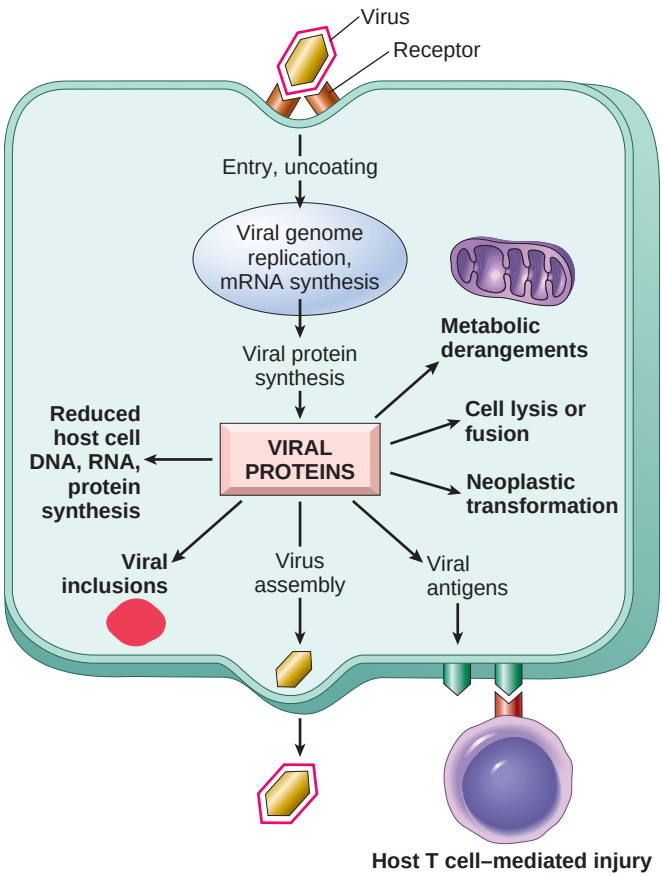

Figure 8-3 Mechanisms by which viruses cause injury to cells.

misfolded proteins that activate the ER stress response; this, too, activates pro-apoptotic pathways. Finally, some viruses encode proteins that are pro-apoptotic; the HIV vpr protein is one such example.

- *Anti-viral immune responses.* Host lymphocytes can recognize and destroy virus-infected cells. Cytotoxic T lymphocytes (CTLs) are important for defense against viral infections, but CTLs also can be responsible for tissue injury, as discussed previously.
- *Transformation of infected cells.* Oncogenic viruses can stimulate cell growth and survival by a variety of mechanisms, including expression of virus-encoded oncogenes, expression of viral proteins that inactivate key tumor suppressors, and insertional mutagenesis, in which expression of host genes is altered by the insertion of the viral genome into the genes or the flanking host genome. The mechanisms of viral transformation are numerous and are discussed in Chapter 7.

Mechanisms of Bacterial Injury

Bacterial Virulence. **Bacterial damage to host tissues depends on the ability of the bacteria to adhere to host cells, to invade cells and tissues, or to deliver toxins.** Pathogenic bacteria have *virulence genes* that encode proteins that confer these properties. An example of the importance of such genes can be found in the various strains of *Salmonella*. All *Salmonella* strains that infect humans are closely related enough to form a single species, meaning that they share many "housekeeping" genes. Differences in a relatively small number of pathogenicity genes determine whether an isolate of *Salmonella* causes life-threatening typhoid fever or self-limited enteritis. Virulence genes are frequently found grouped together in clusters called *pathogenicity islands*.

Mobile genetic elements **such as plasmids and bacteriophages can transmit functionally important genes to bacteria, including genes that influence pathogenicity and drug resistance.** Genes for toxins are sometimes found in plasmids but are more often found in the genomes of bacteriophages, including the genes that encode the toxins responsible for the pathogenesis of cholera, diphtheria and botulism. Genes for acquired antibiotic resistance traits are more frequently found on plasmids, which can spread not only within bacterial species but also between more distantly related organisms. For example, a plasmid with genes for vancomycin resistance can spread not only between species of *Enterococcus*, but also to more distantly related (and virulent) *S. aureus*.

Many bacteria coordinately regulate gene expression within a large population by a process called *quorum sensing*. For example, bacteria can induce expression of virulence factors as they grow to high concentration in tissue. This may allow bacteria growing in discrete host sites, such as an abscess or consolidated pneumonia, to overcome host defenses. *S. aureus* coordinately regulates virulence factors by secreting *autoinducer peptides*. As the bacteria increase in numbers, the level of the autoinducer peptide increases, stimulating toxin production. Within the population, some bacteria produce the autoinducer peptide and others respond to it by secreting toxins. Thus, because of quorum sensing, unicellular bacteria acquire some of the more complex properties of multicellular organisms, in which different cells perform different functions.

Communities of bacteria can also form *biofilms* in which the organisms live within a viscous layer of extracellular polysaccharides that adhere to host tissues or devices such as intravascular catheters and artificial joints. In addition to enhancing adherence to host tissues, biofilms increase the virulence of bacteria by protecting the microbes from immune effector mechanisms and increasing their resistance to antimicrobial drugs. Biofilm formation seems to be particularly important in the persistence and relapse of bacterial endocarditis, artificial joint infections, and respiratory infections in people with cystic fibrosis.

Bacterial Adherence to Host Cells. *Adhesins* are bacterial surface proteins that bind bacteria to host cells or extracellular matrix. Adhesins are limited in structural type but have a broad range of host cell specificity. *Streptococcus pyogenes* adheres to host tissues using the adhesins protein F and teichoic acid, which project from the bacterial cell wall and bind to fibronectin on the surface of host cells and in the extracellular matrix.

Pili are filamentous proteins on the surface of bacteria that act as adhesins. The stalks of pili are composed of conserved repeating subunits, while the variable subunits on the tips of the pili determine the tissue-binding specificity of the bacteria. For example, strains of *E. coli* that cause urinary tract infections specifically express a pilus which binds to a gal(α1-4)gal moiety expressed on uroepithelial cells. Pili can be targets of the host antibody response and,