



Worms You Should Know

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Disclosures of Financial Relationships with Relevant Commercial Interests

- None

Question #1

28-year-old female

- Recurrent crampy abdominal pain for several months
- Just returned home after living for two years in Tanzania
- Colonoscopy reveals small white papules
- Biopsy reveals an egg with eosinophilic granulomatous inflammation

Which is the most likely diagnosis?

- A. Entamoeba histolytica
- B. Ascaris lumbricoides
- C. Wuchereria bancrofti
- D. Schistosoma mansoni
- E. Paragonimus westermani

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Major Helminth Pathogens

TREMATODES

Blood flukes

Schistosoma mansoni
Schistosoma japonicum
Schistosoma haematobium

Liver flukes

Fasciola hepatica
Clonorchis sinensis
Opisthorchis viverrini

Lung flukes

Paragonimus westermani

Intestinal flukes

Fasciolopsis buski
Metagonimus yokagawai

CESTODES

Intestinal tapeworms

Taenia solium
Taenia saginata
Diphyllobothrium latum
Hymenolepis nana

Larval cysts

Taenia solium
Echinococcus granulosus
Echinococcus multilocularis

NEMATODES

Intestinal

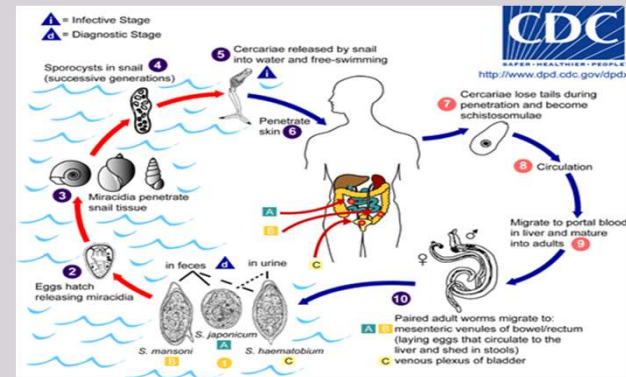
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Gnathostoma spinigerum
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SEE ENLARGED SLIDE FOLLOWING ENTIRE PRESENTATION

Schistosomiasis Life Cycle



Acute Schistosomiasis

Cercarial Dermatitis (Swimmer's Itch)

- Urticarial plaques and pruritic papules
- Occurs upon re-exposure to cercariae penetrating skin in a sensitized individual
- Symptoms develop minutes to days after water exposure
- Can occur with human or avian schistosomes



Katayama Fever

- Fever, myalgias, abdominal pain, headache, diarrhea, urticaria
- Occurs in previously unexposed hosts
- Symptoms typically start 3 - 8 weeks after water exposure
- Eosinophilia, elevated AST and alkaline phosphatase
- No reliable way to confirm diagnosis acutely as serology and stool O/P frequently negative

Chronic Schistosomiasis



Intestinal and hepatosplenic disease

(*S. mansoni* + *Sj*, *Si*, *Smk*, *Sh/b*)

- Granulomatous colitis
- Portal hypertension

Genitourinary disease (*S. haematobium* + *Sh/b*)

- Granulomatous cystitis
- Bladder fibrosis and cancer
- Obstructive uropathy

Pulmonary Disease (*Sm*, *Sh*, *Sj*)

CNS disease

- CNS disease (eggs to brain/spinal cord, esp *S. japonicum*)

Schistosoma species

- *S. mansoni* (*Sm*)
- *S. japonicum* (*Sj*)
- *S. intercalatum* (*Si*)
- *S. mekongi* (*Smk*)
- *S. haematobium* (*Sh*)
- *S. haematobium/S. bovis hybrid* (*Sh/b*)

From Senegal, outbreak 2013 in Corsica, France

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Schistosomiasis

Chronic genital disease

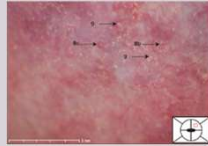
Increasingly recognized
Primarily due to *S. haematobium*

Women (vaginal and cervical lesions)

- Pelvic pain
- Dysmenorrhea
- Dyspareunia
- Post-coital bleeding
- Endometritis/salpingitis

Men

- Epididymitis
- Prostatitis



Sand Grains



Sandy Yellow Patches



Abnormal Vessels



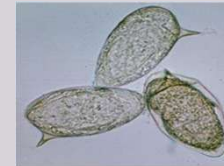
Rubbery Papules

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WHO Female Genital Schistosomiasis Pocket Atlas

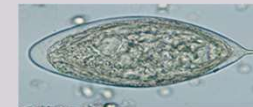
Schistosome Eggs

S. mansoni
(Lateral spine)



CDC DPDx image library

S. haematobium
(Terminal spine)



CDC DPDx image library

Question #2

A 25-year-old Peace Corps worker in Madagascar reports passing thin, white, flat tissue fragments in her stool. The microbiology lab reports the tissue fragments are proglottid segments of *Taenia solium*.

What is a long-term complication that can occur as a result of infection with the larval form of this parasite?

- A. HTLV-1 infection
- B. Bladder cancer
- C. Appendicitis
- D. Liver abscess
- E. Seizures

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<u>TREMATODES</u>	<u>CESTODES</u>	<u>NEMATODES</u>
Blood flukes <i>Schistosoma mansoni</i> <i>Schistosoma japonicum</i> <i>Schistosoma haematobium</i>	Intestinal tapeworms <i>Taenia solium</i> <i>Taenia saginata</i> <i>Diphyllobothrium latum</i> <i>Hymenolepis nana</i>	Intestinal <i>Ascaris lumbricoides</i> <i>Ancylostoma duodenale</i> <i>Necator americanus</i> <i>Trichuris trichiura</i> <i>Strongyloides stercoralis</i> <i>Paracappilaria philippinensis</i> <i>Enterobius vermicularis</i>
Liver flukes <i>Fasciola hepatica</i> <i>Clonorchis sinensis</i> <i>Opisthorchis viverrini</i>	Larval cysts <i>Taenia solium</i> <i>Echinococcus granulosus</i> <i>Echinococcus multilocularis</i>	Tissue Invasive <i>Wuchereria bancrofti</i> <i>Brugia malayi</i> <i>Onchocerca volvulus</i> <i>Loa loa</i> <i>Trichinella spiralis</i> <i>Angiostrongylus cantonensis</i> <i>Anisakis simplex</i> <i>Toxocara canis/cati</i> <i>Baylisascaris procyonis</i> <i>Gnathostoma spinigerum</i> <i>Dracunculus medinensis</i>
Lung flukes <i>Paragonimus westermani</i>		
Intestinal flukes <i>Fasciolopsis buski</i> <i>Metagonimus yokagawai</i>		

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Taenia Life Cycle

The diagram illustrates the life cycle of *Taenia* species, involving humans and intermediate hosts (pigs and cattle).

Stages:

- Humans infected by ingesting raw or undercooked infected meat** (4). This leads to the adult stage in the small intestine.
- Adults in small intestine** (6). The scolex attaches to the intestine.
- Eggs or gravid proglottids in feces and passed into environment**. This includes illustrations for *T. saginata* and *T. solium*.
- Cattle (*T. saginata*) and pigs (*T. solium*) become infected by ingesting vegetation contaminated by eggs or gravid proglottids** (2).
- Oncospheres hatch, penetrate intestinal wall, and circulate to musculature** (5). This leads to the encysted stage in muscle.
- Oncospheres develop into cysticerci in muscle** (3).

Legend:

- ▲ = Infective Stage
- ◆ = Diagnostic Stage

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Taenia Life Cycle

Taenia solium

- Tapeworm is acquired by eating larvae in pork
- Adult tapeworm causes few symptoms

Taenia saginatum

- Acquired by eating larvae in undercooked beef
- Causes few symptoms
- Can grow to 10 m

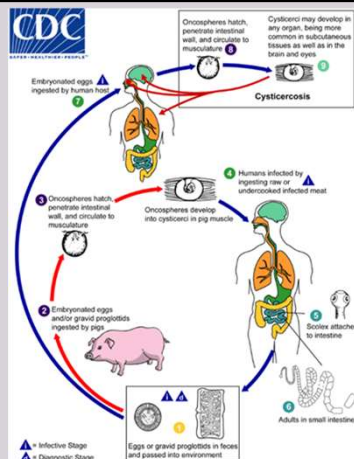
Diphyllobothrium latum (can grow > 10 m)

- Acquired by ingesting fish with larvae
- ***B12 deficiency in up to 40% of patients**

Dx: Eggs/proglottids in stool **Rx:** Praziquantel (not FDA-approved)

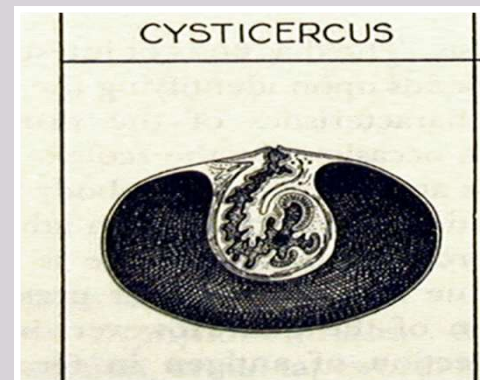


For some cestodes, humans can be infected by the larval stages, and this can cause severe pathology.



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Cysticercus: a fluid filled bladder containing the invaginated head (scolex) of the larval form of a tapeworm



Neva and Brown, Basic Clinical Parasitology 6th Edition

Neurocysticercosis



Neurocysticercosis

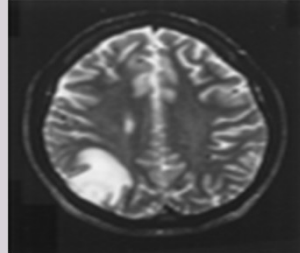
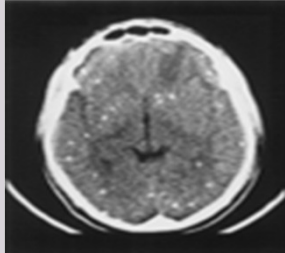
Can cause:

- Seizures
- Hydrocephalus
- Headaches
- Focal neurologic deficits

Neurocysticercosis

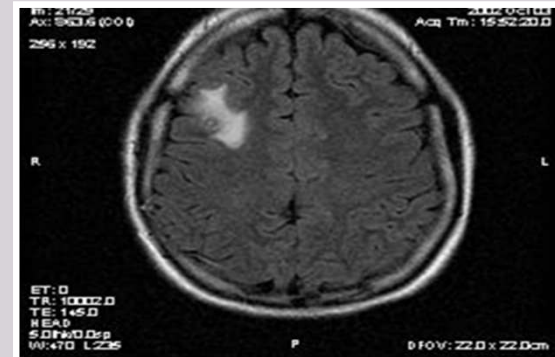
Perilesional edema – typically occurs around dying cysts and is a frequent finding on initial presentation of seizure or terrible headache.

Multiple old calcifications



Cysticercosis

Single Lesion Disease is Diagnostic Challenge



Neurocysticercosis

Diagnosis:

Definitive = tissue biopsy, multiple cystic lesions each with scolex on imaging, retinal cysticercus on funduscopy

Presumptive = suggestive lesions on imaging

Cysticercosis serology → supportive (sensitive if high burden of disease)

qPCR and antigen testing of CSF → sensitive for subarachnoid and intraventricular neurocysticercosis, and can be used to help gauge duration of treatment (available at NIH, contact Dr. Elise O'Connell occonnellem@mail.nih.gov)

Treatment:

Medical therapy decreases risk of future seizures, but has immediate risk of increasing seizures/brain inflammation

If **hydrocephalus** or **diffuse cerebral edema**: initial treatment with steroids and/or surgery (not anti-parasitic Rx)

If no increased ICP: 1-2 viable cysts → albendazole for 1-2 viable cysts

> 2 viable cysts → albendazole + praziquantel

AND corticosteroids started before anti-parasitic therapy

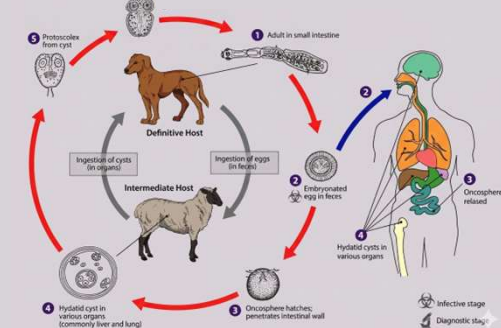
****2017 IDSA Guidelines for Diagnosis and Treatment of Cysticercosis****

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Echinococcus granulosus

DPDx

Adult worms (3-6mm long) live in dog intestines



Humans =
Accidental hosts

Infected by ingestion of
eggs in dog feces

SEE ENLARGED SLIDE FOLLOWING ENTIRE PRESENTATION

Echinococcus granulosus

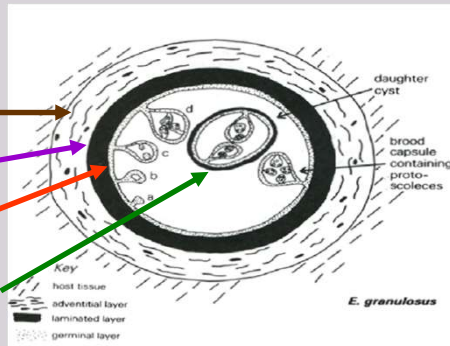
Hydatid cyst = "watery vessel"

Surrounding inflammatory response of
fibrosis and chronic inflammation

Outer **acellular laminated layer**

Inner, **nucleated germinal layer**
(PLURIPOTENTIAL TISSUE!)

Internal cystic fluid and **daughter cysts**



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Echinococcus and Hydatid Disease 1995

Echinococcus granulosus Presentation

Most cysts (65%) in the liver

25% in the lung, usually in the right lower lobe

Rest occur practically everywhere else in the body

Common Presentations

- Allergic symptoms/anaphylaxis due to cyst rupture after trauma
- Cholangitis and biliary obstruction due to rupture into biliary tree
- Peritonitis b/c intraperitoneal rupture
- Pneumonia symptoms due to rupture into the bronchial tree

Uncommon Presentations

- Bone fracture due to bone cysts
- Mechanical rupture of heart with pericardial tamponade
- Hematuria or flank pain due to renal cysts

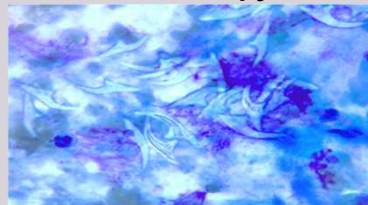
Echinococcus granulosus Diagnosis

Radiology



Clinical Radiology (2006) 61, 737-748

Microscopy



Serology

IgG ELISA about 85% sensitive for liver cysts of *E. granulosus*

Only 50% sensitive in cases of single pulmonary cyst

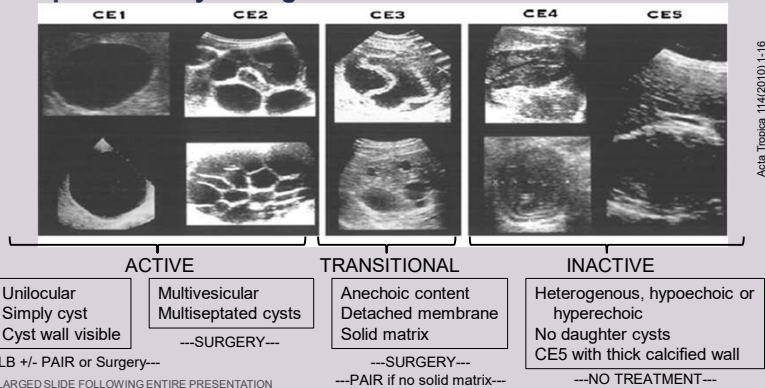
Echinococcus granulosus Treatment

Reasons for not spilling cyst contents

1. Anaphylaxis may occur
2. Spilled protoscolecex can reestablish infection

Typically treat with albendazole for several days
before surgery or PAIR (usually 3d-1wk before, and 1-3 months
after)

Cystic Echinococcus Treatment Depends on Cyst Stage



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Intestinal Helminths - Lifecycles

Strongyloides and Hookworms

SKIN → LUNGS → GUT

Ascaris

INTESTINE → LIVER → LUNGS → INTESTINE

Ascaris lumbricoides

- Large numbers of worms can cause abdominal distention and pain or intestinal obstruction
- Can cause "Loeffler's syndrome" - an eosinophilic pneumonitis with transient pulmonary infiltrates
- Cholangitis and/or pancreatitis b/c aberrant migration



Ascaris lumbricoides

Diagnosis

Will not find eggs until 2-3 months after pulmonary symptoms occur
After 2-3 months, easy to find eggs since females make 200,000/day



Unfertilized



Fertilized

Rx: albendazole or mebendazole

CDC DPDx

Hookworms

Ancylostoma duodenale and *Necator americanus*

also *Ancylostoma ceylanicum* (zoonotic from dogs/cats in Asia)

- MAJOR cause of ANEMIA and protein loss (b/c plasma loss)
- Pneumonitis associated with wheezing, dyspnea, dry cough (usually, a few days to weeks after infection)
- Urticarial rash
- Mild abdominal pain

If sensitized → papulovesicular dermatitis at entry site "ground itch"

If worms migrate laterally → **cutaneous larvae migrans**

(especially dog and cat hookworms, as late as 2-8 wks after exposure to *A. braziliense*)

Hookworms are still endemic in the U.S. → 35% of individuals from a rural community in Alabama had *N. americanus* in their stool samples

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Am. J. Trop. Med. Hyg. 97(5). 2017. pp. 1623-1628

Trichuris trichiura (Whipworm)

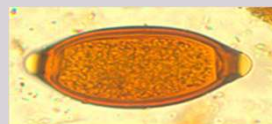
4 cm long nematode

Life cycle: Fecal-oral

In heavy infections:

- Loose and frequent stools
- Tenesmus
- Occ blood to frank blood
- In heavily infected children: rectal prolapse

Dx: eggs are football shaped with two polar plugs



CDC DPDx

Question #3

A 25-year-old female from rural Peru presents with shortness of breath, bilateral interstitial infiltrates, fever, loose stools, hypotension, and *E. coli* bacteremia. She has received > 4 weeks of high dose corticosteroids and cyclophosphamide for a recent diagnosis of lupus nephritis.

Which of the following anthelmintic agents should be included in her treatment regimen?

- Albendazole
- Ivermectin
- Praziquantel
- Pyrantel pamoate
- Diethylcarbamazine

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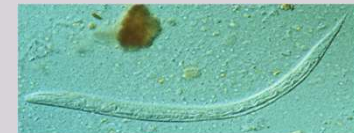
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Strongyloides stercoralis Can complete lifecycle in host!

Usual manifestations

GI: mild abdominal/epigastric pain
Pulm: wheezing, transient infiltrates
Skin: urticarial rashes, larva currens



Hyperinfection syndrome

→ Immunocompromised state steroids, TNF-inhibitors, HTLV-1, malignancy, malnutrition...NOT HIV

→ Large burden of parasites

GI: Nausea, vomiting, abdominal pain, diarrhea, intestinal erosions b/c millions of larvae in intestinal mucosa

Pulmonary: diffuse infiltrates, wheezing, dyspnea, cough

Systemic: fever and hypotension due to gram negative sepsis

-- Often do not see eosinophilia in hyperinfection --

Strongyloides stercoralis

• **Diagnosis**

- Stool o/p (sensitivity is low - 30-60%)
- Serology

• **Treatment of choice:** ivermectin

- Prevention in pts from endemic countries who are about to be immunosuppressed
 - Empirically treat, or check serology and treat if positive

Ivermectin

Activates nematode glutamate-gated chloride channels causing muscle paralysis

Drug of Choice

- Strongyloides
- Onchocerca volvulus (microfilaricidal only)
- Also has activity against Ascaris, whipworm, cutaneous larva migrans, gnathostomiasis AND ectoparasites such as scabies and lice



Image created with Google Imagen3

ADVERSE EFFECTS

- Altered mental status in 13-year-old boy given standard dose for scabies due to a mutation in ABCB1 (aka P glycoprotein 1 and MDR1); *NEJM* 2020; 383:787-789
- Reports of **seizures, ataxia, and confusion** after ingestion of large veterinary doses; *NEJM* 2021; 385:2197-2198

Question #4

A 32-year-old male from Cameroon reports intermittently experiencing a worm crawling across his eye.

Which of the following tests can be used to confirm the most likely diagnosis?

- A. Brain MRI scan
- B. Midnight blood draw
- C. Noon blood draw
- D. Skin snip
- E. Scrotal ultrasound

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Filariae: Tissue-invasive, Thread-like Nematodes, Transmitted By Arthropod Vectors

	<u>Adults</u>	<u>Microfilariae</u>
<i>Wuchereria bancrofti</i> <i>Brugia malayi</i> (Lymphatic filariasis) --Mosquitoes--	Lymphatics	Blood (night)
<i>Loa loa</i> (Eyeworm) --Chrysops flies--	SQ tissues (moving)	Blood (day)
<i>Onchocerciasis</i> (River blindness) --Blackflies--	SQ tissues (nodules)	Skin

Treatment of Filariasis

	<u>Treatment</u>	<u>Avoid</u>
Lymphatic filariasis	DEC	-----
<i>Loa loa</i>	DEC	DEC and Ivermectin if high microfilaria level
Onchocerciasis	Ivermectin	DEC

ADVERSE EFFECTS

- *Loa* with high microfilaremia → encephalopathy and death
- Onchocerciasis → severe skin inflammation and blindness

W. bancrofti and *B. malayi*

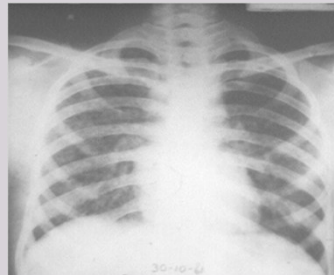


- Asymptomatic microfilaremia
- Lymphangitis
 - Retrograde (filarial lymphangitis)
 - Bacterial skin/soft tissue infections (dermatolymphangioadenitis)
- Lymphatic dysfunction
 - Lymphedema, elephantiasis, hydrocele, chyluria

Tropical Pulmonary Eosinophilia

- Paroxysmal nocturnal asthma
- Pulmonary infiltrates
- Peripheral blood eosinophilia (>3,000/mm³)
- Elevated serum IgE
- Rapid response to anti-filarial therapy

Likely due to excessive immune response to microfilariae in lung vasculature



Lymphatic filariasis Diagnosis

Definitive Diagnosis

- Identification of microfilariae in nighttime blood
- Detection of circulating antigen in blood (only *Wb*)
- Identification of adult worm (by tissue biopsy or ultrasound "filaria dance sign")

Presumptive Diagnosis

- Compatible clinical picture + positive antifilarial antibodies

Treatment

- DEC, doxycycline
- NOTE: Triple drug single dose therapy (DEC/albendazole/ivermectin) is now recommended by W.H.O. for mass drug administration eradication campaigns in areas that are NOT co-endemic for *Loa loa* or *Onchocerca*

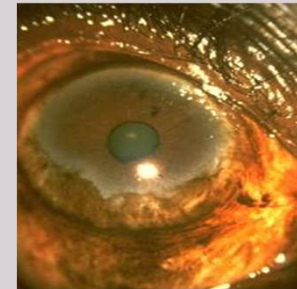
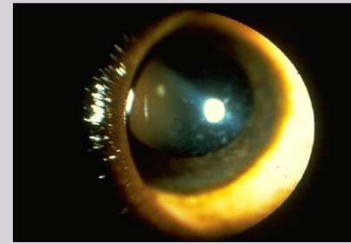
Manifestations of Onchocerciasis

Skin: nodules, pruritus, rash, depigmentation, lichenification



Manifestations of Onchocerciasis

Eye: punctate keratitis, sclerosing keratitis, chorioretinitis



Onchocerciasis

Diagnosis

- Serology
 - Anti-filarial
 - Onchocerca-specific
- Parasitologic: skin snips, nodulectomy



Treatment

- Ivermectin
- Moxidectin (FDA approved in 2018...has much longer half-life)
 - Both are primarily microfilaricidal
 - Therefore, need repeated treatments for many years

(Alternative: **doxycycline** for 6 weeks, which kills endosymbiotic *Wolbachia* bacteria, kills adult worms)

Loiasis

Clinical Manifestations

- Asymptomatic microfilaremia
- Non-specific symptoms
 - Fatigue, urticaria, arthralgias, myalgias
- Calabar swellings
- Eyeworm
- End organ complications (rare)
 - Endomyocardial fibrosis, encephalopathy, renal failure



Calabar Swelling



Loiasis Diagnosis

Definitive Diagnosis

- Identification of adult worm in subconjunctiva
- Detection of Loa microfilaria in **noon blood**

Presumptive Diagnosis

- Compatible clinical picture + positive antifilarial antibodies



CDC DpDx

Possible Question Hints

Freshwater exposure + eosinophilia → Schistosomiasis
Crab/crayfish + pulmonary sx's + eosinophilia → Paragonimus
Cysticercosis → ANY food contaminated with tapeworm eggs
Allergic symptoms after trauma → Echinococcus
itchy feet return to tropics → ground itch due to hookworms
Gram- sepsis after corticosteroids or TNF inhibitor → Strongyloides hyperinfection
Subcutaneous nodules → Onchocerca volvulus
Blood microfilaria night → lymphatic filariasis (day = Loa sax's, skin = Ov)
Muscle pain + eosinophilia → Trichinella
Eosinophilic meningitis → Angiostrongylus
Abdominal pain after sushi → Anisakis
Eosinophilia + F + ↑ AST/ALT in child → visceral larva migrans

Good Luck!

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