everyday CONNECTION

Applied Virology:

The study of viruses has led to the development of a variety of new ways to treat non-viral diseases. Viruses have been used in **gene therapy**. Gene therapy is used to treat genetic diseases such as severe combined immunodeficiency (SCID), a heritable, recessive disease in which children are born with severely compromised immune systems. One common type of SCID is due to the lack of an enzyme, adenosine deaminase (ADA), which breaks down purine bases. To treat this disease by gene therapy, bone marrow cells are taken from a SCID patient and the ADA gene is inserted. This is where viruses come in, and their use relies on their ability to penetrate living cells and bring genes in with them. Viruses such as adenovirus, an upper-respiratory human virus, are modified by the addition of the ADA gene, and the virus then transports this gene into the cell. The modified cells, now capable of making ADA, are then given back to the patients in the hope of curing them. Gene therapy using viruses as carriers of genes (viral vectors), although still experimental, holds promise for the treatment of many genetic diseases. Still, many technological problems need to be solved for this approach to be a viable method for treating genetic disease.

Another medical use for viruses relies on their specificity and ability to kill the cells they infect. **Oncolytic viruses** are engineered in the laboratory specifically to attack and kill cancer cells. A genetically modified adenovirus known as H101 has been used since 2005 in clinical trials in China to treat head and neck cancers. The results have been promising, with a greater short-term response rate to the combination of chemotherapy and viral therapy than to chemotherapy treatment alone. This ongoing research may herald the beginning of a new age of cancer therapy, where viruses are engineered to find and specifically kill cancer cells, regardless of where in the body they may have spread.

A third use of viruses in medicine relies on their specificity and involves using bacteriophages in the treatment of bacterial infections. Bacterial diseases have been treated with antibiotics since the 1940s. However, over time, many bacteria have evolved resistance to antibiotics. A good example is methicillin-resistant *Staphylococcus aureus* (MRSA, pronounced “mersa”), an infection commonly acquired in hospitals. This bacterium is resistant to a variety of antibiotics, making it difficult to treat. The use of bacteriophages specific for such bacteria would bypass their resistance to antibiotics and specifically kill them. Although **phage therapy** is in use in the Republic of Georgia to treat antibiotic-resistant bacteria, its use to treat human diseases has not been approved in most countries. However, the safety of the treatment was confirmed in the United States when the U.S. Food and Drug Administration approved spraying meats with bacteriophages to destroy the food pathogen *Listeria.* As more and more antibiotic-resistant strains of bacteria evolve, the use of bacteriophages might be a potential solution to the problem, and the development of phage therapy is of much interest to researchers worldwide.

21.4 | Other Acellular Entities: Prions and Viroids

By the end of this section, you will be able to do the following:

- Describe prions and their basic properties
- Define viroids and their targets of infection

Prions and viroids are **pathogens** (agents with the ability to cause disease) that have simpler structures than viruses but, in the case of prions, still can produce deadly diseases.

Prions

Prions, so-called because they are proteinaceous, are infectious particles—smaller than viruses—that contain no nucleic acids (neither DNA nor RNA). Historically, the idea of an infectious agent that did not use nucleic acids was considered impossible, but pioneering work by Nobel Prize-winning biologist Stanley Prusiner has convinced the majority of biologists that such agents do indeed exist.

Fatal neurodegenerative diseases, such as kuru in humans and bovine spongiform encephalopathy (BSE) in cattle (commonly known as “mad cow disease”) were shown to be transmitted by prions. The disease was spread by the consumption of meat, nervous tissue, or internal organs between members of the same species. Kuru, native to humans in Papua New Guinea, was spread from human to human via ritualistic cannibalism. BSE, originally detected in the United Kingdom, was spread between cattle by the practice of including cattle nervous tissue in feed for other cattle. Individuals with kuru and BSE show symptoms of loss of motor control and unusual behaviors, such as uncontrolled bursts of laughter with kuru, followed by death. Kuru was controlled by inducing the population to abandon its ritualistic cannibalism.

On the other hand, BSE was initially thought to only affect cattle. Cattle dying of the disease were shown to have developed lesions or “holes” in the brain, causing the brain tissue to resemble a sponge. Later on in the outbreak, however, it was shown that a similar encephalopathy in humans, known as variant Creutzfeldt-Jakob disease (CJD), could be acquired from eating beef from animals infected with BSE, sparking bans by various countries on the importation of British beef and causing considerable economic damage to the British beef industry (**Figure 21.17**). BSE still exists in various areas, and although a rare disease, individuals that acquire CJD are difficult to treat. The disease can be spread from human to human by blood, so many countries have banned blood donation from regions associated with BSE.

The cause of spongiform encephalopathies, such as kuru and BSE, is an infectious structural variant of a normal cellular protein called PrP (prion protein). It is this variant that constitutes the prion particle. PrP exists in two forms, **PrP^{C}**, the normal form of the protein, and **PrP^{SC}**, the infectious form. Once introduced into the body, the PrP^{SC} contained within the prion binds to PrP^{C} and converts it to PrP^{SC}. This leads to an exponential increase of the PrP^{SC} protein, which aggregates. PrP^{SC} is folded abnormally, and the resulting conformation (shape) is directly responsible for the lesions seen in the brains of infected cattle. Thus, although not without some detractors among scientists, the prion seems likely to be an entirely new form of infectious agent, the first one found whose transmission is not reliant upon genes made of DNA or RNA.

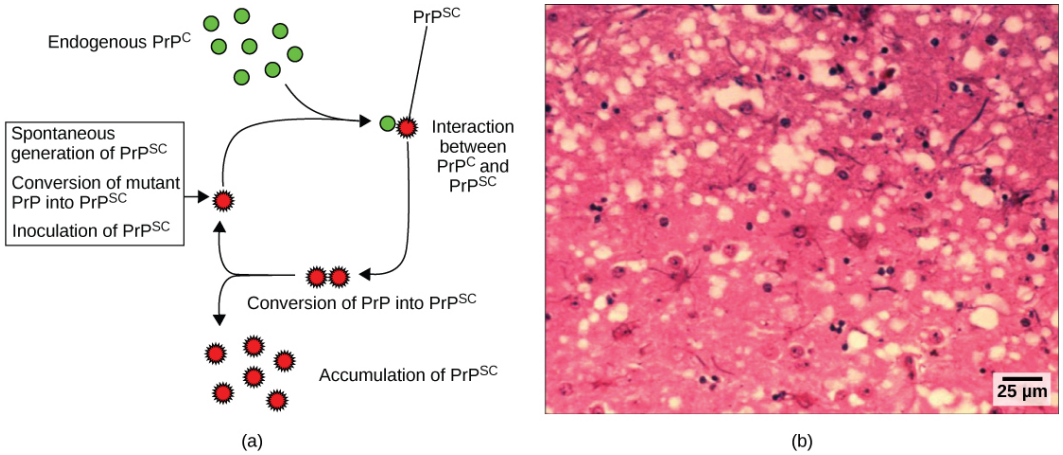

Figure 21.17 Mad Cow Disease in humans. (a) Endogenous normal prion protein (PrP^{C}) is converted into the disease-causing form (PrP^{SC}) when it encounters this variant form of the protein. PrP^{SC} may arise spontaneously in brain tissue, especially if a mutant form of the protein is present, or it may occur via the spread of misfolded prions consumed in food into brain tissue. (b) This prion-infected brain tissue, visualized using light microscopy, shows the vacuoles that give it a spongy texture, typical of transmissible spongiform encephalopathies. (credit b: modification of work by Dr. Al Jenny, USDA APHIS; scale-bar data from Matt Russell)

Viroids

Viroids are plant pathogens: small, single-stranded, circular RNA particles that are much simpler than a virus. They do not have a capsid or outer envelope, but like viruses can reproduce only within a host cell. Viroids do not, however, manufacture any proteins, and they only produce a single, specific RNA molecule. Human diseases caused by viroids have yet to be identified.

Viroids are known to infect plants (**Figure 21.18**) and are responsible for crop failures and the loss of millions of dollars in agricultural revenue each year. Some of the plants they infect include potatoes, cucumbers, tomatoes, chrysanthemums, avocados, and coconut palms.

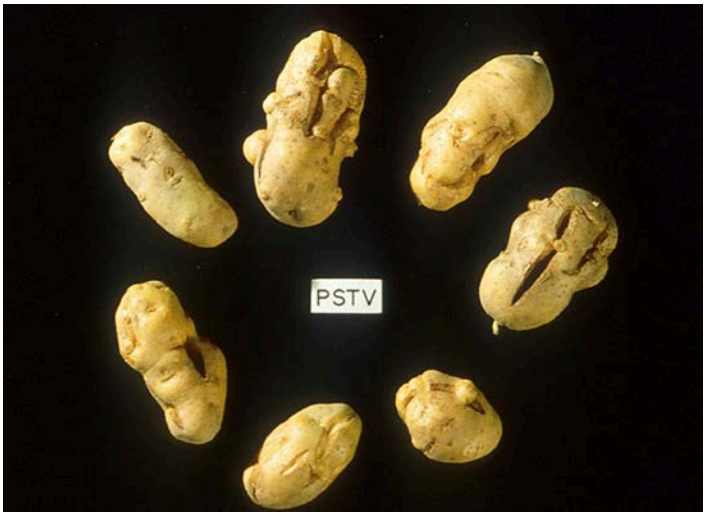

Figure 21.18 These potatoes have been infected by the potato spindle tuber viroid (PSTV), which is typically spread when infected knives are used to cut healthy potatoes, which are then planted. (credit: Pamela Roberts, University of Florida Institute of Food and Agricultural Sciences, USDA ARS)

career CONNECTION

Virologist

Virology is the study of viruses, and a virologist is an individual trained in this discipline. Training in virology can lead to many different career paths. Virologists are actively involved in academic research and teaching in colleges and medical schools. Some virologists treat patients or are involved in the generation and production of vaccines. They might participate in epidemiologic studies (**Figure 21.19**) or become science writers, to name just a few possible careers.

Figure 21.19 This virologist is engaged in fieldwork, sampling eggs from this nest for avian influenza. (credit: Don Becker, USGS EROS, U.S. Fish and Wildlife Service)

If you think you may be interested in a career in virology, find a mentor in the field. Many large medical centers have departments of virology, and smaller hospitals usually have virology labs within their microbiology departments. Volunteer in a virology lab for a semester or work in one over the summer. Discussing the profession and getting a first-hand look at the work will help you decide whether a career in virology is right for you. The American Society of Virology's **website (http://openstaxcollege.org/l/asv)** is a good resource for information regarding training and careers in virology.

KEY TERMS

acellular lacking cells

acute disease disease where the symptoms rise and fall within a short period of time

asymptomatic disease disease where there are no symptoms and the individual is unaware of being infected unless lab tests are performed

attenuation weakening of a virus during vaccine development

AZT anti-HIV drug that inhibits the viral enzyme reverse transcriptase

back mutation when a live virus vaccine reverts back to it disease-causing phenotype

bacteriophage virus that infects bacteria

budding method of exit from the cell used in certain animal viruses, where virions leave the cell individually by capturing a piece of the host plasma membrane

capsid protein coating of the viral core

capsomere protein subunit that makes up the capsid

cell necrosis cell death

chronic infection describes when the virus persists in the body for a long period of time

cytopathic causing cell damage

envelope lipid bilayer that encircles some viruses

fusion method of entry by some enveloped viruses, where the viral envelope fuses with the plasma membrane of the host cell

gall appearance of a plant tumor

gene therapy treatment of genetic disease by adding genes, using viruses to carry the new genes inside the cell

group I virus virus with a dsDNA genome

group II virus virus with an ssDNA genome

group III virus virus with a dsRNA genome

group IV virus virus with an ssRNA genome with positive polarity

group V virus virus with an ssRNA genome with negative polarity

group VI virus virus with an ssRNA genome converted into dsDNA by reverse transcriptase

group VII virus virus with a single-stranded mRNA converted into dsDNA for genome replication

horizontal transmission transmission of a disease between unrelated individuals

hyperplasia abnormally high cell growth and division

hypoplasia abnormally low cell growth and division

intermittent symptom symptom that occurs periodically

latency virus that remains in the body for a long period of time but only causes intermittent symptoms