CHAPTER 23 - Microbial Diseases of the Cardiovascular and Lymphatic System

I. Structure and Function of the Cardiovascular and Lymphatic Systems

A. INTRODUCTION
   1. The heart, blood, and blood vessels make up the cardiovascular system.
   2. Lymph, lymph vessels, lymph nodes, and lymphoid organs constitute the lymphatic system.

B. STRUCTURE AND FUNCTION OF THE CARDIOVASCULAR SYSTEM
   1. The heart circulates substances to and from tissue cells.
   2. Blood is a mixture of plasma and cells.
   3. Plasma transports dissolved substances. Red blood cells carry oxygen. White blood cells are involved in the body’s defense against infection.

C. STRUCTURE AND FUNCTION OF THE LYMPHATIC SYSTEM
   1. Fluid that filters out of capillaries into spaces between tissue cells is called interstitial fluid.
   2. Interstitial fluid enters lymph capillaries and is called lymph.
   3. Vessels called lymphatics return lymph to the blood near the right side of the heart.
   4. Lymph nodes contain fixed macrophages, B cells, and T cells.

II. Bacterial Diseases of the Cardiovascular and Lymphatic Systems

A. Septicemia, Sepsis, and Septic Shock
   1. The growth of microorganisms in blood is called septicemia. Signs include lymphangitis (inflamed lymph vessels). Red streaks, see picture in text.
   2. Septicemia can lead to septic shock, characterized by decreased blood pressure.
   3. Septicemia usually results from a focus of infection in the body, e.g. UTI, pneumonia.
   4. Gram-negative rods are usually implicated. Endotoxin causes the symptoms associated with a severe drop in blood pressure. 250K deaths/yr.
   5. Staph aureus, a gram positive cocci, may cause a toxic sepsis especially in dialysis patients.
   6. Puerperal sepsis begins as an uterine infection following childbirth or abortion; it can progress to peritonitis or septicemia.
   7. Streptococcus pyogenes is the most frequent cause.

B. Bacterial Infections of the Heart

   1. The inner layer of the heart is the endocardium.
2. Subacute bacterial endocarditis is usually caused by alpha-hemolytic streptococci, staphylococci, or enterococci.
   a) Develops slowly
   b) The infection arises from a focus of infection, such as a tooth extraction.
   c) Preexisting heart abnormalities are predisposing factors.
   d) Signs include fever, anemia, and heart murmur.
3. Acute bacterial endocarditis is usually caused by Staphylococcus aureus.
   a) The bacteria causes rapid destruction of heart valves.

C. Rheumatic Fever – Streptococcus pyogenes

1. Rheumatic fever is an autoimmune complication of streptococcal infections.
2. Rheumatic fever is expressed as arthritis or inflammation of the heart. It can result in permanent heart damage.
3. Antibodies against group A beta-hemolytic streptococci react with streptococcal antigens deposited in joints or heart valves or cross-react with the heart muscle.
4. Immune reaction to group M protein in Strep is the cause.
5. Rheumatic fever can follow a streptococcal infection, such as streptococcal sore throat. Streptococci might not be present at the time of rheumatic fever.
6. Prompt treatment of streptococcal infections can reduce the incidence of rheumatic fever. Before antibiotics this was a leading killer of children.
7. Penicillin is administered as a preventive measure against subsequent streptococcal infections.

D. Tularemia – Francisella tularensis

1. Tularemia is caused by Francisella tularensis. The reservoir is small wild mammals, especially rabbits.
2. Signs include ulceration at the site of entry, followed by septicemia and pneumonia.
3. Humans contract tularemia by handling diseased carcasses, eating undercooked meat of diseased animals, being bitten by certain vectors (such as deer flies), or inhaled. Maybe used as a bio weapon.
4. F. tularensis is resistant to phagocytosis, so is a problem in chemotherapy.
5. Laboratory diagnosis is based on an agglutination test on isolated bacteria.

E. Brucellosis (Undulant Fever) - Brucella abortus

1. Brucellosis can be caused by Brucella abortus, B. melitensis (goats), and B. suis (swine).
2. B. abortus most common In US. Get from unpasteurized milk or diseased animal tissue. Mainly in vets, farmers, meat packers. Enters skin, mucous membranes, or GI tract.
3. Domesticated animals (cattle, pigs, goats, and camels) and some wild stocks constitute the reservoir.
4. The bacteria enter through minute breaks in the mucosa or skin, reproduce in macrophages, and spread via lymphatics to liver, spleen, or bone marrow.
5. Signs include malaise and fever that spikes each evening (undulant fever). 104°
6. A vaccine for cattle is available.
7. Diagnosis is based on serological tests.

F. Anthrax – Bacillus anthracis
1. *Bacillus anthracis* causes anthrax. In soil, endospores can survive for up to 60 years.
2. Grazing animals acquire an infection after ingesting the endospores.
3. Human gastrointestinal anthrax (50% mortality) caused by ingestion of endospores has been reported.
4. Humans contract anthrax by handling hides from infected animals. The bacteria enter through cuts in the skin (20% mortality) or through the respiratory tract (100% mortality). Can be used as a bio weapon.
5. Entry through the skin results in a pustule that can progress to septicemia. Entry through the respiratory tract can result in pneumonia.
6. Diagnosis is based on isolation and identification of the bacteria.

G. Gangrene – Clostridium perfringens
1. Soft tissue death from ischemia (loss of blood supply) is called gangrene.
2. Microorganisms grow on nutrients released from gangrenous cells.
3. Ferments carbohydrates and produces CO$_2$ + H$_2$ gases. Organisms produce exotoxins and enzymes that further interfere with blood supply and favor spread of infection. Spreads area of necrosis and toxemia and death may occur.
4. Gangrene is especially susceptible to the growth of anaerobic bacteria such as *Clostridium perfringens*, the causative agent of gas gangrene.
5. *C. perfringens* can invade the uterine wall during improperly performed abortions.
6. Debridement, hyperbaric chambers, and amputation are used to treat gas gangrene.

H. Diseases Caused by Bites and Scratches
1. *Pasteurella multocida*, introduced by the bite of a dog or cat, can cause septicemia.
2. Anaerobic bacteria such as *Clostridium, Bacteroides*, and *Fusobacterium* found in the mouth infect deep animal bites (including human bites).
3. Cat-scratch disease is caused by *Bartonella henselae*. Found in up to 50% of all cats.
   a) Initial sign is a reddish purple papule at infection site.
I. Vector-Transmitted Diseases

1. Plague - Yersinia pestis

   a) Plague is caused by Yersinia pestis. The vector is usually the rat flea (Xenopsylla cheopis).

   b) Normally a disease of rats. Transmitted one to another by rat flea. European rats introduced into US many years ago are primary reservoirs. In far West and Southwest is endemic in wild rodents, esp. ground squirrels, prairie dogs & chipmunks. If host dies the rat flea seeks a replacement. Another rodent or human. Plague infected flea needs to feed because growth of bacteria blocks the flea’s digestive tract and the blood the flea ingests is quickly regurgitated. Don’t always need arthropod vector. Contact from the skinning infected animals, scratches of domestic cats and similar incidents have been reported as causing plague.

   c) Reservoirs for plague include European rats and North American rodents.

   d) Signs of bubonic plague include bruises on the skin and enlarged lymph nodes (buboes).

   e) The bacteria can enter the lungs and cause pneumonic plague.

   f) Pneumonic form especially dangerous. Highly infective due to airborne droplet transmission. Untreated mortality rate is 50-75% and pneumonia is near 100% Organism can survive inside cells.

   g) Laboratory diagnosis is based on isolation and identification of the bacteria.

   h) Antibiotics are effective in treating plague, but they must be administered promptly after exposure to the disease.

   i) Streptomycin and tetracycline can be used prophylactically in those who have been exposed.

2. Relapsing Fever – Borrelia sp.

   a) Relapsing fever is caused by Borrelia species and transmitted by soft ticks.

   b) The reservoir for the disease is rodents.

   c) Signs include fever, jaundice, and rose-colored spots. Relapses recur three or four times after apparent recovery due to antigenic variants.

   d) Laboratory diagnosis is based on the presence of spirochetes in the patient’s blood.

3. Lyme Disease – Borrelia burgdorferi

   a) Lyme disease is caused by Borrelia burgdorferi and is transmitted by a tick (Ixodes).

   b) Lyme disease is prevalent on the U.S. Atlantic Coast.
c) *Ixodes pacificus* – Pacific coast
d) *Ixodes scapularis* – Rest of US
e) *Get rash and flu-like symptoms. A skin lesion spreads from the site of the bite, clearing in the center (bull’s eye rash). Later complications are arthritis, and occasionally heart and neurological abnormalities. Similar to late stage syphilis.*
f) *Field mice provide the animal reservoir.*
g) *Diagnosis is based on serological tests and clinical symptoms.*
h) *Can treat with antibiotics.*

   a) *Epidemic Typhus*
      (1) The human body louse *Pediculus humanus corporis* transmits *Rickettsia prowazekii* in its feces, which are deposited while the louse is feeding.
      (2) Epidemic typhus is prevalent in crowded and unsanitary living conditions that allow the proliferation of lice.
      (3) *Rubbed into wound when host scratches bite*
      (4) The signs of typhus are rash, prolonged high fever, and stupor.
      (5) Tetracyclines and chloramphenicol are used in treatment.

   b) *Endemic Murine Typhus*
      (1) Endemic murine typhus is a less severe disease caused by *Rickettsia typhi* and transmitted from rodents to humans by the rat flea.
      (2) *Actually occurs sporadically rather than in epidemics.*

   c) *Spotted Fevers*
      (1) *Rickettsia rickettsii* is a parasite of ticks (*Dermacentor* species) in the southeastern U.S., Appalachia, and the Rocky Mountain states.
      (2) The rickettsia may be transmitted to humans, in whom it causes tickborne typhus fever.
      (3) Chloramphenicol and tetracyclines effectively treat Rocky Mountain spotted fever, or tickborne typhus.
      (4) Serological tests are used for laboratory diagnosis.
      (5) In the east, dog ticks are mainly responsible, in Rocky Mountains, wood ticks. The rickettsiae are passed among ticks by transovarian passage, infecting tick eggs as they are produced.

III. **VIRAL DISEASES OF THE CARDIOVASCULAR AND LYMPHATIC SYSTEMS**

A. *Infectious Mononucleosis* - *Epstein-Barr virus* (EBV).
   1. *Infectious mononucleosis is caused by the EB virus. Fever, sore throat, swollen lymph glands in neck, general weakness.*
2. The virus multiplies in the parotid glands and is present in saliva (kissing disease). It causes the proliferation of atypical lymphocytes in the blood.
3. The disease is transmitted by the ingestion of saliva from infected individuals.
4. Diagnosis is made by an indirect fluorescent-antibody technique.
5. Have to watch out for ruptured spleen as a complication.

B. Cytomegalovirus (CMV) Inclusion Disease - herpes virus- HHV-5
1. CMV (a herpesvirus- HHV-5) causes intranuclear inclusion bodies and cytomegaly of host cells.
2. CMV is transmitted by saliva, urine, semen, cervical secretions, and human milk.
3. CMV inclusion disease can be asymptomatic, a mild disease, or progressive and fatal. Immunosuppressed patients may develop pneumonia.
4. If the virus crosses the placenta, it can cause congenital infection of the fetus, resulting in impaired mental development, neurological damage, and stillbirth.
5. Babies get CMV – negative blood. Means ab negative. Would be antibody pos for life if have had disease. May be problem with macrophages and T cells. Organism lives inside.
6. Diagnosis is based on isolation of the virus or detection of IgG and IgM antibodies.

C. Classic Viral Hemorrhagic Fevers
(Most hemorrhagic fevers are zoonotic diseases. If medically familiar they are “classic” hemorrhagic fevers.)

1. Yellow fever is caused by an arbovirus (yellow fever virus). The vector is the mosquito Aedes aegypti.
   a) Endemic in Africa and tropical countries in Central and South America. Monkeys are reservoirs of virus.
   b) Signs and symptoms include fever, chills, headache, nausea, and jaundice.
   c) Mortality is high. Liver damage.
   d) Diagnosis is based on the presence of virus-neutralizing antibodies in the host.
   e) No treatment is available, but there is an attenuated, live viral vaccine.

2. Dengue is caused by an arbovirus (dengue fever virus) and is transmitted by the mosquito Aedes aegypti. There are 4 distinct serotypes of dengue fever. > 100 million cases/yr worldwide.
   a) Signs are fever, muscle and joint pain, and rash.
   b) Seldom fatal but are painful, giving disease name of “breakbone fever”.
   c) Mosquito abatement is necessary to control the disease.
   d) Dengue hemorrhagic fever (DHF) occurs when a person is reinfected with a second serotype of dengue virus. This may be rapidly fatal, especially in SE Asian children. Survival of the first type confers immunity to that type but creates a dangerous situation when infected by an other of the 4 types.
D. Emerging Viral Hemorrhagic Fevers
1. Human diseases caused by Marburg, Ebola, and Lassa fever viruses were first noticed in the late 1960s.
   a) Marburg and Ebola are the filoviruses. Lassa is an Arenavirus. “Hot Zone” a popular book on these viruses.
   b) Marburg virus is found in nonhuman primates; Lassa fever viruses are found in rodents.
   c) Rodents are the reservoirs for Argentine and Bolivian hemorrhagic fevers.
2. Hantavirus pulmonary syndrome is caused by Hantavirus. The virus is contracted by inhalation of dried rodent urine, especially in out buildings.
   a) Southwest US. Fatal pulmonary infection causing lungs to fill with fluid. Elsewhere in world are known as hemorrhagic fever with renal syndrome.

IV. PROTOZOA N DISEASES OF THE CARDIOVASCULAR AND LYMPHATIC SYSTEMS
(Have complex life cycles)

A. American Trypanosomiasis (Chagas’ Disease) - Trypanosoma cruzi
1. Trypanosoma cruzi causes Chagas’ disease. The reservoir includes many wild animals. The vector is a reduviid, the ‘kissing bug.’ Lives in thatch roofs and cracks of buildings.
2. Look for trypanosomes in the intestinal tract of the reduviid bug after feeding on patient’s arm, which confirms the diagnosis.
3. Occurs in southern US and throughout Mexico, Central America, and South America. Disease is transmitted to humans when insect bites are contaminated by the insect’s feces. Most damage is caused by inflammatory reactions after transport by blood to the liver, spleen, heart, and so on. One symptom is loss of involuntary muscular contractions in the esophagus and GI tract due to nerve damage. These organs become grossly enlarged: megaesophagus and megacolon. The disease is most dangerous to children, in whom it damages the heart.

B. Toxoplasmosis - Toxoplasma gondii
1. Toxoplasmosis is caused by the sporozoan Toxoplasma gondii.
2. T. gondii undergoes sexual reproduction in the intestinal tract of domestic cats, and oocysts are eliminated in cat feces.
3. Oocysts can be ingested by cattle and other animals.
4. Sporozoites hatch from an oocyst and invade host cells.
5. In the host cell, sporozoites reproduce to form either tissue-invading tachyzoites or bradyzoites.
7. May become chronic as the immune system becomes increasingly effective.
9. Humans contract the infection by ingesting tachyzoites or tissue cysts in undercooked meat from an infected animal or contact with cat feces.
10. Subclinical infections are probably common because the disease symptoms are rather mild. 40% of population is positive for ab.
11. Congenital infections can occur. Signs and symptoms include severe brain damage or vision problems.
12. Toxoplasmosis can be identified by serological tests, but interpretation of the results is uncertain.

C. Malaria - Anopheles mosquito - Plasmodium falciparum – P. vivax – P. malaria & ovale
1. The signs and symptoms of malaria are chills, fever, vomiting, and headache, which occur at intervals of 2-3 days. 300-500 million infected. 2-4 million killed/yr.
2. Malaria is transmitted by Anopheles mosquitoes. The causative agent is any one of four species of Plasmodium.
3. Plasmodium falciparum – Most dangerous and geographically widespread. About 20% of cases.
4. P. vivax – Also widespread. About 80% of cases.
5. P. malaria & ovale – Lower infection rate, geographically restricted, and milder disease.
6. Sporozoites reproduce in the liver and release merozoites into the bloodstream, where they infect red blood cells and produce more merozoites.
7. Laboratory diagnosis is based on microscopic observation of merozoites in red blood cells.
8. New drugs are being developed as the protozoa develop resistance to drugs such as chloroquine. A vaccine is being developed?

D. Leishmaniasis
1. Visceral, cutaneous, and mucocutaneous clinical forms.
2. About 20 species of protozoans that are transmitted by sandflies (very small).
3. Many cases are being dx in veterans from Mediterranean Gulf Wars.
V. HELMINTHIC DISEASES OF THE CARDIOVASCULAR AND LYMPHATIC SYSTEMS

A. Schistosomiasis - *Schistosoma mansoni*
1. Species of the blood fluke *Schistosoma* cause schistosomiasis.
3. Eggs eliminated with feces hatch into larvae that infect the intermediate host, a snail. Free-swimming cercariae are released from the snail and penetrate the skin of a human.
4. The adult flukes live in the veins of the liver or urinary bladder in humans.
5. Adult flukes reproduce, and eggs are excreted or remain in the host.
6. Granulomas are from the host’s defense to eggs that remain in the body.
7. Causes damage such as abscesses and ulcers to the liver and other organs such as the lungs or urinary system.
8. Observation of eggs or flukes in feces, skin tests, or indirect serological tests may be used for diagnosis.
9. Chemotherapy is used to treat the disease; sanitation and snail eradication are used to prevent it.

B. Swimmer’s Itch
1. Swimmer’s itch is a cutaneous allergic reaction to cercariae that penetrate the skin. The definitive host for this fluke is wildfowl.
2. Larvae does not mature in humans.