Self-directed learning

Protozoa and protozoan diseases

Objectives

- Understand the diversity of protozoa
- Describe the different methods of reproduction in protozoa
- Name the 4 classes of protozoa & give examples of protozoa associated with human infections
- Describe the life cycle of *Giardia intestinalis*
- Describe the life cycle of *Trichomonas vaginalis*
- Understand the importance of haemoflagellates in human disease
- Name the 4 important members of the Genus *Plasmodium*
- Describe the life cycle of *Plasmodium* spp
- Understand the importance of malaria
- Understand the importance of *Toxoplasma gondii*
- Understand the importance of *Cryptosporidium* and *Microsporidium*
- Name 4 drugs used to treat malaria
Protozoa generally

Malaria
http://www.who.int/topics/malaria/en/

Protozoa

- Unicellular
- Eukaryotic
- No rigid cell wall
- Complex life cycle involving various stages or forms
  - Many form a resistant cyst stage
  - Sexual and asexual reproduction
- Feed by ingesting particulate matter – usually other cells - phagocytosis
- Mainly found in fresh water & marine habitats; some found in soil or aerial habitats
- Large number parasitic on man & other animals
- Motile – flagella, cilia, amoeboid movement
  - Used to divide them into taxonomic groups
1. Asexual reproduction:

- **fission** – binary or transverse
- **schizogony** - Nucleus undergoes multiple divisions before the cell divides → Cytoplasm forms around each nucleus before division takes place → Gives rise to multiple daughter cells

![Diagram of asexual reproduction]

2. Sexual reproduction

Sometimes an obligatory step in the life cycle, in other cases the organism can reproduce asexually with an occasional round of sexual reproduction.

Two forms:
1. Process often involves production and fusion of gametes
   - Occurs mainly in protozoa with an insect vector stage (also seen in *Cryptosporidium* – an intestinal parasite)
2. Process of conjugation and exchange of genetic material between different mating types in *Ciliophora* (eg *Paramecium* spp)
Sexual reproduction

*Plasmodium* life cycle

http://www38.homepage.villanova.edu

Conjugation in *Paramecium* spp
Protozoan groups

1. Sarcodina
2. Mastigophora
3. Ciliata
4. Sporozoa

Protozoal infections in humans

<table>
<thead>
<tr>
<th>Phylum</th>
<th>Organism</th>
<th>Disease</th>
<th>Habitat/source/vector</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sarcodina (amoeba)</td>
<td><em>Entamoeba histolytica</em></td>
<td>Amoebic dysentery</td>
<td>Contaminated water</td>
</tr>
<tr>
<td>Mastigophora (flagellates)</td>
<td><em>Giardia intestinalis</em></td>
<td>Giardiasis</td>
<td>Contaminated water</td>
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<tr>
<td></td>
<td><em>Trichomonas vaginalis</em></td>
<td>Vaginosis</td>
<td>Vagina</td>
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<tr>
<td></td>
<td><em>Trypanosoma brucei gambiense</em></td>
<td>Sleeping sickness</td>
<td>Tsetse fly</td>
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<tr>
<td></td>
<td><em>Trypanosoma cruzi</em></td>
<td>Chagas disease</td>
<td>Kissing bug</td>
</tr>
<tr>
<td></td>
<td><em>Leishmania spp</em></td>
<td>Cutaneous leishmaniasis</td>
<td>sandflies</td>
</tr>
</tbody>
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# Protozoal infections in humans

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<td>Ciliata</td>
<td><em>Balantidium coli</em></td>
<td>Balantidial dysentery</td>
<td>Contaminated water</td>
</tr>
<tr>
<td>Sporozoa (Ampicomp-lexans)</td>
<td><em>Plasmodium spp</em></td>
<td>Malaria</td>
<td>Anopheles mosquito</td>
</tr>
<tr>
<td></td>
<td><em>Toxoplasma gondii</em></td>
<td>Toxoplasmosis</td>
<td>Raw meat, cat faeces</td>
</tr>
<tr>
<td></td>
<td><em>Cryptosporidium</em></td>
<td>Diarrhoea</td>
<td>Humans, animals</td>
</tr>
<tr>
<td></td>
<td><em>Microsporidium</em></td>
<td>Diarrhoea</td>
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## 1. Sarcodina

- **Amoebae**
  - Large cells surrounded by a membrane – lack a definite shape
  - Move via pseudopodia
  - Absorb nutrients through the membrane or engulf food (phagocytosis)
Sarcodina (amoebae)

- Numbers of species in the intestinal tract of man and animals – mostly non-pathogenic
  - Form cysts – excreted in faeces – ingested by another host via contaminated water, food
- *Entamoeba histolytica* – pathogenic
  - Amoebic dysentery – mostly in tropics/subtropics
  - Not endemic in Australia but seen in travellers
  - Disease ranges from mild diarrhoea to severe dysentery – colitis (blood, pus, mucus in faeces).

2. Mastigophora – flagellates

- Motile by flagella – whip-like action
- Oval in shape
- Reproduce asexually by longitudinal binary fission
- Many form cysts for survival
- Free-living and parasitic species
  - Several important human pathogens
**Giardia intestinalis (lamblia)**

- Common intestinal parasite found throughout the world
- Exists in 2 forms
  - Infective trophozoite stage – 4 pairs of flagella and a sucker – attachment to the intestinal wall
  - Resistant cyst stage shed in faeces – can survive for weeks in a moist environment

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**Giardia intestinalis**

- Contaminated drinking water most common source of infection
- Symptoms may take some weeks to appear
- Symptoms range from abdominal pain and prolonged bouts of diarrhoea to weight loss and lack of energy
**Trichomonas spp**

- Flagellated protozoan – commensal in large percentage of the population
- *Trichomonas hominis* – commensal in the gut
- *Trichomonas vaginalis* – frequent inhabitant of female genital tract
  - Vaginitis characterised by smelly greenish vaginal discharge
  - May occur when pH becomes less acid and allows *T vaginalis* to multiply
  - Sexually transmitted

**Haemoflagellates**

- Flagellates responsible for number of serious diseases – high morbidity, high mortality – cause millions of deaths each year in some parts of the world
- *Trypanosoma brucei gambiense* (West Africa) & *T. brucei rhodesiense* (East Africa) – both carried by tsetse fly – cause sleeping sickness
  - Protozoa affect the nervous system → coma and death
Haemoflagellates

- *Leishmania* spp – cause disease leishmaniasis
- Spread by sandflies
- South & Central America, India, Middle East, Africa
- Some species attack the skin → cutaneous leishmaniasis
- Others cause visceral leishmaniasis (kala-azar) – affects liver, spleen; untreated it is always fatal
- Animals other than humans can be a reservoir – recently leishmania detected in some kangaroos in the Northern Territory
3. Ciliates

- Cells have large number of small hair-like cilia that move in a synchronised way to propel the organism along
- Many ciliates in the environment
- Only pathogen – *Balantidium coli*
  - Large protozoan
  - Causes diarrhoea
  - Although distributed around the world infections are rare

4. Sporozoa

- Non-motile protozoa
- Several important human pathogens
  - *Plasmodium* spp
  - *Toxoplasma* spp
  - *Cryptosporidium*
  - *Microsporidium*
Malaria

• 4 species of Plasmodium
  – P falciparum
  – P vivax
  – P ovale
  – P malariae

• Require an insect vector – female Anopheles mosquito

Plasmodium spp life cycle

1. Mosquito → injects sporozoite into human
   • Sporozoite → liver → asexual reproduction over days & weeks → hundreds of merozoites
2. Merozoites → red blood cells
   – multiply → lysis of RBC → release hundreds more merozoites
   – Typical symptoms (fever, chills, headache, nausea) – recur at regular intervals corresponding with synchronous release of merozoites from RBC
   – Some merozoites → trophozoites → male & female gametes
   – Gametes ingested by feeding mosquito
3. Sexual reproduction stage in the mosquito – takes 7 to 10 days
   – Gametes fuse to form zygote → matures into sporozoite → released through salivary gland of mosquito when it bites a new host
Malaria Cycle – *Plasmodium* carried by *Anopheles* mosquitoes

http://www.soulcare.org

Global distribution of malaria transmission risk, 2003

Hundreds of millions of cases occur each year and more than one million people die of malaria every year, mostly infants, young children and pregnant women and most of them in Africa.
Control of malaria

• Control mosquitoes
  – Insecticides in water to kill larval stages eg DDT – resistance has emerged
  – Personal insecticide to prevent biting
  – Mosquito nets
  – New development – fungal spores

Toxoplasma gondii

• Sporozoan parasite
• Causes mild flu-like illness – toxoplasmosis
• Humans infected from contact with raw/undercooked meat or handling cat faeces (3 or 4 days old)
• More serious illness in immunocompromised people
• Causes congenital defects if a non-immune mother infected in pregnancy
  – Early pregnancy → neurological defects, blindness, still birth
  – Later pregnancy → neurological problems, learning difficulties
Cryptosporidium

- Very small – 3 to 5 μm
- Parasites of the intestinal tract of fishes, reptiles, birds, and mammals
- *Cryptosporidium* isolated from humans is now referred to as *C. parvum*
- Large outbreaks associated with contaminated water
  - Mostly causes mild diarrhoea
- Cryptosporidiosis major infection in immunocompromised people
  - Severe chronic diarrhoea
Microsporidia

- Microsporidia are obligately intracellular, spore-forming
- over 1000 species
- host range is extensive and includes honeybees, fish, mosquitoes, fleas, grasshoppers, rodents, rabbits, and other fur-bearing mammals
- A number of species cause disease in humans
  - Most (but not all) infections associated with AIDS or transplant patients
  - Intestinal infections – chronic diarrhoea

Antiprotozoal drugs

<table>
<thead>
<tr>
<th>Drug</th>
<th>Mode of action</th>
<th>Mechanism of selectivity</th>
<th>Target organism</th>
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<tbody>
<tr>
<td>dapsone</td>
<td>Co-factor synthesis</td>
<td>Unique target</td>
<td><em>Plasmodium</em> spp</td>
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<tr>
<td>proguanil</td>
<td>ditto</td>
<td>Differences in target</td>
<td>ditto</td>
</tr>
<tr>
<td>pyrimethamine</td>
<td>ditto</td>
<td>ditto</td>
<td>ditto</td>
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<tr>
<td>sulphonamides</td>
<td>ditto</td>
<td>ditto</td>
<td>ditto</td>
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<tr>
<td>benznidazole</td>
<td>Nucleic acid synthesis</td>
<td>Activation in parasite</td>
<td><em>Trypanosoma</em> spp</td>
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<tr>
<td>chloroquine</td>
<td>ditto</td>
<td>Differential uptake</td>
<td><em>Plasmodium</em> spp</td>
</tr>
<tr>
<td>mefloquine</td>
<td>ditto</td>
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<td>DNA synthesis</td>
<td>Activation in parasite</td>
<td><em>Giardia</em>, <em>Trichomonas</em>, <em>Entamoeba</em></td>
</tr>
<tr>
<td>pentamidine</td>
<td>ditto</td>
<td>Differential uptake</td>
<td><em>Leishmania</em> spp</td>
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<tr>
<td>quinine</td>
<td>ditto</td>
<td>ditto</td>
<td><em>Plasmodium</em> spp</td>
</tr>
<tr>
<td>tetracycline</td>
<td>Protein function</td>
<td>Differential uptake</td>
<td>ditto</td>
</tr>
<tr>
<td>benzimidazoles</td>
<td>Microtubule function</td>
<td>Differences in target</td>
<td><em>Giardia</em>, <em>Trichomonas</em></td>
</tr>
<tr>
<td>primaquine</td>
<td>Energy metabolism</td>
<td>ditto</td>
<td><em>Trypanosoma</em> spp</td>
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Treatment of malaria

- Antimalarial drugs can be classified according to structure or anti-malarial activity
  - **Anti-malarial activity:**
    - **Tissue schizonticides for causal prophylaxis:** Act on the primary tissue forms of the plasmodia before the parasites start to infect RBCs.
      - Pyrimethamine and Primaquine have this activity
      - Impossible to predict the infection before clinical symptoms begin, this mode of therapy is more theoretical than practical.
    - **Tissue schizonticides for preventing relapse:** Act on the hypnozoites of *P. vivax* and *P. ovale* in the liver that cause relapse of symptoms on reactivation.
      - Primaquine is the prototype drug; pyrimethamine also has such activity.
    - **Blood schizonticides:** Act on the blood forms of the parasite and thereby terminate clinical attacks of malaria. These are the most important drugs in anti-malarial chemotherapy.
      - Include chloroquine, quinine, mefloquine, halofantrine, pyrimethamine, sulfadoxine, sulfones, tetracyclines, artemisins
    - **Gametocytocides:** These drugs destroy the sexual forms of the parasite in the blood and thereby prevent transmission of the infection to the mosquito.
      - Chloroquine and quinine have gametocytocidal activity against *P. vivax* and *P. malariae*, but not against *P. falciparum*.
      - Primaquine has gametocytocidal activity against all plasmodia, including *P. falciparum*.
      - Artemisins
    - **Sporontocides:** These drugs prevent the development of oocysts in the mosquito and thus ablate the transmission.
      - Primaquine and chloroguanide have this action.