Opportunistic Fungal Infections

Patients with opportunistic fungal infections often have an underlying immune or metabolic defect, or have undergone surgery. Normally non-pathogenic fungi such as Mucor, Rhizopus, or Rhizomucor will cause Zygomycosis. Or borderline pathogenic fungi such as Trichosporon, Fusarium, or Penicillium will cause systemic disease.

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Candidiasis

**Candidiasis.** In severely immunocompromised patients (e.g. those receiving chemotherapy) C. albicans, that is part of the normal human flora (see above), can proliferate and disseminate throughout the body.

*Candida* are normal flora organisms, and can be found in the mouth, GI tract, vagina, and on the skin of 20% of normal individuals. Colonization increases with age, pregnancy and hospitalization. Since it is present in or on everyone, it has many opportunities to cause endemic infections in the compromised host.

Nutrition note: Zinc and iron deficiency is also a risk factor for Candidiasis.

*Candida albicans* is the most common opportunistic fungal infection, and is the 4th most common bloodstream infection in hospitals. The clinical spectrum of disease ranges from:

- Mucocutaneous – Oral thrush, yeast vaginitis
- Cutaneous – Skin and nails
- Systemic candidiasis – Fungemia

Other significant pathogens: *C. glabrata, C. krusei, C. parapsilosis, C. tropicalis*
Chromogenic Candida Agar (OCCA) is a selective differential medium that utilises two chromogens to differentiate C. albicans colonies (green) from colonies of C. tropicalis (dark blue), C. krusei (pink brown) and other important Candida species (beige, yellow and brown) in a single incubation.

Germ Tube Test: Incubate yeast cells for 2-3 hours at 37°C with human serum. Germ tube will grow from the mother cells as hyphae begin to develop. **A positive germ tube test is a positive ID of C. albicans.**

*C. albicans* in tissue with blastoconidia budding from the pseudohyphae.
Interiginous or flexural candidiasis showing an extensive erythematous scaling lesion and several smaller satellite lesions caused by *C. albicans*.

Thrush

*C. albicans*: Prosthetic valve endocarditis
Aspergillosis
This term is the name given to a number of different diseases caused by the mould *Aspergillus*. It produces large numbers of spores and occurs world-wide. In the U.S., *A. fumigatus* is the most common species causing disease. It can result in allergic broncopulmonary aspergillosis in those with hypersensitivity to the fungus. The organism can also infect the lungs, inner ear, sinuses and, rarely, the eyes, of previously healthy persons. In the immunosuppressed host, *Aspergillus* can disseminate throughout the body, in which case it is called invasive aspergillosis.

Branched, septate hyphae are suggestive of Aspergillus infection. Similar to Candida and the Zyogmcyetes, Aspergilli rarely infect a normal, immunocompetent host. The most common etiologic agents of aspergillosis in the U.S. are *A. fumigatus*, *A. niger* (large, globose, dark brown conidial heads), and *A. flavus*.

Three clinical types of pulmonary aspergillosis:
- Allergic hypersensitivity
- Aggressive tissue invasion – aspergillosis is primarily a pulmonary disease, but the fungus may be disseminated to any organ, and cause endocarditis, osteomyelitis, otomycosis, and cutaneous lesions.
- Fungus ball (aspergilloma) – characteristically seen in old TB cavities in lungs.

![Aspergillus niger](https://example.com/aspergillus-niger)

![Aspergillus fumigatus](https://example.com/aspergillus-fumigatus)

![Aspergillus flavus](https://example.com/aspergillus-flavus)

![Aspergillus fumigatus showing the classic seporate, branched hyphae.](https://example.com/aspergillus-fumigatus-detailed-view)
**Cryptococcosis**

This disease is a systemic infection caused by the yeast *Cryptococcus neoformans*. Exposure to this pathogen can result in asymptomatic infections and lifelong carriage of the organism. The most common manifestation is a subacute or chronic form of meningitis resulting from the inhalation of the organism. Pulmonary infection can also occur. The disease affects both healthy and immunosuppressed individuals and occurs world-wide. *C. neoformans* can be isolated in large numbers from pigeon droppings in the environment, although such birds do not appear to harbour the yeast.

Most common in AIDS patients. *Cryptococcus. neoformans* can be found in soil worldwide. It is also associated with avian excrement (especially pigeon droppings). At risk individuals become infected after inhaling microscopic, airborne fungal spores. It can spread to other parts of the body and cause serious disease; often pulmonary disease and meningitis.

![C. neoformans micrograph using an India Ink stain](image1)

![Encapsulated C. neoformans yeasts (red) in lungs](image2)

![Diagram of infection process](image3)
Pneumocystosis

Pneumocystis pneumonia (PCP) is caused by *Pneumocystis jiroveci*. *P. jiroveci* was formerly named *Pneumocystis carinii*, and thought to be a protozoan. However, the human organism has been re-classified as a fungus (nucleic acid composition of *Pneumocystis* ribosomal RNA and mitochondrial DNA indicated it is fungal, and is related to Ascomycetes, but the *P. carinii* name was retained specifically for the species found in rats), and was renamed. Pneumocystis species are present in the lungs of many mammals, including humans, but do not cause infections unless the individual is immunosuppressed. PCP was rarely seen prior to the HIV/AIDS epidemic. Most PCP infections are associated with HIV infection.

*P. jiroveci* cannot currently be cultured in any laboratory medium.

There are two predominant life-cycle forms of *Pneumocystis*, the trophic form and the cyst form. It has been hypothesized that the trophic form can conjugate by binary fission and therefore undergo asexual reproduction (a). In addition, there is a sexual cycle (b). Three intermediate cyst stages have been visualized by electron microscopy, and they contain complements of 2, 4 and 8 nuclei, respectively. The mature cyst contains 8 intracystic nuclei. It has been suggested that trophic forms emanate from the intracystic nuclei of the mature cyst as it ruptures, and then undergo vegetative growth or conjugate to re-form the cyst.
**Zygomycosis**

Zygomycetes are usually fast growing fungi characterised by primitive coenocytic (mostly aseptate) hyphae. Asexual spores include chlamydoconidia, conidia and sporangiospores contained in sporangia borne on simple or branched sporangiophores. Sexual reproduction is isogamous producing a thick-walled sexual resting spore called a zygospore.

*Mucor, Rhizopus* (bread mold), *Rhizomucor, Absidia* and *Cunninghamella* species cause opportunistic infections collectively referred to as zygomycoses. Most of these species are not able to survive at 37°C, but there are some thermally tolerant species that are able to infect immunocompromised individuals.

Hematopoietic cell cancer patients (e.g. leukemia) and those with Type 2 diabetes are at high risk for these infections. The diseases present as rhinocerebral, pulmonary or disseminated infections. Without very rapid surgery and therapy, there is high mortality, as these organisms grow very quickly.

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Chest radiograph showing nodular infiltrates on the right and confluent opacity on the left.  

Section from the lung showing numerous hyphae In the wall and lumen of the blood vessel and in the alveoli (Grocott’s stain).

Zygomycoses – skin lesions  
Rhinocerebral zygomycosis