

fungi  
[created by Paul Young 02/10/07]

- *C. neoformans* and *C. gattii* are the most important
- an encapsulated organism
- cause of meningitis and pneumonia in the immunocompromised
- India ink staining and CSF and blood cryptococcal antigen tests are useful

### Cryptococcus

- caused by Zygomycetes fungi - *Rhizopus*, *Rhizomucor*, *Absidia* spp
- broad, non-septate hyphae that branch at 90 degrees

### Mucormycosis

- risk factors are:
  - chronic respiratory acidosis,
  - poorly controlled diabetes,
  - immunosuppression,
  - renal failure,
  - chelation therapy with increased serum iron levels,
  - burns,
  - intravenous drug use
- invasive rhinocerebral, orbital or disseminated black lesions
- usually resistant to azoles (except posaconazole)

### Aspergillus fumigatus

- acute angle, branching, septated, non-pigmented hyphae
- associated diseases include:
  - asthma (type 1 hypersensitivity to spores)
  - allergic bronchopulmonary aspergillosis (type 3 hypersensitivity with recurrent pneumonia & bronchiectasis)
  - aspergilloma (mycetoma)
  - invasive aspergillosis
- serum galactogamman (an *Aspergillus* antigen) may aid diagnosis
- CT may show halo and crescent air signs with aspergilloma and invasive disease

### Pneumocystis jiroveci

- previously known as *P. carinii* & renamed recently as well as reclassified as a fungus on the basis of nucleic acid and biochemical features
- classically causes pneumonia in the immunosuppressed
- may respond to treatment with cotrimoxazole, dapsone or atovaquone
- concomitant corticosteroids should be used in patients with HIV infection and significant hypoxaemia

- For severe sepsis due to *Candida* species, initiate treatment with amphotericin until the identity of the *Candida* species is confirmed.
- If the infection is related to an intravascular catheter, the catheter should be removed to prevent relapse. Initially, use: amphotericin B desoxycholate 0.5 to 1 mg/kg IV, daily.
- For proven *Candida albicans* and other susceptible strains, use: fluconazole 400 mg (child: 10 mg/kg up to 400 mg) IV, daily.
- Following clinical improvement with either IV amphotericin or IV fluconazole, for susceptible species, continue treatment with: fluconazole 400 mg (child: 10 mg/kg up to 400 mg) orally, daily for a total of at least 14 days.
- Some *Candida* (eg *C. krusei*, *C. glabrata*) are resistant to fluconazole; voriconazole or caspofungin may be suitable alternatives.
- Neutropenic patients with hepatosplenic candidiasis need prolonged therapy

### treatment of systemic candidiasis

### Candida spp

- *Candida albicans* is asexual, dimorphic with hyphae, pseudohyphae & chlamydospores
- Other species with increased resistance patterns and varied morphology are
  - C. tropicalis*
  - C. krusei*
  - C. glabrata*
  - C. lusitanae*
  - C. parapsilopsis*
- Azole resistance is increasing with *C. albicans* and is well established for *C. krusei* & *C. glabrata*
- amphotericin resistance is a problem with *C. lusitanae* but it is sensitive to azoles
- Invasive candidiasis is highly likely if:
  - cultured from the blood (especially two at different times of collection)
  - cultured from a sterile site
- Invasive candidiasis is suggested by:
  - culture from tissue or burn wound biopsies
  - culture from two non-contiguous sites
  - identified species is non commensal

### risk factors for invasive Candidaemia

- the incidence of candidaemia amongst unselected ICU patients is only 0.5–2%.
- Invasive fungal infections in such patients are associated with crude mortality rates of 30–40%,
  - such as recent abdominal surgery,
  - gastrointestinal tract perforation,
  - dialysis,
  - central venous catheterization,
  - total parenteral nutrition,
  - broad-spectrum antibiotic therapy and
  - colonization with *Candida* species

Estimated risk	Examples	Incidence without fluconazole prophylaxis (IFIs/100 patients)	Incidence with fluconazole prophylaxis (IFIs/100 patients)	Number avoided/ 100 patients	Number needed to treat to prevent one episode of IFI <sup>1</sup>
Low (<1%)	absence of risk factors <sup>b</sup>	1	0.47	0.53	188 (147–345)
Average (2%)	unselected ICU population <sup>b</sup>	2	0.94	1.06	94 (74–172)
High (11%)	one of diabetes, new onset haemodialysis, TPN prior to ICU entry or broad-spectrum antibiotics <sup>b</sup>	11	5.2	5.8	17 (13–31)
High (17%)	one of diabetes, new onset haemodialysis or TPN prior to ICU entry <sup>c</sup>	17	8.0	9.0	11 (9–20)
Highest (20%)	one of diabetes, new onset haemodialysis or TPN prior to ICU entry, and broad-spectrum antibiotics <sup>c</sup>	20	9.4	10.6	9 (7–17)

IFI, invasive fungal infection; TPN, total parenteral nutrition.

### arguments against prophylaxis with fluconazole

- (i) may predispose to infection or colonization with azole resistant fungal species
- (ii) drug interactions with fluconazole
- (iii) hepatotoxicity of fluconazole
- Certain *Candida* species, such as *C. glabrata* and *C. krusei*, and most filamentous fungi, including *Aspergillus* species, are intrinsically or relatively fluconazole-resistant

### arguments for prophylaxis with fluconazole

- antifungal prophylaxis with fluconazole reduces invasive fungal infections and total mortality across a broad range of clinical settings in non-neutropenic critically ill patients in a systematic review.