Topic: Diseases of Cardiovascular and System

System Structure
• Composed of 3 parts:
  – Heart
  – Blood
  – Blood vessels
• Arteries ➔ connected to veins via capillaries
• Blood composition
  – Serum – liquid part of blood
  – Formed elements – erythrocytes, leukocytes, platelets

Structure – Big Picture
Blood & Lymph System

- **Movement (review)**
  - Right ventricle pumps blood to the lungs
    - Oxygen enters blood and carbon dioxide diffuses out
  - Oxygenated blood returns to the heart through the left ventricle and then to the arteries and capillaries
  - Capillaries carry blood to the surrounding tissues and also leak fluid that is picked up by the lymphatic vessels

Infection Terms

- **Septicemia**
  - Any microbial infection of the blood that produces illness
- **Bacteremia**
  - Bacterial septicemia that is often harmless
- **Toxemia**
  - Release of bacterial toxins into the blood
- **Lymphangitis**
  - Infection and inflammation of the lymphatic vessels

Characteristic streaking presentation of Lymphangitis (sign of Septicemia)
Signs & Symptoms – Septicemia, Bacteremia, Toxemia

- Fever, chills, nausea, vomiting, diarrhea, malaise
- Septic shock can develop rapidly
- Small hemorrhagic lesions called petechiae can develop
- Osteomyelitis can occur when bacteria invade the bones
- Toxemia symptoms vary depending on the toxin
  - Exotoxins – released from living microorganisms
  - Endotoxin – released from Gram-negative bacteria

Characteristic petechiae (bacteremia sign)

Pathogens and virulence factors

- Septicemia and toxemia are caused by various bacteria
- Pathogens are often opportunistic or nosocomial infections
- Gram-negative bacteria cause septicemia more often than Gram-positive bacteria
- Presence of capsule that resists phagocytosis
- Capacity to capture iron needed for bacterial growth
- Endotoxin produced by Gram-negative bacteria
Pathogenesis and Epidemiology

- Septicemia - acquired by direct inoculation of bacteria into the blood
  - Examples include medical procedures, drug users
- Immunocompetent individuals rarely have septicemia
  - Bacterial infections in these people are self-limited
- Gram-negative bacteria are more likely to produce severe septicemia due to release of endotoxin as the bacteria die
  - Endotoxin activates various defensive reactions by the body

Endotoxin Effects

About Septicemia, Bacteremia, Toxemia

- Signs and symptoms are usually **diagnostic**
- Bacteria are cultured from the blood in fewer than half the individuals with indications of sepsis
- **Treatment** requires prompt identification and administration of antimicrobial drugs
- **Prevention** includes immediate treatment of infections, especially in individuals with compromised immune systems
Endocarditis

- Signs and symptoms
  - Fever, fatigue, malaise, tachycardia
- Pathogens
  - Viridans streptococci – half of cases
- Pathogenesis and epidemiology
  - Patients usually have obvious source of infection
  - Patients with abnormal heart have increased risk
- Diagnosis, treatment, and prevention
  - Treat with intravenous antibacterial drugs
  - High-risk patients can be given prophylactic antibiotics when needed

Brucellosis

- Signs and symptoms
  - Fluctuating fever that spikes every afternoon
- Pathogen and virulence factors
  - Caused by Brucella melitensis strains
  - LPS causes some of the signs and symptoms
- Pathogenesis and epidemiology
  - Consumption of contaminated dairy products
  - Contact with animal blood, urine, or placentas
- Diagnosis, treatment, and prevention
  - Usually requires no treatment
  - Attenuated vaccine exists for animals
Tularemia Presentation (*Francisella tularensis*)

- G neg, bacillus
- Entry: tick, ingestion, inhalation
- Presents as fever, chills, headache, diarrhea, joint & muscle pain, progressive fatigue, chest & resp. issues
- Incubate 3-5 days avg (up to 2 wks)
- I.M. streptomycin and tetracycline

Plague – Bubonic and Pneumonic

- **Gram negative cocobacillus (*Yersinia Pestis*)**
  - Bubonic plague is characterized by enlarged, inflamed lymph nodes called buboes
  - Pneumonic plague occurs when the bacterium spreads to the lungs
- **Virulence factors** include adhesins, type III secretion systems, capsules, and antiphagocytic proteins
- **Diagnosis** based on characteristic symptoms; must be diagnosed and treated immediately
- **Treated** with various antimicrobial drugs
- **Prevention** occurs through rodent and flea control and good personal hygiene

Classic Bubo Presentation (lymphnodes)
Advanced Bubonic Plague Presentation
(Yersinia pestis)

- Black Death (dead, infected tissue)
- 1/3 of Europe in middle ages
- Fleas or inhalation

Yersinia pestis Transmission

Lyme Disease

- Epidemiology
  - One of most reported vector-borne diseases in U.S.
  - Two events contribute to increase in Lyme disease
    - Human populations have moved into woodland areas
    - Deer population has been protected
Ticks – the enemy! (Lyme Disease)

Bulls-eye presentation of Lyme Disease

Lyme Disease Bacteria (Borellia burgdorferi)

- Not in 100%
- Initial presentation

- G neg spirochete
-Ticks
- neurological (10%)
- arthritic (80%)
Lyme Disease Life Cycle

About Lyme Disease
- Diagnosis
  - Based on the signs and symptoms of the disease
  - Bacterium rarely detected in the blood
- Treatment
  - In early phases, antimicrobial drugs are used
  - Treatment of later phases is difficult because symptoms are often caused by the immune system
- Prevention
  - Use of repellants containing DEET
  - Use of protective clothing

Erlichiosis & Anaplasmosis
- New – unknown before 1987
- Tick-borne
- Rickettsia, Gram negative, obligate intracellular bacteria:
  - *Ehrlichia chaffeensis* causes erlichiosis
  - *Anaplasma phagocytophilum* causes anaplasmosis
- Live inside phagosomes, prevent fusion w/ lysosomes…
Erlichiosis and Anaplasmosis

- Flulike signs and symptoms
- Pathogen and virulence factors
  - *Ehrlichia chaffeensis* causes erlichiosis (HME – Human monocytic erlichiosis)
  - *Anaplasma phagocytophilum* causes anaplasmosis (HGA – Human granulocytic anaplasmosis)
- Diagnosis, treatment, and prevention
  - Diagnosis difficult due to mild symptoms
  - Treated with antimicrobials
  - Prevention involves avoiding tick-infested areas

Growing Inside Leucocyte!

Distribution of Erlichiosis and Anaplasmosis

- Blue = HME
- Red = HGA
- Purple = Both
Mononucleosis (Viral)

- Signs and symptoms
  - Severe sore throat and fever followed by enlarged lymph nodes
- Pathogen and virulence factors
  - Human herpes virus 4 (HHV-4) or Epstein-Barr Virus (EBV) is the causative agent
  - EBV can cause other conditions depending on the strength of the immune response of an individual

About Epstein-Barr Virus & Infectious Mononucleosis

- Pathogenesis
  - Transmission occurs via saliva
  - EBV infects B lymphocytes
- Diagnosis made based on the presence of large, lobed B lymphocytes and neutropenia
- Treatment focuses on relieving symptoms
  - Most cases resolve without treatment
- Prevention is difficult due to the widespread occurrence of EBV

Other Epstein-Barr Diseases
Cytomegalovirus

– Signs and symptoms
  • Asymptomatic in most cases
  • Neonates and immunodeficient individuals can have complications from CMV infection
– Pathogen and virulence factors
  • Caused by *Cytomegalovirus*
– Pathogenesis and epidemiology
  • Transmitted by direct contact with bodily secretions or across the placenta
  • One of the most common infections of humans
– Diagnosis, treatment, and prevention
  • Fomivirsen administered for eye infections

“Owl-eyes” histology of CMV

Viral Cardiovascular and Systemic Diseases

[INSERT FIGURE 21.14]

[INSERT DISEASE AT A GLANCE 21.5]
Yellow Fever

– Yellow fever virus (Flavivirus genus)
– Mosquito transmission
– Claims to fame:
  • One of most influential diseases in US history
  • 1793 killed ~10% of Philadelphia
  • Has affected the outcome of many battles and campaigns
  • Killed more American soldiers than bullets in Spanish-American war

Yellow Fever

– Signs and symptoms – three stages
  • First stage – fever, headache, muscle aches
  • Second stage – period of remission
  • Third stage – delirium, seizures, coma, hemorrhaging
– Pathogenesis and epidemiology
  • Transmission occurs via the bite of an infected Aedes mosquito
  • Virus travels to the liver, where it replicates
  • Yellow fever cases occur today in South America and Africa

Dengue (Fever & Haemorrhagic Fever)

– Signs and symptoms
  • Two phases of Dengue fever
    – First phase – fever, edema, head and muscle pain
    – Second phase – return of fever and red rash
  • Dengue hemorrhagic fever
    – Internal bleeding, shock, and possibly death
– Pathogens and virulence factors
  • Dengue viruses 1, 2, 3, and 4 are the causative agents
  • Aedes mosquitoes are the vector
Dengue Fever

- Pathogenesis and epidemiology
  - Dengue fever is usually a mild disease
  - Dengue hemorrhagic fever is more severe and can be fatal
- Diagnosis, treatment, and prevention
  - Diagnosis made based on signs and symptoms of someone who has traveled to endemic regions
  - No specific treatment available
  - Prevention requires control of mosquitoes

African Viral Hemorrhagic Fevers (Ebola & Marburg)

- Signs and symptoms
  - Fever, fatigue, minor petechiae that progresses to severe internal hemorrhaging
- Pathogens and virulence factors
  - Caused by *Ebolavirus* or *Marburgvirus*
- Pathogenesis and epidemiology
  - Contact with bodily fluids of infected individual or possibly via contact with an animal host
The culprit- Ebola Virus!

Distribution of African Hemorrhagic Diseases

In Virginia – only monkeys in a research facility

African Viral Hemorrhagic Fever
Diseases (cont.)

- Diagnosis, treatment, and prevention
  - **Diagnosis** based on characteristic symptoms and presence of virus in the blood
  - **Treatment** is supportive care including fluid and electrolyte replacement
  - **Vaccines** are being studied for their efficacy in preventing human disease
Protozoan and Helminthic Cardiovascular and Systemic Diseases

- Protozoa of the phylum Apicomplexa can cause disease in humans
- Life cycles of these parasites are complex and involve at least two types of hosts
Malaria

- Pathogens and virulence factors
  - Four Plasmodium species cause malaria
  - Disease severity depends on the species

- Virulence factors
  - Reproductive cycle occurs within red blood cells, hiding parasite from immune surveillance
  - Malaria secretome injects toxins into host cells
  - Adhesins allow red blood cells to adhere to certain tissues
  - Merozoites form within vesicles and avoid detection
  - Changes in body chemistry attract other mosquitoes

Malaria Pathology

- Pathogenesis
  - *P. falciparum* causes the most severe malaria
  - Certain genetic traits can increase resistance to malaria
    - Sickle-cell trait
    - Hemoglobin C
    - Genetic deficiency of glucose-6-phosphate dehydrogenase
    - Lack of Duffy antigens

- Epidemiology
  - Endemic in over 100 countries, though not in the U.S.
Toxoplasmosis

- Signs and symptoms
  - Majority of cases have no symptoms
  - Symptoms in those with poor immunity
    - Fever, malaise, and inflammation of the lungs, liver, and heart
  - Symptoms in the fetus
    - Stillbirth, epilepsy, mental retardation

- Pathogen and virulence factors
  - *Toxoplasma gondii* is the causative agent
    - Cats are the definitive host

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Toxoplasmosis Life Cycle

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Toxoplasmosis (cont.)

- Pathogenesis and epidemiology
  - consuming undercooked meat containing the parasite
  - Transmission across the placenta can occur
  - Specific mechanism of disease is not yet known

- Diagnosis, treatment, and prevention
  - Diagnosed mainly by detecting organisms in tissues
  - Treatment is usually unnecessary except in AIDS patients, pregnant women, and newborns
  - Prevention is difficult due to the numerous hosts of *T. gondii*
Chagas' Disease

- Caused by *Trypanosoma cruzi* – flagellated protozoan

- Pathogenesis and epidemiology
  - Transmission via bite of infected *Triatoma* (assasin bug) or transfusion with infected blood
  - Progresses through four stages
    - Site of bite swells
    - Stage with generalized symptoms such as fever, swollen lymph nodes, myocarditis
    - Chronic asymptomatic stage that can last years
    - Final stage characterized by congestive heart failure and pseudocyst formation

Chagas' Disease Life Cycle

*Trypanosoma cruzi* in blood

Relative sizes of various *Triatoma*
Schistosomiasis
- Protozoan (blood fluke) that can penetrate skin
- 200 million infected
- Main organisms: 
  S. mansoni, S. haematobium, S. japonicum
- Transient swimmer’s itch then vascular
- Mate for life- lay millions of eggs that trigger immune reactions, renal failure (egg calcifications), splenomegaly, high BP, bladder and ureters

Schistosoma Transmission

Schistosoma (cont.)
Characteristic Schistosoma egg w/ spine

Schistosomiasis Life Cycle

Schistosomiasis
- Diagnosis, treatment, and prevention
  - **Diagnosis** based on identification of eggs in stool or urine sample
  - **Treat** with Praziquantel, the drug of choice
  - **Prevention** depends on avoiding potentially contaminated freshwater