Host-Parasite Interaction in Fungal Infections

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The outcome of host-parasite interactions in fungal infections is determined by the balance between pathogenicity of the organism and the adequacy of the host defenses. A wide variety of host defense mechanisms are involved in protection against fungal infections. These include nonspecific mechanisms such as intact skin and mucus membranes, indigenous microbial flora, and the fungicidal activity of neutrophils and monocytes. Such mechanisms constitute the major host defense against opportunistic fungal infections caused by ubiquitous organisms of low virulence. The effective role of immunoglobulins and complement as opsonins varies with the fungal pathogen involved. Specific immune responses of both the humoral and cell-mediated type develop in response to infections by pathogenic fungi. Antibodies, in general, are not of major importance in protection against these infections. Specifically sensitized T lymphocytes produce lymphokines that activate macrophages. Activated macrophages are the major line of defense against systemic fungal pathogens. The type and degree of impairment in immune responses determines the susceptibility and severity of diseases. The type of immune response also determines the tissue reactions in these diseases and sometimes may be involved in the pathogenesis of the disease process. The role of natural killer cell activity, antibody-dependent cellular cytotoxicity, and biological response modifiers in various fungal infections has been described recently. The microbial factors of importance in fungal infections are adherence, invasion, presence of an antiphagocytic capsule, and ability to grow under altered physiological states of the host. The differences in the virulence of fungal strains is of minor importance in determining the outcome in general. The seriousness of the alteration of the host state rather than the pathogenic properties of the fungus determine the severity of the disease.

Natural immunity to fungal diseases is very high. The two major physiologic barriers to fungal growth within tissue are temperature and redox potential. Most fungi are mesophilic and have an optimal growth range below the temperature of the human body. Their enzymatic pathways function more efficiently at the oxidation-reduction potential of non-living substrates compared to the relatively more reduced state of living metabolizing tissues. A highly efficient set of cellular defenses is present in the human body to combat fungal proliferation.

The establishment of infection depends on exposure to a sufficient inoculum size of the organism and the general resistance of the host. In the first instance infection occurs in patients in endemic areas because of exposure to large numbers of infectious forms of the organism. In the normal host, the majority of such infections are asymptomatic or self-limited and are followed by the development of specific resistance to infection. A similar exposure, however, can lead to local, disseminated and many times fatal infection in the immunocompromised host. Such patients also are susceptible to opportunistic infections caused by ubiquitously present organisms of low virulence. Under such circumstances, the establishment of disease depends entirely on the lowered resistance of the host. The recovery rate from these infections is low especially if the underlying immune defect is persistent and specific immunologic resistance does not develop.

All sectors of the immune system are involved in defense against fungal infections. The relative role played by nonspecific mechanisms such as polymorphonuclear neutrophil (PMN) and macrophage-monoocyte microbial mechanisms, and specific mechanisms like humoral and cell-mediated responses varies with the fungal pathogen involved in infection. The type of immune response to fungal antigens determines the tissue reactions in these diseases, and sometimes these reactions are involved in the pathogenesis of the disease process. The immune defects involved may be as subtle as a slight debilitation, in some cases transient, which may afford the
opportunity for a large inoculum of pathogenic fungi and a smaller inoculum of opportunistic fungi to establish infection. In addition to susceptibility, host factors also determine the severity of the disease and the final outcome of the host-parasite interaction. The differences in the virulence of fungal strains is of minor importance in determining the outcome. In the normal host, fungi induce a pyogenic reaction followed by a granulomatous reaction. The response induced by opportunistic fungi in an immunodeficient host is necrotic and suppurative. Humoral antibodies have generally been thought to play little or no part in protection against fungal diseases. However, recent investigations on the role of natural and antibody-dependent cytotoxicity in infections like cryptococcosis and histoplasmosis have further determined the role of antibody in protection against fungal infections. Also, the antigen presenting function of macrophages, vascular endothelial cells (1), Langerhans cells (2) and possibly B lymphocytes has been recognized. Fungi are poor antigens, a fact that makes the determination and quantitation of immune response difficult. The unavailability of standardized antigens and the prevalence of cross-reactions also makes the interpretation difficult. The environmental and host defense factors involved in infections with different fungi will be the subject of discussion in this review.

Candidiasis

Candida albicans is a member of the indigenous microbial flora of humans. It is found in the gastrointestinal tract, upper respiratory tract, buccal cavity and vaginal tract. Its growth is normally suppressed by other microorganisms found in these areas.

Specific environmental and host factors lead to predisposition to different forms of infection by this opportunistic fungus. Alterations in host defenses, physiology or normal flora must occur before colonization, infection and disease production. The seriousness of the alteration of the host rather than any pathogenic properties of the fungus determine the severity of the disease. In humans the principal portals of entry are indwelling intravenous catheters and the gastrointestinal tract (3). The major host defenses against candidiasis are skin and mucous membranes.

Skin and Mucous Membranes. Normal skin provides a very effective barrier to colonization by Candida spp. by being a physical barrier providing microbial interference, and by the secretion of saturated fatty acids with antifungal properties. Cutaneous involvement and invasion are more likely when skin becomes moist or lacerated. Indwelling lines probably serve as conduits for Candida spp. to enter the bloodstream from the skin. They may also abrade the vascular or cardiac endothelium, leading to platelet and fibrin aggregates which serve as foci for infection and vegetation formation. The incidence of supplicative thrombophlebitis caused by Candida spp. is increasing (4). Both arterial and venous catheters, including pressure monitoring devices, have been reported to become infected by Candida spp. Use of hyperalimentation fluids is an important predisposing factor for hematogenously disseminated candidiasis. Various explanations for this occurrence include the presence of high carbohydrate levels in the bloodstream or locally at the catheter tip (4). Burned skin provides another important portal of entry for invasive candidiasis.

Chronic mucocutaneous candidiasis is a specific entity occurring in patients with genetic defects such as Swiss type agammaglobulinemia or Di George’s syndrome, and endocrinopathies such as juvenile hypoparathyroidism, hypoadrenocorticism or thyromas. Most of these underlying diseases involve defects in cell-mediated immunity. Patients with AIDS with similar defects in cell-mediated immunity also experience this spectrum of Candida infections.

Alterations of the gastrointestinal flora by broad-spectrum antibiotics and mucosal injury caused by stress, chemotherapy and radiation are important factors predisposing to gastrointestinal tract invasion by Candida spp. (5). Agha et al. (5) have speculated that infection by herpes viruses may initiate superficial ulcerations in the esophagus that become secondarily invaded by fungi. Antibiotic and/or adrenal corticosteroid treatment and diabetes mellitus enhance the growth of Candida albicans in the saliva (6). Diabetes has been shown by Taper-Jones et al. (7) to be associated with a 20 % increase in rate of colonization and a fourfold increase in the density of colonization. This increase in rate and degree of colonization could not be correlated with the degree of control of diabetes. However, the level of glucose in saliva was not estimated by these investigators. The investigators also noted an increase in the colonization rate in smokers and denture wearers in diabetic as well as control groups.

The most common clinical infection with Candida albicans is probably vulvovaginal candidiasis. Local factors such as pH, glycogen-glucose concentration and the status of epithelial cells, all under hormonal control, are of prime importance in the occurrence of vaginal candidiasis. A rise in vaginal pH during menstruation correlates with increased symptomatology of vaginal candidiasis. Women on oral contraceptives have a higher rate of asymptomatic colonization as well as symptomatic vaginitis (8). The susceptibility to colonization and infection is higher in women who use a combined estrogenic type of oral contraceptive than in those who use a sequential progesterone-containing one (9).