Pathogenic fungi and parasites

Unit 4
What is Mycology?
Mycology is the study of fungi

- We use fungi to make:
  - Beer
  - Wine
  - Bread
- Some fungi are edible e.g. gourmet mushrooms
- Some fungi are toxic
- Some fungi are pathogens or opportunistic pathogens
What is a fungus?

- Eukaryote – with nucleus
- Do not contain chlorophyll
- Have cell walls
- Produce filamentous structures
- Produce spores
Species of Fungi

• 100,000 – 200,000 species

• About 300 pathogenic for man
Kingdom Fungi

- Ascomycota
- Basidiomycota
- Zygomycota
- Deuteromycota (Fungi Imperfecti, Mitosporic Fungi)
Table 12.3 Characteristics of Major Groups of Fungi

<table>
<thead>
<tr>
<th>Group and Representative Member</th>
<th>Usual Habitat</th>
<th>Some Distinguishing Characteristics</th>
<th>Asexual Reproduction</th>
<th>Sexual Reproduction</th>
</tr>
</thead>
<tbody>
<tr>
<td>Zygomycetes</td>
<td>Terrestrial</td>
<td>Multicellular, coenocytic mycelia (with many haploid nuclei)</td>
<td>Non-Septate</td>
<td>Sexual spores known as zygospores can remain dormant in adverse environment</td>
</tr>
<tr>
<td>Rhizopus stolonifer</td>
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<tr>
<td>(black bread mold)</td>
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<tr>
<td>Basidiomycetes</td>
<td>Terrestrial</td>
<td>Multicellular, uninucleated mycelia. Group includes mushrooms, smuts, rusts that affect the food supply</td>
<td>Sporangiaspores</td>
<td>Produces basidiophores that are borne on club-shaped structures at the tips of the hyphae</td>
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<tr>
<td>Agaricus campestris</td>
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<tr>
<td>(meadow mushroom)</td>
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<tr>
<td>Cryptococcus neoformans</td>
<td></td>
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</tr>
<tr>
<td>Ascomycetes</td>
<td>Terrestrial</td>
<td>Unicellular and multicellular with septated mycelia</td>
<td>Septate</td>
<td>Psycomycetes Involve the formation of an ascus (sac) on specialized hyphae</td>
</tr>
<tr>
<td>Neurospora, Saccharomyces</td>
<td>Terrestrial, on fruit and other organic materials</td>
<td></td>
<td>Is common by budding; conidiospores</td>
<td></td>
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<tr>
<td>cerevisiae (baker's yeast)</td>
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<td></td>
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<td></td>
</tr>
<tr>
<td>Deuteromycetes (Fungi Imperfecti)</td>
<td>Terrestrial</td>
<td>A number of these are human pathogens</td>
<td>Conidia</td>
<td>Absent or unknown</td>
</tr>
<tr>
<td>Penicillium, Aspergillus</td>
<td></td>
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</tr>
</tbody>
</table>
Spore → Germ tube → Hypha → Mycelium
Mold structure

(a) Vegetative Hyphae
- Surface hyphae
- Submerged hyphae
- Hypha

(b) Reproductive Hyphae
- Substrate
- Rhizoids
- Germ tube
- Spore
- Spores

(c) Germination
Septate hyphae
as in *Penicillium*

Nonseptate hyphae
as in *Rhizopus*

(c) Types of hyphae
What is medical mycology?
Diseases associated with fungi

• Hypersensitivity (allergy)
• Mycotic toxin
• Infection
Pathogenic fungi

• Normal host
  – Systemic pathogens – 25 species
  – Cutaneous pathogens – 33 species
  – Subcutaneous pathogens – 10 species

• Immunocompromised host
  – Opportunistic fungi – 300 species
Pathogenicity

- Thermotolerance
- Ability to survive in tissue environment
- Ability to withstand host defenses
MORPHOLOGY

• Yeasts
• Hyphae (filamentous fungi, mycelium)
  – Septate
  – Non-septate (Coenocytic)
• Dimorphic
  – Yeast
  – Mycelium
Dimorphic Fungi

- **Yeast Form**
  - Parasitic form
  - Tissue form
  - Cultured at 37°C

- **Mycelial Form**
  - Saprophytic form
  - Cultured at 25°C
SPORES

Sexual

Asexual

• Arthrospore
• Blastospore
• Chamydospore
• Conidia
  – Microconidia
  – Macroconidia
Establishment of infection with a mycotic agent depends on

1. Inoculum size

2. Pathogenicity of the fungi

3. Resistance of the host
Recent interest in mycology

- Increased frequency of mycotic diseases
- Increased awareness by physicians
- Better trained laboratory personnel
- More invasive procedures used on patients
- Increased use of immunosuppressive drugs
- Increase in immunosuppressive disease
Medical mycology

Clinical Classification
Fungal infection (Mycosis)

• Superficial mycoses

• Systemic mycoses
  – Coccidioidomycosis (Valley Fever)
  – Histoplasmosis
  – Blastomycosis
  – Cryptococcosis

• Opportunistic mycoses
  – *Candida, Cryptococcus, Geotrichum, Aspergillus, Rhizopus, Mucor, Pneumocystis*

  – Two of the most common opportunistic pathogens:
    • *Candida albicans*
    • *Aspergillus fumigatus*
Superficial Fungal Infections

• Invade only dead (keratinized) tissues of skin or its appendages
  – stratum corneum, hair, nails

• Organisms are called dermatophytes
  – *Microsporum*, *Trichophyton*, *Epidermophyton*

• Transmission:
  – person to person, animal to person, occasionally fomites
Signs and symptoms

- Skin - itchy scaly ring lesions that increase slowly in size
- Nails - initially flaky, patchy, discolored - eventually become thickened and grossly deformed.
- Hair - round balding patches with numerous breaks in hair
Dermatophytes
Tinea (ringworm) Lesion
Tinea corporis
Tinea capitis

Common causative agent: *Microsporum canis*

Hair fluoresces under Wood’s lamp
Tinea barbae

Caused by *Trichophyton rubrum*

Ringworm of the beard
Tinea Pedis
“athlete’s foot”
Tinea Pedis
Tinea unguium

Common causative agent: *Trichophyton rubrum*
Systemic mycoses

• Coccidioidomycosis (Valley Fever)
• Histoplasmosis
• Blastomycosis
• Cryptococcosis
Opportunistic fungal infection

• Infections caused by endogenous organisms or ubiquitous saprophytes that have:
  – low virulence
  – Rarely infect healthy people

• Host being infected usually have:
  – Predisposing diseases:
    • Diabetes, cancer, leukemia, etc.
  – Predisposing conditions:
    • Agammaglobulinemia, steroid or antibiotic therapy
Opportunistic fungal infection

• Most commonly caused by:
  – Candida
  – Cryptococcus
  – Aspergillus
  – Rhizopus
  – Mucor
  – Pneumocystis

• Two of the most common opportunistic pathogens:
  – Candida albicans
  – Aspergillus fumigatus
Cryptococcosis

- Causative agent – *Cryptococcus neoformans*
- Opportunistic infection acquired by inhalation of the organism
- Found in:
  - Soil
  - common in bird droppings - pigeons
- Opportunistic infection in immunocompromised patients (e.g. AIDS)
Cryptococcosis

Manifestations
• chronic meningitis (the most common cause of fungal meningitis)
  – symptoms: headache, blurred vision, confusion, depression
• pulmonary infection (the most common form of cryptococcosis)
  – usually asymptomatic, transient and self-limited
• can also disseminate to skin, liver spleen, kidneys, etc.

Diagnosis
• Microscopy examination of CSF
• Culture of the organism from CSF, sputum, urine, blood
Cryptococcosis

Encapsulated yeasts found in CSF of patients chronic suffering from cryptococcal meningitis. (India Ink)
Candidiasis (Moniliasis) caused by Candida albicans

- Yeast - multiplies by blastospore formation (budding), forms pseudohyphae & chlamydospores
- part of normal flora of oral cavity, vagina, GI tract, rectal area
- causes more diverse types of disease than any other fungus in humans: spectrum ranges from superficial to systemic
Candida albicans

Typical moist yeast colonies
Candida albicans

Budding

PAS stain of urine showing budding & pseudohyphae
**Thrush (oral candidiasis)**

- small white flecks or patches covering tongue and mouth
- fairly common in newborns, picked up from mother upon passage through birth canal
- immunocompromised patients e.g. AIDS
- treatment: swish and spit preparations of nystatin and Amphotericin B
• **Intertriginous candidiasis** - moist warm areas of the body touching each other especially in overweight individuals, axillae

• **Vaginal candidiasis** - (the typical yeast infection) 20 million cases per year in U.S. alone - diabetes, antibiotic therapy, oral contraceptives, pregnancy, anything changing population of *Lactobacillus*
**Pneumocystis Pneumonia (pneumocystosis)**

- *Pneumocystis jiroveci (carinii)*
  - originally classified as a protozoan
  - RNA analysis led to reclassification as a fungus
    - most closely related to yeasts
- **Transmission:** airborne spores (1-3um)
- **Epidemiology:** serological tests indicate that most children are infected by age 2 1/2. The infection is asymptomatic and generally eliminated within a year.
- **Most cases occur in people with immunodeficiency.** Uncertain whether newly acquired from inhalation of spores or activation of a latent infection.
Pneumocystis Pneumonia

- **Symptoms:** gradually increasing shortness of breath & rapid breathing, fever slight or absent, 1/2 of the patients have a cough.

- **Opportunistic -** occurs when there are defects in cell-mediated immunity.
  - > 80% of AIDS patients have this infection at some time if prophylaxis is not given

- **Diagnosis:** finding organisms in biopsied lung tissue or bronchial lavage.

- **Treatment -** trimethoprim-sulfamethoxazole
Life Cycle of *Pneumocystis jiroveci* (carinii)

1. The mature cyst contains 8 intracystic bodies.
2. The cyst ruptures, releasing the bodies.
3. The bodies develop into trophozoites.
4. The trophozoites divide.
5. Each trophozoite develops into a mature cyst.

Thick walled cyst found in alveoli of lung. (Silver stain).
Antifungal chemotherapy
All eukaryotic cells contain sterols

• Mammalian cells
  – Cholesterol

• Fungal cells
  – Egosterol
Examples of antifungal agents

1. Polyene derivatives (Inhibits ergosterol synthesis)
   - Amphotericin B
   - Nystatin

2. Azoles (Inhibits ergosterol synthesis)
   - Ketoconazole
   - Fluconazole
   - Itraconazole
   - Voriconazole

3. Griseofulvin (It binds to tubulin, interfering with microtubule function, thus inhibiting mitosis; therefore is a barrier to fungal growth)

4. 5-fluorocytosine (Inhibits RNA synthesis)
Medical Parasitology
Outline

• Classification of important parasites to kingdom and phylum
• Parasitic infections affect communities in poor countries
• Knowledge of their life cycle is necessary for effective prevention and control
• Examples of some important parasitic infections
  – Epidemiology
  – Basic life cycle
  – Clinical presentation
  – Management and control
Parasites

- Organisms that acquires basic nutritional requirements through their host (other living organisms)
- Parasites may be unicellular or multicellular
- **Protozoa**
  - unicellular organisms
  - e.g. Plasmodium (malaria)
- **Metazoa**
  - multicellular organisms
  - e.g. helminths (worms) and arthropods (ticks, lice)
- **An endoparasite**
  - a parasite that lives within another living organism
  - e.g. malaria, Giardia
- **An ectoparasite**
  - a parasite that lives on the external surface of another living organism
  - lice, ticks
Definitions

- **Host**: “the organism in, or on, which the parasite lives and causes harm”
- **Definitive host**: “the organism in which the adult or sexually mature stage of the parasite lives”
- **Intermediate host**: “the organism in which the parasite lives during a period of its development only”
- **Zoonosis**: “a parasitic disease in which an animal is normally the host - but which also infects man”
- **Vector**: “a living carrier (e.g.an arthropod) that transports a pathogenic organism from an infected to a non-infected host”. A typical example is the female *Anopheles* mosquito that transmits malaria
Epidemiology

- Majority of parasitic infections occur
  - In tropical regions
  - In country with poor sanitation and personal hygiene

- Usually entire communities may be infected with multiple different organisms
  - Treatment is neither accessible nor affordable
Some major parasitic infections in the world

<table>
<thead>
<tr>
<th>Parasite</th>
<th>Diseases</th>
<th>No. people infected</th>
<th>Deaths/yr</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Plasmodium</em></td>
<td>malaria</td>
<td>273 million</td>
<td>1.12 million</td>
</tr>
<tr>
<td>Soil transmitted helminths:</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>• Roundworm (<em>Ascaris</em>)</td>
<td>Pnemonitis, intestinal obstruction</td>
<td>2 billion</td>
<td>200,000</td>
</tr>
<tr>
<td>• Whipworm (<em>Trichuris</em>)</td>
<td>Bloody diarrhoea, rectal prolapse</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Hookworm (<em>Ancylostoma and Necator</em>)</td>
<td>Coughing, wheezing, abdominal pain and anaemia</td>
<td></td>
<td></td>
</tr>
<tr>
<td><em>Schistosoma</em></td>
<td>Renal tract and intestinal disease</td>
<td>200 million</td>
<td>15,000</td>
</tr>
<tr>
<td><em>Filariae</em></td>
<td>Lymphatic filariasis and elephantiasis</td>
<td>120 million</td>
<td>Not fatal but 40 Millions disfigured or incapacitated</td>
</tr>
<tr>
<td><em>Trypanosoma cruzi</em></td>
<td>Chagas disease (cardiovascular)</td>
<td>13 million</td>
<td>14,000</td>
</tr>
<tr>
<td><em>African trypanosomes</em></td>
<td>African sleeping sickness</td>
<td>0.3 – 0.5 million</td>
<td>48,000</td>
</tr>
<tr>
<td><em>Leishmania</em></td>
<td>Cutaneous, mucocutaneous and visceral leishmaniasis</td>
<td>12 million; 2 million new cases/yr</td>
<td>50,000</td>
</tr>
<tr>
<td>Sub kingdom</td>
<td>Phylum</td>
<td>Sub-phylum</td>
<td>Genus-examples</td>
</tr>
<tr>
<td>-------------</td>
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<td>----------------</td>
</tr>
<tr>
<td>Protozoa</td>
<td>Sarcomastig-ophora</td>
<td>Sarcodina move by pseudopodia</td>
<td>Entamoeba</td>
</tr>
<tr>
<td></td>
<td>further divided into</td>
<td>Mastigophora move by flagella</td>
<td>Giardia</td>
</tr>
<tr>
<td>Apicomplexa</td>
<td>no organelle of locomotion</td>
<td>Plasmodium</td>
<td>P. falciparum, P. vivax, P. malariae, P. ovale</td>
</tr>
<tr>
<td>Ciliophora</td>
<td>move by cilia</td>
<td>Balantidium</td>
<td>B. coli</td>
</tr>
<tr>
<td>Microspora</td>
<td>Spore-forming</td>
<td>Enterocytozoa</td>
<td>E. bienusi</td>
</tr>
</tbody>
</table>
Examples of important intestinal protozoa

Transmitted by the faecal-oral route and cause diarrhoea

• *Giardia lamblia*: world-wide distribution, lives in the small intestine and results in malabsorption

• *Entamoeba histolytica*: may invade the colon and cause bloody diarrhoea – amoebic dysentery. Also causes ameobic liver abscess.

• *Cryptosporidium parvum*: more prevalent in the immunocompromised
Entamoeba histolytica

Trophozoite with ingested RBCs

Cyst
Giardia lamblia

Trophozoite

Cyst
Examples of important systemic protozoa

Detected in the blood

- *Plasmodium*: the cause of malaria. There are 4 species that infect man: *P. falciparum, P. vivax, P. ovale* and *P. malariae*

- *Toxoplasma gondii*: transmitted by the ingestion of oocysts from cat faeces. Infection can lead to ocular problems and is also a cause of neonatal toxoplasmosis

- *Leishmania*: transmitted by sand flies, can lead to visceral, cutaneous and mucocutaneous leishmaniasis

- *Trypanosoma*: haemoflagellates which cause
  - In Africa - sleeping sickness (transmitted by the Tsetse fly)
  - In South America - Chagas disease (transmitted by the Reduviid bug)
Malaria Endemic Countries, 2003

Note: This map shows countries with endemic malaria. In most of these countries, malaria risk is limited to certain areas.
Vectors of malaria: 
*Anopheles*

Trophozoite

Gametocyte
Toxoplasma

Both oocysts and tissue cysts transform into tachyzoites shortly after ingestion. Tachyzoites localize in neural and muscle tissue and develop into tissue cyst bradyzoites. If a pregnant woman becomes infected, tachyzoites can infect the fetus via the bloodstream.

Diagnostic Stage
1) Serological diagnosis.
   or
2) Direct identification of the parasite from peripheral blood, amniotic fluid, or in tissue sections.

(Immunofluorescence assay to detect anti-tachyzoite antibodies in patients)
Taxonomic classification of helminths

**Subkingdom**

- **Metazoa**
  - **Phylum**
    - **Nematodes**
      - Round worms; appear round in cross section, they have body cavities, a straight alimentary canal and an anus
      - Examples:
        - Ascaris (roundworm)
        - Trichuris (whipworm)
        - Ancylostoma (hookworm)
        - Necator (hookworm)
        - Enterobius (pinworm or threadworm)
        - Strongyloides
    - **Platyhelminthes**
      - Flat worms; dorsoventrally flattened, no body cavity and, if present, the alimentary canal is blind ending
    - **Cestodes**
      - Adult tapeworms are found in the intestine of their host
      - They have a head (scolex) with sucking organs, a segmented body but no alimentary canal
      - Each body segment is hermaphrodite
      - Example: Taenia (tapeworm)
    - **Trematodes**
      - Non-segmented, usually leaf-shaped, with two suckers but no distinct head
      - They have an alimentary canal and are usually hermaphrodite and leaf shaped
      - Schistosomes are the exception. They are thread-like, and have separate sexes
      - Example: Fasciolopsis (liver fluke)
      - Schistosoma (not leaf shaped!)
Examples of important metazoa – intestinal nematodes

- *Ascaris* (roundworm)
  - Found world-wide in conditions of poor hygiene, transmitted by the faecal-oral route
  - Adult worms lives in the small intestine
  - Causes eosinophilia

- *Trichuris* (whipworm)
  - A soil transmitted helminth
  - Prevalent in warm, humid conditions
  - Can cause diarrhoea, rectal prolapse and anaemia in heavily-infected people
Ascaris

Fertilized egg  Unfertilized egg

Heavy intestinal infection

Fertilized egg  Unfertilized egg
Examples of important metazoa – intestinal nematodes

• *Ancylostoma* and *Necator* (hookworms)
  – A major cause of anaemia in the tropics

• *Strongyloides*
  – inhabits the small bowel
  – infection more severe in immunospressed people
    (e.g. HIV/AIDS, malnutrition, intercurrent disease)

• *Enterobius* (pinworm or threadworm)
  – prevalent in cold and temperate climates but rare
    in the tropics
  – found mainly in children
Embryonated eggs ingested by human

1. Eggs on perianal folds. Larvae inside the eggs mature within 4 to 6 hours.

2. Adults in lumen of cecum. Gravid female migrates to perianal region at night to lay eggs.

Adult pinworms
Examples of important metazoa – systemic nematodes

Filaria including:

- *Wuchereria bancrofti* – The major causative agent of lymphatic filariasis
- *Brugia malayi* – Another microfilarial parasite that causes lymphatic filariasis
- *Onchocerca volvulus* – Transmitted by the simulium black fly, this microfilarial parasite can cause visual impairment, blindness (river blindness) and severe itching of the skin in those infected
Adults are found primarily in lymphatic vessels.
Examples of important flatworms - cestodes

1. Intestinal - (“tapeworms”)
   • *Taenia saginata*
     - worldwide
     - acquired by ingestion of contaminated, uncooked beef
     - a common infection but causes minimal symptoms
   • *Taenia solium*
     - worldwide
     - acquired by ingestion of contaminated, uncooked pork that contains cystercerci
     - Less common, but causes cystercicosis – a systemic disease where cysticerci encyst in muscles and in the brain – may lead to epilepsy
Taenia
Examples of important flatworms - cestodes

2. Systemic

- *Echinococcus granulosus* (dog tapeworm) and *Echinicoccus multilocularis* (rodent tapeworm)
  - Hydatid disease occurs when the larval stages of these organisms are ingested
  - The larvae may develop in the human host and cause space-occupying lesions in several organs, e.g. liver, brain
Echinococcus granulosus

1. Scolex attaches to intestine
2. Embryonated egg in feces
3. Oncosphere hatches; penetrates intestinal wall
4. Ingestion of eggs (in feces)
5. Intermediate Host (sheep, goats, swine, etc.)
6. Ingestion of cysts (in organs)

- Protoscolex from cyst
- Definitive Host (dogs & other canidae)
- Adult in small intestine

Hydatid cyst in liver, lungs, etc.

= Infective Stage
= Diagnostic Stage
Examples of important metazoa – trematodes (flukes)

- *Clonorchis sinensis* (liver fluke)- Widespread in China, Japan, Korea and Taiwan, this parasite is acquired by ingestion of infective metacercariae in raw or pickled fish

- *Fasciola hepatica* (liver fluke)- Primarily, a parasite of sheep, humans become infected when they ingest metacercariae that have encysted on watercress. The adult trematode lives in the intra-hepatic bile ducts of the liver. “Fascioliasis” can lead to severe anaemia in humans
Clonorchis sinensis (liver fluke)
Examples of important metazoa – trematodes (flukes)

- *Paragonimus westermani* (lung fluke)- Widespread in the Far East and South east Asia, the parasite is acquired by ingestion of infective metacercariae in raw or pickled crustaceans
  - *Schistosoma haematobium*
  - *S. mansoni*
  - *S. japonicum*
Schistosomiasis (1)

Epidemiology
• 200m people in 74 countries infected, 85% of whom live in sub-Saharan Africa
• S. haematobium - Africa and middle east (most prevalent)
• S. mansoni - Africa and Latin America
• S. japonicum – Pacific region
Schistosomiasis (2)

Life cycle

- Transmission occurs in fresh water
- Infective cercariae released from snails of the genera *Bulinus, Biomphalaria Oncomelania*
- Cercariae penetrate the skin of people who drink, swim or bathe in infected water
- Adult worm live in the veins that drain the urinary system (*S. haematobium*) or mesentric blood vessels intestines (*S. mansoni, S. japonicum*) and release eggs into water in urine or faeces
- Eggs develop into miracidia which then infect snails

*Figure: Bulinus globosus, the intermediate host snail for *S. haematobium* (source: WHO/TDR/Stammers)*

*S. haematobium* cercaria (differential interference contrast microscopy; source: WHO/TDR/Stammers)
Schistosomiasis (3)

**Pathology**

- Shistosoma eggs become trapped in the tissues of the urinary tract (*S. haematobium*) and intestines (*S. mansoni, S. japonicum*)
- This results in inflammatory response and tissue damage

Adult worms of *S. haematobium* are 1-2 cm long (source: WHO/TDR/Stammers)

*S. haematobium* eggs measure 140 x 50 μm (differential interference contrast microscopy; source: WHO/TDR/Stammers)
Schistosomiasis (3)

Symptoms and signs

- Urinary Schistosomiasis:
  - *S. hamatobium*
  - Gross haematuria
  - Dysuria
  - Bladder, ureters and kidneys damaged
    - Cancer of the bladder is common

- Intestinal schistosomiasis
  - *S. mansoni, S. japonicum*
  - Gradual enlargement of liver and spleen intestines
  - Hypertension of the abdominal blood vessels which begin to bleed
  - Blood in the stools

Haematuria due to *S. haematobium* (source: WHO/TDR)
Schistosomiasis (4)

Prevention and control

• Educate people to not urinate or defecate in fresh water supplies
• Eliminate snail vectors by making the water habitat unsuitable (increase water flow, remove vegetation)
• Provide piped water to avoid direct contact with cercariae
• Mass drug treatment of communities to reduce reservoir of infection

Concrete irrigation ditches do not allow breeding of *Oncomelania* snails (source: WHO/TDR/Crump)
Examples of medically important arthropods
Head louse

- *Pediculus capitis*
- Scratching
- Secondary infection
  - louse born typhus
Pubic louse

- **Phthirius pubis**
- **Ptiriosis - sexually transmitted infection**
Fleas

- Black Death
- Plague
- Causative agents: *Yersinia pestis*
Ticks

- Lyme disease
- Causative agent: *Borrelia burgdorferi*
**Sarcoptes scabiei**

- Scabies mite
- Causative agents of scabies