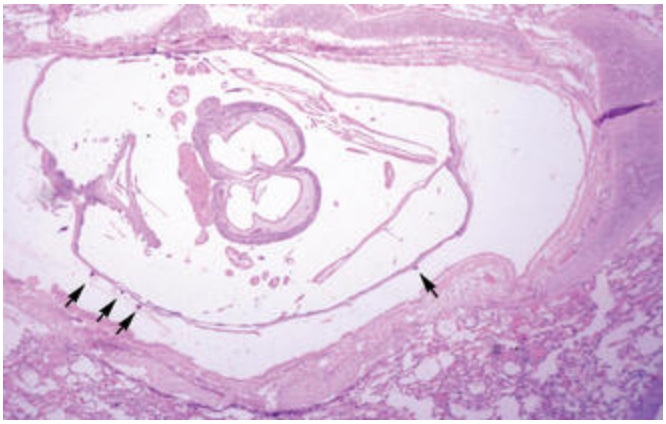

FIGURE 8-1 *Cuterebra* in the lung of a rabbit (×5). The internal organs lie in a body cavity rather than in a parenchymatous matrix; arrows indicate spines on the cuticle.

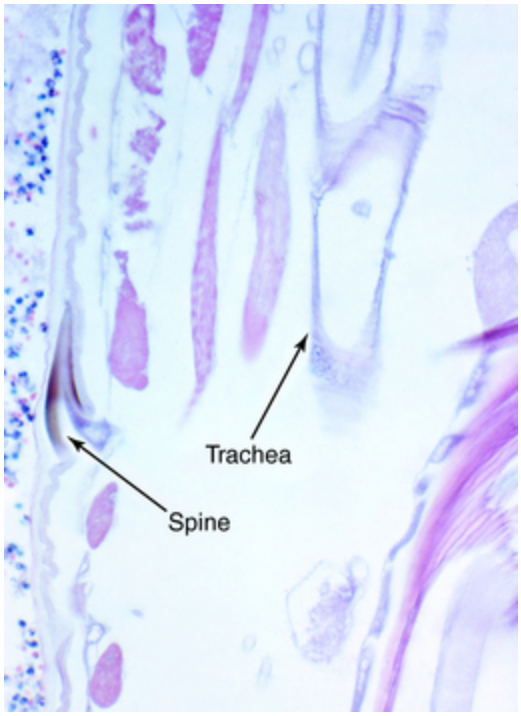

FIGURE 8-2 *Cuterebra* larva (bot) in the brain of a cat (×220).

Mites

Mites tend to be rather small, millimeters or less in size. With many of the species, eggs, larvae (six legs) nymphs (eight legs), and adults (eight legs) are all found in section, and in a section of an adult can

be found all the component parts of a typical arthropod—i.e., segmented legs, spines, and hairs externally, and striated muscles, reproductive organs, intestine, yolk glands, and developing eggs internally, may be seen in section. The mites that live in the skin, *Sarcoptes*, *Notoedres*, *Knemidocoptes*, and *Trixacarus*, are very small and round in appearance, feed at the stratum germinativum and dermis (Figure 8-3), and have spines on their dorsum (Figure 8-4). In some hosts such as the red fox, *Vulpes vulpes*, and pigs, sarcoptic mange is characterized by extraordinary hyperkeratosis (see Figure 8-4), and similar hyperkeratosis occurs in cats with *Notoedres* infections (Figure 8-5). Hyperkeratosis is also typical of mange caused by *Chorioptes* and *Cheyletiella* in certain hosts, but the mites lie more superficially in the stratum corneum.

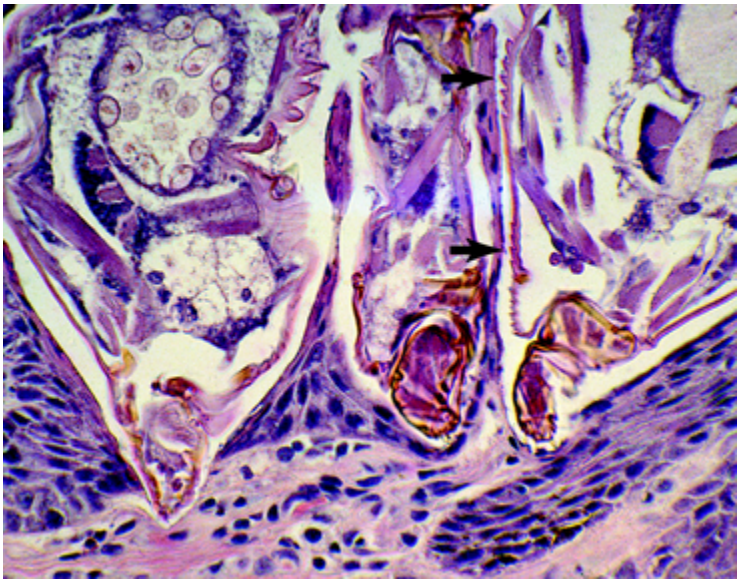

FIGURE 8-3 *Sarcoptes* mites in the skin of a dog (×230); arrows indicate spines on the cuticle.

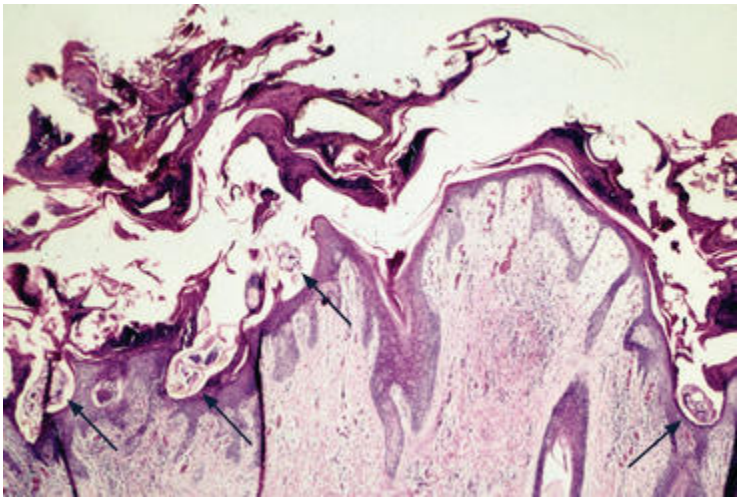

FIGURE 8-4 Hyperkeratosis caused by *Sarcoptes scabiei* in the pig (×22). The mites *(arrows)* are found in the deeper layers of the greatly thickened epidermis.

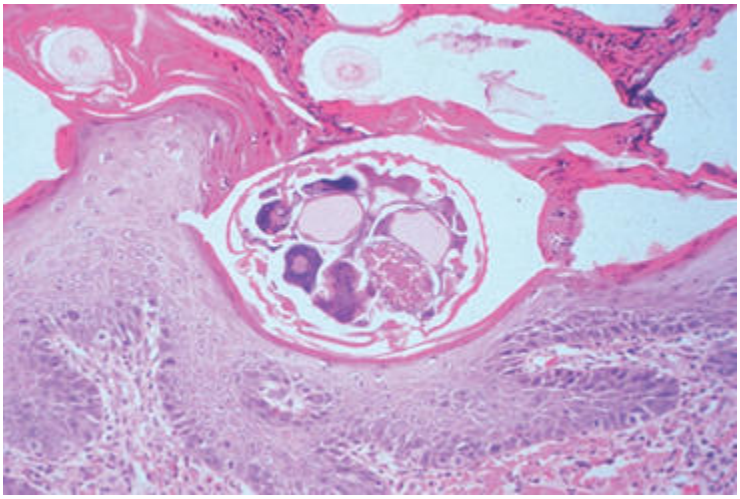

FIGURE 8-5 *Notoedres cati* in the skin of a cat (×150). These mites lie in the stratum corneum.

Demodex organisms are cigar-shaped mites found in hair follicles or with associated sebaceous glands (Figure 8-6); although some such as *Demodex gatoi*, *Demodex criceti*, and *Demodex injai* tend to be superficial. In dogs with severe demodectic mange, *Demodex canis* may be found in the lymph nodes. In goats there can be very large

nodular lesions in the skin, as there can also be occasionally with demodectic mange in cattle and swine (Figure 8-7).

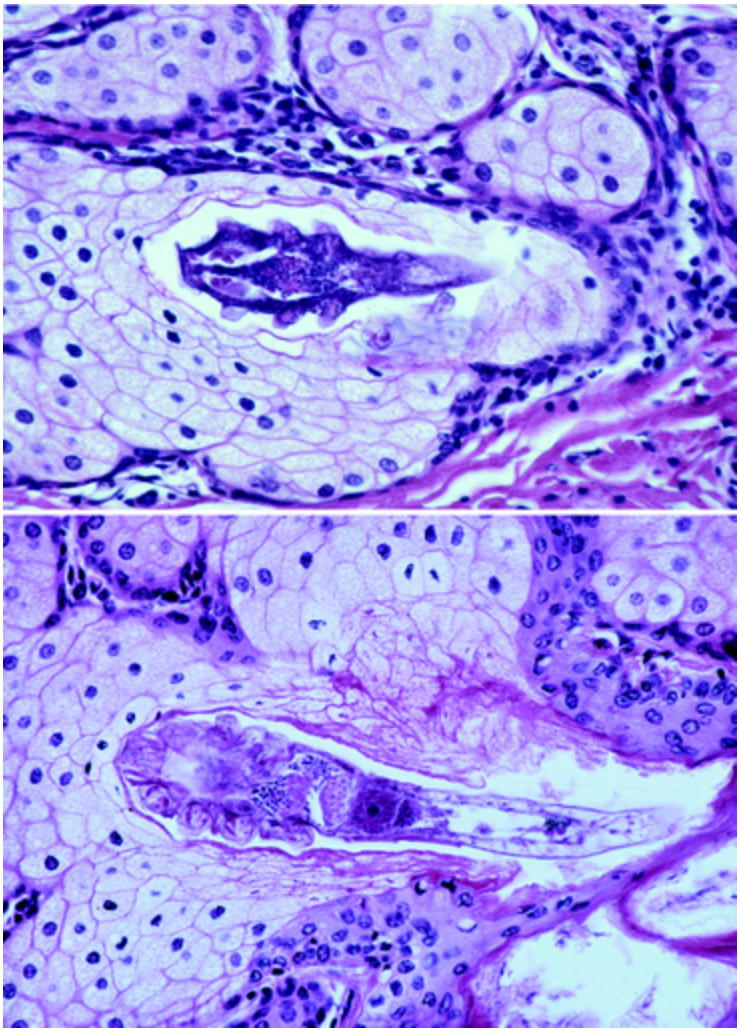

FIGURE 8-6 *Demodex canis* in the hair follicle of the vulva of a ewe. *Top*, Larva. *Bottom*, Adult (×430).

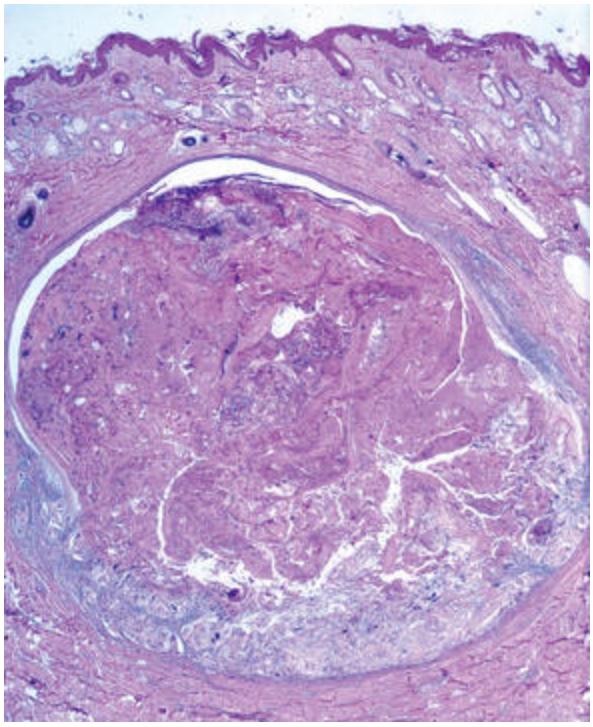

FIGURE 8-7 Demodectic mange in a bull (×16). Demodectic mange in cattle takes the form of nodular accumulations of myriad mites and cellular debris in proportions depending on the age of the lesion.

Mites of the respiratory tract (e.g., *Pneumonyssus* and *Sternostoma*) have more delicate exoskeletons than their ectoparasitic relatives. *Pneumonyssus simicola* and *Pneumonyssoides caninum* of the primate lung and canine nasal passages look very much superficially like any other mesostigmatid mite (Figure 8-8).

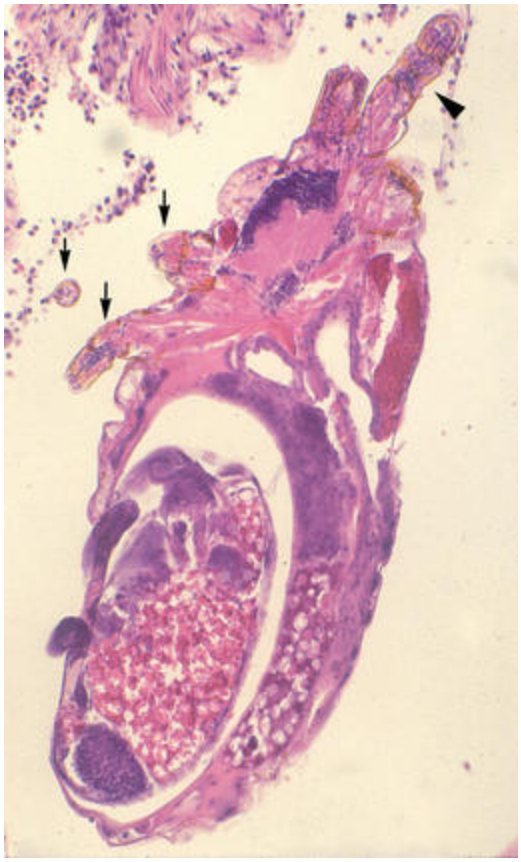

FIGURE 8-8 *Pneumonyssus simicola* in the lung of a rhesus monkey (×92). The mite contains a developing larva. The arrows indicate the legs, and the arrowhead indicates a palp.

Courtesy Dr. Castleman.

Trombiculid larvae (chiggers) feed through a stylostome or feeding tube extending into the dermis (Figure 8-9); very typically the mites are dislodged and all that remains is the very pruritic lesion.

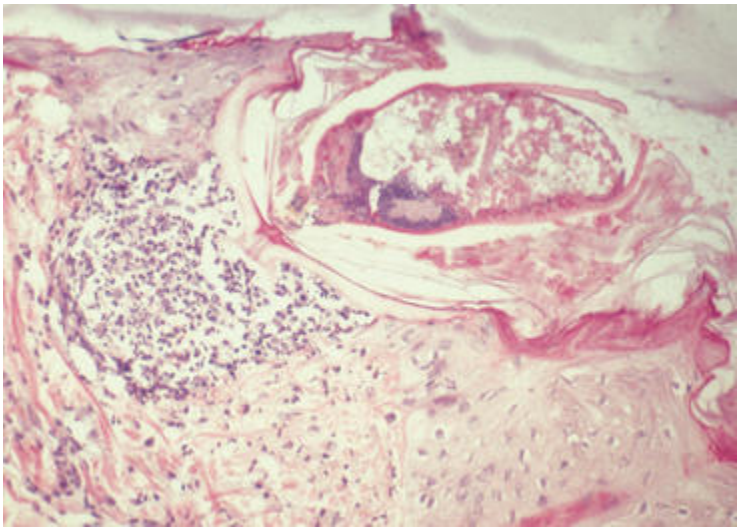

FIGURE 8-9 *Walchia americana* in the skin of a cat (×225). The stylostome or feeding tube extends to an area of dermis infiltrated with inflammatory cells.

Pentastomids

Pentastomids are so called because of the early belief that they had five mouths; in reality, they possess one mouth surrounded by four hooks (see Figure 2-100). The adults of these bizarre crustaceans are wormlike parasites in the respiratory passages of predaceous reptiles, birds, and mammals that for the most part become infected when they ingest nymphs encysted in the tissue of their prey. It is in the vertebrate prey in which the nymphs appear in tissue sections after the host has ingested an egg (Figure 8-10) containing a larva with four or six appendages. The pseudosegmented body of the nymph has a spheric to oval shape covered by a thick cuticle with sclerotized openings, stomata (Figures 8-11 to 8-13). Pentastomids have a complete digestive system with a mouth and an anus, and in section the intestine is often surrounded by large acidophilic glands (see Figures 8-11 and 8-12). These acidophilic glands are a good distinguishing characteristic for this group of organisms; they stain

bright pink with prominent blue nuclei in hematoxylin and eosin (H&E) stained sections. The musculature is striated and located within the subcuticular region.

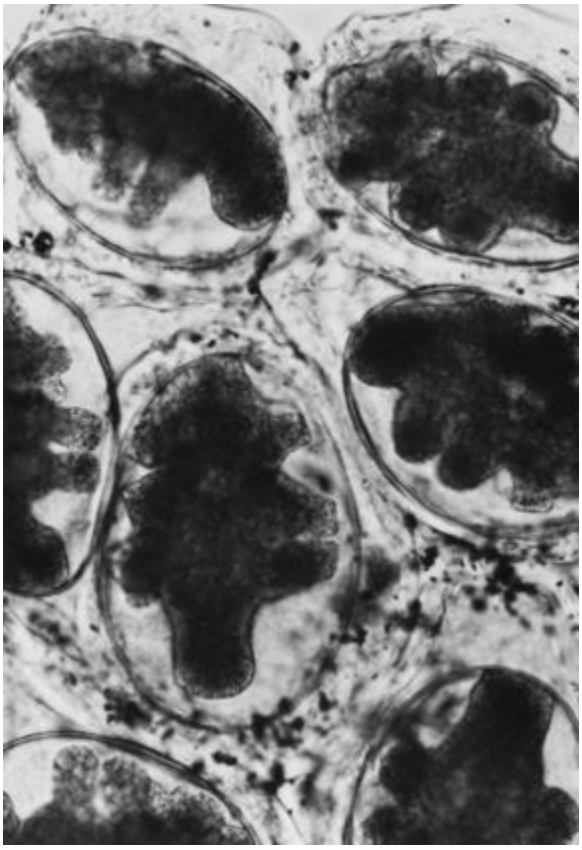

FIGURE 8-10 Pentastomid eggs with developing embryos (×160).

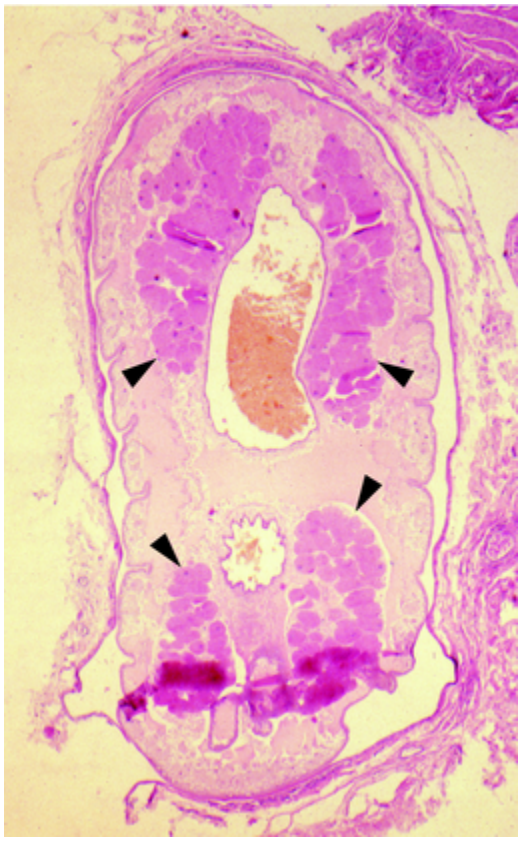

FIGURE 8-11 Pentastomid nymph from near the bladder of a cynomolgus monkey (×94). The cuticle is marked by deep annulations, and the nymph contains large acidophilic glands *(arrowheads)*.

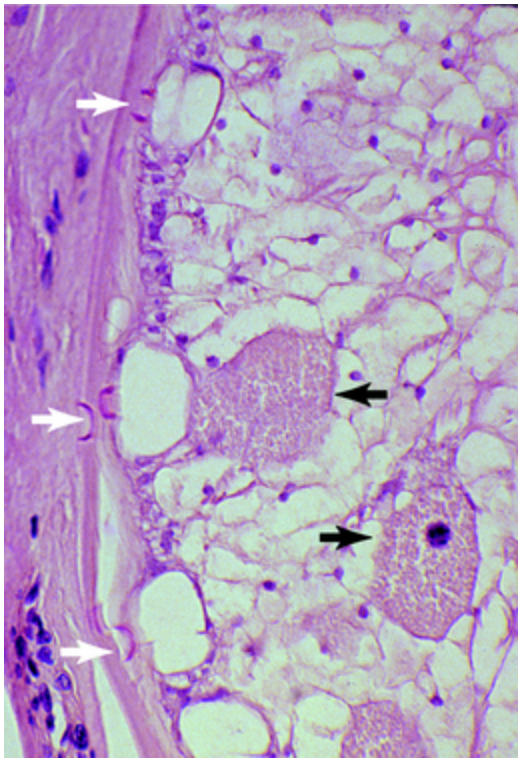

FIGURE 8-12 Pentastomid tissue showing pores *(white arrows)* and acidophilic glands *(black arrows)* (×290).

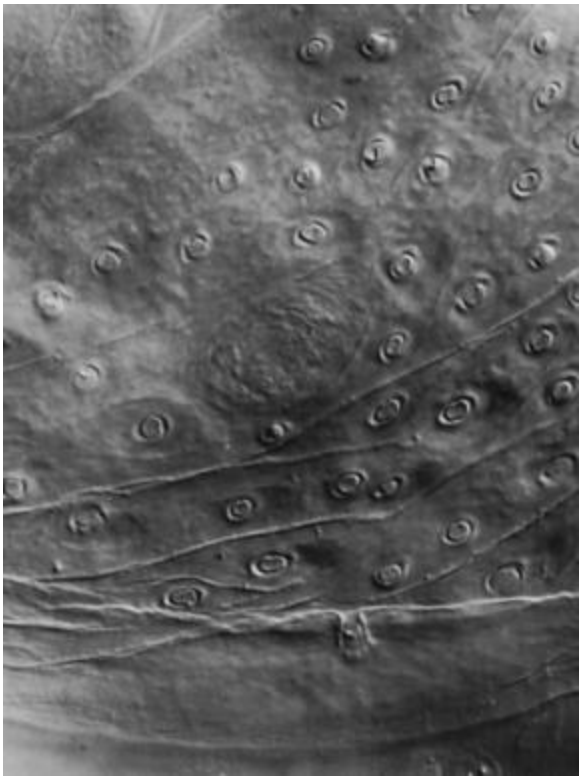

FIGURE 8-13 Surface view of the cuticle of a pentastomid showing the pores (×440).

PROTOZOA

Protozoa that are found in sections tend to be highly specialized individual cells with distinctive nuclei and other structures that may occur singly or in "nests" either within or external to the cells of the host. At the light microscope level, it is often difficult to ascertain many of the details of the individual cells, and often electron microscopy of material will provide the added detail required for a diagnosis. Also, there are often immunohistochemical or in situ hybridization methods that can be used for some infections (e.g., for *Toxoplasma gondii*, *Neospora caninum*, and *Sarcocystis neurona*) to make a definitive diagnosis as to a genus or species of parasite in a particular case.

With a great many of the protozoa it is often difficult to distinguish even distantly related organisms purely on the basis of the structures seen in sections because of preparation, because of the way they are fixed and stained, and because one is working near the working resolution of the light microscope. Therefore a group of amastigotes of *Trypanosoma cruzi* may look very similar to a pseudocyst of rounded zoites of *T. gondii*. This should be fairly straightforward because the amastigotes should be seen to contain the identifying kinetoplast, but they may be visible in only a portion of the organisms, and the typically elongate zoites of *T. gondii* may appear simply as round small nucleated cells in some sections. Often it is very helpful to also take into account the history, clinical signs, and overall pathologic changes seen in a case to aid in making a diagnosis.

Amebas

Amebas are extracellular parasites that feed through the process of engulfing bacteria, cell debris, or other cells as food material. The vast majority of these organisms are free-living parasites or commensals living typically in the large intestine of animals. However, there are two forms that do cause disease. Primates are host to *Entamoeba histolytica*, which can colonize the bowel wall and move to ectopic sites where the organisms establish cysts that most often include the liver, but they can also be found in lungs or brain tissue; reptiles have a similar pathogen, *Entamoeba invadens*, which can cause serious disease in these hosts with extraintestinal lesions. These amebas tend to have nuclei typical of the genus with a central dot of chromatin, the **karyosome, endosome,** or nucleolus, with

chromatin also being clumped around the inner surface of the nuclear membrane. These parasites can also be found to contain erythrocytes, sometimes several, in various states of digestion. The other main group of disease-causing amebas are facultative parasites that include the genera *Naegleria, Acanthamoeba,* and *Balamuthia*, which have infected dogs, sheep, cattle, primates, and horses (Daft et al, 2005). These forms live in the environment but can invade the tissue if they gain access through the nose or through wounds with lesions typically occurring in the brain or skin, but they can be found elsewhere. In sections these amebas tend to appear in clear spaces from artifactual contraction of the surrounding tissues during fixation and specimen preparation, to have foamy cytoplasm, and to have characteristic nuclei that contain a very dense endosome surrounded by a clear halo internal to the nuclear wall (Figure 8-14).

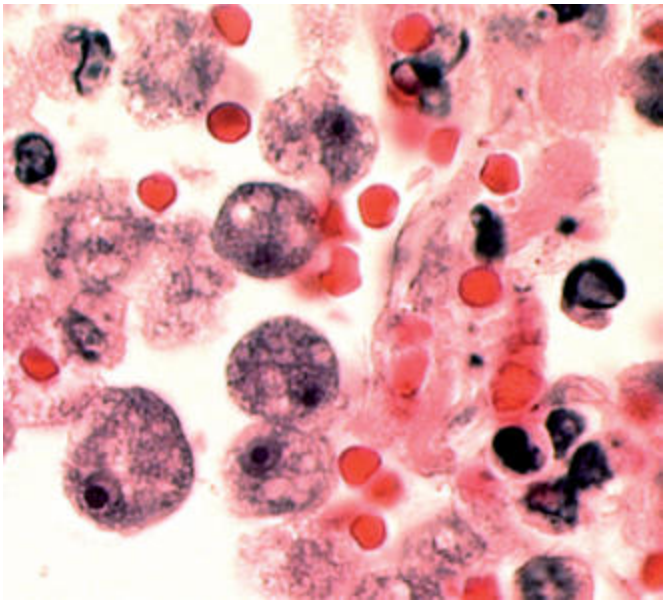

FIGURE 8-14 *Acanthamoeba* in the brain of a horse succumbing to the infection (×1200); note the large nucleolus in the nuclei of each of the ameba parasites.

Courtesy Dr. Govinda Visvesvara.

Flagellates

The typical flagellates that occur in the tissues of vertebrates are two that have what are known as amastigote stages that live within host cells. The amastigotes are small, round to oval bodies measuring 1.5 to 4 mm in diameter (often smaller after tissue processing) and contain a nucleus and a rod-shaped **kinetoplast.** They do not store PAS-positive material. The two groups of organisms that have these stages are *T. cruzi* and various species within the genus *Leishmania*.

Both trypomastigotes and amastigote stages of *T. cruzi* occur in the vertebrate host, but generally only the amastigotes are seen in tissue sections; the trypomastigote stage is found almost exclusively in the blood. *T. cruzi* amastigotes are generally found in muscle cells of the esophagus, colon, and heart, where they may be responsible for megaesophagus, megacolon, and myocarditis (Figure 8-15), respectively.

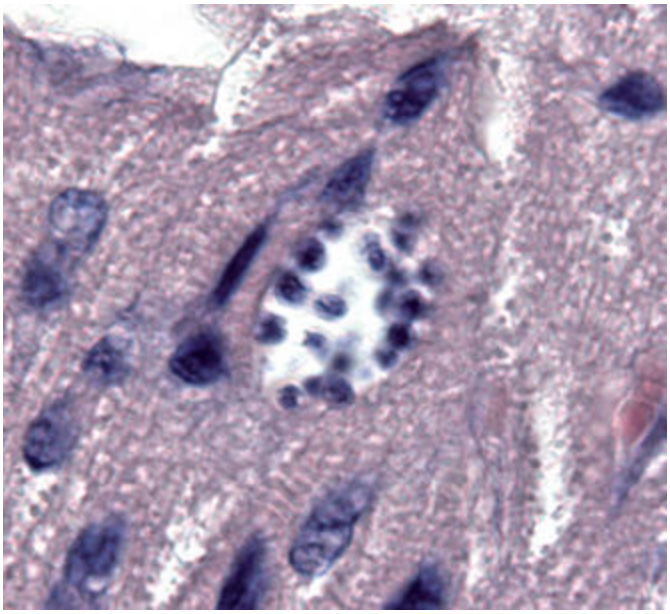

FIGURE 8-15 *Trypanosoma cruzi* amastigotes in cardiac muscle of a dog (×1300). Both nucleus and kinetoplast can be seen in individual organisms.

Courtesy Dr. Stephen C. Barr.

The amastigotes of *Leishmania* parasitize only one cell type in the vertebrate host, the macrophage, typically histiocytes. Therefore they can be found in skin, bone marrow, and visceral organs such as the spleen and Kupffer cells of the liver (Figure 8-16). Again, the diagnostic organelle within the parasite is the kinetoplast, but diagnosing the infection in tissue sections can be somewhat difficult because of the shrinkage of the cells during fixation that can make the visualization of the nucleus and kinetoplast challenging. One of the major differentiations to be considered is whether one is dealing with leishmaniasis or an infection with *Histoplasma* organisms. Needle biopsies or impression touch preps from cutaneous lesions or lymph node and bone marrow aspirates may be prepared and stained with Wright-Giemsa solution, and in these preparations the

full structure of the organism, including both the nucleus and kinetoplast, is generally more clearly visible.

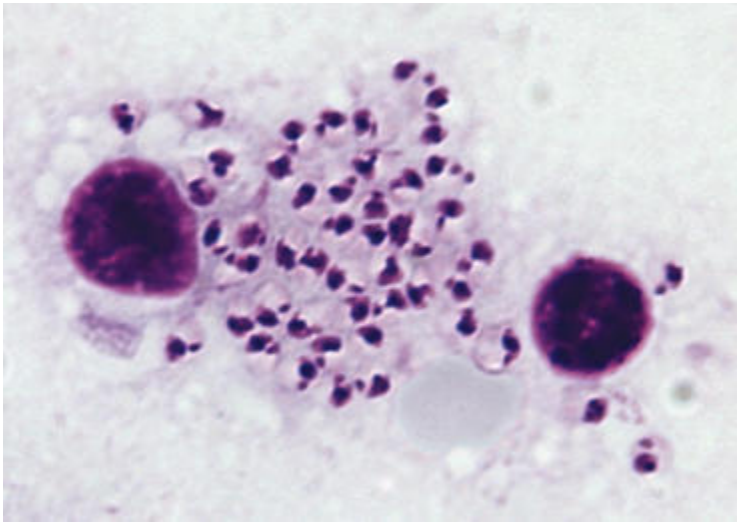

FIGURE 8-16 *Leishmania* amastigotes in a touch prep of an axillary lymph node of a dog (×690). The nucleus and kinetoplast are clearly evident in several of the organisms.

Ciliates

Balantidium coli trophozoites live within the contents of the cecum and colon of pigs but may secondarily invade the wall of the large intestine of swine that have various forms of enteritis. The trophozoites are characterized by their large size and the presence of a **macronucleus** and a **micronucleus** and cilia (Figures 8-17 and 8-18). Rumen ciliates may be found in the lung as a result of terminal inhalation of ruminal contents, in which case there is no evidence of inflammatory reaction. Rumen ciliates may also be found in hepatic vessels in cases of very severe enteritis (Figure 8-19). In horses with severe enteritis, the extravagantly shaped ciliates normally present in the large intestine may secondarily penetrate the submucosa. These ciliates have large, often polymorphic macronuclei, and some have tufts of long cilia.

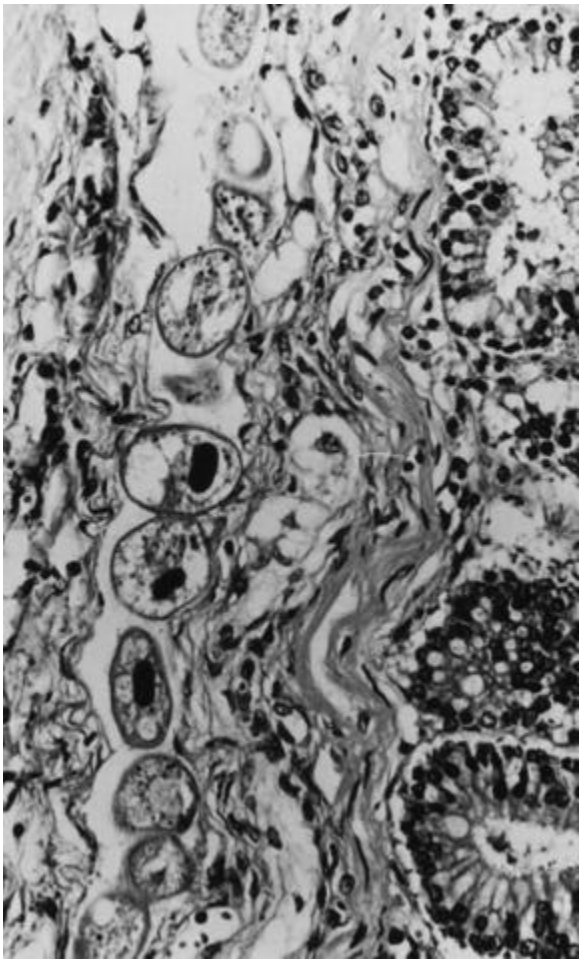

FIGURE 8-17 *Balantidium coli* in the submucosa of the large intestine of a pig (×280).

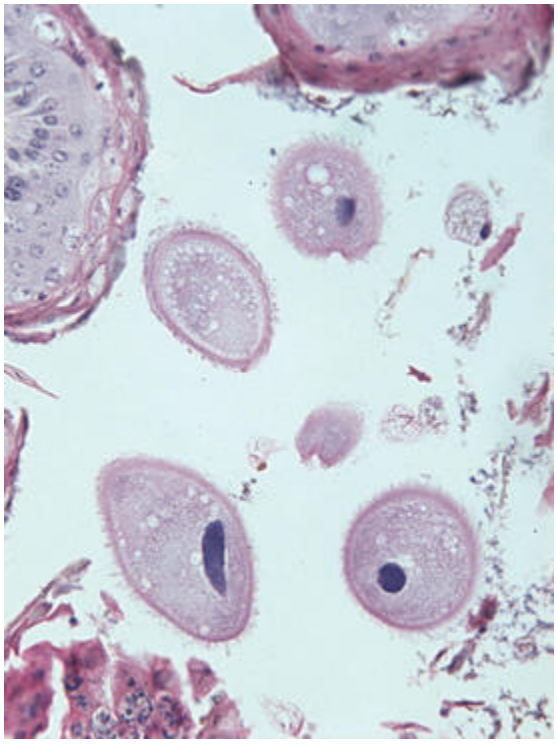

FIGURE 8-18 Rumen ciliates (×360).

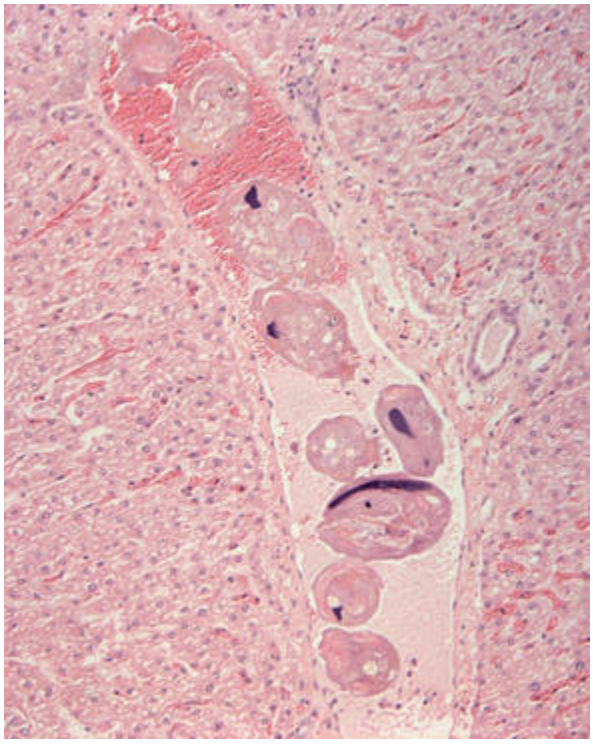

FIGURE 8-19 Ciliate in vein in the liver of a goat with severe suppurative lymphangitis (×250).

Apicomplexa

Coccidia

The coccidia are members of the phylum Apicomplexa. Included in this discussion are members of the genera *Eimeria, Klossiella, Cystoisospora, Hammondia, Besnoitia, Sarcocystis, Neospora,* and *Toxoplasma*. The life history and development of the major genera of coccidians are described in Chapter 3. There seems to be a good deal of consensus around the placement of the genus *Cryptosporidium* within the gregarines rather than with the coccidia, but for convenience, these species are still included in this section. The genera *Eimeria* and *Cryptosporidium* seem to be completely monoxenous, i.e., with transmission always between members of one type of host without any paratenic or intermediate hosts, and almost all the stages seen in section occur within the epithelium of the gastrointestinal tract or rarely the gall bladder. *Klossiella* is also apparently monoxenous, with direct transmission between hosts and almost all stages being found in the epithelium of the renal system. The other coccidia are either facultatively *(Cystoisospora* and *Toxoplasma)* or obligatorily *(Sarcocystis*, *Hammondia*, *Neospora*, and *Besnoitia)* heteroxenous, i.e., having a paratenic or intermediate host. For the heteroxenous species of coccidia, the stages often seen in tissue are the stages causing disease in the prey animal that is serving as the paratenic or intermediate host. A description of the histologic appearance of the various stages follows, but host specificity, site specificity, life cycle, and details of development characteristic of the genera and species of coccidia must also be taken into consideration in arriving at a diagnosis.

Eimeria and *Cystoisospora*

Asexual stages

The infective stage contained in the oocyst is the **sporozoite,** which is a product of a reduction division that occurs in the oocyst (Apicomplexa are haploid except immediately after fusion of the gametes.). When a sporozoite enters a cell, it rounds up as a **trophozoite** in a membrane-lined **parasitophorous vacuole** (Figure 8-20). Not every species of coccidian stays within a parasitophorous vacuole, and this fact can be a useful adjunct in generic and specific diagnoses.

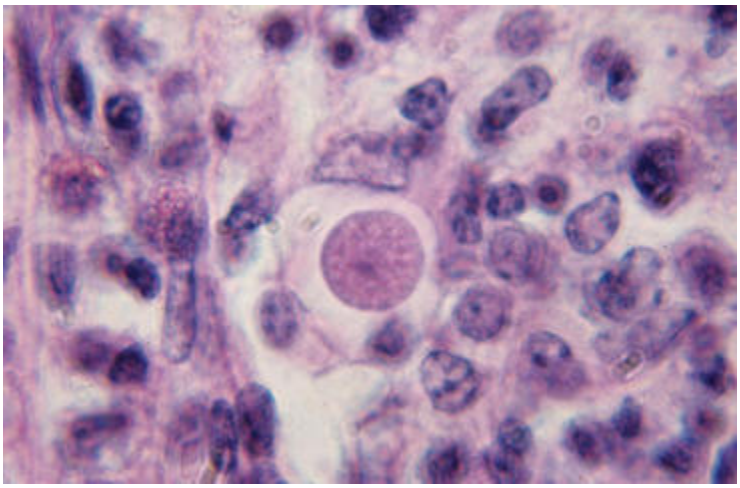

FIGURE 8-20 *Eimeria bovis* trophozoite in an intestinal epithelial cell of a cow (×1300).

Trophozoites multiply asexually within cells by several processes. In the case of *Eimeria* they typically undergo a special type of cellular division called **schizogony** (other terms that describe this form of division with various nuances are **merogony** and **endopolygeny**). In this type of division the apical complex divides into numerous copies around the periphery of the cell, the nucleus

lobulates with portions being associated with each apical complex, and finally the cell membrane contracts and divides to form a few to thousands of individual organisms (Figures 8-21 and 8-22). Depending on the species, schizonts may be found in enterocytes, biliary epithelial cells, endothelial cells, renal epithelial cells, or even uterine epithelial cells. Ordinary meronts contain from less than ten to hundreds of merozoites; some meronts (megaschizonts) (see Figure 8-21) may contain over 100,000 merozoites.

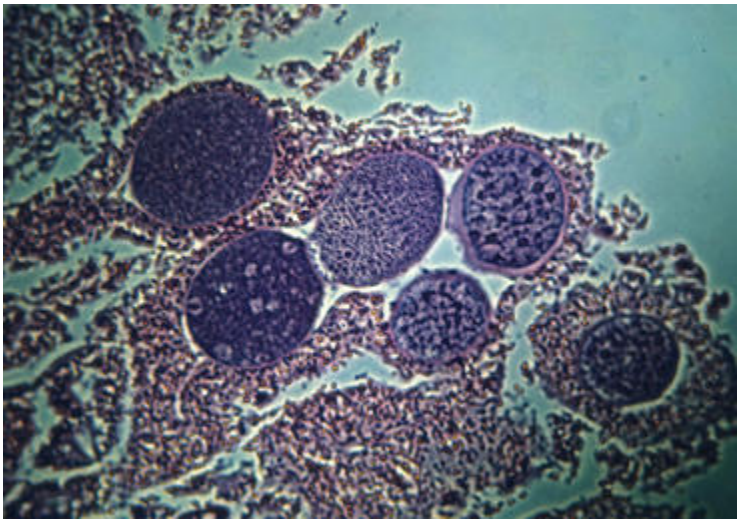

FIGURE 8-21 *Eimeria bovis* schizonts in several stages of development in intestinal epithelial cells of a calf (×250).

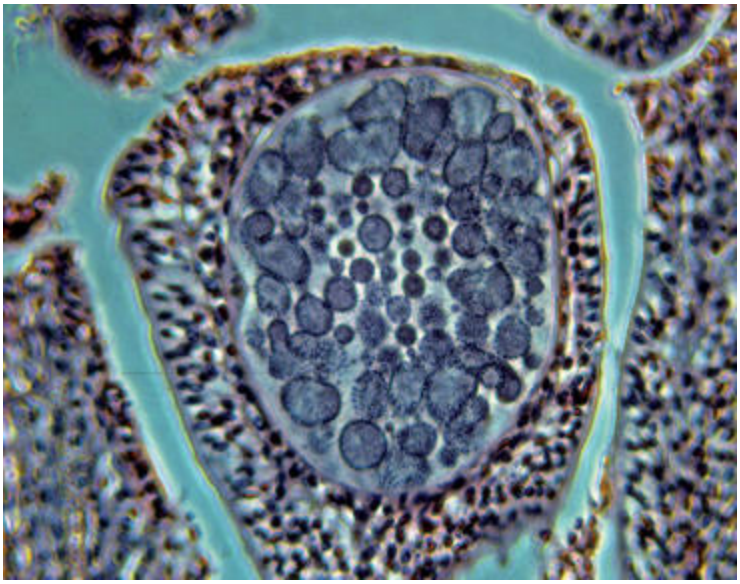

FIGURE 8-22 Another young *Eimeria bovis* schizont in an intestinal epithelial cell of a calf (×400).

Sexual stages

A merozoite produced by the final schizogonic generation enters a fresh host cell and develops into either a male or a female gametocyte. The female gametocyte enlarges, stores food materials, and induces a hypertrophy of both the cytoplasm and the nucleus of its host cell. When mature the female gametocyte is called a **macrogamete** (Figure 8-23). The male gametocyte also induces hypertrophy of the cytoplasm and the nucleus of its host cell (see Figure 8-23) as it undergoes repeated nuclear division and becomes multinucleate. Each nucleus is finally incorporated into a flagellated **microgamete.** (The microgametes of *Cryptosporidium* species are without flagella.) When a macrogamete is penetrated and fertilized by a microgamete, it becomes a **zygote.** Wall-forming bodies, already present in the macrogamete, then become clearly visible as large, spheric, eosinophilic granules in the cytoplasm of the zygote

(see Figure 8-23). These later coalesce to form the oocyst wall (Figure 8-24).

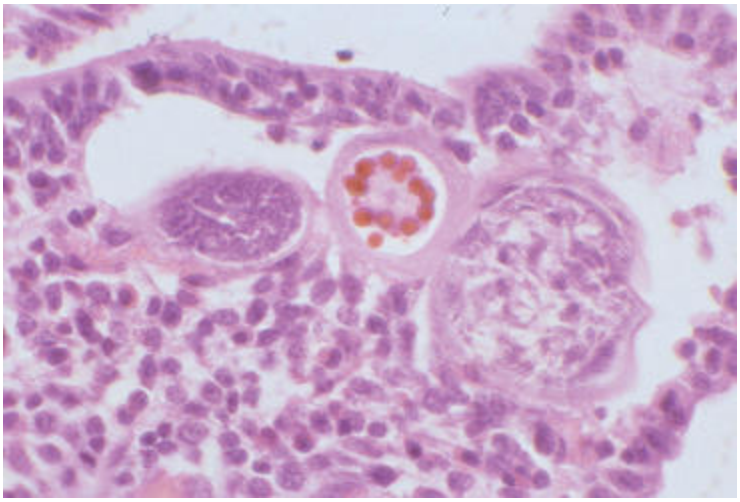

FIGURE 8-23 *Eimeria auburnensis* male gamonts surrounding a developing oocyst in the intestinal epithelial cells of a calf (×1050).

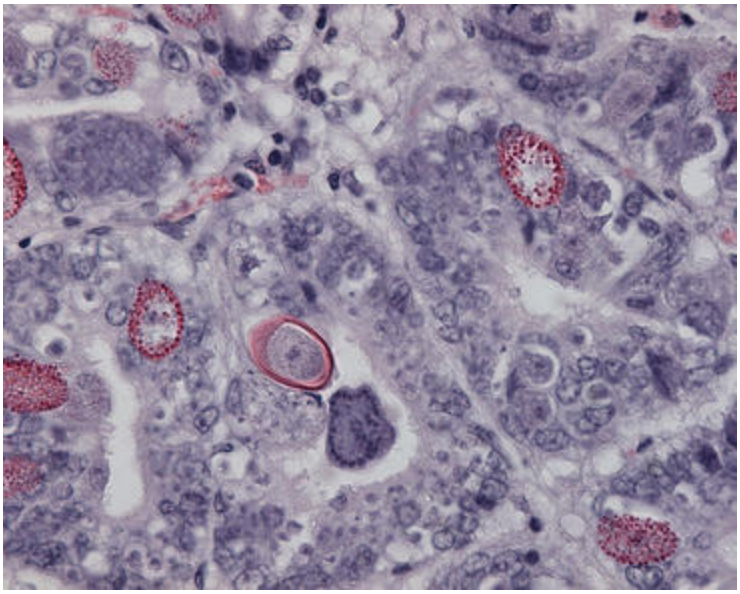

FIGURE 8-24 *Eimeria* oocysts developing in the intestinal epithelium of a goat (×900).

Examples

In the horse, *Eimeria leuckarti* forms large schizonts and very thick-walled and obvious oocysts (Figure 8-25). The oocyst of *Cystoisospora canis* seem to develop within the lamina propria rather than the epithelial cells (Figure 8-26). *Eimeria gilruthi* is atypical in that it forms megaloschizonts in the abomasum that are visible to the naked eye (Figure 8-27). *Eimeria stiedae* of the rabbit lives in and causes proliferation of the biliary epithelium and can produce a lethal hepatitis (Figure 8-28).

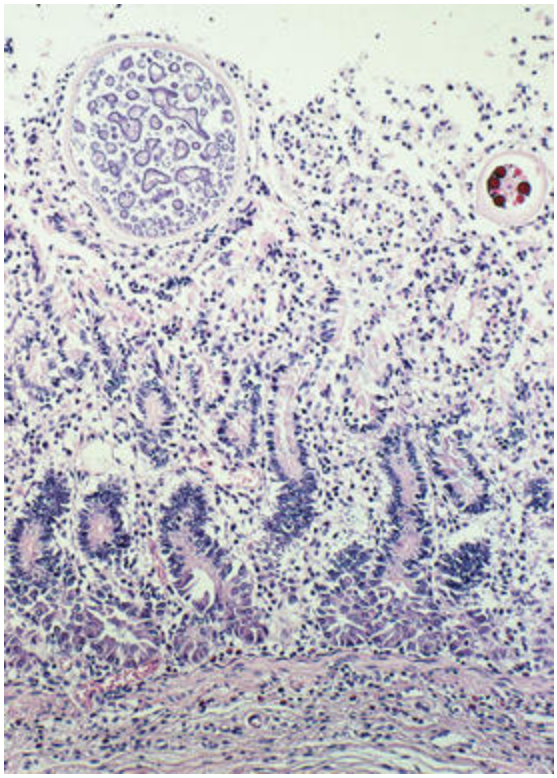

FIGURE 8-25 *Eimeria leuckarti* schizont and developing oocyst in the intestinal mucosa of a foal from Switzerland (×250).

Courtesy Dr. Maja Suter.

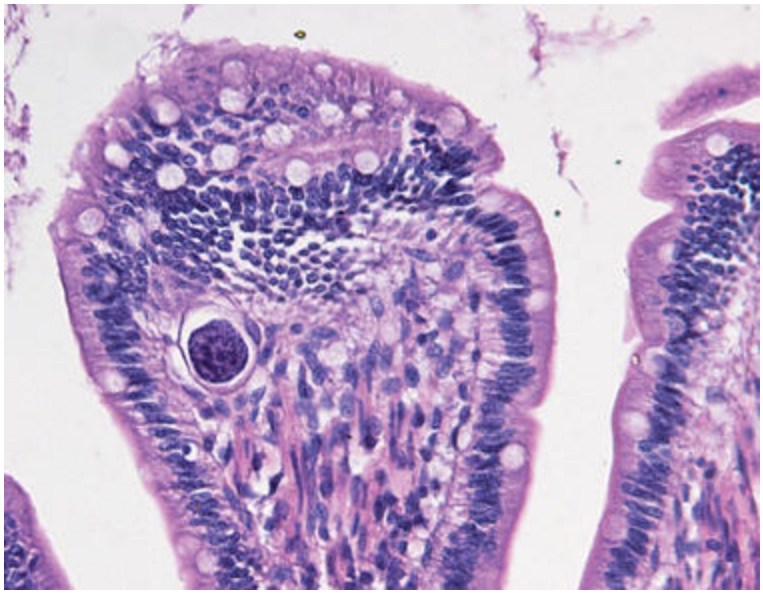

FIGURE 8-26 Oocyst of *Cystoisospora canis* developing in the lamina propria of the colonic mucosa of a dog (×900).

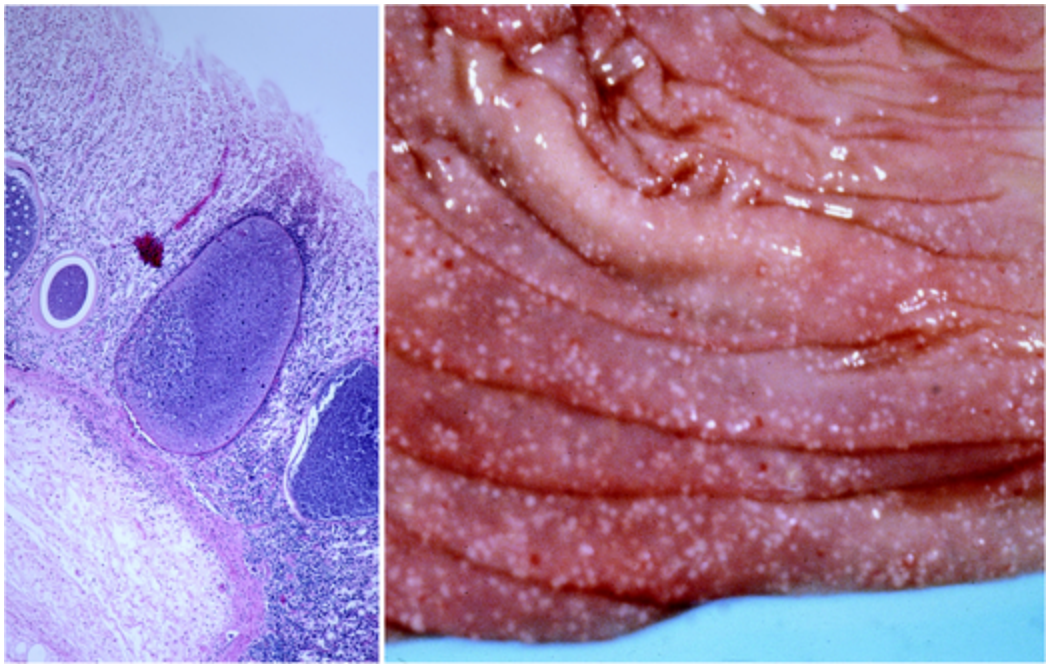

FIGURE 8-27 *Eimeria gilruthi* megaloschizonts in the abomasum of a sheep (histosection on left, ×100; gross on right, ×5).

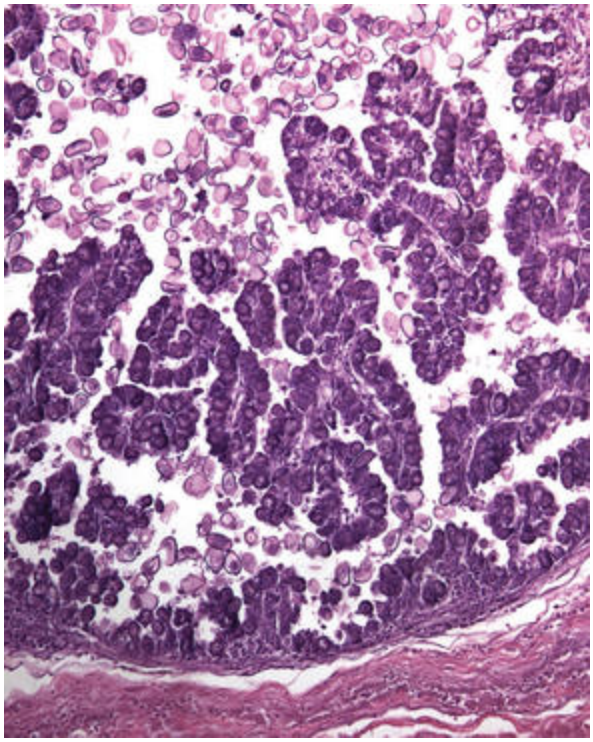

FIGURE 8-28 *Eimeria stiedae* developing in the bile duct epithelium of a rabbit (×100).

Cryptosporidium

The minute (5 to 7 μm) stages appear as basophilic spheres on the luminal surface of epithelial cells of the gastrointestinal tract of vertebrates (Figure 8-29); on rare occasions, typically in the immunocompromised host, infection of respiratory or gall bladder epithelia may also occur. The infection is very superficial and appears to protrude from the surface of the cell, but these are intracellular parasites, and all the stages—schizonts, gametes, oocysts, and so on—form underneath the host cell membrane.

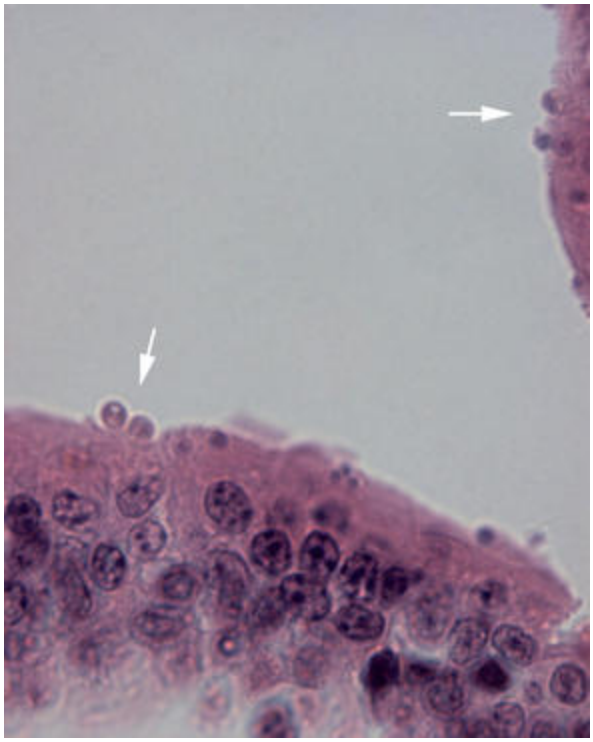

FIGURE 8-29 *Cryptosporidium parvum*. Developing stages *(arrows)* of *Cryptosporidium parvum* on the mucosa of a naturally infected calf.

Klossiella

A parasite of the equine kidney, *Klossiella equi* is usually an accidental histopathologic finding. Schizogony occurs in the glomerular endothelium and in the proximal convoluted tubules of the kidneys. The distinctive sporonts (Figure 8-30) in the renal tubular epithelium produce as many as 40 sporoblasts, which develop into sporocysts, each of which may contain eight to 15 sporozoites. There is a similar species, *Klossiella muris*, which will show up in histologic sections of murine kidneys.

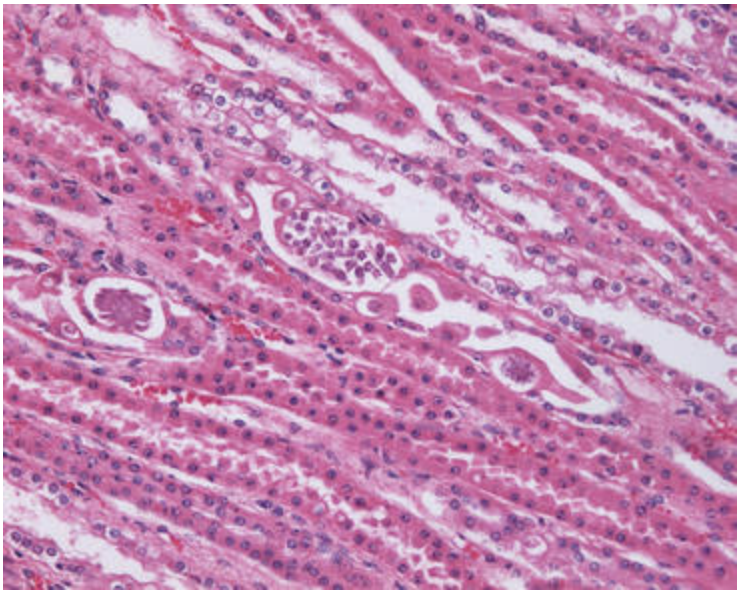

FIGURE 8-30 Sporonts of *Klossiella equi* in the renal tubular epithelium of a horse (×250).

Sarcocystis

The early schizonts of *Sarcocystis* occur in various endothelial cells of different organs (Figure 8-31). **Sarcocysts,** the stages found in the intermediate host, are found in skeletal and cardiac muscle fibers (Figures 8-32 and 8-33); these vary in size from a few micrometers in diameter to macroscopically visible objects, stain intensely with hematoxylin, and are packed full of bradyzoites that are larger than those of *Toxoplasma*. Septa subdivide the interior of the sarcocyst but may escape notice because they stain poorly or not at all with H&E. Often the cyst wall is described as hirsute (hairy) because of the many prolongations that give the cyst its apparent striated border. The hirsute wall and the septa dividing the zoites within the sarcocysts are often diagnostic.

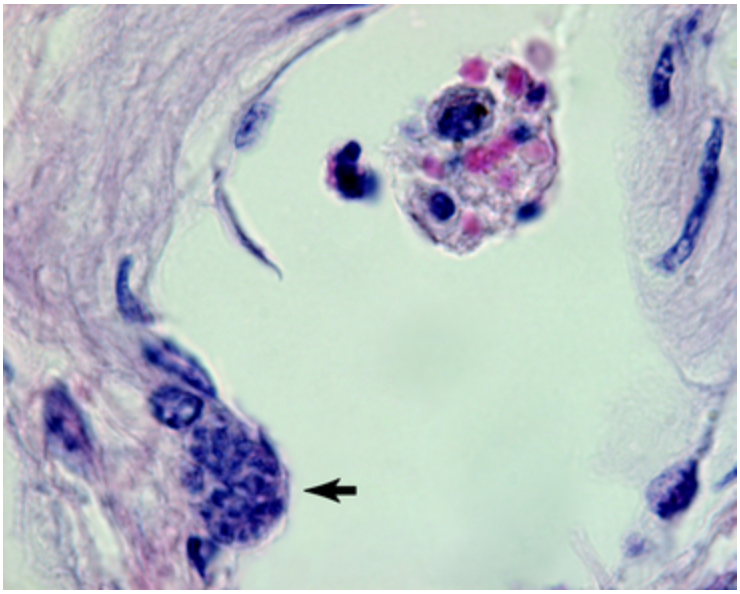

FIGURE 8-31 *Sarcocystis cruzi* schizont *(arrow)* in endothelium of a small artery of a calf with a fatal, naturally acquired infection (×800).

Courtesy Dr. Paul Frelier.

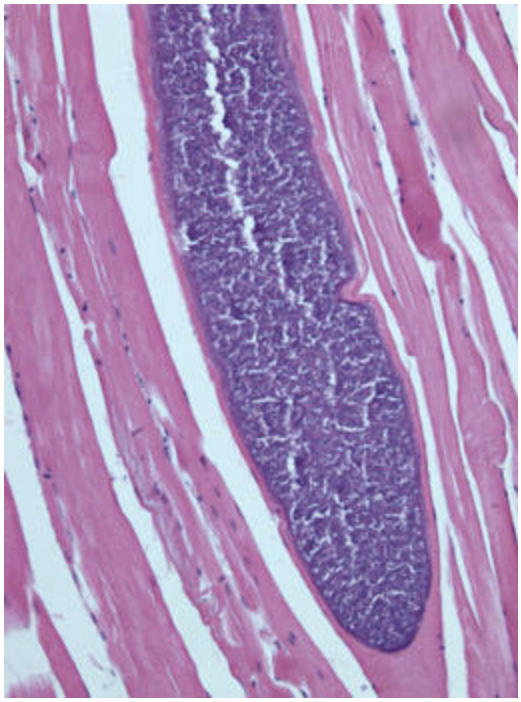

FIGURE 8-32 Sarcocyst of *Sarcocystis muris* in skeletal muscle of a mouse (×200).

Courtesy Dr. Marguerite Frongillo.

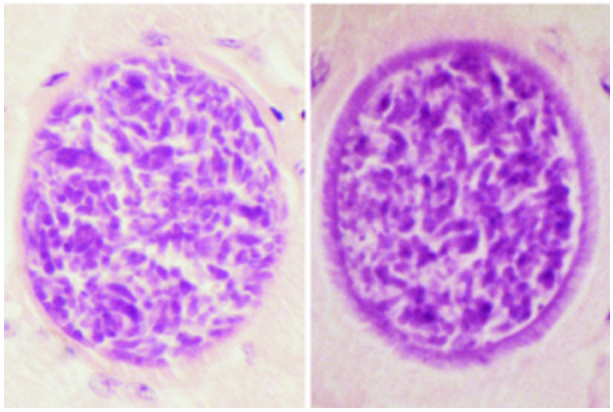

FIGURE 8-33 Sarcocysts of *Sarcocystis cruzi (left)* and *Sarcocystis bovifelis (right)* in skeletal muscle of a cow (×300). The cyst wall of *S. bovifelis* is thicker and appears striated.

Hammondia

Hammondia appears very similar morphologically to *Toxoplasma gondii;* the distinctions are biologic and molecular more than structural. The life cycle is obligatorily heteroxenous, but stages very similar to those described for *Toxoplasma* in the next paragraph are found in the tissues of many warm-blooded vertebrate animals that serve as prey to dogs and cats. These parasites have not been found to cause disseminated disease in immunosuppressed or immunocompromised hosts.

Toxoplasma

The stages that occur within the epithelial cells of the cat are to a great extent comparable to what occurs with *Eimeria* and *Cystoisospora* (Figure 8-34). It is within the genus that the names **tachyzoite** and **bradyzoite** were first used to describe the different life stages that occur in the paratenic hosts. Within these hosts the only form of division that occurs is **endodyogeny** which is similar to schizogony, but only two daughter cells are formed in each

dividing organism. The only schizonts seen with *T. gondii* occur in the intestinal epithelial cells of felids (see Figure 8-34). Tachyzoites divide rapidly and for the most part cannot withstand pepsin digestion for any length of time. Bradyzoites divide slowly, are resistant to pepsin digestion, and form cysts in tissue that are most easily observed in histologic sections of brain stained with PAS, because the slowly dividing forms store PAS-positive material. Cats can have cysts of bradyzoites throughout their bodies just as other hosts (Figure 8-35). Tachyzoites accumulate as "groups" intracellularly; bradyzoites become tightly packed in "intracellular cysts." The latter, when found in striated muscle fibers, might be confused with either sarcocysts or accumulations of *T. cruzi* amastigotes.

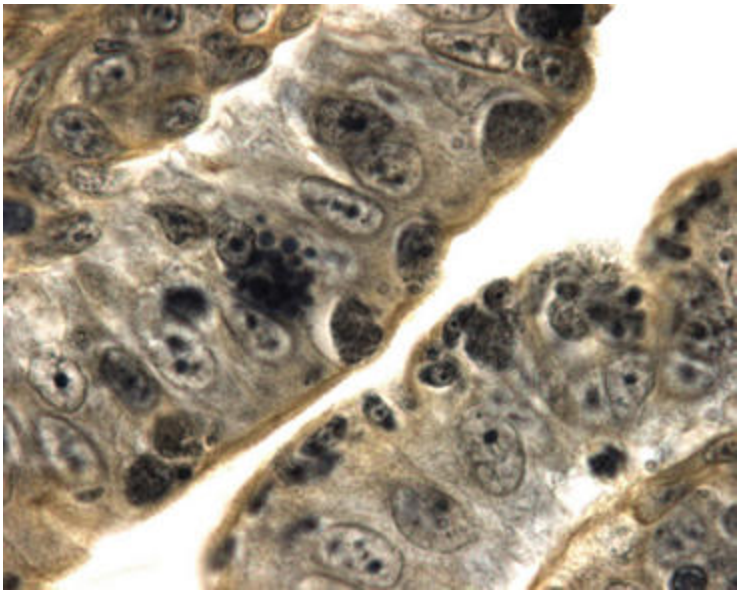

FIGURE 8-34 *Toxoplasma gondii* development stages in the intestinal epithelia of an experimentally infected cat (×800).

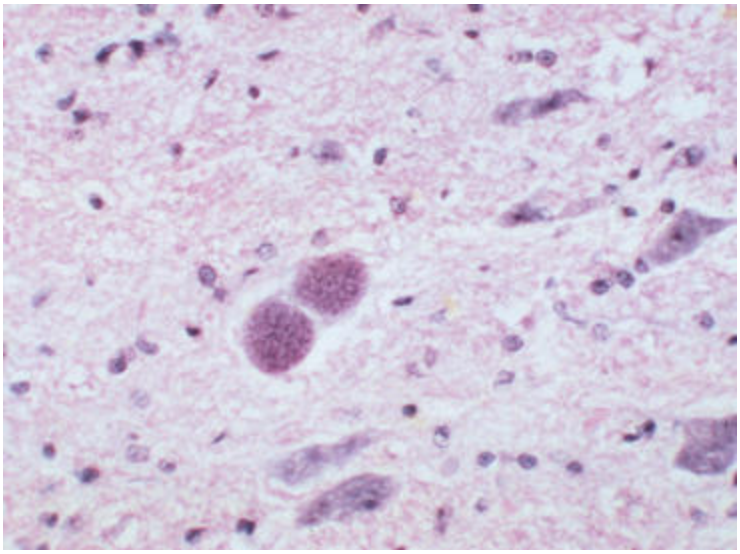

FIGURE 8-35 *Toxoplasma gondii* bradyzoites in a cyst in the brain of a cat (×800).

Neospora

Using the light microscope, the cysts of *N. caninum* are almost indistinguishable from those of *T. gondii*. The major distinction that was recognized in the early description of this species was the thicker "cyst wall" that occurred around bradyzoites (Figure 8-36).

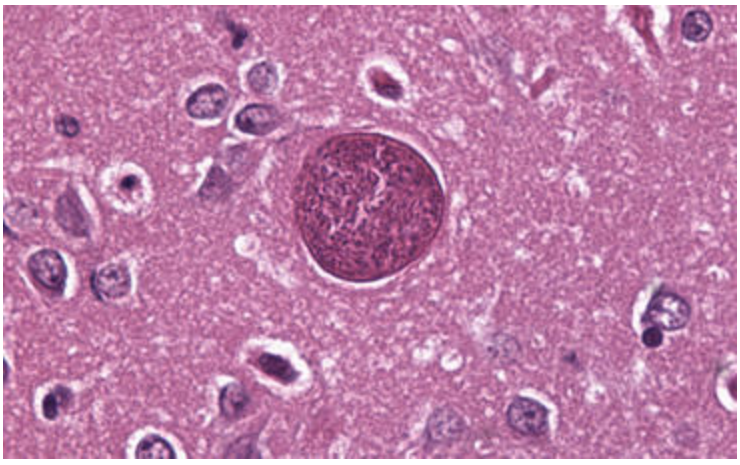

FIGURE 8-36 *Neospora caninum* bradyzoites in a cyst in the brain of a dog (×1200).

Besnoitia

Besnoitia is mainly considered to be exotic to domestic animals in the United States, although wildlife such as opossums can be infected. These organisms described as *Besnoitia bennetti* have been described from donkeys in the United States (Dubey et al, 2005). The typical presentation is very large cysts without septa that are often found in the skin, although viscera may also be affected (Figure 8-37).

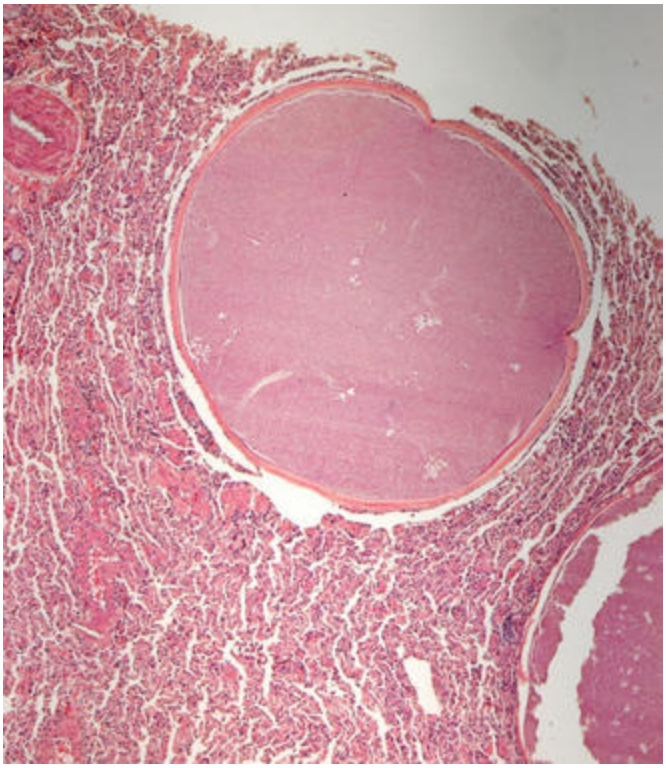

FIGURE 8-37 *Besnoitia* cyst in the lung of an opossum (×40).

Hemosporidians

A number of the Apicomplexa genera have heteroxenous life cycles with the sexual stages occurring in invertebrates and the asexual stages occurring in vertebrates, e.g., *Plasmodium*, *Theileria*,

Hepatocystis, and *Leucocytozoon*. With most of these parasites there is a good deal of description relative to the stages that are found in the blood of the host, whereas very little time is spent describing the various stages, typically schizogonous stages, that may occur in the viscera of hosts that can be seen in sections. *Babesia* infects only red blood cells, whereas *Theileria* infects erythrocytes and lymphocytes; because these are two of the most important haemosporidians of domestic animals, there is little need to focus much attention on the schizont stages that occur in tissues. However, some other species do cause pathology and have stages in the tissues—schizonts that can be quite large and damaging.

Leucocytozoon

There are species in chickens, *Leucocytozoon caulleryi* and *Leucocytozoon simondi,* that produce megaloschizonts in chickens and geese (Figure 8-38), respectively, that can be highly pathogenic. These schizonts can be very large and detrimental to the host.

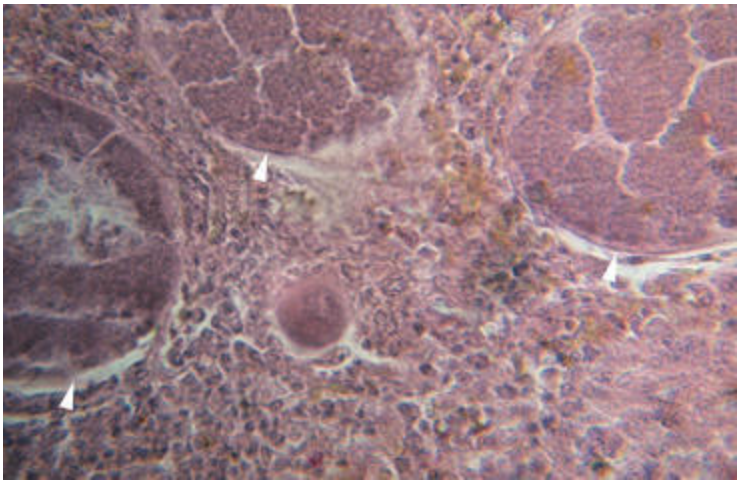

FIGURE 8-38 *Leucocytozoon simondi* megaloschizonts in the liver of a Canada goose (×100).

Hepatozoon

Hepatozoonosis in the United States is associated with *Hepatozoon americanum*, which has cystic stages in the muscle of the host that are associated with chronic muscle pain in these animals. These stages are often used to assist diagnosis, which is still often made as a result of muscle biopsy.

Cytauxzoon

Cytauxzoon is a parasite that kills cats, often very acutely. There are large schizonts that occur within the macrophages and cause them to become enormous. This is the reason for the name of the genus and what makes the infection so deadly for cats. Sections throughout the body will have vessels plugged with these giant cells (Figure 8-39).

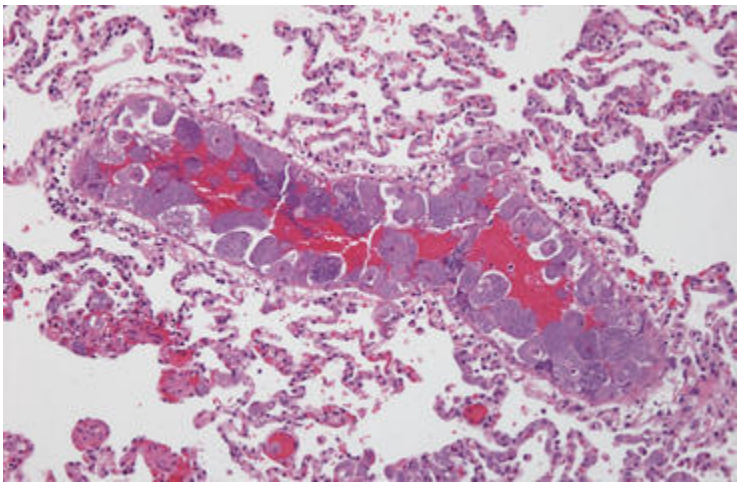

FIGURE 8-39 *Cytauxzoon felis*. A pulmonary vein of a cat filled with multiple, enlarged, mononuclear cells containing schizonts (×100).

HELMINTHS

In terms of examining helminths in section, there are basically two types: solid bodied (the acoelomates) and bodies in which tubes are suspended within a tube (the pseudocoelomates). Trematodes and cestodes are of the solid body type; nematodes and acanthocephalans represent the “hollow” body types. The problem can be that a trematode or cestode may have all sorts of cavities in the various organs that give them the appearance of having a pseudocoele, and nematodes may be so packed with organs and eggs or larvae that one starts to doubt whether one is looking at a nematode or not. The trematodes and cestodes are covered with a syncytial tegument, whereas the nematodes and acanthocephalans are covered with a secreted cuticle.

Trematodes

Most trematodes are parasites of the digestive tract, but these only rarely show up in tissue sections. The trematodes in tissues are typically those in which the adults live in other tissues. Trematodes can be found throughout the bodies of vertebrates, in bile ducts, pancreatic ducts, body cavities, lungs, ureters, blood vessels, and so on. In a few cases larval stages can also be found in domestic animals, where they may or may not be causing disease.

The characteristics of trematodes in sections form a composite group of useful features, but because often the goal is to differentiate trematodes from cestodes, part of the characterization includes how they differ from cestodes. Of course, for almost every characteristic there is one group that composes an exception. Trematodes have a solid but spongy body that usually contains no large cavities and is not divided into cortical and medullary layers

as the body of cestodes is. Trematodes have an intestine that is usually bifurcate ending in a blind cecum. (An example of an exception are the Cyclocoelidae, which have a fusion of the posterior gut so that it forms a continuous loop [Figure 8-40.]) Unlike tapeworms, trematodes do not contain calcareous corpuscles. The body is covered with the syncytial integument that often has spines. There are muscles below the integument, usually an outer circular layer, a middle longitudinal layer, and an inner diagonal layer (which may also be external to the longitudinal layer or absent) (Figure 8-41). There are sex organs in the adult flukes, which are monoecious hermaphrodites except for the Schistosomatidae that have separate males and females. The eggs have typical shapes, and the shells are often brown to golden in sections. There are typically two suckers, one around the mouth and one ventral (often anterior to midbody) (Figures 8-42 and 8-43; see also Figure 8-40), and an excretory system that is difficult to see that empties through a pore at the posterior end of the body.

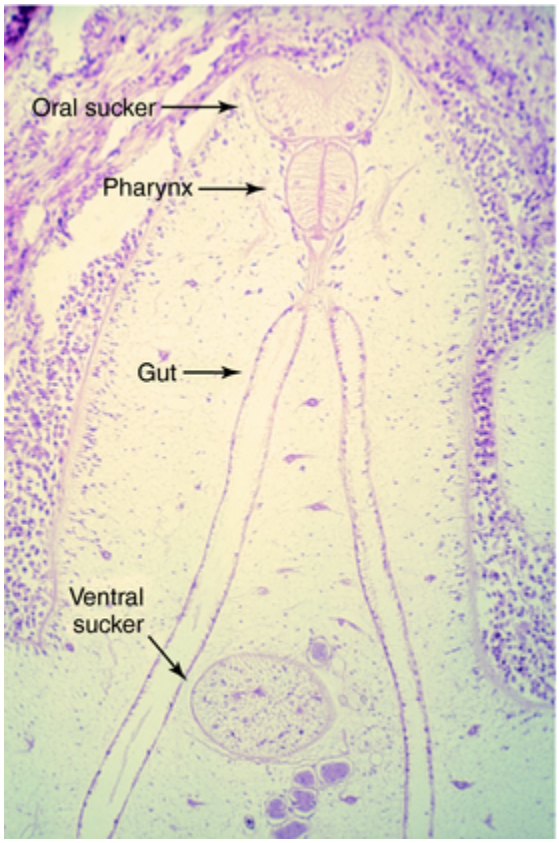

FIGURE 8-40 *Amphimerus pseudofelineus* in the small intestine of an ocelot (×40).

Courtesy Dr. M. Dale Little.

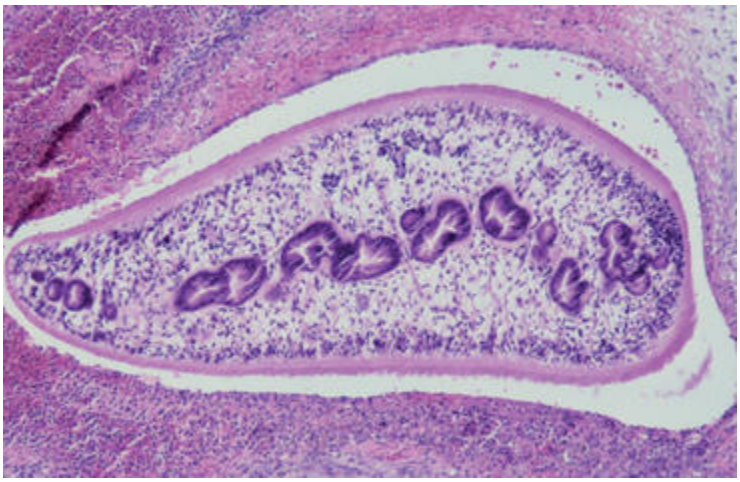

FIGURE 8-41 Migrating larva (marita) of *Fasciola hepatica* in the liver of a cow (×40).

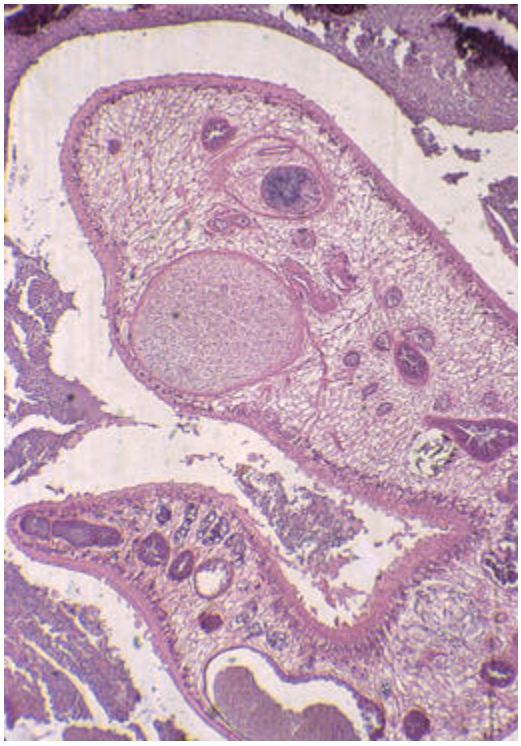

FIGURE 8-42 *Fasciola hepatica* in the bile duct of a cow (×20).

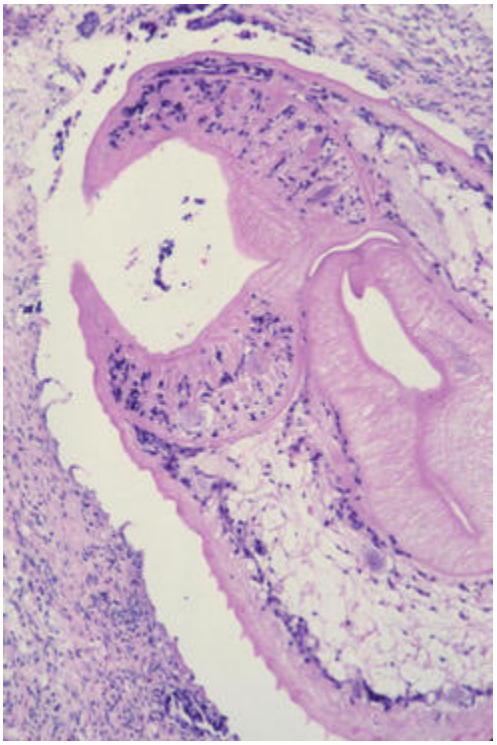

FIGURE 8-43 *Fasciola hepatica* in the bile duct of a rat (×20).

Courtesy Dr. Helen Han Hsu.

Once a trematode is identified as such, the next step is trying to determine the family or genus. This involves calculating or guessing at the overall size and looking at the arrangement of the sex organs, the types of sucker if they are sectioned, and the extent and branching of the intestine and excretory system (Figure 8-44; see also Figure 8-40). If there are eggs, they can be very helpful once the size, shape, type of operculum, and state of development (with or without a miracidium) (Figure 8-45) have been noted. The spines on the surface of the body can also be very helpful in diagnosis, and they will have to be examined for their number, size, and location on the body of the fluke (Figure 8-46).

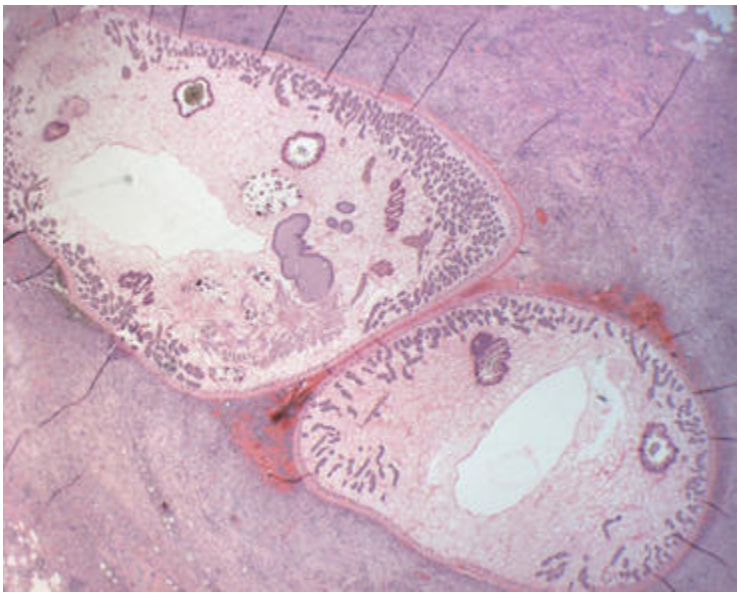

FIGURE 8-44 *Paragonimus kellicotti* in the lung of a cat (×5).

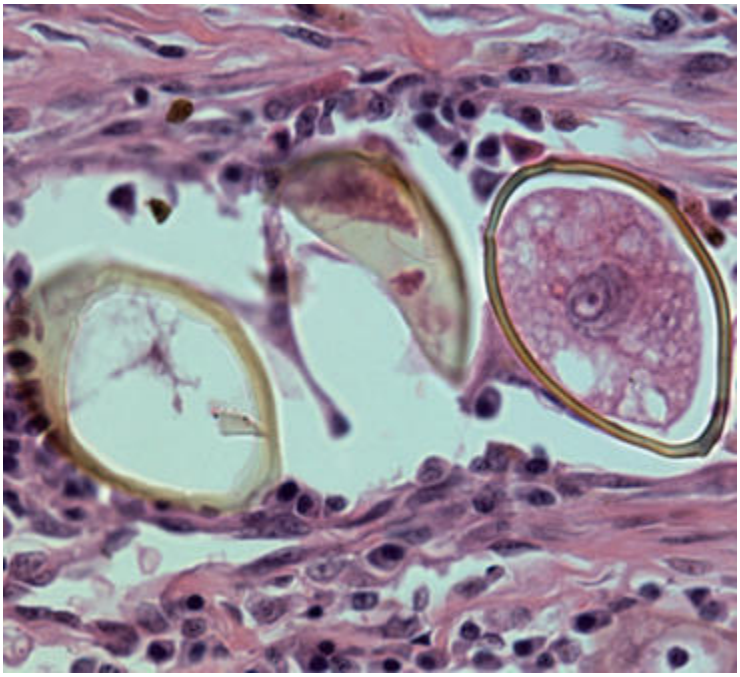

FIGURE 8-45 *Paragonimus kellicotti* eggs in the lung of a cat (×800); note the seated operculum of the shell and the central zygote in the egg on the right.

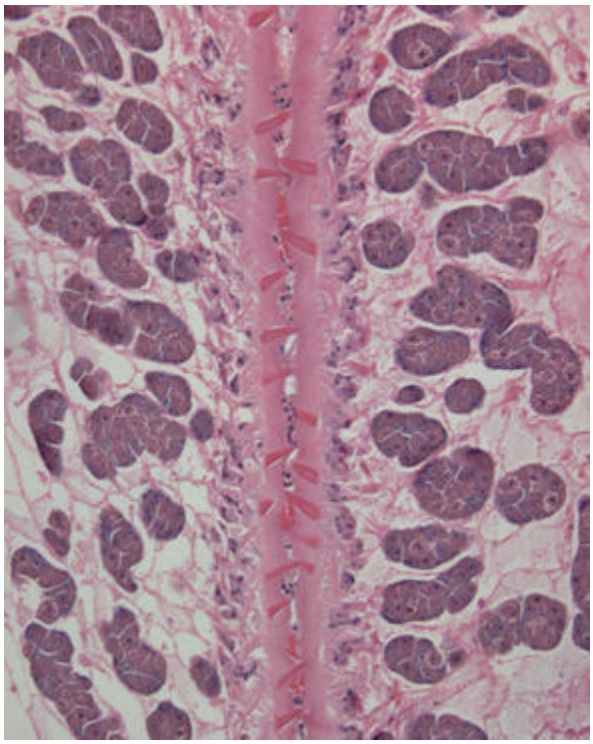

FIGURE 8-46 *Paragonimus kellicotti*, a pair of worms showing the spines on the cuticle and the vitelline glands (×800).

Although both trematodes and cestodes have suckers, the oral sucker of trematodes is connected to a gut (see Figure 8-40), whereas a gut is lacking in cestodes. The ventral sucker of trematodes is not connected to a gut. Sections through the uterus may contain eggs, which by their size, shape, and state of embryonic development may provide clues to the identity of the specimen (Figure 8-47). The arrangement of the sex organs and distribution of vitelline glands in the trematode body are a much-used taxonomic characteristic (see Figures 8-44 and 8-46). For example, these glands lie both dorsal and ventral to the gut in *Fasciola,* but all lie ventral to the gut in *Fascioloides*. The body form of some trematodes is quite distinctive. For example, heterophyids have small bodies with distinct spines and tend to be inserted in intestinal crypts (Figure 8-48), whereas diplostomatids are divided into a flattened forebody and a cylindric hindbody (Figure 8-49). In the dioecious schistosomatids, the slender female is enclosed in the gynecophoral groove of her stouter male partner (Figure 8-50). Adult trematodes lay eggs that can persist in the tissues for long times, causing granulomatous inflammatory reactions in tissues (Figures 8-51 and 8-52).

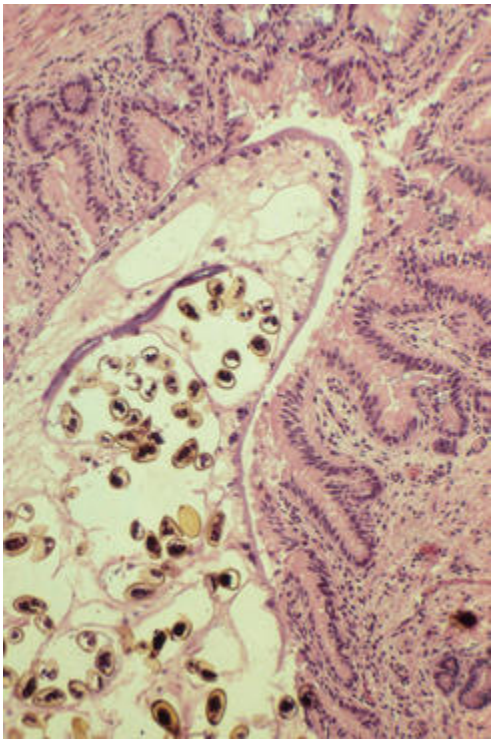

FIGURE 8-47 *Dicrocoelium dendriticum* in the bile duct of a sheep (×40). The typical eggs of this parasite can be seen within the uterus of the fluke.

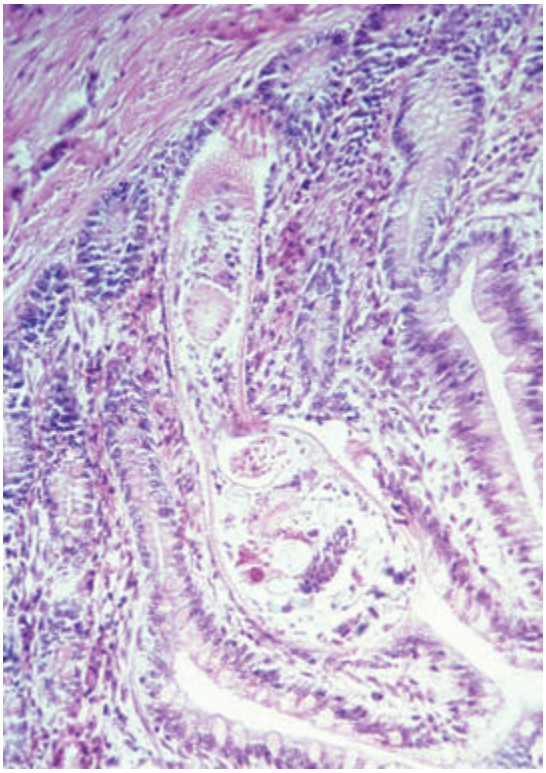

FIGURE 8-48 Heterophyid fluke in the intestine of a raccoon (×40); the spines on the anterior end are quite obvious, as is the relationship of the fluke to the intestinal mucosa.

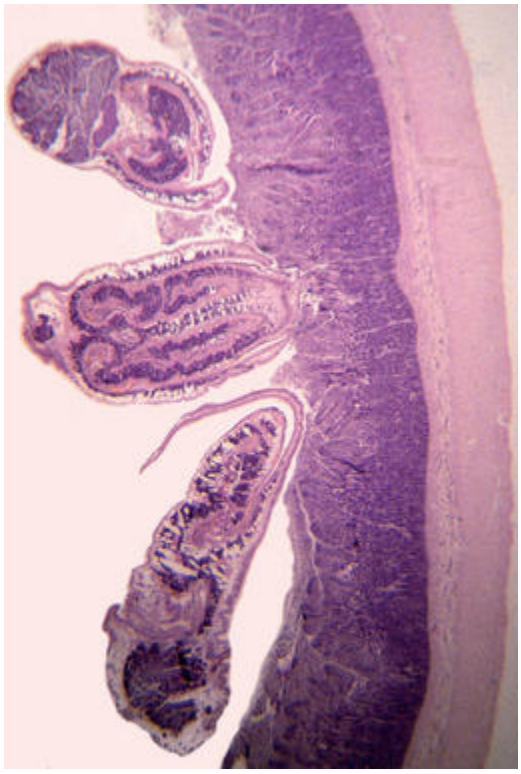

FIGURE 8-49 *Alaria* organisms in the small intestine of a dog (×10). *Alaria*, typical of the family Diplostomatidae, is divided into forebody and hindbody.

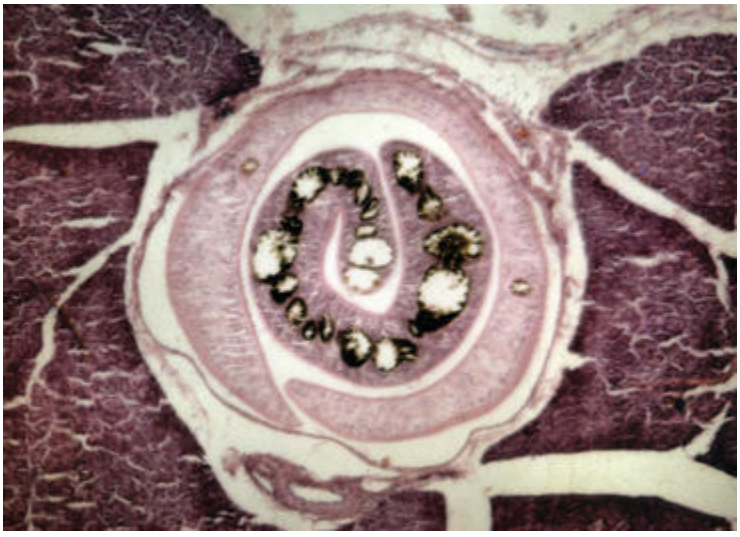

FIGURE 8-50 *Heterobilharzia americana* in a pancreatic vein of a beagle (×80). The smaller female is seen being held in the gynecophorous canal of the male.

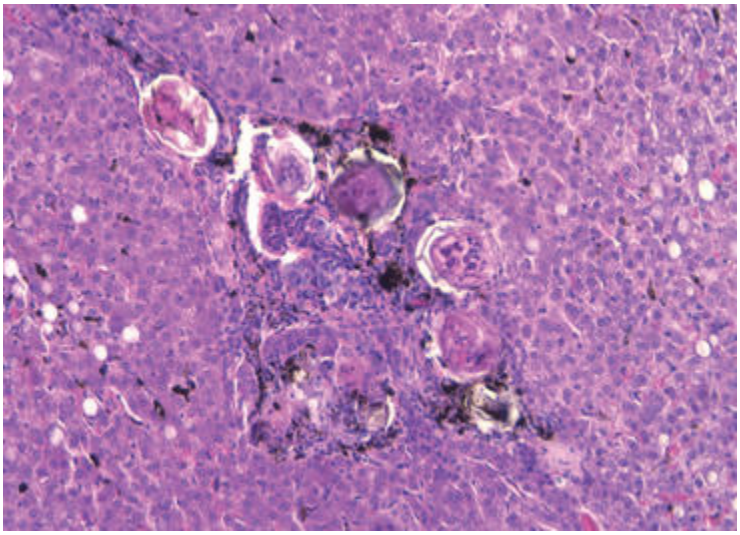

FIGURE 8-51 *Heterobilharzia americana* eggs in the liver of a naturally infected raccoon (×140).

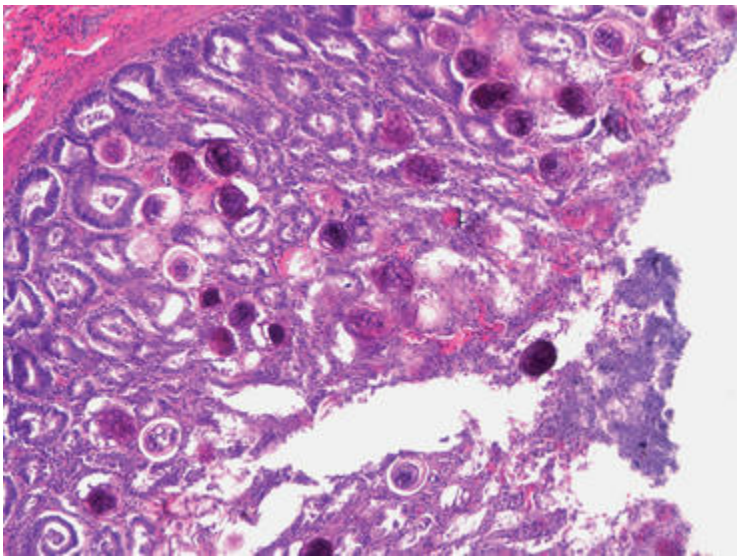

FIGURE 8-52 *Heterobilharzia americana* eggs in the intestine of a naturally infected raccoon (×58).

Larval trematodes, specifically mesocercariae and metacercariae, are not uncommonly seen in tissue sections. They are often rather

small; sometimes they are encountered singly, and other times numerous organisms are present. They are, like adult trematodes, composed of a solid parenchyma body with an outer tegument, but often little other internal structure is seen (Figure 8-53). Because they are immature stages, no reproductive structures are evident. No calcareous corpuscles are present, which helps distinguish them from larval tapeworms.

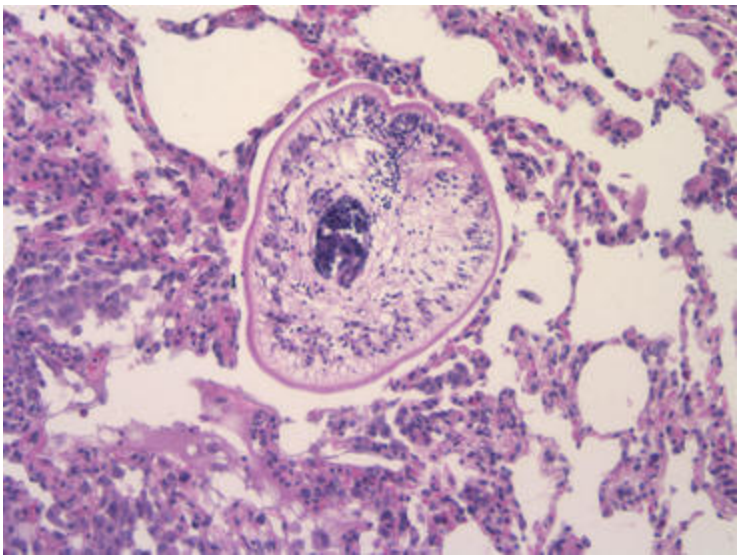

FIGURE 8-53 Mesocercariae of an unidentified trematode in the lung of a raccoon (×125).

Cestodes

Tapeworms seen in sections are most likely to be larval forms, although there is always a chance of seeing a section of a proglottid in an unusual location. Tapeworms, unlike trematodes, have no intestine in any stage of the larvae or adults. Like trematodes, the internal organs of cestodes are embedded in a parenchymatous matrix; there is no body cavity. There are two principal zones of nonstriated muscle fibers, **subtegumental** and **parenchymal**

(Figure 8-54). It is through the tegument that tapeworms absorb their nutrients from the host, and the syncytial surface, especially in adult forms, is thrown into numerous villuslike projections for this purpose. Within the tapeworm, the parenchymal zone divides the parenchyma into a **cortex** lying outside a longitudinal layer of fibers and a **medulla** lying within a transverse layer of muscle fibers; the medulla contains the osmoregulatory ducts and reproductive organs if these are present. **Calcareous corpuscles** are typical of cestode tissues and, especially in larvae, may provide the only evidence that the specimen is a tapeworm (Figures 8-55 and 8-56). Tapeworms are covered by a tegument formed by the cytoplasmic projections of epidermal cells, which appears in histologic sections as a thick, homogeneous noncellular external layer supported by a basal membrane.

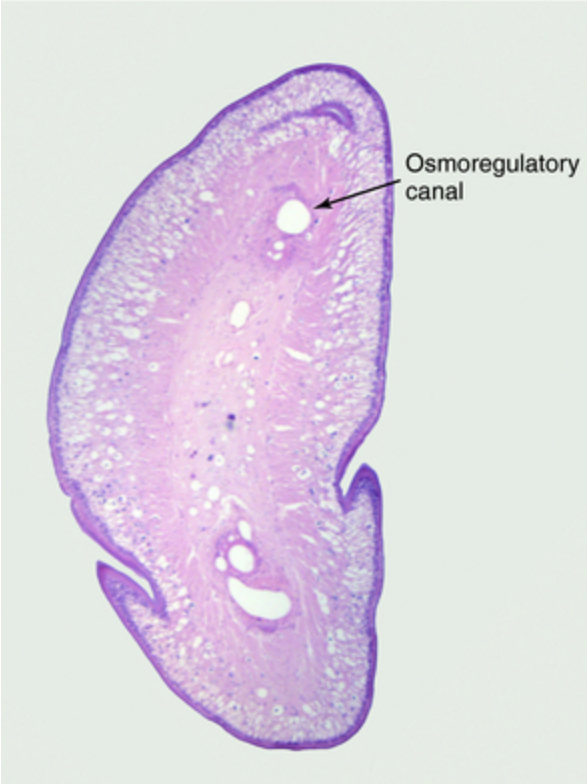

FIGURE 8-54 *Taenia taeniaeformis* strobilocercus from a vole (×20). Cestodes have a solid spongy body with no body cavity and no digestive system. The internal organs of cestodes are embedded in a loose matrix, a parenchymal meshwork of loosely arranged cells divided into distinct outer and inner portions by a system of longitudinal subtegumental and transverse parenchymal muscle fibers.

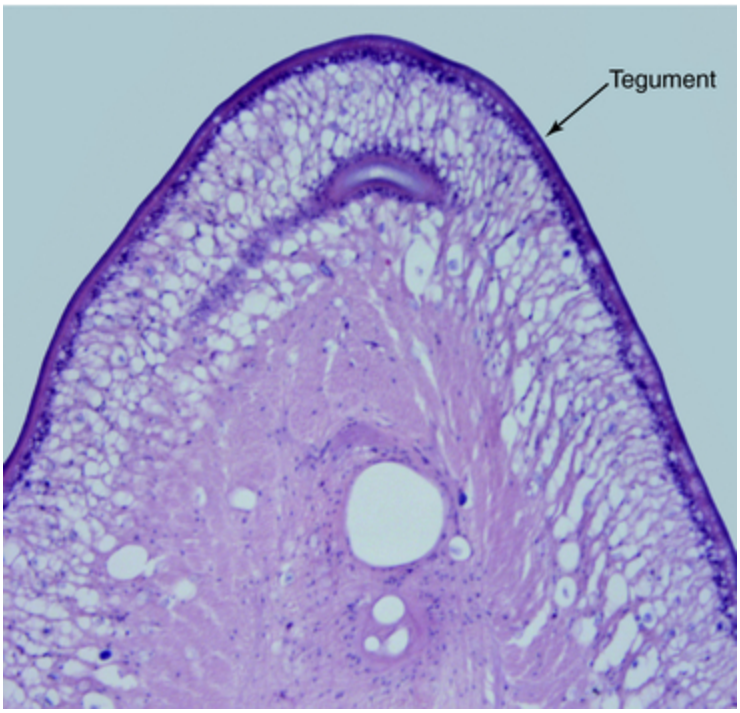

FIGURE 8-55 *Taenia taeniaeformis* strobilocercus at higher power showing the subtegumental and parenchymal muscle layers (×100).

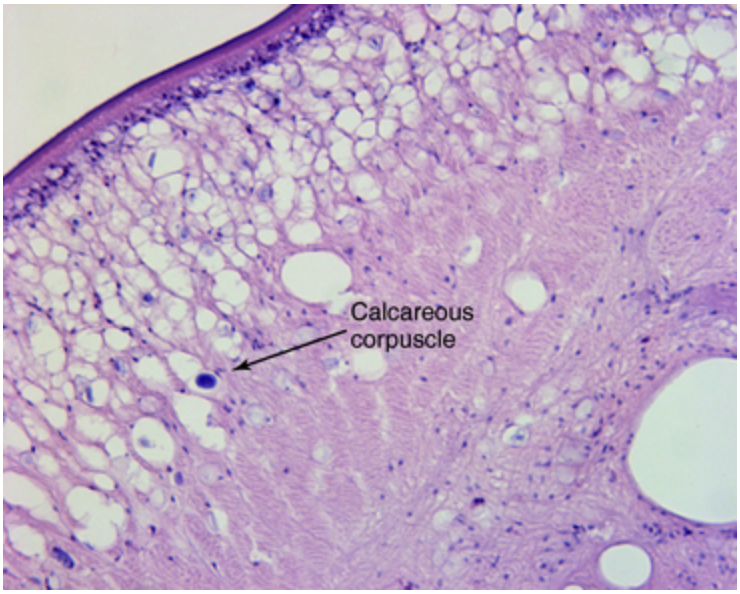

FIGURE 8-56 *Taenia taeniaeformis* strobilocercus at higher power showing calcareous corpuscles (×100).

The larva of a tapeworm that is found in a vertebrate host represents the precursor to the adult form and typically bears the holdfast or scolex of the adult in some rudimentary or embryonic form (Figures 8-57 to 8-68). After the host is ingested, much of the larva will be digested away and the small holdfast will attach to the intestinal mucosa and grow the adult strobila that contains all the varied sexual organs and associated structures. In veterinary medicine, although it often seems as though we are dealing with a huge number of types and forms of bothria, scolices, suckers, and hook shapes, the reality is that compared with the large numbers of tapeworm families with different forms of holdfasts occurring in a wide range of vertebrates (e.g., the Trypanorhyncha or the Tetraphyllidea), we are really dealing only with the few forms that occur in terrestrial mammals. If one is lucky, the sections are through the head of the larva, which aids greatly in being able to identify the parasite beyond the simple designation of larval

tapeworm based on body structure and the presence of calcareous corpuscles, but unfortunately much of the time one has only sections through the body of the larva, and then the diagnosis, based simply on morphology, almost always remains somewhat obtuse.

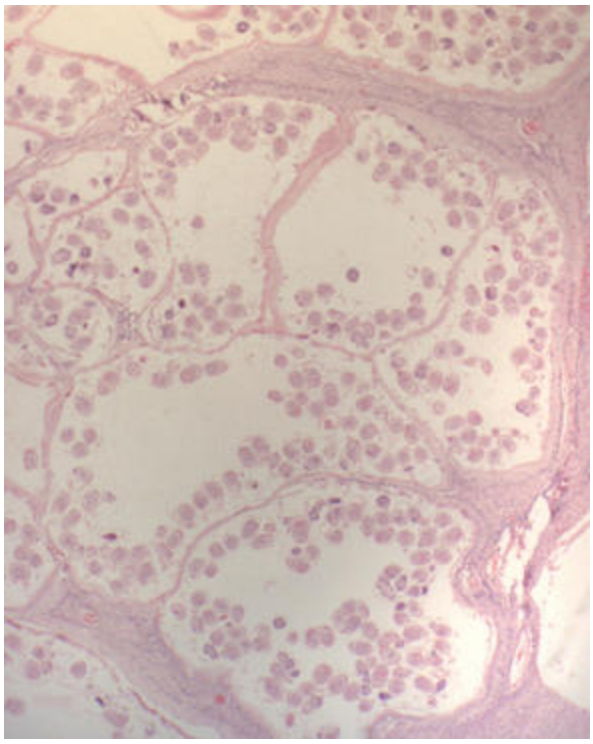

FIGURE 8-57 *Echinococcus multilocularis* alveolar hydatid (×10) showing the multiple germinal areas within the cyst.

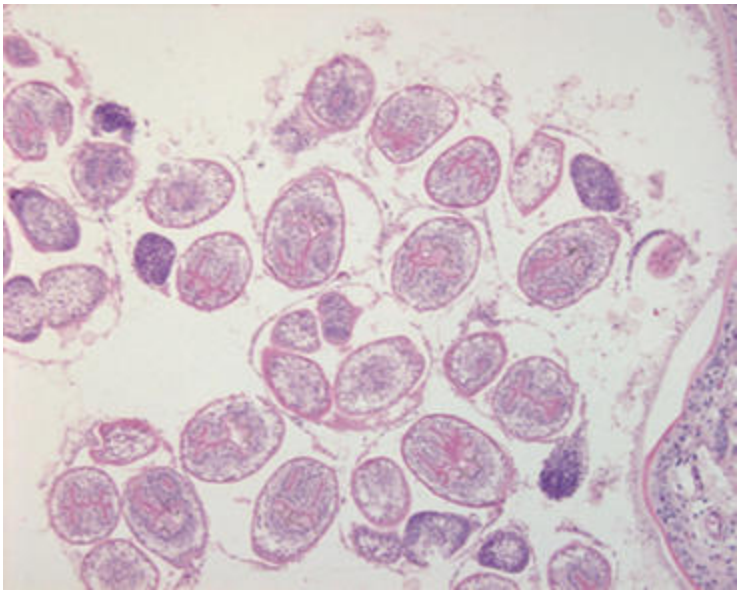

FIGURE 8-58 *Echinococcus multilocularis* alveolar hydatid (×100) showing a number of protoscolices.

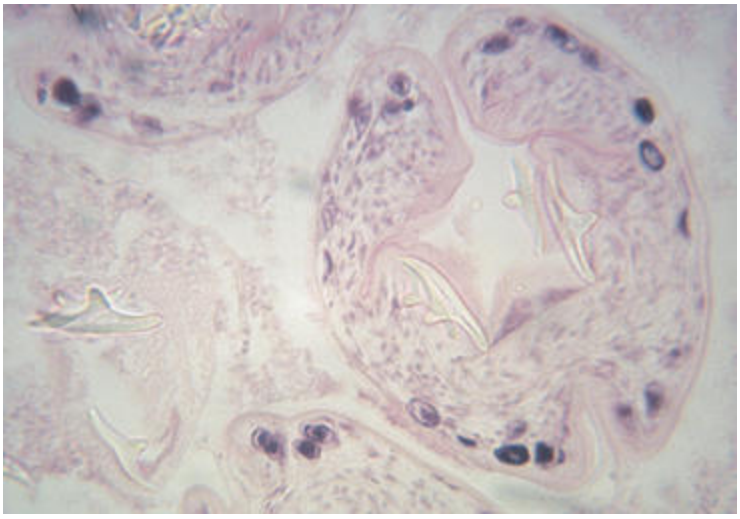

FIGURE 8-59 *Echinococcus vogeli* from an agouti rat *(Dasyprocta leporina)* in Brazil showing the typical clawhammer–shaped taeniid hooks on the protoscolex (×400).

Courtesy Dr. M. Dale Little.

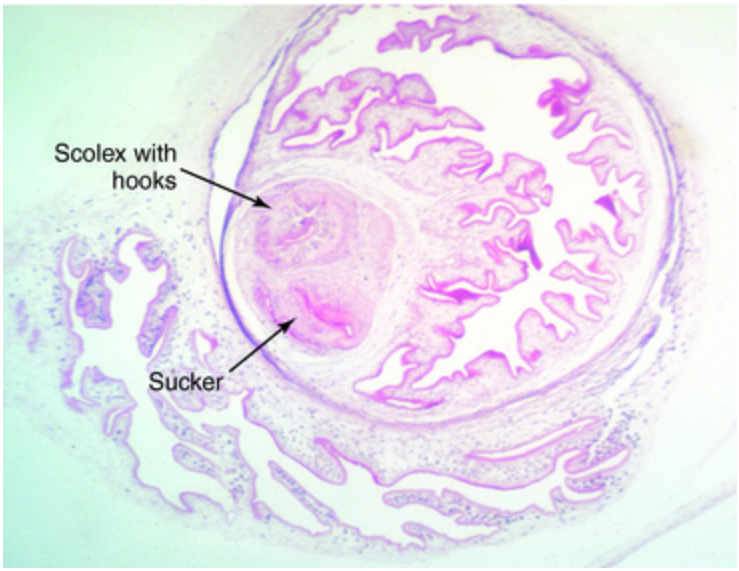

FIGURE 8-60 *Taenia solium* cysticercus in the brain of a dog that can be identified by the shapes and the measurement of the hooks on the scolex (×5).

Courtesy Dr. M. Dale Little.

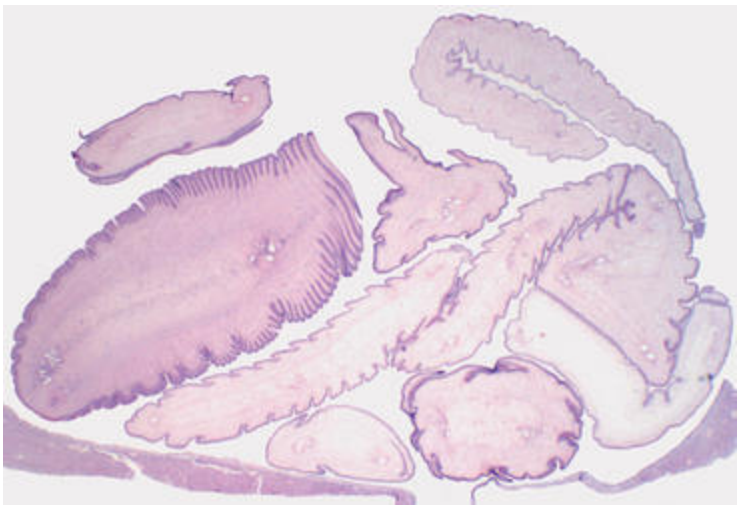

FIGURE 8-61 *Taenia taeniaeformis* strobilocercus encysted in the liver of a meadow vole (×5).

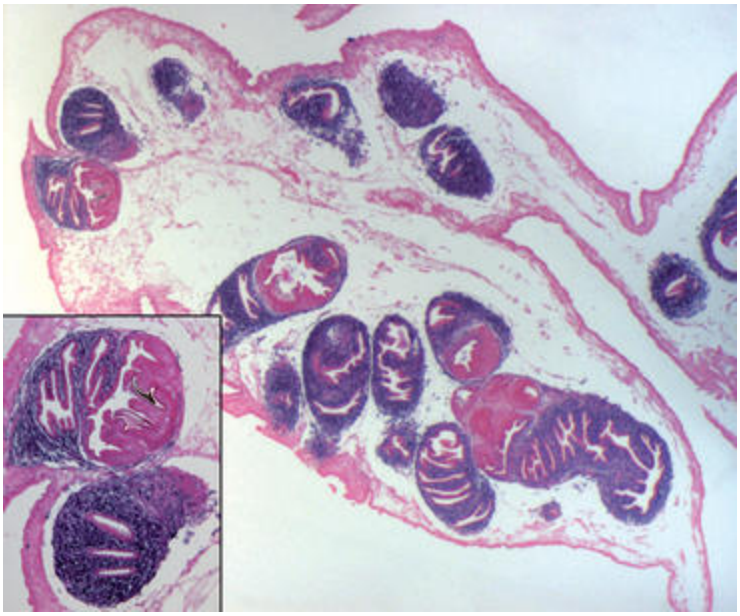

FIGURE 8-62 *Taenia multiceps* coenurus showing several scolices on a thin bladder wall (×45); enlarged view shows the hooks on one of the scolices (×250).

Courtesy Ward's Biological Supply.

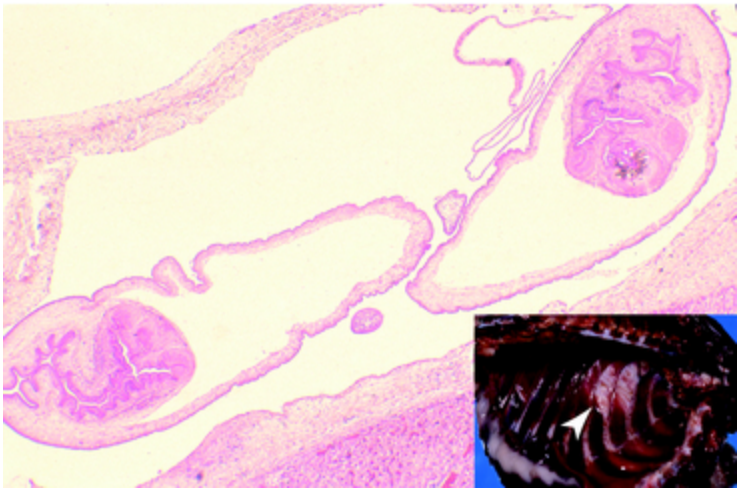

FIGURE 8-63 *Taenia crassiceps*. Cysticerci shown in a gross lesion in a naturally infected woodchuck. Sections through two cysticerci showing each with an inverted scolex (×250). This is an unusual cysticercus in that it proliferates by budding and may be found widely disseminated in various tissues of rodents. *Inset,* Gross specimen of cysticerci *(arrowhead)* in woodchuck at necropsy.

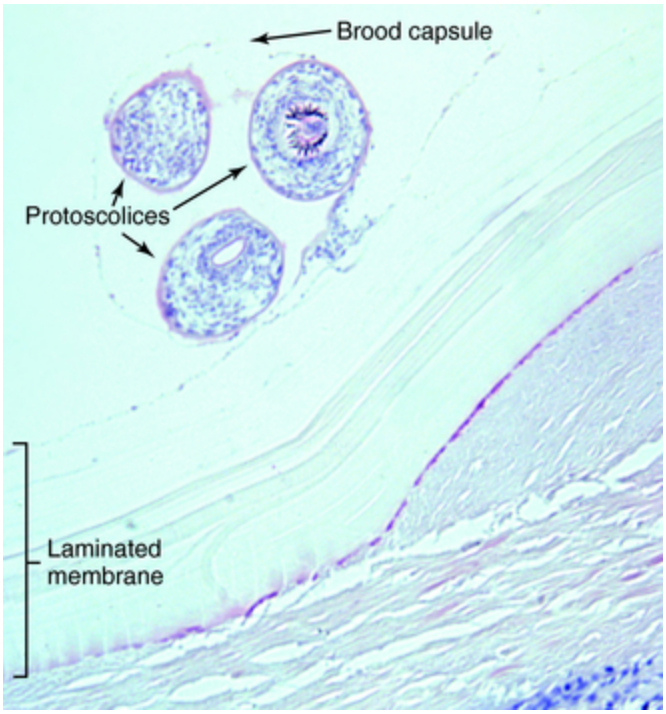

FIGURE 8-64 *Echinococcus granulosus* hydatid cyst (×200).

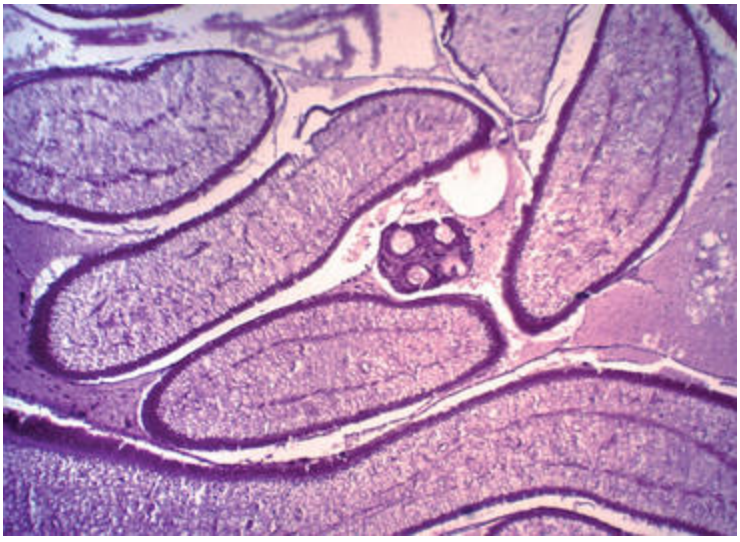

FIGURE 8-65 *Mesocestoides* tetrathyridium from the heart of a rice rat (*Oryzomys* sp.) from Colombia (×40); note the scolex without hooks in the middle of the image.

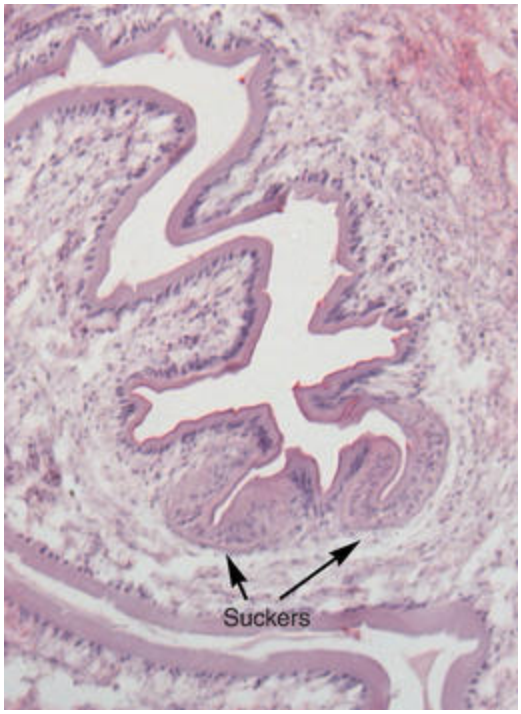

FIGURE 8-66 *Mesocestoides* tetrathyridium from the peritoneal cavity of a baboon (*Papio* sp.); region of scolex shows two suckers *(arrows)* (×200).

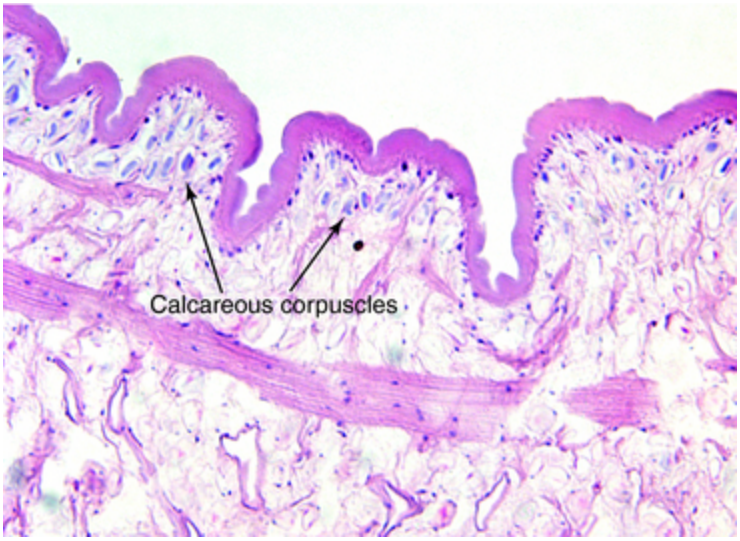

FIGURE 8-67 *Mesocestoides* tetrathyridium of Figure 8-66 parenchyma with large calcareous corpuscles *(arrows)* (×250).

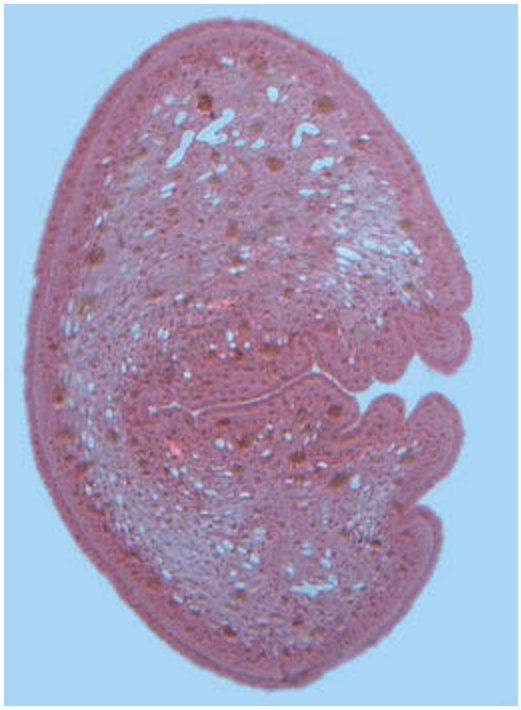

FIGURE 8-68 *Spirometra mansonoides* plerocercoid from the subcutaneous tissues of a mouse (×108).

Because veterinary medicine until very recently focused almost exclusively on the common domestic mammals used as food and human companions, the most common tapeworm larvae seen are those of the taeniid tapeworms that have a mammalian final host and a mammalian intermediate host. The typical taeniid metacestode larvae are the **cysticercus** (see Figure 8-60), the **coenurus** (see Figure 8-62), the **strobilocercus** (see Figures 8-54 to 8-56 and 8-61), the **unilocular hydatid** (see Figures 8-59 and 8-64), and the **alveolar hydatid** (see Figures 8-57 and 8-58). For information on hosts and site specificity, refer to the appropriate host-organ list and details in the previous chapters. If the histologic section includes only the bladder wall of the larvae, there will be little more than calcareous corpuscles to identify it as cestode tissue. A section through the scolex of the larvae that includes the typical

claw-hammer–shaped hooks of this group (see Figure 8-59) identifies the specimen as a taeniid. *Taenia saginata*, the "beef tapeworm" of man, forms an exception in having hooks neither in the larval nor the adult stages. Often the scolex of the tapeworm is inverted in the body and will not evert until the larva is ingested by the final host.

Tentative identification of species of taeniid larvae may be based on their host and site specificity. For example, a cysticercus attached to the peritoneal membranes of a cottontail rabbit is very probably the larva of *Taenia pisiformis*, whereas a cysticercus on the peritoneal membranes of a ruminant of pig is most likely the larva of *Taenia hydatigena*. Further evidence is provided by hook length measurements if both long and short hooks happen to lie in the plane of section or if they can be isolated from the wet tissues. Verster (1969) may be consulted for hook-length data. In the coenurus there is more than one scolex connected to the same bladder wall. *Taenia crassiceps* presents a source of confusion in this regard by forming many cysticerci by budding. These all lie within the same host cysts but are not attached to a common gladder wall (see Figure 8-63). Strobilocerci of *Taenia taeniaeformis* are cysticerci that have precociously begun to elongate and segment as larvae and are found in the liver of rodents (see Figures 8-54 to 8-56 and 8-61).

Hydatid cysts manifest expansive growth and have thick, laminated membranes separating the germinative layer, which bears sessile small scolices (termed *protoscolices*) or brood capsules, from the surrounding host connective tissue capsule. In "sterile hydatid cysts" (cysts without protoscolices), the laminated membrane is the only diagnostic characteristic available. Alveolar hydatids have

much thinner laminated membranes, and their manner of growth is invasive instead of expansive.

The remaining tapeworm larvae that are typically found in the tissues in sections are solid-bodied wormlike threads or ribbons (that can be very long) that course through the tissues or peritoneal cavities of the host. These two larvae are the **tetrathyridium** of the Mesocestoididae (see Figures 8-65 to 8-67) and the **plerocercoid** (or sparganum) of the pseudophyllidean tapeworms (see Figure 8-68). Plerocercoids of *Spirometra* organisms (see Figure 8-67) are ribbonlike larvae that are unsegmented and undifferentiated. They have no bladder, and the scolex is not always developed, so no sections through bothria may be forthcoming no matter how many serial sections are prepared. Observation of calcareous corpuscles in a parenchymatous matrix without evidence of other structures may be the only feature on which to identify a plerocercoid. Tetrathyridia of *Mesocestoides* organisms differ from plerocercoids in that they possess four suckers with no hooks (see Figure 8-66), and their calcareous corpuscles tend to be large but not as dense as those of other larvae (see Figure 8-67). Tetrathyridia can undergo massive asexual proliferation in the intermediate host (often seen in dogs), forming thousands of organisms that are atypical perhaps owing to the rapid multiplication and very difficult to identify as anything other than tapeworm tissue.

Nematodes

Living nematodes are pseudocoelomic animals that have a fluid-filled body. The body externally is covered with a cuticle composed of collagen, and movement occurs by muscles cells in quadrants

along the body wall working in apposition to the cuticle, which allows the worms to move sinusoidally. Nematodes typically have a mouth and an anus connected by a digestive tract. In sections the worms typically appear round and to have the internal organs floating within the pseudocoelomic cavity. The genital primordium appears in larvae, but it tends not to grow to any extent until the worms reach the fourth larval stage. One feature of worms becoming adults after the fourth and final molt of their development is that the vulva of the female finally opens through the cuticle (becomes patent).

In sections (Figures 8-69 and 8-70) the nematode is in most cases divided into two dorsolateral and two ventrolateral **quadrants** by the **hypodermis.** There is a syncytial layer below the cuticle that secretes the cuticle. The hypodermis tends to extend into the body of the worm in dorsal, ventral, and lateral cords, which is what divides the body into its four apparent sections. The **nervous system** of a nematode consists of a major nervous ganglion that typically encircles the esophagus and that has major sets of fibers running through the ventral and dorsal hypodermal cords. Nematodes also have an **excretory-secretory system** that usually empties through an **excretory pore** that is located on the ventral side of the worm near the level of the nerve ring or more anteriorly. The excretory system may have columns that extend posteriorly in the form of arms that extend into each of the lateral cords. In some adenophorean nematodes, there may be cords found in addition to the typical four. Also, in the Trichinelloidea the hypodermis tends to be organized into **bacillary bands** rather than lateral cords, with one in *Trichuris*, two in *Trichinella*, and three or four typical in the

various capillarids. From the bacillary bands, pores can be seen extending from the band through the cuticle.

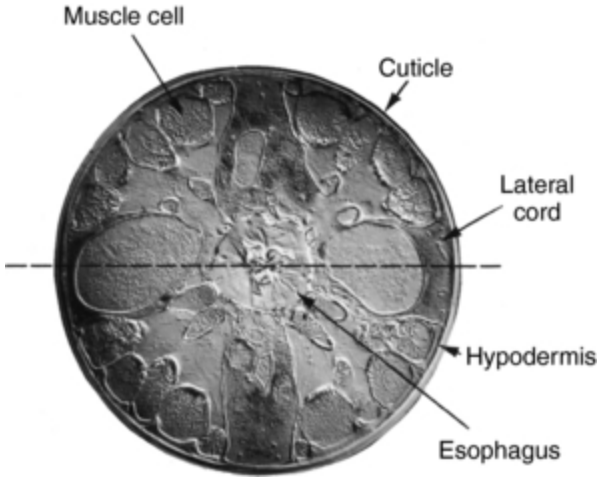

FIGURE 8-69 *Strongylus vulgaris*. Cross-section through the esophageal region of *Strongylus vulgaris* showing the division of somatic musculature into dorsal and ventral fields by the lateral cords. In this particular body region of *S. vulgaris*, the dorsal and ventral cords are exceptionally well developed, and these anatomically separate their respective muscle fields into halves. However, functional separation, expressed in terms of coordinated muscular activity, remains predominantly dorsoventral (×62).

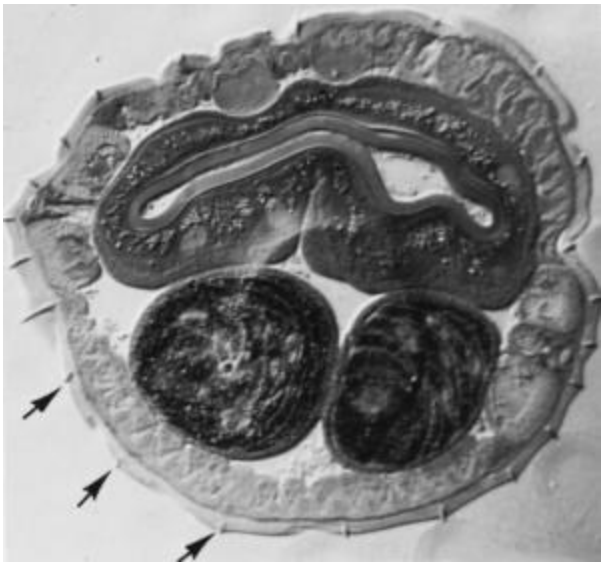

FIGURE 8-70 *Haemonchus contortus* in cross-section at the level of the intestine (×140). The entire circumference of the cuticle is marked by longitudinal ridges *(arrows)*, and the prominent brush border on the luminal surface of the gut is evident.

The **cuticle** covers the external surface of the worm, and, to varying degrees in different groups, the lining of the esophagus, the posterior portion of the digestive tract, the vagina, and the opening of the excretory system. The cuticle may appear layered in histologic sections, especially in forms with thicker cuticles. The cuticle may have major modifications above the lateral hypodermal cord where it forms large wings of cuticle called *cephalic alae* (when only on the head), which may or may not be continuous with **lateral alae** running the length of the worm. Some forms, mainly the Trichostrongyloidea, have numerous additional longitudinal ridges running the length of the body. Adult worms are liable to have all sorts of modifications on the anterior end that are usually less apparent in the larvae; these consist of lips, large buccal capsules, teeth, and so on. The cuticle may also have spines, striations, bosses (thickened bumps), pores (in some Adenophorea), and so on. In adult male nematodes with spicules, the spicules are composed of sclerotized cuticle and have a myriad of forms and shapes with some being spined.

The **muscle cells** of the body that provide locomotion lie along the body underneath the hypodermal layer (Figure 8-71). These muscle cells have their long axis oriented along the length of the worm and vary in number and shape, and the muscle cells of nematodes are unlike those of many other organisms because the muscles send processes to the dorsal and ventral nerve cords rather than having the nerves extending to the muscle cells. When a section has only a few muscle cells (about three to five) per quadrant, this is termed **meromyarian,** and when there are more

cells the worms are described as being **polymyarian.** Muscle cells are also described as to their appearance. If the cells have their contractile elements all oppressed to the hypodermis with an empty cell body above them, they are termed **platymyarian.** If the cells have contractile portions that extend up the side of the cell body, they are called **coelomyarian**. Typically, cells that are platymyarian are few in number per quadrant, hence *meromyarian*, whereas coelomyarian muscle cells tend to be numerous per quadrant and polymyarian. The Ascaridida and Spirurida tend to have polymyarian, coelomyarian muscles; the Rhabditida, Oxyurida, and Strongylida tend to have meromyarian, platymyarian muscles. The Adenophorea are varied.

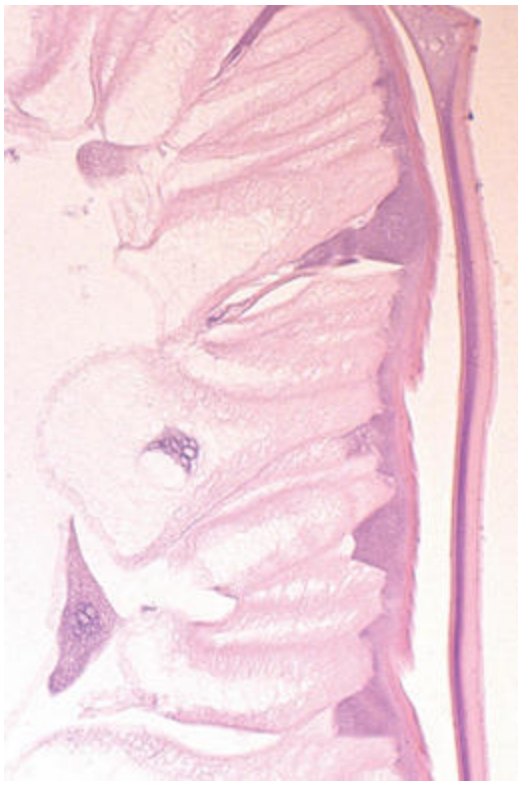

FIGURE 8-71 *Eustrongyloides* sp. (×170) from a great blue heron. Each somatic muscle cell is composed of a basement membrane adjacent to the hypodermis, contractile muscle fibers, and a delicate sarcoplasmic portion containing the nucleus. The

coelomyarian muscle cells have a darkly staining contractile portion extending up the lateral sides of the muscle cell, which gives the cell a cylindric appearance, and an abundant, noncontractile cytoplasmic portion that appears to be empty with most stains.

The digestive tract of the nematodes consists of an esophagus, an intestine, and a rectum (in male nematodes this is actually a cloaca, but the distinction is almost never used). Many of the characteristics of the digestive tract of the adult nematodes are also present in their respective larvae stages. This can be a very useful asset in diagnosis using histologic sections.

The **esophagus** tends to be divided into a dorsal and two subventral portions by a triradiate lumen that is typically lined with cuticle. There are muscles within the esophagus that pull on the lumen to open the esophagus for feeding. Within the different sections there may also be various glandular elements. The esophagus may be muscular throughout its length or may have an anterior portion that is muscular and a posterior portion that is glandular. The Rhabditida have a muscular esophagus typically divided into a distinct corpus, isthmus, and bulbus. The Oxyurida have a muscular esophagus with a large valved bulb before the junction with the intestine. The Strongylida for the most part have a simple muscular esophagus. The Ascaridida have an esophagus that may have a large glandular area, the ventriculus, at its base, and they may also have ventricular ceca. The Spirurida typically have an esophagus that is muscular anteriorly and glandular posteriorly. The Trichinelloidea tend to have a stichosome esophagus (described later), whereas the Dioctophymatoidea have a muscular esophagus with many large branching glands.

The **intestine** of nematodes is fairly simple in all nematodes; it is composed of a single layer of columnar cells that have a microvillous border. In the Strongylida, the intestine is lined with a very few cells (**oligocytous**) that are syncytial and polynucleate, and it will often appear that only two such cells line the lumen at any given section. In the Rhabditida, the intestine appears lined by only two cells at each level. The Oxyurida, Ascaridida, and Spirurida have many cells **(polycytous)** to myriad cells **(myriocytous)** lining the intestinal lumen; these cells tend to be uninucleate for the most part but can vary markedly in height around the lumen, especially within the Spirurida. In the Adenophorea, those we are concerned with typically have a polycytous intestine with uninucleate cells. In most of the nematodes we will see in section, the anus is subterminal, i.e., there is a tail beyond the anus. The only group where this is not the case is the Adenophorea, in which the anus is terminal.

Rhabditida

Pelodera strongyloides larvae are found in the hair follicles of dogs, swine, and cattle (Figure 8-72). They have double lateral alae.

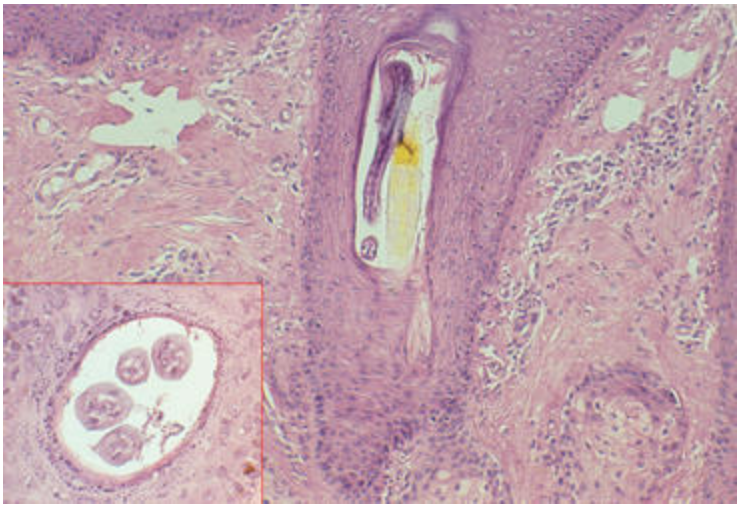

FIGURE 8-72 *Rhabditis (Pelodera) strongyloides* in a hair follicle of a dog (×130). The inset is an enlarged view that shows the double lateral alae (×400).

Halicephalobus gingivalis is another normal saprophytic nematode that has been reported to invade mammalian tissue and disseminate to various sites, most notably the brain (Figure 8-73), with fatal outcome. The infection has been reported widely in horses. These worms are small—adult females are 250 to 450 mm in length by no more than about 25 mm in diameter—and only females and larvae have been reported in tissues, suggesting that they are parthenogenetic. Distinctive features in section, in addition to the small size and location, include the presence of a rhabditoid esophagus, a single genital tube, and a thin body wall in which the cuticle, hypodermis, and muscle layers cannot be distinctly separated.

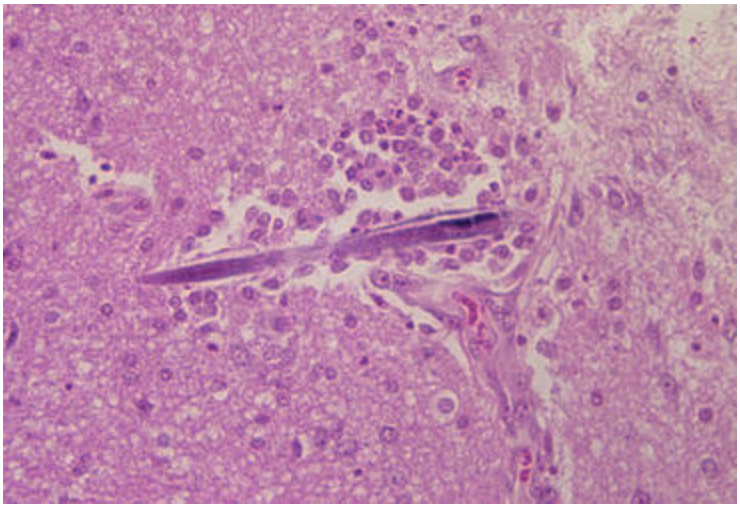

FIGURE 8-73 *Halicephalobus (Micronema) gingivalis* in brain of horse (×200).

Strongyloides is a group of parthenogenetic species, and only female worms and larvae are found in the tissues. The adult parasitic female worms of this species are found deep in the mucous membrane of the small intestine (Figure 8-74) and are characterized by meromyarian and platymyarian muscles, a simple intestine composed of only two cells, and the eggs in utero, which are few in number, lined up in single rows and often with developing larvae. *Strongyloides* larvae (see Figure 7-28) have double lateral alae.

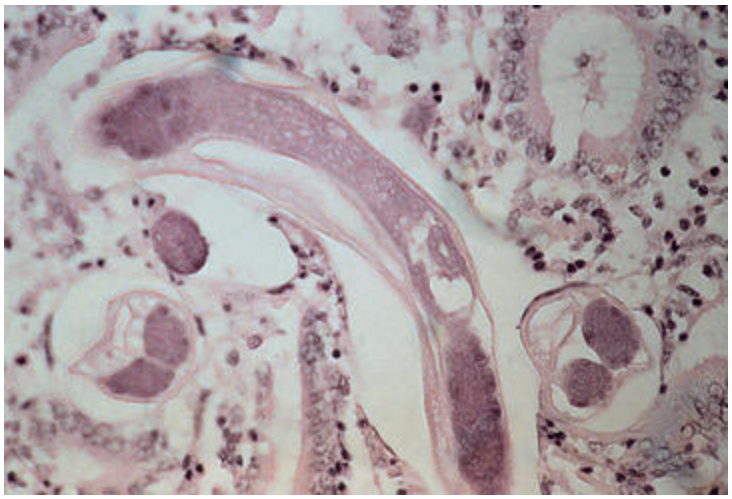

FIGURE 8-74 *Strongyloides westeri* in the mucosa of the small intestine of a horse (×250).

Strongylida

There are four superfamilies: Trichostrongyloidea, Strongyloidea, Ancylostomatoidea, and Metastrongyloidea.

Trichostrongyloidea

The adults of this group tend to be small worms that typically inhabit the stomach or small intestine. In cross-section they are characterized by the small number of platymyarian muscle cells and an intestine composed of few cells, often with prominent nuclei and a microvillus border. Most trichostrongyles, with the exception of *Trichostrongylus* specimens, have marked longitudinal ridges on the surface of the cuticle (Figure 8-75). Fourth-stage larvae are found throughout the mucosa of the stomach and intestine of ruminants and a wide range of other hosts. *Trichostrongylus axei* fourth-stage larvae and juvenile adults are found between the basement membrane and epithelial cells of the abomasal mucosa. *Ostertagia* fourth-stage larvae and juvenile adults are found in dilated gastric glands of the abomasum (Figures 8-76 and 8-77).

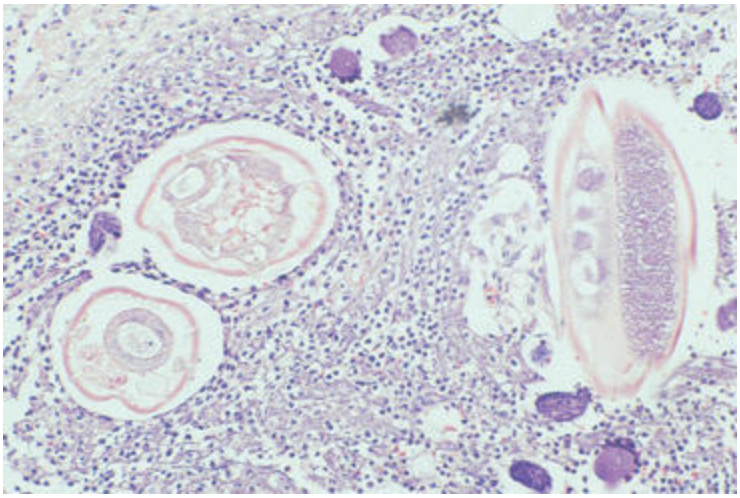

FIGURE 8-75 *Molineus barbatus* in the small intestine of a *Cebus* monkey (×200).

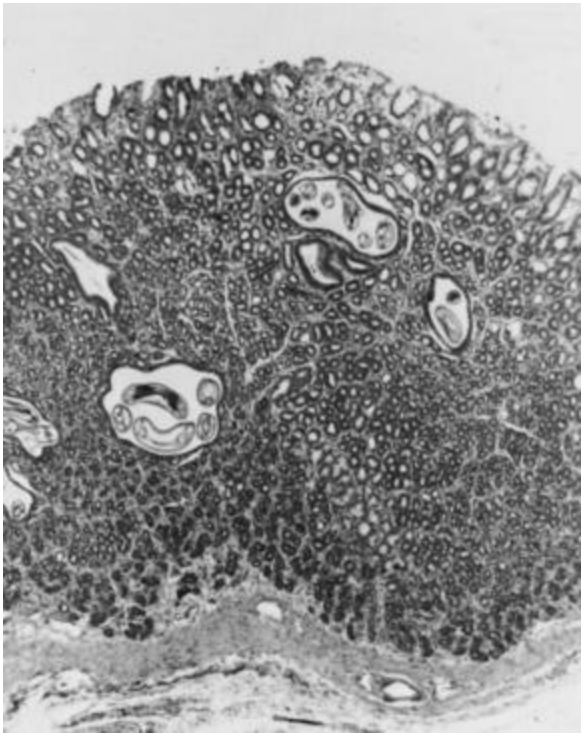

FIGURE 8-76 *Ostertagia ostertagi* in the abomasal mucosa of a heifer (×25).

Courtesy Dr. Lois Roth.

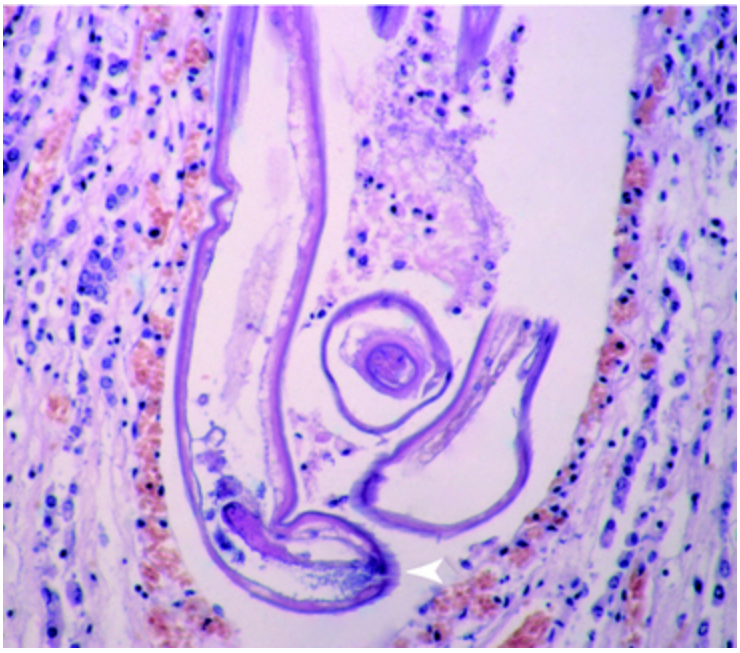

FIGURE 8-77 *Ostertagia ostertagi* in the abomasal mucosa (×200) showing the longitudinal cuticular ridges typical *(arrowhead)* of the superfamily Trichostrongyloidea.

Strongyloidea

Most adult strongyles inhabit the intestinal tract and are larger than the trichostrongyles. In section they exhibit characteristic features, including platymyarian muscles and the typical strongyle intestine. The cuticle is not adorned with ridges. In the strongyles the presence of a large buccal capsule and specialized mouthparts is of great taxonomic value, but these features are often not seen in tissue sections.

Some of the larval stages of strongyles are spent in tissues other than the gut, whereas some form nodules in the intestinal wall. *Strongylus vulgaris*, *Strongylus edentatus*, and *Strongylus equinus* migrate extensively and sometimes erratically in the horse. *S. edentatus* tends to migrate retroperitoneally, and it is characterized by a thick, multilayered cuticle (Figure 8-78). *S. equinus* immature

adults are frequently found in the pancreas; sections through the buccal capsule reveal the presence of teeth at their base (Figures 8-79 to 8-82).

FIGURE 8-78 *Strongylus edentatus*. Cross-section showing the thick, multilayered cuticle of this species (×220).

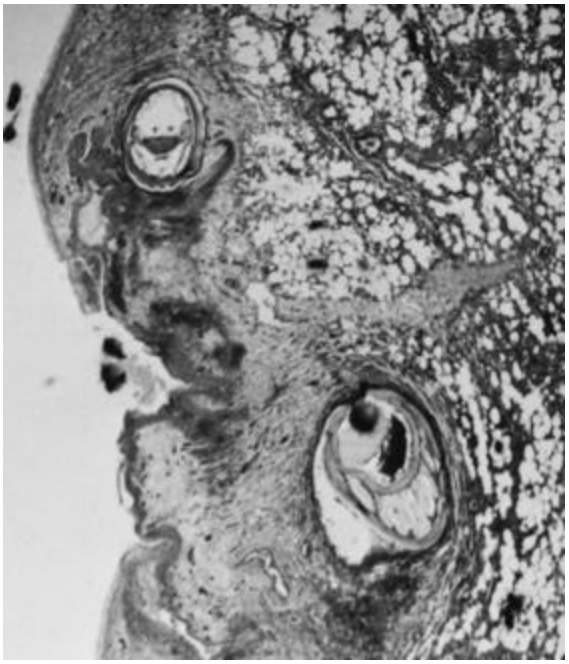

FIGURE 8-79 *Strongylus edentatus* immature male in the lung of a horse (×15). Two sections of worm are visible. The upper is a cross-section near the caudal end of the worm (see also Figure 8-77), and the lower is an oblique section through the buccal capsule (see also Figure 8-78).

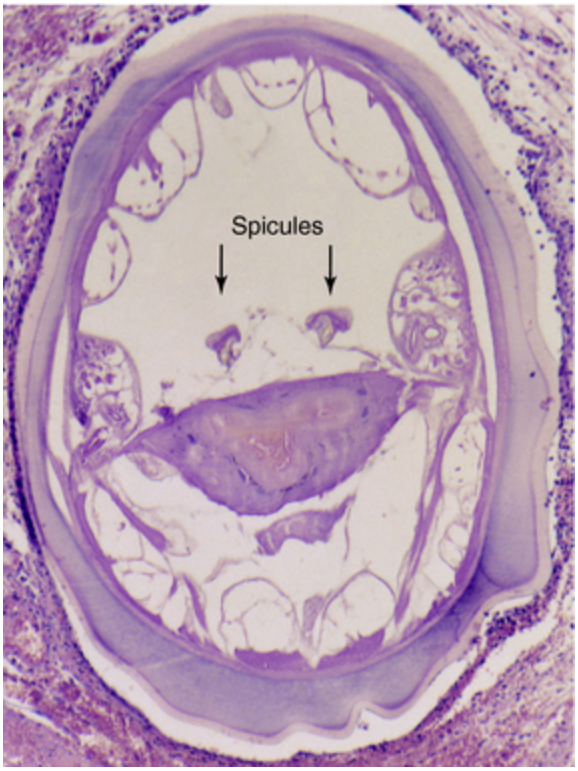

FIGURE 8-80 *Strongylus edentatus*. Higher magnification of Figure 8-79, showing a section through the caudal end of the worm (×100). Note the thick, multilayered cuticle, spicules, and prominent lateral cords. The cytoplasm of the meromyarian-platymyarian muscle cells was lost in histologic processing (see also Figure 8-75).

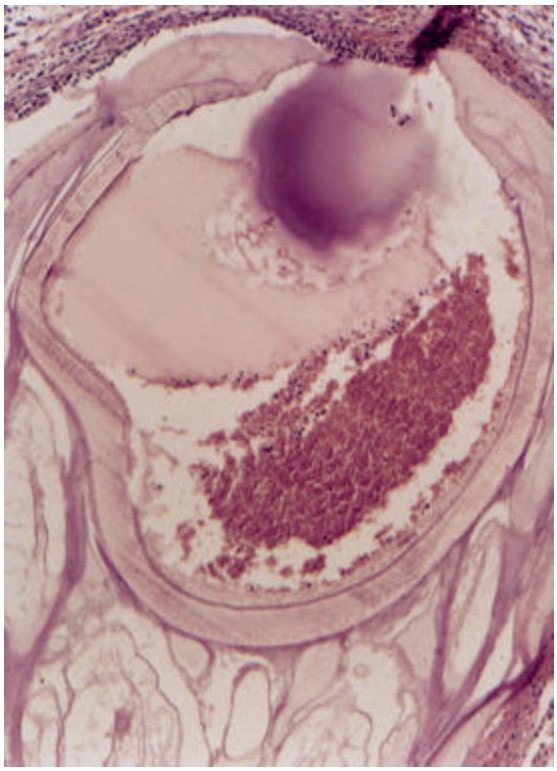

FIGURE 8-81 *Strongylus edentatus*. Higher magnification of Figure 8-79, showing the buccal capsule (×100).

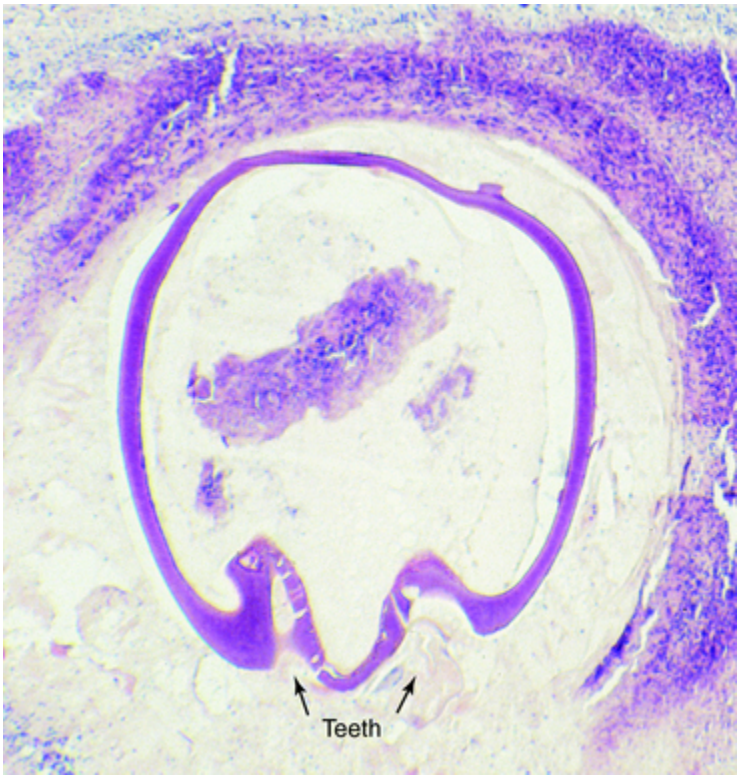

FIGURE 8-82 *Strongylus equinus* immature adult worm in the pancreas of a horse (×100). Although moribund, the teeth *(arrows)* in the base of the buccal capsule are still readily visible and distinguish this species from *S. edentatus*.

Oesophagostomum and related worms are common parasites of livestock and monkeys and have worldwide distribution. They are often referred to as *nodular worms* because developing larvae produce remarkable nodular abscesses in the intestinal wall of the vertebrate host during development leading to the adult stage. Most often seen in section as developing worms inside these nodules (Figures 8-83 and 8-84), the larvae have a relatively thick but smooth cuticle, prominent lateral chords, and muscle cells that are platymyarian and meromyarian, typically with only a small number of muscle cells per quadrant. The gut is composed of a small number of multinucleate cells with a conspicuous microvillous (brush) border.

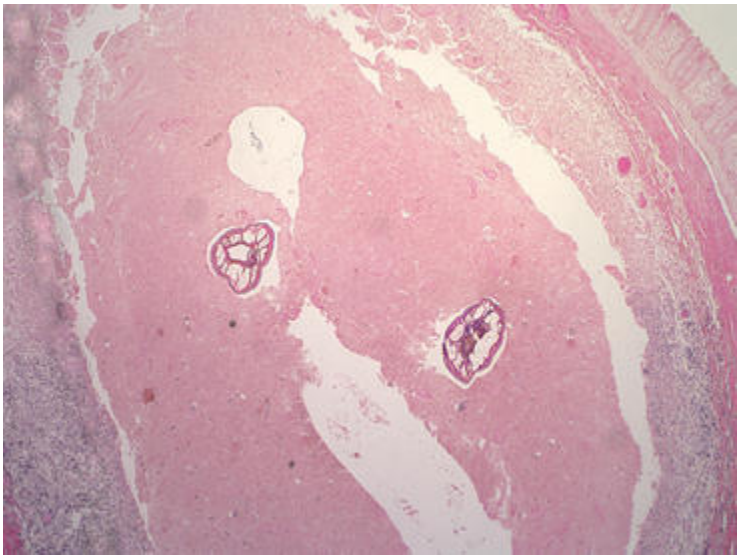

FIGURE 8-83 *Oesophagostomum* sp. Section through a nodule in wall of the large intestine of cynomolgus monkey containing two sections of *Oesophagostomum* larva (×25).

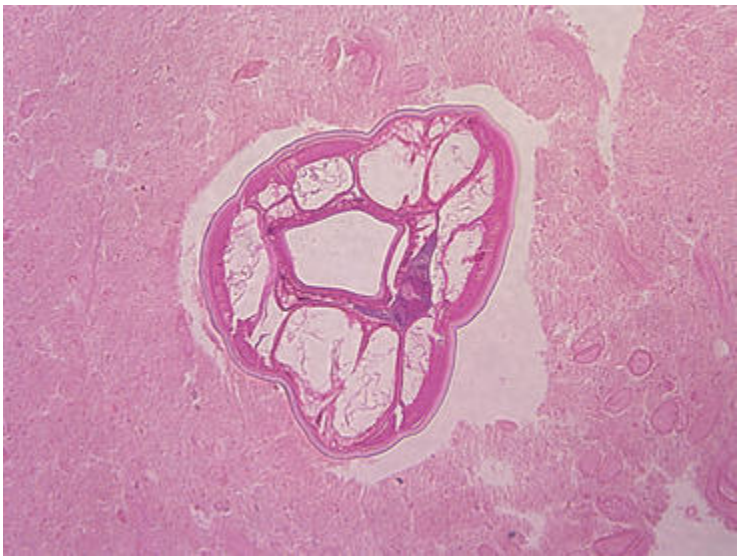

FIGURE 8-84 *Oesophagostomum* sp. Higher magnification of Figure 8-83 showing a section through *Oesophagostomum* larva (×120). Note the small number of platymyarian muscle cells and a prominent brush boarder on the epithelial cells of the gut.

Ancylostomatoidea

The Ancylostomatoidea, typically referred to as *hookworms*, inhabits the gut as adults and have typical strongyle features in section (Figure 8-85). The larvae of hookworms are relatively small, usually only 14 to 16 mm in diameter, and have double lateral alae (Figure 8-86).

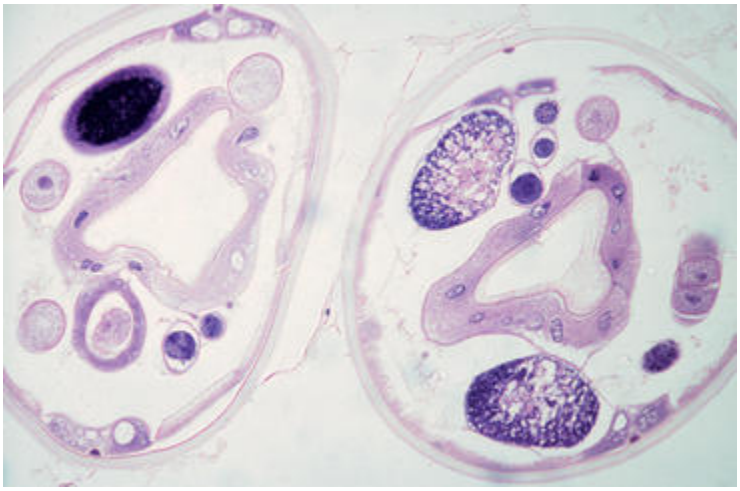

FIGURE 8-85 *Ancylostoma caninum* adult females from the intestine of a dog show the platymyarian muscles and the small number of syncytial intestinal cells (×80).

Courtesy Dr. M. Dale Little.

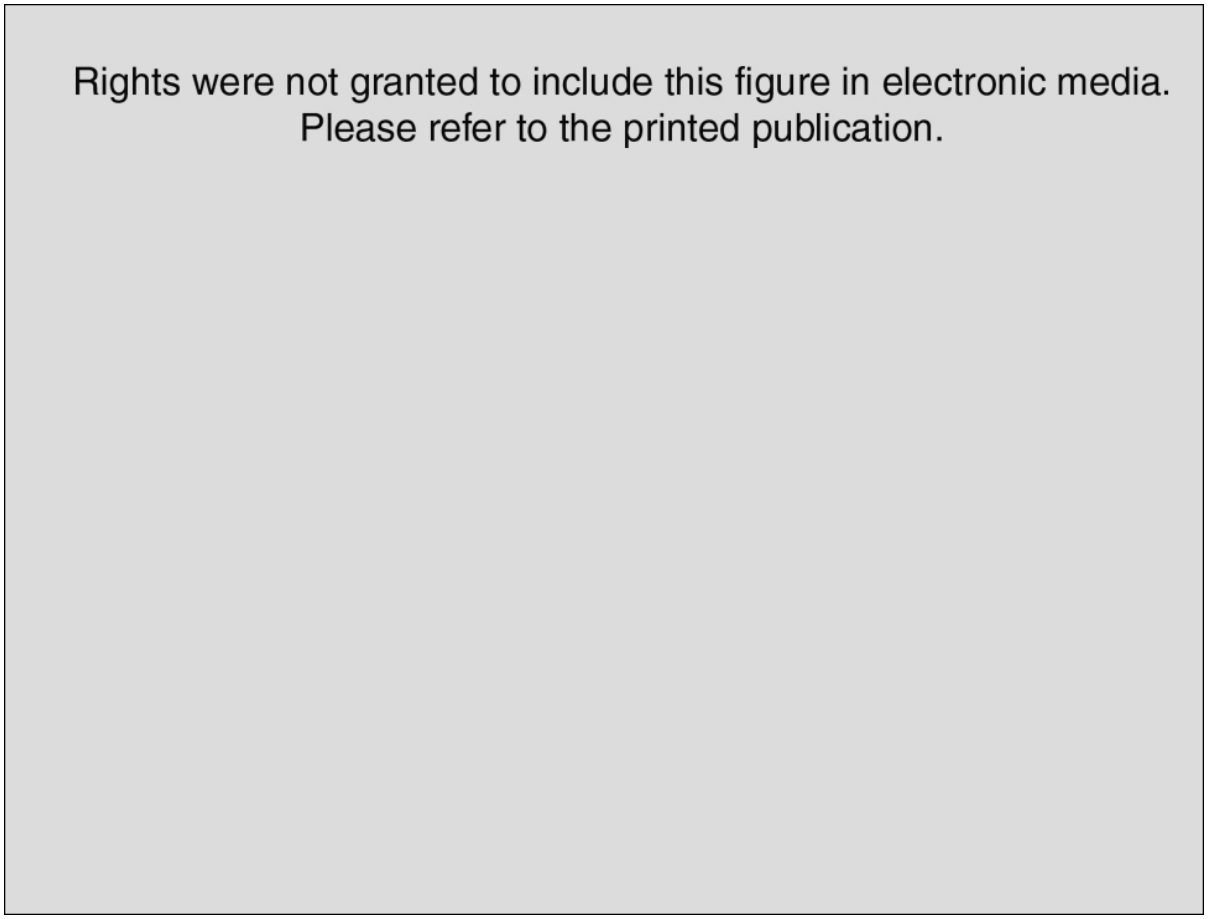

FIGURE 8-86 *Ancylostoma caninum* third-stage larvae within skeletal muscle fibers (×650). Note the double lateral alae.

From Lee KT, Little MD, Beaver PC: Intracellular [muscle-fiber] habitat of Ancylostoma caninum in some mammalian hosts, J Parasitol 61:589, 1975.

Metastrongyloidea

Adult metastrongyles, often referred to as *lungworms*, typically parasitize the lungs or airways, but some may invade blood vessels or the central nervous system. In section the body wall tends to be thin, the musculature is often polymyarian and coelomyarian in nature, and the gut is the typical strongyle type, although the microvilli are less prominent than in other strongyles. Many

metastrongyles contain embryonated eggs or larvae in utero and shed these stages into the surrounding tissues.

Cats are typically host to only a single lungworm, *Aelurostrongylus abstrusus*. Adults, eggs in varying stages of development, and larvae are found in nests in the lung parenchyma (Figure 8-87). Diagnosis is usually fairly easy because domestic cats have few other worms causing similar lesions; however, wild felids may be host to related forms.

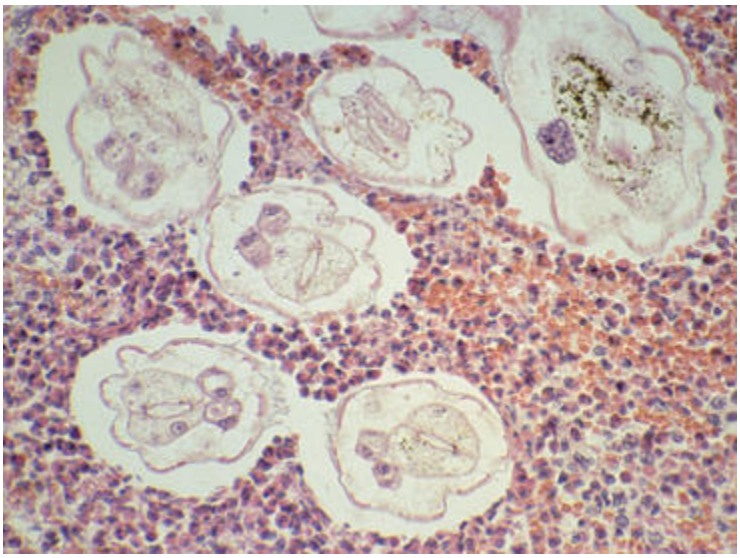

FIGURE 8-87 *Aelurostrongylus abstrusus* adults in section of a nodule in the lung of a cat (×250).

Dogs can be infected with several lungworms, but they tend to live in markedly different locations, making diagnosis easier than it would be otherwise. *Angiostrongylus vasorum* adults may be found in the right side of the heart and pulmonary vessels of dogs, whereas the eggs and larvae are found in the lung parenchyma. This infection was exotic to North America but has now appeared in the far east of Canada (Figure 8-88). *Filaroides hirthi* adults are found in

the lung parenchyma of the dog (Figures 8-89 and 8-90). Eggs contain first-stage larvae when laid, and the eggs do not accumulate in the lung tissue. Autoinfection by *F. hirthi* may lead to a state of hyperinfection in which lung tissue is almost completely replaced by adult worms and larvae may be found widely scattered in lymph nodes, pancreas, intestinal tract, liver, and brain. *Filaroides osleri* adults are found in fibrous nodules projecting into the lumen of the trachea and principal bronchi (Figures 8-91 and 8-92).

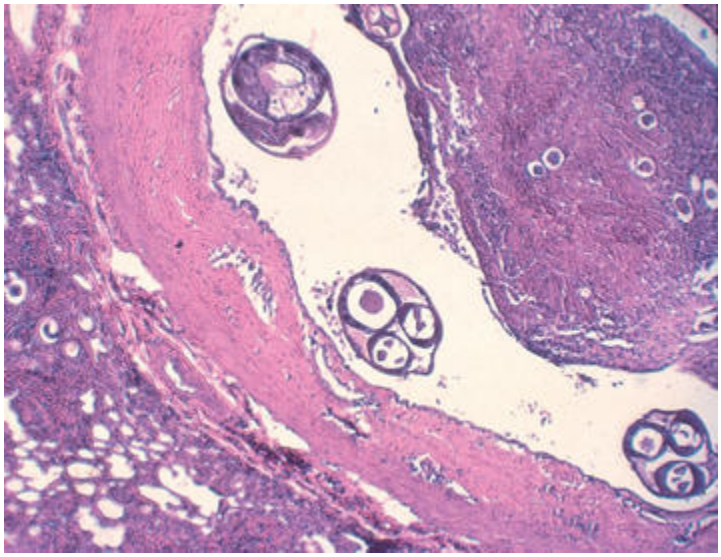

FIGURE 8-88 *Angiostrongylus vasorum* in the pulmonary artery of a dog (×100).

Courtesy Dr. M. Dale Little.

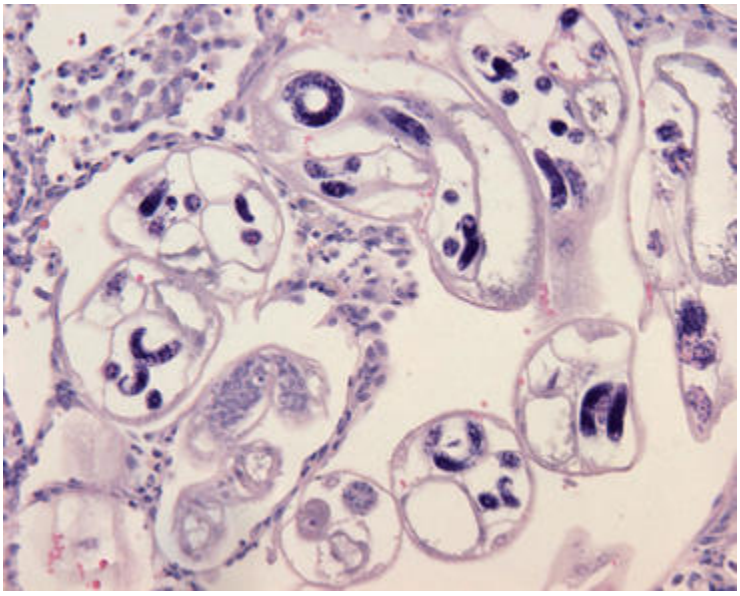

FIGURE 8-89 *Filaroides hirthi* in canine lung tissue (×100). The dark objects are eggs and larvae in the uterus of female worms.

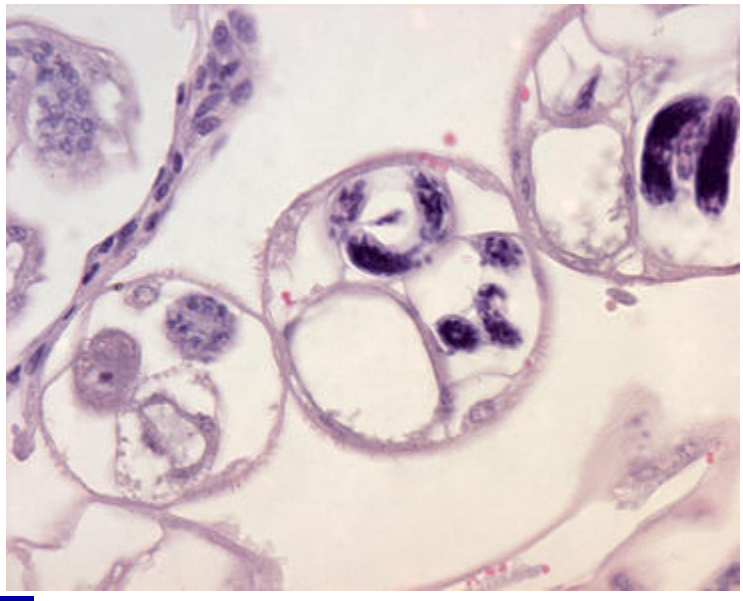

FIGURE 8-90 *Filaroides hirthi*, enlarged view, showing the nature of the intestine, composed of a very few cells (×200).

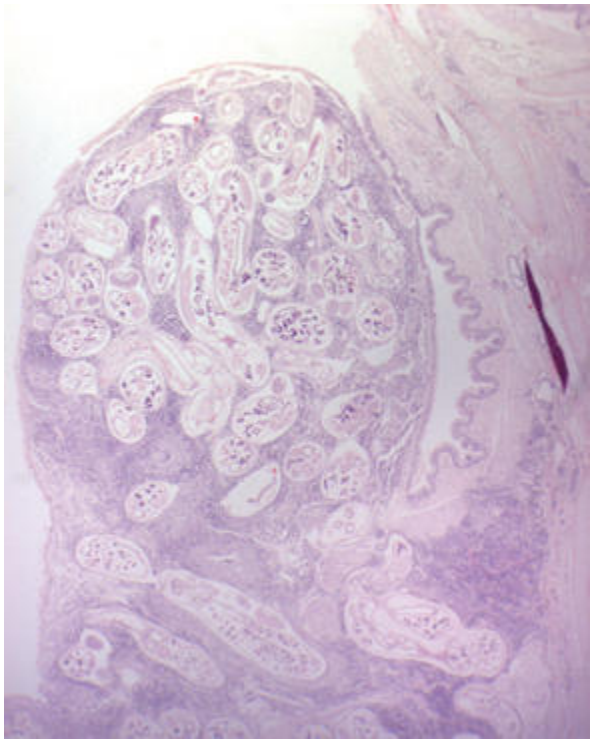

FIGURE 8-91 *Filaroides osleri* in fibrous nodules in the trachea of a dog (×26).

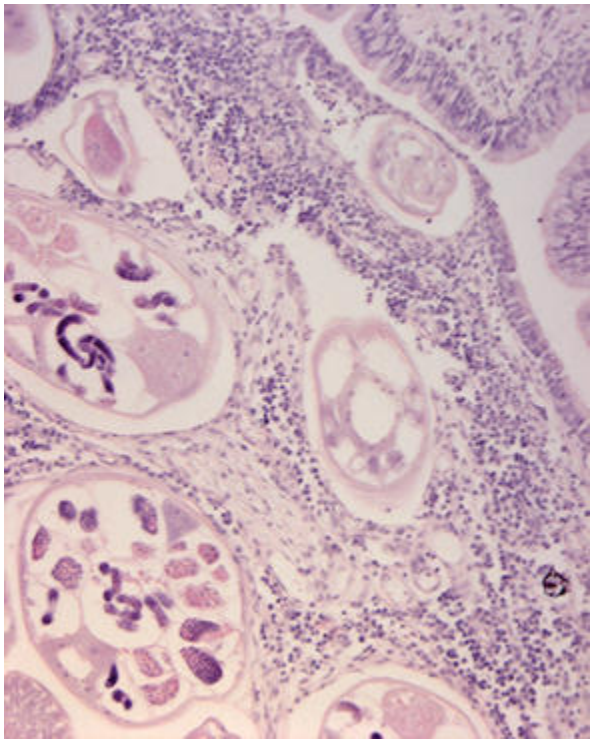

FIGURE 8-92 *Filaroides osleri*, enlarged view, showing the nature of the intestine and the very thin body wall (×180).

Sheep and goats can be host to several species of lungworms. *Muellerius capillaris* is found in nodules in the lung parenchyma. These nodules contain adult worms, eggs in varying stages of development, and larvae. If the tails of larvae can be located in the tissue section, *Muellerius* organisms can be distinguished from *Protostrongylus* organisms (see Figure 7-61). *Protostrongylus* species. adults may be found in either parenchymal nodules or airways. *Dictyocaulus* species (Trichostrongyloidea) adults are found in airways. *Parelaphostrongylus tenuis* adults are found in the meninges and nervous tissue of the spinal cord and brain of sheep and goats (Figures 8-93 and 8-94), but their eggs and larvae, which are indistinguishable from those of *Muellerius* organisms, are found widely scattered in the lung parenchyma rather than concentrated in nests.

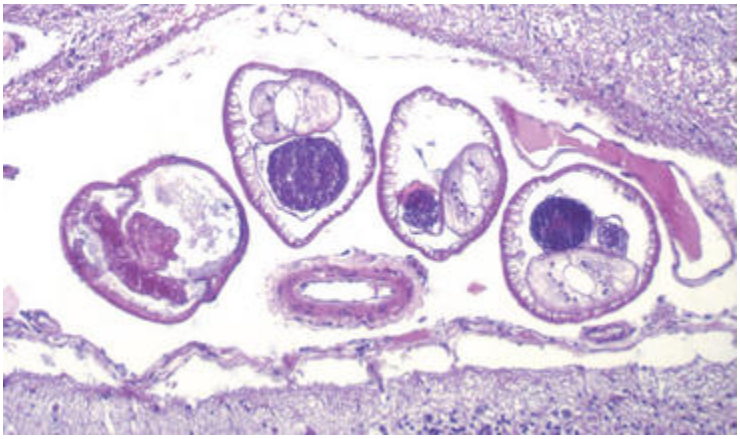

FIGURE 8-93 *Parelaphostrongylus tenuis* in the meninges of a goat (×25).

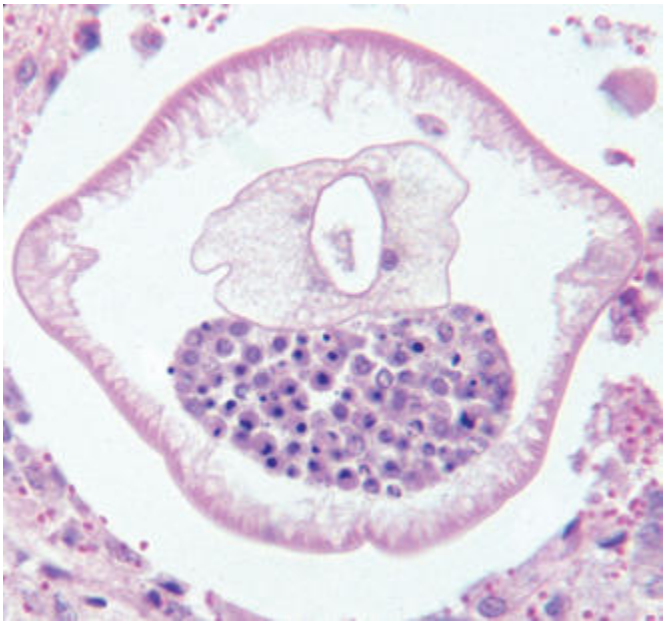

FIGURE 8-94 *Parelaphostrongylus tenuis* (×290) illustrating the nature of the intestine, with very few cells.

Oxyurida

The oxyurids are generally smallish worms that as adults typically inhabit the large intestine or cecum. In section most species have prominent lateral alae. The esophagus has characteristic sections consisting of corpus, isthmus, and terminal bulb which can occasionally be seen in sections. The musculature is platymyarian and meromyarian, and generally only two or three muscle cells are located in each quadrant (Figure 8-95). The intestine is variable but is cuboidal to columnar with a single nucleus per cell. The presence of typical eggs in utero often assists with identification.

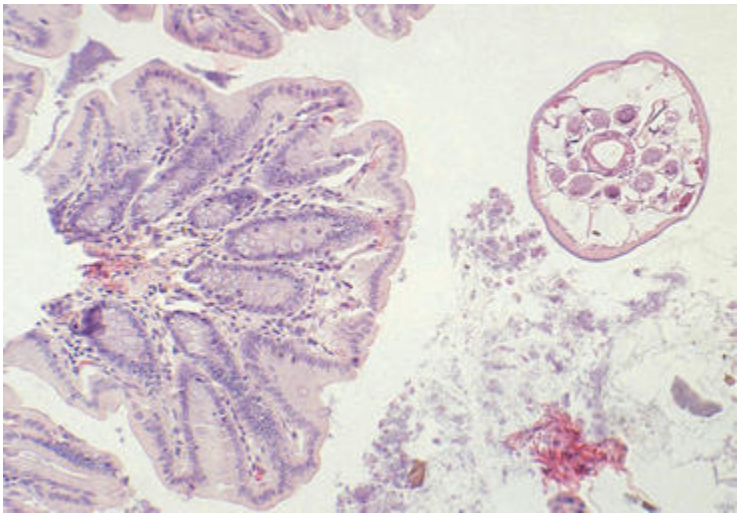

FIGURE 8-95 *Aspiculuris* sp. in the intestine of a rat. This oxyurid (pinworm) has platymyarian muscle cells and at this level of the body lacks lateral alae.

Ascaridida

The ascarids comprise a diverse group of worms, and as adults, some, such as *Ascaris* and *Parascaris* organisms, are the largest of the intestinal nematodes. In tissue section, in addition to their large size, the ascarids characteristically have a thick, multilayered cuticle, polymyarian-coelomyarian muscles (often with cytoplasmic processes that extend into the body cavity), an intestine with numerous columnar epithelial cells and short microvilli, and large lateral cords (Figures 8-96 to 8-98). The Ascaridida are often divided into two large groups or superfamilies. One, the Ascaridoidea, parasitize land-dwelling vertebrates, whereas the second group, the Heterocheiloidea, parasitize birds, fish, and marine mammals. Members of the Ascaridoidea, including the genera *Ascaris*, *Parascaris*, *Toxocara*, *Toxascaris,* and *Baylisascaris*, have three simple lips on the anterior end; a thick, multilayered cuticle; a club-shaped esophagus; columnar epithelial gut cells with a single nucleus near the base of each cell; prominent coelomyarian-

polymyarian muscle; and typical eggs in the uterus that have a thick shell, often wrinkled or sculptured on the surface. Genera in Heterocheiloidea, such as *Anisakis*, *Terranova*, *Contracaecum*, and *Porrocaecum*, have much the same features in section, except all in this group also have a cecum (anteriorly directed), a ventricular appendix (posteriorly directed), or both. These may be obvious if sections are cut through the level of the esophageal-intestinal junction.

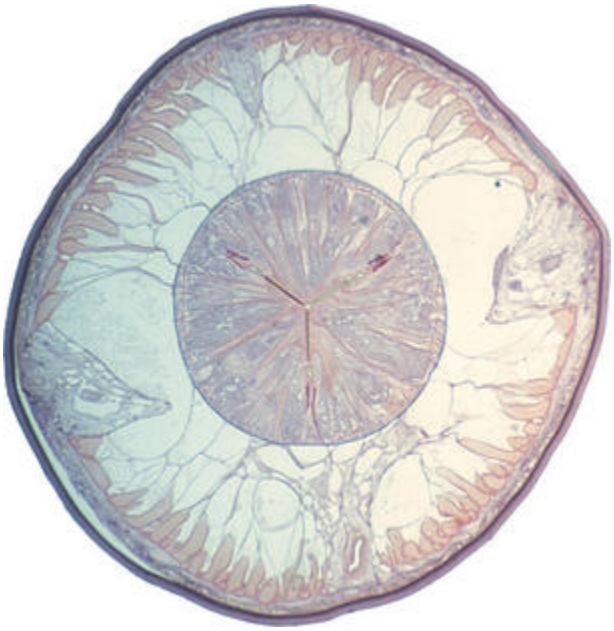

FIGURE 8-96 Cross-section of *Ascaris suum* at the level of the muscular esophagus (×25). The esophagus has a dorsal and two sublateral portions divided by the Y-shaped cuticular lining. The muscles are polymyarian. The lateral cords are prominent, and also visible are the dorsal and ventral nerve cords and the lumen of the excretory duct on the ventral cord.

Courtesy Dr. M. Dale Little.

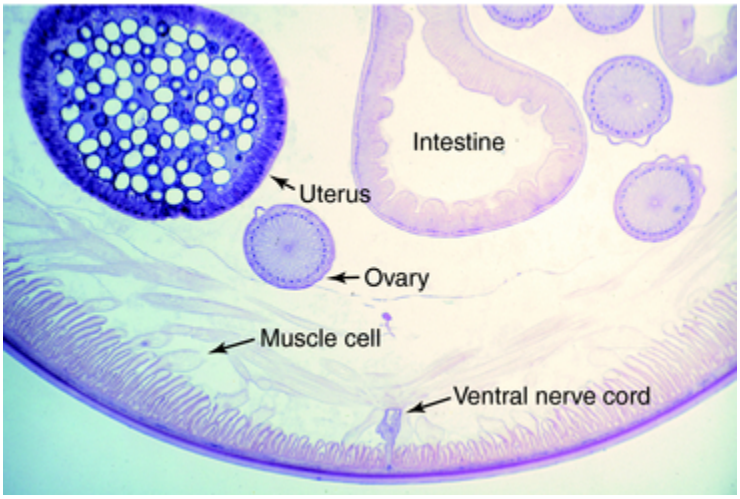

FIGURE 8-97 *Ascaris suum* female (×10) section through mid body showing the many-celled intestine, the ovary with a central rhachis, the uterus full of developing eggs, the ventral nerve cord, and the cytoplasmic portions of the muscle cells extending to the ventral nerve cord.

Courtesy Dr. M. Dale Little.

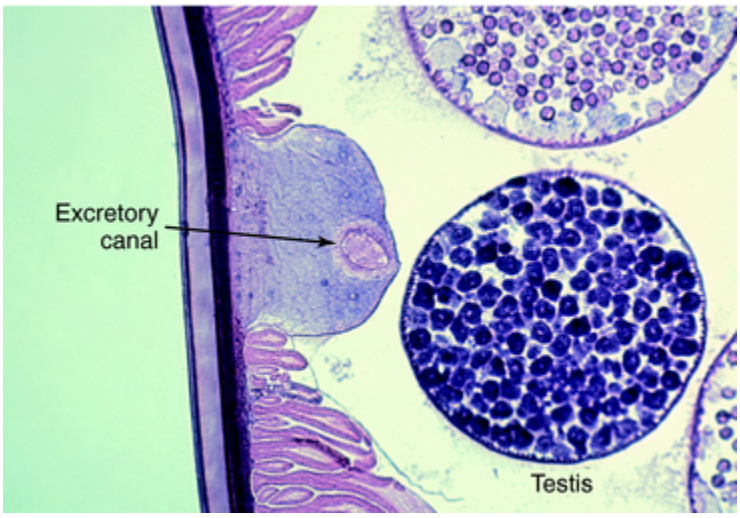

FIGURE 8-98 *Ascaris suum* male (×20) showing a section through the lateral cord with the prominent excretory canal and a section through several loops of the testis.

Courtesy Dr. M. Dale Little.

Those ascarids that parasitize mammals often have larvae that are capable of tissue migration, and larvae of genera such as *Toxocara*

(Figure 8-99), *Baylisascaris* (Figure 8-100), and *Lagochilascaris* (Figure 8-101) cause "larval migrans" syndrome. Ascarid larvae have single lateral cuticular alae. They also have a single excretory cell with H-shaped anterior and posterior projections called *excretory columns*. The presence of single lateral alae and paired excretory columns makes ascarid larvae relatively easy to distinguish in tissue sections (see Figures 8-99 to 8-101). *Toxocara* larvae migrating or arrested in somatic tissues tend not to exceed 21 μm in diameter, but *Baylisascaris* larvae continue to grow as they migrate and may reach 55 to 70 μm in diameter.

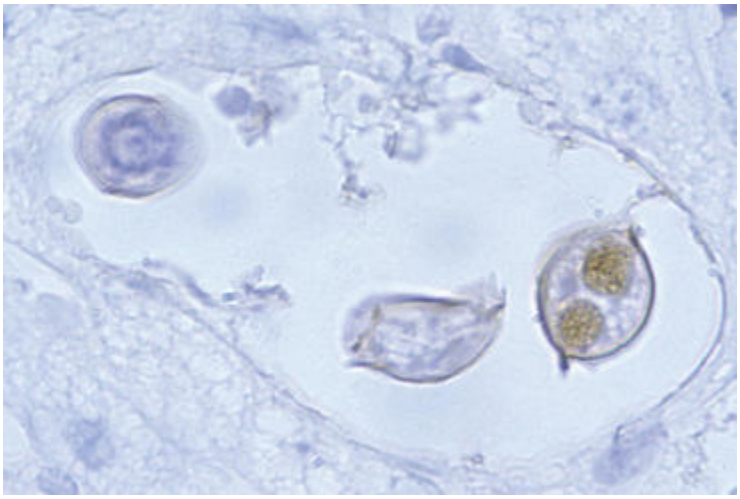

FIGURE 8-99 *Toxocara canis* larva (×650) in an experimentally infected mouse, stained with a monoclonal antibody using immunoperoxidase to show the location of the large branches of the excretory cell that extend posteriad from the single excretory cell along each of the two lateral cords (right section). The section on the left is through the esophagus and is anterior to the branching, and the central section is posteriad to the termination of the excretory columns.

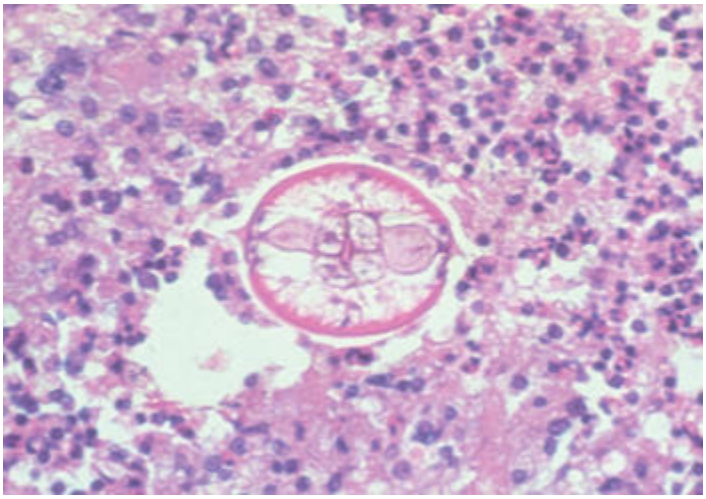

FIGURE 8-100 *Baylisascaris procyonis* (×400) in the brain of a porcupine showing the large excretory columns, the intestine with a patent lumen, and lateral alae.

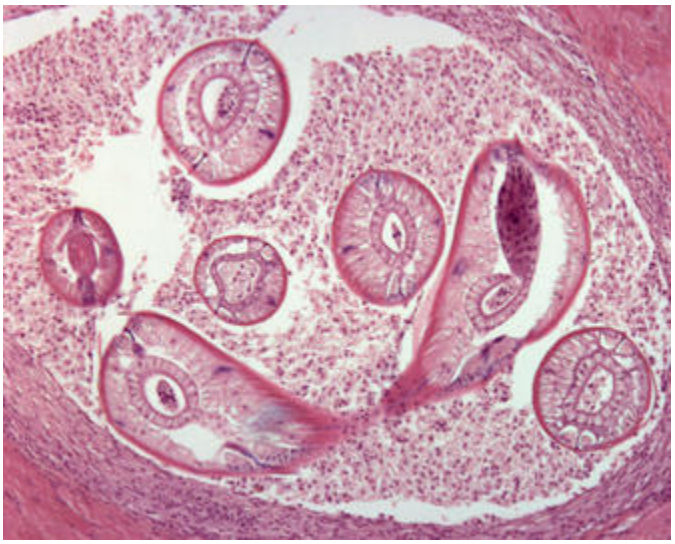

FIGURE 8-101 *Lagochilascaris sprenti* (×100) larvae in an experimentally infected mouse. These ascarid larvae grow quite large, and sections can be seen through the esophagus and through numerous levels of the many-celled intestine.

Spirurida

The order Spirurida consists of the superfamilies Gnathostomatoidea, Physalopteroidea, Rictularioidea, Thelazioidea, Spiruroidea, Dracunculoidea, and Filarioidea. The spirurids

represent an extremely diverse group of nematodes that parasitize a wide range of hosts and anatomic locations in those hosts. As adults, spirurids range in size from thin and threadlike in the case of *Gongylonema*, to stout, robust worms such as *Gnathostoma*, to incredibly long in the case of *Dracunculus*. Some species localize in the lumen of the gut, others are associated with the wall of the gut, and others have moved away from the gut entirely. Despite this variability, there are a number of similarities in both biologic and morphologic aspects. As a group the spirurids use insects as intermediate hosts. In many species, small, thick-shelled eggs containing a well-developed larva are passed in the feces and ingested by an insect intermediate host. In the Dracunculoidea, female worms migrate to the surface and release first-stage larvae into water, where they are ingested by copepods. In the Filarioidea, not only have the adult worms moved away from the gut, but the female worms release motile larvae called **microfilariae** that either circulate in the blood or reside in the skin and are picked up by blood-sucking insects that serve as intermediate hosts. Features of spirurids in tissues include a cuticle that often has some ornamentation, including spines, bosses, transverse striations, or longitudinal ridges. The esophagus tends to be long and divided into an anterior muscular and posterior glandular portion; the glandular portion is very cellular and stains much more intensely. The general spirurid intestine is often large and folded on itself and is composed of many cells, often with the nuclei arranged in a row, a prominent brush border, but a rather weak basement membrane. The lateral cords are prominent, and the musculature is polymyarian-coelomyarian in nature. In most spirurids, female worms contain

small, thick-shelled eggs containing a larva. In the case of the Dracunculoidea and Filarioidea, large numbers of larvae or microfilariae, respectively, are contained in utero. This combination of features makes the spirurids relatively distinctive in sections.

Spirurid larvae are, on occasion, seen in tissue sections and have some of the same morphologic features seen in adult worms, including polymyarian-coelomyarian muscle cells, prominent lateral chords, and a distinctive intestine composed of many tall columnar cells (Figure 8-102).

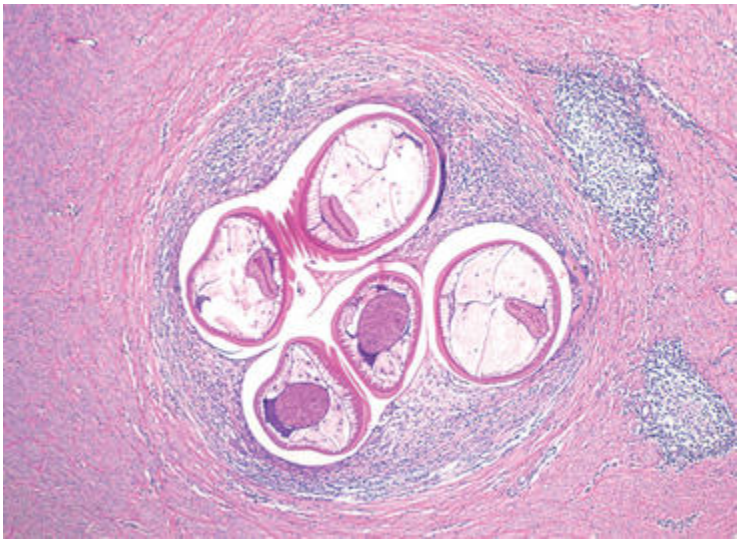

FIGURE 8-102 Spirurid larva in a granuloma in the uterine wall of a rhesus monkey (×36).

Spirocerca lupi (Figures 8-103 to 8-105) provides an example of the superfamily Spiruroidea. The adults typically are found in nodules in the wall of the esophagus and stomach, and sometimes in the wall of the aorta or rectum. In cross-section they are characterized by large lateral cords that project into the body cavity; an intensely stained glandular esophagus (see Figure 8-104); an intestine with a

prominent brush border and many cells with the nuclei lined up in a row, which gives the appearance of three layers; a uterus filled with small eggs containing intensely stained larva; and coelomyarian-polymyarian muscle cells (see Figures 8-103 and 8-104). The larvae have hooks and combs associated with the stoma, although these structures require oil immersion microscopy to be seen properly (see Figure 8-105).

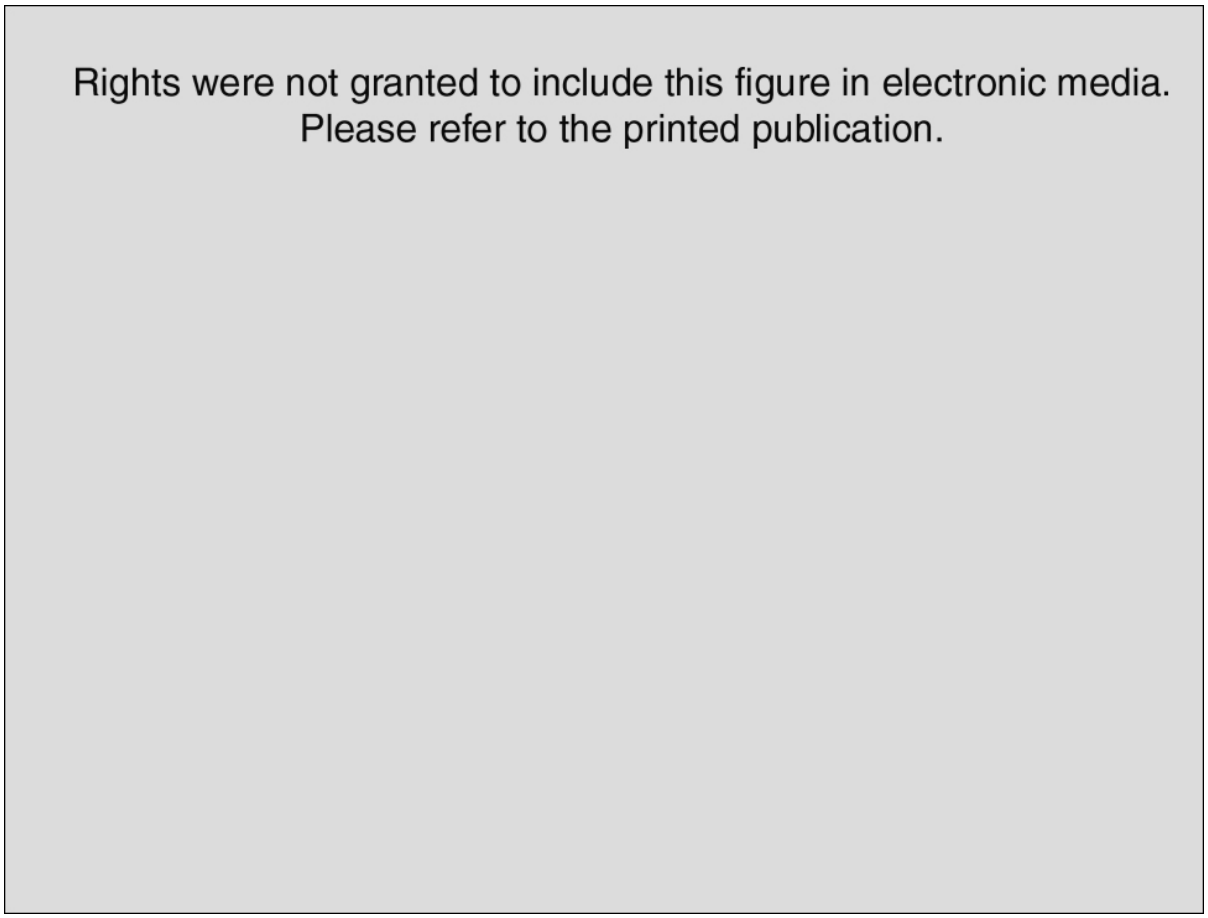

FIGURE 8-103 *Spirocerca lupi* (×22) in a nodule in a dog.

Case described in Georgi ME, Han H, Hartrick DW: Spirocerca lupi [Rudolphi, 1809] nodule in the rectum of a dog from Connecticut, Cornell Vet 70:43, 1980.

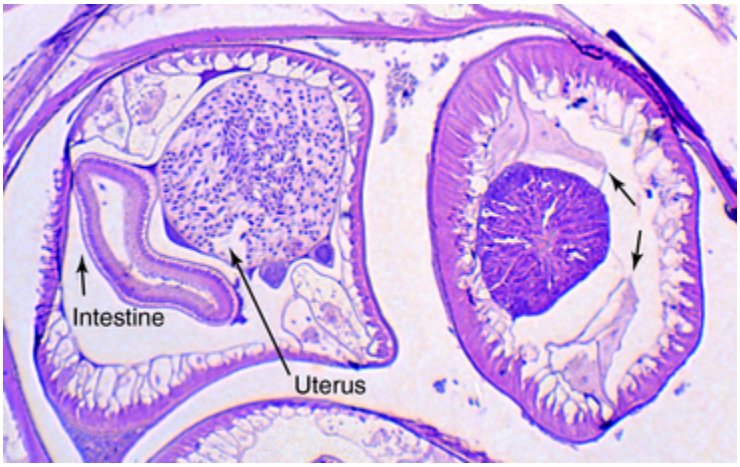

FIGURE 8-104 *Spirocerca lupi* (×50) sections through the region of the glandular esophagus showing the lateral cords *(arrows)* projecting into the pseudocoelom and showing the nature of the intestine, with a prominent brush border and many cells with nuclei lined up in a row and uterus filled with tiny eggs.

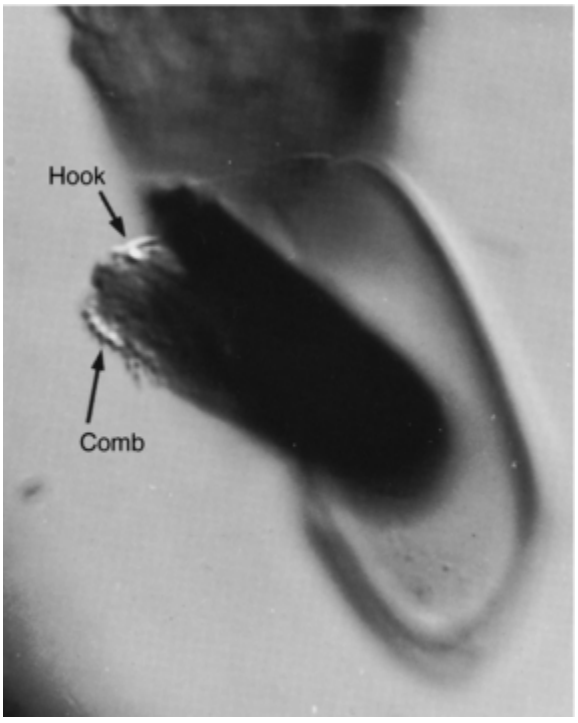

FIGURE 8-105 *Spirocerca lupi* egg with broken shell from which the larva projects (×1800).

The genus *Gongylonema*, another member of the Spiruroidea group, is encountered in the tissues of animals with some frequency and has several distinctive morphologic features. Typically found threaded in the mucosa of the mouth, esophagus (Figure 8-106) or stomach, the members of *Gongylonema* have characteristic spirurid features in section, including a divided esophagus, a polymyarian-coelomyarian musculature, and the presence of small, thick-shelled, embryonated eggs (Figure 8-107). *Gongylonema* organisms are distinctive, however, in that the anterior end has large cervical alae and is covered with cuticular plaques or bosses on the anterior end, and the lateral cords are asymmetric (see Figure 8-107).

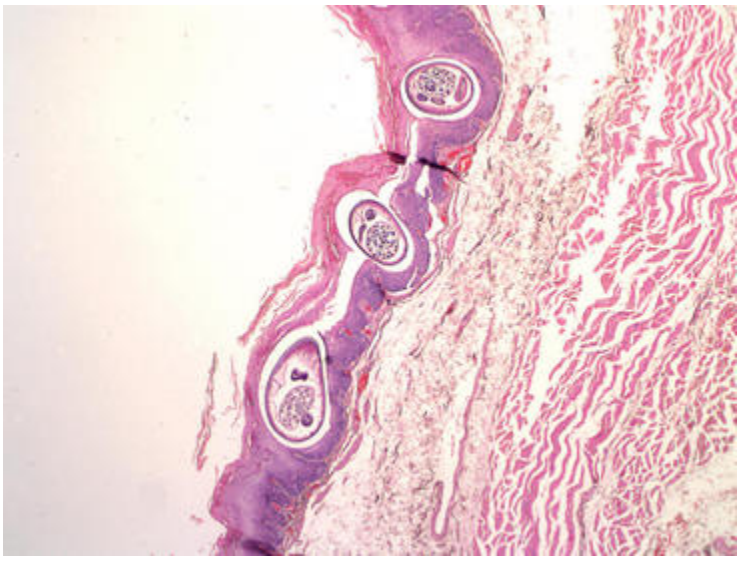

FIGURE 8-106 *Gongylonema* (×22), cross-section through gravid female embedded in esophagus of stumptail macaque monkey.

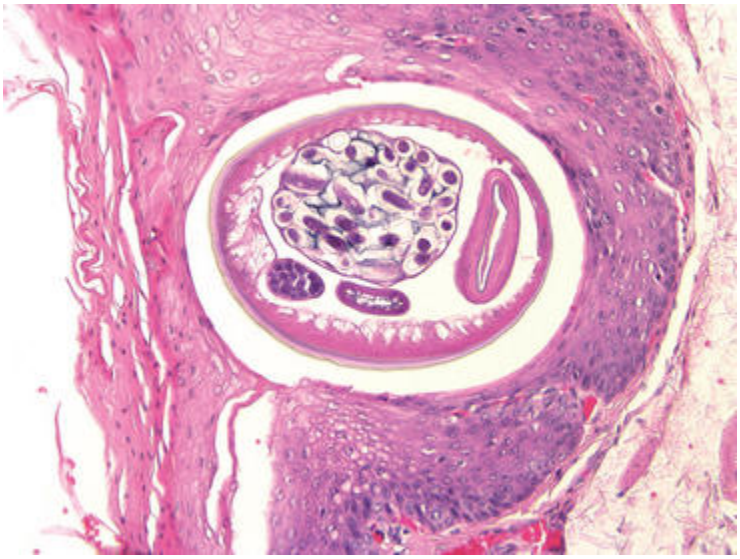

FIGURE 8-107 *Gongylonema* (×125) at a higher magnification showing the presence of unequal lateral chords and embryonated eggs, many containing larvae.

Dracunculus insignis, of the superfamily Dracunculoidea, is characterized by flat lateral cords separating semilunar dorsal and ventral muscle fields composed of coelomyarian-polymyarian muscles, a very reduced intestine, and a large uterus filled with larvae (Figure 8-108).

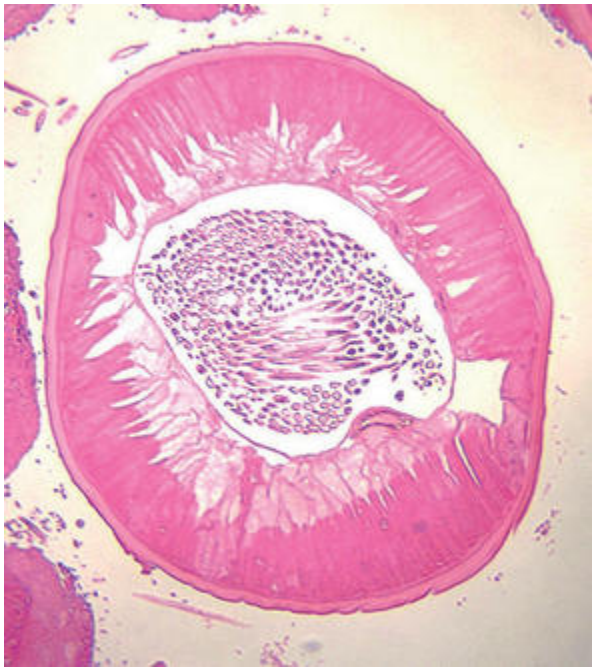

FIGURE 8-108 *Dracunculus insignis* (×60). Cross-section of *Dracunculus insignis* in the subcutaneous tissue of a raccoon. The two lateral chords on either side of the body and heavy dorsal and ventral muscle bands surrounding the uterine tube packed with larvae are evident.

Members of the superfamily Filarioidea, although having many typical spirurid features in section, are relatively distinct. Most distinctive is their location, as adults, in virtually all tissues except the gut. Filarids range greatly in size, from some that are only 1 or 2 cm in length to others such as *Dirofilaria immitis*, where the female worm may reach 30 cm in length by 1 mm in diameter; however, all tend to be slender. The cuticle may be thin or thick and in some groups contains distinctive ridges or striations. The musculature is coelomyarian-polymyarian, the esophagus may be divided but is generally not as prominent as in other spirurids, and the intestine is typically a simple tube. One of the most characteristic features of filarids is the presence of microfilariae filling the uterus. There are

many species of filaria that infect animals, and several examples will serve to illustrate the group.

D. immitis, the dog heartworm, is well recognized for the disease it produces in canines, felines, and humans. The adult worms live in the circulatory system, typically in the chambers and great vessels of the heart. The worms, as just stated, are large; have a thick, multilayered but smooth cuticle; have prominent coelomyarian-polymyarian muscles; have broad lateral cords; have a weak intestine; and, in the female, have paired uteri filled with microfilariae (Figure 8-109). Many other *Dirofilaria*, such as *Dirofilaria repens* of the dog and *Dirofilaria tenuis* of the raccoon, live in subcutaneous locations and are distinctive in that the cuticle has prominent longitudinal ridges marked with transverse striations, giving the external surface a beaded or corn-row appearance (Figure 8-110).

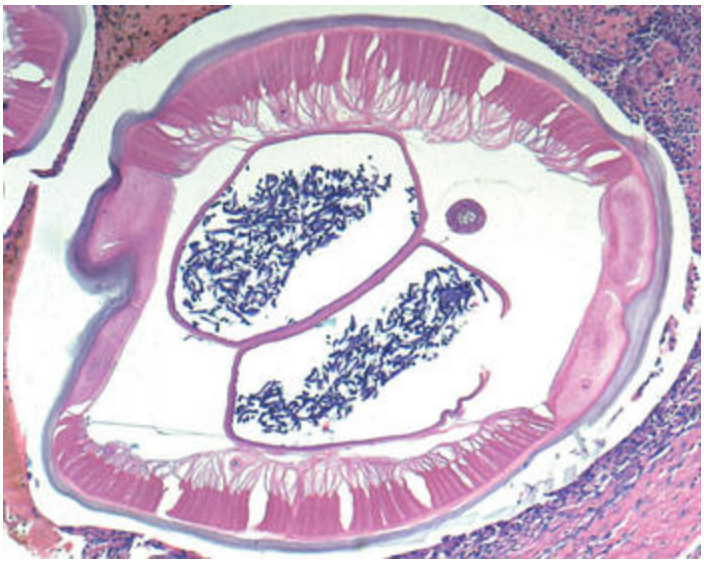

FIGURE 8-109 *Dirofilaria immitis* (×65) in the pulmonary artery of a dog. The thick, smooth cuticle, large coelomyarian-polymyarian muscles, small intestine, and paired uteri are evident.

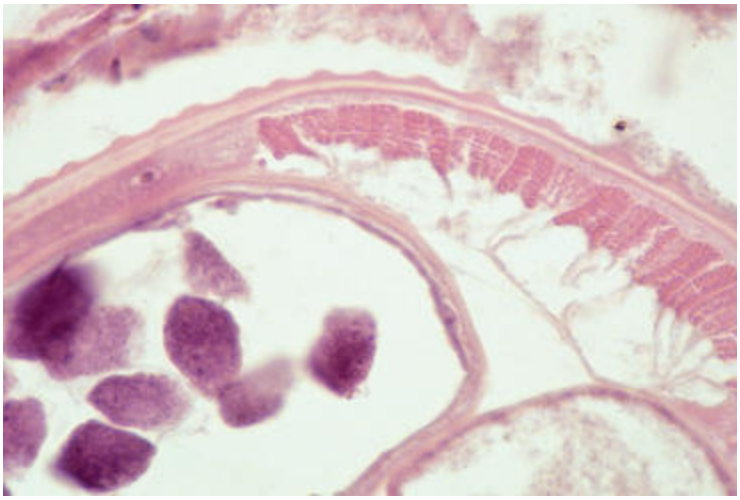

FIGURE 8-110 *Dirofilaria tenuis* (×220), high-power cross-section through a portion of in the subcutaneous tissues of a raccoon. The longitudinal ridges on the surface of the cuticle are evident.

The genus *Onchocerca*, another common filarial infection of domestic animals, provides a good example of specific filarial anatomy in section. Adult female *Onchocerca* organisms are thin and extremely long and have distinctive cuticular structures. These worms possess external circular ridges and striae in the inner layer of the cuticle (Figure 8-111). These ridges and striae not only are specific to the genus *Onchocerca*, but the number of striae per ridge has been shown to have great value in distinguishing various species within the genus. Also distinctive of adult female *Onchocerca* organisms are the muscle cells, which often appear to be weak and poorly developed, and a prominent amount of hypodermal tissue, even underlying the muscle cells (Figure 8-112). As far as it is known, adult *Onchocerca* organisms inhabit dense connective tissue, are tightly coiled, and, in some species, form distinct fibrous nodules.

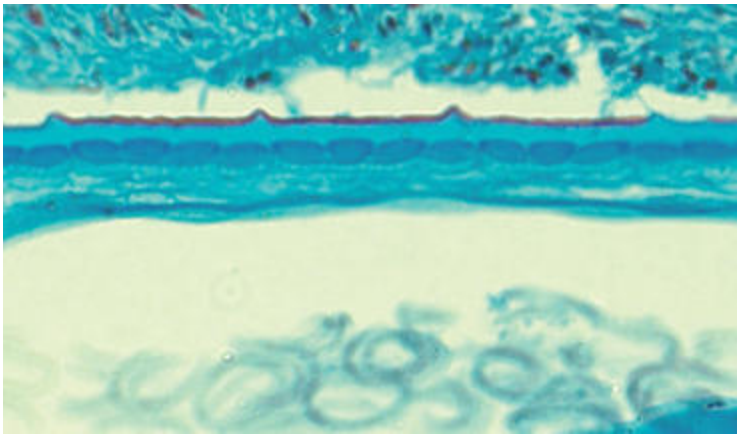

FIGURE 8-111 *Onchocerca cervicalis* (×560) female in the nuchal ligament of a horse. The outer circular cuticular ridges and striae in the inner layer of the cuticle are evident. In *O. cervicalis* there are four striae per ridge, one directly under and three between each ridge.

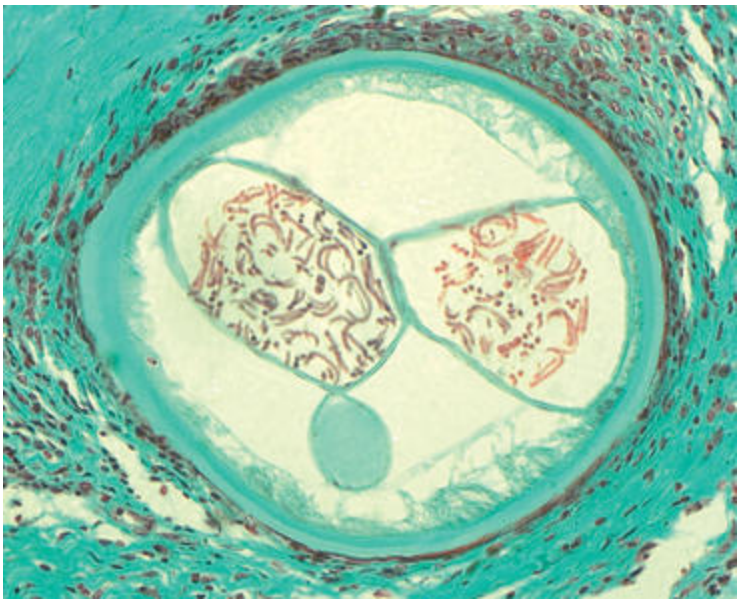

FIGURE 8-112 *Onchocerca cervicalis* (×340) female in cross- section in the nuchal ligament of a horse. The thick cuticle, prominent hypodermal tissue between the cuticle and muscle layers, and wispy muscle cells are all prominent, as are the paired uteri and small intestine.

Enoplida

Trichinelloidea

This group contains the trichinelloids, the trichuroids, the capillarids, and the trichosomoids. In this group the most characteristic feature, both grossly and in section, is the **stichosome esophagus,** a small cylindric tube surrounded by individual **stichocytes** that compose the stichosome. The other distinctive feature of these worms in section is the presence of a bacillary band(s). The **bacillary band** is a specialized section of the cuticle and hypodermis, including specialized hypodermal gland cells. In *Trichuris* there is a single bacillary band in the esophageal region (Figure 8-113), whereas in *Trichinella* and capillarids there are two bacillary bands that run the length of the esophagus. In addition, the female reproductive tract is a single tube, the anus is usually terminal, the muscles are coelomyarian-polymyarian, and the eggs typically have bipolar prominences (plugs) and are frequently in an unembryonated state when passed or seen in tissues. Occasionally, eggs may develop and hatch in utero, as in the case of *Trichinella*. The first-stage larva is typically the infective stage for the definitive host. Most worms in this group display a high order of site specificity and, except for *Trichinella,* a high order of host specificity as well. The host-organ listings should prove helpful in dealing with this group of parasites.

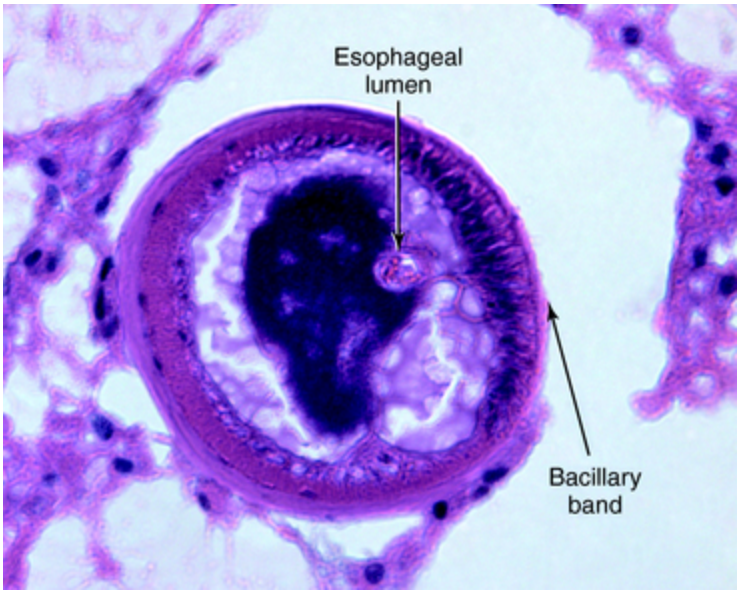

FIGURE 8-113 *Trichuris vulpis* (×500) in the cecum of a dog showing a cross-section of the esophageal region.

Adult *Trichuris,* as their common name *whipworm* suggests, have a whip-shaped body. The thin "whiplash" anterior portion is threaded through the epithelium of the large intestine, whereas the stout "handle" portion normally lies free in the lumen (Figure 8-114). Immature *Trichuris* lie entirely within the mucosa and are of uniform diameter.

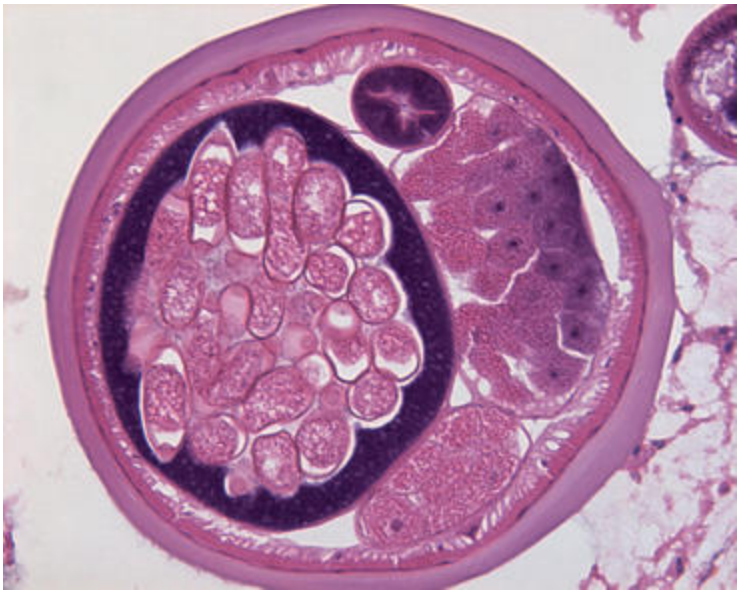

FIGURE 8-114 *Trichuris vulpis* (×250) in the cecum of a dog showing sections through the very small intestine and the thick-walled uterus filled with typical *Trichuris vulpis* eggs.

Adult *Trichinella* are found threaded in the mucosa of the small intestine (Figure 8-115), and in tissue section the adults resemble *Strongyloides*, except that they have a tubular esophagus embedded in the stichosome, male worms exist, and in female worms the uterus contains prelarvae instead of segmenting eggs. *Trichinella* larvae are found characteristically coiled in a "nurse cell" (Figure 8-116) in striated muscle, and they are characterized by stichocytes surrounding the esophagus. Capillarids infecting the intestinal mucosa are somewhat larger than *Trichinella* and have eggs with bipolar plugs in their uteri.

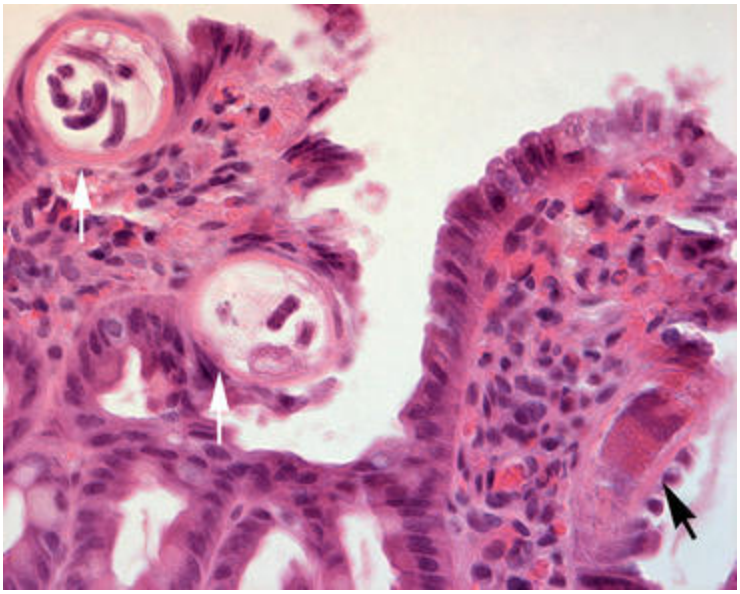

FIGURE 8-115 *Trichinella spiralis* adult in the mucosa of the small intestine of a rat (×480). There are two cross-sections through a female containing prelarvae and a longitudinal section through the stichosome esophagus *(arrows)*.

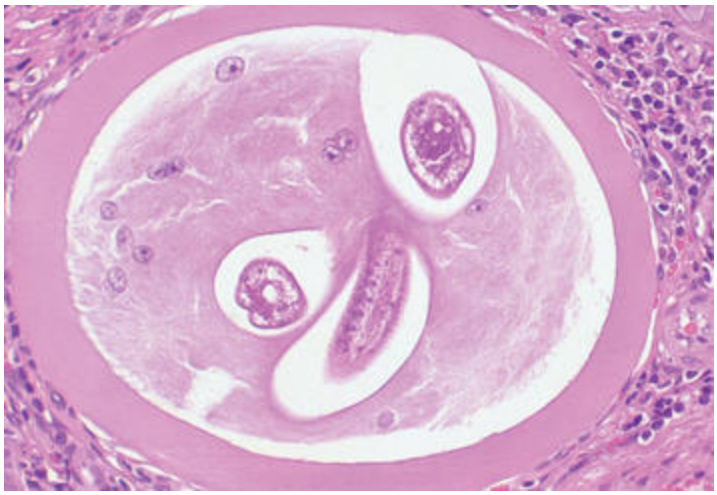

FIGURE 8-116 *Trichinella spiralis* first-stage larvae in a skeletal muscle fiber of a cat (×425).

The presence of single-celled eggs with bipolar plugs in the uterus is the best criterion for identifying capillarids in tissue sections (Figure 8-117). *Trichuris* species have larger eggs and are found only

in the large intestine of mammals, practically the only epithelium in which capillarids will not be found.

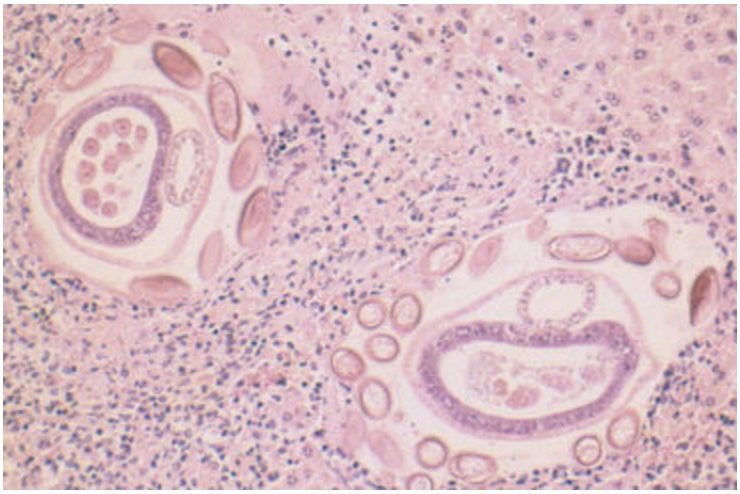

FIGURE 8-117 *Calodium (Capillaria) hepaticum* in the liver of a rat (×360). Eggs with bipolar plugs are visible in the tissue surrounding the worm.

Other common but less frequently seen members of this group include *Anatrichosoma* in the nasal mucosa or palate of primates and marsupials (Figures 8-118 and 8-119) and *Trichosomoides* in the bladder of rats (Figure 8-120). Both have larvated eggs with bipolar plugs, and two or one bacillary band, respectively. *Anatrichosoma*, although occurring in the same general location (i.e., mouth and throat) as *Gongylonema*, can easily be distinguished on morphologic features, including smaller diameter, presence of stichosomes and bacillary bands in the anterior end, and polar plugs in the eggs (see Figure 8-119).

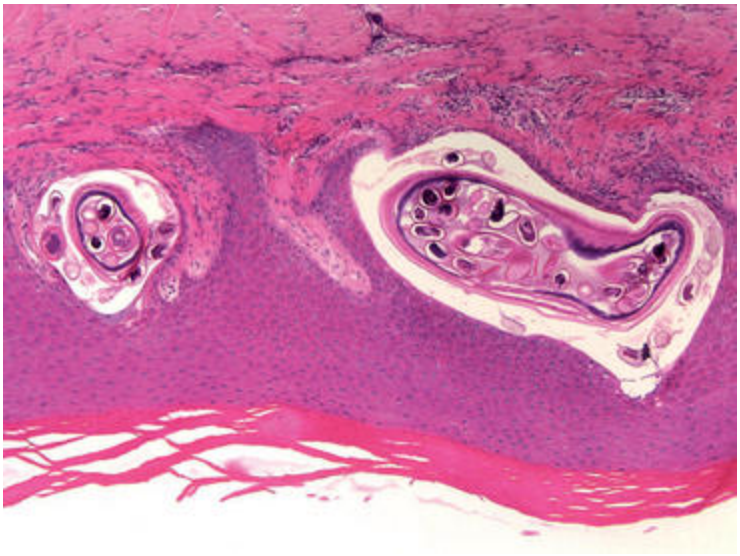

FIGURE 8-118 *Anatrichosoma buccalis.* Cross-section through gravid female *Anatrichosoma buccalis* embedded in palate of opossum (×60).

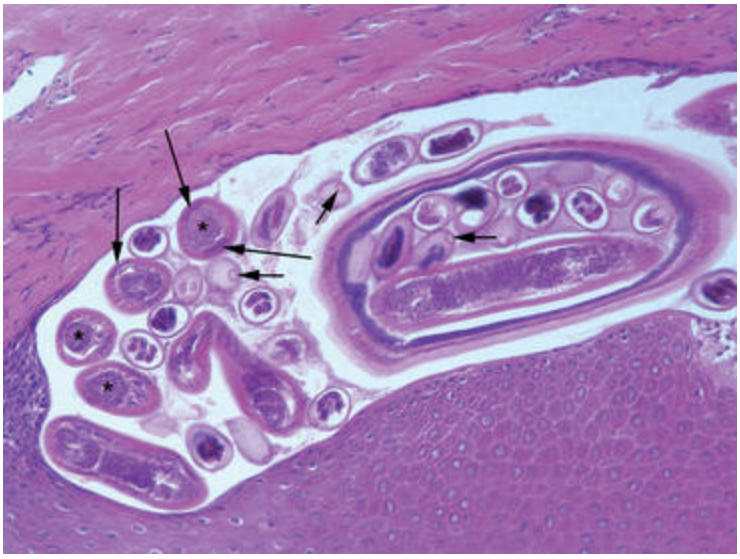

FIGURE 8-119 *Anatrichosoma buccalis*. Higher magnification of worm in Figure 8-114, illustrating stichocytes *(asterisks)*, bacillary bands *(long arrows)*, and polar plugs *(short arrows)* in the eggs (×125).

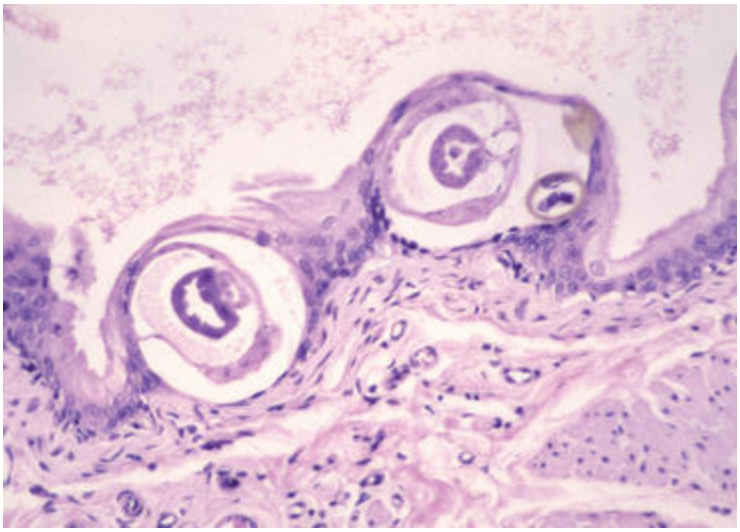

FIGURE 8-120 *Trichosomoides crassicauda* in the urinary bladder mucosa of a rat (×480).

Acanthocephalans

Adult male and female Acanthocephala are pseudocoelomates that live in the intestines of vertebrates where they gain nutrients through their external covering, i.e., they have no intestinal tract (Figure 8-121). Hosts include all vertebrate classes, fish, amphibians, reptiles, birds, and mammals. Eggs passed in feces are ingested by the intermediate host, an arthropod; and infection is acquired through the ingestion of the intermediate host. The wormlike adults possess a spiny proboscis that is used for attachment to the intestinal mucosa and can be retracted inside the body; this why they are often called *thorny* or *spiny-headed worms* (Figure 8-122). The fluid-filled pseudocoelom contains cells of the reproductive system, testes and cement glands in males. Females have a reproductive system wherein balls of ovarian tissue float about and sperm migrate into the pseudocoelom to fertilize the eggs. A "uterine bell" sorts the eggs according to their

developmental stage, and mature eggs, containing a larva called an *acanthor,* pass into the uterus, out of the body, and into the feces. The intermediate host is typically an arthropod in which a stage called a cystacanth develops; the cystacanth can sometimes use vertebrate paratenic hosts, and this is typically the stage that will be seen in histologic sections (Figure 8-123).

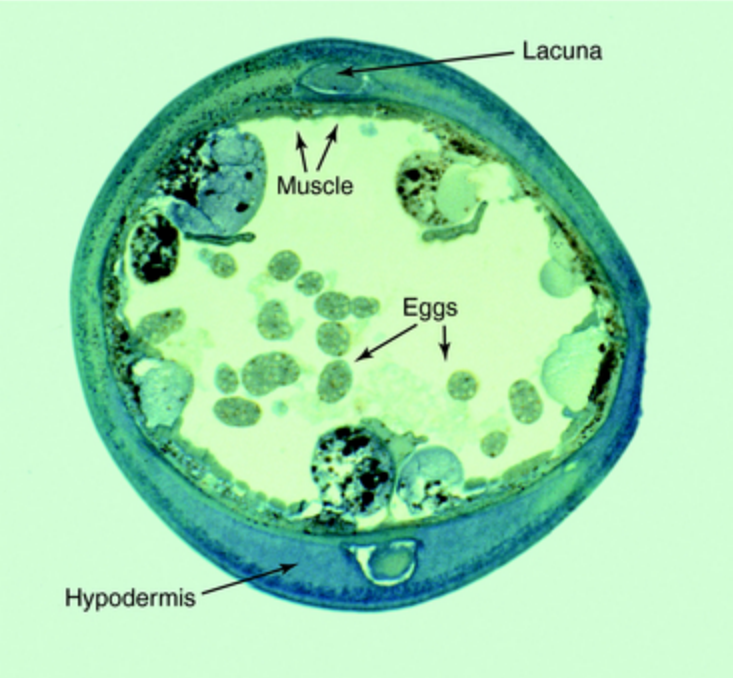

FIGURE 8-121 Cross-section of a female acanthocephalan, *Neoechinorhynchus* (×150). "Eggs" are actually clusters of oogonia called *ovarian balls* that float free in the body cavity.

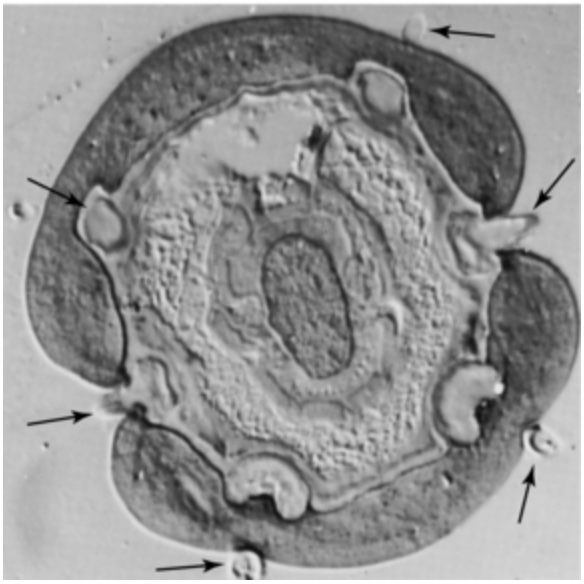

FIGURE 8-122 *Neoechinorhynchus*. Cross-section through the proboscis showing hooks *(arrows)* (×320).

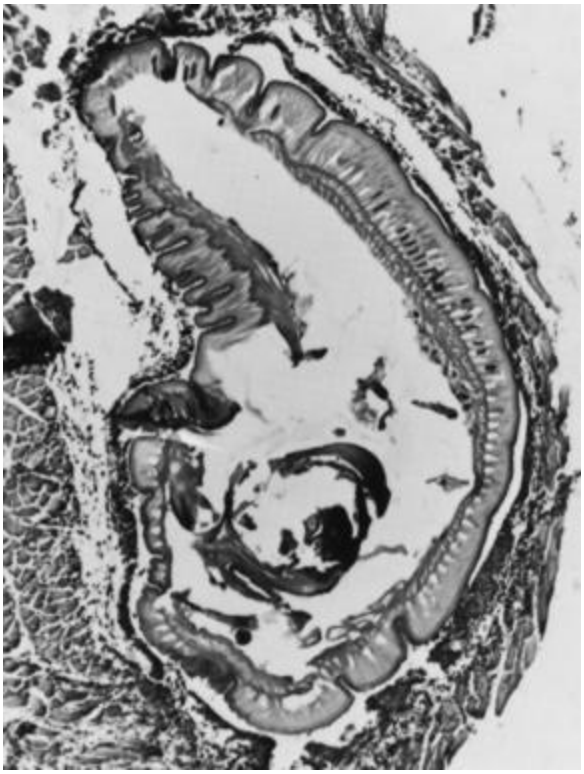

FIGURE 8-123 *Macracanthorhynchus ingens*. Cystacanth in skeletal muscle of a golden hamster *(Mesocricetus auratus)* (×66).

Courtesy Dr. G.R. Fahnestock.

The body wall is thick and multilayered and very distinctive in histologic sections. There is an outer tegument (outer plasma membrane and three fibrous layers that contain lacunae [channels] that may serve as a means of moving nutrients around the body), a thin “dermis” layer, and a layer of circular and longitudinal muscle tubules that highly are distinctive. In the cystacanth there are no reproductive organs, but there are two lemnisci, muscular and glandular structures that serve to evert and retract the thorny proboscis. The thick hypodermis lying external to the muscle layer provides the major clue as to the identity of a cystacanth.

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APPENDIX

Antiparasite Products by Species

Table A-1 Ovine Parasiticides*

Active Ingredient (Dose)	Example Trade Name	Withholding in Days		*Oesophagostomum*	*Telodorsagia*	*Trichostrongylus*	*Nematodirus*	*Marshallagia*	*Haemonchus*	*Cooperia*	*Dictyocaulus*	*Bunostomum*	*Chabertia*	*Strongyloides*	*Trichuris*	*Moniezia*	*Thysanosoma*	*Fasciola hepatica*	*Fascioloides magna*	*Oestrus ovis*	Coccidia
		Milk	Meat																		
Ivermectin (0.2 mg/kg PO)	Ivomec Sheep Drench	NFMS	11	+	+	+	+		+	+	+		+	+	+					+	
Moxidectin (0.2 mg/kg PO)	Cydectin Oral Drench for Sheep†	NFMS	7	+	+	+	+		+	+											
Albendazole (7.5 mg/kg PO)	Valbazen	NFMS	7	+	+	+	+	+	+	+	+		+			+	+	+	+		
Levamisole (8.0 mg/kg PO)	Levasole Sheep Wormer	NFMS	3	+	+	+	+		+	+	+	+	+								
Decoquinate (0.5 mg/kg daily for >28 days PO)	Deccox	NFMS	0																		+
Lasalocid (15 to 70 mg/head/day PO)	Bovatec	0	0																		+

*FDA-approved labeling has been relied on for most of the drugs listed. For a comprehensive listing of off-label usage, see Chapter 6 and/or current literature.
†FDA/CVM MUMS designation.
NFMS, Not for milking sheep; *PO*, orally.

Table A-2 Porcine Parasiticides*

Active Ingredient (Dose)	Example Trade Name	Withholding in Days	*Ascaris*	*Ascarops*	*Oesophagostomum*	*Metastrongylus*	*Strongyloides*	*Stephanurus*	*Hyostrongylus*	*Trichuris*	*Haematopinus*	*Sarcoptes*
Doramectin (0.30 mg/kg IM)	Dectomax Injectable Solution	24	+		+	+	+	+	+		+	+
Ivermectin (0.30 mg/kg SC; 1.8 g (starters, growers, and finishers) or 9.1 g (adult) per ton in feed	Ivomec	18	+	†	+	+	+	†	+		+	+
Fenbendazole (9 mg/kg for 3 to 12 days PO)	Safe-Guard EZ Scoop	0	+		+	+		+	+	+		
Levamisole (8 mg/kg PO)	Levasole	3	+		+	+	+					
Piperazine base (110 mg/kg PO)	Wazine	21	+		+							
Pyrantel tartrate (in feed 800 g/ton for treatment; 96 g/ton for continuous control)	Banminth 48	1	+		+							
Dichlorvos (12.5 mg/kg PO)	Atgard Swine Wormer	0	+	+	+					+		
Amitraz	Taktic	3									+	+

*FDA-approved labeling has been relied on for most of the drugs listed. For a comprehensive listing of off-label usage, see Chapter 6 and/or current literature.
†Ivermectin Premix is effective against *Ascarops* and *Stephanurus*.
IM, intramuscularly; *PO*, orally; *SC*, subcutaneously.

Table A-3 Bovine Parasiticides*

Active Ingredient (Dose)	Example Trade Name	Withholding Period in Days		*Oesophagostomum*	*Ostertagia*	*Trichostrongylus*	*Nematodirus*	*Haemonchus*	*Cooperia*	*Dictyocaulus*	*Bunostomum*	*Strongyloides*	*Trichuris*	*Thelazia*	*Fasciola*	*Moniezia*	*Chorioptes*	*Sarcoptes*	*Psoroptes*	Sucking lice	*Damalinia*	*Haematobia*	*Hypoderma*	Coccidia
		Milk	Meat																					
Doramectin (0.2 mg/kg SC or IM)	Dectomax Injectable	NFD	35	+	+	+		+	+	+	+	+	+	+				+	+	+			+	
Doramectin (0.5 mg/kg pour-on)	Dectomax Pour-On	NFD	45	+	+	+		+	+	+	+		+	+			+	+		+	+	+	+	
Eprinomectin (0.5 mg/kg pour-on)	Ivomec Eprinex Pour-On	0	0	+	+	+	+	+	+	+	+	+	+				+	+		+	+	+	+	
Ivermectin (0.2 mg/kg SC)	Ivomec Injection	NFD	35	+	+	+	+	+	+	+	+							+	+	+			+	
Ivermectin (0.5 mg/kg pour-on)	Ivomec Pour-On	NFD	48	+	+	+		+	+	+		+	+					+		+	+	+	+	
Moxidectin (0.2 mg/kg SC)	Cydectin Injection	NFD	21	+	+	+	+	+	+	+			+						+	+			+	
Moxidectin (0.5 mg/kg pour-on)	Cydectin Pour-On	0	0	+	+	+	+	+	+	+	+						+		+	+	+	+	+	
Ivermectin/clorsulon (0.2 and 2 mg/kg SC)	Ivomec Plus Injection	NFD	49	+	+	+	+	+	+	+	+					+		+	+	+			+	
Clorsulon (7 mg/kg PO)	Curatrem	NFD	8												+									
Albendazole (10 mg/kg PO)	Valbazen	NFD	27	+	+	+	+	+	+	+	+				+	+								
Fenbendazole (5 or 10 mg/kg PO)	Panacur/Safe-Guard	0†	8-13	+	+	+	+	+	+	+	+					‡								
Oxfendazole (4.5 mg/kg PO)	Synanthic	NFD	7	+	+	+		+	+	+	+					+								
Levamisole (6 mg/kg SC or bolus)	Levasole	NFD	2-7	+	+	+	+	+	+	+	+													
Morantel tartrate (10 mg/kg PO)	Rumatel	0	14	+	+	+	+	+	+															
Amprolium (prevention 5 mg/kg PO; 10 mg/kg treatment PO)	Corid	NFD	1																					+
Decoquinate (0.5 mg/kg day PO)	Deccox	NFD	0																					+
Lasalocid (100 to 360 mg/head/day PO)	Bovatec	NFD	0																					+
Monensin (115 to 660 mg/head/day PO)	Rumensin 80	0	0																					+
Sulfaquinoxaline (13 mg/kg/day PO)	Various	NFD	10																					+

*FDA-approved labeling has been relied on for most of the drugs listed. For a comprehensive listing of off-label usage, see Chapter 6 and/or current literature.
†10 mg/kg dose not for dairy cattle (NFD).
‡Not all formulations are approved.
IM, Intramuscularly; *NFD*, not for dairy cattle; *PO*, orally; *SC*, subcutaneously.

Table A-4 Feline Parasiticides*

Active Ingredient (Dose)	Example Trade Name	*Toxocara*	*Ancylostoma tubaeforme*	*Ancylostoma braziliense*	*Dirofilaria*[†]	*Taenia*	*Dipylidium*	Ticks	Fleas	Lice	*Otodectes*
Ivermectin (0.024 mg/kg monthly PO)	Heartgard for Cats		+	+	+						
Milbemycin (2 mg/kg monthly PO)	Interceptor	+	+		+						
Moxidectin (1 mg/kg) and imidacloprid (10 mg/kg) topical	Advantage Multi	+	+		+				+		+
Selamectin (6 mg/kg monthly topical)	Revolution	+	+		+				+		+
Piperazine (55 mg/kg PO)	Pipa-Tabs	+									
Pyrantel pamoate (10 to 20 mg/kg PO)[‡]	Nemex	+	+								
Praziquantel (5 mg/kg) and pyrantel pamoate (20 mg/kg PO)	Drontal	+	+			+	+				
Praziquantel (5-10 mg/kg PO, SC, or IM)	Droncit					+	+				
Emodepside (3 mg/kg) and praziquantel (12 mg/kg) topical	Profender	+	+			+	+				
Epsiprantel (1.25 mg/kg PO)	Cestex					+	+				
Lufenuron (30 mg/kg monthly PO)	Program								+		
Lufenuron (10 mg/kg SC every 6 months)	Program 6-Month Injection								+		
Dinotefuran and pyriproxyfen (topical)	Vectra								+		
Nitenpyram (1 mg/kg daily as needed PO)	Capstar								+		
Imidacloprid (monthly topical)	Advantage								+		
Fipronil (monthly topical)	Frontline							+	+	+	
Fipronil and methoprene (topical)	Frontline Plus							+	+	+	
Metaflumizone (monthly topical)	Promeris								+		
Ivermectin (ear topical)	Acarexx										+
Milbemycin (ear topical)	Milbemite										+

*FDA-approved labeling has been relied on for most of the drugs listed. For a comprehensive listing of off-label usage, see Chapter 6 and/or current literature.
[†]Prevents heartworm infection.
[‡]Commonly used in, but not FDA approved for use in, cats.
IM, Intramuscularly; *PO*, orally; *SC*, subcutaneously.

Table A-5 Canine Parasiticides*

Active Ingredient (Dose)	Example Trade Name	*Toxocara*	*Toxascaris*	*Ancylostoma caninum*	*Ancylostoma braziliense*	*Uncinaria*	*Trichris*	*Dirofilaria*[†]	*Taenia*	*Dipylidium*	*Echinococcus*	Ticks	Fleas	Lice	Mosquitoes	*Otodectes*	*Sarcoptes*
Melarsomine (2.5 mg/kg IM)	Immiticide							+									
Ivermectin (0.006 mg/kg) monthly PO	Heartgard							+									
Ivermectin (0.006 mg/kg) and pyrantel (5 mg/kg) monthly PO	Heartgard Plus	+	+	+	+	+		+									
Milbemycin (0.5 mg/kg) monthly PO	Interceptor	+		+			+	+									
Milbemycin (0.5 mg/kg) and lufenuron (10 mg/kg) monthly PO	Sentinel	+		+			+	+					+				
Moxidectin (2.5 mg/kg) and imidacloprid (10 mg/kg) monthly topical	Advantage Multi	+	+	+		+	+	+					+				
Selamectin (6 mg/kg) monthly topical	Revolution							+				‡	+			+	+
Ivermectin (0.006 mg/kg) and pyrantel pamoate (5 mg/kg) and praziquantel (5 mg/kg) monthly PO	Iverhart Max	+	+	+	+	+		+	+	+							
Fenbendazole (50 mg/kg × 3 days PO)	Panacur	+	+	+		+	+		+								
Febantel (25-62 mg/kg) and praziquantel (5-12 mg/kg) and pyrantel pamoate (5-12 mg/kg) PO	Drontal Plus	+	+	+		+	+		+	+	+						
Pyrantel pamoate (5 mg/kg PO)	Nemex	+	+	+		+											
Pyrantel pamoate (5 mg/kg) and praziquantel (5 mg/kg) PO	Virbantel	+	+	+	+	+			+	+							
Praziquantel (5 to 7.5 mg/kg PO, SC, or IM)	Droncit								+	+	+						
Epsiprantel (5.5 mg/kg PO)	Cestex								+	+							
Piperazine (55 mg/kg PO)	Tasty paste (and others)	+	+														
Lufenuron (10 mg/kg monthly PO)	Program												+				
Dinotefuran and pyriproxyfen and permethrin (topical)	Vectra 3D											+	+		+		
Imidacloprid (monthly topical)	Advantage												+				
Imidacloprid and permethrin (monthly topical)	K9 Advantix											+	+		+		
Nitenpyram (1 mg/kg as needed PO)	Capstar												+				
Spinosad (30 mg/kg PO)	Comfortis												+				
Fipronil (monthly topical)	Frontline											+	+	+			
Fipronil and methoprene (monthly topical)	Frontline Plus											+	+	+			
Amitraz and metaflumizone monthly (monthly topical)	Promeris											+	+				

*FDA-approved labeling has been relied on for most of the drugs listed. For a comprehensive listing of off-label usage, see Chapter 6 and/or current literature.
[†]Melarsomine removes adult heartworm infections; all other products in this column prevent hearthworm infection.
[‡]Approved against *Dermacentor variabilis* only.
IM, Intramuscularly; *PO*, orally; *SC*, subcutaneously.

Table A-6 Equine Parasiticides*

Active Ingredient (Dose)	Example Trade Name	*Parascaris*	*Strongylus*	*Strongylus* Tissue Stages	*Cyathostomes*	Encysted Cyathostomes	*Oxyuris equi*	*Triodontophorus*	*Trichostrongylus*	*Strongyloides*	*Onchocerca*	*Habronema*	*Draschia*	*Dictyocaulus*	*Anoplocephalids*	*Gasterophilus*	Flies	EPM
Ivermectin[†] (0.2 mg/kg PO)	Eqvalan	+	+	+	+	+	+	+	+	+	+	+	+	+		+		
Ivermectin (0.2 mg/kg) and praziquantel (1 mg/kg) PO	Zimecterin Gold	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		
Moxidectin (0.4 mg/kg PO)	Quest	+	+	+	+	+	+	+	+			+				+		
Moxidectin (0.4 mg/kg) and praziquantel (2.5 mg/kg) PO	Quest Plus	+	+	+	+	+	+	+	+			+			+	+		
Fenbendazole (5 mg/kg PO)[‡]	Panacur	+	+	+	+		+											
Fenbendazole (10 mg/kg PO)×5 days[‡]	Panacur Paste 10% Powerpac	+	+	+	+	+	+											
Oxibendazole (10 mg/kg PO)	Anthelcide EQ Equine Wormer	+	+		+		+	+		[§]								
Piperazine (110 mg/kg PO)	Wonder Wormer for Horses	+	+		+		+											
Pyrantel pamoate (6.6 mg/kg PO)	Strongid T	+	+		+		+								[¶]			
Pyrantel tartrate (2.64 mg/kg; daily as top dress)	Strongid C	+	+		+		+								[¶]			
Tetrachlorvinphos (1.54 mg/kg continuous feeding)	Equitrol																+	
Cyromazine (300 mg/horse/day PO)	Solitude IGR																+	
Diflubenzuron (0.15 mg/kg/day PO)	Equitrol II																+	
Nitazoxanide (25 mg/kg/5 days; 50 mg/kg/23 days PO)	Navigator																	+
Ponazuril (5 or 10 mg/kg/28 days PO)	Marquis																	+
Sulfadiazine (20 mg/kg) and pyrimethamine (1 mg/kg) PO for 90 to 270 days	ReBalance Antiprotozoal Oral Suspension																	+

*FDA-approved labeling has been relied on for most of the drugs listed. For a comprehensive listing of off-label usage, see Chapter 6 and/or current literature.
[†]Please note that some generic preparations of ivermectin are not labeled for *Oxyuris equi* or *Triodontophorus*.
[‡]10 mg/kg also recommended for foals with *Parascaris*.
[§]15 mg/kg PO for *Strongyloides*.
[¶]Takes increased amounts of pyrantel; pyrantel tartrate seems to work.
PO, Orally; *EPM*, equine protozoal myeloencephalitis.

Table A-7 Commercial Antiparasite Vaccines*

Marshall W. Lightowlers

Parasite	Vaccine Recipient	Marketing Name	Company[†]	Antigen Type
Antiprotozoal				
Babesia bovis	Cattle	Numerous[‡]	Local[§]	Live attenuated
Babesia bigemina	Cattle	Numerous	Local	Live attenuated
Babesia canis	Dog	Pirodog	Merial	Subunit
B. canis; Babesia rossi	Dog	Nobivac Piro	Intervet	Subunit
Eimeria species[¶]	Chicken	Livacox, Paracox, Eimeriavax	Biopharm, Schering-Plough, Bioproperties	Live attenuated
Eimeria species	Chicken	CoxAbic	ABIC	Subunit
Giardia duodenalis	Dog/cat	GiardiaVax	Fort Dodge Animal Health	Disrupted parasites
Leishmania donovani	Dog	Leishmune	Fort Dodge Animal Health	Subunit
Neospora caninum	Cattle	NeoGuard	Intervet	Killed whole parasites
Sarcocystis neurona	Horse	Sarcocystis Neurona Vaccine	Fort Dodge Animal Health	Killed whole parasites
Theileria annulata	Cattle	Numerous	Local	Live attenuated
Toxoplasma gondii	Sheep	Toxovax	Intervet	Live attenuated
Antihelminth				
Dictylcaulus viviparus	Cattle	Dictol, Bovilis, Huskvac	Intervet	Live attenuated
Antitick				
Boophilus microplus	Cattle	TickGard, Gavac	Intervet, Heber Biotec S.A.	Recombinant subunit

*Marketing and availability of these vaccines are subject to commercial decisions at any time, and hence the list cannot be considered to be accurate or comprehensive on an ongoing basis. These vaccines were being commercially marketed to some extent around the time of writing or in the recent past. An interpretation of the term "vaccine" has been used that excludes the use of situations where a viable, virulent infection is delivered as the immunizing procedure, with or without subsequent drug treatment of the vaccines. Such procedures underlie some immunizing treatments for coccidiosis in poultry and for *Theileria parva*.

[†]Marketing arrangements may lead to vaccines being sold under license in particular regions; hence the company specified may not be responsible for marketing the indicated vaccine in some areas.

[‡]Vaccines prepared using similar methodologies in a number of countries.

[§]A number of different institutes or companies involved with manufacture and marketing.

[¶]Up to seven different species of *Eimeria* may be included in a combined vaccine. Vaccines may be marketed in a number of different variants containing different combinations of different species' oocysts.

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