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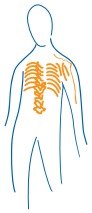

Host Defenses Against Infection

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HOST VERSUS PATHOGEN: VICTORY, DEATH, OR COEXISTENCE

Many factors determine whether we live successfully in symbiosis with our normal microbial flora, whether we can resist exposure to outside pathogens, and whether we live or die in an environment filled with an incredibly wide spectrum of microbes. Factors include age, nutrition, underlying medical conditions (e.g., diabetes mellitus, chronic lung disease), and the nature of the exposure (e.g., microbial virulence, inoculum). The outcome is determined by our host defenses, including barriers (e.g., skin), innate immunity (e.g., phagocytes), and specific responses that include antibodies and T cell–mediated events.

The human host has developed a multilayered host defense system to counter infectious organisms, and the resulting duel between pathogen and human can lead to one of four outcomes: death of the human host, elimination of the pathogen, peaceful coexistence of both in a symbiotic relationship, or an association whose latent nature changes with time and under additional biologic pressures. For example, pneumococcal pneumonia may kill the individual, or the host's defenses may eliminate the organism. *Escherichia coli* and *Bacteroides fragilis* in the gut survive and help to protect the host in a symbiotic relationship. Most individuals exposed to *Mycobacterium tuberculosis* are asymptomatic and latently infected with an inactive nonreplicating organism. Almost one third of the world's population is latently infected, but only about 10% progress to active disease. Immunologic impairment (e.g., human immunodeficiency virus [HIV] infection) and factors such as age increase the risk of progressing from latent to active disease.

The asymptomatic nature of an infection should not automatically be equated with latency or dormancy of the pathogen. For example, chronic HIV-1 infection was incorrectly characterized as having a prolonged latent or silent stage before the host developed immunodeficiency and opportunistic infections. However, most untreated HIV-1–infected individuals harbor actively replicating virus that kill $CD4^+$ T lymphocytes on a daily basis, although the aggregate effects are not appreciated until $CD4^+$ T lymphocyte levels are reduced to below 200 cells/mL after 8 to 10 years of infection. Infected individuals are infectious despite their relatively asymptomatic state, and in resource-rich countries, treatment is recommended regardless of $CD4^+$ T lymphocyte levels. Treatment halts viral immune destruction, reduces viral burden in genital secretions, and decreases an infected individual's risk of transmitting HIV-1.

CATEGORIES OF HOST DEFENSES AND RISKS OF INFECTION

The relative importance of the innate and adaptive defenses is best illustrated by hosts who are deficient in a particular component. For example, chemotherapy leading to the depletion of immune cells such as neutrophils renders the host more susceptible to bacterial and fungal infections. Congenital deficiency of immunoglobulins increases the risk of infections that are usually thwarted by antibody responses such as those associated with *Streptococcus pneumoniae* and *Haemophilus influenzae*. Pharmacologic inhibition of tumor necrosis factor-α (TNF-α) increases the risk of developing active tuberculosis among those with latent infection. Astute clinicians, recognizing the increased incidence of atypical infections such as those caused by *Pneumocystis jirovecii* among young men, sounded the alarm that a novel immunodeficiency syndrome had appeared that was later ascribed to HIV-1.

Host defenses to infection can be classified as nonimmunologic host defenses, innate immunity, and specific or adaptive immunity. Immune host defenses against microbial pathogens are composed of cells and molecules located in peripheral sites, such as the skin and submucosal regions, and in secondary lymphoid tissues, such as the lymph nodes, tonsils, spleen, and Peyer's patches.

For a deeper discussion of these topics, please see Chapters 45 through 50 in Section VII, "Principles of Immunology and Inflammation," in Goldman-Cecil Medicine, *25th Edition.*

Nonimmunologic Host Defenses

Nonimmunologic host defenses include epidermal and mucosal barriers that physically prevent the entry of pathogens into the body. The respiratory tract defenses depend on mucus that entraps pathogens and on ciliary action and cough that continuously clear the mucus and organisms from the lungs and upper airways. Respiratory viruses, including influenza, may inhibit ciliary action or denude the mucous membrane completely, allowing bacteria to colonize and cause infection. Stroke, medications, or other causes of reduced cough reflex may lead to poor clearance of secretions, mucus, and pathogens and cause lung infection. Smoking and industrial exposure to toxins such as silica may similarly reduce lung host defenses, such as reducing ciliary action that leads to infection. In addition to mucus and ciliary action, alveolar macrophages located in the lung