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Human Intestinal Nematodiasis in The United States

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■ *Human intestinal nematodes, all of which can be acquired in the continental United States, can cause a variety of ills including iron deficiency anemia, surgical emergencies, eosinophilic pneumonia, malabsorption, dysentery, myositis, and death. The severity of illness is related to the number of parasites acquired exogenously or the ability of the parasite to multiply within the host. Diagnosis of clinically significant infection can usually be made by stool examination, and appropriate treatment requires an understanding of the life-span and pathogenic potential of the parasite.*

INTESTINAL ROUNDWORMS, while most common in underdeveloped tropical countries, can be acquired here in the United States.

The largest and most common roundworm to involve the intestinal tract of man is Ascaris lumbricoides. Accidental ingestion of fertilized eggs results in release of larvae which penetrate the intestinal blood vessels, are carried to the lungs, break out of alveolar capillaries, migrate up the pulmonary tree, and are swallowed. They mature in the small intestine. Adult ascarids lie free in the lumen of the small intestine, maintaining their position by propulsive muscular activity. The life cycle of Ascaris and other helminths is shown in Table 1.

While the stage of larval migration is usually not clinically recognized, occasionally it may be associated with fever, an irritating cough, wheezing, and striking roentgenographic changes of perihilar nodular or lobar densities. This illness resolves spontaneously in seven to ten days. A high eosinophilia, the presence of a papular or urticarial rash in 15 percent of cases, the usual presentation in adults rather than children, and the greater frequency in populations where climate makes ascariasis a seasonal infection, all support the hypothesis that the pulmonary reaction is primarily allergic in nature.[2]

The pathologic importance of adult ascarids derives from the absorption of nutrients from the diet of the host (sometimes causing protein malnutrition in children with borderline diets) and from the peculiar propensity of the adult worm to migrate through small orifices, thereby causing bizarre and sometimes fatal complications secondary to mechanical obstruction of any hollow viscus. Invasion of bilary or pancreatic ducts may produce obstructive jaundice, intrahepatic abscess, pancreatitis or pancreatic abcess. A single worm, migrating up the esophagus, may suddenly obstruct the upper respiratory tract and cause death. A tangled bolus of worms may cause partial or complete intestinal obstruction (most common in the jejunum), or

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TABLE 1.—*Life-Cycle for Intestinal Roundworms of Man*

Worm	*Usual Extrahuman Cycle in USA*[1]	*Route of Entry*	*Pulmonary Migration*	*Usual Prepatient Period*[2]	*Auto-infection*	*Survival of Adult Worm in Man*	*Duration of Infection*
A. lumbricoides	2 weeks	oral	yes	2-3 months	no	1 year	same
hookworm	2-3 days	skin	yes	5 weeks	no	at least 6 years	same
S. stercoralis	0 to months[3]	skin	yes	2-4 weeks	yes	?	up to 36 years
T. trichiura	3 weeks	oral	no	2-3 months	no	months to 3 years	same
pinworm	6 hours	oral	no	2-4 weeks	yes	2 months	years

1. Period from passage in stool to infectivity for man. These time intervals may varv greatly with climate; thus T. trichiuris infective larvae develop within eggs in 6 months at 15°C and in 11 days at 35°C, while the development of infective larvae in the eggs of A. lumbricoides may take from 5 to over 50 days. The duration of infectivity may be considerably longer in a proper environment; thus A. lumbricoides eggs can remain viable and infective for 6 months to six years.
2. Interval from infection to recovery of diagnostic stage (eggs or larvae) in stool of host.
3. Strongyloides infective larvae may develop directly in man, directly in stool (within 24 hours) or may develop into adults which either produce infective larvae or more free-living adult worms.

intussusception (most common at the ileocecal valve), or volvulus. Peritonitis may follow migration of worms through suture lines of surgical operation on the bowel, or (rarely) migration through unmanipulated bowel or following maturation of an ectopic ascarid in the peritoneal cavity. Sauer et al published an excellent review of bizarre obstructive patterns caused by Ascaris.[2] The most common of all intestinal helminths, A. lumbricoides, usually does nothing, but may, on occasion, do almost anything.

Diagnosis at the stage of larval migration is unusual, but a patchy pneumonia associated with a progressive increase in leukocyte count and a concomitant rise in the number of eosinophiles (up to 70 percent) or the demonstration of eosinophiles in the sputum, is suggestive. The diagnosis can be confirmed occasionally when third stage larvae are found in the sputum or gastric aspirate. If ascaris ova, absent in the stool during the acute illness, appear within six months, a retrospective presumptive diagnosis of Ascaris pneumonia can be made. Serologic tests do not distinguish this illness from other larval migrations; indeed, the highest hemagglutination titers are usually to toxocara rather than Ascaris.[1] Diagnosis of the intestinal phase can be made in 95 percent of cases by microscopic stool examination. In 5 percent only adult male worms are present and no eggs are found in the stools. These cases are identified by history (passing a large round worm) or by accident, such as demonstration of Ascarids on roentgenographic examination of the abdomen.

The most effective treatment of Ascaris is with pyrantel pamoate as outlined in Table 2. (Thiabendazole and piperazine citrate are alternate therapies with lower cure rates.) Because of the rare but ever present possibility of a fatal complication even with a single worm, all infections should be treated. Patients with partial intestinal obstruction due to Ascaris can sometimes be managed by nasogastric suction followed by administering piperazine citrate syrup through the drainage tube and repeating the treatment at 12-hour intervals for six doses.[3] Complete obstruction of any hollow viscus is a surgical emergency, and often the cause cannot be determined before laparotomy. After surgical removal of a worm or worms in such cases, pyrantel therapy for any residual infection is indicated.

Hookworm

Human hookworm infection with Ancyclostoma duodenale or Necator americanus is most common in areas where a warm (70-85°F) rainy (over 40 inches of rainfall per year) climate permits maturation of the infective larval stage in the soil and where children go without shoes. Hookworm infection is, therefore, rarely endemic in California, but is common in the Southeastern United States. Skin penetration may be associated with localized pruritis with or without lesions of creeping eruption (ground itch); or it may go unnoticed. The larvae migrate from cutaneous capillaries to the lungs and then follow a cycle similar to that for Ascaris (Table 1). The adult hookworm is attached to the small bowel mucosa by means of cutting plates or teeth, and derives its nutrition by sucking blood from the host.

Although pulmonary migration is occasionally

TABLE 2.—*Chemotherapy of Intestinal Roundworms*

Worm	*Drug*	*Dose (maximum)*	*Duration*	*Cure rate (Percent)*	*Comment*
A. lumbricoides	pyrantel pamoate Antiminth®	10 mg/kg (1 gram)	1 day	>95	Ascariasis is treated first when several parasites are present, because of the theoretical risk of inciting migration of these worms.
Hookworm	tetrachloro-ethylene	0.12 cc/kg (5 cc)	1 day	>50	Complete worm eradication is not essential; over 90% have reduction in worm burden, all that is necessary to prevent further anemia.
S. stercoralis	thiabendazole Mintezol®	25 mg/kg bid	2 days	>90	Because of autoinfection, worm eradication is always attempted.
T. trichiura	thiabendazole Mintezol®	25 mg/kg bid	2 days	20	Only symptomatic patients are treated.
Pinworm	pyrvinium pamoate Povan®	5 mg/kg (250 mg)	2 days 1 week apart	>90	Only symptomatic patients or families of symptomatic patients are treated.

Note: When more than one worm is present, an alternate drug can be selected for broad spectrum activity. Thiabendazole also has some efficacy against Ascaris, hookworm and pinworm; pyrantel is also effective against pinworm, and pyrvinium pamoate against Strongyloides. Bephenium hydroxynapthoate (Alcopar®) is effective against hookworm and Ascaris. The dose or duration of therapy may differ, however, with mixed infections, and the physician should check the manufacturer's recommendations.

associated with symptoms and some patients complain of abdominal pain simulating that of duodenitis, the majority of infections in the United States are silent. The major pathologic change of hookworm disease is iron deficiency anemia. The importance of any given hookworm infection in the production of iron deficiency anemia can be calculated from the dietary iron plus the number of eggs in the stool. There is an average daily blood loss of 2.1 ml per 1000 Necator americanus eggs per gram of stool, and 4.5 ml lost per 1000 eggs of A. duodenale per gram of stool.[4] Even heavy infections may not cause anemia if the dietary iron is high, but mild infections may bring it about if the diet is borderline. Most adults in the United States have sufficient iron in their diet to tolerate a modest worm burden; they can have hookworm infection without having hookworm disease. Children, particularly those with poor diet, may show severe iron deficiency anemia if heavily infected.

The diagnosis of any clinically significant hookworm infection is easily made by microscopic examination of stool; if concentration techniques are required for demonstration of ova, then it is unlikely there are enough worms present to cause serious pathologic changes. Treatment in the United States should be reserved for food handlers and persons with symptoms or signs of infection; treatment of the asymptomatic carrier for a few worms is not warranted. Most infections will be eradicated by use of tetrachloroethylene (Table 2). In countries where A. duodenale is the primary hookworm, bephenium has been preferred therapy and it has the added advantage that it is also effective against Ascaris.[3] Worm eradication is followed by a very slow correction of iron deficiency anemia; such patients should therefore also receive iron therapy. Indeed, even without worm eradication, iron therapy very promptly corrects hookworm anemia[4] and severe anemia should be corrected before a vermifuge is used.

Strongyloidiasis

Strongyloides stercoralis (threadworm), like hookworm, infects man by skin penetration and pulmonary migration. But no soil phase is required, as it is with hookworm, for maturation of infective larvae. Strongyloides larvae may mature to the infective filariform stage while passing through the large intestine and reinvade the host through the colonic mucosa or perianal skin. Autoinfection is responsible for the extremely heavy intestinal parasitism seen in some patients and the persistence of infection long after the host has left an endemic area.

Although creeping eruption is far oftener caused by threadworm than by hookworm, skin penetration frequently goes unnoticed. All larvae, whether of exogenous or endogenous source, migrate through the lungs. Symptoms of larval migration are similar to those described for As-

caris pneumonia; patients typically have pneumonitis, fever, urticaria and pronounced eosinophilia. X-ray films of the chest may show almost any changes, including diffuse miliary densities very suggestive of tuberculosis. An allergic reaction, as described for ascariasis, is suggested by the common finding of urticaria. Autoinfection also can produce a massive simultaneous pulmonary migration unlikely to occur with an exogenously acquired parasite; in these cases a large part of the pulmonary complex may actually be due to migrating larvae. In fatal cases pulmonary hemorrhages are common.

The adult organisms, which lie embedded in the mucosa of the duodenum and jejunum, usually cause no symptoms. Some patients experience epigastric pain that clinically and radiographically mimics duodenal ulcer. Massive involvement of the small intestine is sometimes associated with frank malabsorption,[5] but some patients tolerate extremely heavy infections without absorption deficiency.[6] Massive autoinfection can occur, often but not always precipitated by corticoid therapy.[7] In such cases patients have vomiting, diarrhea, fever, pulmonary abnormalities; frequently there is neither peripheral eosinophilia nor the presence of parasites in the stool to afford clues to diagnosis. Such cases may be fatal. Major findings at autopsy include the observation of adult forms, larvae and ova in the wall of the small intestine, and severe changes suggestive of granulomatous or ulcerative colitis in the large intestine.[8] Parasites are also found in many other tissues.

The diagnosis of strongyloidiasis is usually made by identification of larvae in fresh stool; Strongyloides ova are rarely found in the stool in the absence of diarrhea, and hookworm larvae, which have subtle morphologic differences from those of S. stercoralis, are not found in fresh stool. The yield from stool examination can be enhanced by suspending approximately 100 grams of fresh stool in fine surgical gauze over a glass, adding lukewarm water to the level of suspended stool so that the bottom of gauze and water are in contact, and waiting one hour for larvae to migrate through the gauze and drop to the bottom of the glass. The sediment is examined for larvae. Eight stool examinations will lead to diagnosis in more than 80 percent of cases, but in some patients, where internal autoinfection is complete, no parasites will be found on stool examination. One duodenal or, better, jejunal drainage specimen is equivalent to eight stool specimens and will establish the diagnosis in almost all cases. The treatment of choice today is with thiabendazole in doses outlined in Table 2. Although the majority of infections are asymptomatic, the possibility of autoinfection and and even death makes treatment advisable.

Trichuriasis

Whipworm infection is acquired by inadvertent ingestion of infective eggs and therefore coexists with A. lumbricoides. The worms mature in the large intestine without a migrational phase, and the adult female can lay several thousand eggs daily. As with hookworm, the soil cycle is required for maturation of eggs to the infective form.

The majority of infections in the United States are light and asymptomatic; symptoms rarely occur in patients with less than 10,000 eggs per gram of stool. When heavy infection produces illness, diarrhea is the most common complaint. Rectal prolapse may follow, with myriads of small white worms seen covering the rectal mucosa. Dysenteric trichuriasis is often associated with amebiasis. Because the Trichuris sucks blood as well as causing dysentery, heavy infections may also cause iron deficiency anemia. One Trichuris ingests approximately 0.005 ml of blood per day, which is 6 to 10 times less than that obtained by N. americanus and 50 times less than by A. duodenale. However, with over 5 million eggs per day—that is, over 800 whipworms—the blood loss may reach 4 ml a day (1.5 mg of iron) which can ultimately cause iron deficiency anemia.[9]

Because only heavy infections produce symptoms, diagnosis can readily be made on microscopic stool examination. Unfortunately treatment is less simple. Thiabendazole (Table 2) generally considered to be the drug of choice, is curative in only 20 percent of cases. Hexylresorcinol retention enemas using about 500 ml of 0.2 percent aqueous suspension for one half hour, repeated at four-day intervals three to four times, may be worthwhile in highly symptomatic patients who do not respond to thiabendazole.[3] The perianal area must be widely protected by petroleum jelly. A new agent, dichlorvos, seems to be promising for treatment, but is currently available only for investigational use in the United

States. A five-day course of treatment with dithiazinine, which is no longer available for clinical use in the United States, was curative in over 95 percent of cases.[3]

Enterobiasis

Pinworm infection, the most prevalent helminth infection in the United States, follows ingestion of the embryonated eggs of Enterobius vermicularis. They mature into adults without extra-intestinal migration and live unattached in the lumen of the lower small intestine and upper large bowel. The gravid adult female migrates, usually at night, to the perianal area and disintegrates, releasing 4,000 to 17,000 sticky eggs. This phenomenon is associated with pruritis ani; resultant scratching transfers eggs to the fingers, thus to the mouth, and external autoinfection ensues. Eggs may also hatch in the anal area and larvae may reinfect through the colon—retroinfection. Eggs also persist on clothing and sheets and probably are spread as an aerosol, leading to infection of the entire family.

Although at least 25 percent of children in general (and half of their family members—including adults) and over 90 percent of children in institutions are infected with pinworms,[10] the vast majority of infections are asymptomatic and unsuspected. Symptomatic patients are usually children, probably owing to their propensity to put fingers in and around body orifices sequentially, leading to heavy autoinfection. The ubiquity of the parasite has led to its incrimination in a variety of conditions which include nagging wives and accident proneness.[11] More reasonable but equally undocumented are rectal bleeding and acute appendicitis; in both, the association of pinworms seems to reflect their geographic prevalence rather than an etiologic role. The only clear-cut pathologic change is one that is essential to the perpetuation of parasitism, pruritis ani; it is possible that mild insomnia and irritability do result from this annoying symptom. More rarely, abdominal pain, urethritis or vaginitis appear to be due to this parasite.

The diagnosis is made by placing cellulose tape, sticky side down, on the perianal area in the morning before bathing, sticking the same tape to a glass slide and examining it microscopically at leisure. Diagnosis is made in virtually all cases if this examination is done on three consecutive mornings. Although eggs are occasionally found in urine and stool, neither method affords a reliable means of diagnosis.

Treatment with pyrvinium pamoate (Table 2) is 80 percent effective in a single dose and a 93 percent cure rate is achieved by repetitive therapy of three weekly doses. Because pinworm is classically a family infection, parasite eradication requires simultaneous treatment of the entire family. A one-day course of treatment for the family is generally recommended only when there is a symptomatic member. Because it is known that eggs are disseminated in the home environment and can remain viable for up to three weeks, vigorous cleaning is often recommended to prevent reinfection; but that measure is ill-advised, for it is ineffective and serves only to place unwarranted importance on this infection.

Trichinosis

Whereas man serves as the only source of his other intestinal nematodes, Trichinella spiralis is a zooinosis and man is an accidental host. Two hosts are necessary for perpetuation of the life-cycle and each host is infected with the larval and the adult form. Man, swine and other carnivores become infected when they ingest meat containing viable larvae. Larvae excyst in the intestine, mature to adults and mate. The fertilized female then burrows into the intestinal mucosa, releasing larvae into blood and lymph. Release of larvae occurs about five days after fertilization and continues for two to six weeks; each female can release more than 1,000 larvae. Larvae that are carried to striated muscle survive, grow rapidly and encyst in about three weeks. They may remain viable for years even when calcification of the cyst wall ensues.

In the absence of cannibalism, man is a dead-end host. He usually becomes infected from eating inadequately cooked pork, often in the form of locally-made sausage, although bear and other wild animal meats have led to occasional outbreaks. Pigs become infected from ingestion of untreated garbage, dead rodents, or the carcasses of other dead animals. The prohibition of feeding uncooked garbage to swine since the mid-1950's and the increasing use of frozen meats* have been important in

*While data is lacking on freezing schedules for large cuts and whole carcasses, in cuts of pork for home use T. spiralis is killed by freezing at 5°F for 20 days or at −20°F for six days.

reducing the incidence of reported trichinosis in the United States from 487 cases in 1948 to 84 cases in 1968.[12] U.S. inspection of pork does not include microscopic examination for the cysts of T. spiralis, and only adequate cooking of pork products insures its safety. Trichinosis is an incidental finding in about 5 percent of autopsies in North America today.[13] Parenthetically, many recent outbreaks of trichinosis, including one in California, have been related to the ingestion of the flesh of wild animals, especially bear meat.

The majority of infections are mild and asymptomatic. Heavy infection may be associated with gastroenteritis at the stage of burrowing of the fertilized adult, but usually this phase goes unnoticed. Initial symptoms typically occur the second week after ingestion of the infected meat, and are characterized by periorbital edema, headache, myalgia, dyspnea, neurologic abnormalities, mucocutaneous hemorrhages, rash and fever. It may be that not all of these manifestations are present in any given patient. Eosinophilia is virtually universal in recognized cases, but may disappear before death. Symptoms continue for up to six weeks, and complete recovery is often delayed for several months. Although larvae do not encyst in the myocardium, pronounced myocarditis is usual in fatal cases.

Fever, myalgia, periorbital edema and splinter hemorrhages under the nails in a patient with eosinophilia strongly suggest the diagnosis of trichinosis. In contrast to most other acute febrile diseases, the erythrocyte sedimentation rate is frequently normal.[14] Creatinuria and elevation of muscle specific enzymes such as creatininephosphokinase (CPK)and lactatedehydrogenase (LDH), such as are seen with myopathy of other kinds, are frequently noted. Specific diagnosis can sometimes be made by serologic testing (complement fixation, fluorescent antibody, and others). A complement fixation test with high specificity is usually positive within one week of illness, but the results may be negative in proved cases.[14] Muscle biopsy of any tender muscle provides the best means of definitive diagnosis. Serial sections may be necessary to demonstrate that the myositis is associated with larval infiltration. A crush preparation of unfixed muscle gives a better yield; motile larvae can usually be demonstrated, often in the tisue fluid at the edge of the specimen. Skin testing is best suited for detection of more remote infection, and may be negative in 15 percent of acute cases.[14] Examination of feces for adult worms is usually unsuccessful.

Because of the extremely variable course of illness, the efficacy of any therapy has been difficult to assess. In most clinically recognized cases the patients do very well with aspirin and supportive therapy, while a few require corticosteroids in full dosage. Thiabendazole, 25 mg per kg of body weight twice a day for 10 to 21 days, has been considered effective in some cases; fever and pain usually resolve within three days, and degenerated larvae can be demonstrated on muscle biopsy following therapy, but other laboratory abnormalities such as eosinophilia and muscle enzyme elevations are unaltered.[14] Drug intolerance, usually nausea and vomiting, may preclude completion of therapy.

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