8.9.6 Angiostrongyliasis 1516

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section 8 Infectious diseases 1516 Uncommon intestinal or tissue nematode infections From time to time a patient may be encountered who harbours an un- usual nematode. Some of these organisms are free-living parasites and the patient has a spurious infection, usually as the result of ingesting the worm, or following the in vitro contamination of a clinical spe- cimen such as faeces or urine. Other individuals may have true infec- tions, with worms being found in either the gastrointestinal tract or the tissues. Many of these infections are with parasites that are poorly adapted to the human host and are unable to complete their devel- opment in humans. Thus, worms in varying stages of development, including larvae, adults, and eggs, may be found in clinical specimens. If there is uncertainty in identifying the worm, help may often be obtained from a veterinary parasitologist, who might be more used to dealing with the species concerned. Sometimes parasites are seen only in histological sections and should be reviewed by a tropical histo- pathologist. The texts by Connor et al.; Gutierrez; and Orihel and Ash provide helpful aids to histopathological identification. FURTHER READING Connor DH, et al. (eds) (1997). Pathology of infectious diseases, Vol. 2, pp. 1305–588. Appleton and Lange, Stamford, CT. Cooper AJ, Hollingsworth TD (2018). The impact of seasonality on the dynamics and control of Ascaris lumbricoides. J Theor Biol, 453, 96–107. Cross JH (1992). Intestinal capillariasis. Clin Microbiol Rev, 5, 120–9. Fuehrer HP, et al. (2011). Capillaria hepatica in man—an overview of hepatic capillariosis and spurious infections. Parasitol Res, 109, 969–79. Gottstein B, et al. (2009). Epidemiology, diagnosis, treatment, and con- trol of trichinellosis. Clin Microbiol Rev, 22, 127–45. Gutierrez Y (2000). Diagnostic pathology of parasitic infections with clinical correlations, 2nd edition. Oxford University Press, Oxford. Herman JS, Chiodini PL (2009). Gnathostomiasis, another emerging imported disease. Clin Microbiol Rev, 22, 484–92. Knopp S, et al. (2012) Nematode infections: soil-transmitted hel- minths and trichinella. Infect Dis Clin North Am, 26, 341–58. Kocięcki J, Kocięcka W, Dmitriew A (2016). Toxocarosis of the organ of sight—the complex pathological and diagnostic problem. Acta Parasitol, 61, 1–9. Leles D, et al. (2012). Are Ascaris lumbricoides and Ascaris suum a single species? Parasit Vectors, 5, 42. Lu LH, et al. (2006). Human intestinal capillariasis (Capillaria philip pinensis) in Taiwan. Am J Trop Med Hyg, 74, 810–13. Luna J, et al. (2018). Updated evidence of the association between toxocariasis and epilepsy: Systematic review and meta-analysis. PLoS

Negl Trop Dis, 12, e0006665. Ojha SC, et al. (2014). Geohelminths: public health significance. J Infect Dev Ctries, 8, 5–16. Orihel TC, Ash LR (1995). Parasites in human tissues. American Society of Clinical Pathologists, Chicago, IL. Shimamura Y, et al. (2016). Common symptoms from an uncommon infection: gastrointestinal anisakiasis. Can J Gastroenterol Hepatol, 2016, 5176502. Wani I, et al. (2010). Intestinal ascariasis in children. World J Surg, 34, 963–8. Woodhall DM, Fiore AE (2014). Toxocariasis: a review for pediatri- cians. J Pediatric Infect Dis Soc, 3, 154–9. World Health Organization (WHO) (2006). Preventive chemotherapy in human helminthiasis. World Health Organization, Geneva. Websites Photographs of the various stages of these parasites and diagrams of their life cycles, may be found at several useful websites: Centers for Disease Control and Prevention. Laboratory investigation of parasites of public health concern. http://www.dpd.cdc.gov/DPDx/ Korean Society for Parasitology. Web atlas of medical parasitology. http://www.atlas.or.kr UK NEQAS Parasitology. http://www.ukneqasmicro.org.uk/parasitology/ 8.9.6 Angiostrongyliasis Richard Knight ESSENTIALS Angiostrongylus cantonensis The rat lungworm causes outbreaks of eosinophilic meningitis pre- dominantly in Southeast Asia, East Asia, Oceania, and the Caribbean. Elsewhere the condition is usually seen in travellers. Human infec- tions follow ingestion of raw snails (the primary intermediate hosts), food contaminated by snail mucus, or one of several paratenic hosts. Clinical manifestations include headache, meningism, vomiting, cranial nerve lesions, and (less commonly) other neurological fea- tures such as seizures. Ocular lesions are quite common. Diagnosis is made by lumbar puncture revealing eosinophilic meningitis, with larval or immature adult worms sometimes seen. Treatment is usu- ally with prednisolone alone, or with albendazole and prednisolone. Mortality is usually below 2%. Prevention is by avoidance of raw high-risk dietary items and unwashed salads. Fig. 8.9.5.22 Egg of Trichuris trichiura. Courtesy of A R Butcher.

8.9.6 Angiostrongyliasis 1517 Angiostrongylus costaricensis The cotton rat is the principal reservoir host. Unwitting ingestion of slugs, the intermediate hosts, in salads or fruit leads to human infections in tropical American countries, especially in Costa Rica, Nicaragua, Guatemala, and Honduras. The organism causes granulomatous le- sions of the right colon and sometimes the liver: most patients present with right-sided or right iliac fossa pain, with tenderness and some- times a palpable mass. Diagnosis is usually made histologically on resected material. Surgery may be necessary, but the value of anthel- minthics is uncertain. Preventive measures include washing and careful inspection of vegetables, and hand washing before meals by children and those preparing salads. Introduction Human disease is caused by two nematode species of the genus Angiostrongylus. Both parasites normally infect rodents, and mol- luscs are the primary intermediate hosts. Angiostrongylid worms with rodent hosts were placed in the genus Parastrongylus in 1986 but this name is no longer used. Infection follows accidental or de- liberate ingestion of molluscs or paratenic hosts. The epidemiology is complex because of multiple potential routes of transmission. Angiostrongylus cantonensis This is the rat lungworm and was first described in 1935 from China. The first known human case, reported in 1944, was a 15-year-old Taiwanese boy with meningoencephalitis, in whose cerebrospinal fluid an immature adult worm was found. Detailed clinicopathological studies were made in 1962 during epidemics of eosinophilic menin- gitis in Tahiti. Aetiology: The biology of the parasite Adult worms live in the pulmonary arteries of rats; larvae from hatched eggs ascend the airways, are swallowed, and so reach the faeces. Molluscs ingest these larvae, and after two moults they are infective when eaten by a rodent. In the rat, infective larval worms migrate to the cerebral grey matter, where they start to mature. They then move to the meninges and enter the venous sinuses, thereby reaching the

pulmonary arteries, where maturation is completed. Infective larvae from a mollusc can also enter, by ingestion, a second or third inter- mediate host, in which they undergo no further development until they enter a mammalian host. Such supernumerary hosts are termed paratenic hosts, and are important sources of infection in humans. Development in humans reaches the immature adult stage, measuring 11 to 15 mm in length. Nearly all will die in the superfi- cial cortex, brainstem, meninges, and occasionally the eye, causing vigorous tissue reactions; very few reach the lungs. Epidemiology The parasite is endemic and causes human outbreaks in Southeast Asia, East Asia, Oceania, and the Caribbean. Sporadic cases are reported in many other countries, usually in travellers. Most recent outbreaks have been in mainland China, Taiwan, Thailand, and Japan. In the Pacific epidemics have occurred in Hawaii, Samoa, and the Solomon Islands. In the Caribbean most cases are reported from Cuba, Costa Rica, and Jamaica; it has also been reported from Ecuador, Brazil, Egypt, and South Africa. It is now present, at least in rats, in several African and tropical American countries including southern USA. All ages can be affected, and outbreaks have occurred after weddings and feasts; infections are often seasonal. The modes of transmission differ geographically, by age and social group, and with time. The principal rodent hosts are Rattus rattus, R. norvegicus, R. alex andrinus, and R. exulans. The prevalence in rats in endemic areas may be 40% or more. The geographical spread and population increase of these peridomestic rodents has increased the zoonotic reservoir; wildlife is now infected in the southern United States of America. Another factor leading to the increase in human infection has been the dispersal by human agency of the edible giant African land snail Lissachatina fulica, from Madagascar in 1800, eastwards across the Indian Ocean and the Pacific, to reach Hawaii in 1936. The freshwater golden apple snail Pomacea canaliculata, which is highly susceptible to the parasite, was recently introduced into Asia, where it has colon- ized paddy fields and caused disease when served raw in restaurants in China, Taiwan, and Japan. The popularity of heliculture, the cultiva- tion of exotic snails for food, and keeping them as pets, facilitates the spread of the parasite. Raw snails are eaten as a delicacy and for me- dicinal purposes; salads may contain small undetected molluscs, their slime trails, or planarians. During food preparation infected mucus from snails may reach the mouth directly or contaminate other foods or water. An outbreak in Taiwan followed the drinking of raw vege- table juice. In Thailand, Pila spp. snails are a seasonal delicacy eaten by all the family, but only young men take them raw with alcohol. Paratenic hosts include freshwater prawns, land and coconut crabs, frogs, and land planarians, which cause infection if eaten raw; drinking-water may contain tiny immature prawns, especially after heavy rains. In Thailand, the yellow tree monitor lizard is an important paratenic host. In the Ryukyu Islands of Japan, patients are usually in- fected by eating raw snails or toad liver for medicinal purposes. Pathology Inflammatory granulomatous lesions, sometimes track-like, occur predominantly in the cortical grey matter and the meninges, but also in the brain stem and cerebellum; nerve roots and the spinal cord may also be affected. Live worms are occasionally found at autopsy, and dead worms are found in many lesions. The number of worms found varies greatly, and may reach several hundred; worm tracks in the tissue and meninges are surrounded by a cuff of eosinophils; Charcot– Leyden crystals derived from eosinophils are numerous. Rarely, adult worms have been found in human lung at autopsy. Ocular infection derives from worms that have migrated across the cribriform plate. Clinical features Illness severity depends mainly on the number of larvae ingested. After an incubation period of 1 to 4 weeks the onset is acute, with headache (intermittent at first), together with nausea and vomiting. There is constitutional upset and frequently menigism; fever is un- usual. The illness is often self-limiting over a period of 4 weeks. Cranial nerve lesions are seen in the optic, abducens, and facial nerves. Less common are seizures, confusion, and radiculopathy

(with paraesthesia, root pains, or weakness). Long-tract signs and impaired consciousness are uncommon, except in severe cases, but spinal cord damage can cause sphincter disturbance.

section 8 Infectious diseases 1518 Fig. 8.9.6.1 Angiostrongylus under the conjunctiva in a Thai girl with a left facial nerve palsy. Copyright D. A. Warrell. Ocular complications include retinitis, retinal haemorrhages, optic neuritis, and larval worms in the vitreous, anterior chamber, or beneath the conjunctiva Fig. 8.9.6.1). Rarely, migration to the lungs produces clinical evidence of pneumonitis. Numerous eosinophils occur in the cerebrospinal fluid, and there is blood eosinophilia. Diagnosis Lumbar puncture reveals high opening pressure, with a clear or lightly turbid cerebrospinal fluid containing 500–2000 cells/mm3 (of which 10–>90% are eosinophils). Protein levels are usually elevated with normal or, less commonly, reduced glucose. Detailed examination at low power reveals larval or immature adult worms in up to 25% of cases, measuring 5–15 mm in length. Cerebrospinal fluid changes may persist for up to 3 months. CT or MRI may reveal focal cortical abnormalities. Serology using antigens from fourth-stage larvae is useful, but cross-reactions with other nematodes can cause difficulty. Commercial serological tests are not yet available. Techniques to de- tect worm antigens in cerebrospinal fluid and serum have also been developed. Parasite DNA can also be detected by PCR. Differential diagnosis is from other helminth infections affecting the nervous system, as eosinophils are otherwise rare in cerebro- spinal fluid. A detailed geographical and dietary history is essential. Conditions to be considered include paragonimiasis, schistosom- iasis, and neurocysticercosis. A particular problem in Thailand is confusion with Gnathostoma spinigerum, which more commonly causes long-tract signs, bloody or xanthochromic cerebrospinal fluid, neck stiffness, and clouding of consciousness. Treatment, prognosis, and control In a recent prospective trial prednisolone alone was as effective as prednisolone plus albendazole. Prednisolone alone for 14 days is now often the recommended treatment, although prednisolone plus albendazole is still used in many centres using albendazole 15 mg/kg daily in divided doses. Treatment hastens recovery and relieves headache and it probably improves the prognosis in severe cases. Repeated lumber puncture has also been used to relieve head- ache. Ocular disease may require laser therapy and larvae in the eye chambers should be removed surgically. Anthelminthics should be avoided in eye involvement. Mortality rates are generally low in uncomplicated cases, but some patients develop encephalitis and pass into coma after about 2 weeks, and their prognosis is then very poor. Most patients improve in 2 to 4 weeks, but focal neurological deficits can persist for longer. Partial relapse after 2 months of illness may represent a reaction to dying worms. Some cases are relatively mild and can be discharged within a few days; during epidemics, mild cases may need only outpatient care. Control measures include health education to limit the inges- tion of raw high-risk dietary items and unwashed salads. Warnings may be necessary regarding raw molluscs, amphibians, and reptiles used for medicinal purposes. Rodents in vegetable gardens and the peridomestic environment should be controlled. Angiostrongylus costaricensis This was first recognized in Costa Rica in 1950 in surgical specimens simulating bowel malignancy. The parasite was described from such specimens in 1967, and the complete life cycle in rodents was eluci- dated over the next 3 years. Aetiology: the biology of the parasite In both the rodent and human hosts, the worms are located in the ileocaecal mesenteric arteries. The cotton rat Sigmodon hispidus is the principal reservoir host, but other species of rodent (including the coatimundi) are also involved, and even dogs and marmosets. In the rodent hosts worm eggs embolize to gut-wall capillaries, and the hatched larvae pass into the gut lumen. Veronicellid slugs, es- pecially Vaginulus plebeius, eat rodent faeces containing larvae, and these develop into infective larvae in the fibromuscular tissue of the mollusc after two moults over a

period of 18 days. Infective larvae can persist in the slug for several months or be shed in slime trails. The prepatent period in rats eating infected slugs is 24 days. In human infections the worms reach maturity, but the embryon- ated eggs do not hatch. Epidemiology Infections occur especially in Costa Rica, Nicaragua, Guatemala, and Honduras, but also sporadically elsewhere in the Americas from the United States of America to Argentina, and some Caribbean islands. Recently, infections have been increasingly recognized from southern Brazil. Small veronicellid slugs are the source of infection in man; infection rates in intermediate hosts can reach 85%. Small or chopped slugs may be unnoticed on fallen fruits or in salads; the mucus of their slime trails also contains infective larvae. Many cases are in schoolchildren, but infants and older persons are also affected. Seropositivity in endemic areas suggests that there are unrecognized infections. Pathology and clinical features Lesions primarily affect the small arteries, producing subacute or chronic granulomatous inflammatory masses in the wall of the

8.9.6 Angiostrongyliasis 1519 caecum, right colon, and less often the small intestine or elsewhere in the colon. Rarely, the predominant feature is ischaemic infarction. The finding of an adult nematode measuring 18 to 42 mm in length within a gut arterial vessel is diagnostic of infection; eggs may be seen in vessels or in tissue, where they are surrounded by eosinophil granulomas. Lesions also occur in regional abdominal lymph nodes or the omentum. Some larvae enter the hepatic artery and cause granulomatous or necrotic lesions in the liver; others enter testicular arteries causing similar lesions of the testis. In a recently reported case an adult worm was shown histologically within a hepatic arteriole. Clinically, most patients present with right-sided or right iliac fossa pain, with tenderness and sometimes a palpable mass in this region. Other features are eosinophilia, fever, diarrhoea, or rectal bleeding. Tender hepatomegaly with high blood eosinophilia occurs in some patients. Serious complications are bowel obstruction and perforation, and rarely testicular infarction. Diagnosis and treatment The confirmation of diagnosis is usually made histologically on re- sected material, PCR can be used to detect parasite antigen. The condition can mimic appendicitis, bowel neoplasm, Meckel’s di- verticulitis, testicular torsion, or other surgical problems. Parasite eggs are not found in faeces, but serology using enzyme-linked im- munosorbent assay (ELISA) or latex agglutination is useful. More recently indirect immunofluorescence using an egg antigen has given good specificity. Serology suggests that subclinical infections may be common. Contrast radiology reveals filling defects and al- tered motility of the terminal ileum, caecum, or ascending colon. Laparoscopy can reveal the bowel and hepatic lesions; biopsy may then be diagnostic. The value of anthelmintic treatment remains unproven; thiaben- dazole or high doses of mebendazole have been used. Surgery is often necessary, but can sometimes be deferred in uncomplicated cases when the diagnosis is strongly suspected, as spontaneous re- mission is common. Preventive measures include washing and careful inspection of vegetables, and hand washing before meals by children and those preparing salads. Rinsing salads in 1.5% bleach kills larvae. FURTHER READING Angiostrongylus cantonensis Cowie RH (2013). Biology, systematics, life cycle, and distribution of Angiostrongylus cantonensis, the cause of rat lungworm disease. Hawaii J Med Public Health, 72 (6 Suppl 2), 6–9. Cowie RH (2013). Pathways for transmission of angiostrongyliasis and the risk of disease associated with them. Hawai J Med Public Health, 72, (6 Suppl 2), 70–4. Cowie RH, et al. (2012). Workshop on research priorities for manage- ment and treatment of angiostrongyliasis. Emerg Infect Dis, 18, e3. Damien KY Ming, et al. (2017). Angiostrongylus cantonensis DNA in cerebrospinal fluid in persons with eosinophil meningitis. Laos Emerg Inf Dis, 23, 2112–13. Eamsobhana P (2014). Eosinophilic meningitis caused by Angiostrongylus cantonensis – a neglected disease with escalating importance. Trop Pubmed, 31, 569–78. Evans-Gilbert T, et al. (2014). Severe eosinophilic

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