

8.9.5 Gut and tissue nematode infections acquired

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section 8 Infectious diseases 1506 worldwide may partly be a result of reduced exposure to the immunosuppressive effects of helminths, and lead to concerns that mass deworming may have detrimental as well as beneficial effects. A trial of experimental hookworm infection as a treatment for asthma did not demonstrate a significant benefit, however hookworm-derived molecules have been demonstrated to have potent immunomodulatory effects in vitro and could form the basis for future drug development. FURTHER READING Bottazzi ME (2015). The human hookworm vaccine: recent updates and prospects for success. *J Helminthol*, 89, 540–4. Buonfrate D, et al. (2015). Novel approaches to the diagnosis of *Strongyloides stercoralis* infection. *Clin Microbiol Infect*, 21, 543–52. George PJ, et al. (2015). Modulation of pro- and anti-inflammatory cytokines in active and latent tuberculosis by coexistent *Strongyloides stercoralis* infection. *Tuberculosis (Edinb)*, 95, 822–8. Karagiannis-Voules DA, et al. (2015). Spatial and temporal distribution of soil-transmitted helminth infection in sub-Saharan Africa: a systematic review and geostatistical meta-analysis. *Lancet Infect Dis*, 15, 74–84. Schär F, et al. (2013). *Strongyloides stercoralis*: global distribution and risk factors. *PLoS Negl Trop Dis*, 7, e2288. World Health Organization (WHO) (2017). Chistosomiasis and soil-transmitted helminthiasis: number of people treated in 2016. *Wkly Epidemiol Rec*, 92, 49–60.

8.9.5 Gut and tissue nematode infections acquired by ingestion

Peter L. Chiodini ESSENTIALS *Ascariasis* *Ascaris lumbricoides* (the human roundworm) is widespread in the tropics and subtropics where sanitation is poor and the soil is contaminated with its eggs. *Ascaris suum* (the pig roundworm) is also capable of infecting humans. Some authorities consider them to be the same species, making *A. suum* a synonym of *A. lumbricoides*. Ingested eggs hatch in the small bowel, the larvae released migrate via the

bloodstream and lungs, then return to the small bowel and develop into adult worms 15 to 30 cm long. Most infections are asymptomatic, but there may be pulmonary infiltrates with eosinophilia, abdominal discomfort and—in children with heavy infections—intestinal obstruction. Infection is diagnosed by finding eggs in the faeces. Treatment is with mebendazole, albendazole, or pyrantel pamoate.

Anisakidosis This is caused by larvae of roundworms in the family Anisakidae, which are parasites of marine mammals. The larvae cannot mature to adult form in humans who thus represent dead-end hosts for these parasites. After ingestion in uncooked fish or squid, immature larvae burrow into the gastric or intestinal mucosa and may cause abdominal pain. Diagnosis is usually made at endoscopy, with treatment by endoscopic removal (if possible) of the larvae, although symptoms resolve spontaneously in most cases.

Capillariasis Intestinal capillariasis, caused by *Paracapillaria philippinensis*, is acquired by ingestion of larvae in undercooked freshwater fish and may cause a severe diarrhoeal disease. Diagnosis is by finding eggs in the stool. Treatment is with albendazole or mebendazole. Prevention is by properly cooking fish.

Hepatic capillariasis—caused by *Capillaria hepatica*, a parasite of wild rodents and other mammals. Ingested eggs hatch and larvae pass to the liver and cause a syndrome similar to visceral larva migrans (see next). Serology is rarely available and definitive diagnosis is made by identifying the parasite or eggs in a liver biopsy. Treatment is usually with albendazole. Adjunctive corticosteroids have been used.

Enterobiasis *Enterobius vermicularis* (threadworm) is cosmopolitan. Ingested eggs develop directly into adult worms in the intestine; fertilized female worms emerge from the rectum at night and deposit eggs on the perianal skin. Most infections are asymptomatic, but pruritus ani may be troublesome at night. Diagnosis is made by finding eggs on clear adhesive tape applied to the perianal skin or identification of worms found on the perianal skin or surface of the stool. Mebendazole or albendazole or pyrantel pamoate are effective in combination with sanitary measures. Recurrent threadworm due to reinfection can be troublesome in a minority of patients.

Gnathostomiasis Gnathostomiasis is due to ingestion of the third stage larva, usually from *Gnathostoma spinigerum*, a parasite of domestic and wild felines and canines, or *G. hispidum*, a parasite of pigs, via raw or undercooked freshwater fish. It is endemic in Southeast Asia, the Indian subcontinent, Southern Africa, Mexico, and Peru, and is increasingly seen in ever-more adventurous travellers. It causes both migratory cutaneous swellings and visceral disease.

Toxocariasis This is due to invasion by larvae of *Toxocara canis* or *T. cati*, acquired by ingestion of eggs from dog or cat faeces contaminating the environment. It occurs in three clinical forms—visceral larva migrans, ocular larva migrans, and covert toxocariasis. Visceral larva migrans usually afflicts children; larvae migrate to the viscera and may be asymptomatic or cause protean manifestations including muscular pain, lassitude, anorexia, cough, urticarial rashes, hepatomegaly, and occasionally splenomegaly, lymphadenopathy and skin lesions, and (rarely) central nervous system involvement resulting in convulsions. Eosinophilia is prominent. While definitive diagnosis is by finding larvae in a liver biopsy this should not be necessary to diagnose visceral larva migrans due to toxocariasis. A negative serological test for toxocara antibody rules out the diagnosis. Most patients recover spontaneously. Severe cases can be treated with albendazole plus adjunctive corticosteroid therapy. Ocular larva migrans is more commonly seen in older children and due to granuloma formation around a larva in the retina.

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Trichinosis This is acquired by ingestion of larvae of *Trichinella spiralis* in undercooked meat, usually pork. Adult

worms in the small bowel produce larvae which seed the muscles and other tissues, where they develop. Most infections are asymptomatic, but heavy infections typically cause diarrhoea, followed by fever and myositis. Definitive diagnosis depends upon finding larvae in muscle biopsies, although this is usually unnecessary; serological tests become positive several weeks after infection. Treatment is mainly symptomatic. Anthelmintic agents are used to kill adults and thus minimize the production of new larvae. Thorough cooking of pork is the best safeguard against infection.

Trichuriasis *Trichuris trichiura* (whipworm) is most prevalent in the tropics and subtropics where sanitation is poor. Ingested eggs hatch in the small bowel and then develop within the gut into adult worms, the anterior end of which becomes embedded in the large bowel mucosa. Very heavy infections may cause dysentery or rectal prolapse. Infection is diagnosed by finding eggs in the faeces. Treatment is with mebendazole or albendazole.

Ascariasis (giant roundworm infection)

Life cycle Ascariasis is an infection caused by the giant roundworm, *Ascaris lumbricoides*. Infection is acquired when an egg is ingested (Fig. 8.9.5.1). The infective larva hatches out in the small intestine (Fig. 8.9.5.2) and penetrates the intestinal wall to enter the portal circulation. From here it enters the systemic circulation and reaches the lungs, where it breaks out of the capillaries into the alveoli and undergoes another moult to become a fourth-stage larva. From the lungs the larva moves up the bronchial tree to the mouth and is then swallowed. In the intestine it moults again to become a sexually mature worm about 6 to 8 weeks after ingestion of the egg. The mature worm is cylindrical with tapering ends and creamy white to light brown in colour (Fig. 8.9.5.3). The female measures 20 to 35 cm in length and 3 to 6 mm in width, whereas the male is 12 to 31 cm long and 2 to 4 mm wide and has a curved tail. Normally, the adult worms live in the lumen of the small intestine, primarily the jejunum. The worm is able to maintain its position in the small intestine by the activity of its somatic muscles; if these are paralysed by anthelmintics it is expelled by peristalsis. The lifespan of an adult worm is usually 1 to 2 years, after which it is expelled spontaneously. The worms mate and eggs are passed in the faeces, with gravid females each producing 200 000 to 250 000 eggs daily. When freshly passed, these eggs are not infective and contain a single cell. This develops in the soil over the next 2–6 weeks (faster in warmer temperatures) into an infective larva. The ova are resistant to chemicals and low temperatures, and may remain viable for up to 10 years in moist soil.

Epidemiology and control Ascariasis is cosmopolitan, and is arguably the most common helminth infection. It is prevalent in areas where there is poor sanitation, with contamination of the soil with eggs. Infection is more common in tropical climates, especially where human faeces are used to fertilize vegetable gardens. Infection is usually acquired by eating contaminated food, or from soil ingested by children when playing and does not induce resistance to reinfection. It is relatively more common in children and intensity of infection peaks in the first decade of life in high transmission areas. In hyperendemic areas with constant warm temperatures and high humidity, children are continuously being infected, so that as some worms are being expelled, others are maturing to take their place. Transmission might only be associated with the Trachea Lungs Pharynx Swallowed female male Circulation Ingested

HUMANS EXTERNAL ENVIRONMENT Fertilized Unfertilized Two cell stage Embryonated egg (infective stage) Eggs in faeces (diagnostic stage) Larva hatches in intestine Advanced cleavage Adults in small intestine Fig. 8.9.5.1 Life cycle of *Ascaris lumbricoides* and *Ascaris suum*.
Fig. 8.9.5.2 Decorticated eggs of *Ascaris lumbricoides*, showing emergence of larvae. Copyright Viqar Zaman.

section 8 Infectious diseases 1508 rainy season in areas that are generally hot and arid. The pig ascarid *A. suum* can infect humans and mature into adult worms and is regarded by some as a

synonym of *A. lumbricoides*. Environmental sanitation is the best control measure, but when this is not possible, mass chemotherapy given at intervals of 6 to 12 months to preschool age and school age children reduces the severity and intensity of infection. Clinical features The first passage of larvae through the lungs usually causes no symptoms or pathological changes, but subsequent infections can be associated with hypersensitivity reactions, causing *Ascaris* pneumonitis (Fig. 8.9.5.4). When this causes fever, cough, dyspnoea, bronchospasm, peripheral eosinophilia, and infiltrates on a chest radiograph that are often migratory, it is known as Löffler's syndrome, but the syndrome is not specific to ascariasis. The condition usually subsides after 7 to 10 days, unless reinfection occurs. In areas where pig farming is common, the larvae of *A. suum* may also produce severe pneumonitis and bronchospasm. Most people with established infection with *A. lumbricoides* are asymptomatic, especially if the worm burden is small. Some might complain of anorexia, nausea, and abdominal discomfort or distension. Heavy infections in children can cause malnutrition and hinder normal development in terms of both stature and cognitive performance. Mechanical complications probably occur in less than 1% of infected individuals. Occasionally, usually in children, large numbers of worms may become entangled to form a bolus that blocks the intestinal lumen, usually near the ileocaecal valve, producing signs and symptoms of acute intestinal obstruction. This might be complicated by perforation, intussusception, volvulus, and death. In some circumstances, such as fever, irritation caused by drugs, anaesthesia, or bowel manipulation during surgery, the worms may migrate to ectopic sites. Migration into the common bile duct can be complicated with cholangitis and liver abscesses, whereas entry into the pancreatic duct might precipitate acute pancreatitis. Worms may migrate into the appendix, occasionally come out through the mouth and nose, and are rarely found in other ectopic locations. Diagnosis Ascariasis is usually diagnosed by finding plentiful numbers of the characteristically oval fertilized eggs measuring 60×30 to $70 \times 50 \mu\text{m}$ in the faeces (Fig. 8.9.5.5). Sometimes the patient brings developing or adult worms that have been passed in the faeces or have emerged from the anus or nose of a sick child. Occasionally, adult worms are outlined in the intestines during barium-meal examination, or are seen at upper gastrointestinal endoscopy. Treatment It is desirable to treat all infected individuals, even when the worm load is small. There are several effective drugs (listed next). None of them is recommended by its manufacturer for use in pregnancy, especially in the first trimester, or children under 1 to 2 years of age, although this has been disputed by some authorities. For preventive chemotherapy, the World Health Organization manual Preventive chemotherapy in human helminthiasis recommends that albendazole or mebendazole be offered in the second and third trimesters of pregnancy in targeted interventions where the prevalence of infection with any soil-transmitted helminth is greater than 20%. • Mebendazole is given as 100 mg twice daily for 3 days in adults and children over 2 years of age. It should not be given in the first trimester of pregnancy. Fig. 8.9.5.3 Adult *Ascaris lumbricoides* (scale in mm). Copyright Viqar Zaman. Fig. 8.9.5.4 *Ascaris lumbricoides* in the lungs, surrounded by an inflammatory reaction. Copyright Viqar Zaman. Fig. 8.9.5.5 Egg of *Ascaris lumbricoides*.

8.9.5 Gut and tissue nematode infections acquired by ingestion 1509 • Albendazole is given as a single dose of 400 mg in adults and children over 2 years of age. It should not be given in the first trimester of pregnancy. • Pyrantel pamoate given in a single dose of 11 mg/kg body weight (maximum 1 g) is effective in curing more than 90% of cases of ascariasis. Side effects are usually mild and the drug is well tolerated. It should not be given in the first trimester of pregnancy. In cases of intestinal obstruction caused by an *Ascaris* bolus, a piperazine salt given at

a dose of 75 mg/kg (maximum 3.5 g) daily for two consecutive days has been recommended as it induces flaccid paralysis of the worms, which may relieve the obstruction. This should be supplemented with decompression of the bowel through an intestinal tube with constant suction; rehydration and restoration of electrolyte balance with intravenous fluids. In most cases this conservative therapy will relieve the obstruction and the child will rapidly recover. If, however, the signs of obstruction persist, laparotomy is required. Obstruction of the biliary tract by *Ascaris* is diagnosed by ultrasound. Anthelmintics are given and worms not passed spontaneously may be removed endoscopically, reducing the need for operation. Surgery is required for gangrenous cholecystitis.

Anisakidosis Life cycle Anisakidosis (previously known as Anisakiasis) is an infection caused by the larvae of various species of nematode belonging to the family Anisakidae, most commonly *Anisakis simplex* and *Pseudoterranova decipiens*. Adults live in the lumen of the intestine of cetaceans (whales, dolphins, and porpoises). Eggs are passed in water, embryonate, and release second-stage larvae which are ingested by crustaceans in which they develop to third-stage larvae. When crustaceans are ingested by fish or squid they enter the muscles of these hosts. Cetaceans and humans become infected by eating infected saltwater fish or squid.

Epidemiology and control The adult worms are commonly found in marine mammals in many parts of the world. Humans are infected when they eat raw or improperly cooked fish or squid. The incidence is highest in Japan, countries on the northern European seaboard and the Pacific coast of the Americas, especially in the South. Infection is prevented by not eating raw, pickled, smoked, or undercooked fish and squid. Larvae are killed by cooking fully to at least 63°C; or freezing solid and storing at minus 20°C for 7 days; or freezing solid at minus 35°C and storing at minus 35°C or below for 15 hours.

Clinical features The larvae do not develop to maturity in humans, but attach themselves to, and then burrow into, the mucosa of the stomach (especially *Pseudoterranova* species) or small intestine (especially *Anisakis* species), and rarely the large bowel (Fig. 8.9.5.6). Symptoms commonly develop 4 to 24 h after eating infected fish. Gastric invasion produces severe epigastric pain, nausea, vomiting, and sometimes haematemesis during the acute stage of the disease. Involvement of the intestine may cause severe lower abdominal pain, which might be misdiagnosed as appendicitis. If symptoms are mild and the patient is left untreated the infection can become chronic, with pseudotumour formation around the parasite. Sometimes the larva precipitates an allergic reaction, with urticaria, angio-oedema, or anaphylaxis.

Diagnosis A definitive diagnosis is made by upper gastrointestinal endoscopy which reveals the lesion and the presence of white or yellow larvae up to 3 cm in length attached to the mucous membrane. Intestinal anisakiasis is more difficult to diagnose, but imaging studies might show thickening of the intestinal wall, and narrowing of the jejunum or ileum. Serology for anti-*Anisakis* IgE or IgG is deployed in some specialist centres.

Treatment In acute infection, an attempt should be made to remove the larva through an endoscope, although in most patients symptoms resolve spontaneously within 2 weeks. In chronic cases, surgical removal of the ulcerated areas or the tumour may be required. No chemotherapy has been proven to be effective in a clinical trial, though albendazole has been reported to be beneficial in a case report.

Capillariasis There are two forms of capillariasis: intestinal capillariasis caused by *Paracapillaria philippinensis*, and hepatic capillariasis caused by *Capillaria hepatica*.

Intestinal capillariasis This infection is caused by a worm still generally referred to as *Capillaria philippinensis*, although it has been renamed *Paracapillaria philippinensis*. Fish-eating birds are the definitive reservoir. Adult *C. philippinensis* measure 2.5 to 4.3 mm in length and produce eggs that are deposited in water and ingested by fish, in which they develop into infective larvae. Humans are infected by eating undercooked freshwater or brackish-water fish. In humans, the parasite has the capacity to autoinfect; female worms produce

eggs that hatch into larvae that reinvade the intestinal mucosa, resulting in prolonged infection, so that the original source and time of infection Fig. 8.9.5.6 Third-stage larva of *Anisakis simplex*, showing the tip of the boring tooth (arrow) ($\times 400$).

section 8 Infectious diseases 1510 may be forgotten. Autoinfection can result in extremely heavy worm loads, especially in immunocompromised patients. The parasite is endemic in parts of South-East Asia, especially the Philippines and Thailand, and has more recently been found in Egypt. Infection is prevented by properly cooking fish. Intestinal capillariasis can be a severe and even fatal disease. Patients often present with abdominal pain, diarrhoea, and bor- borygmi. As the worm load increases, diarrhoea becomes more severe, with anorexia, nausea, and vomiting. Prolonged diarrhoea leads to cachexia. There might also be signs of hypotension and cardiac failure. The mortality rate in untreated cases approaches 20%. The diagnosis is made by finding eggs in the faeces, 36– 45 μm in length by 19–21 μm in breadth (Fig. 8.9.5.7), which can superficially resemble those of *Trichuris trichiura*. Larvae or adult worms may also be present and repeated stool examination may be required in some cases. The parasite might also be found in jejunal aspirate or biopsy. The treatment of choice is albendazole for 10 days. If it is not available, the alternative is mebendazole for 21 days. Stools should be re-examined to ensure the eradication of infection; if not, the course of treatment should be repeated. Supportive measures to overcome malnutrition and diarrhoea are required in severely ill patients. Hepatic capillariasis The adults of *C. hepatica* measure 52–104 mm in length and live in the liver of various mammals, especially rats. Eggs are produced that are retained in the liver parenchyma; they measure 28 $\times$ 48 to 36 $\times$ 66 μm , and have bipolar plugs. The ova eventually reach the soil, either by decomposition of a carcass, or when the host is eaten by another animal and the eggs pass through the gut of that animal and are deposited in the faeces. Eggs embryonate in the soil and can survive there for more than a year. Infective eggs are ingested by another definitive host, then hatch and the larvae reach the liver via the portal system. Human infection with *C. hepatica* occurs when eggs in the soil are accidentally swallowed, but human infection is rare and is usually a dead end for the parasite. Clinical features may resemble those of visceral larva migrans, with tender hepatomegaly, fever, and eosinophilia. The diagnosis is made by identifying the parasite or eggs in a liver biopsy (Fig. 8.9.5.8). The most effective treatment is unclear, although cases have been reported to respond to albendazole which is given as described for intestinal capillariasis.

Enterobiasis (threadworm infection) Life cycle Enterobiasis is an infection caused by the threadworm or pinworm, *Enterobius vermicularis*. Infection is acquired by the ingestion of eggs (Fig. 8.9.5.9). Larvae hatch in the upper intestine and migrate to the region of the caecum, where they mature and copulate. Worms do not invade the tissues. About 1 month after infection, the white thread-like gravid female worms, about 10–13 mm long by 0.3–0.5 mm in diameter, move down the bowel and pass out of the anus at night (Fig. 8.9.5.10). Each worm deposits approximately 10 000 eggs on the perianal skin. The worms then usually die, but sometimes migrate elsewhere, for example, into the vagina. The eggs are infective within a few hours of deposition. Epidemiology and control This worm is found worldwide and is extremely common, being found most frequently in children. Infections are commonly

Fig. 8.9.5.7 Capillaria philippinensis egg ($\times 1400$). Fig. 8.9.5.8 Capillaria hepatica eggs in the liver ($\times 250$). Ingested Embryonated egg (infective stage) HUMANS Penetrates and develops in mucosa Larva hatches in intestine Gravid migrates to perianal region Egg on perianal skin (diagnostic stage) EXTERNAL ENVIRONMENT Fig. 8.9.5.9 Life cycle of *Enterobius vermicularis*.

8.9.5 Gut and tissue nematode infections acquired by ingestion 1511 clustered in families and institutions. Humans are the only reservoir of infection. Eggs can remain viable for up to 3 weeks, and can be transmitted via contaminated clothing, bedding, and dust. Resistance to reinfection does not develop and autoinfection may occur by contamination of the fingers. Clinical features Most infected people are asymptomatic. The most common presenting symptom is pruritus ani. This can be very troublesome and occurs more often during the night, causing restless sleep, especially in children. Persistent itching may lead to inflammation and secondary bacterial infection of the perianal region. Occasionally, adult worms migrate to aberrant sites such as the urethra. In females they may enter the genital tract, causing vulvovaginitis or rarely salpingitis. *E. vermicularis* is sometimes found lodged in the lumen of the appendix (Fig. 8.9.5.11), but whether or not this causes appendicitis is controversial. Diagnosis The eggs are not usually found in the faeces. They are most easily found around the anus first thing in the morning by using cellulose adhesive tape applied with the sticky side against the perianal skin, which is then examined under the microscope; they are $33 \times 55 \mu\text{m}$ in size and flattened on one side (Fig. 8.9.5.12). Sometimes intact worms are passed in the faeces and can easily be recognized by their size and shape. Treatment All the children and adults in a household should be treated at the same time. Several drugs are available, including mebendazole 100 mg in a single dose, repeated after 2 weeks; albendazole 400 mg in a single dose, repeated after 2 weeks; and pyrantel pamoate 11 mg/kg to a maximum dose of 1 g in a single dose, repeated after 2 weeks. Adult threadworm live for no longer than about 6 weeks, so recurrent threadworm infestation is the result of reinfection. Therefore, attention to personal hygiene is an important part of treatment and prevention. The patient should be advised to keep fingernails short; wash hands with soap and water after defaecating and before preparing food; wear close fitting underwear in bed and change it every morning; shower or bath in the morning. The bed linen, mattress cover, soft toys, and towels should be washed at first diagnosis and at least weekly for six weeks thereafter. Over the same time period the bedroom, including the mattress, should be vacuum cleaned and the bathroom and kitchen damp-dusted. Some individuals, often only one member of a household, suffer regular recurrences which can prove very distressing. There is no *in vivo* or *in vitro* assay for anthelmintic drug resistance to this parasite, so it is not possible to assess the potential contribution of drug resistance to this condition. Such cases require management in a parasitology clinic as they might need more intensive treatment regimens under expert supervision. Gnathostomiasis Life cycle There are 12 species of *Gnathostoma*, but only four are known to infect humans: *G. spinigerum*, *G. hispidum*, *G. doloresi* and *G. nipponicum*. Most human cases are due to *G. spinigerum* or *G. hispidum*. Fig. 8.9.5.10 Adult *Enterobius vermicularis* (scale in mm). Copyright Viqar Zaman. Fig. 8.9.5.11 Histological section of *Enterobius vermicularis* in the lumen of the appendix ($\times 250$). Fig. 8.9.5.12 *Enterobius vermicularis* egg.

section 8 Infectious diseases 1512 *G. hispidum* (Fig. 8.9.5.13). *Gnathostoma* does not mature to the adult form in human infections. Its larvae are up to 12.5 mm long and 1.2 mm wide and have a cephalic bulb armed with rows of hooks (see Fig. 8.9.5.14). These enable the larva to move readily through human tissue and inflict substantial damage, especially if nervous tissue is involved. Epidemiology and control Humans are accidental hosts and become infected with the third stage larva after eating raw or undercooked freshwater fish or other intermediate hosts (e.g. snakes, frogs, and chickens, and possibly via ingestion of infected copepods). Given the large variety and wide distribution of its intermediate hosts, it is not possible to eradicate *Gnathostoma* from the environment, so individual protection is required via thorough cooking plus avoidance of

consuming raw or undercooked freshwater fish. Freezing to minus 20°C for 2 to 5 days is also effective. The common practice of marinating fresh fish in lime juice is not effective. Clinical features Cutaneous disease—Gnathostomiasis can present as migratory cutaneous swellings (nodular migratory panniculitis). Visceral disease—Gnathostoma can produce a wide range of presentations, including pleuritic chest pain, pleural effusion, pneumothorax; ocular disease with uveitis, intraocular haemorrhage, or retinal detachment; central nervous system involvement with radiculomyeloencephalitis, eosinophilic meningitis, or subarachnoid haemorrhage.

= Infective Stage = Diagnostic Stage L3 Gnathostomiasis Cutaneous Ocular Visceral Neurological
 Gnathostoma spinigerum Domestic and wild felines and canines are the definitive hosts
 Gnathostoma hispidum Domestic and wild pigs are the definitive host. Unembryonated egg
 Embryonated egg in water. Infected second intermediate host ingested by definitive host. Second intermediate host Paratenic host L2 develops into L3. Copepod first intermediate host L1 develops into L2. Egg hatches and releases L1 larva. 2 1 5 6 4 3 7 L2 L3 L1 L3 develop into adult worms. L3 i i i d d
 Fig. 8.9.5.13 Life cycle of Gnathostoma spinigerum and Gnathostoma hispidum. Courtesy of CDC. Fig. 8.9.5.14 Cephalic bulb of a Gnathostoma larva showing characteristic rows of hooks. Courtesy of P. L. Chiodini.

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Diagnosis Clinical suspicion in cases of eosinophilia, migratory lesions, and exposure history. Occasionally a larva is extruded from the skin spontaneously or removed intact from the eye by an ophthalmologist and its very characteristic morphology then makes diagnosis straightforward. Serology by Western blot is available in specialist centres. Treatment Albendazole 400 mg twice daily for 21 days or ivermectin 200 micrograms per kilogram daily for two days. Repeat courses may be required. Surgical removal is required for ocular lesions.

Toxocariasis Toxocariasis in humans occurs in two clinical forms, visceral larva migrans and ocular larva migrans, and is caused mainly by the migrating larvae of *Toxocara canis*, to a lesser extent *T. cati* and rarely other nematodes. *T. canis* and *T. cati* are parasites that live in the intestines of dogs and cats, which pass eggs in the faeces. Humans, usually young children, become infected by inadvertently ingesting embryonated eggs in the soil. The larvae hatch in the small intestine and migrate to various organs of the body, including the liver, lungs, eyes, and brain. The larvae, which are about 15–20 µm in length, do not mature in humans, but granulomas eventually develop around them (Fig. 8.9.5.15). In a fully formed granuloma the larvae are surrounded by layers of fibrous tissue and inflammation subsides (Fig. 8.9.5.16). Eggs are never seen in human faeces. *Toxocara* infection occurs wherever there are large domestic dog and cat populations in close association with humans and is more common in children. Deworming dogs and stopping children from eating dirt (pica) especially when playing in areas frequented by dogs, are important control measures.

Visceral larva migrans This disease is most often seen in young children, because of pica. Most people remain asymptomatic. In a minority, symptoms consist of muscular pain, lassitude, anorexia, cough, itching, and urticarial rashes. Physical signs might include wheezing and hepatomegaly. Occasionally there is splenomegaly, lymphadenopathy, and skin lesions. Central nervous system involvement can result in convulsions. The acute phase generally lasts for 2–3 weeks, followed by recovery. Sometimes the resolution of all the signs can take up to 18 months. Rarely, the infection ends fatally if a massive number of eggs has been ingested. The hallmark of visceral larva migrans is marked eosinophilia, which can reach a level of 75%. Serological tests for *toxocara* antibody can be helpful; a negative test can rule out the diagnosis, but positive titres are often found in normal individuals. The definitive diagnosis is by finding larvae on biopsy, usually of the liver, but is

seldom indicated. Most patients recover spontaneously; the larvae cannot multiply and eventually die. There is no proven therapy. Anthelmintics, including mebendazole, albendazole, and diethylcarbamazine have been tried, but may be ineffective or precipitate an inflammatory reaction. Corticosteroids and non-steroidal anti-inflammatory agents have been suggested in order to suppress inflammation.

Ocular larva migrans This condition is caused by granuloma formation around a larva in the eye and is most commonly seen in older children. If it is near the macula, impairment of vision or even blindness may result. A rounded swelling, often near the optic disc, might be detected on fundoscopy. The features of visceral larva migrans are usually lacking in ocular larva migrans cases. There is usually no marked peripheral eosinophilia. Diagnosis depends upon positive serology with consistent fundoscopic features; the major differential diagnosis is retinoblastoma. Antibody tests on vitreous or aqueous fluid can be positive when serum antibody tests are negative. Western blot is the assay of choice for use on aqueous or vitreous fluid. Anthelmintic therapy is not routinely given. Visible larvae can be photocoagulated by laser. Vitrectomy has been used in some cases and local and intraocular steroids are used to suppress inflammation.

Fig. 8.9.5.16 Histological section. Granuloma formation in the same animal as Fig. 8.9.5.15 at a later stage when the larva is completely surrounded by fibroblasts ($\times 400$).

Fig. 8.9.5.15 Histological section. Granuloma formation in a monkey experimentally infected with *Toxocara canis*, showing many giant cells and some fibroblastic reaction. The arrow marks the larva ($\times 400$).

section 8 Infectious diseases 1514 Trichinosis (trichinellosis)

Life cycle Trichinosis is an infection usually caused by *Trichinella spiralis* and related species. Humans become infected by eating undercooked meat, usually pork or pork products from domestic and wild pigs (boars) (Fig. 8.9.5.17). After ingestion the larvae are liberated in the stomach, then pass into the small bowel, where they invade the columnar epithelium and develop into adult worms living in the cytoplasm of a row of enterocytes. Male trichinellae are about 1.5×0.05 mm in size and female worms measure 3.5×0.06 mm. Over 2 to 3 weeks or so before they are expelled, female worms release about 500 newborn larvae (Fig. 8.9.5.18), which enter the bloodstream and seed the skeletal muscles. Over the next few weeks the larvae in the muscles increase in size, moult, coil, usually develop a cyst wall and become capable of infecting a new host (Fig. 8.9.5.19); they may remain viable in muscle for several years.

Epidemiology and control *Trichinella* species are widely distributed in many geographical areas among many carnivorous hosts found in three classes of vertebrates: mammals, birds and reptiles (Table 8.9.5.1). Domestic pigs become infected by eating infected scrap from abattoirs or farms. Humans are incidental hosts and are usually infected with *T. spiralis*, but occasionally other species, depending upon the animal eaten. Infection is best prevented by properly cooking meat.

Clinical features Most people with light infections are asymptomatic. In heavy infections, diarrhoea develops in the first week and is associated with abdominal discomfort and vomiting. Fulminating enteritis may develop in patients with extremely heavy infections. Symptoms of larval invasion develop during the second week, and include fever, myositis with pain, swelling, and weakness, usually first involving the extraocular muscles, then the masseters, neck muscles, limb flexors, and lumbar muscles. Some patients may develop one or more

HUMANS Larva in mucosa
Circulation SWINE, OTHER CARNIVORES Adults in small intestine
 Larva released in small intestine
 Encysted larva (infective stage)
 Encysted larva (diagnostic stage)
 Larva deposited in mucosa
 Encysted larva in muscle (diagnostic stage)
 Larva released in small intestine
MEAT (Pork, wild boar, bear) Adults in small intestine

Fig. 8.9.5.17 Life cycle of *Trichinella spiralis*. **Fig. 8.9.5.18** In vitro preparation of infected mouse small bowel, showing adult worms of

Trichinella spiralis surrounded by newborn larvae. Courtesy of D. I. Grove. Fig. 8.9.5.19 *Trichinella spiralis* third-stage larvae in human muscle (×100). Table 8.9.5.1 Major *Trichinella* spp. and their epidemiology

Species	Code	Distribution	Most common hosts
<i>T. spiralis</i>	T1	Worldwide except Australasia	Pig, horse, bear, rodent, fox
<i>T. nativa</i>	T2	Arctic, subarctic	Bear, fox, dog
<i>T. britovi</i>	T3	Temperate, subarctic	Dog, bear, cat, boar
<i>T. pseudospiralis</i>	T4	Cosmopolitan	Bird
<i>T. murrelli</i>	T5	North America	Bear, coyote, dog
<i>T. nelsoni</i>	T6	Subarctic	Bear
<i>T. subzanzibarica</i>	T7	Sub-Saharan Africa	Hyena, cat
<i>T. zimbabwensis</i>	T8	Southern Africa	Lion, panther
<i>T. papuae</i>	T9	Papua New Guinea	Pig, crocodile
<i>T. zimbabwensis</i>	T10	Central Africa	Crocodile, mammals
<i>T. argentine</i>	T11	Argentina	Cougars

8.9.5 Gut and tissue nematode infections acquired by ingestion 1515 of cough, dyspnoea, headache, periorbital oedema, subconjunctival haemorrhages, and a petechial rash. These symptoms slowly subside over several weeks, although symptoms persist longer in a minority of patients. In fulminant infections a potentially fatal myocarditis or meningoencephalitis might develop. **Diagnosis** The diagnosis is suggested by a combination of fever, periorbital oedema, myositis, and eosinophilia in a patient who gives a history of eating undercooked meat, often in the context of an outbreak. Elevated creatine kinase and lactate dehydrogenase levels indicate considerable muscle involvement. Serological tests become positive several weeks after infection. A definitive diagnosis depends upon finding larvae in muscle biopsies, although this is usually unnecessary. **Treatment and prevention** If the diagnosis is made early in the illness, treatment with albendazole or mebendazole for 14 days is given to kill adult worms in the bowel and thus reduce the load of larvae able to invade the muscles. In established infections these benzimidazole agents can also be used, but usually have little influence on the course of the disease. In established symptomatic infections the mainstays of treatment are rest and the administration of corticosteroids, especially in severe cases. Mortality rates as high as 5% have been reported with very heavy parasite loads. Trichinosis in the pig population can be greatly reduced or eliminated by hygienic rearing methods. Larvae in pork may be killed by freezing at -18 °C for 1 week. Whether or not that is done, thorough cooking of pork is the best safeguard against infection in all endemic areas.

Trichuriasis (whipworm infection) Life cycle Trichuriasis is an infection caused by *Trichuris trichiura*. Infection is acquired when an egg is ingested (Fig. 8.9.5.20). The infective larva hatches in the small intestine and enters the mucosal crypts of the caecum, where it moults several times to become an adult worm 30–50 mm long. The anterior three-fifths of the worm are thin and elongated, and the posterior two-fifths bulbous and fleshy. The thin end is embedded in a syncytial tunnel in the large bowel epithelium (Fig. 8.9.5.21). Nearly 3 months after infection the fertilized female worms begin to produce about 10 000 eggs per day. Adult worms live for 1 to 3 years. After passage in the faeces, eggs embryonate in the soil and become infective after several weeks.

Epidemiology and control Trichuriasis has a worldwide distribution, particularly in the warmer parts and is most common in areas where sanitation is poor, especially where human faeces are used as fertilizer in vegetable gardens. Environmental sanitation is the best control measure. Ground-growing fruits and vegetables should be carefully washed. **Clinical features** Most infections are light and asymptomatic. In heavy infections there is colitis and/or proctitis, with the passage of blood and mucus in the faeces. In some cases, prolapse of the oedematous parasitized rectum occurs. Chronic heavy infection can be associated with iron-deficiency anaemia and growth retardation. **Diagnosis** This is based on finding characteristically barrel-shaped eggs 50 × 20 µm in size (Fig. 8.9.5.22) in the faeces. Sigmoidoscopy, proctoscopy, or colonoscopy may show worms attached to the mucous membrane and sometimes intact worms may be passed in the faeces. **Treatment** Benzimidazole anthelmintics (mebendazole or albendazole) are effective when given

for between 3 and 5 days, depending upon the severity of infection. Repeat courses may be required. Ivermectin is an alternative if benzimidazoles cannot be used. EXTERNAL ENVIRONMENT HUMANS Embryonated egg (infective stage) Eggs in faeces (diagnostic stage) Penetrate and develops in mucosa Adults in large intestine Two cell stage Advanced cleavage Larva hatches in intestine Fig. 8.9.5.20 Life cycle of *Trichuris trichiura*. Fig. 8.9.5.21 Histological section. Anterior end of an adult *Trichuris trichiura* embedded superficially in the large bowel mucosa ($\times 250$).

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