289 Tapeworms (Cestodes)

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SHORT VIEW SUMMARY

Definition
- Cestodes are flatworms (platyhelminths) that cause human parasitic infection in the form of intestinal tapeworms or invasive larval cysts (i.e., neurocysticercosis or echinococcosis) (see Table 289.1).

Epidemiology
- *Diphyllobothrium latum,* fish tapeworm, is associated with eating undercooked freshwater fish and is endemic worldwide.
- *Hymenolepis nana* is the most common tapeworm worldwide and is transmitted person to person.
- *Taenia saginata* (beef tapeworm) occurs in cattle-breeding areas of the world.
- *Taenia solium* (pork tapeworm), and consequently neurocysticercosis, is endemic to resource-limited areas including Mexico, Central and South America, Asia, and Africa.
- *Echinococcus granulosus* infection occurs worldwide in livestock-raising areas and primarily is associated with domestic dogs.
- *Echinococcus multilocularis* has a life cycle that involves wild canines and is endemic only in the Northern Hemisphere.

Microbiology
- Mature tapeworms reside in intestines of carnivorous animals.
- Eggs are shed and then pass to an intermediate host, causing cystic infection via dissemination of oncospheres into host tissues.
- A definitive carnivore host ingests cyst-infected tissue, and a tapeworm then develops in intestines.

Diagnosis
- Diagnosis of intestinal tapeworms relies on examination of stool for evidence of eggs or tapeworm segments (proglottids).
- Neurocysticercosis is diagnosed by typical appearance on imaging scans, and diagnosis is supported by clinical symptoms and serologic testing.
- Diagnosis of echinococcosis is made by typical imaging appearance and supported by serology.

Therapy
- The mainstay of therapy for intestinal tapeworms is praziquantel or niclosamide.
- Neurocysticercosis therapy depends on the location and stage of the cyst.
- Parenchymal neurocysticercosis is generally treated with a combination of anthelmintic agents and corticosteroids (albendazole or praziquantel or both).
- Echinococcosis, depending on the stage and species, often requires surgery in combination with anthelmintic agents.

Prevention
- Improved sanitation is essential.
- Education programs on symptoms of infection and keeping livestock in corrals away from humans should be implemented.
- Livestock at market or slaughterhouse should be screened for cysts.
- Dogs should be screened and treated to eliminate *E. granulosus.*
- Prolonged freezing or thorough cooking kills cysts in tissue.

In humans, parasitic cestode infections occur in either of two forms: as mature tapeworms residing in the gastrointestinal tract or as one or more larval cysts (variously called hydatidosis, cysticercosis, coenurosis, or sparganosis) embedded in liver, lung, muscle, brain, eye, or other tissues.[1,1a,1b] The form taken by the infecting parasite depends on which cestode species causes the infection and, to a lesser extent, on the route by which the infection was acquired. Table 289.1 summarizes the common cestode parasites of humans, their typical vectors, and their usual symptoms.

In this chapter, parasite biology and the immunology of cestode infection are discussed, followed by descriptions of individual parasite species: intestinal tapeworms (e.g., *Diphyllobothrium latum, Hymenolepis nana, Taenia saginata,* and *Taenia solium*) and invasive cestode parasites (cysticercosis *[T. solium],* hydatid and alveolar cyst disease [*Echinococcus* spp.], sparganosis, and coenurosis *[Taenia multiceps]*). Diagnosis and therapy, outlined briefly under the individual parasite headings, are discussed in greater detail at the end of each section.

CESTODE BIOLOGY

Parasite Life Cycle

The parasitic cestodes discussed in this chapter are flatworms (platyhelminths) of the orders Pseudophyllidea (*Diphyllobothrium* and *Spirometra*) and Cyclophyllidea (other species), which divide their life cycle between two animal hosts (Fig. 289.1).[1,1a,1b] As mature tapeworms, these parasites reside in the intestinal tract of a definitive host, a carnivorous mammal. Depending on the parasite species, mature tapeworms vary in length from several millimeters (*Echinococcus* spp.) to 25 m *(Diphyllobothrium).*[1,1a,1b]

The tapeworm consists of a head *(scolex),* a neck, and a tail. The head has two or more suckers and in some cases a *rostellum,* or knob of small hooks, used to attach to the wall of the host's intestine (Fig. 289.2A).[2] The scolex is connected by a short neck to the lower portion of the tapeworm, the *strobila,* which is a ribbon-like chain of independent but connected segments called *proglottids* (Fig. 289.2B). Each proglottid has both male and female sexual organs and is responsible for producing the parasite's eggs. Proglottids begin to develop in the neck region of the parasite and then mature and move downward in the strobila as new segments are added from above. The hermaphroditic proglottids become gravid and eventually break free of the tapeworm. Proglottids may degenerate in the stool, releasing eggs (thousands to millions per day) into the feces. Alternatively, intact proglottids may be passed in the stool, with egg release occurring outside the body. In some cases, a section of strobila may be passed in a single day, with no further release of proglottids for several days thereafter. In practical terms, this means that although the number of tapeworm eggs in the stool is usually high, detection of parasite eggs by standard stool examination may be sporadic. Therefore multiple stool samples, rectal swabs, and visual examination of stool and perineum for proglottids may be required to detect a tapeworm infection. For some species of tapeworm (e.g., *T. saginata*), the proglottids are motile. They may migrate within the gastrointestinal tract, causing biliary or appendiceal obstruction, or out of the body, to be found in the perineum.

At the point at which eggs are released, two effective biotypes of parasite can be defined. If the eggs released from the parasite are partially developed, they are called *embryonated.* If the egg embryo has not yet begun its differentiation, the egg is referred to as *nonembryonated.* In

TABLE 289.1 Common Cestode Parasites of Humans, Their Typical Vectors, and Their Usual Symptoms

PARASITE SPECIES	DEVELOPMENTAL STAGE FOUND IN HUMANS	COMMON NAME	TRANSMISSION SOURCE	SYMPTOMS ASSOCIATED WITH INFECTION
Diphyllobothrium latum	Tapeworm	Fish tapeworm	Plerocercoid cysts in freshwater fish	Usually minimal; with prolonged or heavy infection, vitamin B_{12} deficiency
Hymenolepis nana	Tapeworm, cysticercoids	Dwarf tapeworm	Infected humans	Mild abdominal discomfort
Taenia saginata	Tapeworm	Beef tapeworm	Cysts in beef	Abdominal discomfort, proglottid migration
Taenia solium	Tapeworm	Pork tapeworm	Cysticerci in pork	Minimal
Taenia solium (Cysticercus cellulosae)	Cysticerci	Cysticercosis	Eggs from infected humans	Local inflammation, mass effect; if in CNS, seizures, hydrocephalus, arachnoiditis
Echinococcus granulosus	Larval cysts	Hydatid cyst disease	Eggs from infected dogs	Mass effect leading to pain, obstruction of adjacent organs; less commonly, secondary bacterial infection, distal spread of daughter cysts
Echinococcus multilocularis	Larval cysts	Alveolar cyst disease	Eggs from infected canines	Local invasion and mass effect leading to organ dysfunction; distal metastasis possible
Taenia multiceps	Larval cysts	Coenurosis, bladder worm	Eggs from infected dogs	Local inflammation and mass effect
Spirometra mansonoides	Larval cysts	Sparganosis	Cysts from infected copepods, frogs, snakes	Local inflammation and mass effect

CNS, Central nervous system.

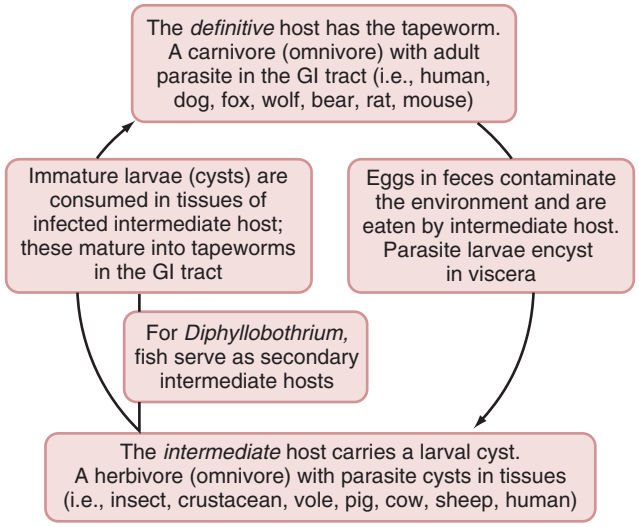

FIG. 289.1 Cestode parasites alternate larval and adult stages in two different hosts. *GI,* Gastrointestinal.

biologic terms, the embryonated egg can immediately infect the next intermediate mammalian or insect host, typically a herbivore or omnivore, through ingestion of food containing the egg.[1,1a,1b] Such eggs, typical of *Echinococcus* spp., *Taenia* spp., and *H. nana,* may lie dormant in grazing areas or become scattered in the home environment and remain infectious for several months to years.[1,1a,1b,3] Once ingested, the egg hatches in the intermediate host's intestine, releasing an *oncosphere,* which penetrates the gut mucosa to reach the circulation. The oncosphere passes to any of several organs to form a parasite cyst, which is variously called a cysticercoid, cysticercus, alveolar cyst, or hydatid cyst, depending on its morphology. The life cycle of these parasites is completed when the carnivorous definitive host consumes the cyst-infected tissues of the intermediate host and the cyst develops into a mature tapeworm in the lumen of the definitive host's intestine.

For nonembryonated eggs, such as those of the fish tapeworm *D. latum,* initial development takes place outside the body in water, after which the eggs hatch to release a free-swimming *coracidium* larva.[2] In time, the coracidium is ingested by a small crustacean called a copepod and then develops into a procercoid larva within the copepod's tissues. When the copepod is ingested by a fish or other intermediate host, the procercoid infects its musculature, developing into the next larval stage, the *plerocercoid* cyst, or *sparganum.* If an uncooked plerocercoid of *D. latum* is ingested by a human, its definitive host, it develops into a mature, intraluminal fish tapeworm. However, if the fish containing the plerocercoid is ingested by another, larger fish, it does not become a tapeworm. It reencysts instead as a plerocercoid in the muscles of the second, larger fish.

Plerocercoid encystment or reencystment is significant in terms of human disease (as *sparganosis*) for cestode species for which humans cannot serve as the definitive host (e.g., *Spirometra mansonoides,* a tapeworm of dogs and felines). Plerocercoids can develop in human tissues if *Spirometra*-infested copepods are ingested in drinking water. Alternatively, human plerocercoid cysts may be acquired via the intestine from another intermediate host (e.g., tadpole, frog, snake) if the meat of that aquatic host is eaten uncooked. Migrating plerocercoid cysts can also transfer directly into the skin or the eye if raw flesh of an aquatic intermediate host is used as a poultice in traditional healing.[2]

As a rule, humans are either definitive or intermediate hosts for a given cestode parasite, but not both. For example, humans are solely definitive hosts (i.e., with tapeworms) for *D. latum* (fish tapeworm) and *T. saginata* (beef tapeworm) and are solely intermediate hosts for *Echinococcus* spp. (hydatid cysts and alveolar cysts), *Spirometra* (sparganosis), and *T. multiceps* (coenurosis). There are two exceptions to this rule. The first is *T. solium,* which develops in humans as a cysticercus if ingested as an egg or as a tapeworm if ingested as a cysticercus in infected pork. It is thus possible for one patient to harbor both cyst and tapeworm forms of *T. solium.* Such dual infection is seen in approximately 25% of cysticercosis cases. The second exception is the dwarf tapeworm, *H. nana,* whose eggs, after ingestion, hatch in the gut and encyst within the wall of the human intestine. After 5 to 7 days, the cyst breaks open, and the larva develops (within the same host) to become a mature tapeworm. The fertile eggs of this tapeworm may directly infect the mucosa, permitting a continued increase in the number of tapeworms in the affected host, without further exposure to environmental egg contamination. In this manner, humans serve as both intermediate and definitive hosts for *H. nana.* Single-host proliferation such as that of *H. nana* is highly unusual among human cestode infections and helminth infections in general. Normally, heavy cestode infections can be acquired only by repeated environmental exposure to eggs or infectious parasite cysts.

Disease Pathogenesis and Immunology

Adult tapeworms in the intestinal tract generally cause minimal local pathology. Reduced nutrient absorption and alteration of gut motility have been described, but there is no firm association of adult tapeworm infection with specific bowel symptoms. An immune response to adult tapeworms provokes eosinophilia and immunoglobulin E (IgE) elevation in some patients, but the immune response does not appear to alter the course of an intraluminal tapeworm infection. In light of the limited

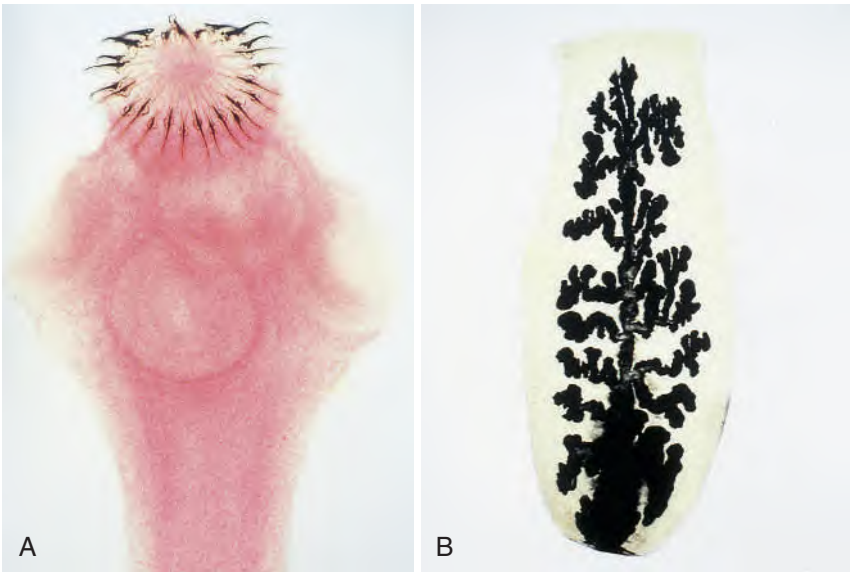

FIG. 289.2 (A) The scolex and (B) a proglottid of the cestode *Taenia solium. (From Ash LR, Orihel TC.* Atlas of Human Parasitology. *3rd ed. Chicago: American Society for Clinical Pathology; 1990.)*

range of potential hosts observed for most adult tapeworms, it has been suggested that host factors, including the presence or absence of specific immunoreactivity, may determine the success of parasite infections in various potential host species.[4]

The immune response to invasive cyst infection is more pronounced but is often unsuccessful in eradicating the cyst in susceptible hosts. Infiltration with neutrophils and eosinophils is followed by local fibrosis, leading to cyst encapsulation and macrophage infiltration. Once the cyst is encapsulated, antigen release may be limited, leading to a reduction in the local inflammatory response. Specific antibody production remains detectable in the serum, however, and delayed-type hypersensitivity may be detected on skin testing. The immune response often increases later as the cyst begins to die and leak antigen or as it erodes into a body cavity, duct, or vessel, increasing local or systemic exposure to antigen. Experimentally, the anticyst immune response appears to limit dissemination of *Echinococcus* spp. after an initial infection.[4,5] Anticyst immunity is also likely to contribute to the spontaneous clearance of *H. nana* infection in older children. There is evidence of increased amounts of IgG subclasses as well as proinflammatory cytokines within the cerebrospinal fluid (CSF) of patients having severe neurocysticercosis.[6] It is unclear if this response contributes to the severity of the disease or is a consequence of severe infection; however, it does not effectively control the infection. Furthermore, symptomatic cysticercosis appears to be related to a depressed cellular immune response compared with the immune response of asymptomatic individuals.[6]

INTESTINAL TAPEWORMS

Diphyllobothrium latum

D. latum, or fish tapeworm, is one of the pseudophyllidean cestodes transmitted via aquatic species.[2] Human infection with *D. latum* is acquired by eating uncooked freshwater fish containing the parasite's plerocercoid cysts. Traditional modes of infection include consumption of dried or smoked fish, which may contain viable cysts if not further cooked, or tasting flavored freshwater fish (e.g., gefilte fish) before cooking. The enthusiasm for raw bar foods such as ceviche, sushi, and sashimi prepared from freshwater fish, especially salmon, has increased the transmission potential for *D. latum* in developed areas of North America.[7,8] Areas of the world in which *D. latum* is highly endemic (>2% prevalence) include specific lake and delta areas of Siberia, Europe (especially Scandinavia and other Baltic countries), North America, Japan, and Chile. In 2006 there was an outbreak in Lake Geneva, Switzerland, caused by freshly caught raw perch served at a wedding.[9] Plerocercoids were also found in 6% to 25% of fish caught in four Italian lakes.[10] Endemicity in rural areas is favored by stable zoonotic transmission through alternative nonhuman definitive hosts including seals, cats, bears, minks, foxes, and wolves.

Human *D. latum* tapeworms are large, reaching up to 25 m (3000–4000 proglottids) in length. It takes 3 to 6 weeks after exposure for the tapeworm to mature. Once established, a *D. latum* parasite may survive 30 years or more. Multiple tapeworms in the same patient are common. Normally, infection is asymptomatic, but a proportion of infected individuals report nonspecific symptoms of weakness (66%), dizziness (53%), salt craving (62%), diarrhea (22%), and intermittent abdominal discomfort.[2]

Prolonged (more than 3 or 4 years) or heavy *D. latum* infection may lead to megaloblastic anemia caused by vitamin B_{12} deficiency. The vitamin B_{12} deficiency is a consequence of two factors: parasite-mediated dissociation of the vitamin B_{12} intrinsic factor complex in the gut lumen (making vitamin B_{12} unavailable to the host) and heavy vitamin uptake and use by the parasite. Megaloblastic anemia may be worsened by concurrent folate deficiency, which also occurs as a consequence of *D. latum* infection. Vitamin B_{12} deficiency may be sufficiently severe to cause injury to the nervous system including peripheral neuropathy and severe combined degeneration of the central nervous system (CNS).

Tapeworm infection may first be suspected based on the patient's history or when contrast studies of the intestine show an intraluminal, ribbon-like filling defect. Definitive diagnosis of *D. latum* infection is made by detection of 45- × 65-mm operculated parasite eggs on stool examination (Fig. 289.3A–B). Recovery of proglottids (with a characteristic central uterus) also establishes the diagnosis.

Treatment is with a single course of niclosamide or praziquantel (see "Therapy").[11] Mild vitamin B_{12} deficiency is reversed by eradicating the tapeworm. Severe vitamin B_{12} deficiency should be treated with parenteral vitamin injections. If a patient presents with vitamin B_{12} deficiency and epidemiologic risk factors for fish tapeworm infection, one should maintain a high index of suspicion for possible infection.

Hymenolepis nana

H. nana, also known as dwarf tapeworm, is a cyclophyllidean tapeworm with embryonated eggs.[2] It is probably the most prevalent tapeworm worldwide, and it is the only tapeworm that can be transmitted directly from human to human. Areas of endemicity (1%–30% prevalence) include Asia, southern and eastern Europe, Central and South America, and Africa.[12] In North America, infection is most frequently found among institutionalized populations (up to 8% prevalence reported in the past)[13] and among malnourished or immunocompromised patients.

Ingestion of parasite eggs on fecally contaminated food or fomites allows the initial infection. Once in the intestine, the eggs hatch to form oncospheres, which penetrate the mucosa to encyst as cysticercoid larvae. The larval cyst ruptures 4 or 5 days later into the lumen to form the relatively small, adult *H. nana* tapeworm (15–50 mm in length). Internal autoinfection may occur as parasite eggs are released from gravid

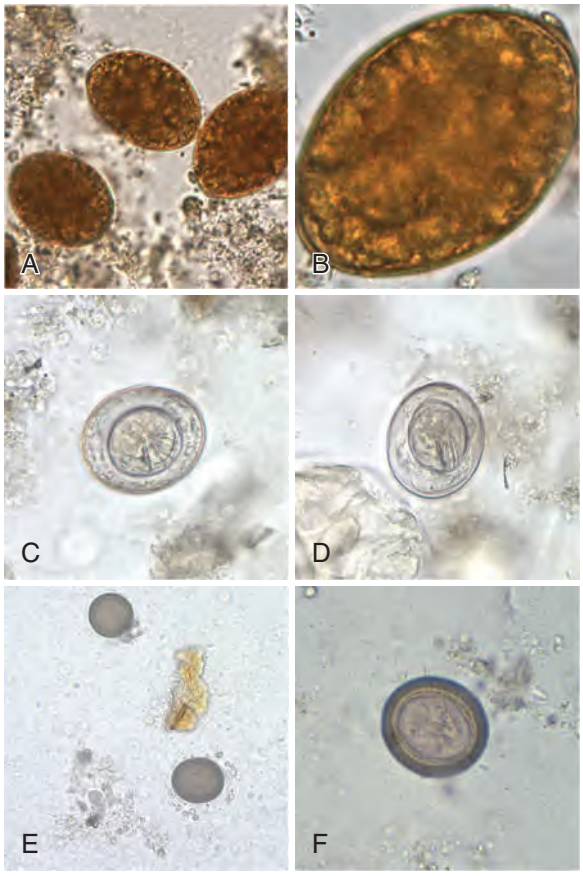

FIG. 289.3 (A–B) Eggs of *Diphyllobothrium latum* (55–75 µm × 40–50 µm) in an iodine-stained wet mount. Note the knob at the abopercular end in (B). (C–D) Eggs of *Hymenolepis nana* (30–50 µm) in an unstained wet mount. Note the presence of hooks in the oncosphere and polar filaments within the space between the oncosphere and outer shell. (E–F) *Taenia* spp. eggs (30–35 µm) in unstained wet mounts. The eggs of *T. solium* and *T. saginata* are indistinguishable from each other as well as from other members of the Taeniidae family.

proglottids in the ileum. In addition, poor sanitary practices promote external (fecal-oral) autoinfection as well as transmission to others sharing the same living quarters. Heavy infection is common among children and may be associated with abdominal cramps, anorexia, dizziness, and diarrhea. In areas of mass drug administration for other soil-transmitted helminth infections, *H. nana* has emerged as a prevalent pathogen because it does not respond to albendazole or mebendazole therapy given for intestinal nematodes.[14] *H. nana* has been associated with anemia and weight loss among affected children.[15]

H. nana infection is diagnosed by identifying the 30- × 47-µm parasite eggs (with their characteristic double membrane) in the stool (Fig. 289.3C–D). Treatment is with praziquantel or niclosamide (see "Therapy").[11] Developing *H. nana* cysticercoids are not as susceptible to drug therapy as adult tapeworms. Because these cysts can emerge several days later to form new tapeworms, effective therapy for *H. nana* requires either higher than usual doses of praziquantel to reach cysticidal levels or more prolonged therapy with niclosamide (to eliminate emerging tapeworms) for 5 to 7 days. Nitazoxanide has also been used to treat infection; it appears to be highly effective and has been used as an alternative therapy after treatment failures with niclosamide.[16]

Taenia saginata

T. saginata, known as the beef tapeworm, is transmitted to humans in the form of infectious larval cysts found in the meat of cattle, which serve as the parasite's usual intermediate host.[1,1a,1b,2] The *T. saginata* tapeworm is common in cattle-breeding areas of the world. Areas with the highest prevalence (up to 27%) are in central Asia, the Near East, and central and East Africa. Areas of lower prevalence (<1%) are found in Europe, Southeast Asia, Central America, and South America. Consumption of measly (i.e., cyst-infected) uncooked or undercooked beef is the usual means of transmission. Rare steak or kebabs and steak tartare are dishes typically associated with *T. saginata* infection. In the definitive human host, adult *T. saginata* tapeworms are long (10 m) and can contain more than 1000 proglottids, each capable of producing thousands of eggs. If, through poor sanitary practices, eggs released in the feces are allowed to reach grazing areas, cattle are subsequently infected with *T. saginata* cysticerci. Alternative intermediate hosts include llamas, buffalo, and giraffes. Humans are the only definitive host.

Symptoms are absent in most patients with *T. saginata* infection. A small number report mild abdominal cramps or malaise. The proglottids of *T. saginata* are motile and occasionally migrate out of the anus, to be found in the perineum or on clothing. The patient may report seeing moving segments in the feces or passing several feet of strobila at one time. These events are often psychologically distressing and are associated with significant anxiety-associated symptoms.

Specific diagnosis of *T. saginata* infection can be established by recovery of parasite proglottids.[1,1a,1b,2] If only eggs are found in the stool, it is important to note that *T. saginata* eggs are morphologically indistinguishable from *T. solium* eggs (Fig. 289.3E–F). With *T. solium* tapeworms there is potential for autoinfection causing cysticercosis; therefore if any *Taenia* spp. eggs are detected, treatment should be given without delay for further speciation. Effective oral treatment for either *T. saginata* or *T. solium* is obtained with praziquantel or niclosamide (see "Therapy").[11]

Taenia solium

Humans can serve as either intermediate or definitive hosts for *T. solium.* Individuals who ingest *T. solium* eggs develop tissue infection with parasite cysts, a condition known as cysticercosis (see "Cysticercosis" for details of this illness). Patients who consume raw or undercooked pork containing infectious larval cysts (cysticerci) acquire the pork tapeworm—that is, the adult form of *T. solium,* which resides in the intestinal tract.[1,1a,1b,2] These tapeworms develop to 2 to 8 m in length and may survive for 10 to 20 years. Some patients harbor both cysticerci and *T. solium* tapeworms, and it is possible for a tapeworm-carrying individual to develop cysticercosis by autoinfection. Areas in which *T. solium* infection is endemic include Mexico, Central America, South America, Africa, Southeast Asia, India, the Philippines, and southern Europe.

Infection with *T. solium* tapeworms is generally asymptomatic unless cysticercosis, caused by autoinfection with parasite eggs, supervenes. If tapeworm infection is diagnosed, one should also have a high index of suspicion for concomitant cysticercosis. The proglottids of *T. solium* are not motile (in contrast to those of *T. saginata*) and do not migrate. Infection with *Taenia* spp. is readily diagnosed by detecting eggs during stool examination, but *T. solium* eggs are indistinguishable from *T. saginata* eggs (see Fig. 289.3E–F). If a proglottid is recovered, the species can be identified based on the characteristic features of the uterine canals in the segment.[1,1a,1b] Species identification is not required for therapy, which can be with either praziquantel or niclosamide.[11]

OTHER SPECIES CAUSING TAPEWORM INFECTION IN HUMANS

Human tapeworm infection also may be caused by *Dipylidium caninum,* a more frequent parasite of dogs and cats, or by *Hymenolepis diminuta,* a tapeworm that usually infects rats.[1,1a,1b,2] Such infections are acquired by consumption of insects (fleas or beetles) containing the larval cysticercoids of these species and are most commonly seen among children. Human infection with tapeworm species related to *D. latum—Diphyllobothrium klebanovskii, Diphyllobothrium dendriticum, Diphyllobothrium ursi,* and *Diphyllobothrium dalliae*—has been described in the Arctic and areas of Siberia. *Diphyllobothrium nihonkaiense,* endemic to Japan, is another related fish tapeworm that can cause infections in humans, and it has been reported in isolated cases in Europe after ingestion of imported fish.[17] *Taenia asiatica,* described in 1993 and confused with *T. saginata* in the past, is found in some countries of Southeast Asia and India. In contrast to *T. saginata* and *T. solium,* this parasite is viscerotropic and is transmissible through ingestion of visceral organs from pigs. It has been found in the muscle of pigs, but, in contrast to *T. solium,* it

does not cause cysticercosis.[15,18] Rarely, other tapeworm species infect humans, particularly individuals with unusual dietary habits such as the consumption of uncooked animal viscera. Infection is diagnosed by identifying characteristic parasite eggs in the stool. Effective treatment is obtained with praziquantel or niclosamide.

DIAGNOSIS

Because mature tapeworm infection is strictly an intraluminal intestinal infection, the most practical approach to diagnosis is examination of the feces for parasite eggs or proglottids. As discussed under "Cestode Biology," egg release in the stool may be variable because of an irregular rate of proglottid detachment and degeneration. Thus examination of stool samples taken on several different days may be required to establish a diagnosis. Sensitivity for egg detection may be improved by formyl ethyl acetate or other concentration techniques. Because cestode eggs are relatively heavy, sedimentation procedures (not flotation) provide a more efficient means to isolate tapeworm eggs. When handling specimens, it is important to remember that *T. solium* eggs are infective for humans and cause cysticercosis. For this reason, precautions should be taken to avoid any potential contamination of fingers or clothing with parasite eggs.

In some cases, intact proglottids are passed in the stool. This is most common with *D. latum, T. saginata, T. solium,* and *D. caninum.* Expelled proglottids tend to degenerate over time, so fixation and staining of specimens are recommended to allow effective microscopic speciation. Although species identification is not essential for treatment, identification of *T. solium* infection is significant and should prompt consideration of possible cysticercosis in the index patient or among his or her household contacts.[19] Proglottids of *D. latum* (fish tapeworm) often pass as short chains of grayish white connected segments, each 11 × 3 mm, with a central uterine structure.[2] Proglottids of the pork tapeworm, *T. solium,* are 11 × 5 mm, with a lateral genital pore and 7 to 13 branches on either side of the central uterine canal. Proglottids of *T. saginata,* the beef tapeworm, have a similar appearance but may be distinguished by the larger number of lateral uterine branches (15–20) in the proglottid. *T. saginata* proglottids are motile and may emerge spontaneously from the anus to be found on the perineum, on the legs, or on clothing. Proglottids of *D. caninum* (23 × 8 mm) are also motile and may be described by the patient (or parent) as whitish, moving cucumber seed–like objects in the stool. *D. caninum* proglottids may also become adherent to perianal hairs and then dry to form a whitish yellow object resembling a small grain of rice. Detection of specific coproantigens in the stool has improved diagnosis of *Taenia* infection and is genus specific. It carries a specificity of up to 95% to 98%. Newer polymerase chain reaction–based tests also show potential to identify infection at a species level.[15]

THERAPY

Tapeworm infection should be treated whenever diagnosed. Safe, effective treatment of intestinal tapeworm infection may be achieved with either praziquantel or niclosamide. Both are well-tolerated oral agents that have direct parasiticidal effects on intraluminal cestode parasites. Although both agents are usually effective and considered first-line therapy, there have been reports of treatment failure, likely secondary to resistance. In some cases, nitazoxanide has been used as an alternative drug and has been found to be safe and effective.[20]

Niclosamide

Niclosamide is a poorly absorbed, narrow-spectrum anthelmintic that is available as 500-mg chewable tablets (e.g., Yomesan; Bayer).[11] However, it is no longer commercially available in the United States. The drug is normally taken as a 2-g (four-tablet) single dose for adults, as a 1.5-g (three-tablet) dose for children weighing more than 34 kg (75 lb), or as a 1-g (two-tablet) dose for children weighing 11 to 34 kg (25–75 lb). A single treatment is effective for *D. latum, T. saginata, D. caninum,* and *T. solium* tapeworms.

Eradication of *H. nana* tapeworm infection requires a more prolonged course of therapy (repeat daily doses for 1 week) because of concomitant infection with maturing *H. nana* cysts, which are not affected by the drug. It is normally recommended that after the first dose, subsequent doses for *H. nana* (i.e., days 2–7) be reduced to 1 g daily for adults and large children (>34 kg) and to 0.5 g daily for small children. These follow-up doses are intended to kill any newly emerging *H. nana* tapeworms and should completely eliminate the infection. Nevertheless, it is appropriate to rescreen the patient's stool for parasite eggs 1 and 3 months after therapy to ensure cure. A repeated cycle of standard dosing (as just outlined) is usually sufficient to eliminate persistent infection.

Niclosamide must be thoroughly chewed before swallowing to obtain the maximal anthelmintic effect. Because the drug is poorly absorbed, the typical side effects of niclosamide are mild, occurring at a rate of approximately 10%.[11] Side effects include malaise, mild abdominal pain, and nausea on the day of administration. High doses of niclosamide have not been shown to have mutagenic effects in animals, and the drug has been placed in US Food and Drug Administration (FDA) pregnancy category B. Normally, treatment should be delayed until after pregnancy, but with *T. solium* there is concern that patients may develop cysticercosis through autoinfection with parasite eggs. Considering the relative risks and benefits, it may be appropriate to treat pregnant women who have *T. solium* tapeworms at the time of diagnosis and not delay therapy. Concern has also been raised about the possibility of internal autoinfection during *T. solium* therapy because of the release and possible retrograde intestinal movement of eggs during therapy. Although such autoinfection has not been documented, some experts recommend a mild laxative 1 or 2 hours after niclosamide treatment to avoid this possibility in *T. solium*–infected patients.

Praziquantel

Praziquantel is a broad-spectrum anthelmintic used to treat both trematode and cestode infections.[11] It is available as a scored, 600-mg coated tablet (e.g., Biltricide, Bayer); it has excellent activity against all tapeworms and is given as a single dose of 5 to 10 mg/kg for both children and adults. The exception to this regimen is *H. nana* infection, for which a higher dose of 25 mg/kg is recommended. If the *H. nana* infection is heavy, it is recommended that the dose be repeated 1 week after the initial therapy. Follow-up stool screening is recommended at 1 and 3 months to ensure eradication of infection.

Mild side effects occur in 10% to 50% of patients treated, depending on the population. Side effects include transient dizziness, headache, malaise, abdominal pain, and nausea. Moderate side effects, including sedation, vomiting, diarrhea, urticaria, rash, fever, and mild transaminitis, are not as common (<10%) and are also transient. Similar to niclosamide, praziquantel is classified in FDA pregnancy category B. However, two well-powered, placebo-controlled randomized trials of praziquantel treatment during pregnancy showed no harm to the fetus and no adverse birth outcomes.[21,22] Potential risks and benefits of treatment should be weighed before use; however, praziquantel appears safe for use in later pregnancy and during lactation.[23]

INVASIVE CESTODE INFECTIONS

Cysticercosis

Cysticercosis is a tissue infection with larval cysts of the cestode *T. solium* in which the patient serves as an intermediate host for the parasite. Infection is acquired by consumption of *T. solium* eggs by fecal-oral transmission from a *T. solium* tapeworm carrier. Prevalence is high wherever *T. solium* tapeworms are common (i.e., Mexico, Central America, South America, Southeast Asia, Africa, China, India, and Nepal),[24,25] and the World Health Organization (WHO) has estimated that there are more than 50,000 deaths per year from neurocysticercosis.[26] In recent years, cases in "nonendemic" countries, in particular the United States, have increased due to both imported cases and locally acquired disease,[27] whereas numbers seem to be decreasing in some highly endemic areas, possibly from better sanitation and public awareness of the disease.[27] A survey of hospitalizations for neurocysticercosis in the United States for the years 2003–2012 found 18,584 hospitalizations, with an estimated cost of greater than $908 million.[28] Nearly three-quarters of the cases were in Hispanic patients. Infected subjects normally harbor multiple cysts in many parts of the body. In areas of endemicity, the cumulative infection risk increases with age, frequent consumption of pork, and poor household hygiene.[29] Symptoms may develop because of local inflammation at the site of involvement; however, apart from CNS and cardiac involvement, serious disease is rare.

Clinical Presentation

Neurocysticercosis, which refers to the most common presentation of cysticercosis, is the term used for human CNS involvement with *T. solium* cysts.[30] Infection may involve any part of the CNS, but symptomatic disease is most often related to intracerebral lesions (causing mass effects, seizures, or both) (Fig. 289.4), intraventricular cysts (causing hydrocephalus), subarachnoid lesions (causing chronic meningitis), and spinal cord lesions (causing cord compression syndrome or meningitis). Seizures, occurring in up to 70% of patients with neurocysticercosis, and intracranial hypertension are the most common clinical manifestations.[26,30] Intraparenchymal cerebral cysts typically enlarge slowly, causing minimal symptoms until years or decades after the onset of infection, when the cysts begin to die. At this point, cysts may lose osmoregulation and begin to swell. They may also leak antigenic material that provokes a severe inflammatory response (cerebritis and meningitis). Both processes contribute to symptoms of focal or generalized seizures, sensorimotor deficits, intellectual impairment, psychiatric disorders, and symptoms of hydrocephalus. The peak incidence of onset of neurologic symptoms is 3 to 5 years after infection but may not occur until 30 years later or even longer. In regions where *T. solium* is endemic, 30% to 50% of patients with seizures have antibodies to *T. solium*, compared with the 2% to 11% prevalence in the general population, suggesting the likelihood that neurocysticercosis is an underlying cause of their disease.[30,31] Further studies using computed tomography (CT) in areas of Guatemala, Mexico, Ecuador, and Honduras have shown that up to 20% of the general population have asymptomatic brain calcifications.[32] However, the strength of the association varies across studies, and good-quality epidemiologic data are often lacking.[33]

Because of their critical location, intraventricular cysts and basilar cysts tend to cause symptoms early during the course of the infection. The symptoms are due to obstruction of CSF flow or local meningeal irritation, which leads to injury to local blood vessels, cranial nerves, or the brainstem.[30] An aggressive form of basilar neurocysticercosis, called *racemose cysticercosis,* has been described in which cysts proliferate at the base of the brain, resulting in mental deterioration, coma, and death. Another severe form of neurocysticercosis, cysticercotic encephalitis, represents a massive infection of the brain parenchyma and induces a significant immune response of the host that complicates treatment regimens. Intraparenchymal spinal cord lesions are often symptomatic early because of direct local pressure effects. When spinal column cysts develop outside the cord itself, the onset of symptoms may be more gradual. The slow onset of external cord compression, arachnoiditis, or radiculopathy may result in a confusing progression of symptoms. In the CNS, multiple cysticerci are the rule, and active symptoms may refer to one or several anatomic locations.

Cysts outside the CNS tend not to be symptomatic. These cysts eventually die and calcify, to be detected incidentally on plain radiographs of the limbs. Although symptomatic cardiac cysticercosis is rarely reported, autopsy reports of patients with cysticercosis have shown cysts involving the heart in up to 23% of cases. Symptoms of cardiac cysticercosis can include heart failure or conduction abnormalities.[34]

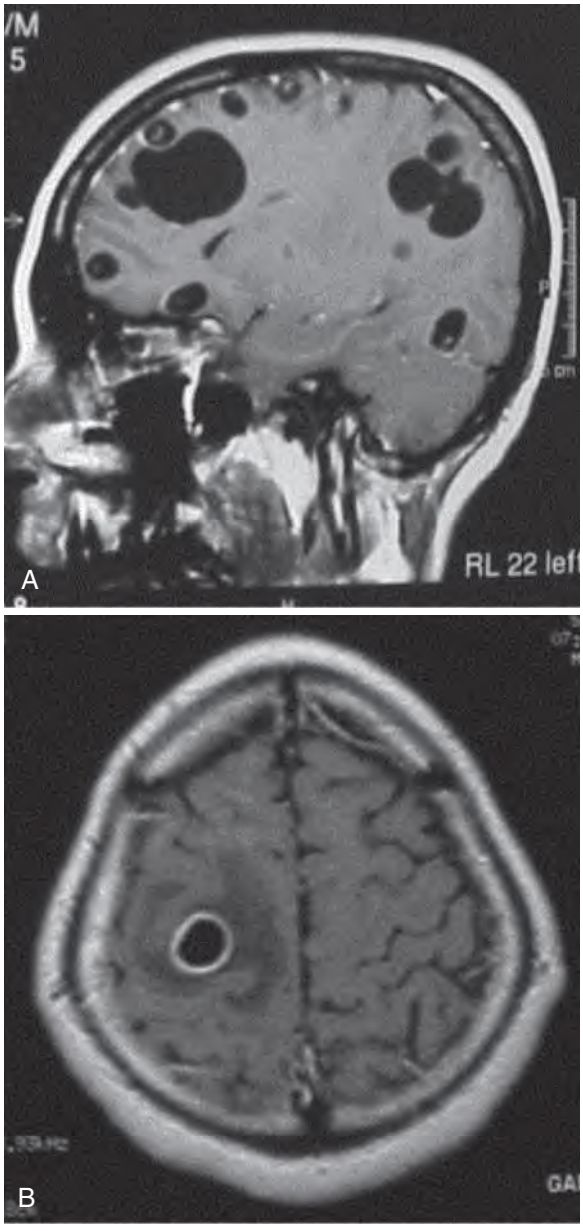

FIG. 289.4 Magnetic resonance images of (A) massive cysticercosis and (B) colloidal cysticercus defined by early signs of inflammation around the cysticercus. *(From Garcia HH, Del Brutto OH. Imaging findings in neurocysticercosis.* Acta Trop. *2003;87:71–78.)*

Diagnosis

The site of involvement and the symptoms experienced determine the best mode of diagnosis and eventual treatment. Travel to or residence in an endemic area significantly increases the likelihood of the diagnosis, although transmission has been documented to occur within the United States in people living in the same household as *T. solium*–infected individuals.[27] Presenting symptoms often suggest a tumor, and a specific diagnosis of cysticercosis is often first suspected on the basis of imaging studies (CT or magnetic resonance imaging [MRI]), which show multiple enhancing and nonenhancing unilocular cysts.[30] Cerebral cysts are usually multiple (an average of 7–10 per patient). Typical radiographic signs on MRI depend on the stage of cyst development. Vesicular cysticerci (small, rounded cysts without edema) often have the pathognomonic eccentric hyperdense nodule representing the scolex. Subsequent stages include colloidal and granular cysticerci, which appear ill-defined with surrounding edema. Lastly, calcified cysts can be detected on CT as hyperdense nodules without contrast enhancement.[35] Multiple cysts can be present in different stages; this pattern is often described as a "starry sky."[36] Ventricular and subarachnoid cysts are less distinct on MRI because CSF and cyst fluid have similar densities, which can present a diagnostic challenge.[36] CSF examination may show lymphocytic or eosinophilic pleocytosis, hypoglycorrhachia, and elevated protein levels. Newer CSF tests using lentil lectin glycoproteins Western blot have shown promising sensitivity (>90%) and specificity (100%) when multiple cysts are present, but decreased sensitivity in the case of single lesions.[30,37] A suspected diagnosis may also be strengthened by serology through enzyme-linked immunotransfer blot that is available commercially or through the US Centers for Disease Control and Prevention (CDC). The serology indicates prior exposure to *T. solium* antigens. Patients infected with other helminths, particularly other cestodes, may have circulating antibodies that cross react with antigens of *T. solium* in some assays.[34,38] However, immunoblotting techniques with the purified glycoprotein fraction of cyst fluid appear to offer a sensitive and specific diagnosis.[32,34,38,39] The sensitivity of antibody testing tends to be high for patients with multiple cysts (94%) but substantially lower for patients with single cysts or calcified cysts (as low as 28%).[40] CT and MRI remain the most effective means of diagnosis, however, and negative serology in the presence of a characteristic scan should not exclude the diagnosis of

cysticercosis.[30] Because the diagnosis can often be challenging, guidelines to assist with diagnosing neurocysticercosis have been proposed based on radiographic appearance, immunoassays, clinical manifestations, and epidemiologic characteristics.[35,41] Newly proposed diagnostic criteria were found to have a sensitivity of 93.2% and a specificity of 81.4% for the diagnosis of neurocysticercosis in a multicenter retrospective cohort.[42] Last, basal subarachnoid cysticercosis has been associated with a higher incidence of concomitant spinal lesions; therefore spinal MRI is recommended in patients with a diagnosis of subarachnoid disease.[43]

Treatment

Although older nonrandomized studies showed mixed results, current general consensus and more recent studies now support anthelmintic and corticosteroid therapy for viable parenchymal lesions.[30,44] Two randomized controlled trials showed benefit of anthelmintic therapy, with reductions in generalized seizures and faster resolution of cysts in one study and faster resolution of active cysts in the other study.[45,46] Despite prior concerning case reports describing increased adverse neurologic events with anthelmintic therapy, neither study showed significant increases in adverse effects with antiparasitic therapy, apart from a slight increase in seizures early in treatment. In addition, the second trial confirmed previous studies that indicated treatment of purely calcified cysts did not provide benefit. Another study of treatment of single active cysts and a meta-analysis provide supporting data for the use of cysticidal agents in the treatment of parenchymal disease.[47,48]

Because, despite antiinflammatory therapy, pericystic inflammation can cause permanent damage to the eye when there is an intraocular cyst, a careful eye examination should always precede treatment to exclude cysticercosis of the eye.[44] Because pharmacologic evidence suggests that concurrent corticosteroid therapy lowers serum praziquantel levels while increasing the circulating levels of albendazole (and its active metabolites) in some patients, many experts now favor the use of albendazole as the drug of first choice when treating a patient with just one or two viable cysts.[49,50] However, albendazole monotherapy has been shown to be only 60% to 70% effective at killing parasites.[51] If repeat MRI scans show persistence of cysts at 6 months following initiation of therapy, a repeat course of drug treatment should be given.[44] Double-blind, randomized, controlled trials have shown the superiority of a combined regimen of albendazole plus praziquantel over albendazole alone at killing parasites and resolving cysts. There were no increased adverse events in these studies.[52,53]

Preferred regimens for multicystic parenchymal disease (more than two viable cysts) involve treatment with albendazole (15 mg/kg/day divided in two doses, with maximum of 1200 mg per day, for 10 days to 2 weeks)[13,44,54] plus a high-dose regimen of praziquantel (50 mg/kg/day divided in three doses per day for 10–14 days). Before, during, and after drug therapy, seizures should be controlled with appropriate antiepileptic medications, and symptomatic hydrocephalus should be relieved by shunting before initiation of anthelmintic treatment.[44] Shunt complications caused by blockage and bacterial infection are common in patients with neurocysticercosis.[55] CNS inflammation should be reduced by concurrent administration of pharmacologic doses of corticosteroid (dexamethasone, 6–8 mg/day divided into three daily doses for 28 days, then a slow tapering off of corticosteroids over 2–8 weeks to avoid rebound symptoms)[56,57]; however, corticosteroids do not necessarily eliminate the risk for serious complications such as infarction[58,59] or intracranial pressure elevation.[49] Anthelmintic treatment is contraindicated in cases of encephalitic or disseminated neurocysticercosis and for ocular disease owing to the intensity of the inflammatory response provoked by drug therapy. For subarachnoid disease, expert opinion supports the use of prolonged courses of anthelmintic agents (2–12 months) owing to variable responses and more frequent relapses than for parenchymal disease. Anthelmintic agents have no role in the treatment of calcified cysts.[54]

Formal, evidence-based consensus guidelines for neurocysticercosis management have been developed by experts from the Infectious Diseases Society of America and the American Society of Tropical Medicine and Hygiene, and these were published by both societies in 2018.[44] Nonetheless, guideline recommendations and the most recent literature should be reviewed in deciding intervention for complex individual patient presentations.

Well-controlled, randomized trials have not yet evaluated the treatment of less common forms of neurocysticercosis (i.e., intraventricular, subarachnoid/basilar, and spinal cysticercosis), and the true value of drug treatment for these forms of the disease is not known.[30] Surgical removal of intraventricular cysts is recommended, where possible, preferably via endoscopic techniques performed by experienced neurosurgeons. Preoperative anthelmintics are not advised in this case, given the fact that the inflammation induced by treatment could prevent adequate removal of the cysts. However, when surgical removal is not possible, drug treatment of intraventricular cysts may prove efficacious. Likewise, owing to the progression and degree of complications of disease with subarachnoid or sylvian fissure cysts, treatment with cysticidal medications is generally recommended, with close attention to the management of intracranial hypertension.[26] Anthelmintic treatment for extensive infections such as diffuse encephalitis is generally not recommended, given the potential adverse effects due to treatment-induced inflammation.

A poor response to either surgical or drug therapy is more common with intraventricular or cisternal cysts and with racemose neurocysticercosis.[44] For these lesions the drug levels achieved in the CSF and cyst during medical therapy are likely to be lower than for parenchymal CNS cysts, making drug failure more likely and often necessitating a longer duration of cysticidal treatment and multiple courses of treatment. Surgical approaches to these areas are difficult, and local inflammation may prevent easy removal of the cyst, although endoscopic removal of ventricular cysts has shown promising results and is recommended if possible.[26] Retained cyst material may result in postoperative recurrence. Nevertheless, successful therapy for ventricular and basilar cysts has been achieved in a small number of patients by either medical or surgical means.[60,61] Individualized therapy, possibly including a combined surgical-medical approach, is recommended in such cases.[30,54]

Spinal cysticercosis presents a challenging scenario as well, due to its sensitive location. Data are limited on the best management of spinal and perispinal disease, and cases should be approached on an individual basis, with consideration of medical or surgical therapy or both. For ocular cysticerci, surgical removal without anthelmintic treatment is recommended.

For symptomatic cysts outside the CNS, the optimal approach is surgical resection. In some cases, lesions may involve critical organs, making surgical removal technically not feasible. In such cases, medical therapy with praziquantel or albendazole may be employed.[11,30]

Echinococcosis (Hydatid and Alveolar Cyst Disease)

When humans serve as inadvertent intermediate hosts for cestodes of *Echinococcus* spp., which are carried as tapeworms by canines such as dogs, wolves, and foxes, disease may result from the development of expanding parasite cysts in visceral organs.[62] This condition, termed *echinococcosis,* has two forms: hydatid or unilocular cyst disease, caused by *Echinococcus granulosus,* and alveolar cyst disease, caused by *Echinococcus multilocularis.* In addition, polycystic or neotropical echinococcosis is caused by either *Echinococcus vogeli* or the much less common *Echinococcus oligarthrus,* both found in Central or South America. *E. vogeli* infections are similar to alveolar cyst disease, whereas *E. oligarthrus* infections appear less aggressive.[63] Sheep, goats, camels, and horses are among the usual intermediate hosts for *E. granulosus;* however, because *E. granulosus* is transmitted by domestic dogs in livestock-raising areas, hydatid disease is prevalent worldwide (in Africa, Middle East, southern Europe, Latin America, and southwestern United States). *E. multilocularis* infections (found in northern areas of Europe, Asia, and North America and in the Arctic regions)[64] and *E. vogeli* infections (found in South American highlands) are transmitted by wild canines and are less common.

Humans acquire echinococcosis by ingesting viable parasite eggs with their food.[62] The parasite eggs are distributed via local environmental contamination by the feces of tapeworm-infected canines. Eggs are partially resistant to desiccation and remain viable for many weeks,[3] allowing delayed transmission to individuals with no direct contact with vector animals. Once in the intestinal tract, the eggs hatch to form oncospheres that penetrate the mucosa and enter the circulation. Oncospheres then encyst in host viscera, developing over time to form mature larval cysts (Fig. 289.5).

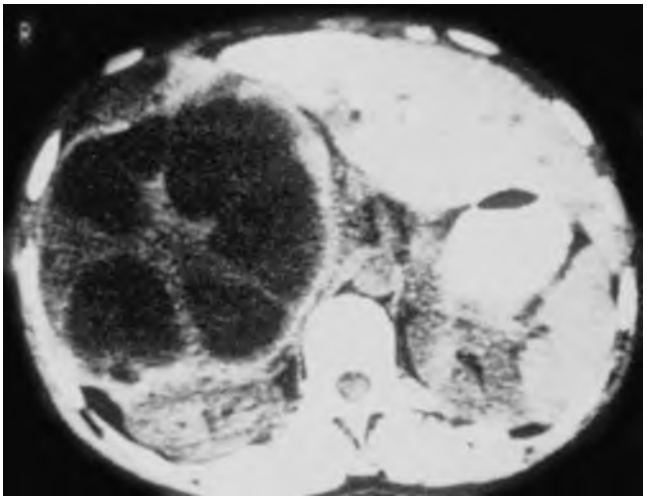

FIG. 289.5 Hydatid cysts of the liver detected on computed tomography scan. Note the well-demarcated wall and characteristic septate internal structures (daughter cysts).

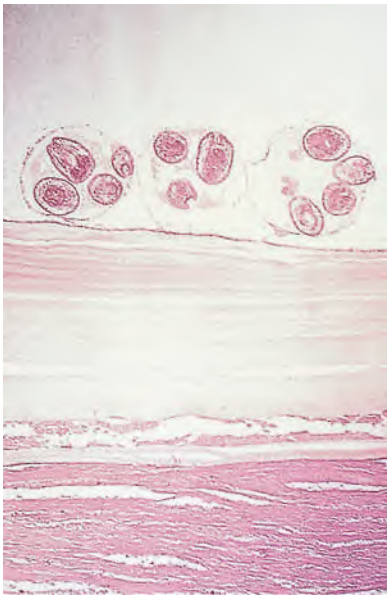

FIG. 289.6 Daughter cyst formation from the germinal membrane of a hydatid cyst. *(From Ash LR, Orihel TC.* Atlas of Human Parasitology. *3rd ed. Chicago: American Society for Clinical Pathology; 1990.)*

Infection with *E. granulosus,* cystic echinococcosis, is estimated to occur in 2% to 6% of endemic populations. Risk factors include unsanitary living conditions, slaughter of livestock in close proximity to humans and dogs, and uncontrolled dog populations. Sheep raising, in particular, is associated with a high prevalence of disease.[65]

Cystic Echinococcosis

Clinical Presentation

The hydatid cysts of *E. granulosus* tend to form in the liver (50%–70% of patients) or lung (20%–30% of patients) but may be found in any organ of the body, including brain, heart, and bones (<10%). They grow to 5 to 10 cm within the first year and can survive for years or even decades. Symptoms are often absent, and infection is detected only incidentally by imaging studies in many cases. When symptoms do occur, they are usually due to the mass effect of the enlarging cyst in a confined space. Hydatid cysts contain a germinal layer that allows asexual budding to form daughter cysts within the primary cyst (Fig. 289.6). If a cyst erodes into the biliary tree or a bronchus, the cyst contents, including daughter cysts, may enter the lumen and cause obstruction or postobstructive bacterial infection. Bacteria may enter the cyst, causing pyogenic abscess formation in the cyst. Cyst leakage or rupture may be associated with a severe allergic reaction to parasite antigens; in the most extreme cases, patients may have anaphylactoid reactions after cyst rupture, including hypotension, syncope, and fever. A dangerous complication of cyst rupture is secondary seeding of daughter cysts into other areas of the body. Their subsequent enlargement may be associated with critical failure of one or more organs, which is associated with significant morbidity and mortality. Fewer than 10% of patients develop such complications, and because the infection is normally self-limited, it is likely that most infections never come to medical attention.[66] Nevertheless, symptomatic cysts should be treated, and asymptomatic cysts should be carefully observed for a number of years to avert complications of infection.

Diagnosis

Infection that is suspected based on imaging studies (ultrasound, CT, and MRI) may be confirmed by a specific enzyme-linked immunosorbent assay and Western blot serology (available in the United States through the CDC) confirming exposure to the parasite.[67,68] Serology is 80% to 100% sensitive and 88% to 96% specific for liver cyst infection but less sensitive for lung (50%–56%) or other organ (25%–56%) involvement. Additional assays continue to be developed using recombinant *Echinococcus* antigens and may provide better diagnostic sensitivity and specificity.[67–69] Eosinophilia is not a consistent or reliable finding. Imaging remains more sensitive (90% with ultrasound and higher with CT and MRI) than serodiagnostic techniques, and a characteristic scan in the presence of negative serologic results still suggests the diagnosis of echinococcosis.[66,70] The WHO has classified the typical imaging patterns on ultrasound to guide treatment decisions (Fig. 289.7). The stages range from undifferentiated cystic lesions (CL) to active (CE1 and CE2), transitional (CE3), and inactive (CE4 and CE5). Transitional cysts are divided into CE3a (detached endocyst present) and CE3b (predominantly solid with daughter vesicles).[71] A WHO working group has provided guidelines for diagnosis based on clinical and diagnostic criteria that define possible, probable, and confirmed cases.[71]

Treatment

There is no one optimal treatment for cystic echinococcosis, and no clinical trials have evaluated and compared all the different options. Expert clinical opinion from the WHO Informal Working Group on Echinococcosis recommends a stage-specific approach.[71] Optimal treatment of symptomatic, complicated cysts (large CE2 to CE3b cysts with multiple daughter vesicles) is surgical resection to remove the cyst in toto. Therapy is also indicated when cysts exert pressure on vital organs or if percutaneous therapy is not available. Traditionally, because of the risk for spreading infection due to cyst rupture, the recommended approach has been to visualize the cyst, remove a fraction of the fluid, and instill a cysticidal agent (hypertonic [30%] saline, cetrimide, or 70%–95% ethanol) to kill the germinal layer and daughter cysts before resection.[1a] The cyst is totally removed 30 minutes after instillation. A number of drains are left in the cyst bed to limit the risk for secondary bacterial infection.

Although time honored, the efficacy of this open surgical approach has not been validated in clinical trials, and given the availability of effective perioperative drug therapy to limit spread, some experts question the need to instill potentially tissue-damaging cysticidal agents during surgery.[1a] Laparoscopic surgery for cyst removal has been performed in less advanced cases (in which spillage of contents is not as likely to occur). In this type of case, the minimally invasive approach may have fewer complications with approximately equal efficacy.[70] Cysts communicating with the biliary tree should not have a cysticidal agent instilled because of the risk for postoperative sclerosing cholangitis,[62,72] and cysticidal agents should not be instilled in lung cysts.

An intermediate intervention for inoperable cysts has been developed, known as the *PAIR* (*p*uncture, *a*spiration, *i*njection, *r*easpiration) procedure.[62,73–75] It has also been recommended as first-line therapy by some experts in cases of CE1 and CE3a cysts.[71] While the patient is receiving anthelmintics to reduce the risk for cyst dissemination, the hydatid cyst may be aspirated with a thin needle under CT guidance.

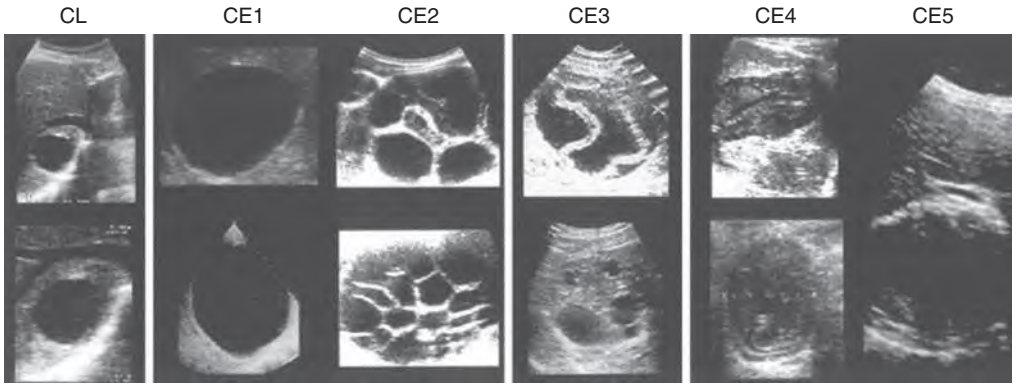

FIG. 289.7 World Health Organization Informal Working Group on Echinococcosis classification of echinococcal cystic lesions as they appear on ultrasound. Lesions are divided into three relevant groups: active (CE1 and CE2), transitional (CE3), and inactive (CE4 and CE5). CL represents an early, undifferentiated cystic lesion. *(From Brunetti E, Kern P, Vuitton DA, Writing Panel for the WHO-IWGE. Expert consensus for the diagnosis and treatment of cystic and alveolar echinococcosis in humans.* Acta Trop. *2010;114:1–16.)*

Approximately 30% of the cyst fluid volume is removed. Detection of protoscolices in the cyst fluid allows confirmation of cyst viability. An equal volume of 95% ethanol or other scolicidal agent (e.g., 0.5% cetrimide) is then instilled into the cyst cavity and allowed to react for 30 minutes before removing the needle. However, to prevent postintervention sclerosis, care must be taken to ensure that the cyst does not communicate with the bile ducts before introducing cysticidal chemicals. Results indicate arrest or involution of cysts after treatment. A modified technique uses a special catheter system to simultaneously evacuate the cyst contents while infusing the scolicidal agent. The PAIR procedure has several specific indications, and the overall experience with PAIR is relatively limited compared with traditional treatment methods. However, there is some evidence, based on meta-analysis, that there are fewer complications and lower recurrence rates with PAIR compared with standard surgery. More studies are needed to confirm this finding.[70]

Most surgeons treat patients perioperatively with an anthelmintic agent active against *Echinococcus* cysts (albendazole and mebendazole)[71,76,77] to limit the risk for intraoperative dissemination of daughter cysts. Preoperative treatment with albendazole for 1 to 3 months has been shown to significantly reduce the number of viable cysts found at surgery.[63] Medical therapy for inoperable cysts with albendazole or mebendazole has provided improvement in most patients (55%–79%) and cure in a smaller percentage (29%).[76,77] Young cysts (CE1) can sometimes be treated with anthelmintics alone.[78] The preferred agent is albendazole because of its greater absorption from the gastrointestinal tract and higher plasma levels. Optimal therapy has not been adequately studied but may need to be prolonged in some cases. Typically, it is given at a dose of 400 mg twice a day (for patients weighing <60 kg, 15 mg/kg/day divided into two doses) for 3 to 6 months. It is no longer recommended to interrupt treatment for 2 weeks every month of treatment.[71] The alternative agent, mebendazole, is poorly absorbed and must be taken at higher doses (50–70 mg/kg/day) for several months to achieve a therapeutic effect.[77]

The response to drug therapy depends on the cyst size and location.[73,77] Bone cysts, which are frequently not amenable to surgery, respond less well to drug treatment than other cysts. The response to drug therapy is best monitored by serial imaging studies; cyst disappearance or shrinkage along with increasing cyst density is thought to indicate a positive response. In cases of uncomplicated CE4 and CE5 cysts, some experts advocate the "watch and wait" approach, although this has not been formally studied.[71]

Alveolar Echinococcosis

Infection with *E. multilocularis* (alveolar cyst disease) is relatively more aggressive. It is much less common in humans, with an incidence in endemic countries ranging from 0.02 to 1.4 per 100,000. However, increasing urban fox populations, with a noted increase in prevalence of parasite infection among foxes, may pose an increasing health concern for humans.[64] For example, in Europe, with the development of an effective rabies vaccine program, fox populations began to increase after the 1980s. In concert, the incidence of alveolar echinococcosis doubled from 2001 to 2005 compared with previous years.[79] *E. multilocularis* cysts reproduce asexually by lateral budding. Their gradual invasion of adjacent tissue is tumor-like, and sections of the parasite may "metastasize" to distal parts of the body.[62] Symptoms are usually of gradual onset, referring to the organ involved, which is most commonly the liver. Complications include biliary tract disease, portal hypertension, and Budd-Chiari syndrome. Consequently, morbidity and mortality are higher than for cystic (hydatid) echinococcosis. Findings of initial imaging studies are usually highly suggestive of carcinoma or sarcoma, and biopsy may provide the first indication of infection. A serologic test, available from the CDC, is highly sensitive and specific and, when combined with characteristic imaging studies, offers an alternative means of establishing the diagnosis.[67,78] The WHO Informal Working Group on Echinococcosis developed a classification similar to cancer staging using the acronym *PMN*: *P* for location of parasite in the liver; *N* for neighboring organs involved, and *M* for metastatic spread.[78] For operable cases, wide surgical resection (e.g., hepatic lobectomy or liver transplantation) is recommended to ensure total removal of the cyst.[71,80] Adjuvant albendazole therapy to reduce cyst size before surgery or limit intraoperative spread has been reported to be beneficial in case series.[81] For inoperable cases, drug therapy with mebendazole or albendazole (lifelong) has provided arrest or cure of disease in some patients.[71] The efficacy of surgical or drug therapy may be monitored by serial imaging and serology.

Advances in the understanding of the molecular biology of *Echinococcus* have led to active investigation of new targets and new drugs for therapy.[78]

Other Invasive Cestodes

Human tissue infection with plerocercoid cysts of several cestode species is referred to collectively as *sparganosis.* These parasites, such as *D. latum,* pass through several developmental stages in copepods and vertebrates.[1,1a,1b] The definitive hosts for tapeworms of these species are usually canines or felines. Humans acquire inadvertent parasite infection by ingestion of copepods (in water) or by consumption of or prolonged exposure to uncooked meat of plerocercoid-infected animals.[82–84]

Sparganosis has been reported in South America, Japan, China, and other areas of Asia in association with traditional use of frog-meat or snake-meat poultices. Infection has rarely been reported from Europe and North America. Sparganosis may be the proliferating or nonproliferating type. Infection acquired in the United States is usually due to *S. mansonoides,* which is nonproliferating. In other areas of the world, proliferating forms are more common. These forms branch by lateral division and may detach to spread to other, distal areas of the body.[82] Clinical presentation typically involves local inflammation at the site of invasion (skin and eye are the most common sites for poultice application). Cerebral sparganosis is a rare and severe complication. There is local lymphocytic and eosinophilic inflammation surrounding the parasites. Tissue injury may be particularly severe in the eye. Diagnosis is usually by biopsy, although serologic testing has been

used in some areas.[2] Treatment is by injection with ethanol, surgical resection, or both. Medical therapy with various anthelmintics has not produced a beneficial effect. *Coenurosis* is a human cyst infection with the cestodes *T. multiceps, Taenia crassiceps,* and *Taenia serialis,* which cause tapeworms in dogs.[85] The cysts are unilocular, with multiple protoscolices, but do not contain daughter cysts. Symptomatic disease is usually associated with involvement of the eye or the CNS. Clinically the cysts may be difficult to distinguish from cysticercosis or hydatid disease. Basal arachnoiditis and hydrocephalus are common. There is no reliable serologic test. Surgical resection is the recommended therapy.[85]

PREVENTION

Prevention of cestode infection depends on interrupting the parasite life cycle. Transmission of human tapeworm infection can be reduced or eliminated by the following sanitary measures: (1) careful disposal of human sewage to limit environmental spread of parasite eggs; (2) limitation of forage areas and use of safe feed for vector animals such as cattle or swine that serve as common intermediate hosts; (3) meat inspection before marketing to exclude meat from cyst-infested carcasses; and (4) prolonged freezing (at <–18°C) or thorough cooking of meat (at >50°C), or both, to kill any cysts in the tissues. Control of fish tapeworm is more difficult to achieve because the infected fish can range freely and there are nonhuman reservoirs for the tapeworm (e.g., bear and seals) that can continue to infect fish despite the presence of good human sanitation.

Prevention of invasive cestode infection is more complex. Because this form of human infection results from egg ingestion and the eggs may have been spread throughout an area by free-ranging definitive hosts such as dogs or humans, infection may be difficult to avoid. It is significant that half of patients with hydatid cysts do not recall specific exposure to dogs, although they may have resided in or visited an area of endemicity. Successful control of *E. granulosus* transmission has been achieved by regular screening and treatment of dogs in areas of endemicity in New Zealand, Tasmania, and the British Isles to eliminate adult tapeworm carriage and local release of eggs.[86] Similar programs to treat rural dogs and foxes have been proposed for control of *E. multilocularis* transmission.[87] Treatment of human carriers in areas in which *T. solium* is endemic, as well as health education campaigns focusing on self-recognition of human tapeworm carriers and the corralling of pigs, has proved effective in controlling transmission of cysticercosis.[32,88,89] However, many barriers, particularly involving socioeconomic factors, still exist. Field trials also indicate that anti-*Echinococcus* and anticysticercus vaccines can significantly reduce infection in farm animals (sheep and pigs), which may further reduce the level of peridomestic transmission.[90]

In areas of good sanitation (e.g., the United States), autochthonous transmission of cysticercosis is rare but can occur in settings in which a person with a *T. solium* tapeworm shares living or cooking quarters with susceptible individuals.[85] Screening of immigrants from *T. solium*–endemic areas and treatment of identified tapeworm infections would eliminate the risk for cysticercosis transmission to nontravelers.

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290 Visceral Larva Migrans and Other Uncommon Helminth Infections

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SHORT VIEW SUMMARY

VISCERAL LARVA MIGRANS

Definition

- Visceral larva migrans (toxocariasis) is caused by *Toxocara canis* and less frequently by *Toxocara cati* and other helminths. It commonly occurs in children and may be manifested by fever, wheezing, hepatomegaly, and other generalized symptoms.

Diagnosis

- Diagnosis is based on finding larvae in affected tissues and the presence of eosinophilia.

Treatment

- Most patients recover without therapy.
- Antiinflammatory drugs may be considered, and albendazole, mebendazole, and diethylcarbamazine have been tried but are of uncertain efficacy.

OCULAR LARVA MIGRANS

Definition

- Ocular larva migrans is caused by *T. canis* larvae in the eye and results in a chorioretinal granuloma or occasionally in panuveitis. Retinal detachment may also occur. There is no specific therapy.

OTHER UNCOMMON HELMINTHS

- Other helminthic infections are anisakiasis, cutaneous larva migrans, eosinophilic meningitis, gnathostomiasis, angiostrongyliasis, eosinophilic gastroenteritis, dirofilariasis, capillariasis, nanophyetiasis, and swimmer's itch.

Most helminths that infect humans are relatively host specific to humans, undergo characteristic migration and development, and are found in typical anatomic locations. However, these helminths sometimes undergo atypical or aborted migrations and cause symptoms or signs because of their unusual or ectopic location. A good example of this is the deposition of schistosomal ova and the subsequent granulomatous inflammatory lesions in the spinal cord or brain. In addition, some helminths of animals can also infect humans. Examples are *Echinococcus granulosus* and *Trichinella spiralis,* which commonly infect humans, migrate and develop normally, and reside in locations similar to those in the animal host. In contrast, other helminths of animals are unable to develop or migrate normally. Commonly, they undergo prolonged aberrant migrations or locate abnormally in the tissues as underdeveloped larvae and incite an eosinophilic inflammation that is responsible for many of the symptoms and signs of these infections. Although a large number of animal parasites may infect humans, most do so rarely. In contrast, some helminths of animals infect humans more commonly and cause distinctive clinical syndromes (Table 290.1), sometimes associated with characteristic epidemiology, exposure history, and geographic locations. More often than not, similar clinical syndromes are caused by a group of related parasites. The diagnosis is suggested on clinical and epidemiologic grounds. Although pathologic examination of tissue can sometimes establish the diagnosis, the detection of larvae is commonly unrewarding. Serologic tests are sometimes helpful (see "Visceral Larva Migrans [Toxocariasis]") but usually are not fully evaluated, are experimental, or are unavailable.

The diagnostic procedures used to detect infections differ for each parasite, so a clear idea of the potential causes is essential. The physician must understand the sensitivity of the diagnostic procedures and the abilities of the laboratory personnel performing them.

VISCERAL LARVA MIGRANS (TOXOCARIASIS)

Visceral larva migrans (VLM) is a syndrome characterized in its most florid state by eosinophilia, fever, and hepatomegaly. It is caused primarily by infection with *Toxocara canis* but also, less frequently, infection with *Toxocara cati* and other helminths.[1,2,3]

Life Cycle in the Dog

T. canis infects dogs and related mammals by a number of mechanisms.[1] Most commonly, ingested eggs hatch in the small intestine, and the resulting larvae migrate to the liver, lung, and eventually the mucus layer of trachea. They are then swallowed and mature in the lumen of the small intestine, where eggs are shed. Other larvae migrate to and remain dormant in the muscles but are capable of development years after the primary infection, particularly in pregnant bitches. During pregnancy, larvae again develop and infect the puppies transplacentally and transmammarily. Infective larvae are commonly found in the feces of the puppies. Eggs are not infectious when passed in the feces and take 3 to 4 weeks to develop. They are hardy and often remain viable for months. Large numbers of viable eggs contaminate the environment because of the high prevalence of infection in dogs and the ability of eggs to survive relatively harsh environmental conditions. Humans become infected mostly from ingesting viable ova that contaminate the soil where dogs defecate. Ingestion of raw organs containing larvae, which is common in some regions, is another means of infection.[4]

Infection in Humans

Prevalence

Toxocariasis is prevalent wherever dogs or cats are found, and *Toxocara* eggs are able to survive. The prevalence of infection or disease in humans is not known, but seroepidemiologic studies show wide differences in prevalence, depending on the population tested. In the United States, seropositivity ranged from 2.8% in an unselected population,[5] to 23.1% in a kindergarten population in the southern United States,[6] to 54% in a selected rural community.[7] None of the seropositive persons had recognizable disease. A review of reported seroprevalence of toxocariasis in North America reported an overall prevalence rate of 13.9% in the United States, with higher rates in Mexico.[8]

Clinical Manifestations

VLM occurs most commonly in children younger than 6 years of age, frequently after ingestion of contaminated soil.[3,5] Disease manifestations vary

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TABLE 290.1 Clinical Syndromes Associated With Unusual Helminth Infections in Humans

CLINICAL SYNDROME	PARASITE	USUAL HOST
Visceral larva migrans	*Toxocara canis* *Toxocara cati* *Baylisascaris procyonis*	Canines Felines Raccoons
Eosinophilic gastroenteritis	*Anisakis* spp. *Phocanema* spp. *Ancylostoma caninum*	Sea mammals Sea mammals Canines
Cutaneous larva migrans	*Ancylostoma braziliense* *Ancylostoma caninum* *Uncinaria stenocephala*	Canines, felines Canines, felines Canines, felines
Eosinophilic meningitis	*Angiostrongylus cantonensis* *Gnathostoma spinigerum*	Rats Felines, other mammals
Pulmonary or cutaneous nodules	*Dirofilaria* spp.	Canines, other mammals
Abdominal angiostrongyliasis	*Angiostrongylus costaricensis*	Cotton rats
Capillariasis	*Capillaria philippinensis*	Birds
Swimmer's itch	*Trichobilharzia* spp.	Birds

and range from asymptomatic infection to fulminant disease and death, but it is increasingly appreciated that most infections are asymptomatic. Individuals who come to medical attention most commonly present with cough, fever, wheezing, and other generalized symptoms.[6,7,9] The liver is the organ most frequently involved, and hepatomegaly is a common finding, although almost any organ can be affected. Splenomegaly occurs in a small number of patients, and lymphadenopathy has been noted. Lung involvement with radiologic findings has been documented in 32% to 44% of patients, but respiratory distress occurs rarely. Skin lesions such as urticaria and nodules have also been described. Seizures have been noted to occur with increased frequency in VLM, but severe neurologic involvement is infrequent.[10] Eye involvement in VLM is unusual but has been documented (see "Ocular Larva Migrans"). Eosinophilia, usually accompanied by leukocytosis, is the hallmark of VLM. Laboratory findings include hypergammaglobulinemia and elevated isohemagglutinin titers to A and B blood group antigens, which are caused by the host's immune response to cross-reacting antigens on the surface of *T. canis* or *T. cati* larvae. Serologically positive populations may be at increased risk for seizures.[11]

Diagnosis

The diagnosis of VLM is usually suggested clinically by the presence of eosinophilia, leukocytosis, or both in a young child also presenting with hepatomegaly or signs and symptoms of other organ involvement. A history of pica and exposure to puppies is common. In the United States, patients are more commonly black and from rural areas.

The diagnosis is definitively confirmed by finding larvae in the affected tissues by histologic examination or by digestion of tissue; however, larvae are frequently not found. Computed tomography scans have demonstrated ill-defined hypodense round lesions in the liver of patients with VLM, the basis of which is unclear.[4] Standard assays including enzyme-linked immunosorbent assay or Western blot using excretory-secretory products of T. canis larvae have been used to confirm the clinical diagnosis for decades.[12] Newer assays using recombinant antigens in a Luminex Bead format have obviated the need for collection of infectious larvae and have led to assays with high sensitivity and less cross-reactivity with other helminths. *Toxocara* antibody titers in populations without clinically apparent VLM vary dramatically, and elevated titers cannot definitively establish the diagnosis.

Differential Diagnosis

Eosinophilia, fever, and hepatomegaly are frequently caused by helminths that migrate through the body. *Baylisascaris procyonis* (an ascarid of raccoons) is a recognized cause of larval migrans in the United States.[13] Other helminth infections include acute schistosomiasis, *Fasciola hepatica* infections, *Ascaris lumbricoides* abscess of the liver, acute liver fluke infections *(Clonorchis sinensis, Opisthorchis viverrini, Fasciola hepatica)*, complications from *Echinococcus* infection of the liver, and *Capillaria hepatica*. Diseases not caused by parasitic infections should also be considered. Children with mild disease may manifest only eosinophilia.

Treatment and Management

Most patients recover without specific therapy. Treatment with antiinflammatory or anthelmintic drugs may be considered for patients with severe complications usually caused by involvement of the brain, lungs, or heart. There is no proven effective therapy, although albendazole, mebendazole, diethylcarbamazine, and other anthelmintics have been used. Injury to the parasite may provoke an intense inflammatory response, leading to worsening of the clinical picture. Corticosteroids are frequently used to control symptoms of infection or to suppress possible potentiation of symptoms caused by the host's immune responses to killed or injured larvae as a consequence of anthelminthic treatment.

Prevention

VLM can be easily prevented by a number of simple but effective measures that prevent *T. canis* or *T. cati* eggs from contaminating the environment and children from ingesting eggs and pica. Dogs, particularly puppies, should be periodically tested and treated for *Toxocara* and other worms. To prevent defecation by dogs and cats in sandboxes where young children play, they should be covered when not in use.

OCULAR LARVA MIGRANS

Ocular larva migrans is caused primarily by an infection of the eye with *T. canis* larvae.[14,15] Although a present or past history of clinically recognized VLM has occasionally been noted, almost all patients present with unilateral eye visual loss without a past history or present systemic symptoms or signs. Presumably, a larva becomes entrapped in the eye by chance, resulting in an eosinophilic inflammatory mass. Children are most commonly affected and, on average, are older (mean, 8.6 years old in one study) than children with VLM. Although the most common lesion is a chorioretinal granuloma in the posterior pole, or occasionally more peripherally, diffuse panuveitis may also be seen. Retinal detachment may occur. This entity was first recognized in the examination of eyes enucleated for the treatment of presumed retinoblastoma, and it remains the most important distinction that ophthalmologists must make in children with subretinal lesions.[14]

Eosinophilia, hepatomegaly, and other signs and symptoms of VLM are usually lacking. The diagnosis is established clinically. Although the serum titers to *Toxocara* larvae are higher than those of a control population,[16] many patients with ocular larva migrans have low or negative titers. However, elevated vitreous[17] and aqueous fluid titers[18] to *Toxocara* larvae, compared with serum levels, appear useful for establishing the diagnosis. There is no specific therapy.

A characteristic clinically recognizable syndrome, diffuse unilateral subacute neuroretinitis is caused by infection with helminth larvae of *B. procyonis* and *Toxocara* spp.[19] and other unidentified nematodes.[20,21] *Angiostrongylus cantonensis* larvae can also involve the eye.[22] A motile larva is commonly found in or below the retina. Photocoagulation is curative. Anthelmintic therapy such as albendazole may be effective.

BAYLISASCARIASIS

B. procyonis, an ascarid of raccoons, is a recognized cause of VLM in humans and many other animals.[23,24,25] The life cycle is similar to that of dog and cat ascarids, and infection occurs after ingestion of ova excreted in raccoon feces that subsequently contaminate soil and the environment. Although the clinical manifestations are similar to those caused by dog and cat ascarids, severe and commonly fatal eosinophilic meningoencephalitis occurs in more than half the cases. Eye involvement is common and is one of the known causes of diffuse unilateral subacute neuroretinitis.[19,20] The diagnosis is established by detecting typical larvae in tissues; an experimental serologic examination is useful.[26] There is no proven therapy. Of the available drugs, albendazole and corticosteroids are most commonly tried.[20]

ANISAKIASIS

Anisakiasis is caused by infection of humans by larvae found in saltwater fish and squid. The definitive hosts are marine mammals. The clinical syndrome is caused by penetration of larvae into the stomach or small intestine. It is characterized by upper or lower abdominal symptoms or both. The diagnosis is suggested by a history of ingesting raw, salted, pickled, smoked, or poorly cooked fish.[27]

Life Cycle in Marine Mammals

Larvae of the family Anisakidae, including *Anisakis, Pseudoterranova,* and occasionally other genera, can accidentally infect humans.[1,28,29,30] The adults are found in the stomach of marine mammals. The eggs, passed in the feces, hatch as free-swimming larvae, are ingested by certain crustaceans, and are eaten by fish and squid. When ingested by appropriate marine mammals such as dolphins, seals, and whales, the larvae burrow head first into the stomach. When consumed by humans, the larvae attempt, many times successfully, to burrow into the stomach or intestine, resulting in typical symptoms.

Clinical Syndrome

Anisakiasis occurs after ingestion of raw or improperly cooked marine fish. The disease, initially recognized in the Netherlands after the ingestion of raw herring, is most frequently reported from Japan, where raw fish is commonly eaten. In the United States, infection is still uncommon but is now more frequently recognized because of increased ingestion of raw fish, particularly Pacific salmon. Cod, halibut, pollack, greenling, herring, anchovies, hake, tuna, sardines, and mackerel are other fish that have been implicated.

Clinical manifestations are caused by penetration of worms into the gastrointestinal tract, usually the stomach but also the lower small intestine, most commonly the ileum.[29,30,31] Occasionally, throat irritation is followed by coughing up the characteristic worm. Initial invasion is associated with acute symptoms, whereas the presence of worms for longer periods causes chronic symptoms. The symptoms and the location of the worms depend on the genus, with *Pseudoterranova* commonly associated with infection of the stomach and *Anisakis* associated with infection of the intestine. Symptoms usually occur within 48 hours after ingestion, but this pattern is variable. With gastric anisakiasis, patients complain of intense abdominal pain, nausea, and vomiting. Small intestinal involvement results in lower abdominal pain and signs of obstruction mimicking those of appendicitis. The incubation period is shorter with gastric involvement, in one series peaking at 6 hours usually without significant eosinophilia. In contrast, small bowel infection symptoms peaked at 48 hours and more commonly caused eosinophilia.[31] Symptoms may be chronic, sometimes lasting for months and, rarely, years. These symptoms are associated with intestinal masses containing the parasite and are sometimes confused with a tumor, regional enteritis, or diverticulitis. Worms are occasionally located ectopically outside the gastrointestinal tract. *Anisakis* larvae in seafood have been implicated as a cause of acute allergic manifestations such as urticaria, pruritus, angioedema, and anaphylaxis, with or without accompanying abdominal gastrointestinal symptoms in patients who ingest raw fish.[32,33,34,35,36] In vitro studies and skin tests indicate that sensitization to *Anisakis* antigen is common in this population, whereas sensitization to fish is uncommon.[30,34,35,36]

Laboratory Findings

Eosinophilia is usually absent in patients with gastric anisakiasis[31] but is usually present in small bowel involvement. Leukocytosis is not consistently present with acute anisakiasis but has been noted in almost two-thirds of patients with intestinal involvement in one series.

Diagnosis

Anisakiasis should be considered in anyone with a history of ingesting raw marine fish and suggestive abdominal symptoms. A definitive diagnosis can be established by endoscopy, radiographic studies, or pathologic examination of tissue. In the upper gastrointestinal tract, worms are found partially embedded in any area of the stomach and may be associated with localized mucosal edema, erosions, or mass lesions.[37,38] Upper gastrointestinal radiographic studies may reveal the outline of a worm associated with mucosal edema or tumor formation. Removing the worm during endoscopy definitively establishes the diagnosis and is curative.[31] Intestinal anisakiasis is diagnosed clinically and suggested radiologically.[31,37] Varied degrees of thickening of the walls and narrowing of the lumen of the ileum or jejunum are found on radiographic studies. High-resolution ultrasonography has demonstrated small intestinal wall thickening and localized ascites around the involved section of bowel. Examination of aspirated ascites has revealed a preponderance of eosinophils.[39] Lesions resolve within 2 to 3 weeks. Removal of the intestinal mass is occasionally required to establish the diagnosis and effectively treat the patient. Most, but not all, resolve spontaneously with conservative management and close observation.[31] Tissues show inflammatory masses, many eosinophils, and the characteristic helminth. Serologic tests are not generally available but may be useful, particularly in patients whose symptoms have lasted longer than 1 week.[40]

Treatment

Symptoms diminish spontaneously in most patients without specific therapy, although the process is hastened by removing worms lodged in the stomach during endoscopy. In one series of intestinal anisakiasis, all 12 patients became asymptomatic by 2 weeks.[37] A report of treatment with albendazole in a case diagnosed only by serology is, at best, suggestive of efficacy.[41] One Japanese investigator commonly prescribed antacids after removing the stomach worms.

Prevention

Larvae resist heating up to 50°C (122°F) as well as pickling, salting, and some methods of smoking. Infection can be prevented by cooking or freezing fish for 24 hours before ingestion.

Cutaneous Larva Migrans (Creeping Eruption)

Cutaneous larva migrans is characterized as serpiginous, reddened, elevated, pruritic skin lesions usually caused by the dog or cat hookworms *Ancylostoma braziliense, Ancylostoma caninum,* or *Uncinaria stenocephala*.[42] Other animal hookworms (including *Bunostomum phlebotomum*), the human hookworms *Strongyloides stercoralis* and *Gnathostoma spinigerum,* and, rarely, insect larvae can cause a similar picture. Patients may also present with folliculitis consisting of follicular papules and pustules in the company of serpiginous tracks.

Similar to human hookworms, *A. braziliense* larvae infect dogs and cats by burrowing through the skin. The adults reside in the intestine and shed eggs, which undergo development into infectious larvae outside the body in places protected from desiccation and temperature extremes, such as sandy, shady areas around beaches or under houses. Infections are most common in warm climates, such as the southeastern United States, and occur in children more commonly than in adults. Larvae penetrate the skin, causing tingling followed by itching; vesicle formation; and typically raised, reddened, serpiginous tracks that mark the route of the parasite.[1,43] With severe infections, individuals may have hundreds of tracks. Little further development of the parasite occurs. Usually there are few, if any, systemic symptoms, although some reports have documented lung infiltrates and, rarely, severe lung dysfunction and recovery of parasites in the sputum. Eosinophilia has been noted with some infections. The skin lesions are readily recognized, and the diagnosis is made clinically. Biopsy specimens usually show an eosinophilic inflammatory infiltrate, but the migrating parasite is usually not identified. Therefore biopsies are usually not indicated to establish the diagnosis.

Without treatment, skin lesions gradually disappear[44] but commonly cause severe itching. Ivermectin given once or twice, if needed, at 200 μg/kg orally is the treatment of choice.[45] Albendazole, 400 to 800 mg/day orally for 3 to 5 days in two divided doses with food, is an effective alternative treatment.[46,47]

EOSINOPHILIC MENINGITIS

Infection of humans with larvae of *A. cantonensis,* the rat lung worm, is characterized by invasion of the brain leading to signs and symptoms of meningitis and encephalitis associated with an eosinophilic pleocytosis in the cerebrospinal fluid (CSF) and peripheral eosinophilia. A number

of other helminths cause eosinophilic meningitis; the most common are *Gnathostoma* spp. and *Taenia solium*. The adults of *A. cantonensis* reside in the lungs of rats[1,22] and produce eggs that hatch into larvae in the lungs. These are swallowed, expelled in the feces, and then either invade or are ingested by susceptible slugs, land snails, or a planarian in which they develop into infectious third-stage larvae. The range of animals carrying infectious larvae is substantially increased because infectious larvae can be transferred unchanged to other animals such as freshwater prawns, land and coconut crabs, and frogs through predation (paretenic hosts). After ingestion by rats, the larvae migrate to the pulmonary arteries and then the lung, enter the blood vessels, and thereby migrate to the brain. Eventually they return to the lungs via the vasculature. In humans, the ingested larvae attempt to recapitulate the migration in the rat and migrate to the brain, leading to eosinophilic meningitis or encephalitis.

Epidemics and sporadic infections occur most commonly in the South Pacific,[48] Southeast Asia,[49] and Taiwan[50] but more recently have been recognized in an increasing number of regions including, but not limited to, Jamaica,[51] Cuba,[52] Egypt,[53] Hawaii, China, Brazil, Ecuador, and the United States.[54,55] The most commonly recognized sources of human infection are raw or undercooked snails, prawns, and crabs. Foods such as leafy vegetables may be contaminated by larvae deposited by slugs or snails. Caesar salad was implicated in one epidemic.[51]

Clinical manifestations vary, and although fatalities occur, particularly with massive infections, most patients have a relatively uncomplicated course.[22,48,49,50,56] During one well-characterized epidemic, the incubation period ranged from 1 to 6 days after ingestion of infected snails.[48] Symptoms include headache, stiff neck, fever, rash, pruritus, abdominal pain, constitutional complaints, nausea, and vomiting. Neurologic involvement varies from no complaint to paresthesias and pain, weakness, various focal neurologic findings (sixth and fourth cranial nerve palsies are frequently noted), coma, and death. Eye involvement has been documented uncommonly and is important to rule out.[22] In general, patients do not appear to be as ill as patients who have bacterial meningitis. Signs of meningitis are frequent but nonspecific. CSF leukocytosis with more than 10% eosinophils is frequent. CSF glucose levels are usually normal, but depressed values have been noted.

The diagnosis is suggested by the clinical presentation, presence of increased eosinophils in the CSF, appropriate travel history, and a history of ingestion of raw or partially cooked implicated foods. PCR detected parasite DNA in randomly collected CSF samples of 78% of patients with positive serology.[57] A number of serologic tests for antibody in serum or CSF appear to be useful in later collected serum but are likely of limited value at presentation.[57] In severe cases, magnetic resonance imaging (MRI) shows meningeal enhancement, tracts in the brain or spinal cord, increased abnormal subcortical and periventricular T2-weighted MRI signals, and enhancing subcortical lesions.[58,59] A heavy worm burden increases the probability of brain involvement.

Symptomatic therapy includes corticosteroids, which have been shown to decrease the duration of headaches in a randomized trial.[60] Evidence for the efficacy of albendazole is controversial.[61–63] Repeated CSF lumbar punctures appear to be helpful for treating associated headaches, presumably by decreasing CSF pressure. Recovery usually occurs within 2 months, although prolonged symptoms and signs are occasionally noted.

GNATHOSTOMIASIS

A characteristic syndrome of intermittent, nonpitting edematous swellings of subcutaneous tissues associated with eosinophilia is caused by migration throughout the body of larvae from a number of species of helminths of the genus *Gnathostoma* (most commonly, *G. spinigerum* in Southeast Asia and *G. binucelatum* in Latin America).[64,65,66] Although cutaneous symptoms are frequent, any organ may be involved, and the most serious manifestations involve migration of larvae into the spinal cord and brain. Most of these infections occur in Southeast Asia, but large numbers have been recognized in Mexico.[67] Endogenous human infections have also been documented in Spain, Peru, Ecuador, India, China, Japan, Bangladesh, Botswana, Zambia, the United States, and other regions.

Life Cycle

The adult worms reside in tumorous burrows in the stomachs of a large number of mammals including cats of various types, dogs, opossums, and raccoons.[1,68] Eggs are shed in the feces, hatch after about 1 week, and are ingested by small crustaceans called *Cyclops*. These crustaceans are subsequently ingested by a variety of other animals, including fish, frogs, and snakes, where they encyst in the muscles as infectious larvae. When eaten by the appropriate definitive host, larvae migrate through the body and eventually invade the stomach, where they mature, mate, and release eggs in the feces. The spectrum of animals that spread infections to humans has broadened considerably because infectious larvae can be passed unaltered from animal to animal after ingestion (paratenic carriage). Most infections occur after eating undercooked freshwater fish, chicken, or pork. However, infectious larvae can also burrow through the skin, or infections may occur after ingestion of *Cyclops* in contaminated water. Rarely, prenatal transmission has been documented.

Clinical Manifestations

Acute signs and symptoms such as nausea, vomiting, gastrointestinal pain, and fever may occur shortly after ingestion and are most likely caused by the initial invasion of the infecting larva into and out of the intestines.[66,69] The most prominent signs, which occur 3 to 4 weeks after ingestion, are intermittent migratory subcutaneous swellings. They may occur anywhere. They are usually nonpitting, often erythematous, and occasionally pruritic and painful. They may also occur as nodules or abscesses or resemble classic cutaneous larva migrans. Eosinophilia is usually present and may be extreme. Migrating larvae may invade any tissue and give rise to symptoms related to specific organs such as the eye, intestines, spinal cord, and brain; involvement of the brain is commonly heralded by radicular nerve signs and symptoms as the worm gains entrance into the central nervous system. Brain involvement results in the most serious complication, eosinophilic encephalomyelitis.[64,65] Although gnathostomiasis is a less frequent cause of encephalomyelitis compared with *A. cantonensis,* it tends to result in permanent neurologic deficits and death because there is more invasion of the brain substance, commonly reflected by hemorrhagic lesions or tracts on computed tomography and MRI.[70] Consistent with this, the CSF has an increased number of red blood cells.

Diagnosis

Although gnathostomiasis was previously a rare diagnosis in nonendemic regions, it is more frequently recognized because of travel and ingestion of undercooked freshwater fishes, as well as by increased recognition of endogenous infections. In some areas of Southeast Asia, gnathostomiasis is a relatively common illness. The diagnosis is suggested when there is a history of intermittent subcutaneous swelling in the presence of eosinophilia and a history of ingesting raw fish or other implicated foods from endemic areas. A positive serology establishes the diagnosis in most cases but is not readily available in nonendemic regions. Usefulness between different geographic regions where infecting species differ has not been proven with all antibody tests.[71] Occasionally, the worms can be isolated from the migratory swellings or from lesions that develop after treatment, but attempts at parasite recovery are mostly unsuccessful.

Differential Diagnosis

The syndrome is relatively distinctive. *Loa loa* may manifest with Calabar swellings and eosinophilia, but the epidemiology is distinctive, and the swellings are not erythematous and do not resemble larval migrans. Cutaneous larval migrans is usually not accompanied by eosinophilia, and there is a distinctive epidemiology. Strongyloidiasis is not commonly associated with swellings and eosinophilia and can be distinguished by a serologic test or stool examination positive for *Strongyloides*.

Treatment

Both ivermectin, 200 μg/kg for two doses, and albendazole, 800 mg/day in two divided doses for 21 days, have resulted in high cure rates, but a high number of relapses over the long-term have been reported.[72,73]

Prevention

Avoiding uncooked or pickled implicated foods prevents infection in most individuals.

ABDOMINAL ANGIOSTRONGYLIASIS

Clinical manifestations of human infections of *Angiostrongylus costaricensis* are caused by penetration and development of the parasite in the lower small bowel and adjacent colon. They are characterized by abdominal pain, vomiting, and a right lower quadrant mass.[74] In the normal host, the rat, adult parasites reside in the arteries and arterioles of the ileocecal area of the intestine. Eggs deposited in the tissue hatch, and the larvae migrate through the intestinal wall into the lumen and are excreted in the feces. Larvae are then ingested by the intermediate host (the slug) and, after further development, are infectious for rats. After ingestion by rats, the larvae most likely undergo a systemic migration, mature in the intestinal lymphatics, and penetrate the arterioles and arteries in the ileocecal area, where they reside as adults. In humans, the parasite follows a similar pattern of migration except that eggs are retained in the tissues, and larvae do not appear in the feces. Adult parasites are found most commonly in the arteries and arterioles around the ileocecum and deposit eggs there. Both the eggs and the worms provoke an inflammatory response, which results in occluded vessels; an accompanying vasculitis; and an eosinophilic, granulomatous, edematous mass.

Infection of humans, most commonly children, has been recognized in Central and South America, occasionally the Caribbean, and rarely Africa and other areas. The manner of human infection is not usually known, but it may occur after accidental ingestion of infected slugs or of foods contaminated with larvae deposited in the mucous slime trail of slugs. Mint was implicated in one small epidemic.[75]

Patients are mildly to moderately ill and complain of abdominal pain and tenderness, vomiting, and fever; a right lower quadrant mass is noted in about 50% of cases.[76] Surgery reveals that the cecum, ascending colon, ileum, and appendix are involved to varied degrees. The syndrome resembles appendicitis except for the usual presence of eosinophilia and leukocytosis in angiostrongyliasis. Perforation occurs uncommonly, and the worms may be found ectopically in extraintestinal sites.[76]

The diagnosis is suspected clinically and confirmed by examination of biopsy or excised specimens. Radiographic findings are nonspecific and show filling defects and spasticity of the ileum, cecum, or colon. Relatively sensitive and specific serologic tests have been described, but they are not widely available.[77]

Most patients undergo laparotomy with removal of the inflamed areas; the natural history of infected children is unclear. It is not known if specific anthelmintic therapy is effective. An alternative treatment is mebendazole, 200 to 400 mg twice a day for 10 days.

Massive *Ascaris* infections may manifest with intestinal masses and may be confused with infections caused by *A. costaricensis*. Infections can be prevented by treating potentially contaminated vegetables with 1.5% bleach at room temperature for 15 minutes.[78]

EOSINOPHILIC GASTROENTERITIS

One cause of eosinophilic gastroenteritis is infection of humans with *Ancylostoma caninum,* a hookworm of dogs.[79,80,81] This syndrome is apparently limited to Northern Australia, although the conditions for human infection are likely present in many regions. After invading the skin, the usually single larva migrates to the ileum or to the colon to a lesser degree, where there is an intense focal response to the worm, including ulceration, inflammatory nodules, inflammation, thickening, and stricture formation. Gastrointestinal pain, nausea, vomiting, diarrhea, and bowel obstruction are common and are almost always accompanied by eosinophilia and leukocytosis. Ova are not produced, but the adult worm can sometimes be seen by endoscopy. Patients respond to a standard course of mebendazole, 100 mg twice a day for 3 days.

DIROFILARIASIS

A number of species of *Dirofilaria,* a filarial nematode that infects animals, accidentally infect humans through the bite of mosquitoes or black flies, most commonly resulting in lung nodules or subcutaneous masses, depending on the species. Two groups of parasites of the genus *Dirofilaria* accidentally infect humans.[13,82] The clinical presentations are generally different, which reflects the final location of the adults in the usual animal host. The adult worms of *Dirofilaria immitis,* the dog heartworm and the only important parasite in the first group, reside in the right side of the heart and the right pulmonary vessels; they are most commonly located in the lungs in humans but may also occur in other areas, mostly the subcutaneous tissues.

D. immitis is transmitted by a mosquito to its most common host, the domesticated dog, and other related mammals. After development in subcutaneous tissues, the parasites migrate as young adults to the right side of the heart and the right pulmonary vessels. In humans, the immature filariae migrate similarly but do not fully develop and die, which causes a local vasculitis leading to pulmonary infarcts. Histologic examination usually reveals a dead worm in an infarct with vasculitis and with granulomatous and occasionally eosinophilic inflammation.

Most infections occur in the southeastern United States through infections and transmission to dogs and by accidental transmission to humans. Persons are asymptomatic in more than 50% of the infections and show a coin lesion on a routine chest radiograph.[83,84] Others complain of cough, chest pain, or hemoptysis, most likely caused by pulmonary infarction. In some cases, lung infiltrates are noted that resolve into nodules.[85] Eosinophilia occurs in less than 15% of cases.

The diagnosis is made with certainty only by biopsy. Although serologic tests are available, their sensitivity and specificity are not adequate to rule out other potential life-threatening conditions such as a tumor.

Adults of the second group of filariae (subgenus *Nochtiella*) reside in the subcutaneous tissues of various mammals and usually cause inflammatory subcutaneous masses in humans.[86,87] These parasites include *D. tenuis* (raccoon), *D. ursi* (bear), *D. subdermata* (porcupine), and *D. repens* (dogs and cats in Europe and Asia). Ocular, primarily conjunctival, infection caused by *D. repens* has been increasingly reported.[82] Patients present with inflammatory subcutaneous masses containing increased numbers of eosinophils. As in infections with *D. immitis,* there are few, if any, systemic symptoms, and eosinophilia is not usually present. The diagnosis is established by biopsy. However, careful inspection of the entire tissue may be needed to find the parasite. Rarely, patent infections in humans occur.[82] Other filariae of animals, such as *Brugia* spp., have also been found in lymphoid or other tissues of humans.

CAPILLARIASIS

Capillaria philippinensis inhabits the small bowel of humans, causing diarrhea and malabsorption.[88,89,90] Infections have been recognized mostly in the Philippines but also in Thailand, Taiwan, Japan, Korea, Egypt, China, Indonesia, and Iran. The life cycle is surmised as follows: water birds harbor the adult worms and excrete ova, which are ingested by freshwater fish that become infected and produce larvae. Humans and birds become infected after eating infected fish possessing infective larvae. These larvae invade the jejunum and ileum, and the resulting adults produce both eggs and larvae. In contrast to almost all helminths that infect humans, with the exception of *S. stercoralis,* the parasite multiplies in the gut. This process is termed *autoinfection* and results in an overwhelming infection. In fulminant cases, autopsies reveal a thickened, edematous small bowel with a flattened mucosa containing a mononuclear infiltrate. Numerous adults, larvae, and eggs are present in both the lumen and the mucosa. Larvae infectious for birds, humans, and other mammals develop in certain freshwater fish after ingestion of eggs. Almost all signs and symptoms are related to progressive diarrhea and malabsorption. Patients complain of borborygmi, abdominal pain, vomiting, weight loss, and malaise, resulting in wasting, abdominal distention, and edema. Fever and eosinophilia are uncommon, although eosinophilia has been noted after therapy. Laboratory examinations document the typical findings of protein-losing enteropathy; fat, mineral, and vitamin malabsorption; and electrolyte loss. The diagnosis is established by detecting the characteristic *Trichuris trichiura*–like ova or larvae in the stool. A serologic test has been developed.

In untreated patients, mortality rates of 33% have been documented, but specific anthelmintic therapy is effective and lifesaving. Therapy with mebendazole, 200 mg orally twice daily for 20 days, or albendazole, 400 mg/day orally for 10 days,[89] is effective. Relapses are treated with prolonged courses of therapy. Infection is prevented by eating only properly cooked freshwater fish.

SWIMMER'S ITCH

Swimmer's itch is also known as *schistosomal dermatitis, cercarial dermatitis,* and *clam digger's itch*. Cercariae, the infective form of a large number of blood flukes of birds such as avian schistosomes (commonly *Trichobilharzia*), those in nonhuman mammals, and less commonly human schistosomes, can cause a characteristic dermatitis in humans that is associated with penetration of the cercariae into the skin.[1] They are produced and then released by various species of mollusks, which are the intermediate hosts. The clinical manifestations in humans are almost always limited to the skin.[91] Infections are frequent in many areas of the world but are particularly common in persons exposed to the freshwater lakes of the northern United States. However, infections also occur after exposure to salt water (clam digger's itch).

Although the clinical manifestations vary after the initial exposure, symptoms are typically mild and sometimes go unnoticed.[92,93] The patient complains of itching, followed by the appearance of macules at the site of penetration of the cercariae. By 24 hours, the macules have disappeared and begin to be replaced by papules. After repeated exposures, reactions occur earlier than 24 hours after exposure and are more severe. Papules are larger and associated with erythema, itching, and edema. The symptoms subside by 4 to 7 days, but in severe cases, they may last weeks.

Infection can be controlled by ridding bathing areas of the molluscan intermediate host or the definitive host or by avoiding infected bodies of water. Treatment is symptomatic. There is no specific anthelmintic therapy.

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The complete reference list is available online at Expert Consult.

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K Ectoparasitic Diseases

291 Introduction to Ectoparasitic Diseases

James H. Diaz

Ectoparasites infest the skin and its appendages, such as the hair and sebaceous glands, and most external orifices, especially the ears, nares, and orbits. Like endoparasites, ectoparasites may be obligatory parasites, programmed to feed on human hosts to complete their life cycles, or facultative parasites, preferring to feed on nonhuman hosts, infesting humans only as accidental or dead-end hosts. Over the past 2 decades, there have been several reports of significant outbreaks of ectoparasitic diseases, principally myiasis, scabies, and tungiasis, both in indigenous populations and in travelers returning from developing nations and even exclusive tropical beach resorts.[1,2] Many common ectoparasites, such as head lice and scabies mites, are also developing increasing resistance to medical therapies, including the safest topical insecticides.[3–6] Other ectoparasites, such as the New World human botfly, *Dermatobia hominis,* and the jigger or chigoe flea, *Tunga penetrans,* are resistant to systemic and topical antiparasitics and can be treated only surgically.

Ectoparasitic diseases have reemerged as unusual, but not uncommon, infectious diseases worldwide, especially in high-risk populations. Indigenous populations of ectoparasite-endemic tropical nations often have recurrent infestations and superinfestations that can result in severe disfigurement from facial cavitary myiasis or permanent disability from tungiasis-associated autoamputations.

TAXONOMY OF ECTOPARASITES

The phylum Arthropoda is the largest phylum of the animal kingdom and includes the subphylum Crustacea and the classes Insecta and Arachnida. All the medically important ectoparasites, including fleas, flies, lice, mites, and ticks, are members of the phylum Arthropoda and have chitinous exoskeletons, segmented bodies, and jointed appendages. Fleas, flies, and lice are six-legged members of the class Insecta, which also includes the mosquitoes and true bugs (order Hemiptera). Mites, including chigger and scabies mites, and ticks are the eight-legged members of the class Arachnida, subclass Acari. The arthropod ectoparasites of medical importance are stratified by taxonomic classes and distinguishing external anatomic characteristics in Table 291.1.

EPIDEMIOLOGY OF ECTOPARASITIC DISEASES

Ectoparasitic diseases share many of the general characteristics of emerging infectious diseases. Commonly shared characteristics of ectoparasitoses and emerging infectious diseases include the following: (1) origination as zoonoses, with disease establishment dependent on arthropod vector competency; (2) introduction into new, susceptible host populations; (3) infection by endemic agents given selective advantages by changing ecologic or socioeconomic conditions; and (4) recent movement from rural to urban endemic areas, often following migrating human host populations seeking better economic opportunities.[7–9]

To assess the potential combined impact of increasing international travel and the relaxation of quarantine regulations for imported animals in the United Kingdom on arthropod-induced ectoparasitic dermatoses, McGarry and colleagues analyzed 73 insect specimens removed from symptomatic patients and submitted to their laboratory for identification at the Liverpool School of Tropical Medicine during the years 1994 to 2000.[10] Of the 73 specimens identified, there were 27 ticks, 24 flies, 15 miscellaneous insects, and 7 mites. Most of the arthropod dermatoses originated in the United Kingdom ($n = 46$; 63%), and were caused by tick bites ($n = 18$), principally *Ixodes ricinus* (the common sheep tick), an important European vector of Lyme disease and neuroborreliosis. Myiasis cases predominated in returning travelers ($n = 18$; 67%), principally furuncular myiasis from larval infestation by *Cordylobia anthropophaga* (n = 9), the tumbu fly, or *Dermatobia hominis* ($n = 4$), the human botfly. Among the arthropod dermatoses caused by miscellaneous arthropods, most were pediculosis pubis caused by infestation with *Phthirus pubis,* the pubic louse ($n = 7$), or hemorrhagic, bullous bite groupings caused by *Cimex lectularius,* the common bedbug ($n = 3$). The authors concluded that exotic ectoparasitic infestations, particularly myiasis, predominated in returning travelers from Africa and Latin America; pubic lice were domestic, likely sexually transmitted, infestations; and bedbug infestations were domestically and internationally acquired, often from exposure to fomites, including bedding and luggage.

MECHANISMS OF ECTOPARASITE-BORNE DISEASES AND INJURIES

The arthropod ectoparasites can threaten human health directly by burrowing into and feeding, dwelling, and reproducing in human skin and orifices (mites, fleas, flies), or by blood or tissue juice sucking (fleas, lice, mites, ticks). The arthropod ectoparasites can also threaten human health indirectly by infectious disease transmission (fleas, mites, ticks). Ticks are the most versatile ectoparasitic arthropods and can transmit a variety of infectious diseases (viral, bacterial, and protozoan) and even inject paralytic toxins (tick paralysis) during their prolonged blood meals. Unlike other ectoparasites, ticks can be infective as males and females at birth (by transovarial pathogen transmission) and throughout all stages of their development (by transstadial pathogen transmission). The most commonly encountered arthropod ectoparasites, excluding ticks, and the major clinical manifestations of their infestations are featured in Table 291.2. The tick-borne pathogens and the clinical manifestations of their infections are featured in Chapter 296, Tables 296.1 through 296.8.

CONCLUSIONS

Recent epidemiologic evidence now supports the endemicity of several ectoparasitic diseases and their arthropod vectors (Table 291.3) and human and animal reservoir hosts throughout the developing world and in many parts of the developed world, including Europe and the United States. Ectoparasitic diseases have also reemerged in regions where they were once effectively controlled. Ectoparasitic diseases will continue to reemerge in the developed world for several reasons, including the following: (1) the globalization of trade and commerce with ectoparasites and their human and animal hosts traveling worldwide on airplanes and container ships; (2) mass movements of populations from rural to urban areas and from developing to developed nations; (3) the worldwide legitimate and illegal trade of exotic animals and animal hides and skins; (3) the accidental and intentional introduction of exotic animal species into new regions with welcoming ecosystems; (4) the

TABLE 291.1 Taxonomy of Arthropods (Phylum Arthropoda) of Major Medical Importance

	COMMON NAMES	NO. OF LEGS, NO. OF BODY SEGMENTS, OTHER IDENTIFYING ANATOMIC FEATURES
Phylum Arthopoda, Class Insecta		
Order Diptera, family Culicidae	Mosquitoes	Six, three, wings
Order Diptera	Flies[a]	Six, three, wings
Order Hemiptera	True bugs (e.g., bedbugs, reduviid bugs)	Six, three, ± wings
Order Hymenoptera	Ants, bees, wasps	Six, three, ± wings
Order Phthiraptera	Lice[a]	Six, three, no wings
Order Siphonaptera	Fleas[a]	Six, three, no wings
Phylum Arthropoda, Class Arachnida		
Subclass Acari	Mites and ticks[a]	Eight, one globose body, no distinct heads[b], no wings
Order Araneae	Spiders	Eight, two, no wings
Order Scorpiones	Scorpions	Eight, two, abdomens with terminal stingers

[a]The arthropod ectoparasites of major medical importance by taxonomic order and distinctive anatomic features.
[b]Mouthparts visible dorsally only in ixodid (hard) ticks.

TABLE 291.2 Common Arthropod Ectoparasites (Excluding Ticks) and Clinical Manifestations of Ectoparasitoses

REPRESENTATIVE SPECIES OF INFESTING ARTHROPOD ECTOPARASITES	COMMON NAMES OF INFESTING ARTHROPOD ECTOPARASITE	GEOGRAPHIC DISTRIBUTION	MAJOR CLINICAL MANIFESTATIONS OF ECTOPARASITOSES
Class Insecta, Order Phthiraptera, Suborder Anoplura	Lice		
Pediculus humanus corporis	Body louse	Worldwide	Pediculosis corporis
Pediculus humanus capitis	Head louse	Worldwide	Pediculosis capitis, trench fever (Bartonella quintana)
Phthirus pubis	Crab (pubic) louse	Worldwide	Pediculosis pubis (phthiriasis)
Order Diptera	Flies		
Family Calliphoridae	Screwworms		
Auchmeromyia senegalensis	Congo floor-maggot fly	Sub-Saharan Africa, Cape Verde Islands	Larvae are nocturnal blood feeders, no myiasis (tissue invasion); wound (cutaneous) myiasis
Callitroga americana	American screwworm	North and Central America	Cavitary (invasive) myiasis
Chrysomyia bezziana	Old World screwworm	Tropical Africa, Asia, Indonesia	Cavitary (invasive) myiasis
Cochliomyia hominivorax	New World screwworm	Central and South America	Furuncular myiasis
Cordylobia anthropophaga	Tumbu (mango) fly	Africa	Furuncular myiasis
Family Oestridae	Botflies		
Cuterebra spp.	Rodent botfly	North and Central America	Furuncular myiasis
Dermatobia hominis	Human botfly	Central and South America	Furuncular myiasis
Order Siphonaptera	Fleas		
Ctenocephalides spp.	Cat *(C. felis)* and dog fleas *(C. canis)*	Worldwide	Bite groupings (mechanical vectors of dog and rat tapeworms, less efficient bubonic plague vectors)
Pulex irritans	Human flea	Worldwide	Bite groupings (efficient plague vector in Chilean Andes)
Tunga penetrans	Chigoe (jigger) flea	Central and South America, Africa Europe, Asia	Tungiasis
Xenopsylla cheopis	Oriental rat flea	Africa, Americas	Most efficient bubonic plague vector
Class Arachnida	Spiders, mites, ticks	Worldwide	
Subclass Acari	Mites and ticks		
Sarcoptes scabiei	Itch (scabies) mite	Worldwide	Scabies, crusted (Norwegian) scabies
Eutrombicula alfreddugesi	Common chigger (redbug chigger)	Worldwide	Chiggers
Leptotrombidium akamushi	Japanese-Asian rodent chigger	Japan, India, Australia	Potential scrub typhus (Tsutsugamushi disease) vector
Leptotrombidium deliensis	Indian-Asian rodent chigger	Eurasia-Eastern Asia, Southeast Asia, India, Australia, Indo-Pacific Islands	Potential scrub typhus (Tsutsugamushi disease) vector

increasing frequency of pyrethroid-resistant strains of ectoparasites, especially head lice and scabies mites; and (5) the growing populations of susceptible, and often immunocompromised, human hosts living in long-term care facilities and in crowded and impoverished periurban communities.[11,12]

The isolation of the trench-fever pathogen, *Bartonella quintana,* in head lice from homeless persons in the United States illustrates how well socioeconomic factors, human behavioral trends, and vector adaptations can support ectoparasite persistence with significant public health consequences.[13] Formerly felt to be susceptible to the safest pyrethroid pesticides and incapable of transmitting infectious diseases, head lice have acquired the capability to harbor *B. quintana* like body lice and potentially to transmit trench fever to new naïve host populations. The eradication of pyrethroid-resistant head lice infestations in homeless persons in crowded shelters and children in schools will require the use of more powerful pesticides with potential for adverse effects, such as carbaryl, lindane, and malathion; or the use of new, safer alternatives, such as oral and topical ivermectin-containing pediculicides.[11]

TABLE 291.3 Selected Infectious Diseases Transmitted by Arthropods

Infectious Disease	Vector
Anaplasmosis (human granulocytotropic)	Hard ticks
Arbovirus diseases (including yellow fever, dengue fever, encephalitis)	Mosquitoes and ticks
Babesiosis	Hard ticks
Boutonneuse fever (tick bite fever; *Rickettsia conorii*)	Hard ticks
Cat scratch disease, cat scratch fever *(Bartonella henselae)*	Cat fleas
Chagas disease (American trypanosomiasis)	Triatomine (kissing) bugs
Colorado tick fever	Hard ticks
Ehrlichiosis, monocytotropic *(Ehrlichia chaffeensis)* and granulocytic *(Ehrlichia ewingii)*	Hard ticks
Endemic relapsing fever *(Borrelia duttonii)*	Soft ticks
Epidemic relapsing fever *(Borrelia recurrentis)*	Human body lice
Epidemic typhus *(Rickettsia prowazekii)*	Human body lice
Filariasis *(Wuchereria bancrofti, Brugia malayi)*	Mosquitoes
Leishmaniasis (*Leishmania* spp.)	*Lutzomyia* sand fly in the Americas, phlebotomid flies elsewhere
Loiasis *(Loa loa)*	Tabanid flies
Lyme disease *(Borrelia burgdorferi)*	Hard ticks
Malaria (*Plasmodium* spp.)	Mosquitoes
Murine typhus *(Rickettsia mooseri)*	Rat fleas, lice
Onchocerciasis *(Onchocerca volvulus)*	Black flies
Plague *(Yersinia pestis)*	Rat fleas
Q fever *(Coxiella burnetii)*	Hard ticks, fleas
Rickettsialpox *(Rickettsia akari)*	Mouse mites
Rocky Mountain spotted fever *(Rickettsia rickettsii)*	Hard ticks
Scrub typhus *(Rickettsia tsutsugamushi)*	Mites (chiggers)
Trench fever *(Bartonella quintana)*	Body lice, potentially head lice
Trypanosomiasis, African sleeping sickness	*Glossina* (tsetse) flies
West Nile fever	Mosquitoes

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292 Lice (Pediculosis)

James H. Diaz

SHORT VIEW SUMMARY

Definition
- Pediculosis is a complex of three different human infestations (head lice, body lice, and pubic lice) with two species of blood-sucking lice: *Pediculus humanus* var. *capitis* or *corporis* and *Phthirus pubis*.

Epidemiology
- Head lice infestations, or pediculosis capitis, are transmitted primarily by head-to-head contact and less commonly by fomites.
- Head lice afflict millions of people annually, mostly school-aged children.
- Body lice infestations, or pediculosis corporis, are transmitted primarily by bodily contact and less commonly by fomites.
- Body lice are associated with poor hygiene and primarily infest the indigent, institutionalized, homeless, refugees, and immunocompromised.
- Pubic lice infestations (phthiriasis) are transmitted primarily during sexual contacts and often coexist with other sexually transmitted diseases.

Microbiology
- Body lice can transmit several bacterial diseases, including (1) relapsing fever caused by *Borrelia recurrentis,* (2) trench fever caused by *Bartonella quintana,* and (3) epidemic typhus caused by *Rickettsia prowazekii. B. quintana* has also been isolated in head lice from homeless persons in the United States, establishing the potential for transmission of trench fever by head lice in addition to body lice.

Diagnosis
- Lice infestations are diagnosed by clinical inspection demonstrating live adult lice, nymphs, and viable eggs, or nits, in their precise human anatomic niches.
- Recently, dermoscopy has been used to immediately distinguish viable nits from hatched, empty nits.
- Dermoscopy may provide a more sensitive screening tool for head lice infestations than inspection alone.

Therapy
- A combination of pharmacologic therapy with topical or oral (ivermectin) pediculicides and physical removal of viable nits by wet combing is required.
- Pharmacotherapy should begin with the least toxic pediculicides, such as pyrethrins.
- Topical or oral ivermectin preparations should be reserved for pyrethrin-resistant cases.

Prevention
- Combinations of sanitizing the environment and eliminating all human reservoirs of head lice in households, apartments, housing complexes, homeless shelters, classrooms, and schools are recommended.
- Prevention strategies for pubic lice are similar to the prevention strategies for body lice and should include hot-cycle washing and drying of all clothing and bedding; institution of basic personal hygiene and sanitation measures; and treatment of sexual contacts with active body or pubic lice infestations.

Pediculosis is a complex of three different human infestations with two species of blood-sucking lice of the insect order Phthiraptera, suborder Anoplura: *Pediculus humanus* and *Phthirus pubis.* Sometime after early humans began to wear clothes, *P. humanus* evolved into two clinically distinct ectoparasitic variants, *P. humanus* var. *corporis,* the body louse (Fig. 292.1), and *P. humanus* var. *capitis,* the head louse (Fig. 292.2). Although morphologically indistinct, these human louse variants do not interbreed, prefer unique anatomic niches on human hosts, and are now considered distinct species. Specifically, head lice *(P. humanus capitis)* leave their hair shaft nests for blood meals on the scalp, and body lice *(P. humanus corporis)* leave their clothes seams nests for blood meals on the body. *Phthirus pubis,* the crab or pubic louse (Fig. 292.3), is morphologically distinct from the two *P. humanus* species, has a crab-shaped body, and prefers to dwell in the hair-bearing areas of the pubic and inguinal areas but may also infest the hairy areas of the axillae, chest, and abdomen and even the eyelashes (phthiriasis palpebrum). Unless mating or egg-laying, pubic lice remain relatively stationary, anchored to the bases of hair shafts while blood-feeding.

Lice are among the oldest ectoparasites of humans and are distributed into three separate mitochondrial clades (A, B, and C) based on their continents of origin.[1] Recently, a new clade of head and body lice (mitochondrial clade D) that were infected by *Bartonella quintana* and *Yersinia pestis* has been discovered in lice-infected persons living in plague-endemic areas of the Democratic Republic of the Congo.[2] Since the analysis of ancient DNA from Old World archeological sites is often compromised by low concentrations in poor specimens, the DNA from ancient head louse eggs or nits detected by reverse-transcriptase polymerase chain reaction (PCR) has recently proven to be valuable in mapping the migration patterns of ancient humans and the spread of their louse-borne infectious diseases such as epidemic typhus, relapsing fever, and trench fever.[1]

EPIDEMIOLOGY

Pediculosis capitis, or head lice infestation, is the most common of the three types of human pediculoses, afflicting millions of people annually, mostly school-aged children, in both developing and industrialized nations. Body lice infestations, or pediculosis corporis, are associated with poor hygiene and low socioeconomic status and occur primarily in the indigent, the institutionalized, the homeless, refugees from civil unrest, and the immunocompromised. Body and head lice are usually transmitted by direct body or head-to-head contact or sharing headgear between infested individuals and, much less commonly, by indirect contact with fomites, such as bedding, clothing, towels, headgear, combs, and brushes. Pubic lice infestations, or phthiriasis, are caused by *P. pubis,* the pubic or crab louse. Pubic lice are more often transmitted during sexual rather than fomite contacts and often coexist with crusted (Norwegian) genital scabies and other sexually transmitted diseases.

Unlike pubic lice, body lice can transmit several bacterial diseases. Homeless, immunocompromised, and refugee populations are at greatest risk for body lice infestations and epidemics of body louse–borne bacterial diseases, including the following: (1) relapsing fever caused by *Borrelia recurrentis,* (2) trench fever caused by *Bartonella quintana,* and (3) epidemic typhus caused by *Rickettsia prowazekii.* Body lice have been recognized as infectious organisms of high importance, not only in displaced populations in evacuee and refugee camps but also in immunocompromised subjects, particularly homeless individuals with acquired immunodeficiency syndrome (AIDS).[3–5]