

Fungi

Fungal Characteristics and
Human Fungal Pathogens





Fungal Taxonomy

- Domain Eukarya

- Kingdom Fungi

- [True Fungi = Eumycota]

- Phylum Zygomycota

- Phylum Basidiomycota

- Phylum Ascomycota

- Phylum Chytridiomycota

- Phylum Deuteromycota [Imperfect Fungi]

Fungal Taxonomic Names

- Phylum
 - -mycota
- Class
 - -mycetes
- Order
 - -ales
- Family
 - -aceae
- Genus
- Species



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Fungal Characteristics

- Heterotrophs
- Mainly terrestrial
- Lack Chlorophyll
 - Dark Habitats
 - Multidirectional
- Spore bearing
- Thallus body
- Types
 - Mushroom
 - Moulds
 - Aerobic, multicelled
 - Yeast
 - FA, single cell
- Cell wall = chitin, glucan
- Cell membrane = ergosterol
- Nucleus
 - Membrane bound
 - Diploid chromosomes
- Cytoplasm
 - Similar to plants
 - Different ribosomal synthesis
 - Different microtubule protein
- Reproduction
 - Sexually (meiotic)
 - Asexually (mitotic)



Nutritional Status

- Saphrophytes
 - Scavengers, recycle
 - Non living materials
- Parasites
 - Feed off living materials
- Mutualists
 - Symbiotic relationship
 - Primarily seen with plants



Beneficial Uses of Fungi

Yeasts Baking brewing	Antibiotics penicillin cephalosporin	Other Drugs cyclosporin
Steroids hormones (reproductive)	Foods cheeses Blue Roquefort	Experimental metabolic pathways studied



Parasitic Fungi Overview

- Cause Disease Directly
 - Actual fungal growth in organism
- Cause Disease Indirectly
 - Allergic reactions
 - Toxin ingestion
- Exhibit Dimorphism [M→Y shift]
 - Mould form (mycelial, filamentous)
 - Yeast form (or spherule form)
 - Change due to temperature, nutrients, CO₂ levels

Mould and Yeast





Laboratory Methods to Identify

- Direct
 - Id organism in specimen fluid
 - Hyphae: aseptate, septate
 - Spore: conidiospore, arthrospore, sporangiospore
 - Yeast: size, thickness of walls, capsule +/-
- Culture
 - Media such as Sabourouds, BHI, Mycosal
- Tissue
 - Stains: KOH, Eosin, India ink
- Serology
 - CF, IFA
- Fluorescence of fungi under UV light



Immunity

■ Normal

■ Skin

- pH
- FA
- Flora
- turnover

■ Respiratory

- cilia

■ Abnormal

■ Immunocompromised

- Burn
- HIV
- Chronic Disease
- GCC
- Cancers
- DM
- Post surgical
- Splenectomized



Fungal Infection Locations

- Superficial
- Cutaneous
- Subcutaneous
- Systemic
 - Lungs
 - Other organ systems
- Opportunistic

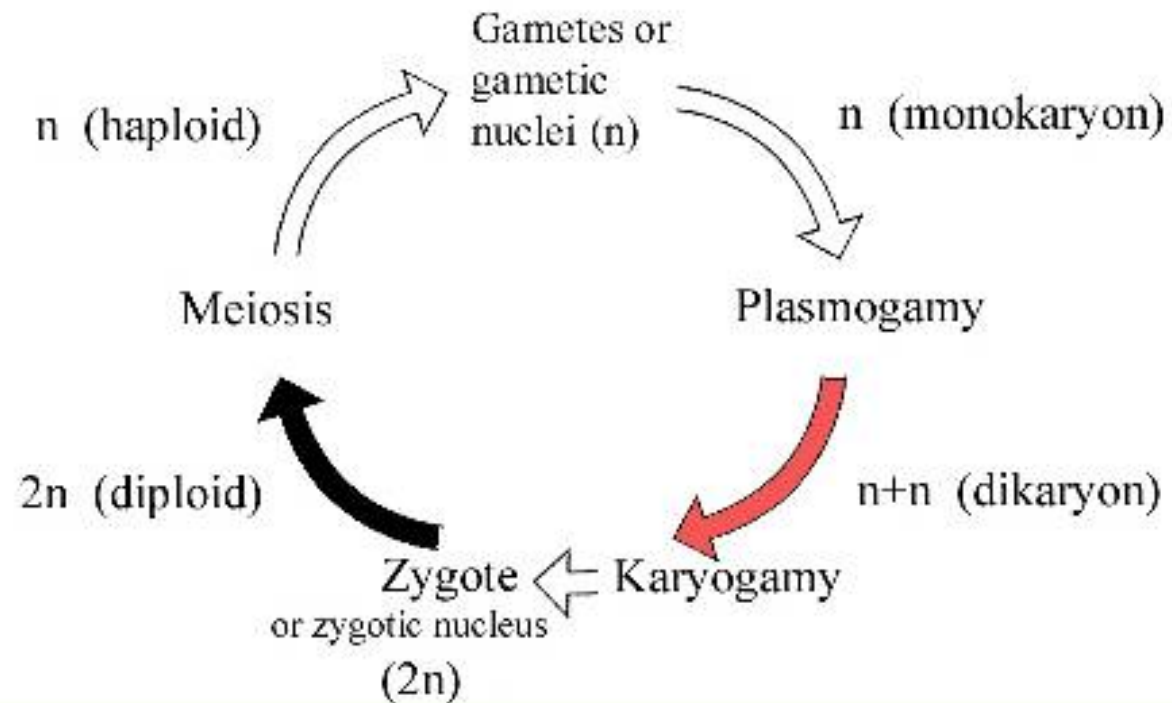


Fungal Mould Reproduction

- Sexual State
 - Meiotic
 - Teleomorph
 - Produce spores (conidia)
- Asexual State
 - Mitotic
 - Anamorph
 - Produce spores (conidia)

Sexual Reproduction of Fungi

Generalized Nuclear Cycle of Fungi





Sexual Reproduction

- Sex organs called gametangia
 - Distinguishable male and female
 - Can bear sex cells (gametes)
 - Can bear sex nuclei (gamete nuclei)
- Homothallic
 - Single mycelium can sexually reproduce
- Heterothallic
 - Two mycelia are required for sexual reproduction



Reproductive Life Cycle

- Growth of hyphae
 - Transverse fissure
- Fragmentation
 - Break off
- Spores
 - Sexual or asexual
 - Disseminate
 - Help in Id of fungus
 - Size, shape, color, number



Sexual Spores

- Zygosporangium

- Zygomycetes

- Sporangium

- Ascospore

- Ascomycetes

- Ascus rupture

- Basidiospore

- Basidiomycetes

- Gill house of basidium, pinches off




Asexual Spores

- Sporangiospores
 - From sac head area called sporangium
 - Rupture to release
 - Zygomycetes
- Conidiospores
 - Free spores, not enclosed in sac
 - Pinched off segments
 - Ascomycetes, Basidiomycetes, Deuteromycetes
 - Types
 - Arthrospores
 - Chlamydospore
 - Blastospore
 - Phialospore
 - Microconidia
 - Macroconidia
 - Porospore

Yeast: *Sacchromyces*





Fungal Yeast Reproduction

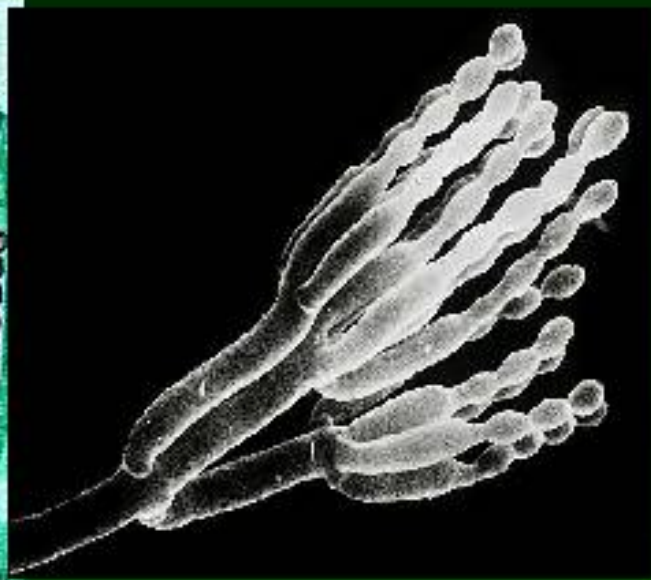
- Diploid Cell (via asexual reproduction)
 - Plentiful food
 - Haploid cells fuse to create diploid
 - Mother cell will bud diploid daughter cells
- Haploid Cell (via sexual reproduction)
 - Starved, Undernourished environment
 - Meiotic division to create 4, $1n$ daughters
 - 4 daughter spores remain inside "mother"
 - Released when favorable environment

Yeast on Sabauroud Agar



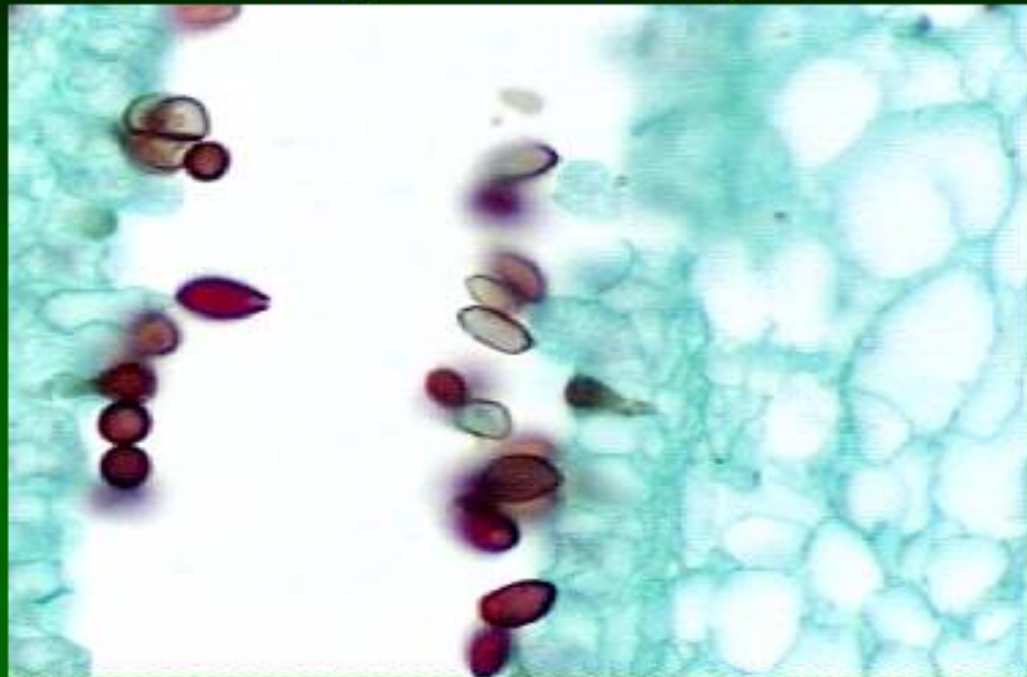
Phyla include most of the yeasts

Ascomycota—sexual spores borne internally in a sac called an ascus-- asexual spores are borne externally as conidia



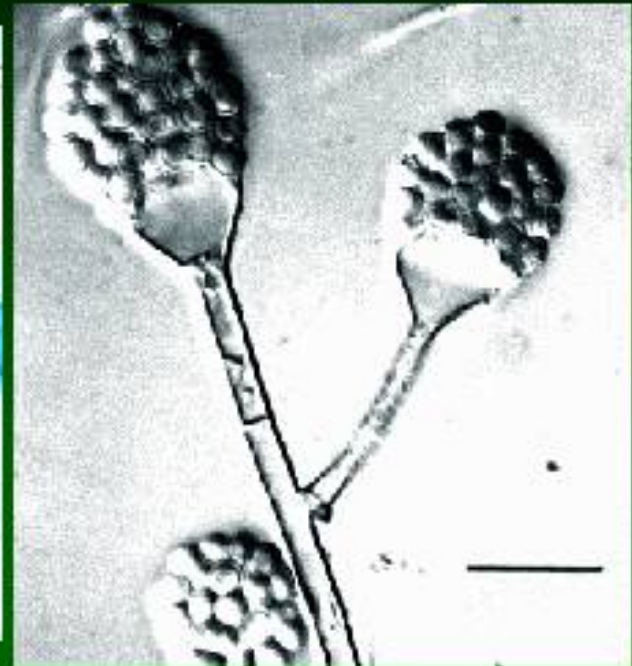
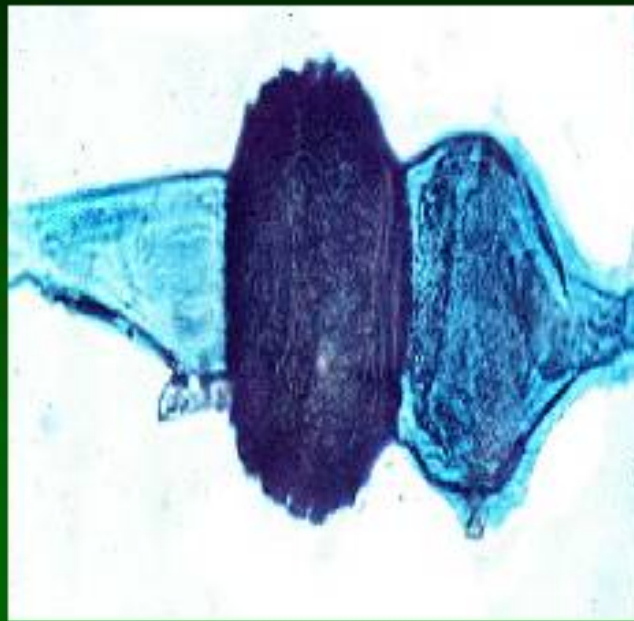
Phyla include mushrooms, puff balls, shelf fungi, rusts, & smuts

Basidiomycota—sexual spores borne externally on a club-shaped structure called a basidium. Usually no asexual spores



Phyla include saprophytic bread moulds and some pathogens

Zygomycota— sexual spores are thick walled resting spores called zygospores -- asexual spores are borne internally in a sporangium



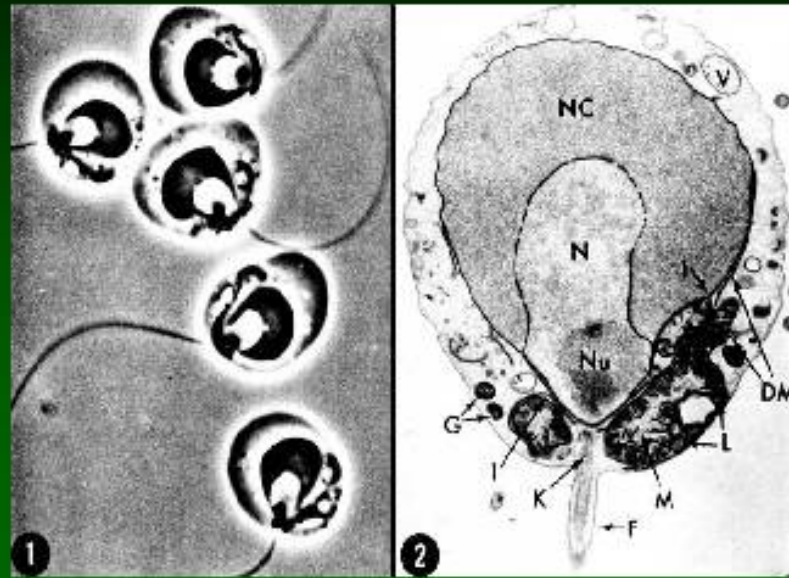
Phyla contain any fungus that has no known sexual repro state

“deuteromycetes” -- no known sexual state, usually reproduces by conidia as asexual state



Fungal Phyla for aquatic, marine

Chytridiomycota — sexual and
asexual spores motile, with posterior flagella



Human Mycoses



Fungal Diseases of the Skin



Sporotrichosis

Sporothrix schenckii

- Dimorphic fungus
- Reservoir: worldwide, tropical
- Transmission: direct soil inoculation
- DX: Special Stains
- TX: Antifungals
- Clinical Course
 - Erythematous
 - Papulonodular
 - ulcerative
 - Lymphocutaneous
 - Joints
 - Osteoarthritis
 - tenosynovitis
 - Pulmonary
 - CNS
 - Disseminated
 - Lymphatic organs
 - GI


Sporothrix yeast phase



Sporothrix infection



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CANDIDIASIS

Candida albicans

- Small yeasts
- Reservoir: soil, food, nosocomial
- Source: Human commensals
- Associated with immunocompromised
- DX: Id organism
- TX: Antifungals
- Candidiasis of MM
 - Oropharynx
 - Vulvovaginal
 - Cutaneous
- Invasive Candidiasis
 - Joints
 - GI: liver, pancreas
 - Urinary
- Miscellaneous
 - Chronic
 - Includes invasive areas
 - CNS
 - Respiratory
 - Neonatal (thrush)

Candidia

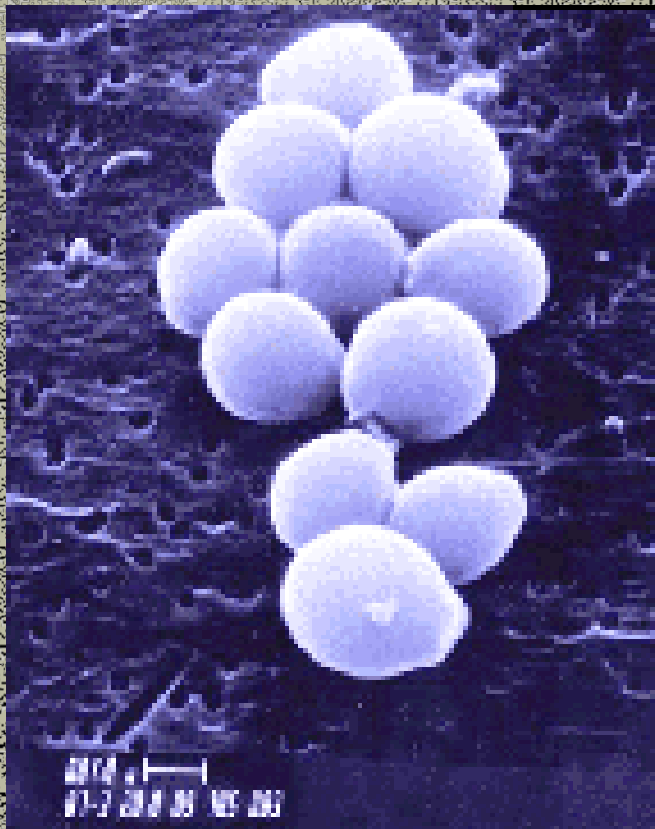
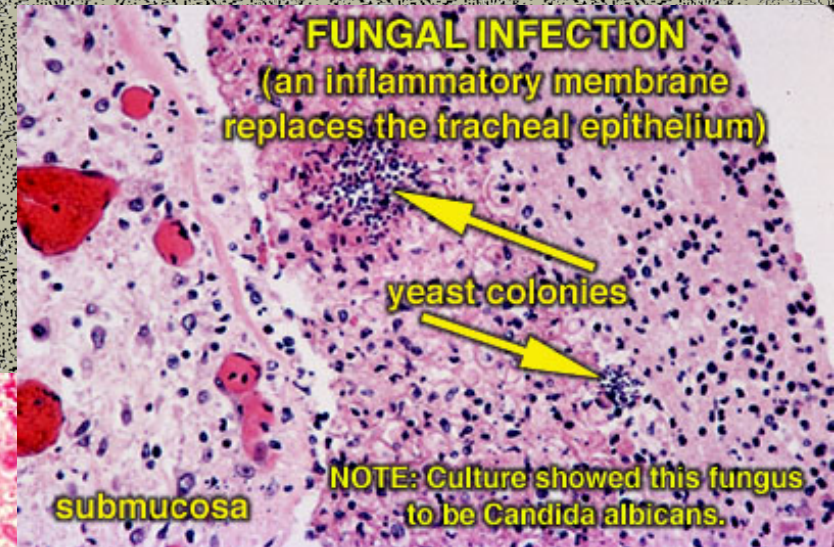
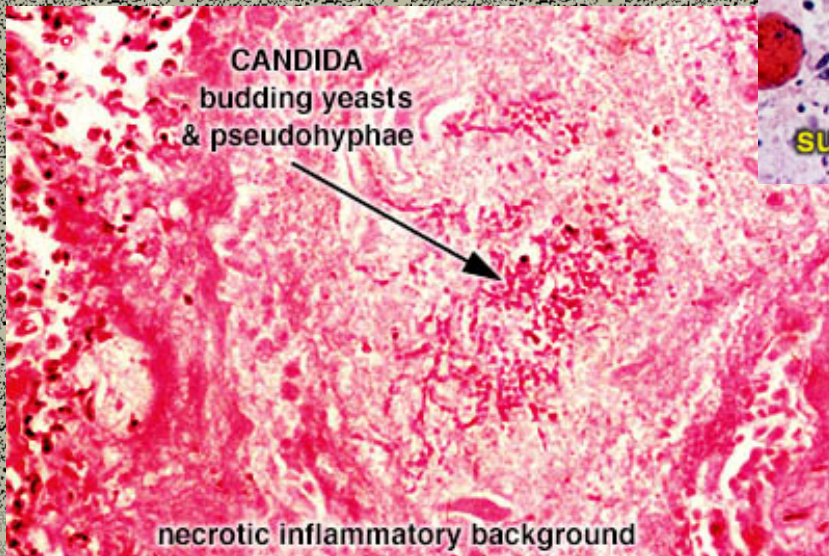


Fig 1

Candidia infections: histology





DERMATOPHYTOSIS

Tinea / Ringworm

- Ubiquitous
- Direct contact
- Colonize keratin layers
- Cause annular lesions with central clearing
- DX: ID organism on selective media or with skin scrapings
- TX: Antifungals
- Tinea capitis
- Tinea corporis
- Tinea cruris
- Tinea pedis
- Tinea unguium
- Tinea favosum

Trichophyton

Microsporum

Epidermophyton

Trichophyton



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Microsporium sp.



Tinea / Ringworm presentation



Image Courtesy of C. Halde
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Trichophyton barbarae

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Human Mycoses

Fungal Infections of the
Nervous System



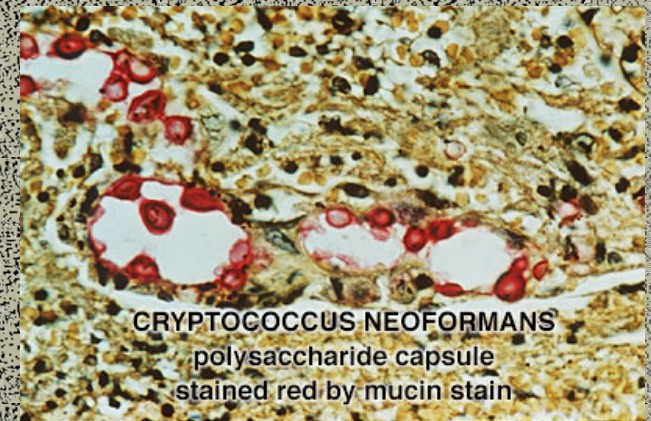
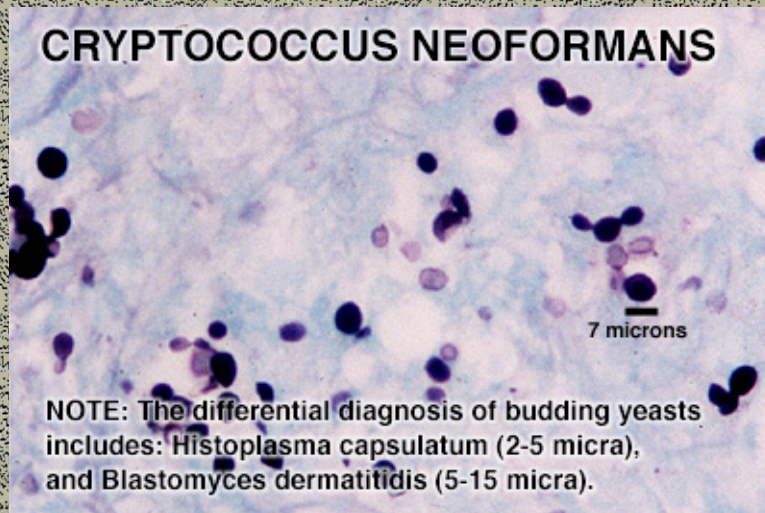


CRYPTOCOCCUS

Cryptococcus neoformans

- Encapsulated
- Worldwide
- Opportunistic
- Inhalation of spores
- Virulence:
 - Enzymes
 - capsule
- DX: Id organism
- TX: Antifungals
- Local in lungs
 - Acute = ARDS
 - Chronic = pneumonia
- Disseminated
 - CNS → meningitis
 - Cutaneous → ulcers
 - GI → inflammation liver, gall bladder, stomach
 - Bone → osteomyelitis
 - Heart → inflammation, all
 - Renal → abscess
 - Eye → inflammation, all

Cryptococcus neoformans infections



Cryptococcus in the brain



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Human Mycoses

Fungal Infections of the
Cardiovascular System





ZYGOMYCOSIS

Rhizomucor, Rhizopus, Absidia

- Zygomycetes group
- Soil, decay
- Opportunistic
- Invades arteries causing embolus
- DX: Autopsy, Culture, Histopath
- TX: Antifungals
- PX: usually fatal
- Rhinocerebral
 - DM
 - Orbital structures
 - Internal Carotid
- Pulmonary
 - Neutropenic
 - dyspnea
 - hemoptysis
- GI
 - Malnutrition
 - Intraabdominal abscess
- Cutaneous
 - Skin trauma, burns
 - Necrotic lesions
- Other areas
 - Bone
 - Heart

Rhizomucor, Rhizopus



Rhizomucor



Rhizopus

Human Mycoses

Fungal Infections of the
Respiratory System

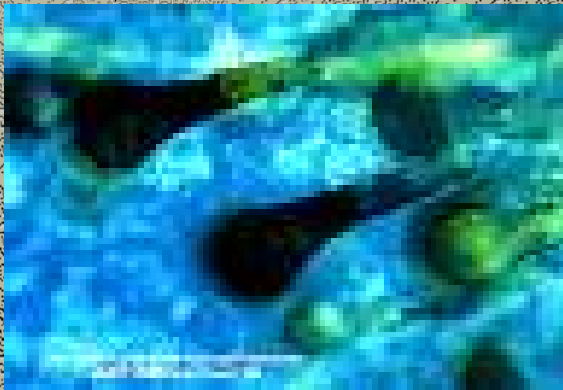


ASPERGILLOSIS

Aspergillus sp.

- Soil, decay
- Inhalation of spores
- Opportunistic
 - Pulmonary Dz
 - Immunocompromised
- DX: Id organism in fluids, culture, histopathology
- TX: Antifungals
- Px: Mortality rate is 50-100%
- Allergic
 - Bronchopulmonary
 - Sinuses and lungs
- Pulmonary
 - Within paranchyma
- Invasive
 - CNS
 - Bone → osteomyelitis
 - Heart → endocarditis
 - Renal → abscess
 - Cutaneous
 - post-op, sx
 - Catheter placement
 - Burn victims
 - Ear

Aspergillosis

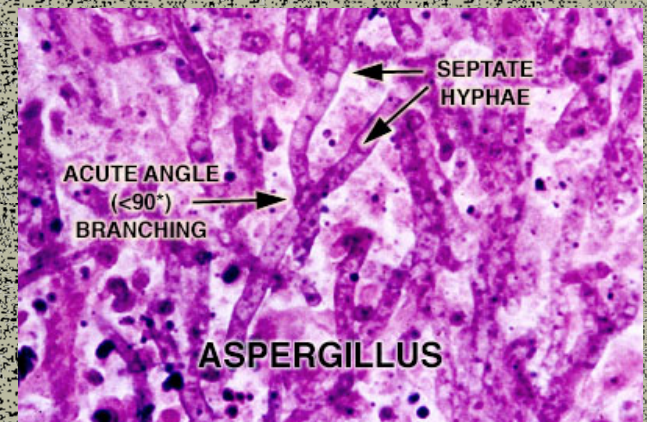
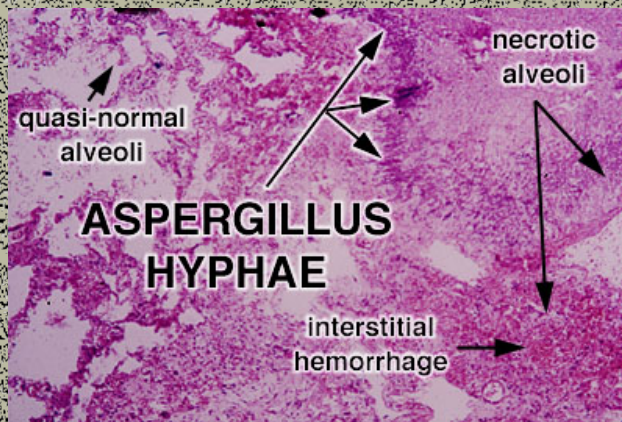
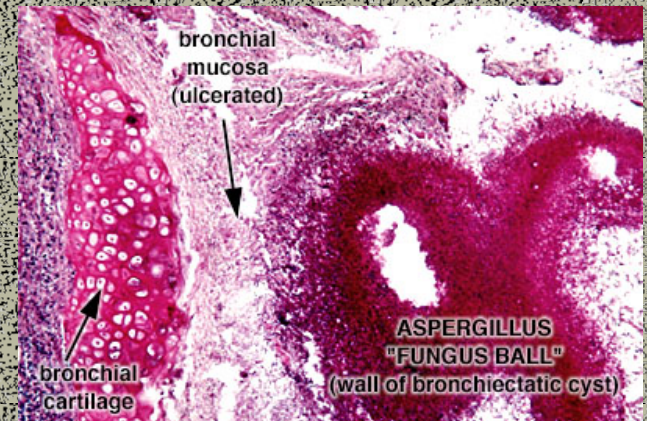



Infections



Culture specimen

Aspergillus histology





Coccidioidomycosis

Coccidioides immitis

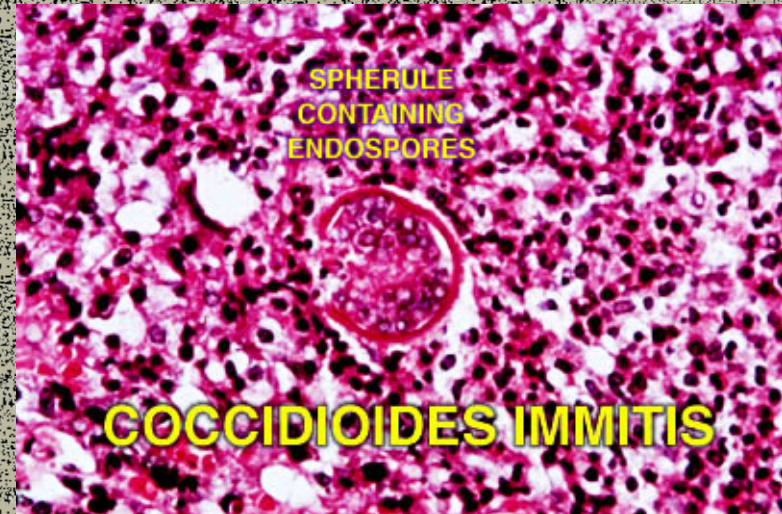
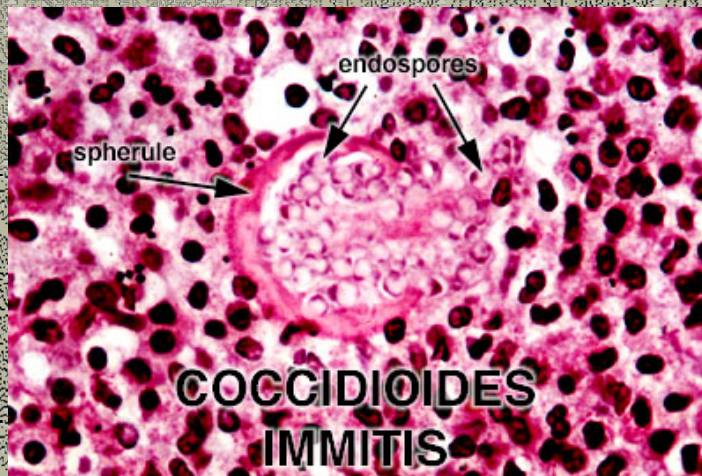
- Dimorphic fungi
- Western hemisphere in arid regions
- Inhalation of spores
- Spores transform to spherules
- DX: CF, RADS, Isolation, Direct ID
- TX: Antifungals
- PX: 90% resolve spontaneously unless immunocompromised
- Asymptomatic
- Acute
 - Respiratory SOB, pain
 - Skin rash
- Chronic
 - Pulmonary Nodules
- Disseminated
 - Skin ulcerative
 - Joints synovitis
 - Meninges hydrocephalus
 - Any other organs
 - Internal linings
 - GI
 - Urogenital
 - Endocrine

Coccidioidomyces



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Coccidioides immitis: Spherules



Coccidioides clinical presentation



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Paracoccidioidomycoses

Paracoccidioides brasiliensis

- South America
- Soil, decayed wood
- Inhalation of blastoconidia
- DX: Id organism in specimens, culture, histopathology
- TX: Antifungals
- PX: good if treated, possibility of relapse
- Asymptomatic
 - Dormant
 - Reappear if immunocompromised
- MM
 - Ulcerations of mouth and oropharynx
- Pulmonary
 - Nodular infiltrates
 - Mimic TB
- Cutaneous
 - Ulcerative
 - Invasive to S.C
- Disseminated
 - GI, liver
 - Bones
 - CNS
 - Male genitourinary tract

Paracoccidioides



KOH

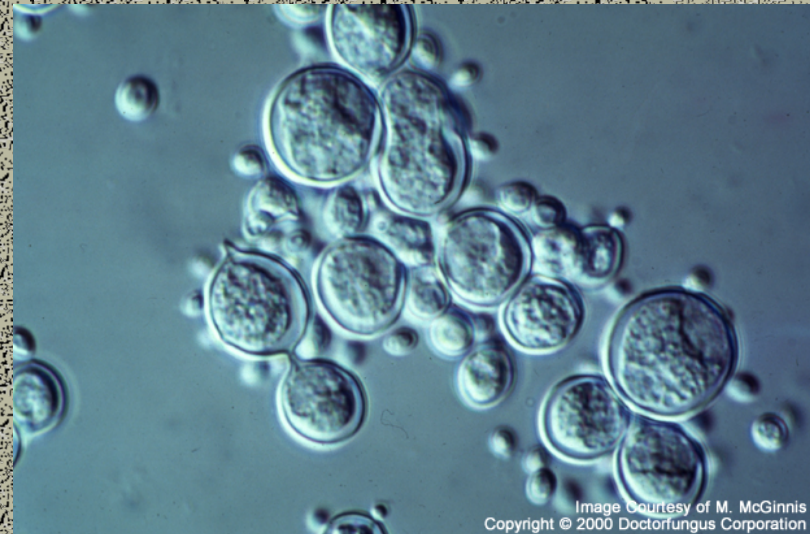


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Microscopic Yeast Phase



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Macroscopic




BLASTOMYCOSES

Blastomyces dermatitidis

- Dimorphic, heterothallic ascomycete
- SC, SE US : Mississippi and Ohio River Valleys
- Source
 - Soil, rotting wood
 - Growth in feces of bats, birds
- Inhalation of conidia
- DX: Direct Id of fluid specimens
Culture Histopathology
- TX: Antifungals
- PX: spontaneous resolution, Tx
CNS Infections
- Asymptomatic
 - 50% of infections
- Acute Pulmonary
 - Mimics bacterial infections
- Chronic Pulmonary
 - Mimics bronchogenic carcinoma
- Disseminated
 - Skin ulcerative
 - Bones, long bones, lytic
 - Genitourinary
 - Male ducts, glands
 - Others
 - CNS
 - Pericardium
 - GI
 - Adrenal Gland

Blastomyces: Yeast Phase





HISTOPLASMOSIS

Histoplasma capsulatum

- Dimorphic fungus
- Soil
- Inhalation of microconidia
- DX: Direct Id of fungi in specimen sample, histopathology, culture
- TX: Antifungals
- PX: most are self limited, Tx if respiratory and disseminated
- Subclinical, benign
- Acute
 - Self limited, flu-like symptoms
 - Pulmonary, pneumonitis, calcification
 - Pericarditis
 - Rheumatological arthritis
- Chronic Pulmonary - TB
- Fibrosing Mediastinitis
 - Fibrous CT in mediastinum
 - Affects surrounding structures
- Disseminated
 - Lymphadenitis
 - Red bone marrow suppression
 - Endocarditis
 - CNS: meningitis, cerebritis
 - GI: ulcers
 - Skin: rash
 - Genitourinary of males
 - Eyes: uveitis, choroiditis

Histoplasmosis

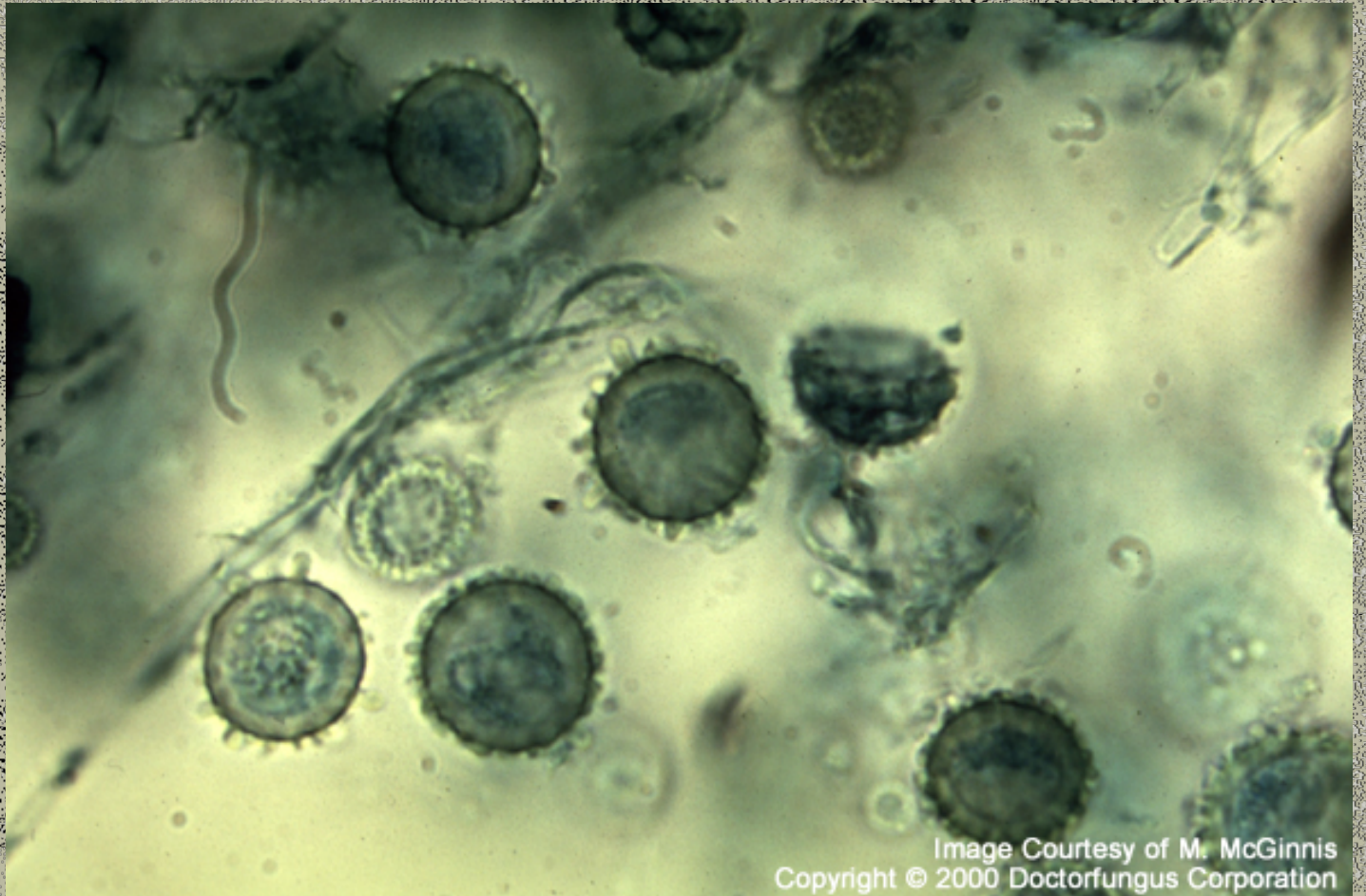
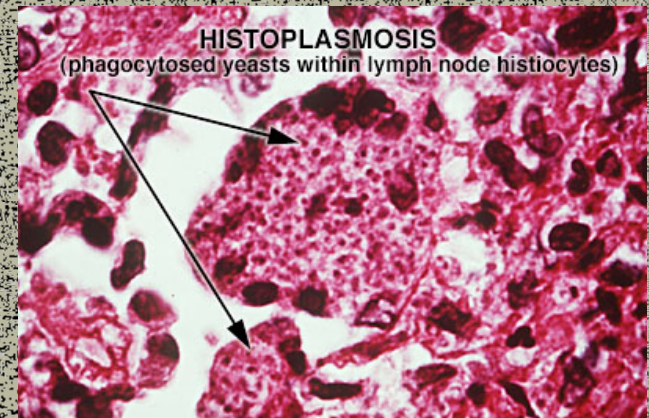
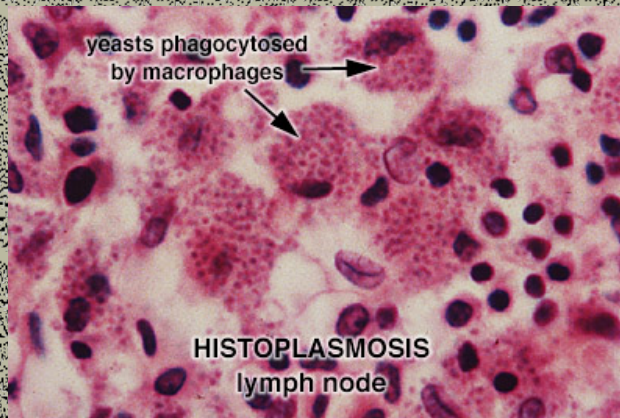
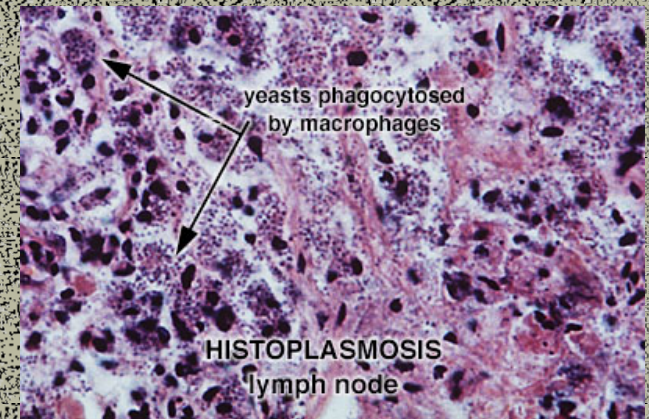
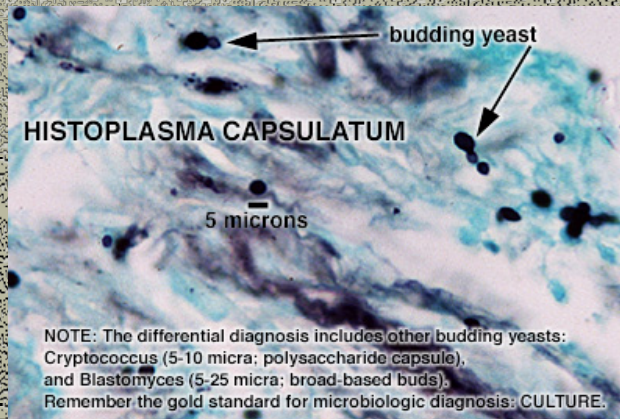


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Histoplasmosis: Disseminated



Histoplasmosis



Culture Id



Cytology



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Clinical Presentation

Human Mycoses



Environmental Moulds



Environmental Exposure

■ Allergic

- Prior Exposure
- Re-exposure
- Respiratory signs
 - Coughing
 - Wheezing
 - Sinus congestion
 - Rhinorrhea
 - Itchy nose
 - Sore throat

■ Mycotoxins

■ Ingestion

■ Ergotism

- *Claviceps*
- Rye products
- Limb gangrene
- Alpha adrenergic blockade

■ Aflatoxins

- *Aspergillus*
- Peanut meal carcinogens

■ Zearalenones

- *Fusarium*
- Estrogen-like steroid
- Precocious puberty

Psychotropic agents



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- Psilocybin
- Psilocin
- Lysergic Acid
Diethylamide

Not all toxins are bad.....

- Penicillium sp.
 - Griseofulvin
 - Antimycotic action
 - Systemic use
 - Disrupts mitotic spindle by binding to microtubule protein





Antifungals

- Macrolides:
 - Bind to ergosterol to disrupt osmotic integrity of plasma membrane
 - Amphotericin B, Nystatin
- Azoles
 - Block ergosterol and chitin synthesis by inhibiting cytochrome P-450 enzymes, causes accumulation of product that replaces ergosterol
 - Topical and/or systemic. Oral, IV, intrathecal, suppository
 - Ketoconazole, Itraconazole, Fluconazole, Clotrimazole, Miconazole
- Allylamines
 - Binds to enzyme involved with ergosterol synthesis, thereby blocking
 - Terbinafine (Lamisil)
- Pyrimidine Analogs
 - RNA incorporation in place of uracil
 - DNA synthesis blockage by enzyme binding
 - Flucytosine → fluracil (RNA) → further metabolites for DNA action
- Miscellaneous
 - Griseofulvin, disrupts mitotic spindle
 - Others with unknown MOA that have antifungal functions
 - Haloprogin, Ciclopirox, Tolnaftate, KI



Fungal Disease Summary

- Zygomycota
 - Rhizopus, Rhizomucor
- Ascomycota
 - Aspergillus, Blastomyces, Histoplasmosis, Dermatophytes, Trichophyton, Microsporium, Epidermophyton
- Deuteromycota
 - Sporothrix, (Para)Coccidioides, Candida
- Basidiomycota
 - Cryptococcus

Questions?



- Would you give an antibiotic to a person with a fungal infection?
- How would you prevent self exposure when working with a patient with a fungal disease?