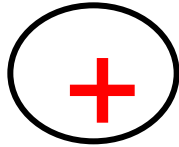


# Fungi as infectious agents

- molds & yeasts are widely distributed in air, dust, fomites & normal flora
- humans are relatively resistant
- fungi are relatively nonpathogenic
- of the 100,000 fungal species, only 300 have been linked to disease in animals
- fungi are the most common plant pathogens
- human mycoses are caused by true pathogens and opportunistic pathogens

# Our ambiguous relationship with fungi

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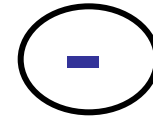


Mushroom cultivation

Antibiotics

Food processing

Transplantation



Mycosis

Mycotoxins

Food spoilage

# Transplantation

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not possible without

Cyclosporin A

Tolypocladium inflatum

Tacrolimus

Streptomyces tsukubaensis

# Fungi as infectious agents

- molds & yeasts are widely distributed in air, dust, fomites & normal flora
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# Examples of Fungal Allergies & Mycotoxicoses

1. asthma, often occurring in seasonal episodes
2. farmer's lung, a chronic & sometimes fatal allergy of agricultural workers exposed to moldy grasses
3. teapicker's lung
4. bagassosis, a condition caused by inhaling moldy dust from processed sugarcane debris
5. bark stripper's disease caused by inhaling spores from logs

# *Candida Albicans infections*

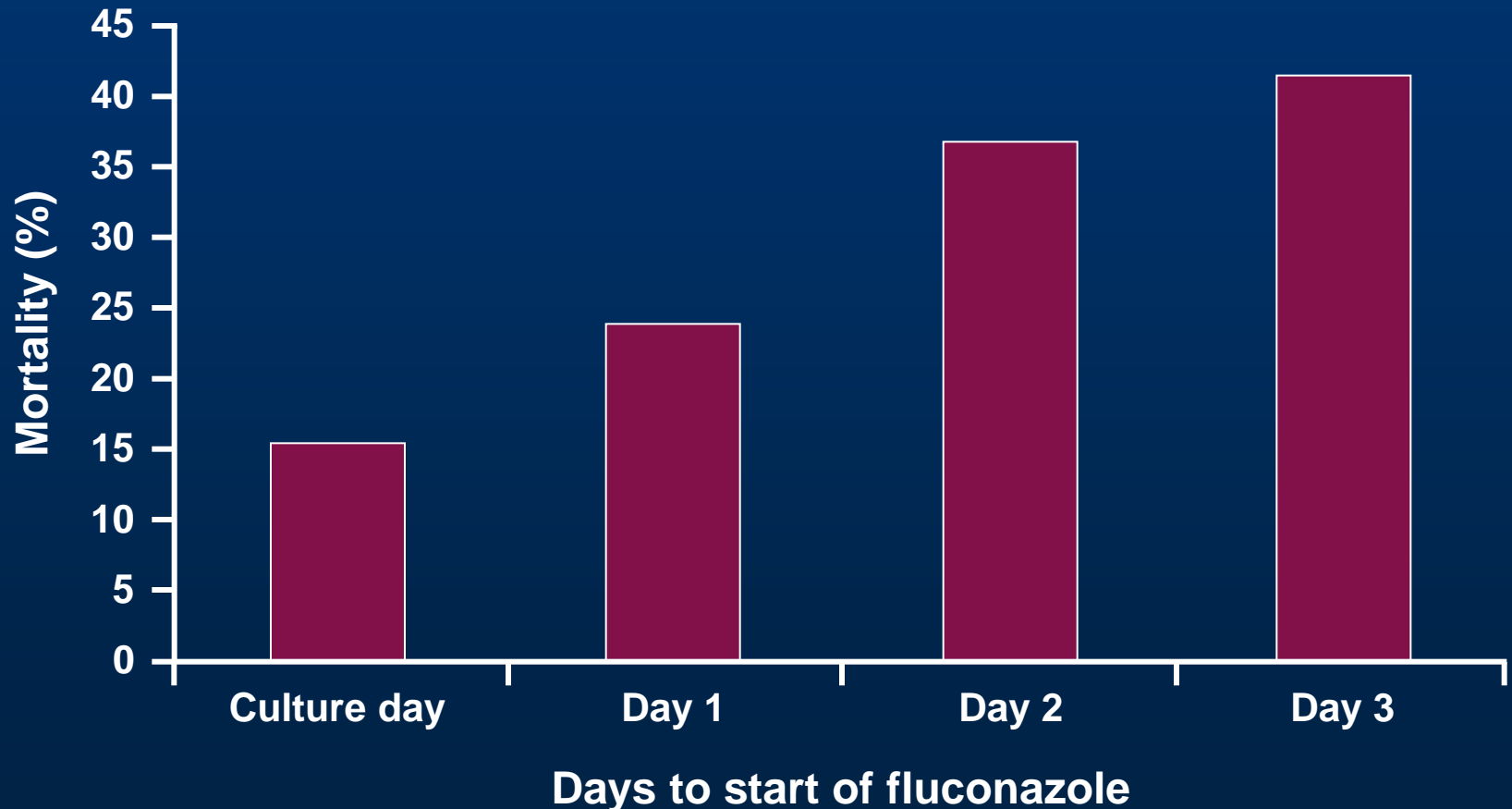
- **Thrush** – occurs as a thick, white, adherent growth on the mucous membranes of mouth & throat
- **Vulvovaginal yeast infection** – painful inflammatory condition of the female genital region that causes ulceration & whitish discharge
- **Cutaneous candidiasis** – occurs in chronically moist areas of skin and burn patients

# Candidaemia in a London teaching hospital

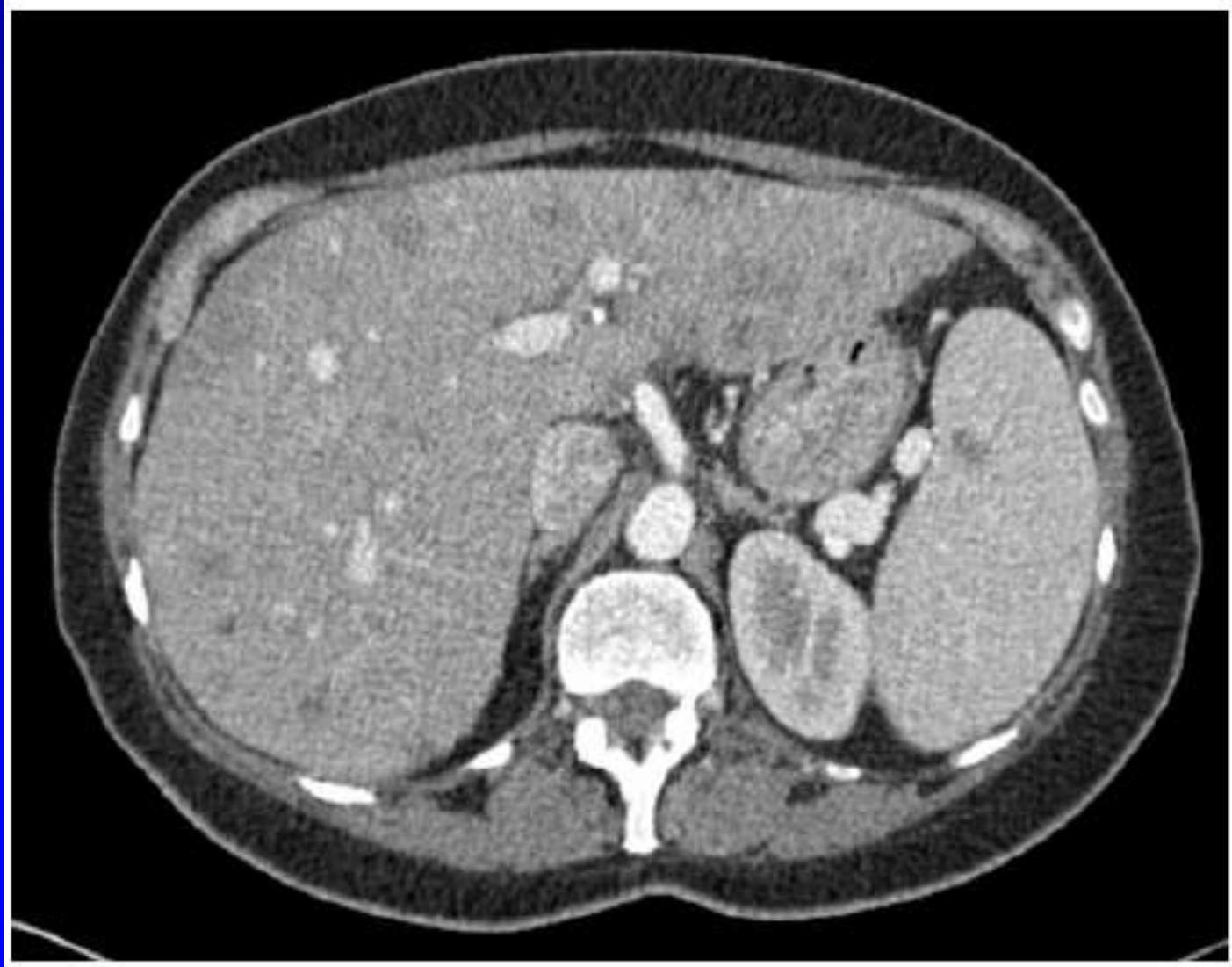
Sources:	IV-lines	77 %
	Urinary tract	7 %
	Gastrointestinal tract	7 %
Serious complications		6 %
Species:	<i>C. albicans</i>	64 %
	<i>C. glabrata</i>	20 %
	<i>C. tropicalis</i>	9 %
	<i>C. parapsilosis</i>	5 %

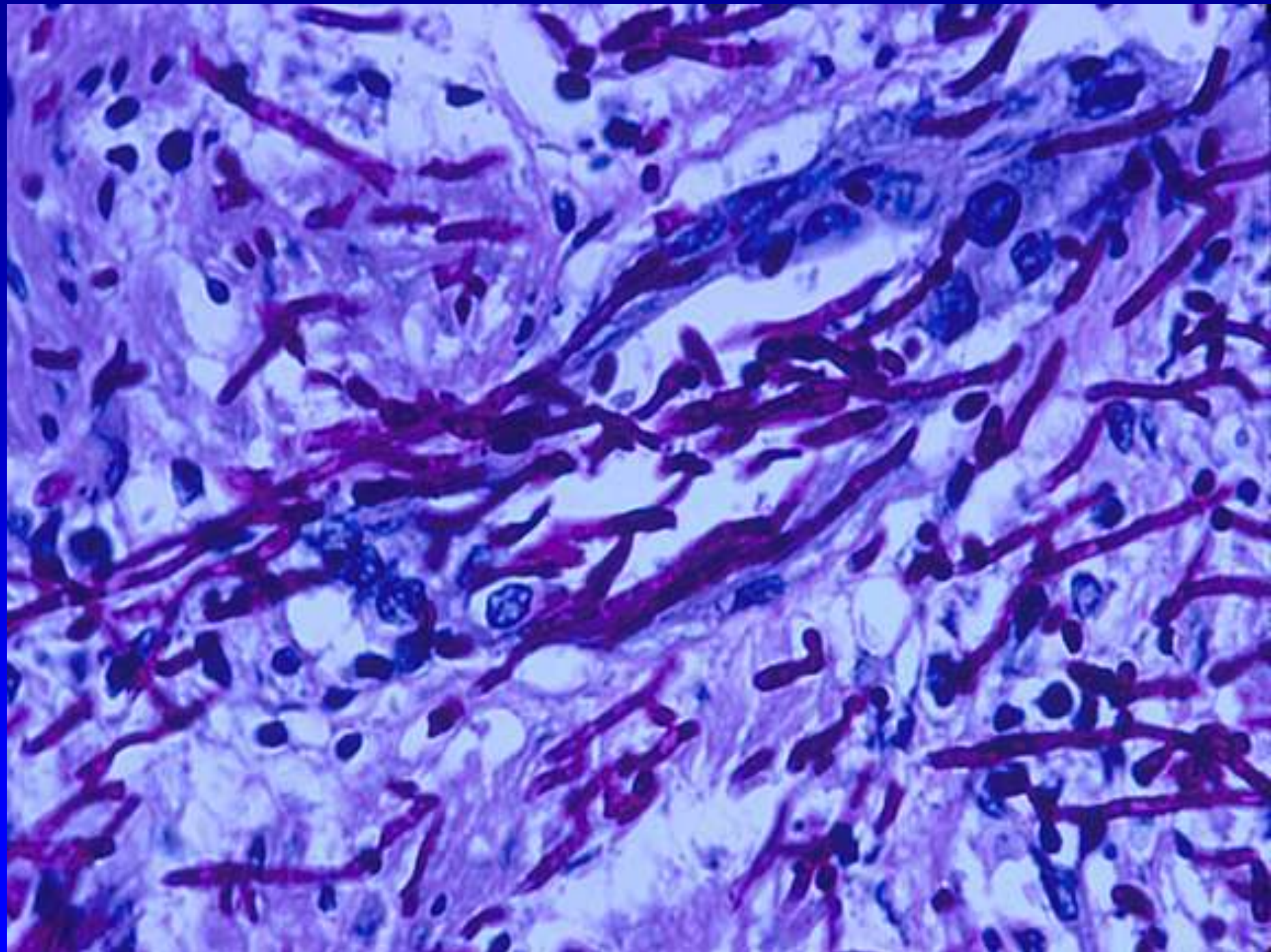
Schelenz, Mycosis 2003

# Impact of delayed treatment on mortality in patients with candidaemia



# Chronic disseminated Candidiasis / hepato-lienal Candidiasis



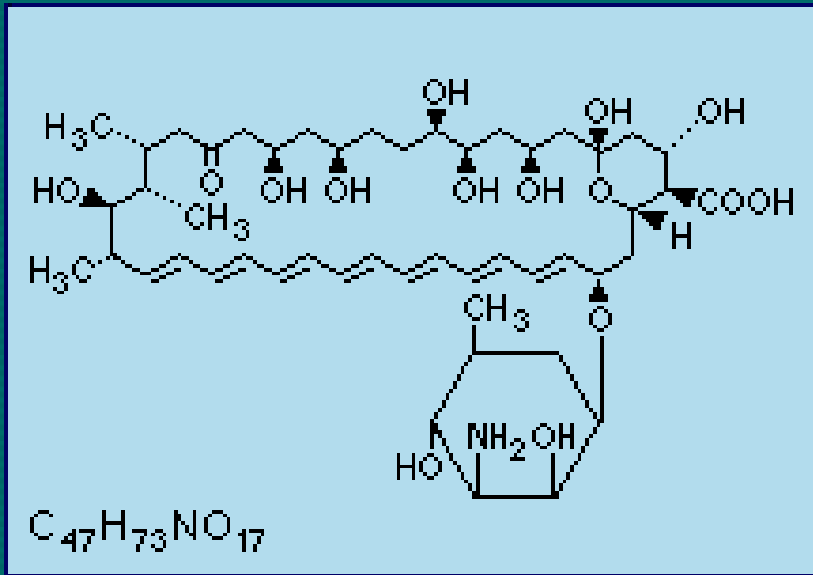


# ENDEMIC MYCOSES IN IMMUNE COMPROMISED PATIENTS

## ➤ Organisms

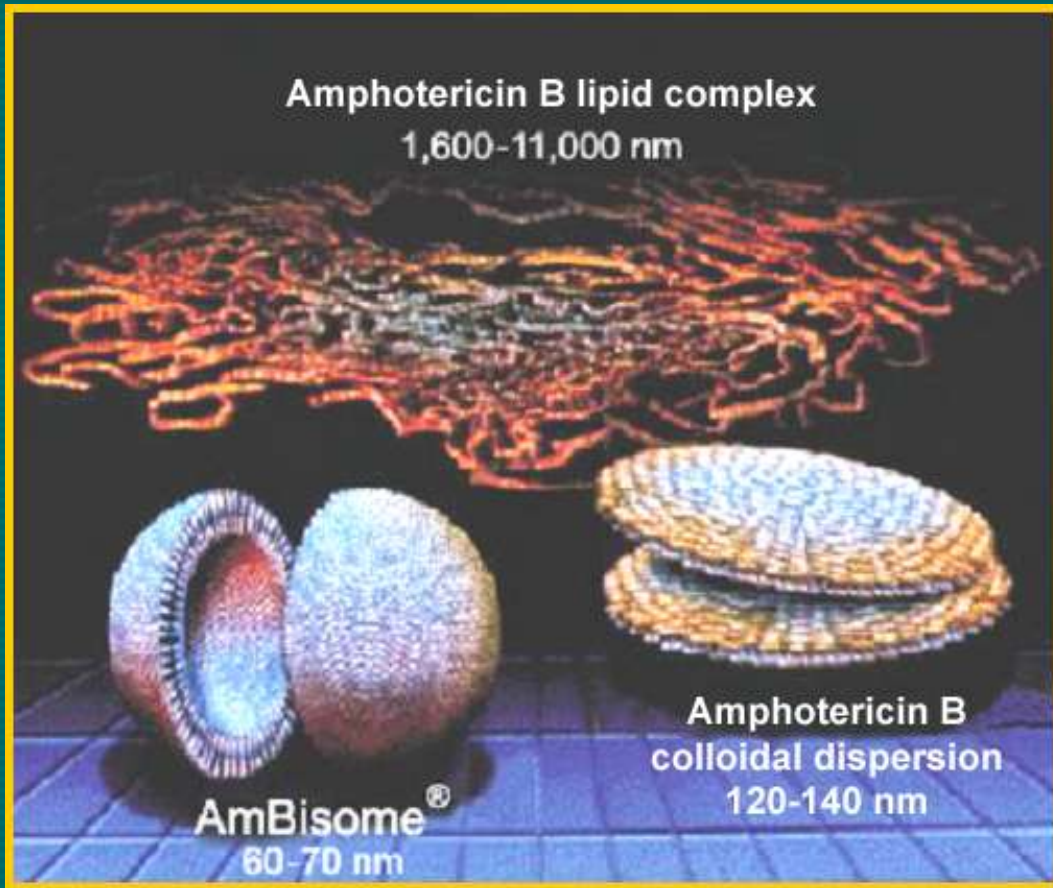
- ✓ *Histoplasma capsulatum*
- ✓ *Blastomyces dermatitidis*
- ✓ *Coccidioides immitis*
- ✓ *Sporothrix schenckii*
- ✓ *Paracoccidioides brasiliensis*
- ✓ *Penicillium marneffeii*

# Amphotericin B is in clinical use since 1960



- A polyene macrolide
- Isolated from *Streptomyces nodosus*
- Insoluble in water
- Solubilized by sodium deoxycholate
- Available for IV use as amphotericin B deoxycholate (Fungizone®)

# Lipid Formulations of Amphotericin B



- AmBisome®: liposomal amphotericin B
- amphotericin B lipid complex
- amphotericin B colloidal dispersion

# Fluconazole

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- Triazol – Goldstandard for the therapy of infections by *C. albicans*
- Oral und parenteral
- Excellent tolerability – Doses up to 1600 mg
- No interference with other drugs
- Prophylaxis

# Treatment of Vaginal Candidiasis

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- Local treatment  
    different azoles
- Oral treatment  
    fluconazole 200-400mg/3 Days

# Treatment of Onychomycosis

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- Oral Treatment  
    fluconazole 200mg once weekly  
    terbinafin

# The New Broad-Spectrum Azoles

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- Voriconazole. **Now licensed**
  - Oral and IV forms
- Posaconazole. Phase III
  - Oral only, at least at present
- Ravuconazole. Phase II. Limited public data
  - Oral for sure, IV is hopeful
- Others for which we don't have time
  - Albaconazole (UR-9825), CS-758, etc.

# The echinocandin class

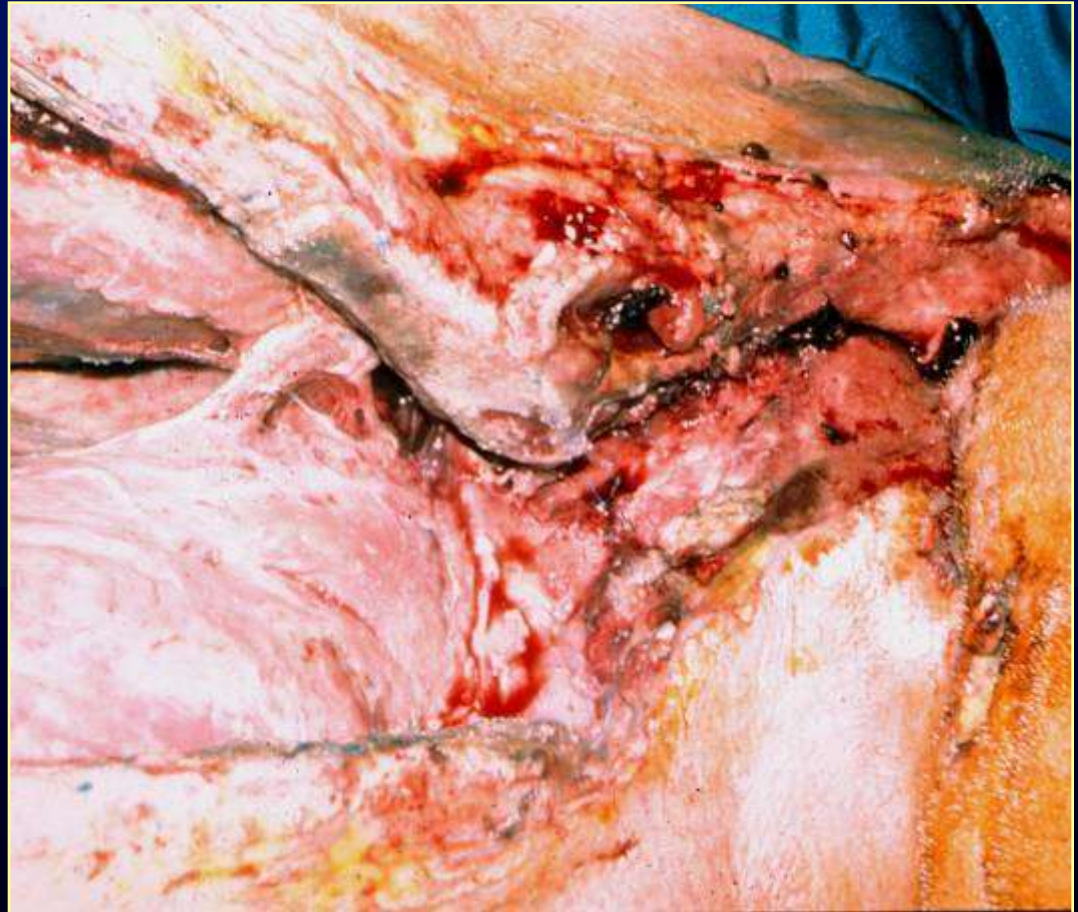
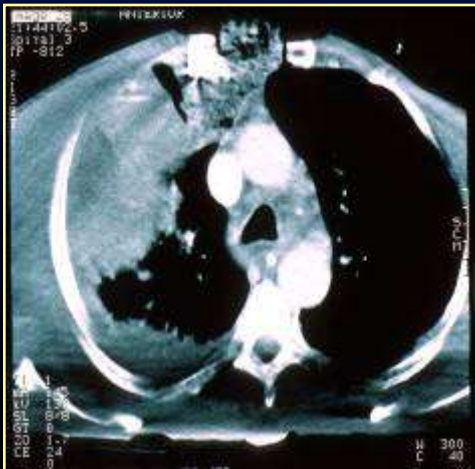
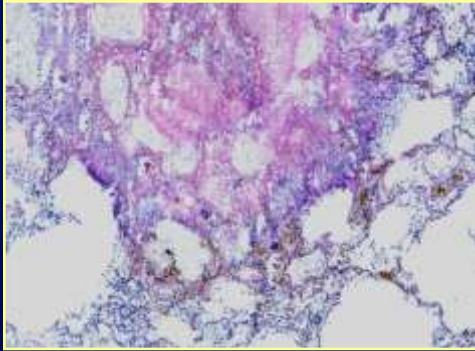
- The three sisters. All are IV only
  - Caspofungin
  - Anidulafungin
  - Micafungin
- Mostly similar
  - Safety: Consistently very clean
  - Non-renal clearance (no adjust in renal fail)
    - Hepatic failure:
      - ◆ A: None for any severity
      - ◆ M: None for moderate, no data for severe
      - ◆ C: 35 mg/d for moderate, no data for severe
  - Drug interactions: More with caspofungin
    - P450 inducers: No effect (A, M), some ↓ (C)
    - Cyclosporine: No effect (A, M), caution (C)
    - Tacrolimus: No effect (A, M), some ↑ (C)

# Aspergillus

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- **Aspergillus fumigatus, flavus, niger**
- **Boden, org. Abfall**
- **„der“ KH Keim**
- **oft opportunistisch**
- **Hyphen**
- **Aspergillosen**
  - **Aspergillom, Lunge**

# Aspergillus- mediastinitis



# Systemic mycoses caused by true pathogens

- *Histoplasma capsulatum*
- *Coccidioides immitis*
- *Blastomyces dermatitidis*
- *Paracoccidioidomycosis brasiliensis*

# *Candida Albicans infections*

- **Thrush** – occurs as a thick, white, adherent growth on the mucous membranes of mouth & throat
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# *Pneumocystis carinii*

- a small, unicellular fungus that causes pneumonia (PCP), the most prominent opportunistic infection in AIDS patients
- this pneumonia forms secretions in the lungs that block breathing & can be rapidly fatal if not controlled with medication
- pentamidine & cotrimoxazole

# *Pneumocystis carinii*

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