More about... Parasitic diseases

Taenia and Echinococcus infections in humans

COLIN NIGEL MENEZES, *MD, MMed (Int Med), Dip HIV Mang (SA), DTM&H, FCP (SA)*
Consultant, Infectious Diseases Unit and Themba Lethu Clinic, Department of Internal Medicine, Helen Joseph Hospital, University of the Witwatersrand, Johannesburg

MARTIN PETER GROBUSCH, *MD, MSc, DTM&H*
Professor, Division of Clinical Microbiology and Infectious Diseases, National Health Laboratory Service and School of Pathology, Faculty of Health Sciences, University of the Witwatersrand, Johannesburg

Corresponding author: Colin Menezes (Colin.Menezes@wits.ac.za)

Important human tapeworms include *Taenia solium, T. saginata, T. asiatica, Echinococcus granulosus* and *E. multilocularis*. Their morphology and reproductive powers are the basis for their survival in the intestine.

Taeniasis and cysticercosis

Human cysticercosis may result from the ingestion of the eggs of *Taenia* species, particularly *T. solium*. Gastrointestinal tapeworm infections result from the ingestion of cysticerci in undercooked meat.

Human cysticercosis with *T. solium* is common in central and South America, South East Asia, eastern and southern Africa.[1,2] In South Africa, the Eastern Cape Province has the highest prevalence owing to the common practice of free-range pig farming and improper sanitation facilities.[2]

Damage depends on the site and number of cysticerci that develop.[1] Infection commonly occurs in the brain (neurocysticercosis), causing seizures, hydrocephalus or focal neurological deficits. Damage from cysticercosis is caused by the severe inflammatory response occurring after the death and disruption of the parasite.[1] Muscles, subcutaneous tissues and the eye may also be affected.[1]

Diagnosis is based on serology, using the enzyme-linked immunosorbent assay (ELISA), although the enzyme-linked immunoblot assay performs much better than the ELISA in clinical settings. The presence of eosinophils in the cerebrospinal fluid may also suggest the diagnosis.[1] Plain radiographs of soft tissues demonstrate the oval or elongated cysts if they are wholly or partially calcified. Plain skull films may show cerebral calcifications. Computed tomography imaging may demonstrate calcified and non-calcified cysts, oedema or intracranial hypertension.[1]

Cysticercosis may require surgery for ophthalmic or brain involvement, but chemotherapy should precede surgery when possible. Tissue infection can be treated with albendazole or praziquantel (combined with corticosteroids in the case of extensive disease to reduce the inflammatory response to the dead cysticerci. Steroid use should be considered when treating non-calcified cerebral cysts). Seizures respond well to anti-epileptic drugs.[1]

On the other hand, *T. saginata* is transmitted as cysticerci in partially cooked or raw beef. *T. asiatica* is found in South East Asia, with pigs being the possible intermediate host.[3]

Symptoms are similar for *T. saginata* and *T. asiatica* infections.[3] These include nausea or vomiting, appetite loss, abdominal pain, and weight loss. A disturbing manifestation is the active crawling of the muscular segments out of the anus.[3]

Diagnosis of *Taenia* species can be made by examination of the number of out-pocketing branches of the uterus in the gravid segments, because the eggs are identical.[1] Perianal scraping with adhesive tape is highly sensitive for *T. saginata* but not for *T. solium*. Coproantigen-detection ELISA may be used to identify *Taenia*-specific molecules in faecal samples, demonstrating current infection.[1] Treatment includes the administration of niclosamide or praziquantel.

Echinococcosis

E. granulosus is common in sheep-raising areas of southern South America, southern and central Russia, East Africa, and the western USA.[4] Many South African cases have been described. A history of rural sheep farming should raise concerns about hydatid disease.

Dogs and sheep are the only final hosts in which the adults are found; humans are the dead end in the cycle.[4]

Echinococcosis (hydatid disease) develops when humans ingest eggs that then hatch in the intestine. Larvae develop, penetrating the intestine, disseminating throughout the body, and concentrating mainly in the liver, but also in the lungs, heart, brain, kidneys, and long bones.[4]

Infected patients may be asymptomatic for many years, but pressure effects eventually develop depending on the site of the hydatid, resulting in collapse of infected parts of the long bones, blindness, and seizures. Rupture of a hydatid cyst may result in anaphylaxis.[4]

Isolated hooks in the sputum suggest rupture of a lung cyst. Serological tests include indirect haemagglutination, latex agglutination or an ELISA.[4] Ultrasound, magnetic resonance and computed axial tomography imaging may demonstrate deep-seated lesions and avascular fluid-filled cysts.[4]

Treatment is mainly by surgical resection. Long courses of albendazole or mebendazole have proved effective, although the results are variable. Percutaneous puncture under sonographic guidance, aspiration of cyst fluid, instillation of a protoscolecidal agent such as 95% methanol or cetrimide, and respiration (PAIR), with albendazole treatment to reduce the danger of subsequently renewed disease from spillage, is an alternative to surgical resection in selected patients and is particularly indicated in uncomplicated single hepatic hydatid cysts.

E. multilocularis normally follows a fox-rodent cycle in northern Siberia, China, Japan and North America. The primary cyst usually forms in the liver. Early radiological imaging by ultrasonography, computed tomography, or magnetic resonance is essential. Serological tests with purified *E. multilocularis* antigens are sensitive and highly specific. Treatment includes long-term albendazole, and surgery.[4]

Infection of the immunocompromised host

Cestode infections should be considered as differential diagnoses of co-infections in HIV/AIDS patients.[5] Little information is available on clinical features, treatment, and outcome of patients in South Africa, where a high prevalence of HIV infection and a large immigrant population exist.

Patients with AIDS are expected to have disease that develops rapidly and manifests early, although symptoms vary depending on the organ involved and the degree of immune deficiency. *T. solium* infection in HIV-infected patients commonly manifests as neurocysticercosis, while hydatid disease presents with cystic lesions in the liver and lungs.[5,6]

Careful consideration of drug interactions that may occur with antiretroviral therapy and the likelihood of the immune reconstitution syndrome (IRIS) developing make the management of such patients challenging.[5]

References

1. Garcia H, Gonzalez A, Evans C, *et al. Taenia solium* cysticercosis. *Lancet* 2003; 362: 547-556.
2. Mafojane N, Appleton C, Krecek R, Michael L, Willingham A. The current status of neurocysticercosis in Eastern and Southern Africa. *Acta Trop* 2003; 87: 25-33.
3. Ito A, Nakao M, Wandra T. Human taeniasis and cysticercosis in Asia. *Lancet* 2003; 362: 1918-1920.
4. McManus D, Zhang W, Li J, Bartley P. Echinococcosis. *Lancet* 2003; 362: 1295-1304.
5. Chopdat N, Menezes CN, John MA, Mahomed N, Grobusch MP. A gardener who coughed up blood. *Lancet* 2007; 370(9597): 1520.
6. Serpa J, Moran A, Goodman J, Giordano T, White A. Neurocysticercosis in the HIV era: A case report and review of the literature. *Am J Trop Med Hyg* 2007; 77: 113-117.

Amoebiasis

DOUG WILSON
Department of Internal Medicine, Edendale Hospital, Pietermaritzburg, KwaZulu-Natal
E-mail: wilsond1@ukzn.ac.za

Entamoeba histolytica is an amoebic parasite that is highly adapted to colonise and invade the human colon. Transmission is by the faeco-oral route. The incidence of invasive infection seems to have declined over the past 15 years in South Africa, probably due to increased access to sanitation in rural and informal settlements, and to frequent prescription of metronidazole for nonspecific diarrhoea. However, 19% of children hospitalised in Venda were found to be infected with *E. histolytica*, as were 2% of schoolchildren. The cholera epidemic in Zimbabwe and outbreaks in South African provinces serve as a sharp reminder of the public health consequences of inadequate sewage management – amoebiasis outbreaks may follow a similar pattern.

Parasite-host interactions

The trophozoite of *E. histolytica* is the pathogenic stage in the parasite's life cycle.

Table I. Common features of amoebic dysentery

Feature	Frequency
Gradual onset over <4 weeks	85%
Diarrhoea	100%
Blood and mucus in stool	95%
Abdominal pain	85%
Weight loss	40%
Fever	35%
Positive stool haeme test	100%

Table II. Differential diagnosis of amoebic dysentery

Infective

- Shigella species
- Non-typhoidal salmonella
- Campylobacter species
- Enterotoxigenic *Escherichia coli*
- *Yersinia enterocolitica*
- Pseudomembranous colitis (*Clostridium difficile*)
- Cytomegalovirus colitis (in HIV-positive patients)

Non-infective

- Ulcerative colitis
- Crohn's disease

To achieve transmission trophozoites form cysts in the bowel lumen that are excreted into the environment. The cysts are protected by a chitinous outer cell wall and are able to remain viable in sewage or free-standing water for several weeks. After human ingestion the cyst excysts into the trophozoite in the small intestine and subsequently comes into contact with colonic mucosa. The ability of the parasite to cause disease is determined by a cell membrane surface lectin protein. If the trophozoite lectin binds to mucin glycoproteins overlying the colonic mucosa an asymptomatic infection is likely to occur. In this scenario the infected host excretes cysts for about 18 months until a humoral (antilectin IgA and IgG) and cell-mediated immune response clears the infection. (There are parallels here with the El Tor biotype of *Vibrio cholerae* that can also establish asymptomatic infection.)

Symptomatic infection is likely to result if the parasite passes through the mucin layer and comes into contact with colonic epithelial cells. The lectin protein binds to glycoproteins on the apical cell wall of colonic mucosal cells. This contact triggers the secretion of potent proteolytic enzymes that lyse cells within 20 minutes and break down fibronectin in the extracellular matrix, initiating the formation of characteristic flask-shaped ulcers through the colonic mucosa. Inflammatory cells, including neutrophils, are also lysed. Cell lysis (and apoptosis) is facilitated by the secretion of an ionophore-like protein that condenses into an ion channel (amoebapore) that perforates the membrane of the target cell. Trophozoites feed on dead cells by phagocytosis.

Trophozoites are carried in the portal vein to the liver where hepatocyte lysis occurs, initiating the formation of micro-abscesses that coalesce into amoebic liver abscesses (ALA).

Clinical presentation

Symptomatic infection occurs in about 10% of cases, ranging from episodic diarrhoea over a period of months to fulminant dysentery with blood, mucus and severe fluid and electrolyte losses. Rectocolitis develops over 1 - 3 weeks, and can progress to toxic megacolon with perforation and peritonitis. Rarely, rectocolitis can lead to the formation of gentiourinary fistulae. Common features of amoebic dysentery are shown in Table I. ALA present with right upper quadrant pain, and can rupture into the peritoneum (acute abdomen), pericardium (tamponade), and lung (pneumonia with pleural effusion), and form fistulas through the intercostal spaces, forming chronic skin ulcers.

Diagnosis

Patients will usually come to medical attention with a history of bloody

diarrhoea. Professor Pudifin recounts how Frank Forman described the rectal examination of a case of amoebic dysentery as 'Putting your finger into a warm and over-ripe tomato'. Amoebic dysentery needs to be distinguished from other causes of dysentery (summarised in Table II) by demonstration of motile amoebae with ingested red blood cells and linear line of movement in a warm stool specimen or, more practically, by positive stool lectin antigen assay or PCR. Microscopy of prepared and fixed stool specimen can demonstrate cysts or trophozoites. Experience is needed to distinguish the microscopic appearance of *E. histolytica* from the morphologically similar and non-pathogenic *E. dispar*. Scrapings or aspirates from the edge of an amoebic ulcer have a very high trophozoite yield.

Serum tests for antibodies directed against *E. histolytica* antigens are highly specific and about 85% sensitive in patients with symptoms for >1week. Importantly, these tests remain strongly positive for years after invasive disease, so a positive test does not necessarily mean active infection.

ALA are associated with a raised white cell count and alkaline phosphatase, with variable transaminase elevation, and infrequently presents with concomitant diarrhoea or positive stool specimens. Diagnosis is confirmed by liver ultrasound scan. Needle aspiration of ALA is useful to exclude pyogenic abscess; recovery of 'anchovy paste' material is common.

Management

Initial management should focus on oral or intravenous rehydration, correction of electrolyte imbalances, and confirmation of the diagnosis of amoebiasis. In South Africa oral metronidazole is the drug of choice for all forms of amoebiasis at a dose of 400 - 800 mg 8-hourly for 5 - 10 days. Widespread use of metronidazole for nonspecific episodes of diarrhoea has raised concerns for the development of resistance, emphasising the importance of establishing the diagnosis before starting treatment (stool antigen tests should be available at primary care clinics). Tetracycline with chloroquine is an alternative regimen, and erythromycin has *in vitro* activity. Clinical trials are needed to demonstrate the efficacy of alternative regimens. Most cases of ALA resolve with high-dose metronidazole with or without additional chloroquine. Percutaneous drainage of ALA is indicated only if rupture is thought to be imminent.

Recommended resources

http://www.youtube.com watch?v=bjODxbG7OpM (accessed 2 May 2009).

http://cache.gettyimages.com/xd/829-78.mov?c=NewsMaker&d=9B6C5E9A385F67CCF559943E93D43A98&k=2&v=1 (accessed 2 May 2009).

Recommended reading

Bansal D, Malla N, Mahajan RC. Drug resistance in amoebiasis. *Indian J Med Res* 2006; 123(2): 115-118.

Ravdin N, Stauffer W. *Entamoeba histolytica* (amebiasis). In: Mandell GL, Bennett JE, Dolin R, eds. *Mandell, Douglas and Bennett's Principles and Practice of Infectious Diseases*. 5th ed. Philadelphia: Churchill Livingstone, 2000: 3097-3107.

Samie A, Obi LC, Bessong PO, Stroup S, Houpt E, Guerrant RL. Prevalence and species distribution of *E. histolytica* and *E. dispar* in the Venda region, Limpopo, South Africa. *Am J Trop Med Hyg* 2006; 75(3): 565-571.

Nematodes

H VAN DER PLAS, *MBCB, FCP (SA), CERT ID (SA), DTM&H*

Senior Specialist, Division of Infectious Diseases and HIV Medicine, Department of Medicine, Groote Schuur Hospital

E-mail: helen.vanderplas@uct.ac.za

Nematodes or roundworms are the most common human parasites and constitute a major health burden, particularly among the poor in developing countries. Several roundworm infections are part of the 14 neglected tropical diseases currently being targeted for control and eradication by the WHO.[1] They can be divided into intestinal and tissue-dwelling roundworms, and further into those parasitic to humans only or zoonotic infections, where the adult worms parasitise animals and humans are accidental hosts (*Toxocara canis*, *Angiostrongylus* species, *Gnathostoma* species, and *Trichinella spiralis).*

Intestinal roundworms

These roundworms are a health burden in developing countries where the frequency of infection is a general indication of the local development of hygiene and sanitation. In most cases transmission to humans results from contact with human waste. Roundworms gain entry to the human host via two routes: by egg ingestion (*Ascaris, Trichuris* and *Enterobius*) or via larvae that penetrate the skin of their host (*Strongyloides* and hookworm). *Trichuris* and *Enterobius* have simple lifecycles as they attach and grow in the intestine after ingestion and start producing eggs. *Ascaris, Strongyloides* and hookworm on the other hand have a larval stage that, after penetration of skin or mucous membranes, travels through the bloodstream to the lungs and migrates up the tracheobronchial tree, where they are swallowed and take up residence as adult worms in the gastrointestinal tract. Infections are generally soil transmitted, with the exception of *Strongyloides* and *Enterobius*, where infection can result from direct transmission and is perpetuated by autoinfection. *Strongyloides* hyperinfection can result from autoinfection in immunocompromised individuals, where infective larvae can cause a severe disseminated illness with a high fatality rate.

Symptoms are directly proportional to the intensity of infection with light infections often asymptomatic and heavy infections causing an array of morbidities, including dietary deficiencies and delayed physical and cognitive development. Common disease symptoms are summarised in Table I. The diagnosis is made with the detection of characteristic eggs on faecal samples, the exception being *Strongyloides,* where rhabditiform larvae in stool are diagnostic. Eosinophilia is a feature in worm infections that have migratory larval stages. Albendazole is the preferred agent, given usually as a single dose of 400 mg; however, single-dose therapy may be unsatisfactory with *Trichuris* and *Strongyloides* infections that require twice-daily treatment for 3 days.[2] Mebendazole and ivermectin are alternative agents that have activity against intestinal roundworms. The WHO has launched mass deworming campaigns in regions where soil-transmitted helminths are prevalent, with the aim to regularly target at least 75% of school-aged children and other high-risk groups by 2010. This public health intervention produces significant benefits to affected communities, particularly children. [4]

Tissue nematodes

These nematodes include the filarial worms; they typically have a complex life cycle with the adult worms residing in the lymphatics or skin and connective tissue, producing microfilariae that circulate in blood or skin. Microfilariae are ingested by insect vectors (mosquitos or flies) where several maturation processes are completed and are transmitted again when they take their blood meal. Transmission of microfilariae requires warm climates, as a high temperature is necessary for the parasites to develop in the vector. Filarial worms are not endemic in South Africa; however, with increasing refugee and immigrant populations and travel to endemic countries clinicians may encounter acute infection in the returning traveller or sequelae from chronic infection. A high eosinophil count (>400 cells/µl) may be the first clue and the diagnosis is made by detecting microfilariae in blood or skin snips or with serological techniques. Treatment involves ivermectin and diethylcarbamazine in combination with albendazole, which

results in rapid and sustained suppression of microfilaria but may not destroy the adult worms. Ideally an opinion from an infectious diseases specialist should be sought to guide diagnosis and treatment.

References

1. Hotez PJ, Molyneux DH, Fenwick A, *et al.* Control of neglected tropical diseases. *N Engl J Med* 2007; 357(10): 1018-1027.
2. Keiser J, Utzinger J. Efficacy of current drugs against soil-transmitted helminth infections: Systematic review and meta-analysis. *JAMA* 2008; 299(16): 1937-1948.
3. Maguire JH. Intestinal nematodes (roundworms). In: Mandell GL, Bennet JE, Dolin R, eds. *Principles and Practice of Infectious Diseases*, vol. 2, 6th ed. Philadelphia: Churchill Livingstone, 2005: 3260-3267.
4. Albonico M, Allen H, Lester Chitsulo L, *et al.* Controlling soil-transmitted helminthiasis in pre-school-age children through preventive chemotherapy. *PLoS Negl Trop Dis* 2008; 2(3): e126.
5. Grove DI. Tissue nematodes including trichinosis, dracunculiasis, and the filariases. In: Mandell GL, Bennet JE, Dolin R, eds. *Principles and Practice of Infectious Diseases*, vol. 2, 6th ed. Philadelphia: Churchill Livingstone, 2005: 268.

Table I. Common disease symptoms (adapted from Mandell *et al.*[3])

Nematode	Trans-mission	Distribution	Duration of infection	Location of adult worm(s)	Clinical mani-festations	Complications	Treatment
Ascaris lumbricoides	Ingestion of infective egg	Tropical regions, temperate zones in warmer months	1 - 2 years	Small bowel	Majority asymptomatic Pulmonary symptoms: transient eosinophilic pneumonitis Gastrointestinal symptoms	Bowel obstruction Biliary and/or pancreatic duct obstruction Intestinal perforation Nutritional deficiency	Albendazole or mebendazole
Trichuris trichuria (whipworm)	Ingestion of infective egg	Tropical regions, temperate zones in warmer months	1 - 3 years	Anchored in caecum and colon	Majority asymptomatic	Rare: *Trichuris* dysentery Rectal prolapse Iron deficiency Growth retardation	Albendazole or mebendazole
Ancylostoma duodenale *Necator americanus* (hookworm)	Penetration of skin by filariform larvae	Tropical regions, temperate zones in warmer months	3 - 5 years (*Necator*) 1 year (*Ancylostoma*)	Small bowel mucosa	Asymptomatic with mild infection 'Ground itch'(where larvae penetrate skin) Transient pneumonitis Gastrointestinal symptoms: pain, diarrhoea	Iron deficiency Protein energy malnutrition Growth retardation in children	Albendazole or mebendazole
Strongyloides stercoralis	Penetration of skin or bowel mucosa of filariform larvae Auto-infection	Warm, humid areas, but can be worldwide	Decades	Small bowel mucosa	Asymptomatic Pulmonary symptoms Gastrointestinal symptoms Papular rash – perianal and thigh Larva currens	*Strongyloides* hyperinfection: dissemination of filariform larvae to many organs Untreated mortality reaches 100%	Albendazole or ivermectin
Enterobius vermicularis (pinworm)	Ingestion of infective eggs Auto-infection	Worldwide	1 month	Caecum, adjacent colon	Asymptomatic Perianal pruritus	Rare: peritoneal or pelvic egg granuloma	Albendazole or mebendazole