Chapter 18

Will Mad Cow Disease Become an Epidemic? Immune System, Bacteria, Viruses, And Other Pathogens

1

Spongiform Encephalopathies

- Class of diseases that _____ _____
- Encephalopathy is a *pathology*, or _____
- Mad cow disease is a type of spongiform encephalopathy that only affects cows; also called *bovine spongiform encephalopathy*, or *BSE*
  - Cows' brains resemble porous, natural sponges filled with holes
  - Symptoms – cows would shake and tremble and rub parts of their bodies against walls or fences; appeared to be irritated or even crazy – thus called mad cow disease

2

Spongiform Encephalopathies

- Spongiform encephalopathies have been diagnosed in sheep
  - Symptoms – their skin becomes so itchy that they scrape off their wool on fences, leading the disease to be called *scrapie*
- In elk and deer, it is called *chronic wasting disease*, due to the emaciated appearance of the affected animals

3

Spongiform Encephalopathies

- Humans have also been affected by spongiform encephalopathies
- *Kuru* – known to affect natives of the eastern highlands of New Guinea
  - Results from the tribal custom of honoring the dead by eating their brains
  - Affected individuals lose coordination and often become demented and eventually die

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Spongiform Encephalopathies

- Creutzfeldt-Jakob Disease (CJD) – affected individuals become very agitated, dizzy, and short-tempered
  - Experience short-term memory loss, lack of coordination, and slurred speech
  - Lethal in all affected humans; very rare and typically affects only the elderly

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Spongiform Encephalopathies

- Recent and alarming trend – increase rate of diagnosis in young British patients
- Autopsy showed their brains looked more similar to those of BSE-infected cattle than CJD-infected humans
- The increased number of people diagnosed with the disease, the structure of their brains, and the lower age of the infected led scientists to believe that BSE was some how being transmitted from infected cows to humans
- This new, transmissible form was named *new-variant CJD (nvCJD)*

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18.1 Infectious Agents

- Genetic diseases are caused by malfunctioning genes, whereas infectious diseases are caused by organisms
- **Pathogens**: _____
- If a pathogen can spread from one organism to another it is _____
- When a pathogen finds a tissue inside the body that will support its growth, it becomes _____
- Bacteria and viruses are the most common infectious _____ (microscopic organisms)

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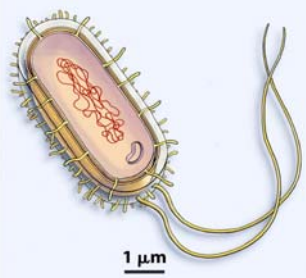
Agent	Disease
Bacteria	• Salmonellosis • Anthrax • Gonorrhea • Botulism • Impetigo • Leprosy • Lyme disease • Tuberculosis • Strep throat • Tetanus • Diphtheria • Bacterial meningitis



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Bacteria

- Very diverse and numerous
  - More in your mouth than there are humans on Earth
- Three common shapes
  - Rod-shaped (_____)
  - Spherical (_____)
  - Spiral (_____)

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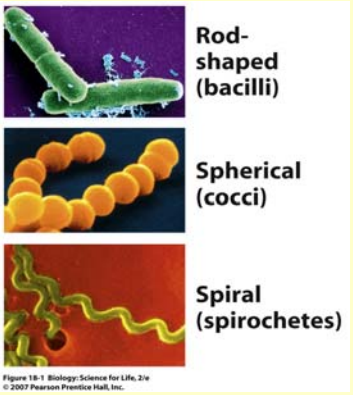

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Bacteria

- Prokaryotic cells
  - Do not have a nucleus
  - DNA is coiled up inside the _____
- Circular genome of double stranded DNA
- Sometimes bacteria contain small extra pieces of DNA called _____

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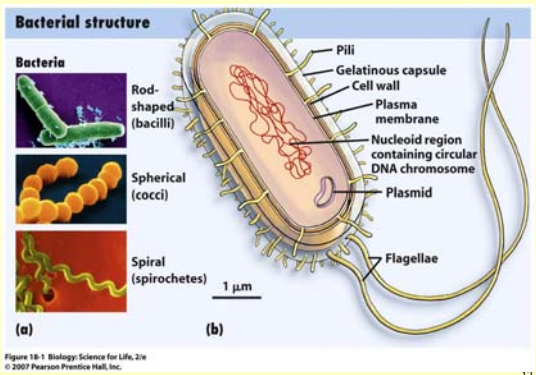

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Bacteria

- Most bacterial cells are surrounded by a _____ that provides rigidity (support) and protection
  - Made of molecules specific to bacteria
- A gelatinous _____ surrounds the cell wall of many bacteria
  - Helps bacteria to attach to tissues they will infect and also evade (escape destruction) the human immune system

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Bacteria

- External _____ can help bacteria move around
- _____ help bacteria attach to each other and exchange genetic information (pass genes to each other)

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Bacteria

- Bacteria divide by _____
  - The chromosome is copied and attached to the plasma membrane
  - The membrane grows and moves the two DNA copies apart
- This asexual reproduction produces identical copies of the bacterial cell

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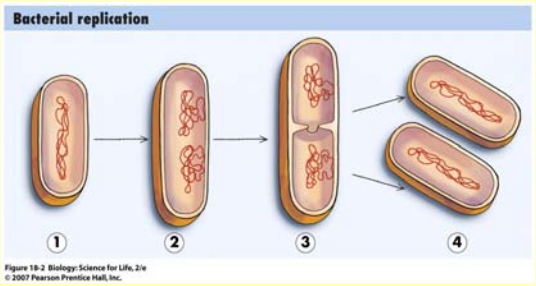

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Bacteria

- The doubling time (time it takes to reproduce) can be as short as 20 minutes, which leads to tremendous numbers quickly
- For example, in 8 hours, a single *Salmonella* bacterium can produce more than 33 million cells
- This is exponential growth and occurs when bacteria are in an area with abundant resources

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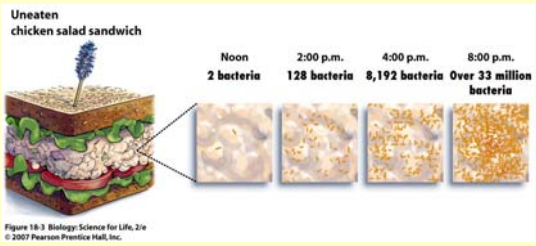

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Bacteria

- Bacteria can live on food, or in a body, causing disease
  - When an infection occurs in your body, the rapidly increasing bacteria support their growth by using your cells' nutrients, effectively preventing your cells from functioning properly
- Bacteria can also cause disease in humans without ever entering the body
  - Molecules secreted by bacterial cells called **toxins** can interfere with the metabolism of humans (cellular processes)

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Bacteria

- Anthrax is caused by the bacterium *Bacillus anthracis*
- Lives in soil and **spores** can get into humans – if inhaled, it can be lethal
- Anthrax isn't a common disease for humans, but it has been used as a weapon of terror
- Anthrax is infectious but not contagious
- When inhaled or in wounds, it produces toxins that produce an accumulation of fluid inside white blood cells called **macrophages**, which then swell and release the toxic chemicals that they normally use to kill bacteria
- Anthrax can be lethal unless immediate antibiotics are administered

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Bacteria

- Some bacteria cause disease and fatalities among humans
- Most bacteria are not harmful to humans and play an important role in nature

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Viruses

- **Viruses** are not considered to be living organisms because:
  - _____
  - _____
  - _____, so they cannot make their own proteins
  - _____
    _____

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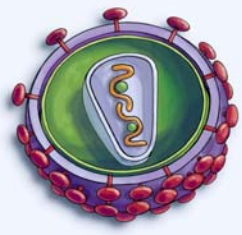
Agent	Disease
Viruses 	• Chicken pox • Measles • Mumps • Influenza • Rabies • Shingles • Smallpox • AIDS • Hepatitis • Viral pneumonia • Viral meningitis • Polio

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Viruses

- Viruses are packets of nucleic acid surrounded by a protein coat
- The virus **genome** (_____) can be DNA or RNA; double- or single-stranded; linear or circular
  - Herpes virus: double-stranded DNA genome
  - Polio virus: single-stranded RNA genome

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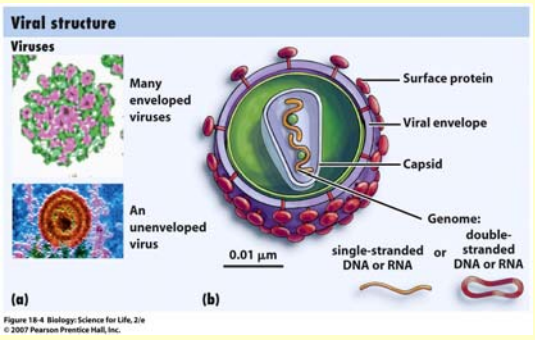

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Viruses

- Viruses have a protein coat surrounding them called a _____
- Some viruses have an additional outer coating called an _____
  - It is derived from the cell membrane of the host cell
  - These viruses are called enveloped viruses

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Viruses

- When the virus enters a cell, it makes copies of itself
- The new viruses leave the cell and infect new cells to continue the infectious process

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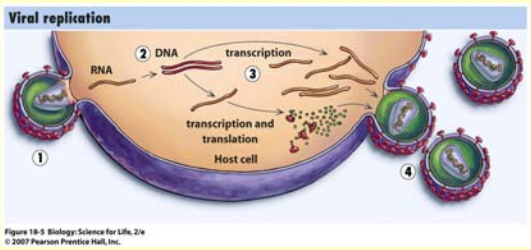

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Viruses

- Some viruses are _____ – dormant for periods of time inside host cells
  - During this time, the virus is not being replicated
  - Example: Herpes virus
- Viruses whose incidence has increased within the past 2 decades or those that seem likely to increase substantially in the near future are called **emerging viruses**
  - Includes SARS (severe acute respiratory syndrome)
    - ✓Causes high fever, chills, and body aches
    - ✓SARS patients can die if the infection causes pneumonia

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Viruses

- Viral infections emerge for various reasons
  - Proliferation of a new agent
  - Detection of a previously unidentified agent
  - Reappearance of a previously known infection
  - Genetic mutation to evade detection by host organism's immune system
- Emergent viruses also arise due to the spread of an existing virus from one species to another
  - For example, the virus causing Ebola jumped to humans from monkeys

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Eukaryotic Pathogens

- _____ are organism that uses host for nutrients and shelter without giving benefits to host
- Parasites are mainly protists and worms

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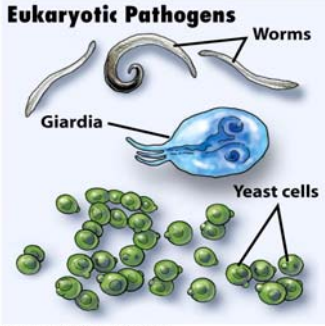
Agent	Disease
Eukaryotic Pathogens 	• Worms cause schistosomiasis, trichinosis, tapeworm • Protists cause amoebic dysentery, giardia, sleeping sickness, and malaria • Fungi cause athlete's foot, oral thrush

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Malaria

- Caused by the eukaryotic pathogen *Plasmodium* and is transmitted by female *Anopheles* mosquitoes
  - In humans, the parasite grow and reproduce in the liver and red blood cells
  - Symptoms include shaking and chills, high fever, and severe headache
  - Damage to kidneys and red blood cells can cause kidney failure and anemia
  - Malaria affects 300 to 500 million people and *kills* nearly 3 million people annually
  - Most common in tropical and subtropical climates

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Schistosomiasis

- Caused by the *Schistosoma* worm
  - Carried by freshwater snails
  - Humans can catch it if in contaminated water
  - The infection causes great discomfort and affects about 200 million humans
  - Symptoms include a rash, itching, chills, fever, cough, and muscle aches
  - This infection is highly prevalent in developing countries where plumbing is lacking

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Infectious Agents

- Infections caused by bacteria, viruses, or eukaryotic parasites have long been known and various treatments (such as chemicals, heat, and radiation) exist
- The class of diseases called **spongiform encephalopathies** are not caused by any of these agents, but rather by infectious agents called prions

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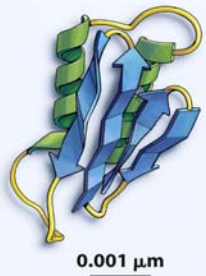
Agent	Disease
Prions 	Spongiform encephalopathies: • Mad cow disease • Scrapie • Chronic wasting disease • Kuru • Creutzfeldt–Jakob disease (CJD)

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Prions

- After a cell synthesizes a protein, the protein folds into its characteristic shape
  - Incorrect folding means that the protein cannot function properly
- A prion is a _____ _____ that, when misfolded, causes spongiform encephalopathy

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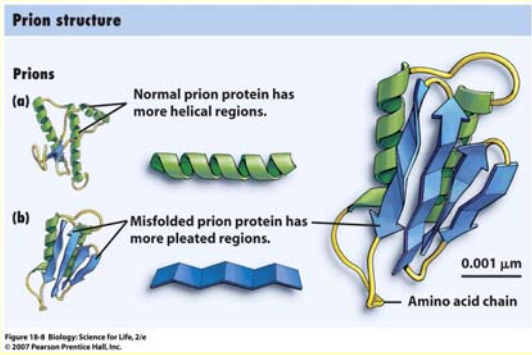

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Prions

- The term *prion* is a shortened form of the term *proteinaceous infectious particle*
- Normal prions are present in the brains of all mammals
- The normal role of the prion in the brain is not clear, but experiments in mice lacking the prion gene, and therefore unable to make the normal version of the protein, indicate that it may protect mammals against dementia and other degenerative disorders associated with aging

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Prions

- CJD is believed to either arise spontaneously when a prion is mistakenly misfolded or caused by a mutation to the gene that encodes the prion protein in humans, leading to the production of a misfolded prion protein
- nvCJD results when an individual is infected by misfolded prion proteins
- When infected with a prion, it searches out properly folded proteins and refolds them into the mutant, disease-causing version

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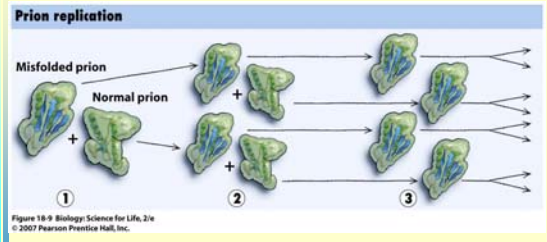

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Prions

- Unlike other infectious agents, prions contain no genetic information
- Unlike other proteins, they don't easily degrade – so they propagate relentlessly

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18.2 Epidemics

- An **epidemic** is a contagious disease that spreads very rapidly in a population
- **Epidemiologists** – scientists who attempt to determine
  - Who is prone to a particular disease
  - Where the risk of the disease is highest
  - When the disease is most likely to occur
- Epidemiologists work to link victims and find common factors
  - These biologists are highly involved in public health policy

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Epidemics

- For an epidemic to occur:
  - Infectious agent must cause disease
  - Must be transmissible from one organism to another
- Transmission is the exchange of pathogen from infected individual to uninfected hosts; occurs in 4 ways…

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Exposure to Infected Body Fluids

- Blood
  - AIDS
  - Hepatitis
- Saliva
  - Mononucleosis
- Semen / vaginal fluid
  - STDs (sexually transmitted diseases)

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Transmission Through an Intermediate Host

- **Vector** – organism that carries disease-causing microorganisms and transmits them from one host to another, such as
  - Mosquitoes for the West Nile virus
  - Deer tick and Western black-legged tick, which carry *Borrelia burgdorferi*, the cause of Lyme disease

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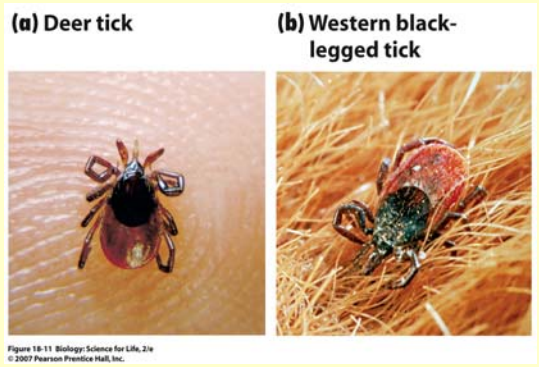

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Inhalation

- Pathogens enter the body along with the air we breathe
- Influenza virus causes the flu
- It is transmitted when an infected person coughs, sneezes or speaks and sends the virus into the air, and other people then inhale the virus
- It can also be caught by touching a surface with the viruses on it and then touching nose or mouth

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Ingestion

- Pathogen enters body with food
- Spongiform encephalopathies are caused when prions are ingested
  - From eating food contaminated by brain or spinal cord tissue
- Scientists believe that cows with mad cow disease ingested misfolded proteins when they ate the remnants of diseased animal that were present in their feed called meat-and bone meal
- Humans become infected with misfolded prions when they eat meat from diseased cows (or from other humans, as in the case with Kuru)

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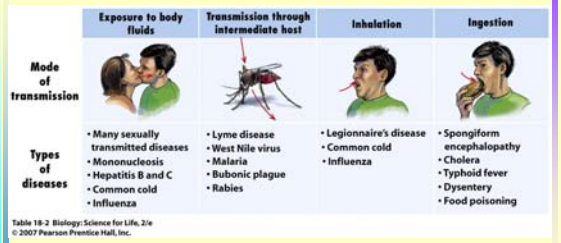

Table 18-2 Biology: Science for Life, 2/e

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18.3 The Body's Response to Infection: The Immune System

- Organisms have evolved defenses against pathogens gaining access to the body
- In humans and most other vertebrates, there are three lines of defense…

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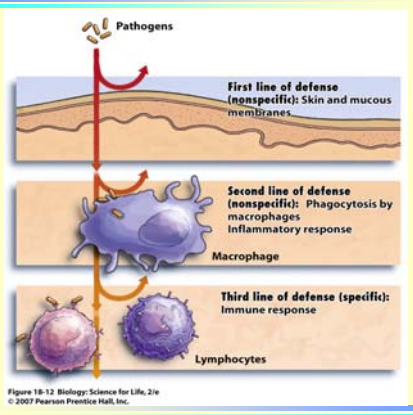

Figure 18-12 Biology: Science for Life, 2/e

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First Line of Defense: Skin and Mucous Membranes

- Skin, secretions, and mucous membranes are physical and chemical barriers that are **nonspecific defenses**:
  - They do not distinguish one pathogen from another
- Skin
  - Keeps out organisms physically
  - Glands in the skin secrete chemicals that slow down the growth of bacteria

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First Line of Defense: Skin and Mucous Membranes

- Tears and saliva contains enzymes that break down bacteria cells
- Mucous Membranes:
  - Line the respiratory system, digestive system, urinary system, and reproductive tract
  - Secrete mucus to trap and remove pathogens

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Second Line of Defense: White Blood Cells, Proteins, and Inflammation.

- Are also nonspecific defenses
- An internal defense system
- White blood cells indiscriminately attack and ingest invaders
- White blood cells called **macrophages** ingest through **phagocytosis**
  - Grab debris or invaders with **pseudopodia** (cellular extensions used for eating and moving)
  - Engulf and bring inside cell
  - Enzymes destroy debris or invaders

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Second Line of Defense: White Blood Cells, Proteins, and Inflammation

- Other white blood cells called **natural killer cells** attack virus infected cells by penetrating their plasma membranes and causing them to burst
- Proteins called interferons and complement proteins defend against pathogens as well

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Second Line of Defense: White Blood Cells, Proteins, and Inflammation

- **Interferons** are proteins that are produced by virus-infected cells to signal other nearby cells to make proteins that inhibit viral reproduction
  - They are released when the infected cells die and they bind to receptors on uninfected cells and stimulate the healthy cells to produce proteins that inhibit viral reproduction

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Second Line of Defense: White Blood Cells, Proteins, and Inflammation

- **Complement proteins** coat surfaces of invaders making them easier for macrophages to engulf
  - The also poke holes in membranes surrounding microbes, causing them to break apart
  - Also amplify the inflammatory response

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Second Line of Defense: White Blood Cells, Proteins, and Inflammation

- The **inflammatory response** is a reaction that produces redness, swelling, pain and fever at infection site
  - Caused by release of chemicals from macrophages
- Inflammation causes blood vessels in the area to leak, allowing fluid and white blood cells into the area causing swelling and pain
- Fever, which is thought to slow growth of microbes in area, is also caused by the macrophages

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Third Line of Defense: Lymphocytes

- If a pathogen makes it past the first 2 nonspecific defense systems, the immune system presents a third line of defense
- Cells of the immune system identify and attack specific microorganisms that are recognized as foreign
- This **specific defense system** consists of millions of white blood cells, called **lymphocytes**
  - They travel throughout the body by moving through spaces b/t cells and tissues or by transport via the blood and the lymphatic system

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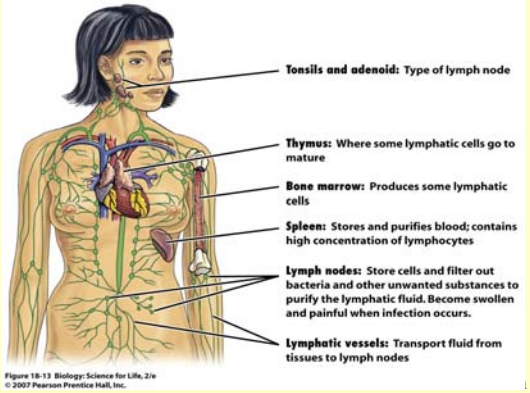

Third Line of Defense: Lymphocytes

- The specific response generated by the immune system is triggered by proteins and carbohydrates on the surface of pathogens, or on cells that have been infected by pathogens
- Molecules that are foreign to the host and stimulate the immune system to react are called **antigens**
  - Found on invading viruses, bacteria, fungi, protozoans, and worms, as well as molecules on the surface of foreign substances such as dust, pollen, and transplanted tissues
  - Present on tissues transplanted from one person to another b/c every individual's cells have a characteristic set of proteins and sugars on their surfaces – this is why transplant patients are given drugs to suppress their immune system

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Third Line of Defense: Lymphocytes

- When antigens are discovered, two types of lymphocytes are produced
  - **B lymphocytes (B cells)**
  - **T lymphocytes (T cells)**
- Like macrophages, B cells and T cells circulate throughout the blood and lymph systems and are concentrated in the spleen and lymph nodes

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Third Line of Defense: Lymphocytes

- B cells and T cells display **specificity –** they recognize specific antigens
- B cells and T cells both eliminate antigens, but in different ways:
  - B cells secrete proteins called **antibodies** that bind to and inactivate antigens
  - T cells attack invaders directly

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Third Line of Defense: Lymphocytes

- Lymphocytes' ability to recognize foreign molecules is based on the presence of proteins whose shape is complementary to a portion of the foreign molecule, called **antigen receptors**
- These receptors are either attached to the surface of the lymphocyte or secreted by the lymphocyte
  - Both B and T cells have receptor molecules on their surfaces, but B cells also secrete antibodies into the surrounding body fluids to locate and destroy antigen

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Third Line of Defense: Lymphocytes

- The ability of the B and T cells to respond to specific antigens begins before birth; thus, we are able to respond to infectious agents the first time we are exposed
- The ability to respond to infection, the **immune response**, results from the increased production of B cells and T cells
- B and T cells recognize different types of antigens
  - B cells recognize and react to small, free-living microorganisms such as bacteria and the toxins they produce
  - T cells recognize and respond to body cells that have gone awry, such as cancer cells or cells that have been invaded by viruses; also respond to transplanted tissues and larger organisms such as fungi and parasitic worms

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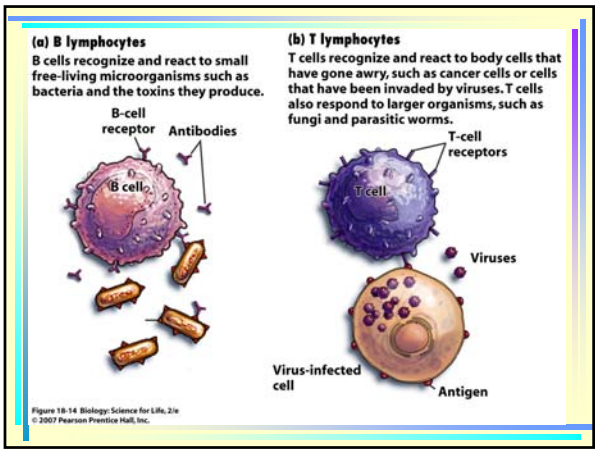

Making B and T Cells

- Lymphocytes are produced from special cells, called **stem cells**, that have the ability to become any other cell type
- Many parts of the body, including bone marrow, retain stem cells that can develop into more specialized cells
- Bone-marrow stem cells enable the bone marrow to produce blood cells throughout the lifetime of a person
- Lymphocytes are produced from stem cells of bone marrow and released into the blood stream
  - B cells continue and complete development in bone marrow
  - T cells finish development in thymus gland, located behind the sternum

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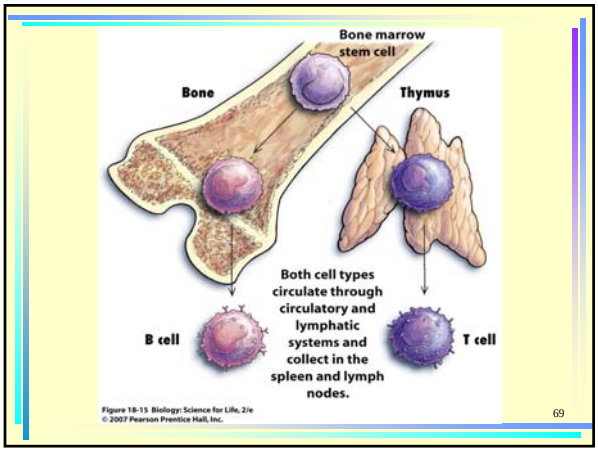

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Antigen Diversity

- Lymphocytes can recognize trillions of different antigens
  - This results from the trillions of different antigen receptors that are produce by B and T cells
- B and T cells have evolved a mechanism to generate an enormous variety of receptors from a limited number of genes
- As the cells develop, each cell's DNA segments that code for the production of receptors rearrange themselves
  - Some portions are cut out, and the remaining DNA segments are joined together
  - Each unique arrangement of DNA encodes a different receptor protein and once synthesized, they move to the surface of the B or T cell and act as antigen receptors

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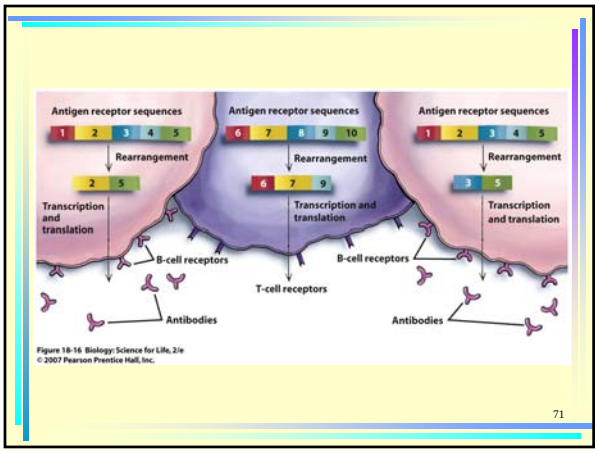

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Self Versus Nonself

- While B and T cells are maturing, their antigen receptors are tested for potential self-reactivity
- Cells of a person have characteristic proteins on their surface, and developing lymphocytes are tested in the thymus to determine whether they will bind to self-proteins
- Any developing lymphocyte whose antigen receptors bind to self-protein is eliminated, making an immune response against one's self less likely
- Lymphocytes whose receptors do not bind are then allowed to develop to maturity

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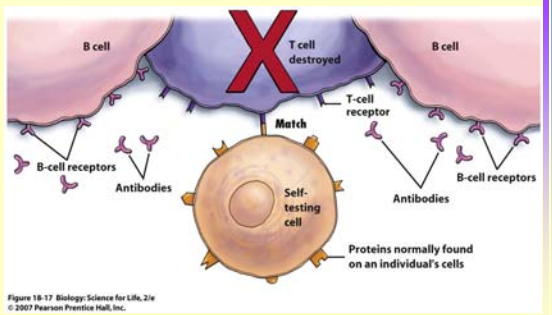

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Self Versus Nonself

- Thus the body normally has no mature lymphocytes that react against self-proteins, and the immune system exhibits self-tolerance
- When this testing fails, the cells of the immune system attack normal body cells
- **Autoimmune diseases:** diseases that result when a person's immune system is attacking normal body cells
  - Multiple sclerosis – occurs when T cells attack a specific protein on nerve cells in the brain
  - Insulin-dependent diabetes - T cells and B cells attack cells that produce the hormone insulin in the pancreas
  - Lupus – occurs when self-antibodies to the nuclei of all cells are formed; the anti-nuclear antibodies build up in cells, causing inflammation of many tissues in the body

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Humoral and Cell-Mediated Immunity

- Major systems of immunity:
  - **Humoral immunity:** B cells operate (so called because antibodies circulate through bodily fluids, which were once called "humours")
  - **Cell-mediated immunity:** T cells operate (because this immunity is dependent on cells)

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Humoral Immunity

- B-cell-mediated immunity that occurs when a B-cell receptor binds to an antigen
- When a B cell encounters an antigen, it immediately makes copies of itself, resulting in a population of identical cells able to help fight the infections
  - This population of cells is called a **clonal population** – all the cells have the same DNA arrangement and they all carry the same receptor on their membrane

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Humoral Immunity

- **Memory cells:** cells of the clonal population that will help the body respond more quickly if the infectious agent is encountered again
  - If subsequent infection occur, the large number of memory cells facilitates a quicker immune response

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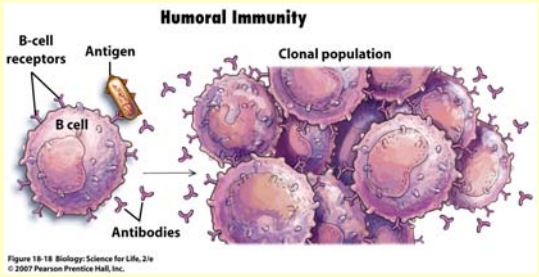
Humoral Immunity

- In addition to memory cells produced, B cells also produce **plasma cells**
  - Do not express receptor antibodies on their membrane; instead they secrete antibodies specific to an antigen
  - The secreted antibodies circulate within body fluids, including tears and saliva; when they encounter an antigen, they bind to it
  - The antigen-antibody complex then combines with complement proteins, which causes the cell to break open
  - Antigen-antibody complex binding also increases phagocytosis and the overall ability of the immune system to destroy invaders

78



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Cell-Mediated Immunity

- T cells also respond to infection by undergoing rapid cell division to produce memory cells
- T cells do not secret antibodies like B cells; they directly attack other cells
- Two types of attacking T cells
  - Cytotoxic T cells
  - Helper T cells

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Cell-Mediated Immunity

- **Cytotoxic T cells** attack and kill body cells that have become infected with a virus
  - When a virus infects a body cell, viral proteins are placed on the surface of the host cell; the cytotoxic T cells recognize these proteins as foreign, bind to them, and destroy the entire cell
  - This is done before the virus has time to replicate by releasing a chemical that causes the plasma membrane of the target cell to leak

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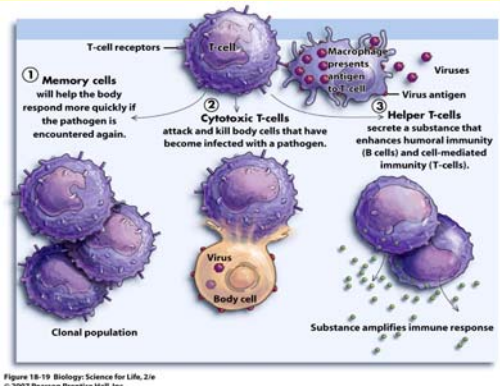
Cell-Mediated Immunity

- **Helper T cells** (also called *T4 cells*) enhance cell-mediated immunity and humoral immunity by secreting a substance that increases the strength of the immune response
- They detect invaders and alert the B and T cells that infection is occurring
- Without helper T cells, there can be almost no immune response
  - The AIDS virus, HIV, infects helper T cell, thus crippling the body's ability to respond to any infection

82



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Cell-Mediated Immunity

- Macrophages also help fight infection by transferring an antigen to their own plasma membrane, thus alerting the immune system, via the T cell, to a foreign antigen present in the body

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There Is No Immune Response to Prions

- An inability to mount an immune response can be the result of an infectious agent carrying antigens for which no amount of DNA rearrangement can yield the proper receptor
- In other cases, one group of people may carry DNA segments that can be rearranged to produce the right receptors, while other groups do not
  - This partly explains why some people do not become ill when exposed to an infectious disease, while others die from the same exposure

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There Is No Immune Response to Prions

- In some instances, an infectious agent is effectively fought for a long period of time and then it changes (reemerges)
- Pathogens undergo evolution in order to evade the immune system
- Many viral and bacterial infections can be prevented by **vaccines** given in an attempt to boost the immune system prior to actual exposure to a pathogen

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There Is No Immune Response to Prions

- Vaccines are made of components of the disease-causing organisms – proteins from plasma membrane of bacterial cell, parts of a virus, or a whole virus that has been inactivated
- The immune system responds to the introduced vaccine's challenge by producing the clonal population of memory cells that will be prepared for a real infection by the virus, if it occur
- Some vaccines require multiple doses before a sufficient response is generated; others require booster shots to maintain protection

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There Is No Immune Response to Prions

- Flu vaccine
  - Because viruses evolve so quickly, a new flu vaccine must be created annually
  - To create, scientists predict which strains of flu viruses will be encountered

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There Is No Immune Response to Prions

- Spongiform encephalopathies do not instigate the immune system to fight
- The prions are abnormally folded proteins, but the proteins are still considered self
- Prions bypass all three lines of defense
- After ingestion, the prions move to the spleen and lymph nodes and refold all the prions there
- Then they move to the brain and spinal cord, refolding normal proteins

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There Is No Immune Response to Prions

- Lack of properly folded proteins leads to death
- Treatment will have to be different from other pathogens because treatment such as heat and radiation, which is generally effective in destroying bacteria and viruses, do not work against prions
  - Treatment will require something that can recognize prions as different from regular proteins
  - Scientists want to figure out how to stabilize the normal prion protein
  - For now, epidemiologists are focused on how to prevent spread

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18.4 Preventing the Spread of Prion Diseases

- It is illegal to import cows, sheep, goats, and deer into the U.S.
- Feeding practices can not include using animal meat or bone meal from other mammals
- Any material made from cow skulls, brains, eyes, vertebral columns, or spinal cords is prohibited for use in human foods or cosmetics
- These measures are aimed at preventing an epidemic of mad cow or the human equivalent (Creutzfeldt-Jakob disease)
- Success could depend on how well farmers and breeders follow government regulations

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