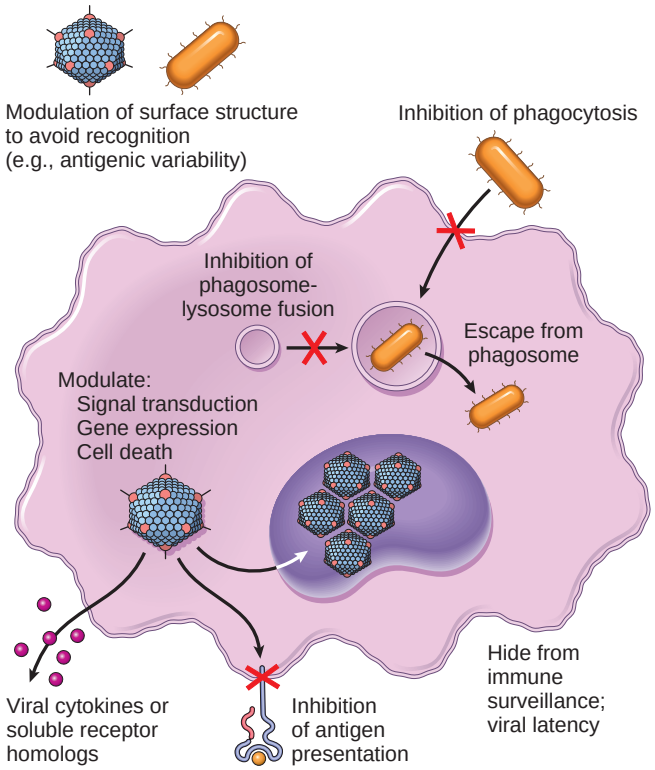


**Figure 8-2** An overview of mechanisms used by viral and bacterial pathogens to evade innate and adaptive immunity. (Modified with permission from Finlay B, McFadden G: Anti-immunology: evasion of the host immune system by bacterial and viral pathogens. Cell 2006;124:767-782.)

- *Antigenic variation.* This is an important mechanism for escape from antibody-mediated host defenses. Antibodies against microbial antigens can block microbial adhesion and uptake into cells, act as opsinins to facilitate phagocytosis, and fix complement, and cytotoxic T cells recognize microbial antigens expressed in the context of MHC molecules on the surface of infected host cells. To escape recognition, microbes have many strategies that allow them to "change their coats" by expressing different surface antigens. Spirochetes belonging to *Borrelia* species and trypanosomes have sophisticated genetic mechanisms that allow them to periodically switch their major surface proteins. Influenza viruses have a complex RNA genome that allows for frequenct recombination events, permitting antigenic "drift" and "shifts". In a less elegant but nevertheless effective fashion, other microbes simply generate numerous genetic variants through mutation. For example, there are over 90 different serotypes of *S. pneumoniae*, each with different capsular polysaccharides. Similarly, the low fidelity of viral RNA polymerases of HIV and many respiratory viruses (including influenza virus) create viral antigenic variation (Table 8-2).
- *Resistance to antimicrobial peptides.* You will recall from Chapter 6 that epithelial cells and some leukocytes produce cationic antimicrobial peptides such as defensins and cathelicidins that are toxic to microbes, in part by forming pores in microbial membranes. These peptides can also augment anti-microbial immunity by inducing the production of pro-inflammatory chemokines and cytokines. Resistance to these peptides is a factor in the virulence of a number of pathogens, including *Shigella* ssp, *S. aureus,* and *Candida.* Microbial strategies to avoid killing by peptides include changes in net surface charge and membrane hydrophobicity that prevent antimicrobial peptide insertion and pore formation, secretion of proteins that inactivate or degrade the peptides, and pumps that export the peptides.
- *Resistance to killing by phagocytes.* Phagocytosis and killing of bacteria by neutrophils and macrophages are a critical host defense against extracellular bacteria; accordingly, pathogens have evolved a wealth of resistance mechanisms at virtually every level of the process. The carbohydrate capsule on the surface of many bacteria that cause pneumonia or meningitis (*S. pneumoniae*, *N. meningitidis*, *H. influenzae*) prevents phagocytosis of the organisms by neutrophils. *E. coli* that cause meningitis in newborns synthesize a special capsule containing sialic acid that will not bind C3b, which is critical for activation of the alternative complement pathway and opsonization-directed phagocytosis. *S. aureus* expresses protein A, which binds the Fc portion of antibodies and so inhibits phagocytosis. Other bacteria make proteins that variously kill phagocytes, prevent their migration, or diminish their oxidative burst. Finally, some pathogens are resistance to intracellular killing in phagocytes, including mycobacteria, *Listeria*, *Cryptococcus neoformans*, and certain protozoa (e.g., leishmania, trypanosomes, toxoplasmas).
- *Evasion of apoptosis and manipulation of host cell metabolism.* Some viruses produce proteins that interfere with apoptosis of the host cell, which may buy them the time necessary to replicate, enter latency, or even transform host cells. Microbes that replicate intracellularly (viruses, some bacteria, fungi and protozoa) also express factors that modulate autophagy, which appears to enhance their ability to evade degradation and to replicate.
- *Resistance to cytokine-, chemokine- and complement-mediated host defense.* Many virues express factors that interfere with the actions of cytokines, chemokines, or complement. For example, some viruses produce soluble homologues of IFN-α/β or IFN-γ receptors that function as "decoys" and sop up and inhibit the actions of secreted IFNs. Viruses also produce proteins that inhibit the JAK/STAT pathway, a key signaling cascade that

**Table 8-2** Mechanisms of Antigenic Variation

| Type | Example | Disease |
|---|---|---|
| High mutation rate | HIV<br>Influenza virus | AIDS<br>Influenza |
| Genetic reassortment | Influenza virus<br>Rotavirus | Influenza<br>Diarrhea |
| Genetic rearrangement (e.g., gene recombination, gene conversion, site-specific inversion) | *Borrelia burgdorferi*<br>*Neisseria gonorrhoeae*<br>*Trypanosoma* sp.<br><br>*Plasmodium* sp. | Lyme disease<br>Gonorrhea<br>African sleeping sickness<br>Malaria |
| Large diversity of serotypes | Rhinoviruses<br>*Streptococcus pneumoniae* | Colds<br>Pneumonia<br>Meningitis |