

- *Endemic mycoses* are caused by dimorphic fungi that can produce serious systemic illness in healthy individuals.
- *Opportunistic mycoses* can cause life-threatening systemic diseases in individuals who are immunosuppressed or who carry implanted prosthetic devices or vascular catheters. Some of the fungi that cause opportunistic mycoses are discussed below; those involving specific organs are discussed in other chapters.

Yeast

Candidiasis

Most *Candida* infections originate when the normal commensal flora breach the skin or mucosal barriers. Residing normally in the skin, mouth, gastrointestinal tract, and vagina, *Candida* species usually live as benign commensals and seldom produce disease in healthy people. *Candida* species, usually *C. albicans*, are the most frequent cause of human fungal infections. These infections may be confined to the skin or mucous membranes or may disseminate widely. In otherwise healthy people *Candida* cause vaginitis and diaper rash. Individuals with diabetes and burn patients are particularly susceptible to superficial candidiasis. In individuals with indwelling intravenous lines or catheters, or undergoing peritoneal dialysis, *Candida* can spread into the bloodstream. Severe disseminated candidiasis most commonly occurs in patients who are neutropenic due to leukemia, chemotherapy, or hematopoietic stem cell transplantation, and may cause shock and disseminated intravascular coagulation.

Pathogenesis. A single strain of *Candida* can be successful as a commensal or a pathogen. *Candida* can shift between different phenotypes. Phenotypic switching involves coordinated regulation of phase-specific genes and provides a way for *Candida* to adapt to changes in the host environment (produced by antibiotic therapy, the immune response, or altered host physiology). These variants can exhibit altered colony morphology, cell shape, antigenicity, and virulence.

Candida produce a large number of functionally distinct adhesins that mediate adherence to host cells and contribute to virulence. These adhesins include (1) an integrin-like protein, which binds to fibrinogen, fibronectin, and laminin; (2) a protein that binds to epithelial cells; and (3) several agglutinins that bind to endothelial cells or fibronectin. Adhesion is an important determinant of virulence, since strains with reduced adherence to cells *in vitro* are avirulent in experimental models *in vivo*. Differential expression of adhesins by yeast and filamentous forms leads to recognition of distinct receptors on host cells.

Candida produce a number of enzymes that contribute to invasiveness, including at least nine secreted aspartyl proteinases, which may promote tissue invasion by degrading extracellular matrix proteins, and catalases, which may enable the organism to resist oxidative killing by phagocytic cells.

The ability of *C. albicans* to grow as biofilms also contributes to its capacity to cause disease. *Candida* biofilms are microbial communities consisting of mixtures of yeast, filamentous forms, and fungal-derived extracellular matrix.

C. albicans can form biofilms on implanted medical devices that reduce the organism's susceptibility to immune responses and antifungal drug therapy.

Neutrophils, macrophages and T_H17 cells are important for protection against *Candida* infection.

- Neutrophils and macrophages phagocytose *Candida*, and oxidative killing by these phagocytes is a first line of host defense. The important role of neutrophils and macrophages is illustrated by the increased risk of *Candida* infections in individuals with neutropenia or defects in NADPH oxidase or myeloperoxidase. Filamentous forms, but not yeast, can escape from phagosomes and enter the cytoplasm and proliferate.
- *Candida* yeast activate dendritic cells through multiple pathways, more so than do the filamentous forms of the fungi. For example, β -1,3-glucan expressed by the yeast engages dectin on dendritic cells and induces IL-6 and IL-23 production, which promotes T_H17 responses. The T_H17 responses elicited by *Candida* are responsible for recruiting neutrophils and monocytes (Chapter 6). These responses are critical for protection against *Candida* infection, as shown by recurrent mucocutaneous candidiasis in individuals with either low T-cell counts due to HIV infection or inherent defects in T_H17 cell development.

MORPHOLOGY

In tissue sections, *C. albicans* can appear as yeast, pseudohyphae, and, less commonly, true hyphae, defined by the presence of septae (Fig. 8-42). Pseudohyphae, an important diagnostic clue, are a chain of budding yeast cells joined end to end at constrictions. All forms may be present together in the same tissue. The organisms may be seen in routine hematoxylin and eosin stains, but a variety of special fungal stains (Gomori methenamine-silver, periodic acid-Schiff) are commonly used to better visualize them.

Most commonly candidiasis takes the form of a superficial infection on mucosal surfaces of the oral cavity (**thrush**). Florid proliferation of the fungi creates gray-white, dirty-looking pseudomembranes composed of matted organisms and inflammatory debris. Deep to the surface, there is mucosal hyperemia and inflammation. This form of candidiasis is seen in newborns, debilitated people, children receiving oral steroids for asthma, and following a course of broad-spectrum antibiotics that destroy competing normal bacterial flora. The other major risk group includes HIV-positive patients; people with oral thrush for no obvious reason should be evaluated for HIV infection.

***Candida* esophagitis** is commonly seen in AIDS patients and in those with hematolymphoid malignancies. These patients present with dysphagia (painful swallowing) and retrosternal pain; endoscopy demonstrates white plaques and pseudomembranes resembling oral thrush on the esophageal mucosa (Fig. 8-42).

***Candida* vaginitis** is common, especially in women who are diabetic, pregnant, or on oral contraceptive pills. It is usually associated with intense itching and a thick, curdlike discharge.

Cutaneous candidiasis can present in many different forms, including infection of the nail proper (onychomycosis), nail folds (paronychia), hair follicles (folliculitis), moist, intertriginous skin, such as armpits or webs of the fingers and toes (intertrigo), and penile skin (balanitis). Diaper rash is a cutaneous