Parasitology
Protozoans, Helminths (worms), Arthropods

Life cycles, hosts
Definitive host: sexual reproduction, intermediate host: asexual reproduction or larval development

Diagnosis
Microscopic examination, blood count (eosinophilia in tissue helminths), serology, nucleic acids

Protozans
Flagellates, amoebas, apicomplexa

Malaria
Plasmodium falciparum, P. vivax, P. malariae are most important species
Fever, anemia, impaired circulation

Malaria life cycle
Mosquito bite: sporozoites enter circulation, form merozoites in liver
Merozoites enter circulation from liver, enter erythrocytes, form trophozoites or gametocytes
Trophozoites form schizonts in erythrocytes, multiply by mitosis, lysis of erythrocyte release more merozoites into circulation which repeat the cycle in erythrocytes
Gametocytes do not lyse blood cells, infected cells taken up by mosquito feeding on infected person
Gametocytes fuse in mosquito, form oocyst in gut wall, divides by meiosis to form sporozoites

Disease
P. falciparum most severe, P. vivax can relapse
Half the world’s population at risk, significant mortality in children and pregnant women

Helminths: nematodes (roundworms), cestodes (tapeworms), trematodes (flukes)
Usually do not multiply within host, disease severity depends on “worm load”, requires multiple infection, some helminths can multiply in host via “autoinfection”

Intestinal nematodes
Adult worm found in gut, infectious form (eggs or larvae) and route (oral or via skin), and site of larval development (circulation or gut) differ depending on species

Tissue nematodes
Human “accidental” host, lifecycle not completed in humans, (e.g. trichinosis)
Human natural host, transmitted by arthropods, e.g. river blindness transmitted by flies

Trematodes
all require a snail species as intermediate host
hermaphroditic EXCEPT Schistosoma

Schistosomiasis
Schistosoma hematobium, S. mansoni, S. japonicum most important species
Life Cycle: adults found in mesenteric or bladder veins; eggs migrate to gut or bladder, passed into fresh water; motile larvae infect snail, multiply asexually, released into water; larvae enter human skin, develop into adults in liver, mate, and migrate to final venous site
Disease: chronic disease is an inflammatory response to retained eggs
most important helminth pathogen, significant morbidity and mortality in Africa

Other trematodes require two intermediate hosts
e.g. Chinese liver fluke (snail, fresh water fish), lung fluke (snail, fresh water crustaceans)
Medical Parasitology

- The study of protozoans, helminths, and arthropods that produce human disease
  - Protozoans
    - Unicellular heterotrophic eukaryotic organisms
    - Traditionally classified by method of motility
      - Flagellates (flagella-mediated motility)
      - Amoebas (pseudopod-mediated motility)
      - Apicomplexa (aka Sporozoa) (no motility)
  - Helminths (worms)
    - Nematodes (round worms)
    - Cestodes (tape worms)
    - Trematodes (flukes, flat worms)
  - Arthropods
    - Insects (fleas, lice, biting and stinging insects)
    - Arachnids (spiders, ticks, mites)

- Diagnosis of protozoan and helminthic infections
  - Microscopic examination
    - Feces, vaginal swabs, blood, tissue specimens
  - Complete blood count
    - Eosinophilia is an important characteristic of helminth infections that have a tissue migration stage
  - Serology
    - Antibody detection methodologies for parasites have become more sensitive and specific
  - Antigen detection
    - Protozoan infections
    - Nucleic acid methods
    - Protozoan infections

- Life cycles, hosts
  - Many parasites require multiple host species
  - Geographic distribution of human disease may depend on the range of the non-human host

- Definitive host
  - Host species in which the parasite reproduces sexually

- Intermediate host
  - Host species in which asexual reproduction or larval development takes place
  - Some parasites require multiple intermediate hosts

- Flagellate protozoa
  - Trichomonas vaginalis – vaginitis
  - Giardia lamblia – diarrhea
  - Trypanosoma cruzi – Chagas disease
  - T. brucei – African sleeping sickness
  - Leishmania spp. – mucocutaneous and visceral lesions

- Amoebas
  - Entamoeba histolytica – diarrhea and liver abscesses
  - Naegleria and Acanthomeba spp. – amebic meningoencephalitis

- Apicomplexa (old name: Sporozoa)
  - Plasmodium spp. – malaria
  - Toxoplasma gondii – congenital infections and encephalitis
  - Cryptosporidium parvum – diarrhea

Malaria

- Plasmodium falciparum, P. vivax, P. malariae, P. ovale, P. knowlesi
  - Sporozoan (apicomplexan) protozoans
  - Transmitted via mosquito vector (female Anopheles mosquitoes)
  - Complex life cycle involving invasion of liver cells, blood cells, and insect gut epithelial cells

- Malaria: fever, anemia, impaired circulation in organs
  - Significant cause of global morbidity and mortality
  - Drug resistance is a significant problem
  - Vector control (mosquito nets) remain the most effective preventive measure

Plasmodium life cycle and pathogenesis

- Gametocytes fuse to form oocyst, invade gut wall, develop into oocyst, sporozoites released and migrate to salivary glands.
- Mosquito ingests blood cells with gametocytes.
- In some blood cells, merozoites form gametocytes, do not lyse.
Malaria

- Pathogenesis
  - Fever: induction of cytokines by lysis of RBCs, release of merozoites
  - Anemia: lysis and phagocytic removal of infected RBCs, removal of uninfected RBCs, reduced production of RBCs
- *P. falciparum* produces most severe disease:
  - Only species that infects all stages of erythrocytes
  - Produces "knobs" on infected erythrocytes which cause cells to adhere to walls of blood vessels and to uninfected erythrocytes causing obstruction in capillaries
  - Cerebral malaria most severe form
  - Obstruction of capillaries in brain
- *P. vivax* and *P. ovale can relapse* months to years after initial disease
- Hepatic schizonts can become dormant, resistant to treatment
- *P. malariae* infects only senescent RBCs, can produce low level chronic infections lasting years

Malaria

- Half the world's population at risk
- 250 million cases per year, 1 million deaths
- Developing world
- Children
- Pregnant women

Helminths (worms)

- Helminths
  - Multicellular, elongated, bilaterally symmetrical eukaryotic animals
  - Range in size <1 mm to >1 m (human pathogens)
  - All have differentiated organs, nervous system, developed reproductive system (but no circulatory system)
  - May require single or multiple host species
  - Usually do NOT multiply within the host, so increasing "worm load" depends on repeated infections
  - There are a couple of important exceptions involving "autoinfection"
    - Serious disease usually requires high worm load, occurs in the developing world

Nematodes (round worms)

- Cylindrical, fusiform shape; tubular alimentary tract with mouth and anus, separate sexes

Gastrointestinal nematodes

- Adult inhabits intestinal tract of host
  - Life cycle can be completed in single host species
  - Eggs or larvae deposited in feces
  - Infections acquired by ingestion of eggs or entry of larvae in skin, depending on species
  - After ingestion and hatching of eggs, larvae may remain in intestine if eggs ingested, or may penetrate gut and enter circulation, or may enter venous circulation from skin
  - Larvae in circulation cannot pass through alveolar capillaries in the lung, break out there, are coughed up and swallowed, and develop into adults in the gut

Intestinal nematodes

- Limited to intestine
  - *Enterobius vermicularis* (pinworm)
    - anal itching (common but not serious)
  - *Trichuris trichiura* (whipworm)
    - diarrhea, blood loss, rectal prolapse

Pulmonary migration

- *Ascaris lumbricoides*
  - Eggs ingested
  - Largest nematode
  - Pulmonary symptoms, diarrhea and maladsorption, obstruction
- *Ancylostoma duodenale* and * Necator americanus* (hookworms)
  - Larvae enter skin
  - Skin rash, pulmonary symptoms, anemia
- *Strongyloides stercoralis*
  - Larva (not eggs) passed in stool, enter skin
  - Pulmonary symptoms, vomiting, diarrhea
  - Autoinfection possible, larva can migrate in same host, massive hyperinfection can occur in immunosuppressed

Tissue nematodes – human can be “accidental” or natural host

- Human is “accidental host”, life cycle not completed
  - *Toxocara canis* – ascarid of dogs – visceral larva migrans
    - Humans ingest eggs, larva enter circulation
    - Larva enter tissue, form granulomas, necrosis, organ dysfunction
  - *Trichinella spiralis* – agent of trichinosis
    - Parasite of carnivorous animals
      - Pigs are most important source of human disease
      - Larva ingested in undercooked meat, form cysts in skeletal muscle
- **Tissue nematodes**
  - Human is natural host, transmission involves arthropod host in which larvae develop
    - *Onchocerca volvulus* – river blindness
      - Transmitted by fly
      - Adults reside in subcutaneous nodules
      - Larva migrate through skin and eye
      - Chronic inflammation in skin and eye from dying larvae
      - ~300,000 cases of blindness per year, most in sub-Saharan Africa
    - *Wuchereria and Brugia* – transmitted by mosquitoes
      - Adults reside in lymphatic system, larva enter blood circulation
      - Lymphatic filariasis – obstruction of lymphatic circulation
      - Swelling of tissue, elephantiasis

- **Helminths**
  - **Cestodes – Tape Worms**
    - *Taenia saginata* – beef tapeworm
      - Similar to pork tapeworm, except humans do not develop cysticerci in tissue.
    - *Diphyllobothrium latum* – fish tapeworm
      - Adult resides in human intestine, eggs passed in feces
      - Eggs hatch in fresh water releasing motile larvae
      - Larvae ingested by copepods
      - Copepods ingested by fish, larvae migrate to fish tissue
      - Humans ingest infected fish, larve develop into adult worms in intestine.
      - Asymptomatic, or weight loss, vitamin deficiency, obstruction
    - *Echinococcus granulosus*
      - Adult resides in intestine of canines, eggs passed in feces
      - Eggs ingested by grazing animals, larvae migrate to tissue and encyst.
      - Canines eat grazing animals, larvae attach in gut and develop into adults completing the cycle.
      - Humans are accidental hosts, ingest eggs from canines, larvae encyst in tissue forming large masses termed hydatid cysts

- **Cestodes**
  - *Taenia solium* – pork tapeworm
    - Adult resides in human intestine, eggs and gravid proglottids passed in feces
    - Pigs eat human feces, eggs hatch, larvae invade gut wall of pig, enter circulation.
    - Larvae encyst in tissue of animal.
    - Humans eat undercooked pork, larvae develop into adult worms.
      - Asymptomatic, or diarrhea and weight loss
    - **What happens if humans ingest infected human feces???
      - Same thing as in pigs!
      - Eggs hatch, larvae invade gut wall and enter circulation, **encyst in tissue.**
        - Especially brain = neurocysticercosis.

- **Helminths**
  - **Trematodes – Flukes**
    - Bilaterally symmetrical, flattened, leaf-shaped worms
    - Blind alimentary canal
    - Mouth and ventral (for attachment and motility) suckers
    - Most are hermaphroditic, schistosomes have separate sexes
    - All have at least one intermediate host, a snail
  - **Schistosoma hematobium, S. mansoni, S. japonicum** – blood flukes
    - Only dioecious (separate sexes) trematode of humans
    - Mating pairs of adults inhabit veins
      - *S. mansoni, S. japonicum* – mesenteric veins (intestine)
      - *S. hematobium* – bladder veins
    - Eggs penetrate walls of veins and migrate to intestinal or urinary tract
    - Eggs penetrate into fresh water via feces or urine
    - Eggs hatch, and motile larve invade snail host
    - Larvae multiply axenally in snail and are released into water
    - Larvae enter skin of humans, migrate to lung and liver
    - Larvae develop into adults, form mating pairs, and migrate to final venous destination
    - **Human disease**
      - Skin rash after exposure, headache, fever abdominal pain during larval migration
      - After 1 – 2 months, acute systemic inflammatory illness occurs as adult worms begin depositing eggs
      - Chronic inflammation, granuloma formation, hemorrhage, liver and spleen enlargement associated with eggs retained in tissue

- **Cestodes**
  - *Dicrocoelium dendriticum*, *D. punctatum* – ♂ and ♀
    - Adult resides in the liver
    - Eggs hatch, and motile larve invade snail host
    - Larvae multiply axenally in snail and are released into water
    - Larvae enter skin of humans, migrate to lung and liver
    - Larvae develop into adults, form mating pairs, and migrate to final venous destination
    - **Human disease**
      - Skin rash after exposure, headache, fever abdominal pain during larval migration
      - After 1 – 2 months, acute systemic inflammatory illness occurs as adult worms begin depositing eggs
      - Chronic inflammation, granuloma formation, hemorrhage, liver and spleen enlargement associated with eggs retained in tissue

- **Trematodes**
  - *Fasciola hepatica* – liver fluke
    - Adult resides in the liver
    - Eggs hatch, and motile larve invade snail host
    - Larvae multiply axenally in snail and are released into water
    - Larvae enter skin of humans, migrate to lung and liver
    - Larvae develop into adults, form mating pairs, and migrate to final venous destination
    - **Human disease**
      - Skin rash after exposure, headache, fever abdominal pain during larval migration
      - After 1 – 2 months, acute systemic inflammatory illness occurs as adult worms begin depositing eggs
      - Chronic inflammation, granuloma formation, hemorrhage, liver and spleen enlargement associated with eggs retained in tissue
• Trematodes
  • *Schistosoma hematobium*, *S. mansoni*, *S. japonicum* – blood flukes
    • Most important helminth pathogen of humans
    • >200 million persons infected, >200,000 deaths per year
    • Occurs in agricultural and fishing populations in developing world
    • Occurs in tropical and subtropical regions worldwide, but 90% of infections occur in sub-Saharan Africa
    • Control efforts directed at treatment of at-risk populations, snail control, control of reservoir hosts, and improved sanitation

• Other trematodes – require two intermediate hosts
  • *Paragonimus westermanii* – Lung fluke
    • Acquired by ingestion of infected fresh water crabs and crayfish
    • Larvae migrate from intestine into peritoneal cavity, through liver, into lung (sometimes into the brain), where adults develop and deposit eggs
      • chronic bronchitis, neurological symptoms (seizures, paralyasis, etc.)
    • Eggs released in sputum, or swallowed and released in feces.
    • Eggs hatch in fresh water, larvae ingested by snail hosts, released and then invade fresh water crabs and crayfish
    • Five million humans infected, most in Far East, but also found in Africa and Central America

• Other trematodes – require two intermediate hosts
  • *Clonorchis sinensis* – Chinese liver fluke
    • Acquired through ingestion of infected fresh water fish (carp)
    • Larvae migrate from intestine into bile ducts
    • Adults develop in bile ducts
      • chronic inflammation, obstruction, bacterial infections, carcinoma
    • Eggs released in bile duct, passed in feces
    • Larvae ingested by snails, transformed, released and penetrate the tissue of fresh water fish where they encyst.
    • 20 million humans infected in Far East
      • Association with use of human feces in fertilizing commercial fish ponds