Mucocutaneous manifestations of helminth infections

Nematodes

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Learning objectives
After completing this learning activity, participants should be able to describe the cutaneous manifestations of infections by nematodes and identify appropriate therapy.

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In the 21st century, despite increased globalization through international travel for business, medical volunteerism, pleasure, and immigration/refugees into the United States, there is little published in the dermatology literature regarding the cutaneous manifestations of helminth infections. Approximately 17% of travelers seek medical care because of cutaneous disorders, many related to infectious etiologies. This review will focus on the cutaneous manifestations of helminth infections and is divided into 2 parts: part I focuses on nematode infections, and part II focuses on trematode and cestode infections. This review highlights the clinical manifestations, transmission, diagnosis, and treatment of helminth infections. Nematodes are roundworms that cause diseases with cutaneous manifestations, such as cutaneous larval migrans, onchocerciasis, filariasis, gnathostomiasis, loiasis, dracunculiasis, strongyloidiasis, ascariasis, streptocerciasis, dirofilariasis, and trichinosis. Tremadotes, also known as flukes, cause schistosomiasis, paragonimiasis, and fascioliasis. Cestodes (tapeworms) are flat, hermaphroditic parasites that cause diseases such as sparganosis, cysticercosis, and echinococcus. (J Am Acad Dermatol 2015;73:929-44.)

Key words: helminth; nematodes; parasite; travel; tropical.

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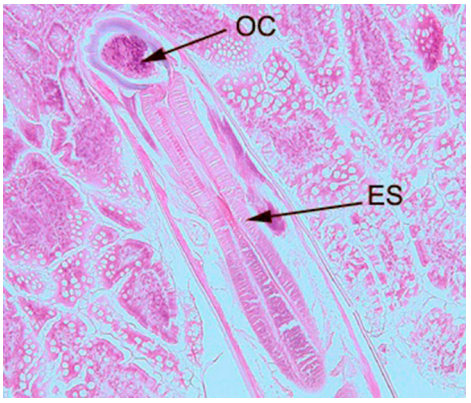

Fig 1. Longitudinal section of an adult hookworm in a bowel biopsy specimen. Note the oral cavity (OC) and esophagus (ES). Courtesy of the Centers for Disease Control and Prevention. (Hematoxylin–eosin stain.)

NEMATODE INFECTIONS

Key points

- **Nematode infections are common parasitoses, with millions of people infected**
- **Prevalence varies, but increases with poverty and tropical climate**
- **Control of nematode infection is based on drug treatment, improved sanitation, and education**

Nematodes are commonly parasitic to humans, with >60 species known to infect man. Nematodes are elongated with symmetrical bodies that contain an intestinal system and a large body cavity. Dermatologists should be familiar with these infections because of their increased presence in the United States, increased travel, and economic globalization.[1-7] In this continuing medical education article, we review the nematode infections with important mucocutaneous manifestations.

CUTANEOUS LARVAL MIGRANS

Key points

- **Cutaneous larval migrans presents with an erythematous, pruritic eruption and is caused by percutaneous penetration of animal hookworms**
- **Infection is caused by filariform larvae burrowing through the skin; common places of infection are sand or soil contaminated with animal feces**
- **The disease is usually self-limited, but patients typically will seek medical treatment**
- **Ivermectin can be used to shorten the clinical course of disease and prevent superinfection.**

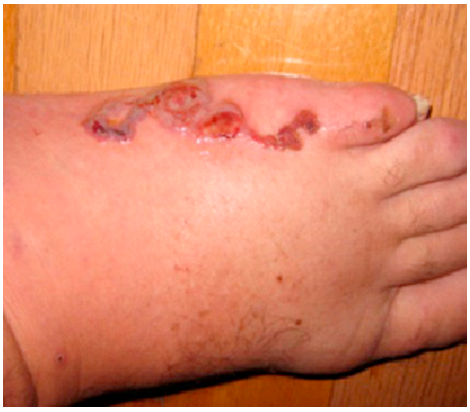

Fig 2. Cutaneous larva migrans on the left foot. Note the elevated, serpiginous track of the hookworm. Courtesy of the Centers for Disease Control and Prevention.

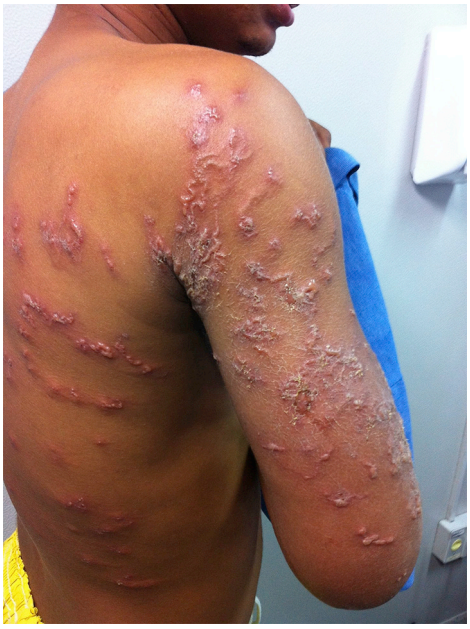

Fig 3. Disseminated cutaneous larva migrans.

Cutaneous larval migrans (CLM) usually affects tourists and inhabitants of tropical and subtropical climates, such as the southeastern United States, South America, Southeast Asia, and Africa. CLM is caused by larval migration of animal hookworms, most commonly *Ancylostoma braziliense, Ancylostoma ceylanicum*, and *Ancylostoma caninum*.

Life cycle

The life cycle begins as larvae attach to the skin of their definitive animal host (usually nondomesticated cats or dogs), eventually arriving to the pulmonary system. The larvae are subsequently swallowed, entering the gastrointestinal tract. Adult larvae (Fig 1) then shed eggs that are eliminated in

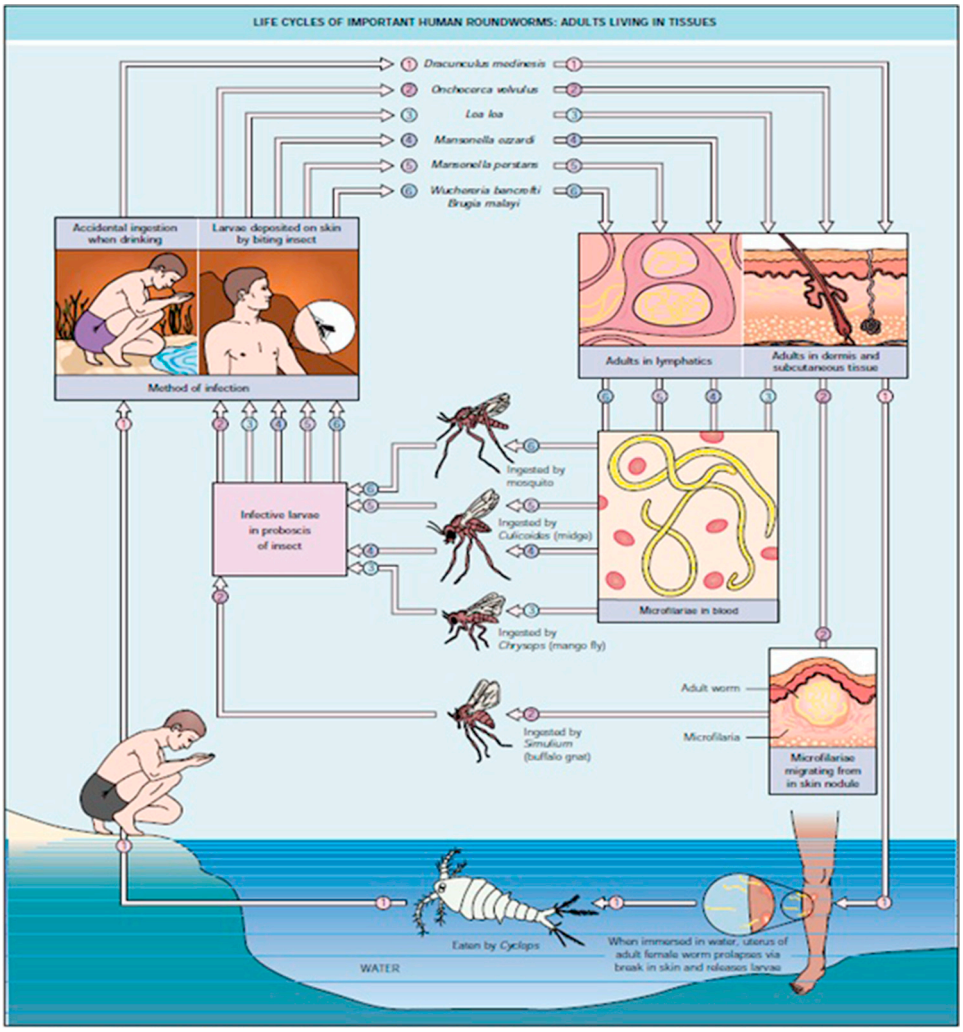

Fig 4. Lifecycle of onchocerciasis, filariasis, *Loa loa*, and Streptocerciasis. Used with permission from Cross JH. Helminths. In: Armstrong D, Cohen J, editors. Infectious diseases. London: Mosby; 1999.

the animal's feces. The larvae continue their life cycle in sand or soil. The mature filariform larvae then infiltrate humans via exposed skin surfaces to begin their new subcutaneous journey.[8] However, in humans, the larvae are sequestered in the dermis and cannot penetrate further to complete their life cycle because of their lack of specific collagenases. Humans are the end hosts.

Presentation

CLM is characterized by pruritic, erythematous papules or a linear or serpiginous elevated mobile track. The hookworm migrates through the skin at about 1 mm to 3 cm per day (Fig 2). The most commonly affected areas are the feet, buttocks, thighs, and lower legs, but lesions can appear anywhere (Fig 3).[9] Intense itching usually begins within a few minutes to a few days after filariform larvae penetration. Symptoms are self-limited and resolve after the nematode dies (approximately 2-8 weeks). Complications of CLM include impetiginization caused by scratching, excoriations, vesiculobullous lesions,[10] and, rarely, folliculitis or erythema multiforme.

Diagnosis

CLM is diagnosed clinically based on history and physical examination. Patients will usually report recent exposure to contaminated sand or soil. The laboratory workup will occasionally reveal eosinophilia or increased immunoglobulin E levels. Obtaining a biopsy specimen is rarely helpful and infrequently reveals larvae given that they have usually migrated away from the site of entry at the time of sampling.

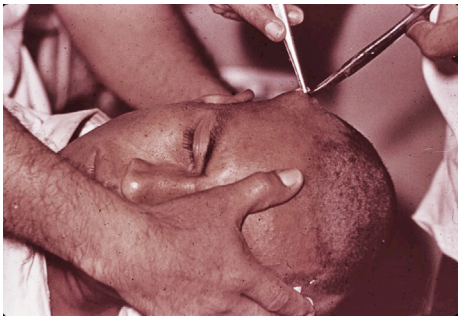

Fig 5. Surgical removal of an onchocercoma. Courtesy of the American Society of Tropical Medicine and Hygiene.

ONCHOCERCIASIS

Key points

- **Onchocerciasis is a common tropical disease with dermatologic, ocular, and systemic manifestations**
- **There are many cutaneous manifestations of the disease, including onchocercoma, which is a palpable onchcercal nodule most commonly found at bony prominences**
- **The disease is also known as "river blindness" because it is the second most common cause of blindness caused by infection**
- **Ivermectin and doxycycline are used to treat the disease**

Onchocerciasis, also known as river blindness, is a parasitic infectious disease caused by the filarial nematode *Onchocerca volvulus*. The disease is transmitted by the bite of a female black fly (Fig 4) and affects >27 million people, with most cases in sub-Saharan Africa[11]—although there have been imported cases reported in the United States.[12] The disease has many cutaneous manifestations, including severe pruritus, eczematous dermatitis, lichenification, and subcutaneous and dermal atrophy.

Life cycle

The cycle begins when a black fly ingests microfilariae (MF) of *O volvulus* from the skin of an infected human host. Within the fly, the MF pass through 2 molts to an infective stage (L3) over a period of 1 to 3 weeks, and at the next blood meal the fly deposits the larvae within the skin of a new human host. The larvae remain in the dermis and subcutaneous tissue, where they undergo 2 additional molts to mature into hair-like adult worms. After maturation, the female adults, now 30 to 80 cm in length, become encapsulated in deep subcutaneous nodules. Once fertilized, the adult females release MF, which can move from the nodules into both subcutaneous tissues and the eyes of the host.

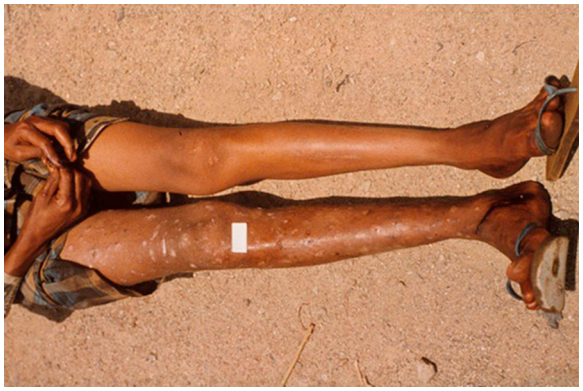

Fig 6. A 14-year-old boy with localized lichenified onchocerciasis on the right lower extremity. Courtesy of the American Society of Tropical Medicine and Hygiene.

Presentation

Onchocercoma is the most distinct cutaneous manifestation of the disease. Onchocercoma is a firm, painless, freely mobile subcutaneous nodule that is often located over a bony prominence. A lesion is typically 1 to 3 cm in diameter (Fig 5). The disease also encompasses many other cutaneous manifestations (Fig 6), and a classification system was developed by Murdoch et al[13] in 1993 (Table I).

In conjunction with these 5 main categories of disease (acute papular onchodermatitis, chronic papular onchodermatitis, lichenified onchodermatitis, atrophy, and depigmentation), lymphedema of the lower extremities and even elephantiasis may occur in areas of Africa where onchocerciasis is endemic. The groin region may become swollen, with enlarged lymph nodes. "Hanging groin"—a merging of enlarged lymph nodes enclosed by a segment of atrophic and stretched abdominal skin—may also be a feature of chronic onchocerciasis (Fig 7).

Diagnosis

One of the first signs of the infection is severe eosinophilia (up to 40%). The criterion standard of diagnosis is microscopic examination of MF that emerge from bloodless skin snips (Fig 8).[14] A skin snip is a specialized way of obtaining a biopsy specimen. After an area of skin is wiped with alcohol, it is elevated with the tip of a needle and a small segment of the tented skin is shaved off with a razor blade or scalpel. This piece of skin is placed on a slide under a cover slip and immersed in isotonic saline. After 15 to 20 minutes, the preparation is examined for the presence of motile MF that emerge from the tissue.

The diagnosis may also be made through the microscopic examination of subcutaneous nodules

Table I. Cutaneous manifestations of onchocerciasis

Classification	Dermatologic description	Location
Acute papular onchodermatitis	Small, 1-3 mm in diameter, pruritic papules that may progress into vesicles or pustules; may be associated with erythema and edema (Fig 6)	Extremities and trunk
Chronic papular onchodermatitis	Flat-topped, hyperpigmented, pruritic papules typically 3-9 mm in diameter	Buttocks, waist area, and shoulders
Lichenified onchodermatitis	Hyperpigmented, lichenified plaques with associated edema and lymphadenopathy	Extremity (typically limited to 1)
Atrophy	Loss of skin elasticity and excessive wrinkling; may be associated with decreased sweating and hair growth	Buttocks, waist, and upper aspect of the thighs
Depigmentation	Often referred to as "leopard skin"; patches of complete pigment loss are seen except for perifollicular islands of retained normal pigmentation	Anterior shins, less commonly on the abdomen or lateral aspect of the groin

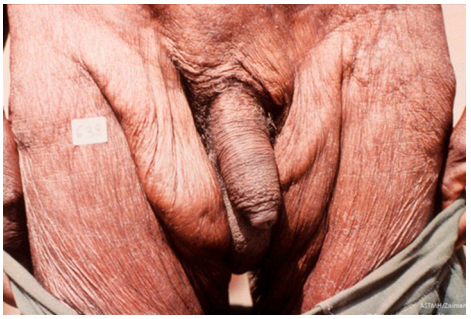

Fig 7. A 52-year-old man with hanging groin caused by onchocerciasis. Courtesy of the American Society of Tropical Medicine and Hygiene.

that have been removed surgically. The pathology reveals coiled adult female worms on the histologic sections of the nodules. The biopsy results of an involved patch of skin may feature an inflammatory reaction made up of eosinophils, neutrophils and macrophages. At times, the worm may emerge from the skin and mimic *Dracunculus medinensis*.[15]

GNATHOSTOMIASIS

Key points

- **The classic diagnostic triad of gnathostomiasis features intermittent migratory swellings/nodules, eosinophilia, and a history of travel to an area of endemicity**
- **The migratory nature of the subcutaneous swellings/nodules help differentiate gnathostomiasis from other causes of subcutaneous nodules**
- **Surgical removal or albendazole are the treatments of choice**

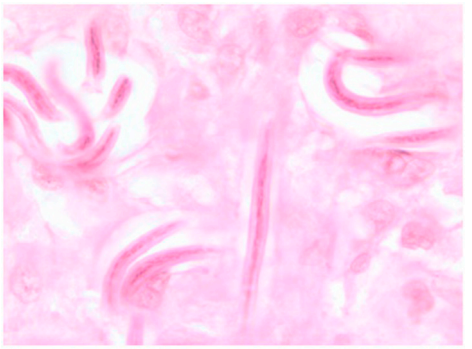

Fig 8. Microfilariae of *Onchocerca volvulus* from a skin nodule of a patient from Zambia. Courtesy of the Centers for Disease Control and Prevention. (Hematoxylin–eosin stain; original magnification, ×1000.)

Human gnathostomiasis is a food-borne parasitic zoonotic disease caused by the ingestion of larvae of the genus Gnathostoma, seen mostly in tropical and subtropical regions, such as Southeast Asia, Japan, Central and South America, and South Africa.[16] There are increased recent reports of disease in tourists returning from endemic areas. The classic triad of intermittent migratory swellings, eosinophilia, and a history of travel to Southeast Asia or other areas of endemicity should alert physicians to the diagnosis.[17]

Life cycle

Humans are accidental hosts in which the parasite fails to reach sexual maturity. The definitive hosts are carnivores, especially fish-eating mammals, where the adult worm (Fig 9) lives coiled up in the wall of the stomach, producing a tumor-like mass. In the definitive hosts, the adult worm, which reaches 13 to

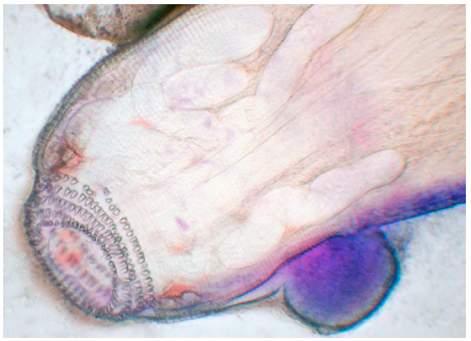

Fig 9. Adult worm seen in gnathostomiasis.

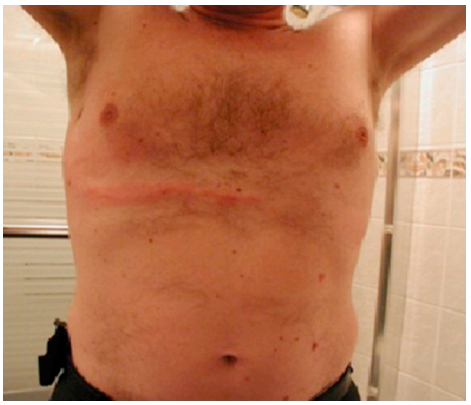

Fig 10. Gnathostomiasis. Note the nodular migratory eosinophilic panniculitis.

55 mm in length, releases eggs into the stomach that are then passed in the feces. Eggs are hatched in freshwater and release first-stage larvae (L1) that mature into third-stage larvae (L3) via 2 intermediate hosts.[16,18] Humans usually become infected with *Gnathostoma* spp. by eating raw or inadequately cooked freshwater fish or other intermediate hosts, such as snakes, frogs, and chickens.

Presentation

Patients may develop nonspecific symptoms, such as malaise, fever, urticaria, anorexia, nausea, vomiting, diarrhea, and epigastric or right upper quadrant pain. These symptoms occur as the larva excysts and migrates through the stomach, intestinal wall, and the liver and may last for 2 to 3 weeks.[19] The worm then migrates to the skin through the subcutaneous tissue, causing the typical migratory swellings and from there may penetrate into deeper tissues.

Cutaneous gnathostomiasis is the most common manifestation of infection. It typically presents with poorly defined, erythematous, edematous, round or oval, pruritic or painful, 5- to 15-cm plaques or indurated, deep-seated nodules that form along the route of larval migration.[20] These edematous

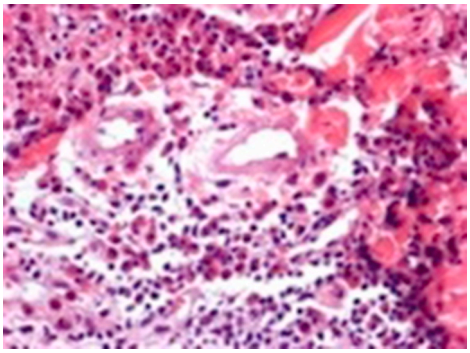

Fig 11. Gnathostomiasis. Note the dense eosinophil infiltration; there was no parasite found in this specimen.

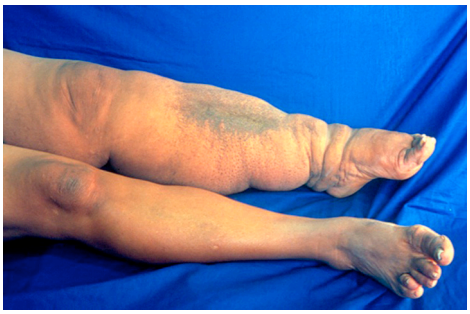

Fig 12. Lymphedema of the left lower extremity caused by lymphatic filariasis.

swellings are intermittent (nodular migratory panniculitis), usually affecting the trunk or upper limbs (Fig 10). They usually occur within 4 weeks of ingestion of the larvae and last for up to 2 weeks. As the larva migrates, subcutaneous hemorrhages may be seen along its tracks, which are pathognomonic of gnathostomiasis and can help differentiate it from other causes of larva migrans (eg, sparganosis or strongyloidiasis).

Episodes of swelling slowly become less intense and shorter in duration, but in untreated patients symptoms may recur intermittently for up to 10 to 12 years. Other less common manifestations of cutaneous gnathostomiasis include skin abscesses or nodules that tend to occur when the larva is migrating more superficially.

Diagnosis

The diagnosis of gnathostomiasis is most commonly made with after a biopsy specimen of the skin is obtained. Expected histologic findings include a dense perivascular and interstitial eosinophilic infiltrate occupying mainly the subcutaneous fat and the dermis (Fig 11).[21] Flame figures, reminiscent of eosinophilic cellulitis, can be present around collagen bundles in the dermis. It is extremely difficult to find the worm on histologic examination

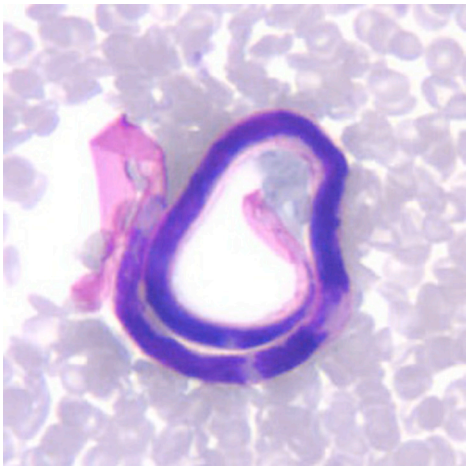

Fig 13. Peripheral blood smear showing microfilaria of *Brugia malayi*. Courtesy of the Centers for Disease Control and Prevention. (Giemsa stain.)

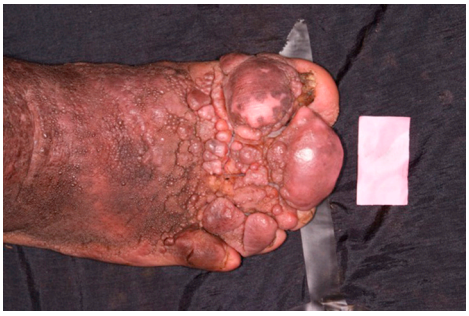

Fig 14. Marked swelling and disfiguration of the right foot caused by podoconiosis. There are multiple firm nodules and hyperkeratotic papillomas.

because the area of infiltration encompasses several centimeters, while the larva measures 2.5 to 12.5 mm long and 0.4 to 1.2 mm wide.[20]

FILARIASIS

Key points

- **Filariasis is caused by the nematodes *Wuchereria bancrofti*, *Brugia malayi*, and *Brugia timori***
- **Filariasis presents with lymphedema, primarily in the lower extremity**
- **Chronic inflammation leads to nonpitting edema and hardening of the tissues, resulting in hyperkeratosis and hyperpigmentation of the skin; fissuring of the skin follows**
- **Lymphedema is initially reversible; however, persistent infection and compromise to the lymphatic system leads to elephantiasis**

Life cycle

Filariasis, or elephantiasis, is a tropical disease characterized by thickening of the skin and

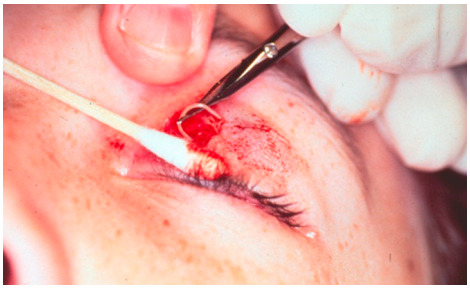

Fig 15. Surgical removal of an adult *Loa loa* worm. Courtesy of Curt Samlaska, MD.

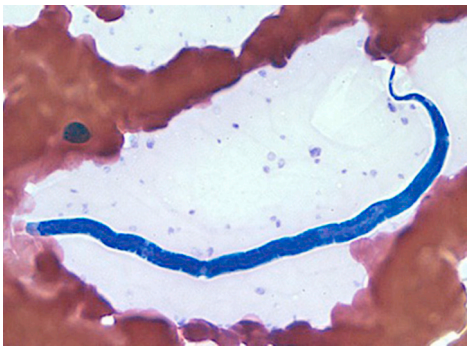

Fig 16. Microfilaria of *Loa loa* in a peripheral blood smear. Courtesy of the Centers for Disease Control and Prevention. (Giemsa stain.)

underlying tissues, especially in the legs and male genitals.[22] There are 3 types of nematodes that cause this disease: *Wuchereria bancrofti*, which causes 90% of cases; *Brugia malayi* and *Brugia timori* cause the remaining 10% of cases, most of which are restricted to south and east Asia. Filariasis affects >120 million people in areas of Asia, Africa, the Pacific Islands, several of the Caribbean Islands, and South America.[23] The disease occurs when infected mosquitoes bite a human and deposit L3 larvae into the skin. The larvae then migrate to the lymphatic system, where they develop into adult worms (Fig 4).

Presentation

Lymphatic filariasis manifests primary as lymphedema of the extremities, genitalia, and breasts (Fig 12). The skin turns warty and thickens with cracks and folds. The affected areas are swollen, painful, and often have a foul smell.

The most common acute manifestation of lymphatic filariasis is acute adenolymphangitis (ALA). ALA is characterized by episodes of fever attacks, inflamed lymph nodes in the groin and axillae, and localized areas of warmth, swelling, redness, and pain. ALA is thought to occur as an immune-mediated response to dying adult worms. ALA episodes recur several times a year, with the

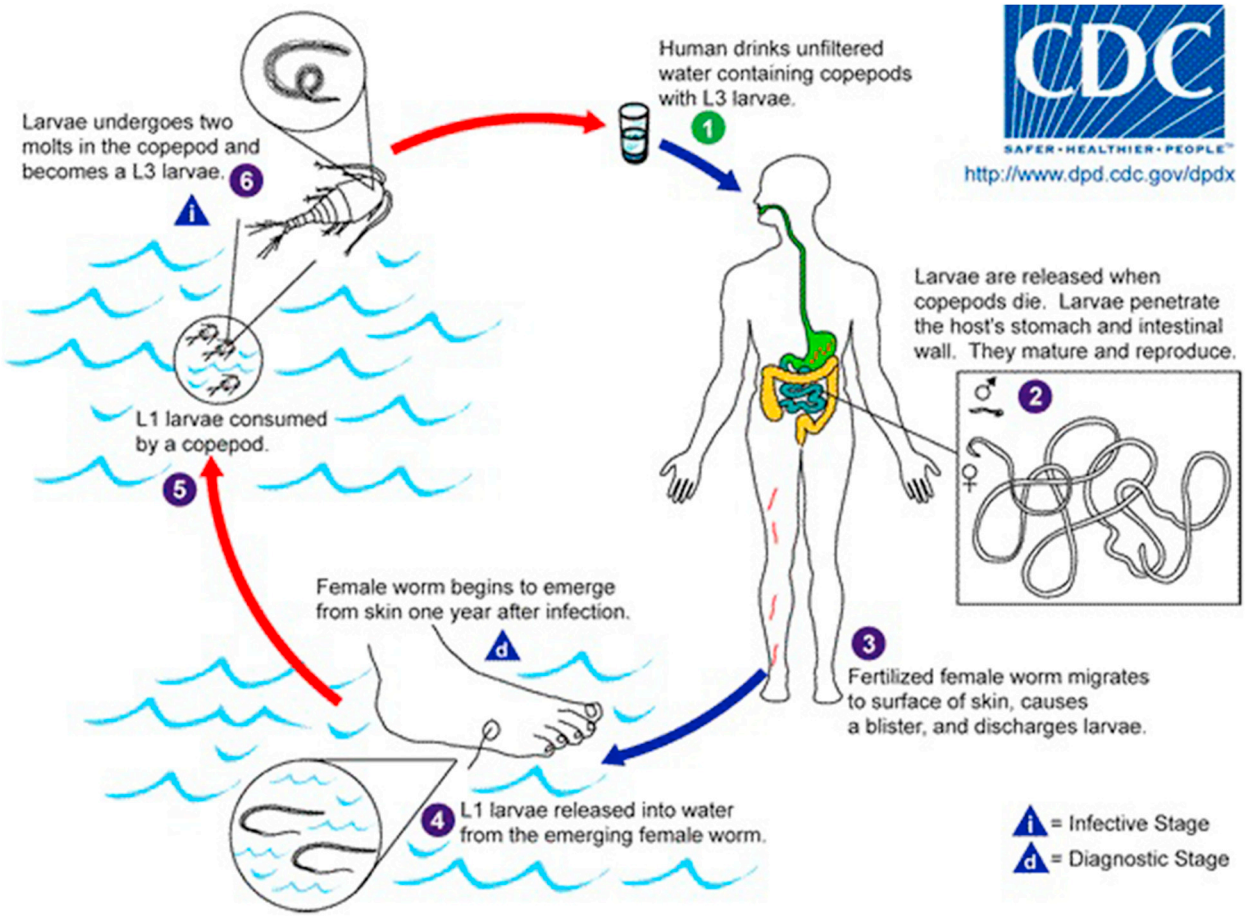

Fig 17. Lifecycle of dracunculiasis. Note that the lesions are intensely painful and patients find relief by having the lesion come in contact with water. Courtesy of the Centers for Disease Control and Prevention.

attacks increasing in frequency and in respect to the degree of lymphedema. This is responsible for elephantiasis of the limbs and the external genitalia. Elephantiasis is a disfiguring, chronic manifestation and presents months to years after initial infection as severe swelling of the extremities, scrotum, vulva, and breasts.[24]

Another acute manifestation of lymphatic filariasis is acute filarial lymphangitis (AFL), which is rare and presents when adult worms are destroyed in the lymph vessels or lymph nodes either spontaneously or by drug administration. Patients present with small, tender nodules at the site of the dying worms.

Diagnosis

Definitive diagnosis can be made by circulating antigen detection. The most useful antigen detection test is the immunochromatographic test (ICT). This test detects antigens released by adult filarial worms. The test is convenient, mobile, and inexpensive.[25,26] If circulating antigen testing is not available, examination of blood smears for MF can be performed. Blood must be taken between 10 PM and 2 AM because of the "nocturnal periodicity" of the filaria. MF can be detected in peripheral blood during the early stages of filariasis, even before clinical manifestations develop (Fig 13). This highly reliable method was the diagnostic standard for many years and is still used in many regions. This test is not useful once lymphedema is present because MF are absent from the blood during this stage.[27] Patients will also have high eosinophilia (>10%).

Differential diagnosis

Podoconiosis, also known as "mossy foot," is a noncommunicable, noninfectious tropical lymphedema and an important differential for filariasis. It is a common cause of lower leg lymphedema in tropical volcanic highland areas (>1000 meters above sea level) with high annual rainfall. It is characterized by below the knee bilateral lower

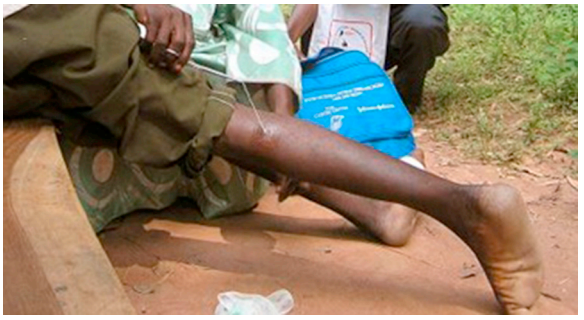

Fig 18. A Guinea worm extracted from the right lower leg of a Nigerian man. Only a few millimeters are removed each day. The extracted portion of the worm is then wrapped around a small stick or piece of gauze. Courtesy of the Centers for Disease Control and Prevention.

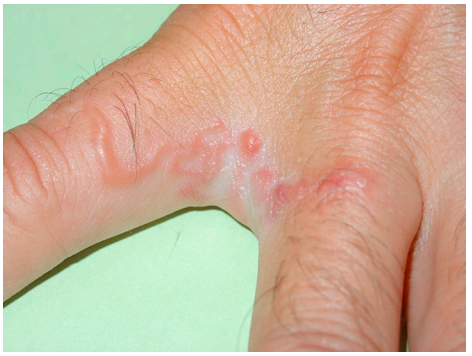

Fig 19. Larva migrans found in the interdigital space between the 4th and 5th digits of the right hand cased by Strongyloidiasis infection. Note that the lesions are more commonly found in the perianal and truncal regions. Courtesy of Penvadee Pattanaprichakul, MD.

limb elephantiasis in barefoot subsistence farmers in farmland areas with red soils derived from alkaline volcanic rock. Although it has only recently been formally designated a "neglected tropical disease" by the World Health Organization,[28] it contributes to a significant public health burden in 10 countries across tropical Africa, Northern India, and Central and South America. There has been recent association of variants in human leukocyte antigen class II loci with the disease, suggesting it may be a T cell–mediated inflammatory disease.[29]

In podoconiosis, persistent lymphedema (Fig 14) is typically below the knee and not associated with scrotal involvement or hydrocoele. Skin changes include the so-called "mossy" hyperkeratosis and series of hard bands or nodules interspersed with deep cracks, folds, and fissures in the skin that harbor mixed infections leading to a strikingly offensive odor in affected individuals.

There are no diagnostic tests for podoconiosis. Exclusion of LF and other causes of lower limb lymphedema should be excluded before settling on the diagnosis. Treatment is challenging, but simple interventions can lead to substantial improvements in both objective measurements of lymphedema and significant improvement in quality of life.[30] Measures include daily washing of the feet and wearing of socks and shoes to prevent contact with the irritant soil responsible for the disease. Debulking surgery has shown to only provide short-term benefit, with subsequent return of lymphedema.

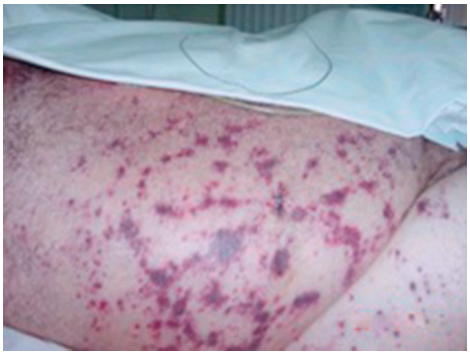

Fig 20. Disseminated Strongyloidiasis. Note the retiform purpura caused by vessel occlusion and dermal invasion of the larvae.

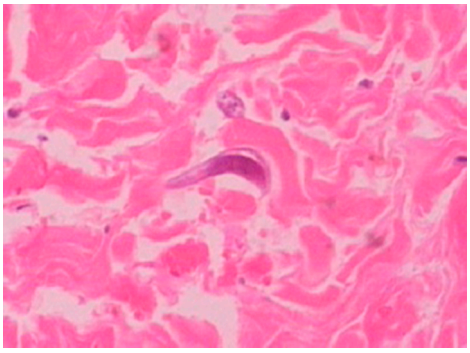

Fig 21. *Strongyloides stercoralis* larvae among the reticular dermis and capillaries. There is no inflammatory reaction.

LOIASIS

Key points

- **Loiasis, also known as African eye worm, is caused by the filarial nematode *Loa loa*; the vector is a deerfly from the genus Chrysops**
- **The manifestations of disease include transient localized subcutaneous swellings (known as Calabar swellings), which have been reported in approximately 50% of patients**
- **Migration of the adult worm across the conjunctiva of the eye occurs in approximately 70% of patients**
- **The treatments of choice are diethylcarbamazine and albendazole**

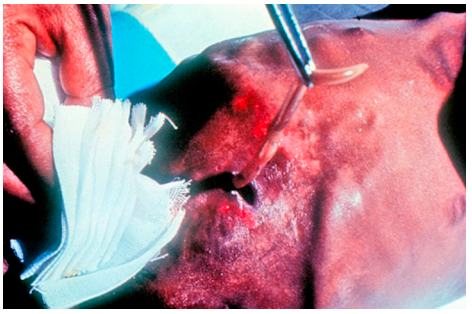

Fig 22. Extraction of *Ascaris lumbricoides*.

Life cycle

Loa loa, also known as African eye worm, is found in West and Central Africa. It is estimated that 3 to 13 million people were infected in 2010.[31] The 2 main signs of disease are localized subcutaneous swellings and migration of the worm across the conjunctiva. The vector of the disease is a deerfly from the genus Chrysops, which transmits the parasite when it bites a human, most commonly during the rainy season (Fig 4).

Presentation

Most infected people are asymptomatic, especially when they live in endemic areas. Travelers experience symptoms more commonly. Patients present with subcutaneous swellings on the limbs, known as Calabar swellings, which are localized, elastic, cold, transient, painless, pruritic, and migratory.[31] They are often found near the joints.

The disease can also present as recurrent migratory focal angioedema caused by adult filariae. A raised outline of the skin is occasionally visible, showing the underlying mature filariae. It may involve the limbs and large joints and may present with pain and pruritus. The periorbital area is often affected and the MF may also be seen in the conjunctiva (eye worm disease; Fig 15).

Diagnosis

Loiasis should be considered in patients with a history of travel to an endemic area who present with unexplained peripheral eosinophilia, ocular symptoms, and/or Calabar swellings. The standard diagnostic test is the demonstration of MF on a daytime, Giemsa-stained blood smear (Fig 16) or demonstration of an adult worm removed from subcutaneous or conjunctival tissue. Polymerase chain reaction testing for loiasis is approved in the United States.[32]

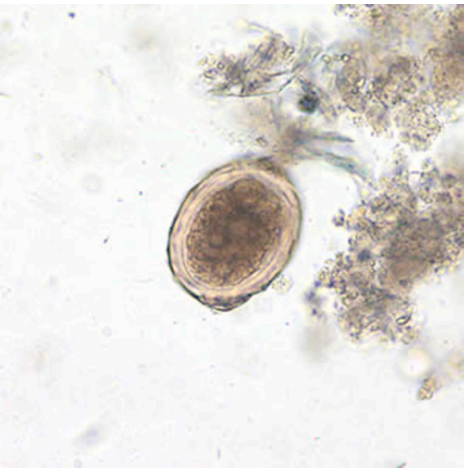

Fig 23. Fertilized egg of *Ascaris lumbricoides* in an unstained wet mount. Courtesy of the Centers for Disease Control and Prevention. (Original magnification: ×200.)

DRACUNCULIASIS

Key points

- **Dracunculiasis is transmitted by drinking stagnant water contaminated with copepods containing infective Guinea worm larvae**
- **Approximately 1 year after infection, a fertilized female worm migrates to the surface of the skin and induces an extremely painful papular lesion; when the infected patient soaks the lesion in water, the worm releases larvae, relieving the discomfort**
- **To remove the worm, it is slowly coiled out over the course of a few days to a month with a small rod, match, or stick**

Dracunculiasis, also known as Guinea worm disease, is a parasitic infection once common in the tropics that is caused by *Dracunculus medinensis*; in recent years it has been nearly eradicated. In 2013, there were 148 reported cases: 113 in south Sudan, 14 in Chad, 11 in Mali, 7 in Ethiopia, and 3 in Sudan.[33]

Life cycle

The life cycle begins with human ingestion of unfiltered water containing copepods (tiny aquatic crustaceans, approximately 2-3 mm long) that serve as intermediate hosts. After human ingestion, the copepods are killed by gastric juices and release larvae that penetrate the host stomach and small intestine, which provides an entryway into the abdominal cavity and retroperitoneal space. Here the larvae mature into adults and copulate. Adult females grow to 60 to 100 cm. All of the male worms die in the human host, but the females migrate to subcutaneous tissue. Here the females mature for approximately a year before epicutaneous migration occurs (Fig 17).

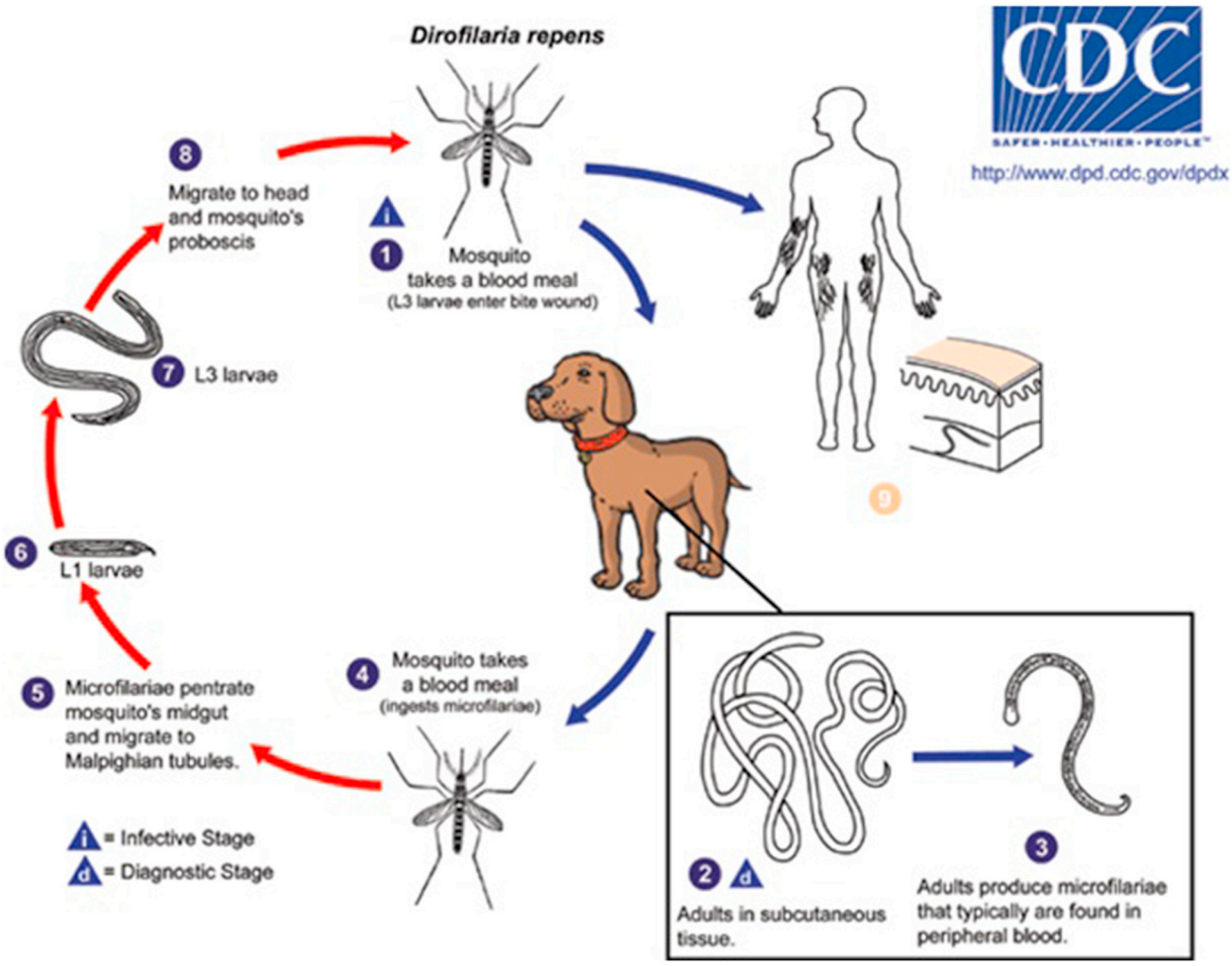

Fig 24. Life cycle of *Dirofilaria repens*. Courtesy of the Centers for Disease Control and Prevention.

Presentation

During subcutaneous migration, patients typically complain of intense pain localized to the path of travel. Patients may also complain of nonspecific symptoms, such as nausea, vomiting, fever, and syncope.

Approximately 1 year after initial ingestion and after epicutaneous migration, urticaria and an erythematous papulonodular lesion are noticed. The lesion is evanescent, being followed by a vesiculobullous lesion with surrounding induration, which causes the patient an intense burning sensation relieved by submerging the lesion in water. There is usually a distinct primary lesion, but a patient may have >20 worms extruding at any given time. Once the lesions are immersed in water, the adult female releases hundreds of thousands of Guinea worm larvae, leaving the water supply contaminated.[34,35]

If the worm ruptures in the subcutaneous tissue, it causes cellulitis or can heal with calcification. About half of patients have secondary bacterial infections at the site of the vesiculobullous lesion; this is a major cause of morbidity.[34]

Diagnosis

Diagnosis is made by clinical observation of a worm extruding from a skin lesion (Fig 18) or from a suspected ulcer with a wet smear revealing motile larvae on microscopic examination. Patients usually have eosinophilia with an increased erythrocyte sedimentation rate.

STRONGYLOIDIASIS

Key points

- **Strongyloidiasis is typically a gastrointestinal disorder; however, larvae may emerge to the patient's perirectal skin to produce a**

Table II. Other nematode infections[43-54]

Infection	Epidemiology and transmission	Presentation	Diagnosis
Ascariasis (Fig 22)	Most common helminthic infection worldwide; estimated prevalence rate in the US is 2%; infection in humans occurs with ingestion of water or food contaminated with fertilized Ascaris ova	Urticaria (most common); dermatographism; cutaneous manifestations are typically associated with the pulmonary disease termed Loeffler syndrome or Ascaris pneumonia; prevalence of dermatologic manifestations is approximately 20-25%	Eosinophilia; stool examination reveals characteristic trilayered ova (Fig 23)
Streptocerciasis	*Mansonella streptocerca* is confined to Central and West Africa; the disease is transmitted by biting midges (Culicoides midges; Fig 4)	Usually asymptomatic; most common dermatologic manifestations include pruritus, especially over the thorax and shoulder; lichenification; hypopigmented macules; and lymphadenopathy; does not cause subcutaneous nodules	Identification of MF in the skin; females are on average 27 mm in length; the MF are shorter and thinner than those in *Onchocera volvulus*; the posterior end of the MF may be bent like a shepherd's crook; patients typically have an eosinophilia
Dirofilaria	Humans are infected with dirofilaria larvae (Fig 24) through mosquito bites (usually Aedes or Culex); most common in the Mediterranean, but has been described in many areas, including the US	Subcutaneous nodule, either tender or nontender; occasionally migratory; may be associated with an abscess; commonly found on the eyelids, scrotum, breasts, arms, and legs	Histologic examination; species identification can be made by analysis of the length and morphology of the parasite; patients do not typically exhibit eosinophilia
Trichinosis	Trichinella is found worldwide and is a serious health concern in areas where raw or undercooked meat is consumed; pigs are the most common source of human infection, and raw or undercooked meat is the main mode of transmission; in the US, this is typically from consumption of home-prepared sausage	Myalgia is the most common complaint (~90% of cases); fever and weakness are also commonly reported; periorbital edema is the most common dermatologic manifestation; occasionally, a nonpruritic urticarial and morbilliform exanthem appears during the parenteral phase in week 3 of infection; the clinical triad of fever, myalgia, and periorbital swelling should alert the dermatologist to the disease; migration to the distal extremities may result in subungual splinter hemorrhages	Eosinophilia; increased creatine phosphokinase; screening ELISA test detects anti-Trichinella IgG; confirmatory test: indirect immunofluorescence

ELISA, Enzyme-linked immunosorbent assay; *IgG*, immunoglobulin G; *MF*, microfilariae.

distinctive cutaneous eruption termed "larva currens"

- **Larva currens is characterized by a serpiginous, raised, erythematous track that migrates at 5 to 15 cm per hour, much faster than the creeping eruption of cutaneous larval migrans**
- **Hyperinfection with Strongyloides can cause a rapidly progressive and diffuse petechial "thumbprint purpura" eruption that is fatal if untreated**
- **Ivermectin is the treatment of choice**

Strongyloidiasis is caused by the human parasite *Strongyloides stercoralis*. Strongyloidiasis is

Table III. Treatment of nematode infections[55-59]

Disease	Treatment*	Dosing	Comment
Cutaneous larva migrans	Ivermectin†	0.15-0.2 mg/kg QD PO × 1 or 2 days	The disease is essentially self-limited, with antihelminthic therapy relieving symptoms and preventing secondary bacterial infection
Onchocerciasis	Ivermectin	0.15-0.2 mg/kg PO × 1 dose; may repeat in 3-12 months for the life of an adult worm	Ivermectin reduces skin microfilarial worms, but it does not eradiate infection.[55]
	Doxycycline	100 mg QD PO × 6 wks	Doxycycline kills *Wolbachia sp.*, a bacterium necessary for the nematode to reproduce[56]
	Surgical removal (nodulectomy)		
Gnathostomiasis	Albendazole	400-800 mg PO QD × 21 days[57]	
	Ivermectin (for pediatric patients)	0.2 mg/kg PO × 2 doses taken 48 hrs apart	
	Surgical removal		
Filariasis	DEC	200 mg PO q12h × 12 days, repeat 10 days later, or 6 mg/kg/day PO × 12 days (pediatric dose), repeat 10 days later	DEC is no longer approved by the FDA, but physicians can obtain the medication from the CDC after the diagnosis has been confirmed; this therapy should be avoided in patients with concurrent onchocerciasis, as it can worsen eye disease; DEC should also be avoided in patients with loiasis because encephalopathy or death may ensue. Patients with lymphedema or elephantiasis will not likely benefit from DEC because most of these patients are not actively infected with the parasite[58]
	Doxycycline	200 mg QD PO × 6-8 wks	Doxycycline kills *Wolbachia sp.*, a bacterium necessary for the nematode to reproduce
	Ivermectin	0.15-0.2 mg/kg PO × 1 dose	Treatment of choice for patients with concurrent onchocerciasis
Loiasis	DEC	200 mg QD PO × 21 days	
	Albendazole	200 mg BID PO × 21 days	
	Surgical removal		Effective if there is only a single adult worm
Dracunculiasis	Thiabenazole	25-37.5 mg/kg PO BID × 3 days	Pharmacologic therapy can be used to decrease inflammation to aid worm removal, but these therapies are not parasiticidal
	Metronidazole	200-400 mg PO TID × 3 days	
	Surgical removal		
Strongyloidiasis	Ivermectin	0.2 mg/kg QD PO × 2 days	
Ascariasis	Albendazole	400 mg PO × 1 dose	
Mansonella	DEC	6 mg/kg/day PO × 12 days	Before administering DEC, onchocerciasis should be excluded because of the possible exacerbation of ocular disease in these patients
	Ivermectin	0.15 mg/kg × 1	Reduces microfilarial load, but efficacy is unknown[59]

Continued

Table III. Cont'd

Disease	Treatment*	Dosing	Comment
Dirofilaria	Surgical removal		Often the lesions calcify without any treatment
Trichinosis	Albendazole	5 mg/kg/day × 7 days	
	Mebendazole	5 mg/kg/day × 8 to 14 days	
	Thiabendazole	25 mg/kg/day for 8 to 14 days	
	Prednisone	30-60 mg QD PO × 10-14 days	Used in conjunction with antihelmintics to help control inflammatory response

BID, Twice daily; *CDC*, Centers for Disease Control and Prevention; *DEC*, diethylcarbazine; *FDA*, US Food and Drug Administration; *PO*, per os; *QD*, once daily; *TID*, three times daily.
*The preferred treatment is listed first.
†Ivermectin safety in children <15 kg is not known and the drug is not recommended for pregnant or lactating females.

a worldwide disease most commonly found in tropical and subtropical regions that causes mild symptoms in immunocompetent individuals but severe and life-threatening symptoms to immunocompromised individuals.

Life cycle

The life cycle begins with direct contact with free-living filariform larvae, usually through contaminated soil. The larvae penetrate the skin on contact and migrate through the body, eventually reaching the small intestine where they mature into adult nematodes and lay their eggs. Noninfective larvae hatch from the eggs and are then either excreted in stool or remain in the intestinal tract to develop into the infective filariform larvae, which migrate towards the perianal opening. There they penetrate the skin and rapidly extend outward, causing cutaneous manifestations.

Unique among helminthic parasites, *S stercoralis* is able to complete its life cycle inside of the human host. Autoinfection occurs when the filariform larvae enter the circulatory system, are carried into the lungs, and are then swallowed into the intestinal tract, repeating the cycle.[36]

Presentation

Most patients with strongyloidiasis are asymptomatic or do not experience major symptoms. Acute infection is generally characterized by gastrointestinal and pulmonary symptoms. Chronic infection is characterized by dermatologic symptoms. Other patients have eosinophilia that persists for years with the absence of any symptoms. As the larvae migrate out of the intestinal tract, they may reach the perianal skin and move outward. Here they cause a classic urticarial eruption that is centered perianally and extends to the buttocks, thighs, and abdomen in a linear or serpiginous pattern. The rash is thought to be an allergic response to the migrating larvae. Specific to strongyloidiasis is the rate at which the rash extends, noted to be from 5 to 15 cm per hour and gives rise to the name "larva currens" (Fig 19). This rash may last a few hours to days, but autoinfection cycles can cause the rash to recur for weeks to years.

In immunocompromised individuals, hyperinfection with Strongyloides can cause a rapidly progressive and diffuse petechial "thumbprint purpura" eruption, characteristically radiating from the periumbilical area (Fig 20).[37-40] These skin manifestations are thought to be attributed to dermal invasion of a large number of larvae that migrate through the vessel walls.[41] Hyperinfection is usually present with other systemic involvement, such as sepsis or septic shock, and signifies a poor prognosis with high rates of fatality.

Diagnosis

The criterion standard for diagnosis of strongyloidiasis is microscopic stool examination to visualize the larvae. The serum immunoglobulin E level is usually elevated, in line with other migrating helminth infections. Enzyme-linked immunosorbent assay for specific anti-Strongyloides immunoglobulin G antibodies is sometimes used as a screening assay.[42] On histologic examination, the filariform larvae may be seen (Fig 21).

CONCLUSION

Other nematode infections with cutaneous manifestations include ascariasis, streptocerciasis, dirofilaria, and trichinosis (Figs 22 to 24 and Table II). In conclusion—and considering that there is no vaccine available to prevent nematode infections—the most effective management is treatment (Table III) and prevention. Dracunculiasis is the second (after smallpox) human infectious disease scheduled for eradication and the first infectious disease to be eradicated without the use of a vaccine. Prevention of other nematode

infections depends on the epidemiology: controlling arthropod vectors for onchocerciasis, filariasis, streptocerciasis, dirofilariasis and loiasis; cooking food thoroughly for gnathostomiasis and trichinosis, wearing shoes to prevent cutaneous larval migrans and strongyloidiasis, and providing clean drinking water for ascariasis. Therefore, most improvements in sanitary conditions and public health will lead to reductions in nematode infections.

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