Infectious Diseases: Fungal Infections

Northeast Regional Medical Center

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Disclosures

• No financial relationships exist with commercial interests
Classification of Fungal Diseases

• Superficial
  – Do not have the ability to invade hair, skin, nails

• Cutaneous
  – Dermatophytes

• Deep
  – Localized subcutaneous (implantation or dermal spread)
  – Dimorphic systemic (hematogenous spread)
  – Opportunistic (immunocompromised patients)
<table>
<thead>
<tr>
<th>Name</th>
<th>Mechanism of Action</th>
<th>Characteristic</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>TRIAZOLEs</strong></td>
<td></td>
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<tr>
<td>Itraconazole</td>
<td>Blocks ergosterol synthesis by inhibiting <strong>14a-demethylase</strong></td>
<td>Fungistatic, lipophilic, needs <strong>acidic</strong> milieu for absorption</td>
</tr>
<tr>
<td></td>
<td></td>
<td>SE: ↑ LFTs, ↓ WBC, ↑ TG, nephrotoxicity, <strong>CHF worsening</strong></td>
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<td></td>
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<td>Tx: dimorphic fungi, aspergillosis, candidiasis, superficial dermatophytes, onychomycosis, sporotrichosis</td>
</tr>
<tr>
<td>Voriconazole</td>
<td><strong>Inhibits cyt p450</strong> (↑ levels of digoxin, cyclosporine, etc.) Category C</td>
<td><strong>SE: visual disturbances</strong></td>
</tr>
<tr>
<td>Fluconazole</td>
<td><strong>Inhibits cyt p450</strong> (↑ levels of digoxin, cyclosporine, etc.) Category C</td>
<td>Fungistatic, crosses blood–brain barrier</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Tx: candidiasis, pityriasis versicolor (PV), cryptococcosis, histoplasmosis, superficial dermatophytes, coccidioidomycosis</td>
</tr>
<tr>
<td>Name</td>
<td>Mechanism of Action</td>
<td>Characteristic</td>
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<tr>
<td><strong>IMIDAZOLES</strong></td>
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<tr>
<td>Ketoconazole</td>
<td>Inhibits <strong>14a-demethylase</strong> Category C</td>
<td>Fungistatic, lipophilic, needs <strong>acidic</strong> milieu for absorption, ↑ absorption with food, <strong>inhibits cytochrome p450</strong> SE: <strong>fulminant hepatitis</strong> (rare), ↑ LFTs (15%), gynecomastia Tx: dermatophytes, candidiasis, dimorphic fungi, PV</td>
</tr>
<tr>
<td><strong>ALLYLAMINES</strong></td>
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</tr>
<tr>
<td>Terbinafine (Lamisil)</td>
<td>Inhibits <strong>squalene epoxidase</strong> (first step of ergosterol synthesis) <strong>Category B</strong></td>
<td><strong>Fungicidal</strong>, biotransformed in liver, <strong>does NOT inhibit cyt p450</strong> SE: nausea, metallic taste, liver damage, <strong>drug-induced LE</strong> Tx: onychomycosis, tinea corporis, tinea pedis</td>
</tr>
<tr>
<td>Name</td>
<td>Mechanism of Action</td>
<td>Characteristic</td>
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<tr>
<td><strong>POLYENES</strong></td>
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</tr>
<tr>
<td><strong>Amphotericin B</strong></td>
<td>Binds ergosterol and forms membrane pores</td>
<td><strong>Category B</strong> SE: acute reaction after infusion (fever, chills, nausea, tachypnea), nephrotoxicity, agranulocytosis, seizures, arrhythmias</td>
</tr>
<tr>
<td><strong>OTHERS</strong></td>
<td></td>
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<tr>
<td><strong>Caspofungin</strong></td>
<td>Inhibits synthesis of glucan (fungal cell wall)</td>
<td>IV administration</td>
</tr>
<tr>
<td></td>
<td>Category C</td>
<td>Tx: candidiasis and aspergillosis</td>
</tr>
<tr>
<td><strong>Griseofulvin</strong></td>
<td>Disrupts microtubule function (metaphase arrest)</td>
<td>Fungistatic, ↑ absorption w/ fatty meal, induces cytochrome p450 (may ↓ warfarin level), resistance seen in <em>T. rubrum</em></td>
</tr>
<tr>
<td></td>
<td>Category C</td>
<td>SE: headache, paresthesia, photosensitivity, drug-induced LE, worsens acute intermittent porphyria</td>
</tr>
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<td></td>
<td></td>
<td>Tx: dermatophytes (NOT yeast or bacteria)</td>
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</tbody>
</table>
Superficial Fungal Infections

- Pityriasis Versicolor
- Tinea nigra
- Black piedra
- White piedra
Pityriasis versicolor

- *Malassezia furfur & M. globosa*, yeast phase of *Pityrosporum orbiculare*
  - Part of normal skin flora
- Hypo or hyperpigmented coalescing scaly macule commonly presents on the trunk/upper arms
  - Decreased pigmentation secondary to the inhibitory effects of dicarboxylic acids on tyrosinase (acids result from metabolism of surface lipids by the yeast)
  - Increased pigment due to PIPA
- Favors oily areas of skin and more common in summer time
- A/w seb derm, AD & neonatal cephalic pustulosis (*M. sympodialis*)
- Dx with KOH- “spaghetti and meat balls”
- Tx with topical or oral antifungals.
  - Terbinafine & griseofulvin ineffective
  - Do not use oral ketoconazole—hepatotoxicity
Tinea Nigra

- *Hortaea werneckii* - a black yeast found in hot humid environments
  - Common in tropics and the gulf coast
- One or several brown/black patches on palms or soles
- Pigment confined to stratum corneum and scrapes off easily
- KOH prep- hyphae appear brown/gold
- Culture to identify organism
- Topical antifungals (clotrimazole, miconazole, ketoconazole) are effective
  - Griseofulvin not effective
Black and White Piedra

- Hyphae, arthrospores and bacteria adhere to each other to form nodules or 'stones' along hair shaft
- Hair breakage may occur
- Black Piedra - *Piedraia hortae* – Firm adherent nodule on the face and scalp
- White Piedra - *Trichosporon ovoides* or *T. inkin* - Soft, less adherent nodules in the axilla & pubic hair
  - Can cause **fungemia**, fever, lung infiltrates, renal failure, purpuro-necrotic skin lesions in immunosuppressed
- Tx: shaving hair
- Oral and topical antifungals
  - Black Piedra
    - Oral & topical terbinafine
  - White Piedra
    - Oral Itraconazole
    - Topical Imidazoles
    - Ciclopirox olamine
    - Selenium sulfide
    - Chlorhexidine solutions
    - Zinc pyrithione
    - Amphotericin B lotion
Dermatophytoses

• Fungal infections caused by three genera of fungi (Dermatophytes)
  – Unique ability to invade and multiply within *keratinized tissue* (hair, skin and nails)
    • *Trichophyton*
    • *Microsporum*
    • *Epidermophyton*
• “Tinea” precedes the Latin name for the involved body site
  – Capitis, faciei, barbae, corporis, cruris, pedis, manuum, unguium
• Scaly annular plaques that spread *centrifugally* from the point of skin invasion
  – Initially circinate and then may become serpiginous
Tinea Coporis

- Any dermatophyte can potentially cause tinea corporis
  - MC: *T. rubrum, T. mentagrophytes*
- Tinea imbricata – *T. concentricum*
- Lesions can also be vesicular, granulomatous or verrucous in appearance

Majocchi's Granuloma

- Usually caused by *T. rubrum*
- Represents a deep dermatophyte folliculitis in which the wall of the follicle is disrupted
- Perifollicular papulopustules or granulomatous
Tinea Cruris

- Inguinal region, upper thighs
  - Occasional extension onto the abdomen and buttocks
  - Scrotum is usually spared (candidiasis if involved)
- MC: *E. floccosum, T. rubrum and T. mentagrophytes*
- Check feet for *T. pedis* or onychomycosis
Tinea Mannum
- Usually **non-inflammatory** and often unilateral
  - There is diffuse **hyperkeratosis** of the **palms** and digits that fails to respond to emollients
- Moccasin-type tinea pedis is often present
  - Share clinical features such as chronicity and hyperkeratosis
  - “**Two feet and one hand syndrome**” = dermatophytid (id) reaction
- Other presentations include exfoliative, vesicular and papular variants

Tinea Pedis
- Soles and interdigital web spaces
- MC: *T. rubrum*, *T. mentagrophytes*, *E. floccosum*
- Four major clinical types of tinea pedis
  - Moccasin, interdigital, inflammatory, and ulcerative
Tinea Capitis

- Common in **children**
  - Predilection for African descent
- MC: *T. tonsurans* >> *M. canis*
- Alopecia with or without scale is the most common presentation
  - Discrete patches or involve the entire scalp
  - “Comma,” “corkscrew,” and dystrophic broken hairs
  - Posterior cervical and posterior auricular lymphadenopathy
  - Alopecia is reversible with treatment
Kerion
• Boggy, purulent plaques with abscess formation and associated alopecia
• Variant of endothrix
• Can result in permanent scarring

Favus
• MC: *T. schoenleinii, T. violaceum, M. gypseum*
• Thick, yellow crusts composed of hyphae and skin debris (“scutula”)
Diagnosis

- **KOH** (potassium hydroxide)
- **Culture**
  - **Sabouraud Dextrose Agar (SDA)**: gold standard
  - **Modified SDA** (Mycosel or Mycobiotic): SDA + cycloheximide + chloramphenicol
- **DTM** (dermatophyte test media)
  - Peptones, dextrose, cycloheximide, phenol red, chlortetracycline, and gentamicin
  - Dermatophytes turn media from **amber to red color** due to alkaline by-products
  - Non-dermatophytes cause media to turn yellow (or stay amber-colored)
- **H&E**
  - **Gomori methenamine silver (GMS)**: outlines fungal elements black
  - **Periodic acid-Schiff (PAS)**: outlines fungal elements magenta with green background
  - **Fontana-Masson**: stains dematiaceous fungi
Treatment

• Uncomplicated tinea corporis, cruris, pedis
  – Topical antifungals 1-2x/day 2-4 weeks
    • i.e., ketoconazole, econazole, terbinafine
  – Extensive -> oral medication
    • Terbinafine 250 mg/day x 1 wk, fluconazole 150-200 mg/wk x 2-4 wk, itraconazole
      – Baseline LFTs for terbinafine
      – Fluconazole contraindicated with coadministration of drugs that cause QT prolongation
      – Itraconazole contraindicated with congestive heart failure

• Tinea capitis, kerion, majocchi’s granuloma
  – Need oral medication due to involvement of the hair follicle
    • Children: Griseofulvin 20–25 mg/kg/day (microsize suspension) × 6–8 weeks, terbinafine
      – Both are considered very safe
    • Treat until negative fungal culture

• Zeasorb AF powder can be used for prevention
  – Feet and body folds
4 Types of Onychomycosis

1. Distal Subungual Onychomycosis
   - *T. rubrum* is most common cause
   - Begins distally, involves nail bed, nail plate, and hyponychium

2. White Superficial Onychomycosis (WSO)
   - *T. mentagrophytes* is most common cause
   - Organisms invade surface of toenail plate
   - *T. rubrum* is more common in *HIV positive* patients

3. Proximal White Subungual Onychomycosis
   - *T. rubrum* is most common cause
   - Organisms enter the cuticle; leukonychia in the proximal nail plate near lunula
   - May be a sign of *HIV infection*

4. Candida onychomycosis
   - Destruction of nail and massive nailbed hyperkeratosis
   - Usually in patients with mucocutaneous candidiasis
Onychomycosis Diagnosis

• No single method gives 100% accurate results
• KOH of clippings or curettings of subungual debris
  – Chlorazol black E can be added to improve sensitivity
• Histopathologic examination with PAS stain
• Culture
  – Sabouraud agar with chloramphenicol & cycloheximide (mycosel) agar
    • Slow, but identifies genus and species
  – DTM
Onychomycosis Treatment

• Many patients do not seek treatment
  – Patients with diabetes or peripheral neuropathy should be treated
• Topical treatment ciclopirox nail laquers: modestly effective
  – Thymol in EtOH
  – Efinaconazole (Jublia, 14 alpha demethylase inhibitor) or Tavaborole (Kerydin, inhibits aminoacyl-tRNA synthetase) daily for 48 weeks
• Oral therapy: better cure rate, especially if all nails involved
  – Terbinafine
    • 250mg/day for 6-8 weeks (fingernails) and 12-16 weeks (toenails)
    • Monitor liver function
    • Potential for SCLE development
  – Itraconazole
    • Pulsing is recommended
    • Associated with CHF and drug interactions (strong CYP3A4 inhibitor)
Candidiasis

- **C. albicans**
  - Common inhabitant of GI, GU, and skin
  - Oral (Thrush)
    - Affects Newborns, children
      - May be the first manifestation of AIDS
    - **Side effect of Secukinumab and Ixekizumab**
      - Metallic taste
  - Perleche (angular cheilitis)
    - May be due to ill-fitting dentures or from exaggerated skin folds
    - Riboflavin/nutritional deficiencies
  - Intertrigo
  - Chronic paronychia
    - Associated with exposure to moisture/irritants
  - Diaper dermatitis
    - Erythematous patches in groin, satellite lesions, and maceration
Candida Diagnosis

- KOH prep
  - Spores and **pseudohyphae** under microscope
- Gram stain
  - Dense, gram positive ovoid bodies
- Histopathology
  - Budding yeast and pseudohyphae in stratum corneum
  - PAS staining beneficial
  - Pseudohyphae **vertically** oriented
  - Neutrophils in stratum corneum
  - Hyperkeratosis and crusting
- Culture on sabouraud glucose agar
Candidiasis Treatment

• Terbinafine not effective

• Oral Thrush
  – Nystatin suspension
  – Clotrimazole troches
  – Fluconazole

• Perleche
  – Anticandidal creams
  – Barrier creams/ointments
  – Properly fit dentures
  – Fillers

• Intertrigo
  – Topical antifungals
    • May combine with mild topical steroid for short duration
  – Iodoquinol and hydrocortisone

• Chronic paronychia
  – Topical anticandidals
    • +/- topical steroids
  – Oral fluconazole if refractory
  – Avoid moisture and irritants

• Diaper dermatitis
  – Topical anticandidal agents
    • Clotrimazole, econazole, ketoconazole, miconazole, oxiconazole, naftifine, nystatin
  – Compounding with zinc oxide ointment for barrier
  – If recurrent, consider oral nystatin
Sporotrichosis

- *Sporothrix schenckii*
- Direct inoculation by thorn/splinter
  - Gardeners, florists, farmer
- 3 different forms
  - Lymphocutaneous-MC
    - Subcutaneous nodule, + ulceration, with ascending lymphatic spread
  - Fixed cutaneous- 20%
    - Single subcutaneous nodule, + ulceration, no lymphatic spread
  - Disseminated- rare
    - Involves bones, joints, meninges, pulmonary, genitourinary tract
- Sporotrichoid spread “CAT N SPLAT”
  - Cat scratch
  - Anthrax
  - Tuberculosis
  - Nocardia
  - Sporotrichosis
  - Leishmaniasis
  - Atypical mycobacteria
  - Tularemia
Sporotrichosis

- **Histology**
  - Palisading granuloma
  - Cigar shaped yeast in tissue (rarely seen)
  - Stellate abscess (CLATS)
    - Cat scratch
    - Lymphogranuloma venereum
    - Atypical mycobacterium
    - Tularemia
    - Sporotrichosis
  - **Asteroid bodies**
    - Yeast cell with surrounding eosinophilic fringe (represents reaction between host and fungus)—“Splendore-Hoepli” phenomenon (MN BASS)
      - M-ycetoma
      - N-ocardia
      - B-otryomycosis
      - A-ctinomycosis
      - S-porotrichosis
      - S-arcoidosis
- **Treatment**
  - Itraconazole, terbinafine, potassium iodide
Chromoblastomycosis (Chromomycosis)

- Caused by
  - Compact—*Fonsecaea compacta*
  - Dead—*Cladosporium carrionii*
  - Wet—*Rhinocladiella aquaspersa*
  - Warty—*Phialophora verrucosa*
  - Feet—*Fonsecaea (Phialophora) pedrosi - MC*

- Affects the lower extremities

- Due to direct inoculation of organism from penetrating trauma
  - Farmers account for 75% of cases

- Begin as small, pink, scaly papule → verrucous plaques or nodules, with scarring
  - Slowly progressive
  - Risk of squamous cell carcinoma in long standing lesions
Chromoblastomycosis

- **Histologically**
  - Pseudopeitheliomatosus hyperplasia with intraepidermal pustule
    - **Here**—halogeneoderma
    - **Come**—chromoblastomycosis
    - **Big**—blastomycosis
    - **Green**—granuloma inguinale
    - **Leafy**—leishmaniasis
    - **Vegetables**—pemphigus vegetans
  - Dermal granulomatous reaction
  - **Sclerotic bodies (medlar bodies, copper pennies)**
    - Fungi in clusters- brown thick walled cells

- **Treatment- difficult**
  - Small lesions- excision, cryotherapy
  - Extensive lesions- itraconazole 200-400mg/day x 6-12 months
  - Terbinafine, cryotherapy, CO2, PDT, Amphotericin/itraconazole combination
Mycetoma (Madura Foot, Maduromycosis)

- Chronic, granulomatous, subcutaneous inflammatory disease
- Found in soil and plants
  - Increased prevalence in Mexico, Central/South America, India, and Africa
- Etiology
  - Actinomycetoma = filamentous bacteria
    - *Nocardia, Actinomadura, and Streptomyces*
  - Eumycetoma = true fungi
    - *Madurella grisea, M. Mycetomatis, Leptoshaeria senegalensis, Exophilai jeanselmei, Phialophor verrucosa, C geniculate, Pseduallescheria boydii, A. Recifei, Fusarium monoliform, Nocardia asteroides, Actinomadura madurae*
- Organisms enter by traumatic inoculation - commonly foot
- Triad- tumefaction, sinuses, draining grains
- Instep or toe webs
  - Painless, nontender, firm nodule(s)
  - Underlying fascia/bone may become involved
Mycetoma

- **Histology**
  - Actinomycetoma
    - Sinus tracts with neutrophils (resembles stellate abscesses)
    - Grains with suppurative foci
    - Grains made of filamentous bacteria
    - Smooth *splendore-hoepli phenomenon* at periphery
  - Eumycetoma
    - Grains are composed of fungal hyphae

- **Radiographs will show bone involvement**
  - MRI may show “dot in a circle” sign = grains

- **Treatment**
  - Actinomycetoma
    - Actinomyces - penicillin
    - Nocardia - sulfonamide
    - Rifampicin/cotrimoxazole, or imipenem
  - Eumycetoma - more resistant
    - Surgical removal, voriconazole, itraconazole
## Colors of Grains and Geographic Distribution of Eumycotic and Actinomycotic Mycetomas

<table>
<thead>
<tr>
<th>Pathogen</th>
<th>Grain color</th>
<th>Geographic distribution</th>
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</thead>
<tbody>
<tr>
<td><strong>Eumycotic</strong></td>
<td></td>
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<tr>
<td><em>Madurella mycetomatis</em></td>
<td>Black</td>
<td>North, Central and South America; Caribbean, Africa, Europe, Middle East, Asia</td>
</tr>
<tr>
<td><em>Madurella grisea</em></td>
<td>Black</td>
<td>North, Central and South America; Africa, Asia</td>
</tr>
<tr>
<td><em>Leptosphaeria senegalensis</em></td>
<td>Black</td>
<td>Africa, Asia</td>
</tr>
<tr>
<td><em>Pseudallescheria boydii</em></td>
<td>White</td>
<td>North, Central and South America; Africa, Oceania, Asia, Europe</td>
</tr>
<tr>
<td><em>Acremonium</em> spp.</td>
<td>White</td>
<td>North, Central and South America; Asia, Europe, Oceania</td>
</tr>
<tr>
<td><strong>Actinomycotic</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td><em>Nocardia brasiliensis</em> †</td>
<td>White</td>
<td>Worldwide (all <em>Nocardia</em> spp.)</td>
</tr>
<tr>
<td><em>Nocardia asteroides</em> ‡</td>
<td>White</td>
<td></td>
</tr>
<tr>
<td><em>Nocardia caviae</em></td>
<td>Yellow–white</td>
<td></td>
</tr>
<tr>
<td><em>Actinomyces israelii</em> $</td>
<td>Yellow–white</td>
<td>Worldwide</td>
</tr>
<tr>
<td><em>Actinomadura madurae</em></td>
<td>Pink or white</td>
<td>Worldwide</td>
</tr>
<tr>
<td><em>Actinomadura pelletieri</em></td>
<td>Red</td>
<td>North and South America, Africa, India</td>
</tr>
<tr>
<td><em>Streptomyces somaliensis</em></td>
<td>Brown or yellow</td>
<td>Africa (arid regions)</td>
</tr>
</tbody>
</table>
Keloidal Blastomycosis
(Lobomycosis, Lacaziosis)

- *Lacazia loboi*
- Central/South America - acquired from water, soil, vegetation
  - Associated with dolphins
- Ears, face, upper extremities
- Painless, smooth surface nodules
  - Keloid like lesions
  - Increase in size with invasion of surrounding skin or lymphatics
Keloidal Blastomycosis (Lobomycosis, Lacaziosis)

• Histology
  – Organisms are thick walled, refractile, spherules
  – Attached to one another with narrow connections- “brass knuckles” or “chain of coins” “pop beads”

• TX
  – Surgical excision treatment of choice
  – Itraconazole 100mg/day, clofazimine 100mg/day
  – Combination therapy with excision and itraconazole or cryotherapy
Blastomycosis (Gilchrist Disease)

- *Blastomyces dermatitidis*
- Epidemiology:
  - Endemic to North America *(Mississippi/Ohio river valleys/Great Lakes)*
  - Found mainly in soil
- Pathogenesis:
  - Inhalation of organisms
- Histology:
  - Broad-based bud
  - Thick double-contoured wall
  - Pseudo epitheliomatous hyperplasia with intraepidermal pustules
    - Here Come Big Green Leafy Vegetables
Blastomycosis

• Clinical Variants
  – Primary pulmonary Infection:
    • Typically asymptomatic/self limited, can mimic TB or pneumonia
    • 80% cases with dissemination to skin
  – Cutaneous Infection:
    • Typically after pulmonary infection
    • Variable presentation; papulopustules, well-demarcated verrucous plaques with crusting and pustules especially at border
    • +/- central ulceration, healing begins centrally and heals with cribriform scarring

• Treatment: oral antifungal
  – Severe or progressive: Amphotericin B
  – Mild-Mod: Itraconazole, Ketoconazole, Fluconazole
Histoplasmosis

- Darling’s disease, Cave disease, Ohio valley disease,
- *Histoplasma capsulatum*
- Found in soil, frequently in bat/bird feces
  - Transmission via inhalation of airborne spores
- Southeastern or central US
- Clinical:
  - Immunocompetent: asymptomatic primary pulmonary infection with rare skin findings
  - Immunocompromised (HIV): umbilicated papules, nodules, +/- ulceration (oral ulcers common)
    - Molluscum like lesions (CCHIP)- coccidiodomycosis, cryptococcosis, histoplasmosis, penicilliosis
- Histology:
  - Lacks a true capsule- surrounded by pseudocapsule
  - Organisms within histiocyte
    - P—enicillium marneffei
    - H—histoplasmosis
    - G—ranuloma inguinale
    - R—hinoscleroma
    - L—eishmanaisis
- Treatment: spontaneous healing/itraconazole, amphotericin B
Coccidiodomycosis

- Valley fever, desert rheumatism, San Joaquin valley fever, California disease
- *Coccidioides immitis* – thought to be most virulent of all fungi
- Found in soil of Southwestern US
  - Arthroconidia inhaled via dust particles
- Clinical:
  - Pulmonary: MC
    - Flu-like symptoms, hilar adenopathy, pulmonary infiltrate, erythema nodosum (favorable prognostic sign)
  - Disseminated:
    - < 1% cases; targets joints, viscera, brain, skin
  - Cutaneous:
    - Very rare, due to inoculation; indurated nodule → ulcerate with sporotrichoid pattern
- Histology:
  - Spherules with double refractile, thick walls loaded with endospores
- Treatment:
  - (+) Meningitis: Fluconazole or Amphotericin B
  - (-) Meningitis: Itraconazole, Ketoconazole, Voriconazole
Paracoccidioidomycosis

- South American Blastomycosis, Brazilian Blastomycosis
- *Paracoccidioides brasiliensis*
- Endemic to Central and South America
  - Infection via inhalation
- Clinical:
  - Primary Pulmonary Infection:
    - Resembles pneumonia, +/- dissemination to skin and other organs
  - Cutaneous Infection:
    - Slow-growing painful verrucous or ulcerative nodules typically around mouth with painful oral and nasal mucosal ulcerations
- Histology:
  - Pseudoepitheliomatous hyperplasia
  - Large round organism with multiple narrow-based buds radiating outward *(mariner’s wheel)*
  - Lacks thick refractile wall and eccentric nucleus (seen in blastomycosis)
- Treatment:
  - Preferred treatment: Itraconazole
  - Others: Amphotericin B, systemic azoles and sulfonamides
Cryptococcosis

- *Cryptococcus neoformans*
- Found in *pigeon droppings*, soil, and dust
  - Transmission via inhalation
- Clinical:
  - Begins as localized pulmonary infection (90%):
    - Immunocompetent: asymptomatic or mild infection
    - Immunocompromised:
      - Disseminated disease-poly morphous (molluscum-like umbilicated papules)
  - 10% hematogenously disseminate to organs (CNS/Skin)
- Histology:
  - Encapsulated yeast - stains w/ mucicarmine, PAS, alcian blue
  - India ink stains yeast (capsule appears are clear halo)
- Treatment:
  - Amphotericin B + 5-fluorocytosine
Aspergillosis

- Invasive fungal infection by non pigmented mold
- *Aspergillus flavus* (MC primary cutaneous pathogen), *A. fumigatus, A. niger*
- Ubiquitous in nature (soil, decaying vegetation, dust, leaves)
  - Risk factors for invasive aspergillosis: neutropenia, bone marrow transplantation, age
- Pathogenesis:
  - Direct inoculation of the skin or hematogenous spread
- Typical portals of entry: IV catheters, burns, trauma, surgical wounds
- Primary cutaneous aspergillosis: erythematous macules → necrotic papules, hemorrhagic bullae, ulcers
  - May have pulmonary disease and disseminated disease w/hematogenous spread
- Histology:
  - *Dichotomous branching at 45-60°*, often involving blood vessels
- Treatment:
  - Invasive Aspergillosis: Voriconazole, TOC
  - Amphotericin B, Itraconazole
Mucormycosis (Zygomycosis)

- Found in nature (soil, fruits, decaying vegetation)
  - Transmission typically via inhalation
- Risk factors: neutropenia, diabetes mellitus, metabolic acidosis, severe burns, immunosuppression
- Histology:
  - Large ribbon-like hyphae with 90° branching (wider than Aspergillus)
  - Ring-shaped on cross section
  - Tend to invade blood vessels and form thrombi
- Clinical:
  - Rhinocerebral
    - Diabetic patients with sinus infection under poor control → dissemination/rapid contiguous spread → indurated necrotic plaque, facial edema, orbital cellulitis, bloody nasal discharge and cavernous sinus thrombosis
  - Local cutaneous- secondary infection following burn
- Treatment:
  - Amphotericin B and debridement
References