**Human Fungal Pathogens**

**Medical Mycology**: Study of human pathogenic fungi.

**Mycoses**: Fungal diseases of animals.

Relatively few human pathogenic fungi, but with wide geographical and host ranges.

Difficult to treat.

**Human Pathogenic Fungi**

- History on causes of disease:
  - Early people thought disease due to demons, evil spirits, etc.
  - Later more elaborate stories, e.g. Pandora, Aesculapius, Hygeia, Panacea.
  - **Hippocrates**, 350 B.C., disease result of disproportionate relationship of body humor: Blood, bile and phlegm - Humor Theory

**Human Pathogenic Fungi**

- History on causes of disease:
  - **Marcus Terentius Varro**, 23 B.C. thought disease caused by unseen particles.
  - **Girolamo Francastoro**, 1546
    - First description of typhus.
    - Disease passed from person to person or fomite
  - **Antoine Van Leeuwenhoek**, 1674 observed “animalcules” with microscope.

**Human Pathogenic Fungi**

- History on causes of disease:
  - **Agostino Bassi** 1835 discovered that a fungus (*Beauveria bassiana*) caused disease in silk worms (=Muscocardine).
  - **David Gruby** (1841) Proved *favus*, disease of scalp, caused by fungus by inoculation experiments.
  - Note that they preceded Pasteur's Germ Theory of 1862. Why no credit?

**Human Pathogenic Fungi**

- **Sabouraud** (1892) published large number of articles on fungus disorder of skin.
  - Did not understand pleomorphism.
- Progress also slow in medical mycology due to lack of expertise by doctors.
  - In part, lack of knowledge and urgency due to infrequency of diseases.
Human Pathogenic Fungi

- Emmons (1934) redefined dermatophyte species according to mycological standards and Rules of Botanical Nomenclature.

- Potentially, any fungus seems to be able to cause human diseases. Even the most unlikely species:
  
  *Schizophyllum commune*, a common wood decomposing mushroom has been found living in human sputum and fingernail.

Human Pathogenic Fungi

- Potentially, any fungus seems to be able to cause human diseases. Even the most unlikely species (continue):

  *Ustilago maydis* (Corn Smut) is known to cause skin lesion

Human Pathogenic Fungi

- Categories of infections can be divided into three groups:
  - **Superficial or Cutaneous Infections**: This category is equivalent to the obligate parasites.
  - **Subcutaneous Infections**: Introduced through breaks in skin and is localized.
  - **Systemic Infections**: Infections that become wide-spread. Sometimes growing throughout the body.

Superficial Infections (Ringworm and Related Diseases)

- Most well known of fungal diseases.
- Have been recorded in various medical literature for thousands of years.
  - Greek called it *Herpes*, literally circle or ring-form.
  - Romans called it *Tinea*, believed it to be caused by a worm.
- More prevalent in the past than in the present.
- **Ringworm Infections**: Common where there is overcrowding and conditions are unsanitary.
Ringworm

- More prevalent in the past than in the present (continue).
- Individuals with ringworm were segregated to prevent spread of disease.
- Although cause of disease was unknown, segregation indicates knowledge that it was contagious.

Ecology of fungi causing Ringworm:
- Zoophilic or "animal loving": Species infecting mostly animals, e.g. cats, dogs, cows and other farm animals, but readily transmitted to people.
- Anthrophilic "man loving": Species infecting people and not transmitted to animals.
- Geophilic or "soil loving": Infects both human and animals. Facultative parasite.

Unanswered questions concerning ringworm:
- Contagious, but not uncommon for only one person in large family to have disease.
- When infection occurs, it is usually in a restricted area. Why not the whole body?
- Why are some people more susceptible to ringworm than others?

Types of Ringworm:
- Tinea corporis or ringworm of the body caused by a variety of species.

The common name ringworm is combination of Greek & Roman common name, Herpes (round), Tinea (worm).

Types of Ringworm:
- Tinea capitis or ringworm of the scalp caused by a variety of species.

Individual with inflammatory ringworm of scalp.  Individual with "black dot" ringworm of scalp.

Individual with ringworm of hand.  Individual with ringworm of feet = athlete’s foot.
Types of Ringworm:
- **Fungus Nail** commonly caused by *Trichophyton rubrum*.
  - Individual with infected finger nails.
  - Individual with infected toe nails.

- **Tinea versicolor** superficial infection of skin caused by *Malassezia furfur*.
  - Individual with dark circles on lighter skin.
  - Individual with white circles on dark skin.

**Diseases often chronic and difficult to treat.**
Numerous treatments. Some success with griseofulvin, clotrimazole and selenium sulfide.

Intermediate Infections
- Infections that enter through openings of the skin.
- Penetration through wound may be considerable, but normally will remain localized.
- In rare instances may become systemic.

Intermediate Infections
- **Chromoblastomycosis**: Disease limited to skin and subcutaneous tissue.
  - Characterized by warty, ulcerated and crusted lesions.
  - Majority of cases occur on feet or on legs, below knee.
  - This suggest that fungi inoculated through skin while walking barefoot, in contact with soil.
Early initial lesion of chromoblastomycosis.

Chronic form with raised warty areas. Usually amputation must occur.

Intermediate Infections
- Treatments not very satisfactory.
- Treatments include surgical excision, cryosurgery, or topical antifungal chemicals.

Intermediate Infections
- *Candida albicans*: Disease commonly referred to as *Candidiasis*.
- Disease usually confined to skin and mucous membranes, but can cause lesions, which may be fatal.
- *Oral candidiasis* usually occur in children.

Intermediate Infections
- Dimorphic fungus.
- Disease is unusual in that it is normally found in the body.
- For reasons unknown, it may cause severe and even fatal infections in various parts of body.

Intermediate Infections
- *Candida albicans*
- Oral candidiasis, showing yeast phase.

Candidiasis can also occur where there is excessive moisture build up, such as between fingers and under creases of breast.

Systemic Mycosis
**Systemic Infections**
- Fungi involved are normally saprobes.
- Infections occur through breaks in skin or enters through nose or mouth.
- Fungus is able to adapt itself to the hostile environment of the human body.
- Species of fungi usually dimorphic, mycelial as saprobe, yeast after entering body.

**Intermediate Infections**
- A dozen or so species of fungi causing this category of disease.
- Diseases are internal and can spread throughout the body.
- Potentially most harmful, but actually seldom results in death or even harmful effect.

**Examples of Systemic Infections:**
- **Histoplasmosis**
  - Only known to occur in people and dogs. Infection in other domestic animals unknown.
  - Disease is caused by *Histoplasma capsulatum* (= *Ajellomyces capsulatum*), an Ascomycota.
  - May be isolated from soil, but sporulation occurs in excreta of birds.

**Examples of Systemic Infections:**
- **Histoplasmosis**
  - Infections occur from inhalation of spores of fungus sporulating on bird droppings.
  - Also probable entry is direct inoculation into skin or mucous membrane.
  - Once entry is achieved, it is thought to enter bloodstream in some cases where many body parts involved.

**Examples of Systemic Infections:**
- **Histoplasmosis**
  - Disease ranges in severity from asymptomatic to those leading to death.
  - First three cases of disease recorded in Panama Canal Zone, in 1905-06.
  - In those cases, massive infection of lungs, spleen, liver and lymph nodes revealed.

**Examples of Systemic Infections:**
- **Histoplasmosis**
  - Until the 1940's, it was thought to be a rare disease with few known occurrences of the disease.
  - In 1940, many men being tested for military service were discovered to have healed over pulmonary lesions.
  - Histoplasmin skin test indicated positive test for Histoplasmosis.
Examples of Systemic Infections:

- **Histoplasmosis**
  - Rounded, calcified bodies distributed in both lungs, indicating possibility of Histoplasmosis.

- **Histoplasmosis**
  - Symptom would soon subside and person would be immune to disease.
  - Symptoms of most diseases for systemic mycoses similar to Histoplasmosis.
  - Skin test verifies diseases.

- **Histoplasmosis**
  - Disease was little known until 1997, when Bob Dylan almost died from disease.
  - Caused inflammation of sac around heart.

- **Histoplasmosis**
  - It was estimated that as much as 20% of population in this country may have contracted disease.
  - Great majority had no symptoms and others with miscellaneous aches and pains or even a slight cough with flu-like symptoms.

- **Histoplasmosis**
  - Symptom would soon subside and person would be immune to disease.
  - Symptoms of most diseases for systemic mycoses similar to Histoplasmosis.
  - Skin test verifies diseases.

- **Histoplasmosis**
  - Disease very similar to Histoplasmosis and a parallel history.
  - Caused by *Coccidioides immitis*.
  - Very common in Kern County, in San Joaquin Valley, in California.
  - Skin test, with coccidioidin, indicate 90% of population had the disease.

- **Histoplasmosis**
  - Lesion in tongue
  - Spores in lung tissue

- **Histoplasmosis**
  - Cutaneous lesion on lip
● **Examples of Systemic Infections:**
  - **Coccidiomycosis**
    - Again, once an infection has occurred, person is immune to further infections.
    - Symptoms similar to those of other systemic diseases.
    - Disease should be suspect if recent visit to endemic area has been made.
  - Symptoms on left is an example of direct cutaneous inoculation of fungus. Rare and distinct from other diseases.

● **Examples of Systemic Infections:**
  - **Coccidiomycosis**
    - More severe symptoms not that different from other systemic diseases.
    - Coccidioidin skin test would indicate presence of disease.

● **Overall, mycoses are difficult to treat. Why?**
  - Fungi are eukaryotes.
  - Because of infrequent occurrence, not as much research carried out.
  - Since AIDS has reached epidemic proportions and transplants becoming common-place, mycoses is becoming more important.

● **Some treatments:**
  - **Nystatin**: Antibiotic derived from Streptomyces. Effective against oral candidiasis.
  - **Amphotericin B (Fungizone)**: Antibiotic that is effective against several systemic mycoses. Administered intravenously.
  - **Micanazole (Monistat)**: Also used for systemic mycoses, but with side effects. Nausea and inflammation of blood vessels.
Some treatments:

- **Griseofulvin**: Antibiotic derived from *Penicillium griseofulvum*. Taken orally, one gram/day. Treatment for athlete foot and fungus nail.
- A number of other treatments for athlete foot, jock itch and ringworm also available over the counter:
  - Tolnaftate (=Tinactin)
  - Miconazole (=Monistat)
  - Canesten (=Clotrimazole)