Endemic Mycoses

• Prior Guidelines Issued in 2000

• Updated in 2007/2008

  – Sporotrichosis

  – Blastomycosis

  – Histoplasmosis
Common Themes

- Increased role for lipid formulations of Amphotericin B
- Step down therapy with AmB followed by azoles
- Possible role of voriconazole and posaconazole
- Therapeutic drug monitoring
Clinical Practice Guidelines for the Management of Sporotrichosis: 2007 Update by the Infectious Diseases Society of America

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CID 2007:45 (15 November)
Sporotrichosis

- *Sporothrix schenckii*

- Usual inoculation is cutaneous

- Manifestations
  - Cutaneous/lymphocutaneous disease
  - Osteoarticular disease
  - Pulmonary
  - Disseminated
  - Meningitis
Unchanged Recommendations

- **Cutaneous/Lymphocutaneous Disease**
  - Itraconazole preferred
  - 2-4 weeks after lesions resolve (3-6 months)
  - Local hyperthermia therapy
  - Terbinafine
  - SSKI
Unchanged Recommendations

- **Osteoarticular**
  - Itraconazole x 12 months

- **Mild to moderate pulmonary disease**
  - Itraconazole x 12 months
  - Surgical resection in select cases
Changes in Guidelines: Sporotrichosis

2000

• Cutaneous
  – Itraconazole 100-200 mg
  – Fluconazole 2nd line

• Osteoarticular
  – Fluconazole 3rd line

2007

• Cutaneous
  – Itraconazole 200 mg
  – Fluconazole only if itra, SSKI, or terbinafine are ineffective

• Osteoarticular
  – Fluconazole not recommended
Changes in Guidelines: Sporotrichosis

2000
- Severe disease
  - Amphotericin B deoxycholate

- Meningitis
  - AmB deoxycholate 1-2 gm

2007
- Severe disease
  - Lipid AmB followed by itraconazole

- Meningitis
  - Lipid AmB 4-6 weeks followed by itraconazole
Changes in Guidelines: Sporotrichosis

• Role of voriconazole and posaconazole
  – No published data
  – Voriconazole has no \textit{in vitro} activity
Clinical Practice Guidelines for the Management of Blastomycosis: 2008 Update by the Infectious Diseases Society of America

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CID 2008:46 (15 June)
Blastomycosis

- *Blastomyces dermatitidis*

- Inhalational inoculation

- Manifestations
  - Pulmonary
  - Cutaneous
  - Osteoarticular
  - Genitourinary
  - CNS
  - Virtually any organ
Unchanged Recommendations

• Mild to moderate pulmonary disease
  – Itraconazole x 6-12 months

• Mild to moderate disseminated disease
  – Itraconazole x 6-12 months

• Osteoarticular
  – Itraconazole x 12 months
Changes in Guidelines: Blastomycosis

2000

- **Severe Disease**
  - AmB deoxycholate 1.5-2.5 gm total

- **Immunosuppressed**
  - AmB deoxycholate 1.5-2.5 gm, followed by oral azole therapy indefinitely

2008

- **Severe Disease**
  - Lipid AmB 1-2 weeks, followed by itraconazole

- **Immunosuppressed**
  - Lipid AmB 1-2 weeks, followed by oral azole therapy at least 12 months
### Changes in Guidelines: Blastomycosis

<table>
<thead>
<tr>
<th>Year</th>
<th>CNS Disease</th>
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<tbody>
<tr>
<td>2000</td>
<td>- AmB deoxycholate 2 gm total</td>
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<tr>
<td>2008</td>
<td>- Lipid AmB 4-6 weeks, followed by itraconazole, voriconazole, or high dose fluconazole</td>
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</tbody>
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Changes in Guidelines: Blastomycosis

- Ketoconazole and fluconazole largely removed from guidelines

- Voriconazole and posaconazole have activity against *B. dermatitidis*

- Clinical reports of successful treatment with voriconazole, especially CNS disease

- No reports yet of posaconazole use for *B. dermatitidis*
Changes in Guidelines: Blastomycosis

• Therapeutic Drug Monitoring
  – Itraconazole levels 2 weeks after starting therapy
    • 1.0-10.0 μg/mL
  – Voriconazole levels?
Clinical Practice Guidelines for the Management of Patients with Histoplasmosis: 2007 Update by the Infectious Diseases Society of America

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CID 2007:45 (1 October)
Histoplasmosis

- *Histoplasma capsulatum*

- Inhalational exposure

- Manifestations
  - Asymptomatic infection
  - Pulmonary/Mediastinal disease
  - Disseminated
  - CNS
  - Visceral involvement, especially mucosal involvement
  - Rheumatologic manifestations
Unchanged Recommendations

• No indication for antifungal therapy
  – Localized pulmonary disease
    • Symptoms < than 4 weeks
  – Rheumatologic complications
  – Pericarditis
    • Unless steroids given for severe pericarditis
  – Histoplasmosoma
  – Broncholithiasis
  – Asymptomatic granulomatous mediastinitis
Unchanged Recommendations

- **Treatment recommended**
  - Acute pulmonary disease, > 4 wks symptoms
  - Severe pulmonary disease
    - Antifungal therapy + steroids
  - Chronic cavitary pulmonary disease
  - Mild to moderate disseminated disease
    - Itraconazole
Changes in Guidelines: Histoplasmosis

**2000**
- Severe disease
  - Amphotericin B, sometimes for entire course

- CNS disease
  - Amphotericin B 3 months, then fluconazole

**2007**
- Severe disease
  - Lipid AmB, followed by itraconazole

- CNS disease
  - Liposomal AmB 4-6 weeks, then itraconazole
Changes in Guidelines: Histoplasmosis

• Antifungal discontinuation in AIDS patients
  – At least 1 year of itraconazole
  – Negative blood cultures
  – Serum and urine antigen levels <2 ng/mL
  – CD4 > 150 cells/mm³
  – On HAART
Changes in Guidelines: Histoplasmosis

- Voriconazole and posaconazole have activity against *H. capsulatum*

- Decreased voriconazole sensitivity in patients that have failed fluconazole therapy

- After itraconazole, all other azoles are considered second-line alternatives
Changes in Guidelines

• Therapeutic Drug Monitoring
  – Itraconazole
    • 1.0-10.0 μg/mL
  – Voriconazole
    • Trough at least 0.5 μg/mL
    • Peak at least 2 μg/mL
  – Posaconazole
    • Random level at least 0.5 μg/mL
Thank You