Chronic Meningitis
with an emphasis on fungal meningitis

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A meningeal inflammatory process persisting under observation for at least 4 weeks with failure of clinical improvement or with clinical worsening.
Ainslee B.

- 24 year old woman in horse industry
- June 2004 – admitted with severe headaches and diplopia
  - Travel to SW USA
  - Exam shows papilledema and R 6th n palsy
  - CSF OP 50; WBC 50 (lymphs); glucose 17/90; protein 66; +OCBs and ↑IgG
  - All microbiological studies negative
  - Discharged as viral meningitis
- Recovers w/o treatment
Ainslee B.

- August 2008 – returns with headaches, imbalance, and visual problems
  - Exam shows papilledema
  - CSF OP 25; WBCs 5; protein 121; glucose 10; +OCB; ↑IgG
  - MRI, MRA, and MRV negative
  - All studies negative but CSF histoplasma CF 1:8 yeast and 1:1 for mycelial phase
- Five weeks of IV Ambisome followed by Voriconazole and Diamox indefinitely
- February 2010 – doing well
Chronic Meningitis
Epidemiology

- Dependent on population risk factors
  - New Zealand study representative of developed world
  - < 1% of all meningitis
    » 83 cases v. 1000 bacterial or viral meningitis
  - Causative agent identified in 66%
    » TB (60%)
    » Carcinoma (13%)
    » Cryptococcus neoformans (11%)

Anderson and Willoughby Q J Med 1987;63:283
Chronic Meningitis

Epidemiology

- Dependent on geography
- Examples
  - Coccidioidomycosis in American Southwest
  - Histoplasmosis in Ohio River Valley
  - Cysticercosis in Mexico and South and Central America
  - Angiostrongylus cantenensis in China
Chronic Meningitis
Infectious etiologies

- Viral meningitis (HIV, Mollaret’s {HSV-2})
- Tuberculous meningitis
- Syphilis and neuroborreliosis (Lyme)
- Nocardiosis
- Parameningeal infection
- Fungal meningitis
- Parasitic infection
Chronic Meningitis
Non-infectious etiologies

- Neoplastic meningitis
- Sarcoidosis
- Granulomatous angiitis
- SLE and other vasculitides
- Behcet’s disease
- Vogt-Koyanagi-Harada syndrome
- Allergic and hypersensitivity meningitis
- Chronic meningitis of unknown etiology
Fungi

- Eukaryotic organisms
  - Include yeasts, molds, and mushrooms
- Cell walls contain chitin
  - Versus cellulose in plant cell walls
  - Chitin combined with glucans unlike arthropod
- May grow as single celled yeasts reproducing by budding or binary fission
- Most grow as hyphae (cylindrical structures 2-10μm in diameter)
  - Dimorphic fungi can switch between yeast and hyphal forms
- All have a common ancestor
## Classification of Disease Causing Fungi

<table>
<thead>
<tr>
<th>Classification</th>
<th>Infectious diseases - Mycoses and Mesomycetozoa (B35-B40, 110-118)</th>
<th>[hide]</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Superficial and cutaneous (dermatomycosis):</strong> Tinea=skin; Piedra (exothyrix/endothyrix)-hair</td>
<td><strong>Ascomycota</strong></td>
<td><strong>Dermatophyte</strong> (Dermatophytosis)</td>
</tr>
<tr>
<td><strong>By location</strong></td>
<td><strong>Tinea barbae/Tinea capitis (Kerion)</strong></td>
<td><strong>Epidermophyton floccosum</strong></td>
</tr>
<tr>
<td></td>
<td><strong>Tinea corporis (ringworm)</strong></td>
<td><strong>Microsporum canis</strong></td>
</tr>
<tr>
<td></td>
<td><strong>Tinea cruris</strong></td>
<td><strong>Microsporum audouini</strong></td>
</tr>
<tr>
<td></td>
<td><strong>Tinea pedis (Athlete’s foot)</strong></td>
<td><strong>Trichophyton interdigitale/macrophilites</strong></td>
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<tr>
<td></td>
<td><strong>Tinea unguium</strong></td>
<td><strong>Trichophyton tonsurans</strong></td>
</tr>
<tr>
<td></td>
<td><strong>Oidiodermatophytosis</strong></td>
<td><strong>Trichophyton schoenleinii</strong></td>
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<tr>
<td></td>
<td></td>
<td><strong>Trichophyton rubrum</strong></td>
</tr>
<tr>
<td><strong>Other</strong></td>
<td>Hortaea werneckii (Tinea nigra)</td>
<td>Pedraia hortae (Black piedra)</td>
</tr>
<tr>
<td><strong>Basidiomycota</strong></td>
<td>Malassezia furfur (Tinea versicolor)</td>
<td>Trichosporon spp. (White piedra)</td>
</tr>
</tbody>
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</thead>
<tbody>
<tr>
<td><strong>Subcutaneous, systemic, and opportunistic</strong></td>
<td><strong>Ascomycota</strong></td>
<td><strong>Dimorphic (yeast-mold)</strong></td>
</tr>
<tr>
<td><strong>Oxynemata</strong></td>
<td><strong>Coccidioides immitis/Coccidioides posadasii</strong> (Coccidioidomyosis)</td>
<td><strong>Histoplasma capsulatum</strong> (Histoplasmosis)</td>
</tr>
<tr>
<td></td>
<td><strong>Lecanicillium lecanii</strong> (Leptospirosis)</td>
<td><strong>Paracoccidioides brasiliensis</strong> (Paracoccidioidomycosis)</td>
</tr>
<tr>
<td></td>
<td><strong>Blastomyces dermatitidis</strong> (Blastomycosis)</td>
<td><strong>Sporothrix schenckii</strong> (Sporothrixosis)</td>
</tr>
<tr>
<td></td>
<td><strong>Penicillium marneffei</strong></td>
<td></td>
</tr>
<tr>
<td><strong>Other</strong></td>
<td><strong>Candida auris</strong> (Candidiasis, Oral, Esophageal, Chronic mucocutaneous)</td>
<td><strong>C. glabrata</strong></td>
</tr>
<tr>
<td></td>
<td><strong>C. tropicalis</strong></td>
<td><strong>C. lusitaniae</strong></td>
</tr>
<tr>
<td></td>
<td><strong>Pneumocystis jiroveci</strong> (Pneumocystosis, Pneumocystis pneumonia)</td>
<td></td>
</tr>
<tr>
<td><strong>Yeast-like</strong></td>
<td><strong>Aspergillus</strong> (Aspergillosis, Aspergilloma, Allergic bronchopulmonary aspergillosis)</td>
<td><strong>Exophiala jeaneselmei</strong> (Eumycetoma)</td>
</tr>
<tr>
<td></td>
<td><strong>Fusarium oxysporum/Fusarium oxysporum</strong> (Fusariosis)</td>
<td><strong>Phialophora verrucosa</strong> (Chromoblastomycosis)</td>
</tr>
<tr>
<td></td>
<td><strong>Geotrichum candidum</strong> (Geotrichosis)</td>
<td><strong>Pseudoallescheria boydii</strong> (Allescheriasis)</td>
</tr>
<tr>
<td><strong>Basidiomycota</strong></td>
<td>Cryptococcus sp. (Cryptococcosis)</td>
<td></td>
</tr>
<tr>
<td><strong>Zygomycota</strong></td>
<td><strong>Mucorales</strong> (Mucormycosis)</td>
<td><strong>Rhizopus oryzae</strong></td>
</tr>
<tr>
<td></td>
<td><strong>Mucor indicus</strong></td>
<td><strong>Apicillium remus</strong></td>
</tr>
<tr>
<td></td>
<td><strong>Absidia cornifera</strong></td>
<td><strong>Syncephalastrum racemosum</strong></td>
</tr>
<tr>
<td></td>
<td><strong>Entheromorphales</strong> (Entheromycosis)</td>
<td><strong>Basidiobolus ranarum</strong> (Basidiobolomycosis)</td>
</tr>
<tr>
<td></td>
<td></td>
<td><strong>Conidiobolus coronatus/Conidiobolus incongruus</strong> (Conidiobolomycosis)</td>
</tr>
<tr>
<td><strong>Mycosporidia</strong> (Mycosporidiosis)</td>
<td><strong>Enterocytozoon bieneusi</strong></td>
<td><strong>Entercocoilozoon intestinalis</strong></td>
</tr>
<tr>
<td><strong>Mesomycetozoa</strong></td>
<td><strong>Rhinosporidium seeberi</strong> (Rhinosporidiosis)</td>
<td></td>
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</tbody>
</table>
Percentage of fungal meningitis relative to other types

Figure 1. More than half of all meningitis-related hospitalizations was for the viral form of the disease, 2006.

Fungal meningitis inversely related to wealth

Figure 4. The distribution of meningitis-related hospitalizations was inversely related to wealth, particularly among those hospitalized with fungal/other meningitis, 2006*

* Based on all-listed diagnoses.

Higher mortality with fungal meningitis than with other forms.

Figure 5. In-hospital mortality for meningitis increased substantially among patients 45 years and older, 2006*.

* Based on all-listed diagnoses.

<table>
<thead>
<tr>
<th>Predisposing factor</th>
<th>Typical fungi</th>
</tr>
</thead>
<tbody>
<tr>
<td>prematurity</td>
<td>candida</td>
</tr>
<tr>
<td>inherited immune deficiency - CGD, SCID, etc</td>
<td>candida, cryptococcus, aspergillus</td>
</tr>
<tr>
<td>corticosteroids</td>
<td>cryptococcus, candida</td>
</tr>
<tr>
<td>cytotoxic agents</td>
<td>aspergillus, candida</td>
</tr>
<tr>
<td>HIV/AIDS</td>
<td>cryptococcus, histoplasmosis</td>
</tr>
<tr>
<td>alcoholism</td>
<td>sporothrix</td>
</tr>
<tr>
<td>iron chelator therapy</td>
<td>zygomycetes</td>
</tr>
<tr>
<td>IV drug abuse</td>
<td>zygomycetes, candida</td>
</tr>
<tr>
<td>diabetic ketoacidosis</td>
<td>zygomycetes</td>
</tr>
<tr>
<td>trauma, surgery, FB</td>
<td>candida, dematiaceous fungi</td>
</tr>
<tr>
<td>near-drowning</td>
<td>pseuodallescheria</td>
</tr>
</tbody>
</table>
Pathological spectrum of CNS fungal infection

<table>
<thead>
<tr>
<th>SPECIES</th>
<th>Meningitis</th>
<th>Abscess</th>
<th>Infarct</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>True yeast</strong></td>
<td>++++</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>cryptococcus, histoplasmosis,</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>blastomycosis</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Pseudohyphae</strong></td>
<td>++</td>
<td>++</td>
<td>-</td>
</tr>
<tr>
<td>candida</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>True hyphae</strong></td>
<td>+</td>
<td>+++</td>
<td>++++</td>
</tr>
<tr>
<td>aspergillus, zygomycetes</td>
<td></td>
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</tr>
</tbody>
</table>

International Neuroinfectious Disease Conference
Addis Ababa, Ethiopia, on February 27-28, 2010
True Yeast
Cryptococcus neoformans

History

- 1861 - *C. neoformans* first identified
- 1894 - Busse isolates the organism
- 1895 - Buschke describes tibial gumma
- 1914 - Verse describes *C. neoformans* meningitis
- 1956 - Introduction of amphotericin
Cryptococcus neoformans

Synonyms

- Cryptococcus neoformans
- Cryptococcus histolytica
- Torulopsis neoformans
- Torula histolytica
- European blastomycosis
- Saccharomyosis
- “Champignon” (French)
Cryptococcus neoformans
Epidemiology

- Ubiquitous
  - var. *neoformans* A-D: worldwide
  - var. *gatti*: Australia, SE Asia, Central Africa, Southern California

- prior to AIDS: 3 M:F
- age range: 30-50 years (>2/3s)
- all races affected
Cryptococcus neoformans
Associated disorders

- AIDS (1.9-11% of all AIDS patients)
- Corticosteroid therapy
- Leukemia and lymphoma
- Diabetes mellitus, cirrhosis, renal disease
- Sarcoidosis, SLE
- TB
- Idiopathic CD4 lymphopenia
Cryptococcus neoformans
Characteristics

- Variety *neoformans* capsular types (A-D) and *gatti* (B and C)
- Commonest fungal infection of CNS
- Bird excreta, soil, fruits, animals, man
- ↑dairy workers and immunosuppressed
- Lesions of lung, skin, mucous membranes, bone
Cryptococcus neoformans
Identification

- Grows at 27°C, but not at 44°C
- Hydrolyzes urea
- Virulent in mice
- Ability to assimilate carbon and nitrogen compounds
- Mucinuous capsule (only encapsulated fungus to invade the CNS)
Cryptococcus neoformans
Cryptococcus neoformans Pathogenesis

- Respiratory tract is usual portal of entry; occasionally skin or mucous membrane
- CNS most common site of clinical infection
- Other organ systems affected:
  - respiratory ("coin" lesion of lungs)
  - lymph nodes
  - skin and eyes
  - bone
Cryptococcus neoformans
Pathogenesis
Cryptococcus neoformans
Properties enabling CNS invasion

- Receptor on CNS cells for yeast ligand
- Ability to grow at 37°C
- Melanin production by yeast (antioxidant)
- Production of capsule (protective)
- Resistance against *C. neoformans*
  chiefly CMI: corticosteroid therapy and HIV
Cryptococcal meningitis

Signs and symptoms (Sabetta and Andriole 1985)

- Headache 87%
- Fever 60%
- Nausea and vomiting 53%
- Altered mental status 52%
- Meningeal signs 50%
- Visual disturbances 33%
- Cranial nerve palsies 32%
Cryptococcal meningitis

Signs and symptoms (Sabetta and Andriole 1985)

- Papilledema 28%
- Ataxia 26%
- Seizures 15%
- Aphasia 10%
- No signs or symptoms 10%
Cryptococcal neoformans

Radiographic findings

- CT and MRI usually normal
  - meningeal inflammation typically minimal
- rarely focal mass lesions
  - cryptococcomas: indistinguishable from pyogenic abscess
  - pseudocysts: CSF equivalent w/o contrast+, "soap bubble" appearance
  - choroid plexus granulomas
Cryptococcal neoformans
Radiographic findings

Lacunar infarct of right basal ganglia on CT scan
Cryptococcal neoformans
Radiographic findings

Contrast enhanced FLAIR (A and C) and T1WI (B and D)
Cryptococcal neoformans
Radiographic findings – IRIS in AIDS

Small cerebellar lesion

Meningeal enhancement

2 weeks after the initiation of HAART

Cryptococcal meningitis
CSF findings

- ↑ WBC (<800 cells; lymph) 97%
- ↑ protein (<600 mg/dl) 90%
- ↑ opening pressure 64%
- ↓ glucose (15-35 mg/dl) 55%
- + India ink 57%
- + culture 75%
- + crypt Ag (latex agg>CF) >95%
Cryptococcal meningitis
AIDS vs. non-AIDS: [++<25%; ++<50%; +++<75%; ++++<100%]

<table>
<thead>
<tr>
<th>Findings</th>
<th>AIDS</th>
<th>non-AIDS</th>
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<tbody>
<tr>
<td>symptoms&lt;1-2 weeks</td>
<td>+</td>
<td>++</td>
</tr>
<tr>
<td>+India ink</td>
<td>++++</td>
<td>++</td>
</tr>
<tr>
<td>CSF Ag titer&gt;1:1024</td>
<td>++++</td>
<td>+</td>
</tr>
<tr>
<td>+serum Ag</td>
<td>+++</td>
<td>++</td>
</tr>
<tr>
<td>↓CSF WBC</td>
<td>++++</td>
<td>+</td>
</tr>
<tr>
<td>↓CD4 count</td>
<td>++++</td>
<td>+</td>
</tr>
<tr>
<td>cryptococcemia</td>
<td>+++</td>
<td>+</td>
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</table>
Cryptococcal meningitis
AIDS vs. non-AIDS: [+<25%; ++<50%; +++<75%; ++++<100%]

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<thead>
<tr>
<th>Findings</th>
<th>AIDS</th>
<th>non-AIDS</th>
</tr>
</thead>
<tbody>
<tr>
<td>extracranial sites</td>
<td>+++</td>
<td>+</td>
</tr>
<tr>
<td>parenchym. lesions</td>
<td>++</td>
<td>+</td>
</tr>
<tr>
<td>increased ICP</td>
<td>++</td>
<td>+</td>
</tr>
<tr>
<td>var neoformans</td>
<td>++++</td>
<td>+++</td>
</tr>
<tr>
<td>suppressive Rx</td>
<td>++++</td>
<td>+</td>
</tr>
<tr>
<td>+ initial response</td>
<td>++++</td>
<td>+++++</td>
</tr>
<tr>
<td>relapse</td>
<td>+</td>
<td>+</td>
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</tbody>
</table>
Cryptococcus neoformans

Histopathology

- Meningitis/meningoencephalitis 67%
- Cysts 18%
- Granulomas (cryptococcomas) 8%
- Encephalitis 4%
- Abscesses 2%
Cryptococcus neoformans
Histopathology
Cryptococcal meningitis
A Proposed Management Algorithm

Algorithm 24(A) Management of cryptococcal meningitis

Features suggestive of cryptococcal or other causes of meningitis:
- Fever, headache, ± neck rigidity

Evaluation:
- Examination for mental state & focal signs
- Serum cryptococcal antigen, blood culture, CXR
- CT brain

Any focal signs or space-occupying lesions on CT scan

Yes
No

Investigate and treat intracranial effusions
Perform lumbar puncture:
- Protein, sugar, cell counts, AFB smear
- Gram stain & Indian ink stain
- Cryptococcal antigen, VDRL
- Culture

Diagnosis of cryptococcal meningitis

- Amphotericin B ± flucytosine induction treatment
- Monitor treatment response and side effects

Yes
No

Response

- Look for other causes of meningitis if CSF suggests so
- Fluconazole induction, followed by maintenance

Yes
No
Cryptococcal meningitis

Treatment

- Induction (2 weeks)
  - Amphotericin B 0.7 mg/dk/d
  - +/- flucytosine

- Maintenance (8 weeks)
  - fluconazole 400 to 800 mg/d or
  - itraconazole

- Secondary prophylaxis (AIDS patients)
  - fluconazole 200 mg/d
Cryptococcus neoformans

Side effects of treatment

- **Amphotericin**
  - fever, chills, H/A, N&V, phlebitis, cardiotoxicity, nephrotoxicity, hypomagnesemia, hypokalemia, hepatotoxicity, cytopenias

- **5-Flucytosine**
  - cytopenias, nephrotoxicity, hepatotoxicity, confusion, H/A, hallucinations

- **Fluconazole**
  - nausea and vomiting, headache, skin rash, abd pain, diarrhea, hepatotoxicity, seizures
Cryptococcus neoformans
Prognostic factors

- ↑ CSF opening pressure
- + India ink test
- ↓ CSF leukocyte count
- CSF hypoglycorrhachia
- ↑ CSF cryptococcal Ag titer
- + blood culture
- C. neoformans at extraneural sites

Diamond and Bennett 1974
Histoplasma capsulatum

Epidemiology

- Endemic to Ohio River valley, central Mississippi valley, Appalachian Mountains
- Sources: soil, domestic and wild animals
- Asymptomatic disease common:
  - primary pulmonary infection
  - RES affected
- Most commonly symptomatic in 1st year of life and 5-6 decades
- Incidence in AIDS is as high as 26% in endemic areas to <1% in non-endemic
Histoplasma capsulatum
Systemic features

- Symptoms develop in 3-17 days
  - typically 12-14 days following exposure

- Constellation of symptoms include:
  - Fever
  - Chest Pain
  - Weight loss
  - Dry Cough
  - Headache
  - Sweats
  - Chills
  - Fatigue
  - Hemoptysis
  - Night sweats
Histoplasma capsulatum
Chest X-ray
Histoplasma capsulatum
Dissemination to the CNS

- Dissemination usual in immunosuppression
- CNS disease in 10-25% with dissemination
  - meningitis (basal)
  - IC mass lesions
- CNS disease may occur many years after apparent cure
- Culture negative biopsy may be mistaken for sarcoidosis
Histoplasma capsulatum
Clinical features

◆ Symptoms:
  – Headache, confusion

◆ Signs:
  – Altered LOC
  – Cranial neuropathies
  – Seizures, personality change, focal features in 10%
  – Meningismus (10%)
Histoplasma capsulatum Diagnosis

- Chest X-ray normal in 33%
- CSF with monocytic pleocytosis, ↑protein, ↓glucose
  - Occasionally persistent neutrophilic pleocytosis
- Positive CSF cultures in 50%-66%
- Blood culture + in 50%
- Bone marrow culture + 33-60%
  - Culture negative bx may be mistaken for sarcoidosis
- + Serum and CSF histoplasma Ag – specific
  - 95% of urine + and 85% of blood in HIV+
- + Serum and CSF histoplasma Ab
Histoplasma capsulatum

Treatment

- CNS disease requires amphotericin
  - Liposomal ambisome or ambisome lipid complex
  - Decreases risk of renal toxicity

- Itraconazole
  - Oral itraconazole may be started after 2 weeks
  - Check liver functions
  - Check serum levels after 2 weeks (>1 µg/ml)

Avoid fluconazole
Coccidioides immitis
Epidemiology

- Dimorphic yeast
- Endemic to San Joaquin valley & Arizona
- Found in soil - inhaled into lungs
- Predisposing factors for dissemination:
  - pregnancy, DM, immunodeficient states
  - More common in African Americans and Latinos
Coccidioides immitis
In culture
Coccidioides immitis
Clinical manifestations

◆ Six main presentations
  – Asymptomatic
    » Most common
  – Pulmonary
  – Skin
  – Soft tissue
  – Skeletal
  – Meningitis
Coccidioides immitis

Features of severe infection

- Loss of body weight >10% baseline
- Intense night sweating >3 weeks
- Infiltrates involving >50% of one lung or portions of both lungs
  - prominent or persistent hilar lymphadenopathy.
- Anti-coccidioidal complement fixing antibody titer >1:16.
- Failure of dermal hypersensitivity to coccoidal Ags
- Symptoms may also persist for >2 months.
Coccidioides immitis Neuropathology

- Meningitis alone (13%)
- Meningitis with cerebritis (78%)
- Scattered miliary granulomas (9%)
Coccidioides immititis
Diagnosis

- Brain imaging
  - Normal or meningeal features
- CSF
  - Presence of eosinophils (>10 eos/ml$^3$) - ≤30%
  - Some eosinophils in 70%
- Diagnosis
  - + CSF Complement fixations - Ab to C. immititis
  - + CSF cultures for C. immititis
Coccidioides immitis Treatment

- **Ambisome** for meningitis or refractory cases
  - Direct port into the CSF may be required
  - Lifetime Rx with imidazole may be needed

- **Fluconazole** is first line.
  - Good CSF penetration
  - Effective in ~75% of patients

- **Itraconazole** is equally effective
  - Poor CSF penetration

- **Voriconazole**
  - Broad spectrum in vitro agent
  - Good efficacy either PO or IV
  - Efficacy is nearly as good as ambisome
  - Visual changes (~20%) & hallucinations (~5%)
Actinomycosis

- Endemic in Africa, India and S. and C. America
- Most commonly skin infection following traumatic inoculation of organism
  - Maduromycosis (mycetoma pedis)
- CNS infection reported
Pseudoallescheria boydii

P. Boydii in transplant patient
Blastomycosis dermatitidis

- Uncommon infection
- Most common in USA
- M:F ratio of ~10:1
- **Transmission** by inhalation from decomposing vegetation and rotting wood
- Usually indolent with chronic progression
- **Skin lesions** in exposed areas
- CXR with nodular infiltrates in ~65% of cases
Blastomycosis dermatitidis

- Uncommon cause of meningitis
- Also causes vertebral osteomyelitis
- Treatment
  - Liposomal amphotericin B
  - Voriconazole may be used as follow on therapy or in amphotericin intolerant
Sporotrichosis schenckii

- Found worldwide
- In soil, moss, rose thorns, hay
- Typically chronic skin infection
- Forms
  - Cutaneous
  - Pulmonary
  - Disseminated – including CNS
- To 1987 – only 15 cases in world literature of CNS sporotrichosis
- Dx:
  - Difficult to culture
  - CSF/blood Ab to Sporotrichosis

True Hyphae
Mucormycosis (phycomycosis)

- Mucoraceae (*Rhizopus, Mucor, Absidia*)
- Ubiquitous bread & fruit mold, soil, manure
- 1885- described with brain abscesses
- Most aggressive fungal infection
- Worldwide distribution and all ages
- Classic triad:
  - Diabetic ketoacidosis
  - Naso-orbital necrotizing infection
  - Meningoencephalitis
Mucormycosis (phycomycosis)

- 95% immunocompromised:  
  - diabetes mellitus 70%  
  - hematologic malignancy (lung or dissemin.)  
  - renal transplant  
  - IVDA (m.c. cause of IC fungal abscess)  
  - Rx with desferroxamine

- Pathology:  
  - hyphae invade arterial walls, spread into brain  
  - 1/3 thromb int carotid artery (hemorrh. infarct)  
  - cavernous sinus thrombosis common
Mucormycosis (phycomycosis)

- **Symptoms:** facial pain, diplopia, lacrimation, nasal stuffiness or discharge, fever, lethargy
- **Signs:** nasal ulcer, nasal discharge, facial swelling, cranial nerve abn, ophthalmoplegia, focal deficits, seizures
- **Radiographic studies:** bone erosion & sinus opacification; BG m.c. site of abscess
- **CSF:** non-specific; cultures negative
Mucormycosis (phycomycosis)

Morbidity and mortality:
- >90% before amphotericin
- now >70% DM and ~20% others
- 70% with residual deficits

Treatment
- correction of metabolic abnormality
- exenteration of infected tissues
- amphotericin B
- hyperbaric O₂
Aspergillosis

- "aspergillum": sprinkles holy water
- 1897 - sphenoid lesion w/spread to optic chiasm and internal carotid artery
- ubiquitous: soil, water, organic debri
- >9 of 200 species cause CNS lesions
- worldwide distribution
- no sex or age predilection
Aspergillosis

★ Risk factors:
  – neutropenia: hematologic neoplasms, organ & BM transplants
  – DM, IVDA, hepatic disease, Cushings
  – sarcoidosis, TB

★ Pathology:
  – vasculitis and infarct
  – cerebritis and abscess
  – granuloma (rare)
Aspergillosis

- lungs site of primary infection
- two patterns of CNS infection
  - direct extension from paranasal sinuses
  - hematologic dissemination
    - CNS involved in 15% of pulmonary cases
    - CNS in 40-60% of all disseminated cases
- stroke syndrome m.c. manifestation
- serological studies experimental
- Rx: extirpation/drainage and AmphoB
Pseudohyphae
Candida

- *C. albicans* >90%; other species <10%
- Normal flora: skin, oropharynx, gut, vagina
  - blood seeded by gut, IV lines, endocarditis
- Compromised neutrophil function
- At autopsy, most common fungal brain dis.
- Pathology:
  - microabscess - typical lesion
  - full sized abscess in <14%
  - meningitis/ependymitis probably <15%
Candida

- Clinical manifestations are non-specific:
  - confusion, drowsiness, stupor, fever
- Meningitic signs m.c. than w/other fungi
- Focal signs with full-sized abscess
- Usually very ill and on IV antibiotics
- CSF non-specific; cultures negative
- Frequent presence of Candida at other sites
- Rx: AmphoB w or w/o oral flucytosine
"I'd say it's a fungal infection."