The cardiovascular system consists of the heart, blood, and blood vessels. The lymphatic system consists of the lymph, lymphatic vessels, lymph nodes, and lymphoid organs (tonsils, appendix, thymus gland, and spleen). The function of the cardiovascular system is to circulate blood throughout the body's tissues so it can deliver certain substances to cells and remove other substances from them. Some plasma filters out of the blood capillaries and into spaces between the tissue cells (interstitial spaces). The fluid circulating between tissue cells is called interstitial fluid. Lymphatic capillaries surrounding the tissue cells are larger and more permeable than the blood capillaries and as the interstitial fluid moves around the tissue cells it is picked up by the lymphatic capillaries and the fluid is now known as lymph. Eventually all the lymph is returned to the blood of the veins. The cardiovascular and lymphatic systems transport fluids throughout the body and they unite the organs and tissues of the body, delivering, exchanging, and removing cells and molecules. Because both systems circulate various substances throughout the body, they can serve as vehicles for the spread of infection. The lymphatic capillaries readily pick up microorganisms or their products. At various regions along the lymphatic system, lymph nodes, which contain macrophages, help to clear the lymph of microorganisms. The cardiovascular and lymphatic systems do not support normal flora, but are occasionally contaminated by pathogens. At times, the number of microorganisms circulating through the lymph nodes is so great that the nodes become infected, enlarged, and tender. Lymph nodes contain T lymphocytes which carry out important immune defense functions and B lymphocytes produce antibodies against the infectious agent.

Diseases of the cardiovascular and lymphatic systems frequently affect several other systems because the infectious agents are easily disseminated through blood and lymph. Although blood is usually sterile, moderate numbers of microorganisms are usually not harmful. When microorganisms enter the bloodstream from a wound or other infection, bacteremia, a brief, asymptomatic period in which bacteria circulate in the blood but do not multiply, can occur. Immune defenses ordinarily eliminate these microorganisms. If the defenses of the blood and lymph systems fail, the microorganisms can undergo rapid multiplication, resulting in septicemia, or blood poisoning. The bacteria can then be disseminated to other tissues and organs. Symptoms of septicemia include fever, shock, and lymphangitis (red streaks due to inflamed lymphatic vessels beneath the skin from the site of infection). Sometimes the red streaks end at a lymph node, where the lymphocytes attempt to stop the invading microorganisms. A person suffering from septicemia can exhibit symptoms of septic shock, which is life-threatening. The small arteries and vessels are constricted and may collapse, peripheral blood circulation decreases, and peripheral tissues become oxygen-starved. The person develops rapid breathing and heartbeat, a drop in blood pressure, and mental confusion. The extremities become cool and
may turn blue. Coma and death may result.

The microorganisms most frequently associated with septicemia are Gram negative rods, although a few Gram positive bacteria and fungi are also implicated. The Gram negative rods include, *Escherichia coli*, *Enterobacter aerogenes*, *Serratia marcescens*, *Proteus mirabilis*, *Pseudomonas aeruginosa*, *Klebsiella* spp., and *Bacteriodes* spp. These bacteria enter the blood from a focus of infection in the body. The endotoxins produced by these organisms when the cells lyse are directly responsible for septic shock. Once released they damage blood vessels, causing low blood pressure and shock. Antibiotics often worsen the situation by causing cell lysis of a large number of bacteria resulting in the release of endotoxins from their cell walls. More damage is caused to the blood vessels and blood pressure drops even further. A few cases of septic shock are caused by exotoxins.

One-third of all septicemia cases are *nosocomial* (hospital-acquired) and appear within 24 hours after an invasive medical procedure, such as catherization or insertion of feeding tubes, have been performed. Septicemia has a mortality rate of 50-70% and accounts for about 100,000 deaths per year in the U.S.

There are three categories of infection of the heart:

1. **endocarditis** - infection of the heart’s inner lining or endocardium. It is usually bacterial, but occasionally fungal.

2. **myocarditis** - infection of the heart muscle itself, or myocardium. It is usually viral, but rarely bacterial or fungal. A unique form of infectious myocarditis is American trypanosomiasis or Chagas’ disease, which is caused by a protozoan.

3. **pericarditis** - infection of the heart’s surrounding membrane, or pericardium. It is usually viral, but occasionally bacterial or fungal.

**Bacterial Diseases**

1. **Bacterial or Infective Endocarditis**

Bacterial endocarditis is a life-threatening infection and inflammation of the endocardium and valves of the heart. Microorganisms from another body site of infection are transported to the heart. Bacteria that adhere to and multiply on the endocardium become surrounded by clotlike material from the blood. The masses of bacteria and clots are called vegetations. Bacteria in vegetations are protected from the body’s defenses and from bloodborne antibodies. As vegetations grow, pieces break off, forming emboli that can lodge in small blood vessels and interrupt blood supply to distant organs. Emboli can cause death if they
travel to the brain or kidneys. Vegetations can damage heart valves resulting in an inadequate blood pressure to supply vital organs. The result is **congestive heart failure** (accumulation of fluids around the heart).

Bacterial endocarditis is divided into **acute** and **subacute**.

**Acute Bacterial Endocarditis**

a. **causative agent:** *Staphylococcus aureus*

b. **method of transmission:** Intravenous drugs and serum postoperative infections.

c. **symptoms:** It is more rapidly progressive than subacute and it causes rapid destruction of the heart valves. It is frequently fatal within a few days or weeks if untreated. Fever, fatigue, malaise, valve damage, and heart failure occur.

d. **prevention:** Avoid intravenous drug abuse.

e. **treatment:** cephalosporins, penicillinase-resistant penicillins, followed by surgical repair of damaged valves.

**Subacute Bacterial Endocarditis**

a. **causative agent:** *Streptococcus pyogenes*

b. **method of transmission:** The bacteria enter the bloodstream from infected tonsils or following tooth extraction. It usually occurs in people who have abnormal or defective hearts which allows the bacteria to adhere to the endocardium and valves.

c. **symptoms:** It starts more gradually, progresses more slowly, and lasts longer than acute bacterial endocarditis. Fever and fatigue may last months, anemia, general weakness, and heart murmurs occur.

d. **prevention:** People who have heart defects should take penicillin before dental surgery or other minor surgery.

e. **treatment:** penicillin
2. **Tularemia**

   a. **causative agent:** Francisella tularensis - it is a pleomorphic (able to change forms) organism which exhibits one of several forms depending on how the infection is acquired.

   b. **method of transmission:** It is most frequently acquired through minor skin abrasions and by rubbing the eyes after handling infected small wild mammals. 90% of all cases are contracted from rabbits. Transmission is also by ingestion of infected inadequately cooked meat (squirrel, rabbit, and deer). It can also be spread by the bites of arthropods, such as deer flies, ticks, or rabbit lice.

   c. **symptoms:** Entry through the skin results in local inflammation and a small ulcer at the site of infection. After a 48 hour incubation period, symptoms begin with an abrupt high fever (104-106°F), with chills and shaking. After about a week, fatigue, debilitating headache, and buboes (regional lymph node swelling) occur. The lymph nodes may contain pockets filled with pus.

   d. **prevention:** Avoid contact with infected animals, wear gloves when handling or skinning animals, and in tick-infested areas wear protective clothing and search clothing and skin for ticks. An attenuated live vaccine is available for high-risk laboratory workers.

   e. **treatment:** Streptomycin, gentamicin, or tetracycline, but prolonged administration is necessary to prevent relapses. Naturally acquired immunity is usually permanent, but recurrences have been reported.

3. **Brucellosis (Undulant Fever)**

   a. **causative agent:** Brucella abortis (cattle), B. suis (swine), B. melitensis (sheep and goats), and B. canis (dogs)

   b. **method of transmission:** Direct contact with infected animals or their secretions on farms or in slaughterhouses, consuming infected unpasteurized dairy products, direct contact with skin abrasions, and through the respiratory tract by way of aerosols.

   c. **symptoms:** Inside the host the facultative intracellular parasites are ingested by macrophages, multiply and move through the lymphatic system into the bloodstream where they cause acute bacteremia within 1 to 6 weeks. A gradual onset of symptoms occurs which includes a cyclic or undulating fever that is high in the afternoon and low at night after profuse sweating, fatigue, headache, and loss of appetite. The bacteria may spread to the
lymph nodes, liver, and spleen, causing them to enlarge, and jaundice may result.

d. prevention: Eliminate infected animals from domestic herds, immunization of animal herds, pasteurize milk and dairy products, provide education and protective clothing for workers with occupational exposure.

e. treatment: Tetracycline and streptomycin, gentamicin, or rifampin may be added in severe cases. Prolonged treatment is necessary because the bacteria are in macrophages and resistant to antibiotic therapy. Recovery is usually spontaneous, but chronic aches and nervousness may develop.

4. Relapsing Fever

a. causative agent: Borrelia hermsii, B. turicatae, B. parkeri (Gram negative spirals)

b. method of transmission: Salivary secretions from the bites of soft ticks that feed on rodents.

c. symptoms: It is characterized by alternating fever and nonfever periods. After an incubation period of 3-5 days, there is a sudden onset of chills, high fever (greater than 105°F), jaundice, and rose-colored spots. The fever persists for 3-7 days and subsides. After 7 to 10 days a fever recurs for 2 to 3 days. Three to four relapses may occur, each shorter and less severe. Relapses are explained by changes in the microorganisms' antigens. The body's immune response destroys most of the antigens, but a few bacteria remain and have surface antigens the immune system fails to recognize. The bacteria multiply and cause a relapse. Each relapse reproduces a new population of bacteria that have evaded the immune defense mechanisms. The disease is particularly dangerous in pregnant women because it can cross the placenta and infect the fetus.

d. prevention: Tick control. Ticks feed mainly at night for about a half an hour. Victims such as campers or occupants of houses infested with tick-carrying rodents never realize they have been bitten.

e. treatment: tetracycline, chloramphenicol, penicillin, or erythromycin.
5. **Lyme Disease** (Lyme Borreliosis)

   It is the most common tickborne disease in the U.S.
   a. **causative agent:** *Borrelia burgdorferi* (spirochete)
   b. **method of transmission:** Deer and field mice are the most important animal reservoirs. It is transmitted by the bite of a tick (*Ixodes* spp.) that feeds on infected animals.
   c. **symptoms:** There are three stages and one, two, or all three may occur. The first stage is usually a rash that appears at the bite site 3-32 days after the bite. It is a red area that clears in the center as it expands to about 15cm in diameter and it resembles a bull’s-eye. In a couple of weeks flu-like symptoms occur during the second stage as the rash fades. Heartbeat becomes irregular, headache, stiff neck, muscle aches, and fatigue occur. Bacteria spread to the lymph nodes, blood, and eventually other organs such as the brain, joints, heart, liver, spleen, and kidneys. After 6 months the third stage occurs which includes facial paralysis, meningitis, and encephalitis. Arthritis may occur and become chronic which lasts for several years. The bacteria can cross the placenta and infect the fetus.
   d. **prevention:** Avoid tick bites and rodent infested areas. Wear protective clothing and check clothing and skin for ticks.
   e. **treatment:** Early diagnosis is crucial because the infection is easier to cure. Doxycycline, amoxicillin, or erythromycin. In the later stages they may have to be administered intravenously.

6. **Rocky Mountain Spotted Fever**

   a. **causative agent:** *Rickettsia rickettsii*
   b. **method of transmission:** The reservoir is arthropods including ticks (*Dermacentor*), lice, and fleas. It is transmitted by salivary secretions from bites.
   c. **symptoms:** It is a severe disease characterized by fever and a rash. The bacteria multiplies in the smooth lining of blood vessels, and damages capillaries in the skin resulting in leaking of blood into the tissues and producing a spotty rash. The rash is sometimes mistaken for measles. Early symptoms include fever, headache, vomiting, and the rash within 1 week of the bite. Eventually the rash covers the entire body, including the palms and soles. It becomes dark, and slightly raised, sometimes resembling tiny bruises. In severe cases, internal organs suffer similar capillary damage. 20% of untreated cases of overwhelming infection with abnormal blood clotting leads to shock and death. Children
are more likely to become infected, but adults are more likely to die.

d. prevention: Wear protective clothing and vigilantly inspect clothing, skin, and especially hair during visits to tick-infested areas.

e. treatment: Tetracycline and chloramphenicol are the only affective antibiotics.

7. Endemic or Murine Typhus

a. causative agent: Rickettsia typhi

b. method of transmission: Rat fleas (Xenopsylla cheopis) from infected rats, mice, or squirrels defecate while biting, infecting the humans they bite.

c. symptoms: Humans rub the microorganisms into the bite wounds or transfer them to mucous membranes. After 10-14 days incubation, abrupt onset of fever, chills, and a crushing headache occur, followed by a rash in 3-5 days.

d. prevention: Avoid rat-infested areas and eliminate rodents. Rat control is the best preventive measure for the disease. People who work in mice or rat-infested areas (shipyards or grain storage elevators) are most at risk.

e. treatment: The disease is self-limiting and lasts about 2 weeks if untreated. Tetracycline or chloramphenicol can be administered.

8. Cat-Scratch Fever

a. causative agent: Afipia felis (Gram negative rod), Rochalimaea henselae (rickettsia)

b. method of transmission: Cats acquire the microorganisms from the environment and carry them on their claws or in their mouth. When a cat scratches, bites, or lick, it transmits the microorganisms to humans.

c. symptoms: After 3 to 10 days symptoms begin with a pustule or papule (raised area) at the infection site that progresses to a rash, swelling of the lymph nodes (usually under the arm pit or in the groin), and prolonged fever, headache, swollen glands, and conjunctivitis which last for a few weeks.
d. **prevention**: Avoid cat scratches, bites, and licks, and keep cats indoors.

e. **treatment**: Rifampin, tetracycline, doxycycline, trimethoprim-sulfamethoxazole, or ciprofloxacin.

9. **Rat Bite Fever**

   a. **causative agent**: *Streptobacillus moniliformis*

   b. **method of transmission**: It is present in 50% of all wild and laboratory rats. Most cases result from bites of wild rats and half occur in children under 12 years of age living in overcrowded, unsanitary conditions. It can also result from bites and secretions of mice, squirrels, dogs, and cats.

   c. **symptoms**: It begins as a localized infection at the bite site that heals promptly. In 1-3 days a headache begins and new lesions appear elsewhere, except on the palms and soles. The fever is recurrent, arthritislike symptoms (inflammation, pain, and stiffness), and infection of the lymphatic vessels occur.

   d. **prevention**: Eradication of rats and disinfection of bite sites.

   e. **treatment**: streptomycin or penicillin.

**Viral Diseases**

1. **Dengue Fever** *(Breakbone Fever)*

   a. **causative agent**: flavivirus

   b. **method of transmission**: *Aedes albopictus*, an aggressive biting mosquito is an effective carrier of the virus and can transmit it from person to person.

   c. **symptoms**: 2 to 7 days after the bite, high fever, headache, loss of appetite, nausea, weakness, and in some cases a rash occur. Severe bone and joint pain (breakbone) may occur.

   d. **prevention**: Mosquito control is the primary method of preventing the disease. Avoid bites of mosquitoes by wearing protective clothing and mosquito repellant.
2. Infectious Mononucleosis (Mono)
   It is sometimes referred to as the "kissing disease".
   a. causative agent: Epstein-Barr virus (EBV)
   b. method of transmission: Transfer of saliva from the parotid glands by kissing, and the sharing of drinking glasses and eating utensils. By midlife 90% of U.S. residents have been infected with EBV.
   c. symptoms: After an incubation period of 4-7 weeks, fever, sore throat, swollen lymph nodes in the neck, general weakness, fatigue, and an enlarged spleen occur. B lymphocytes proliferate and are counteracted by T lymphocyte proliferation, and after recovery, the virus remains latent in a small number of B lymphocytes. Major complications involving the central nervous system or fatal rupturing of the spleen may occur, but is rare.
   d. prevention: Peak of incidence occurs between 15 to 25 years of age and college populations have a high incidence. Avoid kissing and sharing glasses and eating utensils with infected individuals.
   e. treatment: It is self-limiting, recovery is complete in a few (4-6) weeks, and immunity is permanent.

Protozoan Diseases

Worldwide, protozoans are among the most common pathogens of the cardiovascular and lymphatic systems. Protozoans that cause disease often have complex life cycles and their presence may severely affect humans.

1. Toxoplasmosis
   a. causative agent: Toxoplasma gondi - It is an intracellular parasite and can invade many tissues.
   b. method of transmission: It infects many warm-blooded animals both domestic and wild. Humans usually become infected through contact with feces of domestic cats that forage for natural foods, especially infected rodents. Another common means of transmission is the consumption of raw or undercooked meat (steak tartare or raw ground beef). The organism can be transferred
across the placenta of an infected mother to the fetus. The microorganism undergoes its only sexual phase in the intestinal tract of cats. Oocysts are shed in the cats feces and contaminate food and water that can be ingested by other animals. The oocysts contain sporozoites that invade host animal cells and form trophozoites called tachyzoites. The intracellular parasites reproduce rapidly (tachys means rapid), and the increased numbers cause the rupture of the host cell, with the release of more tachyzoites. As the immune system becomes increasingly effective, the disease enters a chronic phase in which the infected host cells develop a wall to form a tissue cyst. The numerous parasites called brachyzoites (brachys means slow) within the cysts reproduce very slowly, if at all and persist for years, especially in the brain. Tachyzoites or tissue cysts are ingested in undercooked meat.

c. symptoms: It causes mild lymph node inflammation in most humans and the infection is usually asymptomatic. It can be serious in developing fetuses, newborn infants, and sometimes in young children. Congenital defects, including accumulation of cerebrospinal fluid, seizures, convulsions, deafness, abnormally small head, blindness, mental retardation, and disorders of movement may occur. It can also be responsible for stillbirths and spontaneous abortions. If infection occurs after birth, the symptoms are similar to, but less severe than, those seen in fetuses. Infants may have an enlarged spleen and liver, and a rash.

d. prevention: Cook meat well and avoid infected cat feces. Pregnant women should avoid contact with raw meat and cat feces, and cats should be kept out of sandboxes where children play, especially if the child might carry the microorganism to a pregnant woman. Oocysts in cat feces are not infective for the first 24 to 48 hours after they are passed and infection can be minimized by emptying litter boxes daily and by keeping cats indoors.

e. treatment: It is usually self-limiting. Pyrimethamine and trisulfapyridine or sulfadiazole used in combination, but no treatment can reverse permanent damage from prenatal infection.

2. Babesiosis

a. causative agent: Babesia microti

b. method of transmission: Small rodents are the reservoir for the protozoan and it is transmitted by the bite of a tick (Ixodes) that is the same vector for Lyme disease. The protozoan enters the blood by way of the bite of an infected tick and invades and multiplies in the erythrocytes (red blood cells).
c. **symptoms:** Many cases are asymptomatic, but when symptoms appear they usually begin with sudden high fever, chills, headache, fatigue, and muscle pain. Anemia and jaundice may occur as red blood cells are destroyed. The symptoms usually last for several weeks and are followed by a prolonged carrier state. It is fatal in individuals that have had their spleen removed, elderly, and the immunosuppressed.

d. **prevention:** Avoid tick bites, wear protective clothing, and search clothing and skin for ticks.

e. **treatment:** Chloroquine and clindamycin in combination. Most individuals recover without treatment.

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**Helminth Disease**

**Schistosomiasis (Bilharzia)**

This disease is not contracted in the U.S., but more than 400,000 immigrants to the U.S. have the disease.

a. **causative agent:** *Schistosoma* spp. (blood fluke)

b. **method of transmission:** The life cycle begins when water is contaminated with infected human feces or urine. The eggs in the feces or urine hatch into infective larva called *miracidia*. The *miracidia* infect a particular species of freshwater snail and develop into a larva called *cercariae*. The *cercariae* are released and penetrate the skin of humans as they wade in the water. The *cercariae* enter the blood, where they mature into male and female worms. The female lives in a groove in the males’ body and they produce enormous numbers of eggs. The eggs pass from the blood into nearby organs and are excreted in the feces or urine.

c. **symptoms:** A person can remain infected for decades because the schistosomes acquire on their surface a host-derived antigen that keeps them from being recognized and eliminated by the immune system. As the worms multiply, the individual experiences fever, fatigue, and pain in the affected organ (small intestine, colon, or urinary bladder depending on the species). Eventually, the infected tissues become so severely irritated that the body reacts against them as a foreign body, producing *granulomas*.

d. **prevention:** Improved sanitation and controlling vector snails. The snail vectors are not found in the U.S.

e. **treatment:** praziquantel or oxiamineiquine.