
Chronic Meningitis

with an emphasis on fungal
meningitis

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Chronic Meningitis Definition

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

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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%)

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

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Chronic Meningitis

Infectious etiologies

- ◆ Viral meningitis (HIV, Mollaret's {HSV-2})
- ◆ Tuberculous meningitis
- ◆ Syphilis and neuroborreliosis (Lyme)
- ◆ Nocardiosis
- ◆ Parameningeal infection
- ◆ Fungal meningitis
- ◆ Parasitic infection

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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

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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 2-10 μ m in diameter)
 - Dimorphic fungi can switch between yeast and hyphal forms
- ◆ All have a common ancestor

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Classification of Disease Causing Fungi

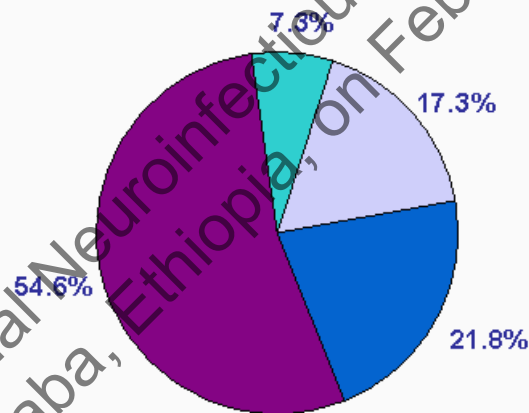
v · d · e				Infectious diseases · Mycoses and Mesomycetozoa (B35-B49, 110-118)		[hide]
Superficial and cutaneous (dermatomycosis): Tinea=skin; Piedra (exothrix/endothrix)=hair	Ascomycota	Dermatophyte (Dermatophytosis)	By location	Tinea barbae/Tinea capitis (Kerion) · Tinea corporis (Ringworm) · Tinea cruris · Tinea manuum · Tinea pedis (Athlete's foot) · Tinea unguium/Onychomycosis		
			By organism	Epidermophyton floccosum · Microsporum canis · Microsporum audouinii · Trichophyton interdigitale/trichoglyphes · Trichophyton tonsurans · Trichophyton schoenleinii · Trichophyton rubrum		
	Other	Hortaea werneckii (Tinea nigra) · Piedraia hortae (Black piedra)				
	Basidiomycota	Malassezia furfur (Tinea versicolor) · Trichosporon beigelii (White piedra)				
Subcutaneous, systemic, and opportunistic	Ascomycota	Dimorphic (yeast+mold)	Onygenales	Coccidioides immitis/Coccidioides posadasii (Coccidioidomycosis) · Histoplasma capsulatum (Histoplasmosis) · Lacazia loboi (Lobo's disease) · Paracoccidioides brasiliensis (Paracoccidioidomycosis)		
			Other	Blastomyces dermatitidis (Blastomycosis) · Sporothrix schenckii (Sporotrichosis) · Penicillium marneffei (Penicilliosis)		
		Yeast-like	Candida albicans (Candidiasis, Oral, Esophageal, Chronic mucocutaneous) · C. glabrata · C. tropicalis · C. lusitanae · Pneumocystis jirovecii (Pneumocystosis, Pneumocystis pneumonia)			
	Mold-like	Aspergillus (Aspergillosis, Aspergilloma, Allergic bronchopulmonary aspergillosis) · Exophiala jeanselmei (Eumycetoma) · Fonsecaea pedrosoi/Fonsecaea compacta/Phialophora verrucosa (Chromoblastomycosis) · Geotrichum candidum (Geotrichosis) · Pseudallescheria boydii (Allescheriasis)				
		Basidiomycota	Cryptococcus neoformans (Cryptococcosis)			
Zygomycota (Zygomycosis)	Mucorales (Mucormycosis)	Rhizopus oryzae · Mucor indicus · Absidia corymbifera · Syncephalastrum racemosum				
		Entomophthorales (Entomophthoramycosis)	Basidiobolus ranarum (Basidiobolomycosis) · Conidiobolus coronatus/Conidiobolus incongruus (Conidiobolomycosis)			
	Microsporidia (Microsporidiosis)	Enterocytozoon bieneusi/Encephalitozoon intestinalis				
Mesomycetozoa	Rhinosporidium seeberi (Rhinosporidiosis)					

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*

■ Bacterial ■ Viral ■ Fungal/Other ■ Non-Specific



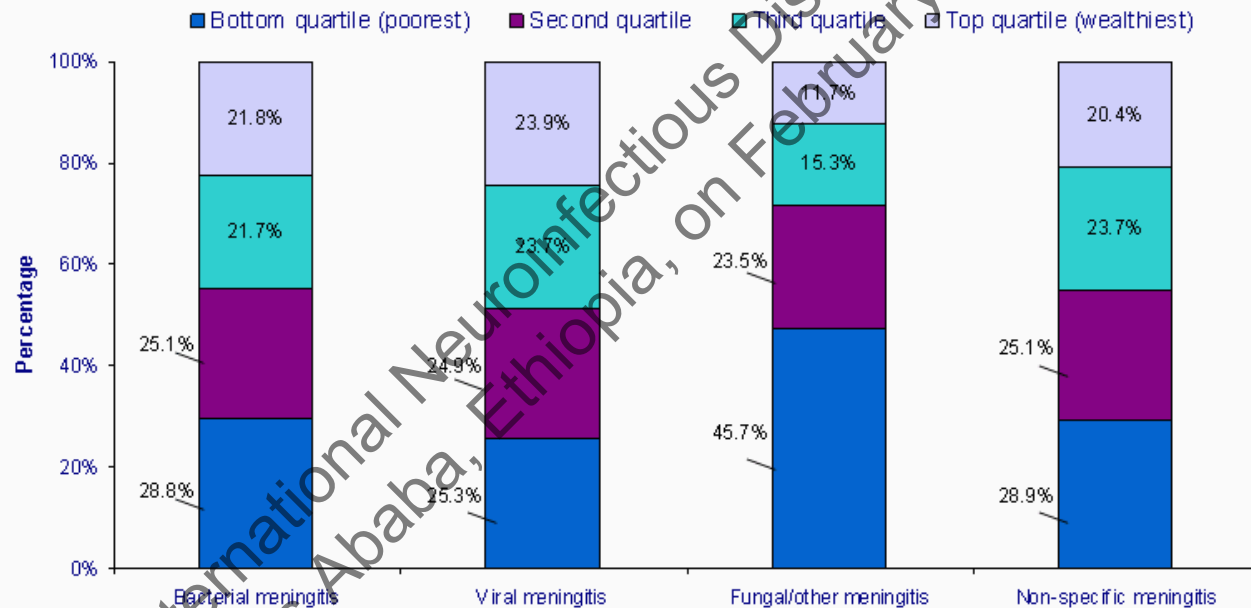
* Based on all listed diagnoses.

Source: AHRQ, Center for Delivery, Organization, and Markets, Healthcare Cost and Utilization Project, HCUPnet, Nationwide Inpatient Sample, 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*



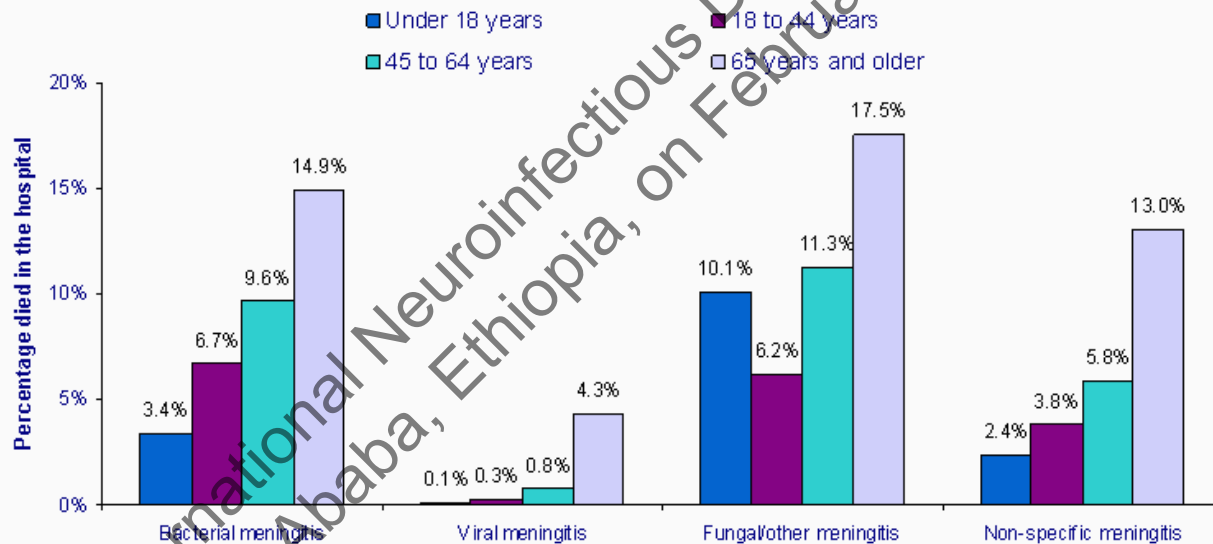
* Based on all-listed diagnoses.

Source: AHRQ, Center for Delivery, Organization, and Markets, Healthcare Cost and Utilization Project, HCUPnet, Nationwide Inpatient Sample, 2006.

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.

Source: AHRQ, Center for Delivery, Organization, and Markets, Healthcare Cost and Utilization Project, HCUPnet, Nationwide Inpatient Sample, 2006.

CNS FUNGI - Predisposing factors

Predisposing factor	Typical fungi
<i>prematurity</i>	candida
<i>inherited immune deficiency - CGD, SCID, etc</i>	candida, cryptococcus, aspergillus
<i>corticosteroids</i>	cryptococcus, candida
<i>cytotoxic agents</i>	aspergillus, candida
<i>HIV/AIDS</i>	cryptococcus, histoplasmosis
<i>alcoholism</i>	sporothrix
<i>iron chelator therapy</i>	zygomycetes
<i>IV drug abuse</i>	zygomycetes, candida
<i>diabetic ketoacidosis</i>	zygomycetes
<i>trauma, surgery, FB</i>	candida, dematiaceous fungi
<i>near-drowning</i>	pseudallescheria

Pathological spectrum of CNS fungal infection

<u>SPECIES</u>	<u>Meningitis</u>	<u>Abscess</u>	<u>Infarct</u>
<i>True yeast</i> cryptococcus, histoplasmosis, blastomycosis	++++	+	+
<i>Pseudohyphae</i> candida	++	++ microabscesses	-
<i>True hyphae</i> aspergillus, zygomycetes	+	+++ macroabscesses	++++

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True Yeast

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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

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Cryptococcus neoformans

Synonyms

- ◆ Cryptococcus neoformans
- ◆ Cryptococcus histolytica
- ◆ Torulopsis neoformans
- ◆ Torula histolytica
- ◆ European blastomycosis
- ◆ Saccharomycosis
- ◆ “Champignon” (French)

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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

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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

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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

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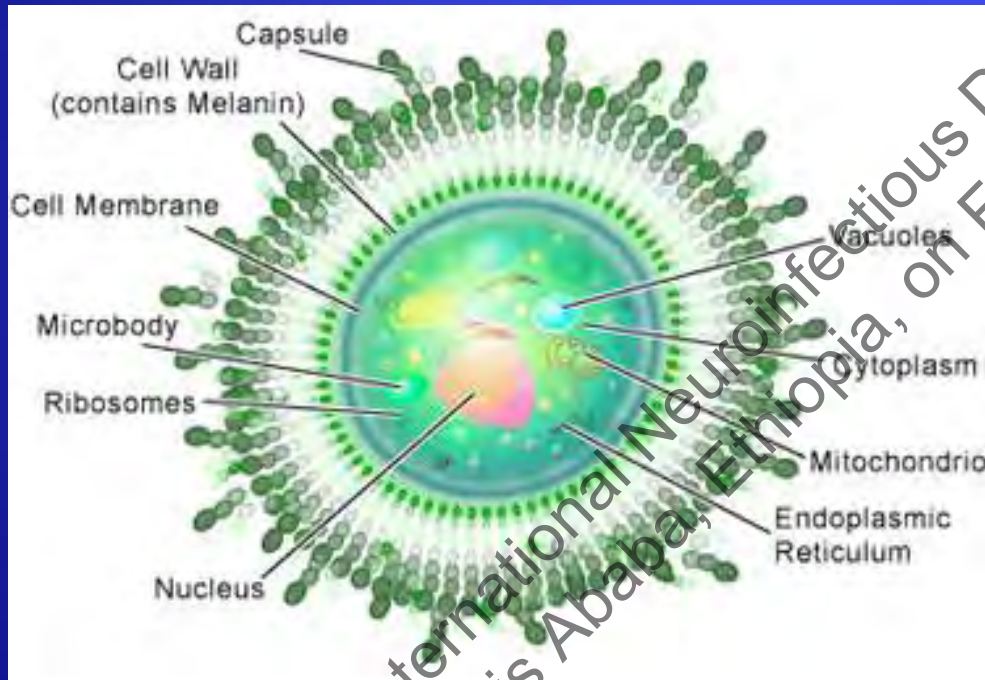
Cryptococcus neoformans

Identification

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

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Cryptococcus neoformans



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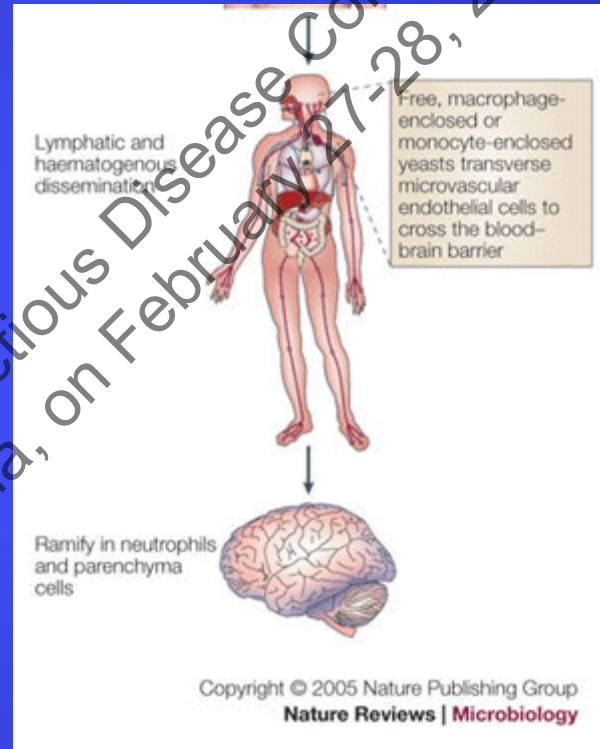
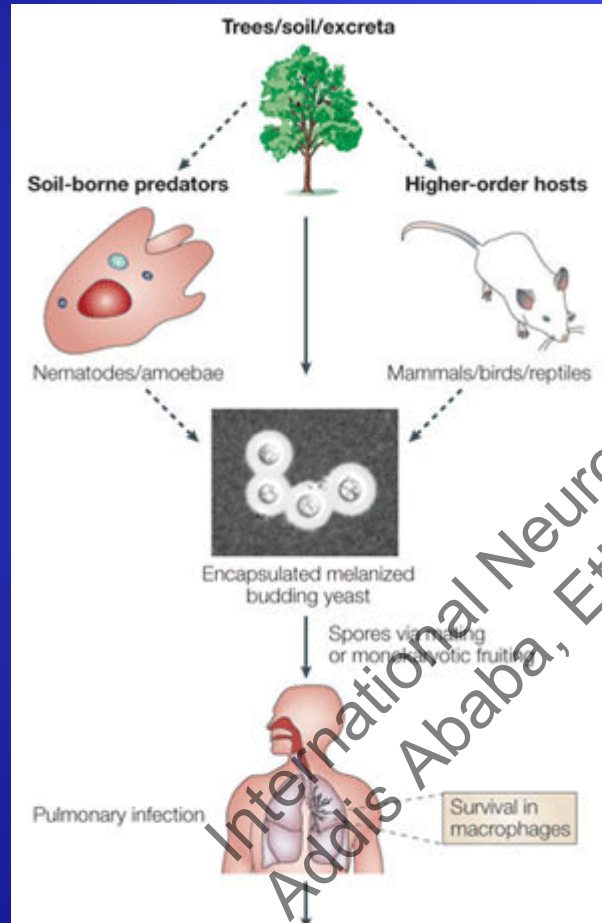
Cryptococcus neoformans

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 CMV: 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%

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Cryptococcal meningitis

Signs and symptoms (Sabetta and Andriole 1985)

◆ Papilledema	28%
◆ Ataxia	26%
◆ Seizures	15%
◆ Aphasia	10%
◆ No signs or symptoms	10%

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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

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Cryptococcal neoformans

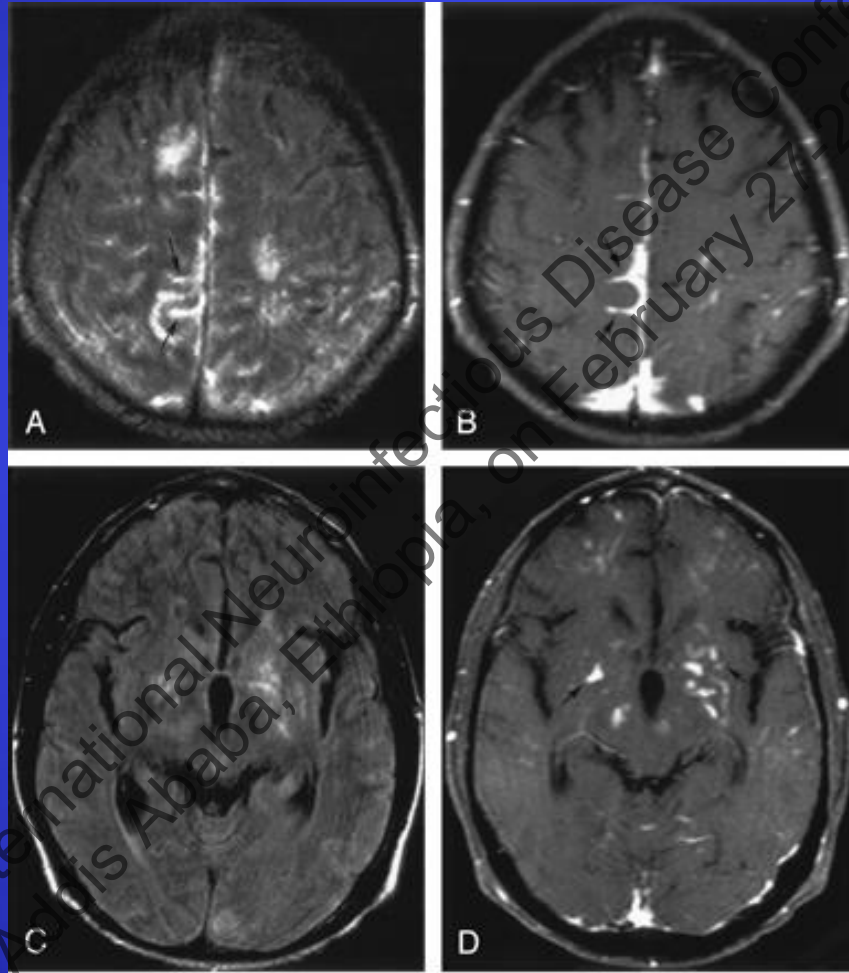
Radiographic findings



Lacunar infarct of right basal ganglia on CT scan

Cryptococcal neoformans

Radiographic findings

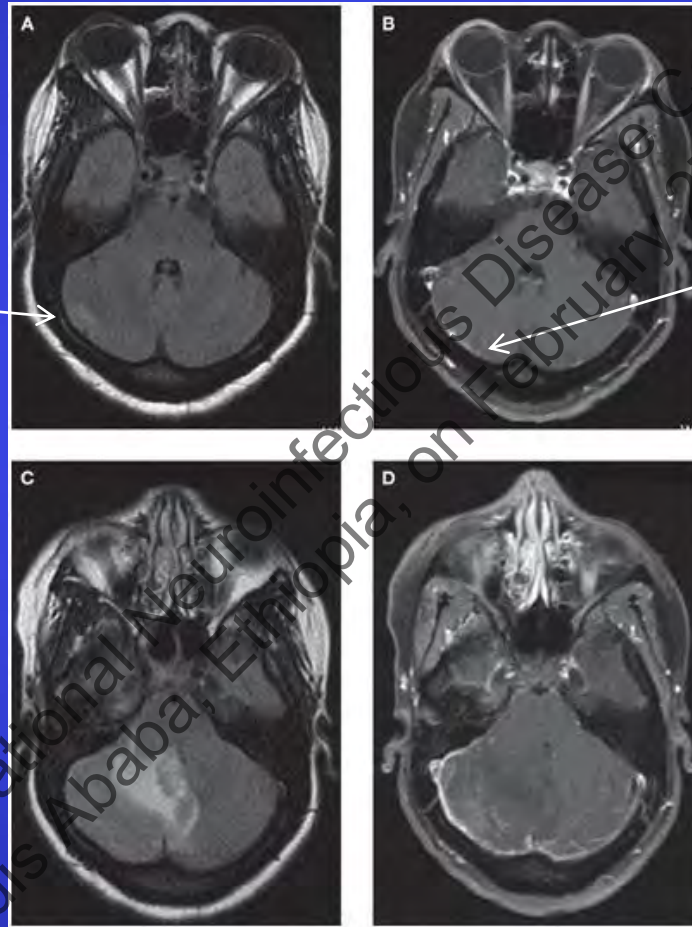


Contrast enhanced FLAIR (A and C) and T1WI (B and D)

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%

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Cryptococcal meningitis

AIDS vs. non-AIDS: [+<25%; ++<50%; +++<75%; ++++<100%]

Findings	AIDS	non-AIDS
symptoms<1-2 weeks	+	++
+India ink	++++	++
CSF Ag titer>1:1024	+++	+
+serum Ag	+++	++
↓CSF WBC	++++	+
↓CD4 count	++++	+
cryptococemia	+++	+

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Cryptococcal meningitis

AIDS vs. non-AIDS: [+<25%; ++<50%; +++<75%; ++++<100%]

Findings	AIDS	non-AIDS
extracranial sites	+++	+
parenchym. lesions	++	+
increased ICP	+	+
<i>var neoformans</i>	++++	+++
suppressiv Rx	++++	+
+ initial response	++++	++++
relapse	+	+

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Cryptococcus neoformans

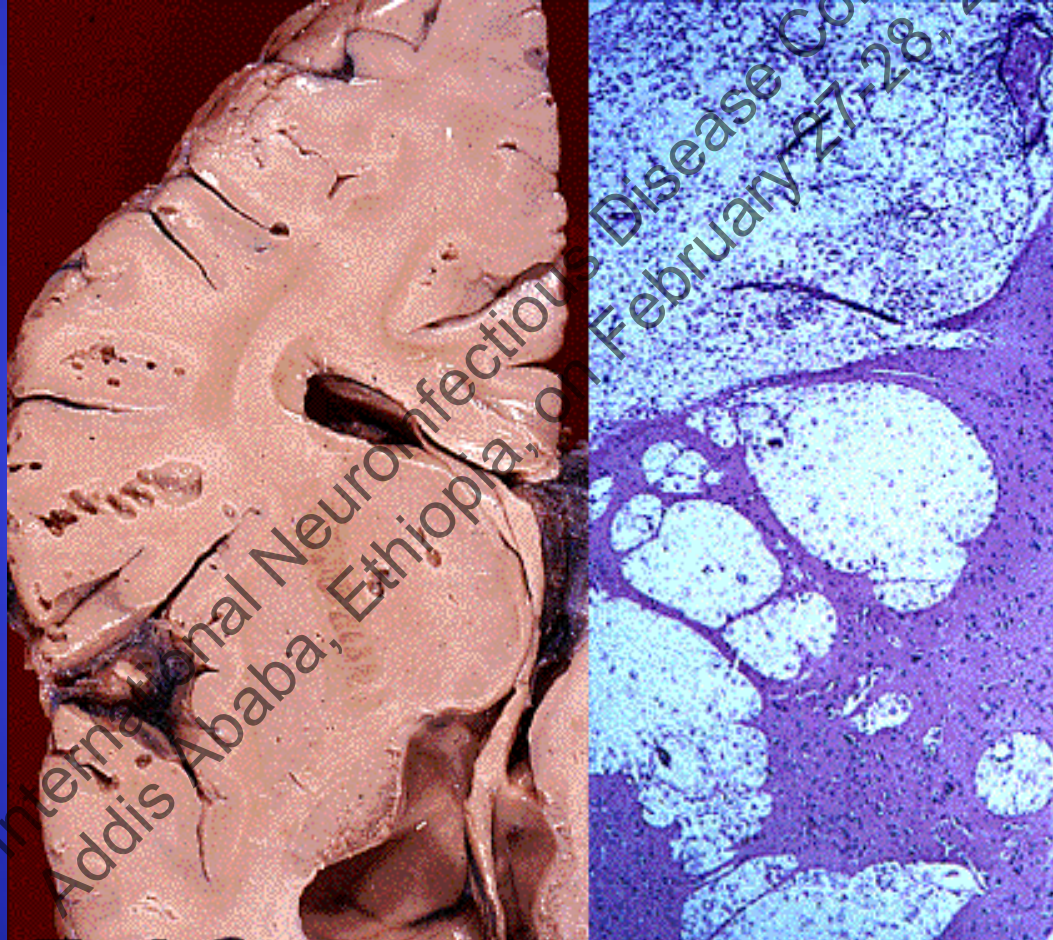
Histopathology

- ◆ Meningitis/meningoencephalitis
67%
- ◆ Cysts 18%
- ◆ Granulomas (cryptococcomas)
8%
- ◆ Encephalitis 4%
- ◆ Abscesses 2%

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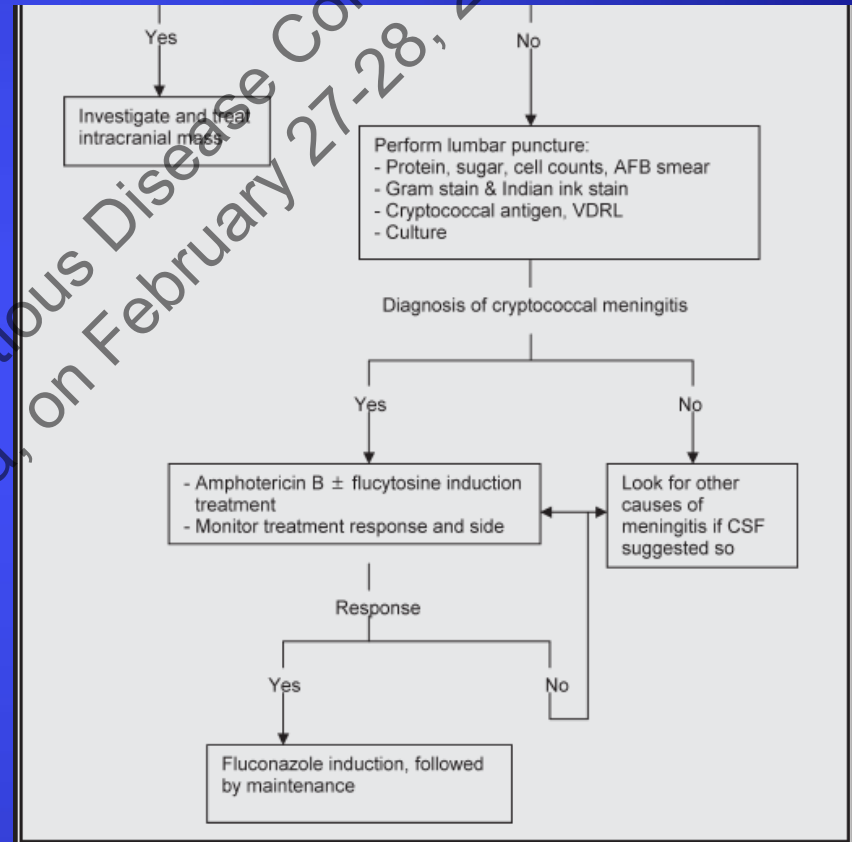
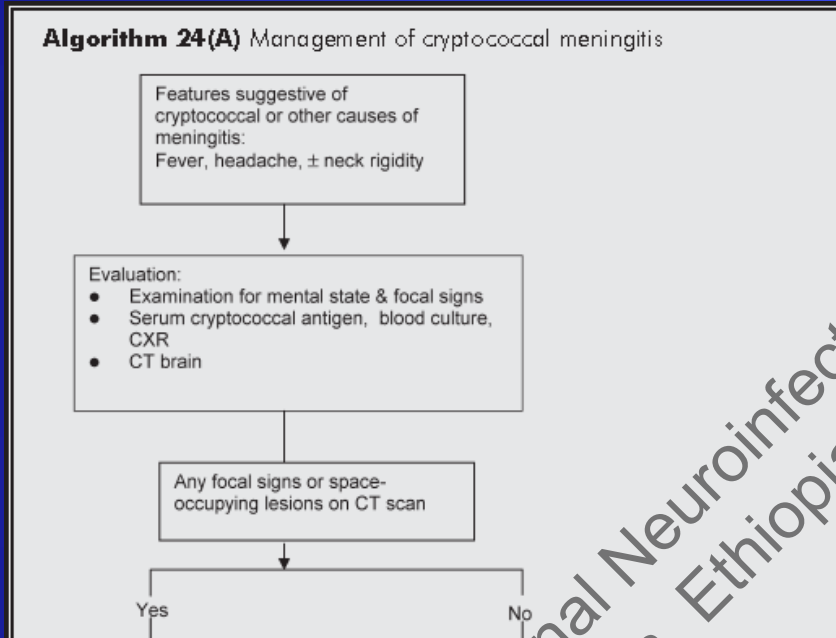
Cryptococcus neoformans

Histopathology



Cryptococcal meningitis

A Proposed Management Algorithm



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Cryptococcal meningitis

Treatment

- ◆ Induction (2 weeks)
 - Amphotericin B 0.7 mg/kg/d
 - +/- flucytosine
- ◆ Maintenance (8 weeks)
 - fluconazole 400 to 800 mg/d or
 - itraconazole
- ◆ Secondary prophylaxis (AIDS patients)
 - fluconazole 200 mg/d

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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

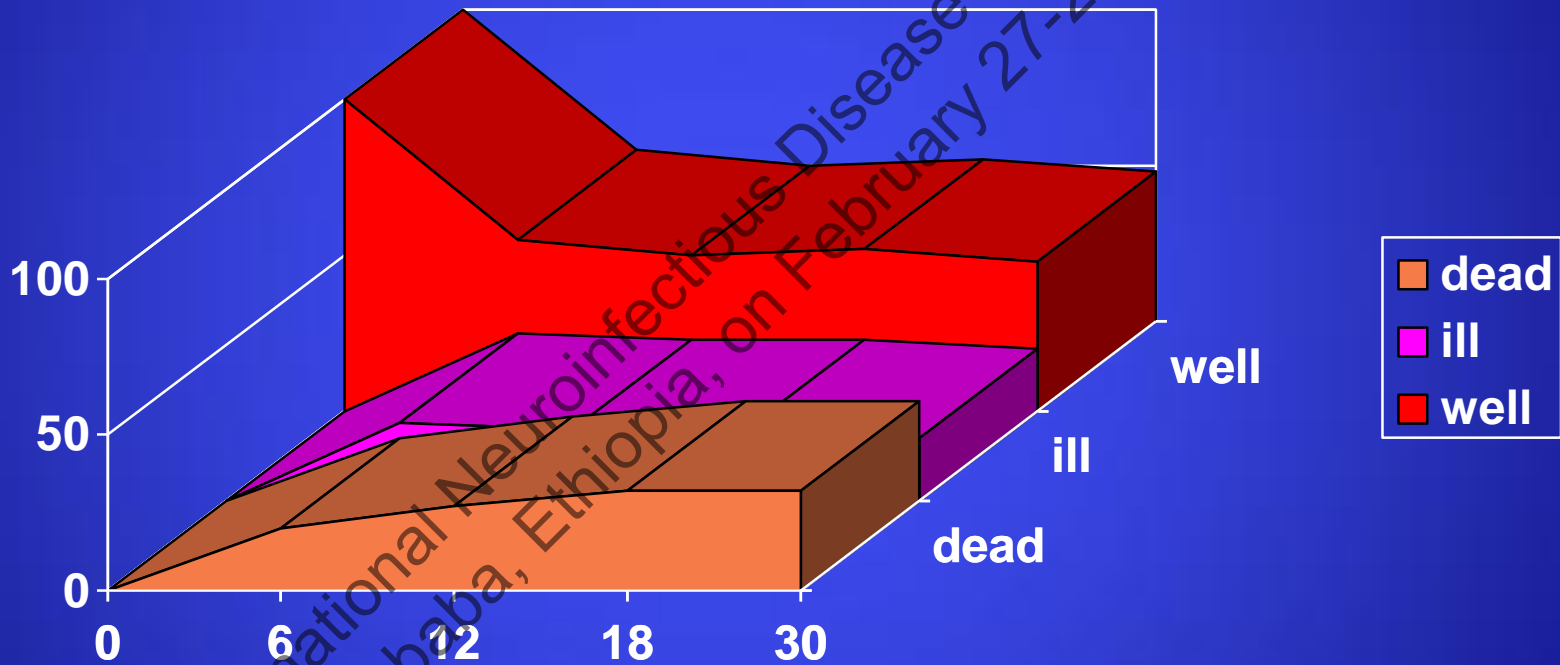
- nausea and vomiting, headache, skin rash, abd pain, diarrhea, hepatotoxicity, seizures

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

Cryptococcal meningitis - Survival



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

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Histoplasma capsulatum

Chest X-ray



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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%)

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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

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Histoplasma capsulatum

Treatment

- ◆ CNS disease requires amphotericin
 - Liposomal amphotericin or amphotericin 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 ($>1\mu\text{g/ml}$)

Coccidioides immitis

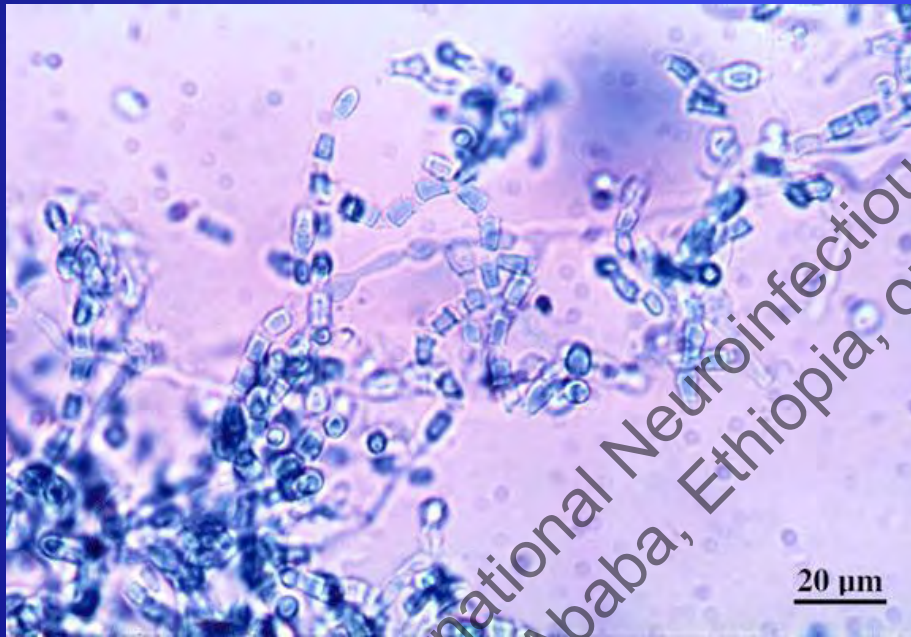
Epidemiology

- ◆ 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

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Coccidioides immitis

In culture



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Coccidioides immitis

Clinical manifestations

- ◆ Six main presentations
 - Asymptomatic
 - » Most common
 - Pulmonary
 - Skin
 - Soft tissue
 - Skeletal
 - Meningitis



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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.

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Coccidioides immitis

Neuropathology

- ◆ Meningitis alone (13%)
- ◆ Meningitis with cerebritis (78%)
- ◆ Scattered miliary granulomas (9%)

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Coccidioides immitis

Diagnosis

- ◆ Brain imaging
 - Normal or meningeal features
- ◆ CSF
 - Presence of eosinophils (>10 eos/ml³) - $\leq 30\%$
 - Some eosinophils in 70%
- ◆ Diagnosis
 - + CSF Complement fixations - Ab to C. immitis
 - + CSF cultures for C. immitis

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%)

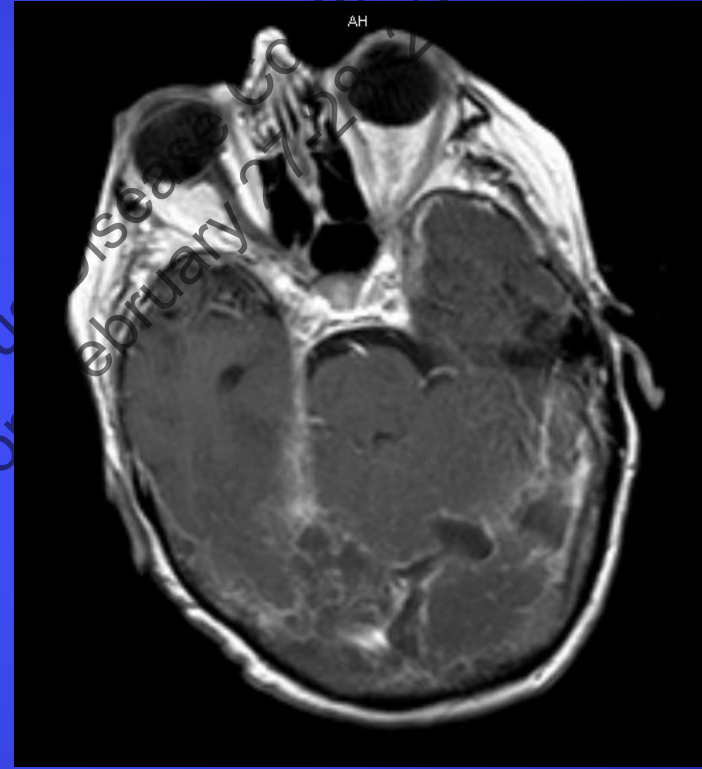
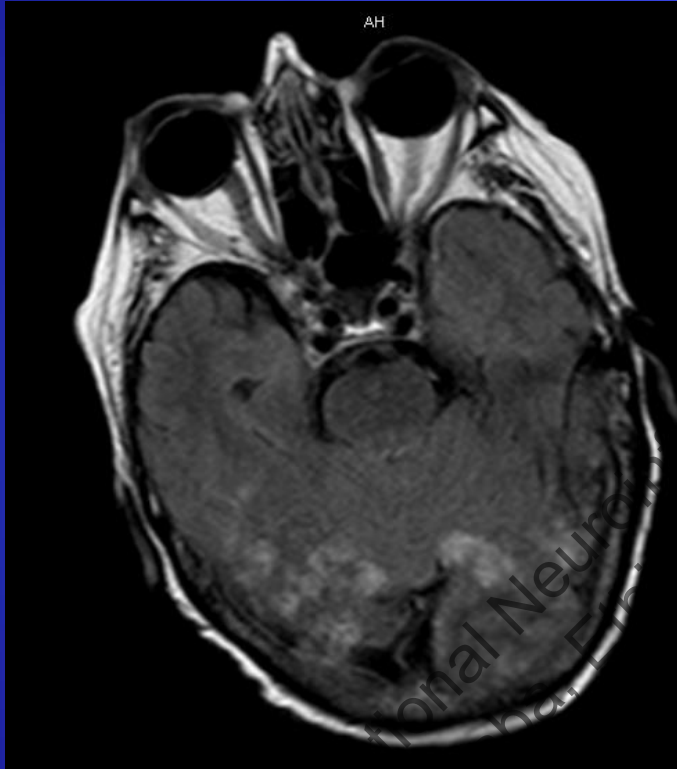
Actinomycosis

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



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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



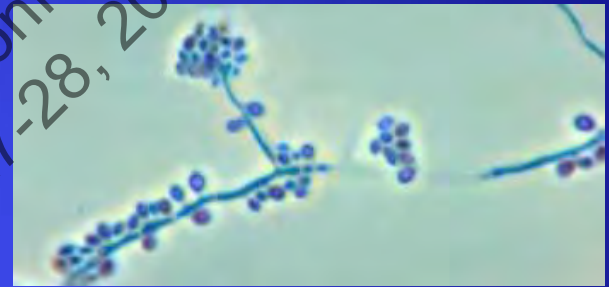
Blastomycosis dermatitidis

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

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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

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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 deferoxamine
- ◆ 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

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Aspergillosis

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

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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)

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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

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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

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"I'd say it's a fungal infection."