Epidemiology of Fungal Diseases

Epidemiology of Mycoses
- Mycosis (pl., mycoses) - an infection caused by a fungus
- Two broad categories of mycoses
  - Nosocomial (hospital acquired)
  - Community acquired
- Nosocomial infections are considered opportunistic in origin
- Community-acquired infections can be opportunistic, but also include endemic mycoses

Epidemiology of Mycoses (cont.)
- Over the past 20 years, both nosocomial and community-acquired mycoses have increased dramatically
- Excluding HIV/AIDS patients, mycoses are the 7th most common cause of infectious disease

Nosocomial Mycoses
- Between 1979 and 2000, the number of sepsis cases due to fungi increased 207%
- Between 1995 and 2002, 9.5% of bloodstream infections were due to fungi, of which the vast majority were Candida species (the fourth leading cause of such infections)

Nosocomial Mycoses (cont.)
- From 1980 to 1990, a separate study noted a marked increase in nosocomial mycotic infections regardless of institution type
  - Teaching hospitals
    - Large (>500 beds): 2.4% to 6.6%
    - Small (<500 beds): 2.1% to 3.5%
  - Non-teaching hospitals
    - Large (>200 beds): 1.2% to 2.5%
    - Small (<200 beds): 0.9% to 2.4%
Nosocomial Mycoses (cont.)

- These increases occurred regardless of:
  - Body site (4 studied)
  - Major specialty service provided
  - Subspecialty service provided
- Deaths due to fungal infections increased nearly three-fold from 1980 (680 deaths) to 1990 (2300 deaths)
- Fungemia patients were more likely to die than those bloodstream infections by other types of microbes

Nosocomial Mycoses (cont.)

- Independent risk factors for fungemia (i.e., those determined to enhance infection alone)
  - Number and duration of antimicrobial agents
  - Chemotherapy
  - Previous colonization
  - Indwelling catheter
  - Neutropenia
  - Hemodialysis

Nosocomial Mycoses (cont.)

- Organ transplant patients experience the highest risk of fungal infection
  - Rates of fungal infection by type of transplant
    - Renal, <5%
    - Bone marrow, 2-30%
    - Heart, 10-35%
    - Liver, 28-42%
  - Risk factors include large corticosteroid doses, tissue rejection, poor tissue function, hyperglycemia, leukopenia, and age

Nosocomial Mycoses (cont.)

- Molecular epidemiology
  - Increased emphasis on characterizing pathogens at the subspecies level to:
    - Better define infectious process
    - Modes of transmission
  - Classically, epidemiology was based upon physiological factors
  - Today, epidemiological studies tend to be DNA-based using a variety of molecular methods

Nosocomial Mycoses (cont.)

- Molecular methods include
  - RFLP (restriction fragment length polymorphisms) analysis
Nosocomial Mycoses (cont.)
- Molecular methods include
  - RFLP (restriction fragment length polymorphisms) analysis
  - Electrophoretic karyotyping
  - Various "satellite" typing methods

Nosocomial Mycoses (cont.)
- Protein-based methods include
  - Immunoblot fingerprinting
  - Polyacrylamide gel electrophoresis
  - Multilocus enzyme electrophoresis

Key question asked by epidemiology - are two or more isolates associated with an outbreak "the same" or "different"?
- If different, probably reflect different sources or modes of infection
- If same, infection is assumed to be cross-contamination from one patient to another, or from a common source
- Typing methods can also help distinguish between a relapse of infection or the acquisition of a new one

Epidemiology data can also be used to help develop strategies of prevention and control which must consider if the origin of infection is
- Endogenous - mainly yeast infections, particular Candida and Candida-like species
- Exogenous - mainly mold species, but also yeasts from contaminated sources

Community-Acquired Mycoses
- Etiological agents of community-acquired fungal infections include
  - Endemic dimorphic fungi
    - Blastomyces dermatitidis
    - Coccidioides immitis and C. posadasii
  - Histoplasma capsulatum var. capsulatum and H. capsulatum var. duboisi
  - Paracoccidioides brasiliensis
  - Penicillium marneffei

Histoplasma capsulatum mold and yeast phases (above) and dimorphism in Coccidioides immitis (below).
Community-Acquired Mycoses (cont.)

- Opportunistic pathogens
  - Candida species and other yeast and yeast-like fungi
  - Non-pigmented (in vivo) molds causing hyalophyphomycosis
  - Pigmented (in vivo) molds causing phaeohyphomycosis
  - Subcutaneous pathogens causing sporotrichosis, chromoblastomycosis, and mycetoma
  - Zygomycetes

Community-Acquired Mycoses (cont.)

- Endemic, dimorphic fungi
  - Acquired in specific geographic regions
  - Afflict both immune competent and immunocompromised individuals, but more common in HIV-infected persons and organ transplant recipients
  - Endemic regions
    - Histoplasma capsulatum
      - var. capsulatum - Ohio River valley of the U.S. and Latin America
      - var. duboisii - portions of Africa

Community-Acquired Mycoses (cont.)

- Coccidioides spp. - desert southwestern U.S., northern Mexico, and Central America
- Paracoccidioides brasiliensis - Central and South America
- Blastomyces dermatitidis - Ohio River and Mississippi valley areas of U.S. and portions of Africa
- Penicillium marneffei - southeast Asia

Laboratory Diagnosis

- Diagnosis of a fungal infection is complicated and requires diverse expertise
- Most common methods are traditional, i.e., isolation, culture, and observation
- "Gold standard" is the recovery of the etiological agent from the clinical specimen
- Current methods include a mixture of the traditional, commercially-available kits, and new molecular approaches.
Laboratory Diagnosis (cont.)

- A proper means to diagnosis includes the following:
  - Specimen selection
    - Proper anatomical site
    - Use of suitable container for transport
  - Specimen collection
    - Choose an active lesion
    - Use aseptic technique
    - Obtain an appropriate quantity
    - Use sterile, appropriately labeled containers

Laboratory Diagnosis (cont.)

- Specimen transport and storage
  - Examine microscopically as soon as possible
  - Transport immediately using pertinent transport media if required
  - Do not freeze specimens
  - Do not refrigerate if not likely to contain contaminating microbes
  - Do not desiccate
  - Plate onto appropriate media

Laboratory Diagnosis (cont.)

- Culture: most infectious agents identified growth from clinical specimens
  - Media - various media have been developed, some quite traditional, and have been very successful in helping identify etiological agents
  - Incubation conditions
    - Optimal temperature: 30°C (range 25-30°C)
    - Need a humid environment
    - Incubation period of 4-6 weeks often used
    - To assess form transitions, dimorphic fungi cultured at 35-37°C

Laboratory Diagnosis (cont.)

- Direct microscopic examination
  - Requires recovery and identification of fungus from cultures or examination of infected tissue
  - Trained individual can often make diagnosis based upon this examination
  - Types of observations
    - Wet mounts (unstained)
    - Stained preparations
      - Fungal cells
      - Tissue samples

Laboratory Diagnosis (cont.)

- Methods of identification and diagnosis
  - Morphology - some fungi exhibit characteristic cellular features both in vitro
  - Histopathology - some fungi exhibit characteristic cellular features both in vitro
  - Nucleic acid probes
  - Serology
  - Radiological surveys