Parasitology: *Don't Be Buggin'*

CLASS CESTODA: THE FLAT TAPEWORMS

GENERAL FEATURES

Adult worms colonize the DEFINATIVE HOST. Attach at the scolex. Proglottids are hermaphroditic segments → most mature at the posterior end. Gravid proglottids are shed in the feces.

INTERMEDIEATE HOSTS ingest eggs → develop into cystecerci → cause major illness via tissue dissemination. This occurs with *Taenia solium* and *Echinococcus granulosus*.

MORPHOLOGY: *Taenia solium* scolex has specialized hooks for avid attachment; the proglottids and eggs are nearly indistinguishable from *T. saginata*. *Diphyllobothrium* proglottids are fairly unique.

TX: Generally use single dose of praziquantel for adult worms
Long-course therapy with albendazole or prazquantel is necessary for *Taenia solium* cystercerci

Taenia saginata: BEEF TAPEWORM

DH: Humans
IH: Cattle
TMX: Ingestion of beef with seeded cystercerci (larvae)
LC: Terminal gravid proglottids shed in feces → eggs released to environment → ingested by cattle → rupture → implantation of oncospheres in intestinal mucosa → hematogenous spread as cysticerus→ infection of all tissues → human ingestion → development in GI tract (typically beyond jejunum): adult worms may live for > 20 yrs
PATH: NVD, occasional weight loss, bowel obstruction
Rarely, reinfection occurs, and may lead to hyperinfection; but this is independent of immune status
DX: Discovery of proglottids in stool, distinguish from *T. solium* via morphology of proglottids
The eggs to *T. solium* and *saginata* are identical by LM

Taenia solium: PORK TAPEWORM

DH: Humans
IH: Pigs *and* Humans
TMX: Ingestion of undercooked pork with seeded cystercerci → definitive host
Ingestion of **eggs** → intermediate host
LC: Identical to *T. saginata* BUT eggs are also infective → mature to form cysticerci
Adult worms may live for > 20 yrs
EPI: lower prevalence than *saginata*.
Seen in areas where swine are in contact with human feces

PATH: The cystercerci may disseminate to any tissue in humans (intermediate host).
Neurocystercercosis is a highly fatal infection of the entire brain parenchyma
Reinfection does occur: eggs in feces are incidentally ingested → thus infection with the adult stage may actually progress to cystercercosis
DX: Proglottids in stool
Cysticercosis: calcified dead cysts may be visualized by plain film; viable cysts via CT/MRI (> 1 cm in diameter)
PREV: Cooking prevents infection with adult stage; cystercerci may also be obliterated by freezing.

Diphyllobothrium latum: **FISH TAPEWORM**
DH: Humans
IH: small crustacean → continued maturation in fresh-water fish
Dual intermediate hosts
TMX: Ingestion of undercooked fish with seeded plerocercoid (larvae)
LC: Eggs are shed into water → free-living coricidium → ingestion via small crustaceans (copepods) → encysts to form pro-cercoid → ingestion by fish (freshwater only) → re-encystation as plerocercoid (final larval stage) → ingestion by humans → maturation to adult form in human GI tract (ileum and beyond)
EPI: Most common in Scandinavia
PATH: Similar to *T. saginata*.
B12 deficiency due to massive absorption
DX: The proglottids are drastically different than beef and pork tapeworm
TX: single dose of praziquantel + B12 supplementation
PREV: cooking and freezing effectively prevents transmission

Echinococcus granulosus: **HYDATID DISEASE**
DH: Wild and domestic dogs
IH: Ungulates, Humans
TMX: Ingestion of eggs shed in dog feces
LC: Eggs shed by dog → ingested by intermediate hosts (mainly ungulates, sheep, moose, elk, humans) → larvae emerge and implant in liver and lungs → development of the hyaditid cyst → death of IH → ingestion of carcass by dogs → maturation of protoscolices to adult worms
EPI: occurs in areas with pastoral cycles; dogs must be fed offal; pastoral and sylvian cycles (North America); humans may be intermediate host with some burial customs
PATH: If eggs are ingested, the cysts silently seed various tissues
Liver > Lungs, Kidney, Bone
Latent period is followed by cyst rupture (usually traumatic) and release of protoscolices
May be associated with anaphylaxis
Circulating Ig against hydatid cyst Ags (non-neutralizing)
DX: Presents as a slowly enlarging mass on CT; Serology
TX: percutaneous drainage of cyst + injeciton of hypertonic saline or EtOH + caourse of albendazole
PREV: Disposal of offal, deworming of dogs

CLASS TREMATODA: THE FLUKES

GENERAL FEATURES

Flukes: hermaphroditic reproduction, broad flattened morphology
Schistosome: sexual reproduction, dimorphic elongated morphologies (male and female)
GENERAL LC: miracadium hatches from egg → IH is always a mollusk → serves as host for asexual replication → production of motile cercariae
→ schistosomes: invasion of DH (humans)
→ flukes: maturation to metacercariae → invade second IH (fish, aquatic plants)
→ by ingestion by DH (humans)

Schistosoma mansoni, japonicum, hematobium : **THE BLOOD FLUKES**

These have various vascular tropisms (predominantly veins)
S. mansoni : inferior mesenteric vessels and distribution (descending colon)
S. japonium : superior mesenteric vessels and distribution (small bowel)
S. hematobium : vessels of the vescicular plexus (venous drainage of bladder)

DH: Humans
IH: Mollusks
TMX: Percutaneous invasion by free-living cerceria (released from snails) in water
EPI: Distribution is dependent on species
S. mansoni: Africa, Middle East, Asia, S America
S. japonicum: Japan, China, Philippines
S. hematobium: equivalenent to *mansoni*
Maintenance of LC requires colonization of water supply by appropriate snails and contamination with human waste (urine or feces)
Peak TMX in 10 – 20 yrs

LC: Eggs are shed into the water in feces or urine → emergence of miracidium → infection of mollusk → 2x cycles of asexual reproduction → release of motile cercaria → percutaneous invasion of humans → enters portal circulation → maturation to adult form → mating within venous system → continuous and massive production of eggs → release into environment OR seeding in tissues → inflammation

PATH

Early: Intense pruritic rash
Hypersensitivity reaction with subsequent exposures
Fever and headache correspond to migration of the schistosomula to final venous site

Middle: High-grade fever 1 – 2 mos. after exposure → corresponds to release of first cohort of eggs
Immune complex disease (Katayama Syndrome)
Arthralgia, lymphadenopathy, splenomegaly, encephalitis (*S. japonicum*)
S. japonicum is associated with more severe disease due to highest egg load
This phase resolves within 2 -3 mos.

Chronic: 5 – 15 years after initial infection
Eggs implant in the liver, GI tract and bladder (depends on species)
Antigen production by miracidia result in granulomatous reponse and intense Eosinphilia (surrounding the non-viable eggs)
S. mansoni and *japonicum*: intestinal mucosal ulceration, periportal fibrosis → portal HTN + hepatosplenomegaly → mortality via ruptured varices
Higher mortality with *S. japonicum* due to egg load
S. hematobium: bladder fibrosis and incontinence → uremia, dysuria, and ascending infections; bladder carcinoma

Thus, the tissue damage is due to massive granulomatous inflammation + eosinophilic infiltrates

Schistosome Dermatitis: A benign subcutaneous infection by non-pathogenic species; the organism dies *in situ* ; rash resolves within 1 wk; treat with topical steroids and antihistamines.

DX: ID can be achieved via observation of egg in feces or urine
TX: praziquantel → allows for immune control of adult worms
MAIN: most of the pathogenesis is due to granulomatous inflammation around eggs

Fasciola hepatica and *Clonorchis sinensis* : **THE LIVER FLUKES**
DH: Sheep, cattle, cats, dogs, humans
IH: Snails (both) → aquatic plants (*Fasciola*) or fresh-water fish (*Clonorchis*)
TMX: Ingestion of encysted metaceracia on aquatic plants or in undercooked fish
EPI: Distribution is dependent on species
Clonorchis: found in E Asia ; associated with use of human feces in fish farms
Fasicola: worldwide; associated with sheep and cattle farms
LC: Eggs are shed into water or soil → emergence of miracidia → infection of mollusks (both) → release of cercaria → enycstation in fish and on plants (secondary IH) → emergence of metacercaria → ingestion by humans → infection of the biliary system → descent of eggs through the hepatobiliary circulation in both spp.
Chlonorchis: ascending migration through the bile duct
Fasciola: invasion of the intestinal mucosa → invasion of liver capsule → forms tracks through liver during migration to the bile duct
PATH: Biliary injury (seen with both species) and secondary hepatic dysfunction
Fasciola results in severe liver injury
DX: History of travel + RUQ pain
CT and U/S
Gold standard: observation of eggs in stool
TX: *Clonorchis* treated with praziquentel or albendazole
Fasciola treated with triclabendazole
PREV: If humans are major definitive host → control waste (avoid contamination of water)
Proper food processing
MAIN: require two IH, eggs are shed in the stool via biliary circulation

CLASS NEMATODA: THE ROUNDWORMS

GENERAL FEATURES

These worms may be freely motile in the gut lumen, anchored, or distributed throughout tissues

All demonstrate sexual reproduction

Humans are the DH for all species EXCEPT: *Tococara canis*, *Anisakis* spp, *Dirofilaria Immitis*; incidental hosts for *Trichinella* (although may serve as DH)

Filarial worms are TMX by vectors

Enterobius Vermicularis: THE PINWORM

DH: Humans

IH: None (soil)

TMX: Ingestion of eggs

EPI: more prevalent in lowere SES; associated with daycares and peds

LC: Nocturnal emergence of gravid females from anus → generation of eggs → perianal scratching → desposition of eggs in environement → ingested by human → emergence and mating in the small bowel → migration to colon

PATH: Intense perianal pruritis

Secondary infection and auto-infection due to excoriation

In females: infection of the UG tract → secondary bacterial infection

DX: Clinical : perianal pruritis, insomnia

Observation of eggs; requires serial observation due to irregular migration of females

TX: requires two courses of therapy with praziquental (due to hatching of egg cohort after clearance of adult worms)

MAIN: perianal pruritis

Trichuris trichuria: WHIPWORM

DH: Humans

IH: None (soil)

TMX: Ingestion of eggs after maturation in soil

EPI: Worldwide distribution

More prevalent in tropical countries due to soil conditions

In U.S: may be found in S East, usually lower SES

Association with use of human feces as fertilizer

LC: Gravid females produce eggs → shed in feces → obligate maturation in the soil → ingestion (usually by peds after recreation in soil, or unwashed foliage) → emergence and mating in small bowel → migration to colon

PATH: Disruption of colonic mucosa → dysentery, rectal prolapsed, anemia due to chronic blood loss

Light worm burdern usually does not cause clinical illness

Hemorrhage attachment site (colon) may result in bacteremia

DX: Observation of eggs in stool ONLY

MAIN: hemorrhagic colitis, bacteremia, prolapse

Ascaris Lumbricoides: **ASCARIASIS**
DH: Humans
IH: None (soil)
TMX: Ingestion of eggs after development in soil
LC: Eggs shed in feces → maturation in soil (3 wks) → ingestion by peds or via unwashed foliage → emergence of larvae in the mucosa → enters venous circulation → eventual migration to the lungs → entry into the alveolar airspace → coughed and swallowed → maturation and mating in the small bowel WITHOUT attachment to mucosa
Occasionally, the adult worm may be shed in the feces
EPI: Association with use of human feces as fertilizer
Found in tropical countries, and lower SES areas of S East U.S
PATH: Ectopic infection (nasopharynx, bile duct)
Intestinal obstruction
With stress → migration to remote sites
Malnutrition leads to delayed mental and physical development
Eosinophilic inflammation during migration through lungs may lead to asthma
Light worm burdens are usually subclinical, despite continued reproduction
DX: Observation of eggs in stool ONLY
MAIN: unattached (large worms) causing malnutrition or obstructive symptoms

Necator americanus and *Ancylostoma duodenale* : **HOOKWORM**
DH: Humans
IH: None (soil)
TMX: Percutaneous invasion by the filariform larvae
EPI: Prevalent within the S East U.S
Associated with poor public hygiene; farming practices in which shoes are not worn
A very prevalent infection worldwide: major cause of DALY
LC: Filariform larvae → penetration of skin → implantation in the lung parenchyma → emergence in the alveolar space → coughed and swallowed → maturation in the intestine → anchored → eggs shed in feces → maturation in soil and emergence of feeding larvae
PATH: Initial pedal pruritis
Bronchitis due to initial passage through lungs
Chronic infection may lead to asthma-like response (similar to *Ascaris*)
Asthma becomes more severe with recurrent infections
Chronic: **anemia** results in delayed mental and physical development in peds
DX: Anemia + eggs in stool
The fecal egg count is correlated total worm burden
Association with use of human feces as fertilizer
MAIN*:* chronic iron deficiency anemia, initial pedal pruritis

Storngyloides stercoralis
DH: Humans
IH: None
TMX: Invasion : percutaneous infection via filariform larvae
Ingestion: contamination of food by rhabdiform larvae
EPI: Distribution equivalent to that of Hookworm
Also seen in farming practices in which shoes are not worn
LC
Direct: adult females in gut → eggs → emergence of larvae in mucosa → migration to lumen → shedding of larvae in feces → form filariform larvae in soil → percutaneous invasion (similar to Hookworm)
Thus, there is no amplification in either host or environment
Indirect: Filariform larvae in soil may mature to adults → sexual amplification → generation of larvae → resume direct cycle
Thus, there is amplification within the environment (soil)
Autoinfection: perianal larvae may mature to form filariform stages → percutaneous re-infection through the perianal epithelium or rectal mucosa
Amplification within host
Horizontal TMX is also possible
This cycle may result in chronic infections (if immunocompetent), potentially > 30 yrs after primary exposure
PATH: Pulmonary manifestations (asthma-like illness)
Rash on buttocks, back, and legs (usually serpiginous) : indicative of autoinfection
Chronic malabsoption and dysentery : seen with high worm burdens only
Severe infection with immunosuppression may lead to disseminated infection → bowel perforation
DX: Larvae in stool and duodenal aspirate
Examination of sputum (if pulmonary symptoms)
TX: ivermectin + albendazole; prolonged therapy necessary for hyperinfection
PREV: shoes, hygiene, proper food processing (prevent ingestion of rhabditiform larvae)
MAIN: causes hyperinfection if immunocompromised

Toxocara canis: **VISCERAL LARVA MIGRANS**
DH: Dogs : free-living adults
IH: Humans : disseminated larvae
TMX: Ingestion of eggs after maturation in soil
EPI: High prevalence of infection in U.S dogs
Warmer climates favor egg development
Most commonly TMX by puppies to peds
LC: Identical to *Ascaris* in dogs → eggs deposited in soil undergo obligatory development → ingestion of eggs by humans → similar to *Ascaris* in humans EXCEPT larvae burrow through the intestine and into the circulation → **generalized parasitemia** (larvae may be found in any tissue)

PATH: Typically self-limiting
Necrosis with heavy worm load
VLM: ocular, pulmonary, neurologic, splenomegaly
DX: Triad of eosinophilia, HSM, hyperglobinemia
NO eggs will be found in stool since progression to adult stage within humans is RARE
PREV: disposal of dog feces, de-wormign dogs
TX: only required for severe disease (albendazole + corticosteroids)
MAIN: this a generalized parasitema that is usually self-limited; puppies in warm climates

Anisakis spp. : **FISH ROUNDWORM**
DH: Marine cetacenas (whales, dophins), seals, sea lions
IH: Humans
TMX: Ingestion of raw seafood (sushi)
LC: Excystation in the gastric environment → incomplete maturation in humans
PATH: Presents as gastric peptic ulcer (due to irritation of the gastric mucosa by existed worms)
DX: Direct observation of worm attached to gastric mucosa (endoscope)
TX: manual extraction of worm
MAIN: presents similarly to PUD; associated with raw seafood (rather than undercooked fish); humans are an unsuitable host

Trichinella spiralis: **TRICHINOSIS**
DH: Bears, swine, walrus, humans; any carnivore, including humans (incidental host)
IH: Humans
TMX: Ingestion of undercooked pork with encysted larvae
EPI: This is actually *less common* in underdeveloped countries due to lower meat consumption
Usually not found in Islamic and Judaic cultures
Strongest association: self-prepared sausage, uncooked walrus
LC: Ingestion of encysted larvae → release of larvae in gastric acid → maturation and mating in small bowel → implantation of female in the enteric mucosa → emergence of larvae → invasion of circulation and lymphatics → intracellular seeding of skeletal muscle → encystations → encapsulated spiral
PATH: Severity is dependent on cyst load
> 100 cysts/gm: fulminant disease, may be fatal
Fever, myalgia, weakness
Cardiac dysfunction and neuropathy
Conjunctivitis
The tissue damage is due to intense inflammation around cysts and destruction of muscle
DX: Eosinophilia, serology, muscle Bx
TX: Mebendazole + Corticosteroids
PREV: cooking pork; extended freezing
MAIN: seen in self-prepared sausage; humans are both DH and IH (cessation of amplification after a single round of excystation)

Wuchereria bancrofti and *Brugia malayi*: **ELEPHANTIASIS**
DH: Humans
IH: Anopheles and Culex mosquitos
TMX: Insect vector
EPI: Prevalent in tropical regions fo Africa, Asia, S Pacific, S America
LC: Adults are located in lymphatics → maturation and mating in the lymph vessels produces microfilariae → escape into venous circulation → daytime residence in the pulmonary vessels → nocturnal emergence into peripheral circulation → mosquito blood meal → development to larvae (infectious stage) → TMX to human on next blood meal → migration to lympahtics → maturation to adults
PATH: Progressive granulomatous inflammation and fibrosis leading to lymphatic obstruction
Elephantiasis: occursin < 10% of all infections in endemic areas
This is the end-result of chronic lymph obstruction
Affects extremities, genitalia, breasts
The effects are seen even after clearance of the organism
DX: peripheral smear demonstrates microfilariae
MAIN: the adult worms represent the pathogenic stage (cause lymphatic inflammation); larvae are infectious; microfilariae allow for motility and residence in the pulmonary vessels

Onchocerca volvulus: **RIVER BLINDNESS**
DH: Humans
IH: Blackflies
TMX: Insect vector
LC: Similar to *Wuchereria* → blackfly bite → introduce larvae → may reside in subcutaneous nodules for 15 yrs → microfilariae escape and migrate through subcutaneous tissue → (may invade the eye) → fly bloodmeal
PATH: Fibrosis of the epidermis (Lizard skin, Hanging Groin)
Ocular invasion leads to blindness due to inflammation
Requires co-infection with *Wolbachia*
MAIN: the microfilariae are the pathogenic stage; reside in subcutaneous nodules, but may become migratory, leading to blindness

Loa Loa: **EYE WORM (LOAIASIS)**
LC: similar to *Onchocerca*, but adults (not microfilariae) are capable of subcutaneous migration
EPI: less prevalent than *Onchocerca*
PATH: Infection is usually less severe

Dirofilaria Immitis: **DOG HEART WORM**
DH: Dogs
IH: Mosquitoes, Humans (rare incidental host)
TMX: Mosquito vector
LC: Mosquito blood meal → injection of microfilariae → immature adults form nodules in lungs → (results in minor pulmonary symptoms) → rarely mature to travel to the heart
PATH: Forms nodules visible on CXR

PROTOZOANS: LUMINAL PARASITES

Trichomonas vaginalis

TMX: Sexual contact; non-sexual due to poor hygiene (rare)
LC: there is only a single trophozoite stage → replicates via binary fission
EPI: Cosmopolitan distribution. Leading non-viral STI in U.S. Peak incidence 16 – 35 yrs.
PATH: Universally symptomatic in females: persistent vaginitis with frothy exudates
Typically asymptomatic in maes: NSU; can involve prostate and seminal vesicles
DX: LM demonstrates motile organisms, culture
TX: DOC is Metonidazole; screen all partners (including asymptomatic males), screen for co-infections
PREV: barrier protection
MAIN: the leading non-viral STI, universally symptomatic in females; TX requires screening of all partners

Giardia lamblia

RESERVOIR: wild and domestic animals
TMX: F/O
Classically: backpacker drinking unpurified water
Receptive anal intercourse
EPI: Cosmopolitan distribution with endemic pattern (developing nations)
Point-source epidemics in day cares, resorts, and due to water contamination
LC
Infectious cysts ingested → excystation in human small bowel → binucleate trophozoites → binary fission → adherence to brush border epithelium → migration to the colon → encystations → cysts shed in feces
PATH: Onset of symptoms at 2 weeks
Ranges from asymptomatic infection to flatus + non-bloody diarrhea
Acute phase is self-limiting within 4 wks
BUT chronic infection may be established with continual shedding of cysts
Malabsorption syndromes
DX: Stool Ag test, cysts in stool (rarely trophozoites)
TX: DOC is Tinidazole; or Paromcin in pregnant women
PREV: hygiene, boiling water, iodine tablets, filters
MAIN: the trophozoites adhere to the intestinal epithelium via a ventral disc (thus: rarely shed in the stool); may lead to asymptomatic shedding of cysts

Entamoeba histolytica : **AMEBIASIS** *and* **AMEBIC DYSENTERY**

TMX: F/O
Receptive anal intercourse
EPI: Cosmopolitan distribution with endemic pattern (developing nations)
Point-source epidemics due to water contamination and colonic irrigation
Also associated with use of human fecal fertilizer
U.S endemics seen in communal settings and receptive anal intercourse

LC
Infectious cysts ingested → excystation in human small bowel → quadrinucleate metacysts → binary fission → formation of 8 trophozoites → migration to the colon → binary fission → encystation → cycts shed in feces

PATH: The disease causes affliction on a spectrum
Asymptomatic: carriers may shed numerous cysts
Limited: intermittent flatus + abdominal pain + diarrhea; may become chronic
Amebic Dysentery: severe bloody diarrhea, due to invasion of colonic mucosa by trophozoites ; forms characteristic ulcers
Invasive Amebiasis: hematogenous spread from GI tract → most commonly causes hepatic abscess; may involve CNS and direct extension to lungs
May occur without history of dysentery
Recurrence invasive disease is rare, possibly due to development of humoral immunity
DX: LM trophozoites and cysts in stool or sigmoid aspirate; trophozoites contain RBCs; stool Ag assay or PCR
Get Travel Hx: endemic to many countries
TX: Invasive disease treated with metronidazole, GI phase treated with Paromycin
PREV: hygiene, sanitation

PROTOZOANS: HEMOFLAGELLATES (KINETOPLASTIDS)

GENERAL FEATURES

The LC alternates between mammalian hosts and insect vectors
Replication via binary fission only
They can be detected by the basophilic Giemsa stain
Intracellular: *Leishmania* spp. And *T. cruzi*
Extracellular: *T. brucei* spp. (African *Trypanosoma*) → parasitemia

Leishmania spp. : LEISHMANIASIS

RESERVOIR: wild and domestic animals → zoonosis
Human host only (India) → urban cycle sustained by anthropophilic sandfly
TMX: vector-borne; via the Sandfly
EPI: Occurs in tropical and subtropical climates
Demonstrates both sylvatic and urban cycles of transmission
LC
Infectious promastigotes introduced to humans during blood meal → invasion of monocytes and macrophages (this is an intracellular organism) → differentiation to amastigote form → replication within the phagolysosome → rupture of cell → amastigotes released to the circulation

PATH: Disease course is determined by species

L. major, *L. braziliensis*, ***L. tropica***, *L. Mexicana*: **Cutaneous**

IP 1 – 8 wks → ulceration at bite site → + satellite lesions → macrophages with **intracellular amastigotes** may be isolated from the ulcer

The lesion usually resolves within 3 – 12 mos. → may progress (metastasize) to develop into mucocutaneous disease

Infection confers strain-specific immunity

L. braziliensis, (*L. Mexicana*) : **Mucocutaneous**

Primary cutaneous lesion → metastasis years after healing of primary ulcer → destruction of nasophagyngeal mucosa

The lesions do not contain a high parasite load

L. chagasi, ***L. donovani***, *L, infantum* : **Visceral**

Rapid dissemination into circulation → onset of recurrent fevers at 2 – 12 mos.

Invasion of viscera

Malabsorption syndrome (cachexia), Hepatosplenomegaly (cytopenias)

Mortality is due to secondary infections

May have subclinical infection and acquired immunities if endemic

In all cases: successful treatment leads to immunity

DX: Amastigotes in skin or visceral Bx

TX

Cutaneous: spontaneous resolution; *L. major* treated with fluconazole

Mucocutaneous: Antimony or AmphoB

Visceral: miltefosine

PREV: Vector control ; avoid sandfly environment

T. brucei spp. **: AFRICAN TRYPANOSOMIASIS (SLEEPING SICKNESS)**

RESERVOIR: Varies between subspecies

T. brucei brucei : cattle; NOT a human pathogen

T. brucei rhodesiense: wild game; East/Central Africa → **acute zoonosis**

T. brucei gambiense : humans; West Africa → **chronic vector-transmitted parasitemia**

TMX: vector-borne; via the **Tsetse Fly** ; concentrates near rivers and forested areas

EPI: Confined to sub-Saharan Africa

The disease is universally fate if untreated

The Tsetse fly preferentially infects humans, and is more likely to transmit the Gambian Form (chronic infection)

LC

The metacyclic form is transmitted to humans during a bloodmeal → results in primary parasitemia → the short form is ingested by fly → matures from procyclic to metacyclic form in vector : secondary waves of parasitemia continue to occur in the human host

PATH: Disease course is determined by species

Gambian

Early: painful chancre at bite appears within 7 d. → dissemination to bloodstream

Middle: onset of recurrent waves of parasitemia at 2 – 3 wks → recurrent fevers
Associated with lymphadenopathy (Winterbottom Sign) and anemia

Recurrent fever + LN + anemia

Late: CNS invasion at 6 mos. – 2 yrs → perivascular inflammation → cerebral edema → increasing global neurologic deficits

Mortality due to secondary infections

Rhodesian

The timecourse is compressed; mortality within 6 – 9 mos.

There is an initially vigorous humoral response converting to immunosuppression. Recurrent waves of parasetemia, each with antigenic drift, allows for evasion.

DX: Motile organisms on blood drop or CSF, card agglutination, Giemsa stain

TX

Early: Pentamidine

Late: Melarsoprol or Eflornithine for CNS penetrance

PREV: Vector control , prophylactic IM pentamadine (Gambian only), early Tx , avoid Tsete fly environment, monitor population

T. cruzi **: AMERICAN TRYPANOSOMIASIS (CHAGAS' DISEASE)**

RESERVOIR: rats, dogs, cats, possums

TMX: vector-borne; via the Reduvid (Assassin) genera of bugs ; transfusion, IVDA

EPI: Endemic to South and Central America

Mainly occurs in mud hatch dwellings

Infected Redivid bugs may be found in S West U/S, but do not TMX infection

Contaminated blood supply in S America

LC

Reduvid bugs are nocturnal → pass infectious trypomastigotes in feces → rubbed into conjunctive → intracellular invasion of neurons and myocytes → differentiation to amastigotes in cytoplasm → division → mature to trypomastigotes → rupture and release to circulation

PATH: The disease can be described in terms of acute and chronic phases

Acute: **2 – 4 mos. after infection**

Febrile illness with chagoma (at eyelid, known as Romana's Sign)

High-level parasitemia (due to rupture of host cells → release of trypomastigotes)

Peds are susceptible to more severe primary illness → organism disseminates readily to tissues

Adults usually suppress the infection (AMI and CMI)

Chronic: **10 – 20 yrs after infection**

May be reactivated by immune suppression

No promastogotes in circulation
Amastigotes reside in cells (neurons and myocardium), resulting in progressive tissue destruction
Trypomastigotes are NOT detectable in the peripheral blood
Common manifestations: dilated cardiomyopahty, esophageal dysmotility (Achalasia), megacolon
Susceptible to sudden cardiac death

DX: Trypomastogites on LM blood mount; xenodiagnosis with unifected Reduvid bugs
TX
Acute: Nifurtimox or Benznidazole
Chronic: None
PREV: Vector control, improved housing conditions, screen blood blanks

PROTOZOANS: APICOMPLEXIANS (SPOROZOA)

GENERAL FEATURES

These organisms have fairly complex LCs
ALL obligate intracellular : apical complex allows for host cell invasion
Have both asexual (schizogony) and sexual reproductive stages
The sexual cycle occurs intracellularly, in the intestinal epithelium of the definitive host
OTHER ORGANISMS: *Isospora* and *Sarcocytis* cause an enteric disease similar to *Cryptosporidia*
Babesia causes a malaria-like illness in asplenic patients

Cryptosporidium hominis and *parvum*
RESERVOIR: wild and domestic animals (including livestock)
TMX: F/O
EPI: Cosmipolitan, endemic to developing nations
In U.S, transmission occurs in day cares and communal settings
This is a significant rate of nosocomial infections
OOcysts are highly infective!
Massive epidemic in Milwaukee
LC
Infectious oocysts ingested → release four sporozoites in small bowel lumen → sporozoites invade brush border cells → asexual reproduction (schizogony) for 2x cycles → GEN2 merozoites (progeny) re-invade epithelium → differentiated into gametes → fusion → diploid oocyte → meiosis → oocyst containing four infectious sporozoites → thin-walled oocyts rupture and cause re-infection; thick-walled cysts are passed in feces
(Thus, the asexual and sexual cycles are both intracellular, within the same host)
PATH: This is an opportunistic infection (esp. in pts with HIV)
2 wk IP → profuse watery diarrhea (can be > 12 L/d) → resolution within 1 – 2 wks
Thus, similar to Giardiasis: but shorter duration and greater volume loss

If immunocompromised, the infection may be persistent and severe, leading to AIDS wasting syndrome

DX: LM demonstrates **acid-fast** 'cup and saucer' cysts, DFA

TX

Oral rehydration: important if immunocompromised
Restoration of immune function (ART therapy) in HIV patients
Short course of nitrazoxanide

PREV: 1μm absolute water filter, boiling, avoid infectious stool

Toxoplasma gondii : **TOXOPLASMOSIS**

RESERVOIR: cats, mice, sheep, cows

DH: cats

IH: sheep, humans

TMX: F/O : ingestion of infectious oocysts
Undercooked meat: ingestion of tissue cysts (this is the **most common route**)
Transplacental, if primary infection during pregnancy

EPI: Cosmopolitan distribution
Urban TMX is associated with undercooking and cat litter
50% seropositive in U.S

LC

In the DH: CATS shed immature oocytes, subsequently ingested by IH (mouse, human)
Cat ingests an infected mouse→ mouse tissue cysts are released → excystation in GI tract and release of bradyzoites → enters schizogony and sexual reproduction in the intestinal epithelium, similar to the cryptosporidium LC → shed immature oocysts in feces

Natural (Propagating) Cycle
→ ingestion by **mouse** or **livestock** (lamb, beef) → emergence of sporozoites from oocyst → invasion of IH intestinal epithelium → asexual reproduction → tachyzoites → dissemination throughout host tissues (ANY nucleated cell!) → continued phases of asexual reproduction → differentiation to encysted bradyzoites (favors muscle and CNS) → dormant cysts are viable throughout IH lifespan

Incidental Cycle
→ ingestion of oocysts (from cat litter box) and encysted bradyzoites (from undercooked lamb and beef) by humans → [GI invasion, replication, systemic dissemination and seeding of cysts] → rupture is highly morbid in immunocompromised pts, releasing tachyzoites

Thus, asexual replication can occur within human hosts

PATH: This is an **opportunistic infection**
The acute infection is similar to mononucleosis and may be asymptomatic
Host immunity gains rapid control of the infection → lifelong latent infection
Re-activation is prevented if immunocompetent
In immunosuppressed: primary and reactivated infection become fulminant

Leads to *Toxoplasma* encephalitis in AIDS pts → significant mortality

Transpancental: occurs if primary infection is acquired before the third trimester → abortion, MR, defects, chorioretinitis (if less severe)

DX: Serology

No titre: no infection
IgM +ve: early acute primary or reactivation
Rising IgG: late acute primary or reactivation
Stable or declining IgG: chronic infection

The IgM may be positive for 18 mos, but usually is undetectable > 6 mos (chronic infection)
Also: CNS Bx; in AIDS pts with seizure, do MRI to look for ring-enhancing lesions

TX

Pyremethamine:Sulfadiazine is effective against the tachyzoite stage
Ifpregnant: spiramycin
Treat: immunocompromised, acute infection during pregnancy, chorioretinitis

PREV: frequent litter changes; if immunocompromised, avoid undercooked meat and cats; prophylactic TMP-Sulfa if CD4+ < 100 cells

Plasmodium spp. : **MALARIA**

RESERVOIR: Humans
DH: The Anopheles Mosquito (F)
TMX: Vector-borne (mosquito)
Congenital infection
IVDA
EPI: Cosmopolitan distribution

The incidence of fatal disease is highest in peds (1 – 5 yrs) and G1 females

LC

Infectious sporozoites introduced during a blood meal → rapid migration and invasion of hepatocytes → intrahepatic intracellular schizogony (7 d.) → emergence from liver → invasion of erythrocytes → fever onset is coincident with intra-RBC cycle of schizogony (ring stage → trophozoite → schizont → merozoite) → released from lysed RBCs → other RBCs infected → development of gametes → ingested by feeding mosquito → secual reproduction in mosquito → migration of sporozoites to salivary glands

Thus: Schizogony occurs within hepatocytes and RBCs
Sexual stages occur within the mosquito GI epithelium (but gametes are generated within RBCs)
P. vivax and *P. ovale* can establish latent hepatic infections

PATH: Illness is defined by cyclic fevers and paxoxysms (rigors followed by massive fever, due to endogenous TNF and IL-1)

The tempo of fever is characteristic of species
P. vivax: 48 hr cycle + severe 10 hr paroxysm
P. malariae: 72 hr cycle + severe 10 hr paraoxysm
P. falciparum: 48 hr cycle + protracted 16 – 36 hr paroxysm
P. ovale: 48 hr cycle + limited 10 hr paraoxysm

Hemolytic anemia + Sequestration of infected erythrocytes (*P. falciparum* only)
Pyogenic vasodilation → dropped ECF → hypotension → tissue hypoxia and acidosis
    Hypoxia + Hypoglycemia + Acidosis may lead to cerebral malaria
The clinical syndrome: rigors, fever, splenomegaly, anemia, myalgia, headache
    Complicated malaria: cerebral disease and severe anemia; will become fulminant if asplenic
Cerebral malaria, thrombocytopenia, and intravascular hemolysis occur with *P. falciparum* only
Progressive renal failure occurs with *P. malariae*

IMM
Immunity develops slowly, and requires multiple primary infection → declines rapidly once removed from endemic areas
Asplenic patients are at highest risk of severe illness
DX: Peripheral Blood Smear with Giemsa stain
    P. falciparum: multiple ring stages + banana-shaped gametocyts without trophozoites or schizonts (these stages causes the erythrocyte to adhere to the endothelium, so they are will not be detected)
TX
    Chloroquine, mefloquine, quinine, doxycycline
PREV: mosquito nets, chemoprophylaxis

GUIDELINE for **TREATMENT** of **PARASITIC INFECTIONS**

ROUNDWORMS → **Benzimidazoles** (Mebendazole and Albendazole)
EXCEPT *Strongyloides* → Ivermectin
FILARIAL WORMS→ **Ivermectin**
TAPEWORMS → **Praziquantel** for adultworm stages
Albendazole for cysticercosis
FLUKES → **Praziquantel**
May need to use Bithionol for some *Fasciola* infections
LUMINAL (GI, GU) PROTOZOA → **Metronidazole**

T. cruzi → Nifurtimox + Benznidazole
T. brucei spp. → Melarsoprol : begin treatment early in the disease course
Eflornithine : may be used for the CNS phase

TOXOPLASMA → Pyamethamine + Sulfamethoxazole or Metronidazole

MALARIA PROPYLAXIS → **Chloroquine** if traveling to areas with endemic chloroquine-sensitive strains
Mefloquine if traveling to areas with *chloroquine resistance*
Doxycyline if traveling to regions with Mefloquine resistance
Chlorquanide (U.K only)
Primaquine to clear latent hepatic infection

ACUTE MALARIA → **Chloroquine** for *P. ovale* and *P. malariae*, as well as sensitive strains of *P. falciparum* and *P. vivax*
Quinine + Doxycycline for acute infection with CQ-resistant strains
Atovaquone + Chloruanide (**Malarone**) for acute infections with CQ-resistant strains
High dose **Mefliquone**

ANTI-HELMINTHICS

GENERAL STRATEGY

Ascaris lumbircoides: mebendazole, pyrantel pamoate + albendazole
Hookworm (*Necator* and *Ancylostoma*): restore hematologic status; drug therapy equivalent to *Ascaris*
Whipworm (*Tricuris*): mebendazole, albendazole, axantel pamoate
Strongyloides: ivermectin
Enterobius: drug therapy equivalent to *Ascaris*
Trichinosis: mebendazole, albendazole effective ONLY against early infection; corticosterioids to suppress reaction to chronic infection
Filarial Worms (*Wuchereria, Onchocerca*): diethylcarbamazine, ivermectin

Schistosoma: Praziquantel
Clonorchis: Praziquantel
Fasciola: Bithionol (available from CDC only) or triclabendazole

Taenia saginata: praziquantel 4 mos.
Taenia solium: praziquantel treats both adult worm infection and cystercercosis; albendazole treats cystercercosis
Diphyllobothrium: praziquantel or niclosamide
Echinococcus: long-term albendazole + surgical resection

ALBENDAZOLE

CLASS: Benzimidazole

TX: broad spectrum against **nematode** infections

First-line therapy for roundworm, hookworm, pinworm, and whipworm

Also effective for cystic echinococcosis and *Taenia solium* cystercercosis

MECH: inhibits polymerization of worm β-tubulin

PHARM: The active metabolite (albendazole sulfoxide) has a high volume of distribution → increased activity against deeply encysted organisms

Treatment usually only requires **single dose**

AR: low systemic toxicity; teratogenicity

CI: pregnant women, cirrhosis

MEBENDAZOLE

CLASS: Benzimidazole

TX: broad spectrum against **nematode** infections

First-line therapy for roundworm, hookworm, and whipworm

MECH: inhibits polymerization of worm β-tubulin

PHARM: Low oral biovailability due to non-absorption + first-pass metabolism

AR: low systemic toxicity; teratogenicity

CI: pregnancy women and peds < 2 yrs

IVERMECTIN

CLASS: Avermectin

TX: DOC for treatment of onchocerciasis

Effective against filarial worm infections (EXCECPT *Loa Loa*)

Also covers most **nematodes** (*Strongyloides*, *Ascaris,* whipworm, pinworm)

MECH: **Increased conductance of Cl- through glutamate channels** in **nematodes only** → tonic paralysis of worm pharyngeal muscles

Not active against filarial stages

Cidal against developing larvae

Inhibits emergence of microfilariae from adult uterus → lowers organism load in cutaneous vessels → reduce vector TMX of *Onchocerca* (black Tsetse fly)

PHARM: Long half-life due to slow clearance, large Vd, and enterohepatic circulation

Treatment usually only requires **single-dose**

AR: low systemic toxicity; CNS toxicity may develop if there is damage to BBB

CI: pregnant women, cirrhosis

PRAZIQUANTEL

TX: DOC for **cestode** and **trematode** infections
First-line therapy for schistosomiasis
Fluke infections require higher dosages; tapeworm infections may be eradicated with a single dose
MECH: Low-dose: increases worm muscular activity → spastic paralysis
High-dose: disruption of tegument → calcium influx → blebbing → increased host immune susceptibility
PHARM: Inactivated by hepatic metabolism
AR: abdominal distress, headache, dizziness, sedation
CI: pregnant women

ANTI-PROTOZOAN AGENTS (NON-MALARIA)

GENERAL STRATEGY

Entamoeba histolytica: metronidazole is active against luminal and systemic infection
Trcihomonas: metronidazole
Giardia: metronidazole or tinidazole
Cryptosporidium: parmamycin (if prengnant) or nitazoxamide
Cyclospora and *Isospora* : TMP-Sulfa

T. cruzi: acute infection may be treated (limited efficacy) with nifertimox and benznidazole; long-term therapy limited by significant toxicity
T. brucei : melasoprol for early infection, eflornathine for CNS disease
Leishmania spp. : pentavalent antimony

Toxoplasma: pyrimethamin + sulfadiazine; spiramycin if pregnant; metronidazole

METRONIDAZOLE

TX: DOC for *Trichomonas* vaginitis, *Giardia*, and ALL forms of symptomatic amebiasis
MECH: anaerobic bacteria + liver result in reduction of the nitro group, forming a highly reactive radical → oxidative damage to DNA and proteins
PHARM: good distribution
AR: headache, dry mouth, metallic taste, anorexia, NVD, disulfuram-like reaction with EtOH
CI: pregnant women in third trimester

ANTI-MALARIA AGENTS

GENERAL STRATEGY

Blood Szhizonticides: these agents terminate the circulating erythrocyte stage (clinical disease) of malaria

Thus, they may be used for treatment of active disease and for chemoprophylaxis

Chloroquine, Quinine, Mefloquine

Tissue Schizonticides: these agnets act within hepatocytes to prevent the initial intra-hepatic schizogony that precedes active malarial disease

Thus, the primary role of these drugs is in prophylaxis

Primaquine, Chlorguanide

Gametocides and Sporontocides: activity against the sexual stages

Not used clinically

Could theoretically be active within infected mosquitoes (sporontocides) or prevent TMX of gametes during blood meal (gametocides)

QUININE

CLASS: Blood schizonticide; quinolone ring derivative

TX: The DOC for chloroquine-resistant strains of malaria; no longer in widespread use

MECH: Weak base → concentrates in food vacuole of *Plasmodium* → inhibits polymerization of heme → increased toxicity to the organism

Free Heme generates ROSs (Fenton reaction)

PHARM: nearly complete oral absorption

AR

Tinnitus, headaches, nausea, blurred vision

Hypersensitivity: flushing, pruritis, hemolysis

May develop 'Balckwater Fever' → massive intravascular hemolysis resulting in hemoglobinemia and renal failure

Hypoglycemia due to increased insulin secretion

Hypotonia due to decreased NMJ excitability

CHLOROQUINE

CLASS: Blood schizonticide; quinolone ring derivative

TX: Used to terminate clinical malaria and for prophylaxis (suppressive)

MECH: Equivalent to QUININE

PHARM: high Vd, so dosing must be carefully titrated

AR: High doses cause hypotension, arrhythmias

> 5 g: may be lethal

CI: hepatic disease, G6PDH deficiency (will cause brisk hemolysis)

MEFLOQUINE

CLASS: Blood schizonticide; quinolone ring derivative

TX: DOC for prophylaxis in areas in which malaria is highly chloroquine-resistant

(This may be accomplished with weekly low doses)

High doses may be sued to treat CQ-resistant clinical disease

MECH: concentrates in food vacuoles but DOES NOT inhibit heme polymerization; instead, causes osmotic swelling

RES: resistance is rapidly evolving; usually associated with MDR malaria

PHARM: slow and incomplete absorption

AR: nausea, lassitude, dizziness, fatigue, seizures, psychosis

CI: pregnant women, Hx of psychosis

PRIMAQUINE

CLASS: Tissue Schizonticide; quinolone ring derivative
TX: DOC for **clearance of latent hepatic schizonts** (*P. vivax* and *P. ovale*)
Weak activity against *P. falciparum* hepatic schizonts
Significant gametocidal activity against all types of malaria
MECH: unknown; may be converted to an oxidative metabolite
RES: some resistance seen in *P. vivax*
PHARM: complete absorption with high Vd; rapidly converted to weak metabolites
AR: hypotension (IM), methemoglobinemia
CI: G6PDH deficiency

CHLORGUANIDE (PROGUANIL)

CLASS: Tissue Schizonticide; quinolone ring derivative
TX: **Malaria prophylaxis** at the tissue schizont level
Also used to terminate clinical disease when co-formulated with atovaquone (Malarone)
MECH: converted to CYCLOGUANIL → **inhibits DHFR** and parasitic DNA synthesis
RES: due to mutation at the drug binding site, decreasing affinity
PHARM: significant ethnic variation in generation of the active metabolite (CYP2C conversion)
AR: no significant toxicity

ATOVAQUONE

CLASS: Hydroxynapthoquinone
TX: combined with Chlorquanide (as Malarone) for treatment of acute chloroquine-resistant malaria
MECH: inhibits electron transport (ubiquinone analog)
PHARM: very low oral bioavailability; increased absorption with fatty meal
AR: maculopapular rash, fever, NVD, headache
GI symptoms may limit absorption