Micro 5

Antiparasitics

*Anthelmintics, Pediculicides, Miticidies, Antifungals*

PHRM 203
Allison Beale
Helminths

The parasitic worms

- **Phylum/Class Nematodes**
  - “Thread” worms
    - “Round” worms
      - *Ascaris lumbricoides*
      - *Anisakis sp.*
    - “Whip” worms
      - *Trichuriasis*
    - “Filarial” worms
      - *Onchocerca volvulus*
      - *Wuchereria bancrofti*
    - “Spiral” worms
      - *Trichinella spiralis*
    - “Hook” worms (Strongyles)
      - *Necator americanus*
    - “Pin” worms
      - *Enterobius vermicularis*

- **Phylum/Class Cestodes**
  - “Tape” worms
    - *Hymenolepis nana*
    - *Taenia solium*
      - Neurocysticercosis = most common brain parasite
    - *Echinococcus granulosus* - Hydatid d.

- **Phylum/Class Trematodes**
  - “Flukes”
    - >20K species
    - Blood versus tissue
      - Schistosomiasis
      - Fascioliasis

Phylum Platyhelminthes
% World Population with Helminth infections

<table>
<thead>
<tr>
<th>Percentage</th>
<th>Helminth</th>
</tr>
</thead>
<tbody>
<tr>
<td>30%</td>
<td>Ascaris</td>
</tr>
<tr>
<td>~22%</td>
<td>Hookworms</td>
</tr>
<tr>
<td>~18%</td>
<td>Trichuris</td>
</tr>
<tr>
<td>~14%</td>
<td>Filarias</td>
</tr>
<tr>
<td>10%</td>
<td>Enterobius</td>
</tr>
<tr>
<td>4%</td>
<td>Schistosomes</td>
</tr>
<tr>
<td>2%</td>
<td>Tape Worms</td>
</tr>
<tr>
<td>1%</td>
<td>Trichinella</td>
</tr>
</tbody>
</table>

Key:  N= Nematode;  C = Cestode;  T=Trematode

(Note controlled in US by Federal Swine Health Protection Act)
Cestodes (tape worms)

*Hymenolepis nana*
Human tape worm

*Echinococcus granulosis*
“Dog” tape worm

*Taenia solium*
Pork tape worm

**Treatment**: Albendazole, Mebendazole or Praziquantel

Proglottid – 80K eggs ea.

Scolex
Trematodes *(flukes):* Schistosomes

Ascites a result of eggs physically blocking hepatic blood vessels

WHO photos of children with Schistosomiasis. It affects 200M people in the world.

**Schistosomiasis**

2nd most significant disease after malaria

Chronic infection with significant morbidity & mortality

4,000 years of recorded human disease (including Egyptian hieroglyphic for the fluke)

*Swimmer’s itch caused by a schistosome sp. that dies upon burrowing in human skin!*

**Treatment:** Praziquantel or metrifonate
Trematodes (flukes): *Fasciola*

Life cycle of *M. yokogawai*

Cysts ingested by eating infected fresh water fish

Emerge in mammal intestines and develop into adults, shedding eggs into feces

May cause systemic infection & eggs will embolize to brain, spinal cord or heart

Fresh water snails infected and release larvae that encyst on fish

Treatment: Praziquantel (CDC photo)

Adult *Metagonimus yokogawai*
Intestinal fluke of humans
10-15% prevalence in Japan
Nematodes (Thread worms)

Filaria: Loa loa (Loiasis)
Treatment: diethylcarbamazine

Pin worms: Enterobius vermicularis
Treatment: OTC Pyrantel

Filaria: Elephantiasis

Hookworms: N. americanus
Treatment: Albendazole

PHRM 203 - Anthelmintics & Antifungals
Nematodes: Ascarids

- Humans – definitive host
  - *Ascaris lumbricoides*
    - Affects 1.4B people
    - Not Reportable in Hawaii!
- Humans – aberrant host
  - *Anisakis sp.*
  - *Toxocara canis/cati*
  - *Baylisascaris procyonis*
  - *Ascaris suum*
Nematodes (Ascarids)
Anisakis sp.

Increasingly seen due to popularity of sashimi and sea food in general

Common in Japan

Treatment: Albendazole or Ivermectin

Symptoms: severe abdominal pain within hours of ingestion, with nausea and vomiting. Symptoms may mimic Crohn’s disease.

Prevent infection by cooking fish or freezing (>1 wk).
Toxocara canis & T. cati Public Health

• Estimate 10,000 human cases/yr in U.S.
  – 700 cases of Ocular Larva Migrans or OLM/yr

• 5-14% seropositive in US
  – Accidental host, self-limiting
    – Corticosteroids/Albendazole

• Risk factors:
  – Children
  – Pica (dirt consumption)
  – Dog/cat ownership
Larva Migrans

- Migration / presence of non-human hosted helminthic larvae within the tissues of a human
- Named by location:
  - Visceral larva migrans (VLM)
  - Ocular larva migrans (OLM)
  - Neural larva migrans (NLM)

Hookworm in a 10yr old girl’s foot
Larva Migrans

• VLM
  – Larvae lodged in liver, lungs, heart, muscle
  – Hook worms and whip worms are seen in skin

• OLM
  – Inflammation and retinal scarring
  – Vision loss (progressive or sudden blindness) - unilateral without systemic signs
  – May be misdiagnosed as retinoblastoma
  – Loa Loa (*Mansonella streptocerca*, a filarial nematode)

• NLM
  – Meningitis, encephalitis, epilepsy
  – Neurocysticercosis (*Taenia solium*, the pork tape worm)
Nematodes: Filaria

- **Lymphatic**
  - **Elephantiasis**
    - Mosquito vector
    - Diethylcarbamazine for most

- **Subcutaneous fat**
  - **Loa Loa**
    - Deer fly vector
  - **River blindness (Onchocerciasis)**
    - Black fly vector
    - 2\(^{nd}\) leading cause of blindness
    - Merck, free **Ivermectin**
  - **Guinea worms**
    - Water fleas (drink water containing the crustacean)

*Dracunculus medinensis*, the guinea worm, must be pulled out over the course of months, there is no drug therapy.
Wolbachia

- Endosymbiotic bacteria
  - WIDESPREAD in insects
  - Filarial worms also have
    - Kill bacteria with doxycycline
      - Sterilizes and kills filarial nematodes
# Anthelmintics


<table>
<thead>
<tr>
<th>Drug</th>
<th>Indication</th>
</tr>
</thead>
<tbody>
<tr>
<td>Albendazole (Albenza) 🍼🎨</td>
<td>Broad spectrum anthelminth. GI and tissue nematodes and cysts of certain cestodes. <strong>Hydatid disease, Neurocysticercosis</strong>, filariasis, hookworms</td>
</tr>
<tr>
<td>Ivermectin (Stromectol) 🍼🎨</td>
<td>Broad spectrum anthelminth, miticide and pediculocide. Threadworms, <strong>strongyloidiasis, onchocerciasis</strong>, filariasis</td>
</tr>
<tr>
<td>Mebendazole (Vermox) 🍼🎨</td>
<td>Broad spectrum anthelminths. GI nematodes. Pinworms, roundworms, whipworms, hookworms</td>
</tr>
<tr>
<td>Praziquantel (Biltricide) 🍼🎨</td>
<td>Active against cesodes and trematodes. Mainly used against <strong>Schistosomes (flukes)</strong> but also against <em>H. nana</em></td>
</tr>
<tr>
<td>Pyrantel (PinX) 🍼🎨</td>
<td>Pinworms, roundworms and hookworms. Used against trichuriasis (whip worms). - Also available OTC</td>
</tr>
<tr>
<td>Diethylcarbamazine (Hetrazan) 🍼🎨</td>
<td>Only against specific filaria: W. bancrofti, B. malayi or B. timori as well as loiasis. Not used for onchocerciasis.</td>
</tr>
</tbody>
</table>
## Anthelmintic Mechanisms

**Goodman and Gilman’s the Pharmacological Basis of Therapeutics 11th Ed. McGraw Hill 2006**

<table>
<thead>
<tr>
<th>Drug</th>
<th>Mechanism</th>
</tr>
</thead>
<tbody>
<tr>
<td>Albendazole (Albenza)</td>
<td>- Polymerization of worm tubulin into microtubules and inhibition of the helminth-specific enzyme fumarate reductase</td>
</tr>
<tr>
<td>Ivermectin (Stromectol)</td>
<td>- Binds to glutamate-gated chloride ion channels in invertebrate nerve and muscle cells → ↑ permeability of cell membranes to Cl⁻, hyperpolarizing the nerve or muscle cell and kills the parasite.</td>
</tr>
<tr>
<td>Praziquantel (Biltricide)</td>
<td><em>Unknown</em> may alter Ca⁺⁺ uptake (leading to paralysis) or adenosine uptake (blocking metabolism)</td>
</tr>
<tr>
<td>Pyrantel (PinX)</td>
<td>- Neuromuscular blocking agent (very poorly absorbed in man)</td>
</tr>
<tr>
<td>Diethylcarbamazine</td>
<td>- Arachidonic acid metabolism in microfilaria</td>
</tr>
</tbody>
</table>

PHRM 203 - Anthelmintics & Antifungals
Ectoparasites & Fungi

- Lice - Head, body and pubic
- Ringworm - fungi Dermatophytes
- Mange – mites Sarcoptes

Courtesy of William D. James, MD
Scabies

- An arthropod – skin mite
- *Sarcoptes scabiei var. hominis.*
- Obligate parasite
- Species specific (different for humans and animals)
- AKA
  - Mange (10-20 mites)
  - Norwegian mites (Crusted)
    - 1,000’s to millions of mites

Often a problem in nursing homes
Lice

- **Three Types**
  - *Pediculus humanus*
    - *capitus* (head)
      - Common in school kids
    - *humanus* (body)
      - Common in the homeless
  - *Pthirus pubis* (pubic) = “crabs”
    - Sexually active adults

Lice cause itching and a characteristic excoriated skin rash that looks like a scrape. They may also transmit diseases, including relapsing fever, typhus, and trench fever.
# Scabicides & Pediculicidies

<table>
<thead>
<tr>
<th>Drug</th>
<th>Route</th>
<th>Indication</th>
<th>Scabies</th>
<th>Lice</th>
<th>Nematodes</th>
</tr>
</thead>
<tbody>
<tr>
<td>25% benzyl benzoate lotion*</td>
<td>Topical</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td></td>
</tr>
<tr>
<td>5% Permethrin cream 🎥 B (Elimite, NIX cream, Acticin)</td>
<td>Topical</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td></td>
</tr>
<tr>
<td>5% monosulfiram soap (Temosol)*</td>
<td>Topical</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td></td>
</tr>
<tr>
<td>Crotamiton (Eurax)</td>
<td></td>
<td>✓</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Piperonyl butoxide/pyrethrins (RID, Tisit, Licide)</td>
<td></td>
<td></td>
<td></td>
<td>✓</td>
<td></td>
</tr>
<tr>
<td>Ivermectin (Stromectol, Sklice)</td>
<td>PO, topical</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
</tbody>
</table>

* May not be available in the US, or may be used off-label in the US
Mycooses

- **Deep**
  - Invasive aspergillosis
    - Often fatal
  - Blastomycosis
  - Candidiasis
  - Cryptococcosis
    - Bird droppings
  - Coccidioidomycosis
    - Soil
  - Histoplasmosis
    - Bird/bat droppings
  - Mucormycosis
  - Pseudallescheriasis
  - Sporotrichosis
    - Rose Gardener’s D.

- **Superficial**
  - Candidiasis
    - Vulvovaginal
    - Oropharyngeal
    - Cutaneous
  - Ringworm

Aspergillosis 2nd most common serious fungal infection after Candida.
Candida

- Candidiasis
  - *Candida albicans*
  - Normal flora in 40-80% of healthy people
    - Skin, mouth, vagina
  - Pathogenic
    - Δ’ d immune status
    - Δ’ d normal flora
    - Δ’ d physiology

Treatment: OTCs *clotrimazole* (Lotrimin) or Rx *Nystatin*, *Amphotericin B* & *fluconazole* (Diflucan)
Cryptococcosis

- *Cryptococcus neoformans*
  - Meningitis
  - Pulmonary disease
- Inhalation of soil/dust
- Usually no symptoms in healthy people
- Potentially fatal in immunocompromised
  - HIV
  - Corticosteroids

Cryptosporidiosis!
Coccidioidomycosis

- “Valley Fever”
  - *Coccidioides immitis* or *posadasii*
  - Flu-like illness that may become chronic pulmonary infection or systemic infection
  - Incidence increasing

 Cryptosporidiosis & Cryptococcosis!
Ringworm

• Several different species of fungi, not worms
  – *Epidermophyton*
  – *Microsporum*
  – *Trichophyton*

• Grow only in keratinized tissue
  – Stops at living tissue
  – Infects the hair shaft

• Can live in humans, animals, and soil

• Sometimes a zoonotic disease

* Tinea corpus – skin
* Tinea cruris – groin
* Tinea pedis – foot/toes
* Onychomycosis - nailbed
Ringworm: Transmission

- Direct
  - Skin-to-skin contact with an infected person or pet

- Indirect/Fomite
  - Infected individual touched object
  - Hats, combs, brushes, bed linens, stuffed animals, telephones, gym mats, shower stalls, etc.

- Rarely, by contact with soil
Ringworm: Treatment

• Ringworm usually responds well to self-care within 4 weeks without having to see a doctor
  – Keep skin clean and dry
  – Over-the-counter antifungal or drying powders, lotions, or creams
  – Wash sheets and nightclothes every day while infected.

• Antifungals
  – Prescription and OTC
  – Miconazole, clotrimazole, etc.
# Systemic Antifungals

<table>
<thead>
<tr>
<th>Drug</th>
<th>Indication</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amphotericin B (Amphotec, Fungizone) 🌴fung B</td>
<td>Aspergillosis, Blastomycosis, Candidiasis, Coccidioidomycosis, Cryptococcosis, Histoplasmosis, Mucormycosis, Sporotrichosis</td>
</tr>
<tr>
<td>Capsofungin acetate (Cancidas)</td>
<td>Candidiasis, invasive aspergillosis in patients refractory to other treatments</td>
</tr>
<tr>
<td>5-Fluorocytosine (Flucytosine)</td>
<td>Cryptococcosis, candidiasis</td>
</tr>
<tr>
<td>Fluconazole (Diflucan) 🌴fung C</td>
<td>Systemic, vulvovaginal and oropharyngeal Candidiasis, Coccidioidomycosis. Cryptococcal meningitis.</td>
</tr>
<tr>
<td>Griseofulvin</td>
<td>Tinea sp. (Ringworm)</td>
</tr>
<tr>
<td>Terbinafine (Lamisil)</td>
<td>Tinea sp. (Ringworm)</td>
</tr>
</tbody>
</table>
Amphotericin B

• Indications
  – ONLY potentially life threatening fungal inf

• ADRs
  – Administer IV slowly under close watch
    • Fever, shaking chills, hypotension, anorexia, nausea, vomiting, headache, and tachypnea are common 1 to 3 hours after starting IV
    • Inject no > 1.5 mg/kg

- Only for life-threatening fungal infections
- May cause fatal cardio or cardiopulmonary arrest
Fluconazole (Diflucan)

- ADRs
  - Liver failure, SJS, anaphylaxis, arrhythmias
  - LOTS (& LOTS) of drug interactions

Oral hypoglycemics
Coumarin-type anticoagulants
Phenytoin
Cyclosporine
Rifampin
Theophylline

Mostly for serious Candida infections

PO, IV

Terfenadine
Cisapride
Astemizole
Rifabutin
Tacrolimus
Short-term benzodiazepines

POTENT ↓
P450

D
# Topical Antifungals

<table>
<thead>
<tr>
<th>Drug</th>
<th>Indication</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clotrimazole (Lotrimin)</td>
<td>Vulvovaginal, Oropharyngeal and Cutaneous candidiasis; Tinea sp. (Ringworm)</td>
</tr>
<tr>
<td></td>
<td>Topical (creams, spray, solution, lozenges/troches)</td>
</tr>
<tr>
<td>Ketoconazole</td>
<td>Cutaneous candidiasis, Tinea sp. (Ringworm)</td>
</tr>
<tr>
<td>Nystatin</td>
<td>Vulvovaginal, Oropharyngeal and Cutaneous candidiasis</td>
</tr>
<tr>
<td>Miconazole</td>
<td>Vulvovaginal and Cutaneous candidiasis; Tinea sp. (Ringworm)</td>
</tr>
<tr>
<td>Terbinafine (Lamisil)</td>
<td>Onychomycosis of the toenail or fingernail due to Tinea sp.</td>
</tr>
<tr>
<td>Tolnaftate</td>
<td>Tinea sp. (Ringworm)</td>
</tr>
</tbody>
</table>