Cutaneous Larva Migrans: “The Creeping Eruption”

Background
Cutaneous larva migrants (CLM), frequently termed “creeping eruption,” is a parasitic skin infection that is caused by the filariform larvae of various animal hookworm nematodes. CLM has a worldwide distribution wherever humans have had skin contact with soil contaminated with infected animal feces. The disease most commonly occurs in subtropical and tropical regions, but may also occur in temperate climates particularly during the summer months and during rainy seasons. In the United States, CLM is seen in individuals living in the southeastern states, Florida and the Gulf Coast states, in travelers returning from sandy beaches and in military personnel returning from tropical postings. Children develop the disease by walking barefoot in sandy areas or playing in dirt or sandboxes that contain infected animal feces. Electricians, plumbers, utility workers and pest exterminators who have contact with soil under houses or at construction sites are at risk, as are fishermen, hunters, farmers and gardeners who handle contaminated soil.

Causative Agents

*Ancylostomabraziliense*, a hookworm of wild and domestic dogs and cats is the most commonly identified etiologic agent of CLM. *A. braziliense* is distributed throughout the tropics and subtropics, especially on the warm sandy beaches of the southeastern and Gulf
Coast states, the Caribbean and Southeast Asia where dogs and cats are permitted to defecate. *Ancylostomacaninum* (dog hookworm), *Ancylostomaceylanicum* (dog and cat hookworm) and *Ancylostomatubaeform* (cat hookworm) may also produce cutaneous lesions. Whereas the skin lesions of *A. braziliense* may persist for months, the skin lesions that are seen with other *Ancylostoma* species resolve within several weeks. A number of other nematodes have been associated with CLM-like lesions. *Strongyloides* species such as *S. papillosus*, *S. westeri*, *S. stercoralis*, *S. procyonis* and *S. myopotami*, nematodes found in the small intestine of mammals, migrate more quickly in human skin than hookworm larva to form skin eruptions called *larva currens* (“racing larva”). *Gnathostoma* species, a dog and cat roundworm found in Southeast Asia and *Dirofilaria repens*, a filarial nematode of dogs, *Medical Parasitology* cats and wild carnivores, can travel through the skin and cause dermatitis, swelling and subcutaneous nodules. *Uncinariastenocephala* (dog hookworm) and *Bunostomumphlebotomum* (cattle hookworm) may also cause cutaneous disease. *Ancylostomaduodenale* and *Necatoramericanus*, human hookworms, that, upon larval migration in the skin, produce a pruritic dermatitis (“grounditch”) similar to CLM of animal hookworms. Free-living nematodes such as *Pelodermastrongyloides* have also been described as a rare cause of cutaneous infection in humans.
Life Cycle
Unlike the classical hookworm life cycle, the cycle of the organisms that are typically associated with CLM is much abbreviated. *A. braziliense* third stage infective larvae (L3) enter the epidermis and migrate laterally in epidermis, generally unable to penetrate the basement membrane of the epidermal dermal junction. Humans are thus incidental dead-end hosts.
Disease Signs and Symptoms

The most common portals of entry by the larvae are the exposed areas of the body such as the dorsum of the feet, lower legs, arms and hands. The buttocks, thighs and abdomen also may be involved, probably due to lying directly on contaminated sand. CLM also occurs in the interdigital spaces of the toes, the anogenital region, knees and rarely on the face. Symptoms usually occur within the first hours of larval infection, although, occasionally, the larvae may lie dormant for several weeks. The first sign of infection is a stinging, tingling or burning sensation at the site of larval entry, followed by the development of an edematous, erythematous pruritic papule. The larvae migrate laterally from the papule and form raised 2-4 mm wide serpiginous tracks. These tracks mark the migratory route of the larvae and may advance from a few millimeters to several centimeters each day, hence the name “creeping eruption.” As they burrow, the larvae produce hydrolytic enzymes that provoke the intense inflammatory reaction that characterizes CLM. In heavy infections, an individual may have hundreds of tracts. Severe inflammatory reactions may cause such an intense pruritis that individuals are unable to sleep, develop anorexia and even become psychotic. Secondary bacterial infections such as impetigo or cellulitis from scratching the skin are common complications.

CLM is usually a self-limited disease. The larvae, unable to complete their life cycle, die in the epidermis within several weeks to months if left untreated. There are reports of larvae that have migrated for over one year. The skin lesions ultimately resolve
although there may be scarring. Rarely larva may migrate past the dermis to cause myositis, pneumonitis (Loffler’s syndrome) or an eosinophilic enteritis (viz., *A. caninum*) of the small intestine. A pruritic folliculitis is another uncommon form of CLM that presents with serpiginous tracks interspersed with papules and pustules confined to a particular area of the body, usually the buttocks.

**Cutaneous Larva Migrans**

**Diagnosis**

The diagnosis of CLM is based on a history of exposure and the characteristic clinical appearance of the skin eruption. There may be a delay in diagnosis in chronic cases due to superimposed allergic dermatitis, secondary bacterial infection or lack of recognition of CLM by health care personnel. Peripheral eosinophilia and increased IgE levels are found in a minority of patients. Skin biopsies are usually not effective at establishing the diagnosis. Histologic examination usually reveals only an eosinophilic infiltrate or a nonspecific inflammatory response, although, occasionally, a skin biopsy taken at the leading edge of the track may contain alarva trapped in a follicular canal, stratum corneum or dermis. The differential diagnosis of CLM should also include cercarial dermatitis (“swimmer’s itch”), migratory myiasis, scabies, jelly fish sting, photoallergic dermatitis, epidermal dermatophytosis, erythema chronicum migrans of Lyme disease and photoallergic dermatitis. Vesicular lesions may be mistaken for viral infections or phytophotodermatitis.
Prevention and Prophylaxis

CLM can be prevented by avoiding skin contact with soil contaminated withinfected animal feces. In geographic areas where the infection is endemic, one should avoid touching soil with bare hands, walking barefoot or lying directly on moist,warm, shady soil or warm, dry, sandy beaches protected from tidal movement. Beaches should also be kept free of dogs and cats. Pets should be examined.

Lecture 2 Dr. Jabar Etaby

Visceral Larva Migrans

VLM occurs primarily in young and preschool children. Most infections are asymptomatic, but fulminant disease and death do occur. Children come to medical attention with unexplained prolonged fever, cough, hepatosplenomegaly, wheezing and eosinophilia. Other clinical signs and symptoms include lymphadenopathy, skin lesions, pruritus, anemia, failure to thrive, decreased appetite, nausea, vomiting, headache and pneumonia, as well as behavioral and sleep disturbances. In children with toxocariasis, pica or geographia are common. Myocarditis, respiratory failure or seizures may complicate overwhelming infection. Other less frequently reported complications included multiple ecchymosed with eosinophilia, pyogenic live abscess, urticaria or prurigo, HenochSchonlein purpura, nephrotic syndrome, secondary thrombocytosis and eosinophilic arthritis. There is a report of VLM mimicking lymphoma with hilar and mediastinal
lymphadenopathy and another of systemic vasculitis with lymphocytic temporal arteritis. Both of these two complications occurred in patients over 60 years of age. Toxocariasis has been suggested to be an environmental risk factor for asthma among children living in urban areas, but supportive evidence for this hypothesis is lacking. Central nervous system involvement is a rare complication reported more frequently in adults. Toxocariasis should be considered as a causative agent in patients with eosinophilic meningoencephalitis or meningitis. *T. canis* has been reported to cause epileptic seizures, particularly late-onset partial epilepsy.

**Ocular Larva Migrans**

Ocular toxocariasis occurs primarily in young adults and older children who present with unilateral visual loss over days to weeks. OLM follows entrapment of a larva in the eye causing an intense eosinophilic inflammatory reaction. Posteriorpole granuloma is the most common form of OLM in children between 6 and 14 years and causes decreased vision. Peripheral granuloma is usually seen at an older age in association with macular heterotropia, strabismus and decreased vision. Endophthalmitis occurs in younger children aged 2 to 9 years in whom there is marked visual impairment with evidence of vitritis and anterior uveitis. Retinal detachment may be seen on fundoscopic examination. OLM should be included in the differential diagnosis of any child with leukocoria.
Diagnosis
The presence of eosinophilia in a child with unexplained fever, abdominal pain, hepatosplenomegaly and multisystem illness raises the possibility of VLM, especially if there is a history of geographia or pica and contact with puppies. For a child with unilateral visual loss and strabismus, a diagnosis of OLM must be excluded. In OLM the blood eosinophil count is frequently not elevated. Leukocytosis, hypergammaglobulinemia, increased anti-Toxocara IgE serum concentration and elevated isohemagglutinin titers to A and B blood group antigens may be present in VLM. The diagnosis of both VLM and OLM is usually based on serologic tests. However, serologic tests do not reliably distinguish between recent and past infection.

The most frequently performed test is the enzyme-linked immunosorbent assay (ELISA) which uses Toxocara excretory-secretory antigens of the second-stage larvae. *Baylisascarisasis and Toxocaraisis*. This test is sufficiently specific to be the best indirect diagnostic assay. At a titer of greater than 1:32 the sensitivity of this test for diagnosing VLM is about 78%. The ELISA is less reliable for the diagnosis of OLM. The presence of elevated vitreous and aqueous fluid titers relative to serum titers supports the diagnosis of OLM.

Microscopy
A definitive diagnosis of VLM is based upon the visualization of the larvae in infected tissue such as lung, liver, or brain. In OLM the larvae may be seen in the enucleated eye.

Molecular Diagnostics and Radiographic
In OLM, ultrasound biomicroscopy has been used to detect the morphologic changes of peripheral vitreoretinal toxocariasis. Ultrasonographic findings of hepatic toxocariasis complicating VLM may include ill-defined focal lesions, hepatosplenomegaly, the presence of biliary sludge and dilatation and periportal lymphadenopathy. If present, follow-up CT scan or MR imaging should be considered following treatment. In patients with cerebral granulomatous toxocariasis, multiple subcortical, cortical, or white matter lesions that were hypoattenuating on CT scan, hyperintense on T2-weighted MR images and homogeneously enhancing have been reported. These findings are nonspecific. It has been suggested, nonetheless, that serial MR imaging may be used to monitor the course of disease treated with anthelminthic therapy.

Follow-Up after Treatment
Within a week of treatment there is usually a rise in eosinophilia accompanied by improvement in clinical parameters. By 4 weeks post-therapy, eosinophilia has usually resolved and the antitoxocara IgE has become negative.

Prevention and Control
Exposure to toxocariasis occurs primarily in overcrowded urban areas where children are in close contact with dogs and cats. Public education and control efforts should be directed at limiting exposure of children to soil contaminated with *Toxocara* eggs in public parks, playgrounds, sandboxes, home gardens and other areas where
children congregate. Dogs and cats should be restricted from entering public areas where children play. Dog owners should clean up after their pets have defecated and have their pets wormed regularly. Children should wash their hands after playing in a park or coming in close contact with dogs, especially puppies and cats.
Filariasis

Generalized Life Cycles of Filarids

1. Infective microfilariae transmitted to human by biting insect intermediate host

   - Culex, Anopheles
   - Manson, Anopheles
   - Brugia malayi
   - Wuchereria bancrofti

   Intermediate host

2. Microfilariae ingested by insect with blood meal. Microfilariae develop in insect to infective stage

   - In lymphatics
     - Brugia malayi
     - Wuchereria bancrofti

   - In subcutaneous tissue
     - Loa loa
     - Onchocerca volvulus

   Intermediate host

   - Chrysops
   - Simulium
   - Onchocerca volvulus
   - Loa loa
Onchocerca volvulus (blinding worm)

Life cycle

No periodicity

Subcutaneous nodule
Adult female & male filariae

Cellular reaction, then fibrosis

Larvae mature to adults in subcutaneous tissue

Microfilariae migrate to other sites, not to enter bloodstream

Maturation time
5 days or more

Dermatitis

Microfilariae

Unsheathed—tail is tapered and free of nucleus

150–300 μm x 3–5 μm

Adults

Diameter 6.42 cm, x 130–210 μm

L 14–60 cm, x 375–400 μm

Pathology and Clinical features

Fibrous nodules develop around the adult worms, especially over the iliac crest. There may be some lymphatic obstruction; elephantiasis has been noted in Africa. The microfilariae cause itching, excoriation, urticaria, depigmentation, lichenification, 'sowda' and lymphadenopathy. When invading the eye, they can cause inflammatory lesions in any part of the eye such as sclerotic keratitis, choroidoretinitis and optic atrophy. Blindness may ensue.

Where microfilariae cannot be demonstrated, a Mazzotti test (DEC provocation test) can be useful.

Laboratory diagnosis

Eosinophilia

Adult worms can be detected in excised nodules, microfilariae in the anterior chamber of the eye (slit lamp), skin snips and rarely in blood and urine.

Specific serodiagnosis by ELISA and PCR for parasite DNA on skin samples is in use.

Distribution

17 million infected worldwide.

Nematode (round) worms 15
**Epidemiology:** In Africa onchocerciasis is prevalent throughout the eastern, central and western Africa, where it is the major cause of blindness. In the Americas it is found in Guatemala, Mexico, Colombia and Venezuela. The disease is confined to neighborhoods of low elevation with rapidly flowing small streams where black flies breed. Man is the only host.

**Morphology:** Adult female onchocerca measure 50 cm x 300 µm, male worms are much smaller. Infective larvae of *O. volvulus* are 500 µm x 25 µm.

**Life cycle:** Infective larvae are injected into human skin by the female black fly (*Simulium damnosum*) where they develop into adult worms in 8-10 months. The adults usually inhabit as group of worms (2-3 females and 1-2 males) tightly coiled. The gravid female releases microfilarial larvae, which are usually distributed in the skin.

They are picked up by the black fly during a blood meal. The larvae migrate from the gut of the black fly to the thoracic muscle where they develop into infective larvae in 6-8 days. These larvae migrate to the head of the fly and then are transmitted to a second host.

**Diagnosis:** Diagnosis is based on symptoms, history of exposure to black flies and presence of microfilaria in nodules.

**Treatment and control:** Diethylcarbamazine is effective in killing the worm. Destruction of microfilaria produces extreme allergic reaction which can be controlled with corticosteroids. Prevention measures include vector control, treatment of infected individuals and avoidance of black fly.
Wuchereria bancrofti and W. (Brugia) malayi (elephantiasis)
**Epidemiology:** *W. bancrofti* is strictly a human pathogen and is distributed in tropical areas worldwide, whereas *B. malayi* infects a number of wild and domestic animals and is restricted to South-East Asia. Mosquitoes are vectors for both parasites.
Morphology: These two organisms are very similar in morphology and the disease they cause. Adult female *W. bancrofti* found in lymph nodes and lymphatic channels are 10 cm x 250 µm whereas males are only half the size. Microfilaria found in blood are only 260 µm x 10 µm. Adult *B. malayi* are only half the size and its microfilaria are only slightly smaller than *W. bancrofti*.

Life cycle: Filariform larvae enter the human body during the mosquito bite and migrate to tissues. There they may take up to a year to mature and produce microfilaria which migrate to lymphatics and, at night, enter the blood circulation. Mosquitos are infected during the blood meal. The microfilaria grow 4-5 fold in mosquito in 10-14 days and become infective for man.

Symptoms: Symptoms include lymphadenitis and recurrent high fever, every 8-10 weeks, which lasts 3-7 days. There is progressively lymphadenitis due to inflammatory response to the parasite lodged in the lymphatic channels and tissues. As the worm dies, the reaction continues and produces a fibro-proliferative granuloma which obstructs lymph channels and causes lymphedema and elephantiasis. The stretched skin is susceptible to traumatic injury and infections. Microfilaria cause eosinophilia and some splenomegaly. Not all infections lead to elephantiasis.

Prognosis, in the absence of elephantiasis, is good.
**Diagnosis:** Diagnosis is based on history of mosquito bite in endemic areas, clinical findings, and presence of microfilaria in blood samples collected at night.

**Treatment and control:** Diethylcarbamazine quickly kills the adultsworms or sterilizes the female. It is given 2 gm/kg orally for 14 days. Steroids are help alleviate inflammatory symptoms. Cooler climate reduces the inflammatory reaction.
Loasis is limited to the areas of African equatorial rain forest. The incidence in endemic areas varies greatly (8-75 percent). The larger, female organism is 60 mm x 500 µm; males are 35 x 300 µm in size. The circulating microfilaria are 300 µm x 7 µm; the infective larvae in the fly are 200 µm x 30 µm. The life cycle of Loa loa is
identical to that of onchocerca except that the vector for this worm is the deer fly. The infection results in subcutaneous (Calabar) swelling, measuring 5-10 cm in diameter, marked by erythema and angioedema, usually in the extremities. The organism migrates under the skin at a rate of up to an inch every two minutes. Consequently, the swelling appears spontaneously, persists for 4-7 days and disappears, and is known as fugitive or Calabar swelling. The worm usually causes no serious problems, except when passing through the orbital conjunctiva or the nose bridge. The diagnosis is based on symptoms, history of deer fly bite and presence of eosinophilia. Recovery of worm from the conjunctiva is confirmatory.

Treatment and control are the same as those for onchocerciasis.

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<th>Wuchereriabancrofti; W. brugiamalayi (elephantiasis)</th>
<th>Mosquito bite</th>
<th>Recurrent fever, lymphadenitis, splenomegaly, lymphedema, elephantiasis</th>
<th>Medical history, physical examination, microfilaria in blood (night sample)</th>
<th>Mebendazole; Diethylcarbamazine</th>
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<td>Onchocerca volvulus</td>
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<td>Nodular and erythematous dermal lesions, eosinophilia,</td>
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