MEDICAL MYCOLOGY

I. Opportunistic Mycoses
A. What is an opportunist?

B. Factors in opportunism:
   Host: Debilitating primary diseases
   Immune deficiency
   Treatment
   *Occur exclusively in compromised pt.
   Organism: Present in environment
   Number available

C. Common opportunistic fungi:

- Cryptococcus neoformans
- Candida species
- Aspergillus species
- Zygomycetes (Phycomycetes)

1. Cryptococcosis:
   a. Etiologic agent: Cryptococcus neoformans
      (sexual state: Filobasidiella neoformans)
   b. Cryptococcus as a primary etiologic agent
   c. Cryptococcus as an opportunist *May not always be opportunistic.
   d. Clinical Forms: Pulmonary → 10^5 pm in az; inhalation of yeast
      CNS → menigitis in disseminated
      Disseminated → skin, bone
   e. Diagnosis
      1. Mycology
         Direct Examination
         Budding yeast, usually has capsule
         (Polysaccharide)
Culture
White to pink, yeast colony on
Sabouraud Agar
Grows on all primary microbiological media

2. Histopathology
   H&E: Budding yeast surrounded by
   unstained capsule
   GMS: Budding yeast (may be confused with
   H. capsulatum)
   *NARROW BUD BASE
   Mucicarmine: Stains capsule red
   *USE THIS IF UNSURE w/ GMS

3. Serology
   Latex Agglutination: Detects capsular
   antigen of C. neoformans
   (Highly sensitive for cryptococcal meningitis)
   *Even in CSF.
   e. Other Cryptococcus sp of clinical importance:
      Cryptococcus terreus
      C. albidos
      C. diffiusens
      C. laurentii

2. Candidiasis
   a. Etiologic agents--Candida sp.
      *We will see all of these in our practices
      *These indicate immunocompromised
b. Predisposing factors to Candidiasis:
1. Debilitating diseases (all types)
2. Immunosuppression
3. Antibiotic therapy (long term) destruction of flora
4. I.V. catheterization
5. Urinary tract catheterization

C. Manifestations of Candidiasis:
1. Systemic → fatal
   * often cancer pt.
2. Cutaneous
3. Subcutaneous
4. Allergic

d. Diagnosis:

1. Mycology:

   Direct Examination:
   Demonstrate pseudohyphae in fresh clinical specimens

   Culture:
   Isolate pure culture on Sabouraud Agar
   Observe pseudohyphae
   Identify by biochemical tests

2. Histopathology:

   Pseudohyphae in tissue, stained by H&E, PAS & MS

3. Serology:
   Latex Agglutination Test for Candida antigen. Not reliable for screening; lacks sensitivity.

3. Other Yeast of Medical Importance:
   Rhodotorula sp
   Trichosporon sp

4. Aspergillosis:

   a. Etiologic agents—Aspergillus sp. → found everywhere

      Most common: A. fumigatus → most common opp. az. in USA
      A. flavus
      A. niger
      A. terreus

* don't know Tx.
b. Predisposing Factors to Aspergillosis:
   1. PMN defect
   2. Leukopenia
   3. Corticosteroid therapy
   4. Immunosuppressive therapy
   5. Parenteral drug use → use contaminated material to cut their drugs
   6. Antibiotic therapy

c. Common Clinical Forms of Aspergillosis:
   Allergic → huge # allergies
   Broncho-pulmonary → common
   Fungus ball → rare (need pre-existing cavity, i.e. TB)
   Invasive → getting more common w/ severely compromised
   Rhinofacial → conidia in sinus & may invade
   Cerebral

   bronchi opens up by mass of hyphae
   & may invade

   Compromised pt → fungus ball grows, even across bone to invade eye & brain. → rapidly fatal

d. Diagnosis:

   1. Mycology:
      Direct Examination:
      Observe hyphal fragments in fresh specimen.
      Hyphae, 3-6 μ in width, septate.
      Culture:
      Grows on most laboratory media in 2-3 days.

   2. Histopathology:
      H&E, PAS, GMS; septate, branched hyphae in tissue.
      This is proof of invasion.

   3. Serology:
      Precipitin Test (ID): Increased number of bands indicate disease.
      Complement Fixation Test: High titer or rising titer is significant.
      Immunofluorescence test for galactomannans of Aspergillus cell wall
5. **Zygomycosis**

   a. Etiologic agents—(most common)
      
      *Mucor* sp  
      *Rhizopus* sp  
      *Absidia* sp  

   b. Predisposing factors to zygomycosis:
      
      1. Diabetes Mellitus  
      2. Hematologic malignancies  
      3. Severe burns  
      4. Malnutrition  
      5. Leukopenia  
      6. Transplantation  
      7. IV drug abuse  

   c. Clinical Forms:
      
      1. **Rhinocerebral** → most common, starts as sinusitis
      2. **Pulmonary** → rare
      3. **Gastrointestinal** → only in trauma/accidents that impact abdomen
      4. **Disseminated**

   d. Diagnosis:
      
      1. **Mycology**:
         
         Direct Examination:
         
         Observe hyphae in fresh specimen
         
         *Hyphae nonseptate, 6-8 μ in width*
         
         
         Culture:
         
         *MOLD* Grows well and rapidly on most fungal media.
         
         Will not grow in presence of cyclohexamide.
         
         Sporangiofores arise from non-septate hyphae bearing sporangia containing numerous sporangiospores
         
      2. **Histopathology**:
         
         H&E, PAS, MS: Broad, nonseptate, ribbon-like hyphae in tissue
         
      3. **Serology**:
         
         None available
      
   D. Treatment of Fungal Diseases:
### ANTIFUNGAL AGENTS

<table>
<thead>
<tr>
<th>AGENT</th>
<th>MECHANISM OF ACTION</th>
<th>ROUTE</th>
<th>CLINICAL USE</th>
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<tbody>
<tr>
<td>POLYENES</td>
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<tr>
<td>Nystatin</td>
<td>Binds to sterols (ergosterol) causing disruption of cytoplasmic membrane</td>
<td>Topical</td>
<td>Most fungi</td>
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<td>Amphotericin B</td>
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<td>Intravenous</td>
<td>Most fungi</td>
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<td>AZOLES</td>
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<tr>
<td>Ketoconazole</td>
<td>Demethylase block of ergosterol synthesis</td>
<td>Oral</td>
<td>Candida, Cryptococcus,Dimorphic fungi</td>
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<tr>
<td>Fluconazole</td>
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<td>Oral, IV</td>
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<td>Itraconazole</td>
<td></td>
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<td>Clotrimazole</td>
<td>Demethylase block of ergosterol synthesis</td>
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<tr>
<td>Miconazole</td>
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<tr>
<td>Voriconazole</td>
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<td>Candida, some other yeasts and molds</td>
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<td>ECHINOCANDINS</td>
<td>Block glucan synthesis</td>
<td>Intravenous</td>
<td>Aspergillus, Candida</td>
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