Fungi & Parasites

Lecture 6
Pathology and Clinical Science 1 (BIOC211)
Department of Bioscience

Text Reference:
Learning Outcomes

- Characteristics
- Classification
- Biochemistry
- Reproduction
- Pathogenic organisms of clinical importance
- Common treatments
### Characteristics - Fungi

- Large diverse group of organisms
- Very few are truly pathogenic
- More commonly opportunistic
- Unicellular or multi-cellular
- Require an organic source of carbon for growth
- Distinguished from plants and algae
  - have no chlorophyll and
  - cannot photosynthesise
## Characteristics - Fungi

- Fungi are of enormous importance commercially in baking, brewing and in pharmaceuticals.
- Fungi have no chlorophyll and cannot photosynthesise.
- Some form part of the body's normal flora.
- A number of fungi are associated with disease.
- Pathogenic species invade tissues.
- The study of fungi is known as mycology and fungal infections are known as mycoses.
Classification-Fungi

Fungal pathogens can be classified

♦ on the basis of their growth forms

♦ the type of infection they cause
GROWTH FORMS - FUNGI

Two main types of fungi that cause disease in humans:

Fungi have Dimorphism which is the ability to grow in two separate forms

- Filamentous fungi (moulds)
- Yeasts

Ref: Mim’s Medical Microbiology 4th edn
# Yeasts

- Unicellular
- Spherical to oval in shape bounded by a cell wall
- Slightly larger than bacteria
- Contain various subcellular organelles
- Growth is asexual through the process of budding
- Pathogenic strains commonly exhibit dimorphism (e.g. budding or hyphae)

Yeast reproducing by budding.

Circular scars can be seen on the surface of the larger cell, representing sites of previous budding.

# Yeasts

- **Budding**
  - A small outgrowth appears on the parent cell which gradually enlarges and separates forming a daughter cell.

- Dimorphism is the ability to grow in two separate forms.

- *Candida albicans*
  - Responsible for thrush.
  - Several forms of growth at 28 degrees and also in the host tissues.
  - At 28 degrees it may exhibit a single celled budding yeast form or produce filaments or hyphae.
## CANDIDA SPP

- Endogenous organism
- Found in 40-80% of normal human beings
- May be commensal or pathogenic
- Frequently infects skin and mucosa
- In culture or tissue, oval, budding yeast cells
- Pseudohyphae formation

*Photo courtesy: Rethika Ravi
ARL pathology*
CANDIDA SPP

Cutaneous

Mucosal


CANDIDA SPP
LABORATORY DIAGNOSIS

GERM TUBE TEST

BLOOD AGAR

Photo courtesy: Rethika Ravi
ARL pathology

Treatment:

- For mucocutaneous form: topical nystatin, ketoconazole, fluconazole
- For systemic infection: Amphotericin B
Structure of filamentous fungi

(a) Vegetative structure of fungi

Hypha

(b) Types of asexual spores

Conidiophore

Conidiospores

Sporangiophore

Sporangium

Sporangiospores

Blastospores

Macroconidia

Microconidia

Moulds

- Capable of growth in many different habitats
- Consist of long filaments called hyphae
- The hyphae branch to form a dense mat of filaments called a mycellium.
- Reproduction is via the production of spores.
- Spores are easily dispersed on air currents.

Photo courtesy: Rethika Ravi
ARL pathology
**Aspergillus spp**

- Ubiquitous saprophyte
- Grows on and derives its nourishment from dead or decaying organic matter.
- Most common human pathogen. Distributed worldwide.
- Inhaled. Can lead to alveolar fibrosis.
- Commonly found in soil, food, paint, air vents, disinfectants
- Fungus ball (Aspergilloma)—recognized by x-ray, may be mistaken for TB cavity
- Patients cough up the fungus elements
- Aggressive tissue invasion

*Photo courtesy: Rethika Ravi ARL pathology*
Aspergillus spp

- **Specimens:** sputum, other respiratory specimens, or lung biopsy
- **Microscopic Examination:** with KOH, presence of hyaline branching septate hyphae

**Culture**
- require 1-3 weeks for growth
- assumes a variety of colors
- species differentiation is based on spore formation as well as their color, shape and texture

**Diagnosis:** serology testing

**Treatment:** Amphotericin

# IMPORTANCE OF FUNGI IN CAUSING DISEASE

- About 300 species are identified as pathogens in humans and animals.
- Some cause only minor health problems but those that invade deeper tissues can be life threatening.
- These systemic forms have become much more serious problems as medical advances have taken place, e.g. immunosuppressive and antibiotic therapies, transplantation, invasive procedures and AIDS.
TYPES OF FUNGAL INFECTIONS

Four types of infection (mycoses) are recognized:

1. Superficial mycoses
   - where the fungus grows on body surfaces

2. Cutaneous mycoses
   - extend deeper into the epidermis, and also include invasive hair and nail diseases.

http://www.your-doctor.net/dermatology_atlas/rwx/rwx/Mycosis_fungoides_annular.jpg

3. Subcutaneous mycoses
   ▪ chronic, localized infections of the skin

4. Systemic or deep mycoses
   ▪ with involvement of internal organs
   ▪ Capable of infecting individuals with normal immunity and in patients with compromised immune systems

Photo courtesy: Rethika Ravi
ARL pathology

http://3.bp.blogspot.com/-An_L0UWfSlg/USj01FjsvlI/AAAAAAAAJM0/hwmW5SsyU_w/s320/Lymphocutaneous+Sporotrichosis3.png
### TRANSMISSION OF INFECTIONS

1. **The superficial mycoses** are spread by person-to-person contact or from animal-to-human contact.

2. **The subcutaneous mycoses** infect humans via the skin.

3. **The deep mycoses** often result from the opportunistic growth of fungi.

4. Free-living fungi can also cause disease.

5. This occurs indirectly when toxins produced by fungi are present in items used as food or when their spores are inhaled.
HARMFUL EFFECTS OF FUNGI

Apart from causing infections, fungi can have other harmful effects:

Allergic reactions:
- Allergic bronchopulmonary
- Workers in farm industries can contract *Aspergillus spp*
- The introduction of spores into sensitized lungs causes a hypersensitivity reaction

Fungal toxins:
- Some fungi produce chemicals that are toxic to humans
- Poisonous mushroom /toadstools
- Symptoms such as nausea, severe diarrhoea, damage to body systems, muscle spasms and death may occur
- Aflatoxin from *Aspergillus* has been linked to the occurrence of liver cancer
DIAGNOSIS

- Diagnosis of fungal infections is very difficult because:
  - The symptoms are often not definitive
  - Laboratory growth of fungi is very slow

- Fungal infections are usually suspected if the patient is immunocompromised and does not respond to empirical antibacterial therapy
TREATMENT

Drug therapies that may increase risk of fungal infections:
- Anti-neoplastic drugs
- Steroids
- Immunosuppressive drugs
- Antibiotics: over-use or inappropriate use of antibiotics alter the normal flora allowing fungal overgrowth

IMPROVING TREATMENT
- New Drugs
- New therapeutic regimen
- Aggressive therapy
- Conjunctive therapy
TREATMENT

New Drugs
- Third generation azoles
- New classes of antifungal agents

Combination Therapy
- Simultaneously administering two drugs
- Sequential Tx with two or more drugs
- Alternate Administration of two or more

AGGRESSIVE THERAPY FOR IMMUNOCOMPROMISED PATIENTS
- Prophylactic – Anti-fungal agents at, or near, the time of chemotherapy
- Empirical – Start therapy when patient at risk, i.e., fever and/or infiltrate without response to anti-bacterials
- Pre-emptive – When there is some additional evidence of fungal infection (serology, isolate, etc.)
## Summary of fungi that cause important human diseases

<table>
<thead>
<tr>
<th>Type</th>
<th>Anatomic location</th>
<th>Representative disease</th>
<th>Causative organism(s)</th>
<th>Growth form</th>
</tr>
</thead>
<tbody>
<tr>
<td>Superficial</td>
<td>Hair shaft, dead layer of skin</td>
<td>Pityrasis versicolor, tinea nigra, piedra</td>
<td><em>Trichosporon, Malassezia, Exophiala</em></td>
<td>Y/F</td>
</tr>
<tr>
<td>Cutaneous</td>
<td>Epidermis, hair, nails</td>
<td>Tinea (ringworm)</td>
<td><em>Microsporum, Trichophyton, Epidermophyton</em></td>
<td>F</td>
</tr>
<tr>
<td>Subcutaneous</td>
<td>Dermis, subcutis</td>
<td>Sporotrichosis</td>
<td><em>Sporothrix</em></td>
<td>Ya</td>
</tr>
<tr>
<td>Systemic</td>
<td>Internal organs</td>
<td>Coccidioidomycosis</td>
<td><em>Coccidioides</em></td>
<td>Formc</td>
</tr>
<tr>
<td>Opportunistic</td>
<td>Internal organs</td>
<td>Cryptococcosis</td>
<td><em>Cryptococcus</em></td>
<td>Y</td>
</tr>
</tbody>
</table>

growth from the body

c *Coccidioides* has an unusual growth form with yeast-like endospores within a spherule

b also forms pseudohyphae

Y, yeast; F, filamentous; N/A, Y/F forms are not applicable.
PARASITES

Protozoa

Scabies

Flea

Protozoa

Mosquito

Images: Courtesy of Dr. Rethika Ravi
Characteristics - Parasites

- Very diverse group
- By definition an organism that derives its nutrients from another living organism
- From single cell to relatively larger multicellular organisms
- Most parasites are pathogenic.
Three major groups - Parasites

- Protozoa
- Helminths
- Anthropods
Protozoa

- unicellular organisms with no cell wall
- Some have a specialised mouth and anal pore
- Thousands of species
- Often motile (flagella)
Protozoa

- larger than bacteria
- Generally found in water
- A number exist as parasites in humans, animals and insects
- Can be intracellular or extracellular parasites
- Infections are more serious in the immuno-compromised
- Route of transmission varies
- Life cycles can be complex

*Paramoecium spp*

Images: Courtesy of Dr. Rethika Ravi
Diagrammatic representation of three different protozoa:

(a) Flagellate

(b) Ciliate

(c) Amoeba

Examples

<table>
<thead>
<tr>
<th>Examples in food and water:</th>
</tr>
</thead>
<tbody>
<tr>
<td>▪ <em>Entamoebae hystolytica</em> (amoebic dysentry)</td>
</tr>
<tr>
<td>▪ <em>Giardia intestinalis</em> (Giardiasis)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Examples in insect vectors</th>
</tr>
</thead>
<tbody>
<tr>
<td>▪ <em>Plasmodium</em> spp.: Malaria from mosquito</td>
</tr>
<tr>
<td>▪ <em>Trypanosoma brucei gambiense</em>: sleeping sickness from the Tsetse fly</td>
</tr>
<tr>
<td>▪ <em>Leishmania</em> spp: Leishmaniasis from sand flies</td>
</tr>
</tbody>
</table>
Protozoa use a variety of routes to infect humans

The occurrence of protozoan parasites in the body

*can also occur in other sites

- CNS amebae
- malaria
- Toxoplasma
- trypanosomes
- blood
- malaria
- trypanosomes
- liver
- Entamoeba
- Leishmania
- intestine
- Cryptosporidium
- Entamoeba
- Giardia
- Cyclospora
- Microsporidia*
- skin
- Leishmania
### ENTAMOEBA HISTOLYTICA

- Infections with *E. histolytica* could be asymptomatic or pathogenic.

- Two main species isolated: *E. histolytica* being invasive and *E. dispar* being non-invasive

- *E. histolytica* occurs worldwide.

- Reproduction of these stages is by simple binary fission.

- These cysts can survive in the external environment and act as the infective stages.
### ENTAMOEBA HISTOLYTICA

- Transmission can also take place as a result of anal sexual activity
- The cysts pass intact through the stomach when swallowed
- These adhere to the epithelial cells
- They can invade the mucosa and feed on host tissues

*E. histolytica* infection can be diagnosed in asymptomatic patients from the presence of characteristic four-nucleate cysts in the stool
Characteristics of cysts (size and number of nuclei) are used to differentiate pathogenic from non-pathogenic protozoa.

- A red blood cell is shown for comparison.
Sigmoidoscopy

*Amoebic colitis.* Sigmoidoscopic view showing deep ulcers and overlying purulent exudate.
**Giardia spp**

Trophozoite of *Giardia lamblia* attached to the mucosal surface of the small intestine

- Epidemics of giardiasis have occurred when public drinking supplies have become contaminated.
- *Giardia* can be passed from person to person.
- *Giardia* may also be transmitted sexually among homosexual men.
| **Cryptosporidium parvum** is an important cause of diarrhea in humans |
| Cross-infection from animals to humans does occur |
| The parasite has a complex life cycle. |
| Transmission requires ingestion of the resistant oocyst stage |
## CRYPTOSPORIDIUM SPP

- Invades epithelial cells of small intestine

- Transmission probably occurs most often via drinking water contaminated by oocysts, either from other humans or from animals

- In 1993, *C. parvum* caused a massive outbreak of watery diarrhea affecting 403,000 people in Milwaukee, USA

- It was transmitted through the public water supply and probably originated from cattle.
CRYPTOSPORIDIUM SPP

- Diarrhea ranges from moderate to severe
- Diagnosed by routine fecal examinations
- Concentration techniques and special staining
- Only immunocompromised patients need treatment for *C. parvum* diarrhea
- Highly active antiretroviral therapy (HAART) in individuals with AIDS
Protozoan infections of the gastrointestinal tract

(A) *Entamoeba histolytica*. Trophozoite
(B) *Giardia lamblia*
(C) Cyst of *E. histolytica*
(D) Oval cyst of *G. lamblia*
Helminths

- **Helminths**
  - multi-cellular organisms (worms)
  - Generally linked with poor sanitation and low socioeconomic conditions
  - Widespread in third world
  - Rarely fatal on their own
  - Contribute to morbidity
  - Complex life cycle

*Image Courtesy of Dr. Rethika Ravi*
Different types of helminths are:

- Cestodes (Tapeworms)
- Trematodes (flukes)
- Nematodes (roundworms)
## Helminths

- **Variety of infectious routes**
- **Life cycle has three stages**
  - *Ovum*
  - *Larvae*
  - *Adult*
- **Diagnosis**
  - Presence of ovum in stools

*Image Courtesy of Dr. Rethika Ravi*
Helminths - Transmission

1. Swallowing infective eggs or larvae via the fecal-oral route

2. Swallowing infective larvae in the tissues of another host
Helminths - Transmission

3. active penetration of the skin by larval stages

4. the bite of an infected blood-sucking insect vector
LIFE CYCLE OF SCHISTOSOMIASIS

- **Schistosomiasis** is a parasitic disease caused by several species of fluke of the genus *Schistosoma*.
- Schistosomiasis is often a chronic illness.
- The urinary form of Schistosomiasis is associated with increased risks for bladder cancer in adults.
- Schistosomiasis is the second most socioeconomically devastating parasitic disease after malaria.
- This disease is most commonly found in developing countries like Asia, Africa, and South America.
Schistosomiasis Lifecycle

Images: Courtesy of Dr. Rethika Ravi
### Parasitic infections affecting the liver

<table>
<thead>
<tr>
<th>(A) Egg of <em>S. mansoni</em></th>
</tr>
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<tbody>
<tr>
<td>(B) Pipe-stem cirrhosis in the liver</td>
</tr>
<tr>
<td>(C) Cellular reaction around an egg in the liver.</td>
</tr>
<tr>
<td>(D) Massive hepatosplenomegaly and ascites due to portal obstruction</td>
</tr>
</tbody>
</table>
### LIFE CYCLE - TAPEWORM

- Consuming larvae in raw or undercooked meat or in the feces of a human tapeworm carrier.

- Relatively harmless.

- Humans can also act as the intermediate hosts.

- A human infected with adult *T. solium* can ingest eggs either through fecal contamination or, possibly, from proglottids carried into the stomach by reverse peristalsis.

- Once eggs are ingested, oncospheres hatch in the intestine.
## LIFE CYCLE - TAPEWORM

- In humans, cysts can cause serious infections if they localize in the brain, resulting in neurocysticercosis
- The parasite life cycle is completed, resulting in human tapeworm infection, when humans ingest undercooked pork containing cysticerci
- Cysts evaginate and attach to the small intestine by their scolex
- Adult tapeworms develop, (up to 2 to 7 m in length and produce less than 1000 pro-glottids, each with approximately 50,000 eggs) and reside in the small intestine for years
Tapeworm Lifecycle

Cysticerci are ingested in rare or undercooked meat

Eggs hatch, larvae burrow through intestinal wall, enter bloodstream, and encyst in muscles as cysticerci

Cow becomes infected when it eats contaminated grass

Mature proglottid will disintegrate and release eggs

Adult worm attaches to mucosa of small intestine

Anthropods

<table>
<thead>
<tr>
<th><strong>Arthropods</strong> (Ectoparasites)-insects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Exist in a parasitic relationship on the outside surface of the human body E.g. fleas, scabies, lice, ticks, mites</td>
</tr>
<tr>
<td>A number can harbour bacteria and so cause infection</td>
</tr>
<tr>
<td>Common diseases are due to transmission of infectious agents such as bacteria</td>
</tr>
<tr>
<td>Scratching the bite allows the bacteria to penetrate the skin and enter the new host</td>
</tr>
</tbody>
</table>
Examples of Parasitic Infections

Scabies

Pediculosis capitis (head lice)


http://3.bp.blogspot.com/-ugU3lqYzOx0/UFIZTFou9cl/AAAAAAAAEGQ/_RwApMIFjvY/s1600/head-lice.jpg
### DIAGNOSIS

- Doctors suspect a parasitic infection in people who have typical symptoms or have live in or traveled to an area where sanitation is poor or where such an infection is known to occur.

- Laboratory analysis of specimens, to identify proteins released by the parasite.

- Blood, stool, urine, or phlegm (sputum) may be taken.

- Tissue samples that may contain the parasite.
<table>
<thead>
<tr>
<th></th>
<th>A biopsy of lung or intestinal tissue</th>
</tr>
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<tbody>
<tr>
<td></td>
<td>A sample of skin may be snipped.</td>
</tr>
<tr>
<td></td>
<td>Eggs or cysts may be found in the person's stool</td>
</tr>
</tbody>
</table>
# TREATMENT

- Parasitic infection can be treated with a variety of drugs

- Community measures for prevention

- Care in drinking from potentially contaminated natural waters

- Several anti-helminthic drugs are available

- Antibiotics, laxatives, and antacids should not be used until after the stool sample has been collected.
Readings and Resources

Resources:

- **Set Textbooks:**

- **Additional textbooks:**
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