Epidemiology of Fungal Diseases

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

- Contributing factors to increased mycoses:
  - Growing population of immune compromised individuals
  - Mobile population/immigration
  - More older adults with chronic medical conditions
  - Aggressive medical therapies
    - Surgery
    - Antibiotics
    - Chemotherapies/Organ transplants
  - Environmental changes

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

- From 1980 to 1990, a marked increase was noted 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

Disclaimer:
This lecture slide presentation is intended solely for educational purposes. Many of the images contained herein are the property of the original owner, as indicated within the figure itself or within the figure legend. These images are used only for illustrative purposes within the context of this lecture material. Use of these images outside the purpose of this presentation may violate the rights of the original owner. Dr. Cooper and Youngstown State University assume no responsibility for the unauthorized use of the material contained herein.
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
  - Electrophoretic karyotyping
Nosocomial Mycoses (cont.)
- Protein-based methods include
  • Immunoblot fingerprinting
  • Polyacrylamide gel electrophoresis
  • Multilocus enzyme electrophoresis

Protein production (A) of rTbGS and immunoblot analysis of the same protein (B).

Nosocomial Mycoses (cont.)
- 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

Nosocomial Mycoses (cont.)
- 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
  – Opportunistic pathogens
    • Candida species and other yeast and yeast-like fungi
    • Non-pigmented (in vivo) molds causing hyalohyphomycosis
    • Pigmented (in vivo) molds causing phaeohyphomycosis
    • Subcutaneous pathogens causing sporotrichosis, chromoblastomycosis, and mycetoma
    • Zygometes

Community-Acquired Mycoses (cont.)
- Histoplasma capsulatum var. capsulatum and H. capsulatum var. dubosii
- Paracoccidioides brasiliensis
- Penicillium marneffei

Community-Acquired Mycoses (cont.)
- Blastomyces dermatitidis mold and yeast phases (plasmod and dimorphic yeast form)
  • Blastomyces dermatitidis in vivo mold and yeast forms (plasmod and dimorphic yeast form) - Sources: www.bact.wisc.edu/Microtextbook/index.php?module=Book&func=displayarticle&art_id=112

Community-Acquired Mycoses (cont.)
- Histoplasma capsulatum and H. capsulatum var. dubosii
- Paracoccidioides brasiliensis
- Penicillium marneffei

Community-Acquired Mycoses (cont.)
- Histoplasma capsulatum and H. capsulatum var. dubosii
- Paracoccidioides brasiliensis
- Penicillium marneffei

Community-Acquired Mycoses (cont.)
- Histoplasma capsulatum and H. capsulatum var. dubosii
- Paracoccidioides brasiliensis
- Penicillium marneffei
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. *dubosi* - portions of Africa

- *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

Community-Acquired Mycoses (cont.)

- Opportunistic fungal pathogens
  - Includes virtually any fungus present in the environment
  - Incidence is unknown because these types of infections are not required to be reported
  - Among the most notable is *Cryptococcus neoformans*
    - Rare infection prior to HIV pandemic
    - Two varieties
      - var. *neoformans* - worldwide distribution
      - var. *gattii* - tropical and subtropical regions

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
  - 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