CHAPTER 22 - Microbial Diseases of the Nervous System

I. STRUCTURE AND FUNCTION OF THE NERVOUS SYSTEM fig 22.2

A. The central nervous system (CNS) consists of the brain, which is protected by the skull bones, and the spinal cord, which is protected by the backbone.
B. The peripheral nervous system (PNS) consists of the nerves that branch from the CNS.
C. The CNS is covered by three layers of membranes called meninges: the dura mater, arachnoid mater, and pia mater. Cerebrospinal fluid (CSF) circulates between the arachnoid and the pia mater in the subarachnoid space.
D. The blood-brain barrier normally prevents many substances, including most antibiotics, from entering the brain.
E. Microorganisms can enter the CNS through trauma, along peripheral nerves, and through the bloodstream and lymphatic system (most common). Inflammation alters the permeability of the blood-brain barrier.
F. An infection of the meninges is called meningitis. An infection of the brain is called encephalitis.

II. BACTERIAL DISEASES OF THE NERVOUS SYSTEM

A. Bacterial Meningitis
- Meningitis can be caused by viruses, bacteria, fungi, and protozoa.
- The three major causes of bacterial meningitis are Hemophilus influenzae (GNR), Streptococcus pneumoniae (GPC), and Neisseria meningitidis (GNC). Also Group B Strep.
- Nearly 50 species of opportunistic bacteria can cause meningitis.

1. Hemophilus influenzae
   a) H. influenzae is part of the normal throat microbiota.
   b) H. influenzae requires blood factors for growth: X and V; there are six types of H. influenzae based on capsule differences.
   c) H. influenzae type b is the most common cause of meningitis in children under 4 years old. Following a viral infection of respiratory tract can invade bloodstream and then invade meninges.
   d) Now have vaccine = Hib. A conjugated vaccine directed against the capsular polysaccharide antigen..

2. Neisseria meningitidis
   a) N. meningitidis causes meningococcal meningitis. This bacterium is found in the throats of healthy carriers.
b) The bacteria probably gain access to the meninges through the bloodstream. The bacteria may be found in leukocytes in CSF.

c) Symptoms are due to endotoxin with severe shock. Early antibiotic therapy helps reduce mortality. The disease occurs most often in young children < 2 years.

d) Military recruits and college dorm students are at risk too. Vaccination with purified capsular polysaccharide to prevent epidemics is recommended.

e) Some types cause widespread epidemics in US (type C) Africa (type A).

3. Streptococcus pneumoniae

a) S. pneumoniae is commonly found in the nasopharynx (70% healthy carriers). Gram Pos encapsulated diplococci.

b) Elderly patients and young children (1mo to 4yr) are most susceptible to S. pneumoniae meningitis. It is rare but has a high mortality rate.

c) The vaccine for pneumococcal pneumonia may provide some protection against pneumococcal meningitis. Antibiotic resistant strains are common.

4. Listeria monocytogenes

a) Listeria monocytogenes causes meningitis in newborns (via pregnant women). L. monocytogenes can cross the placenta and cause spontaneous abortion and stillbirth. In adults: the immunosuppressed, and cancer patients.

b) Proliferates within bacterial cells where it avoids the immune system.

c) GPR can grow in refrigerator temperature

d) Acquired by ingestion of contaminated food, it may be asymptomatic in healthy adults. A well recognized animal pathogen.

5. Diagnosis and Treatment of the Most Common Types of Bacterial Meningitis

a) Broad spectrum cephalosporins may be administered before identification of the pathogen.

b) Diagnosis is based on isolation and identification or direct antigen detection of the bacteria in CSF.

c) Cultures are usually made on blood agar and incubated in an atmosphere containing increased CO₂.

6. Tetanus –Clostridium tetani
a) Tetanus is caused by a localized infection of a wound by Clostridium tetani endospores. 1 million cases worldwide each year.
b) Obligate anaerobic spore forming GPR found commonly in soil, esp. those contaminated with animal waste
c) C. tetani produces the neurotoxin tetanospasmin, which causes the symptoms of tetanus: spasms, contraction of muscles controlling the jaw, and death resulting from spasms of respiratory muscles.
d) Opposing muscles contract simultaneously so joints become ‘locked’.
e) C. tetani is an anaerobe that will grow in deep, unclean wounds and wounds with little bleeding.
f) Acquired immunity results from DPT immunization in childhood that includes tetanus toxoid.
g) Following an injury, an immunized person may receive a booster of tetanus toxoid. An unimmunized person may receive (human) tetanus immune globulin.
h) Debridement (removal of tissue) and antibiotics may be used to control the active infection.

7. Botulism – Clostridium botulinum

a) Botulism is caused by an exotoxin produced by C. botulinum growing in foods.
b) Obligate anaerobic spore forming GPR.
c) Serological types of botulinum toxin vary in virulence, with type A being the most virulent and found in the Western US.
d) The toxin is a neurotoxin that inhibits the transmission of nerve impulses by preventing the release of ACh at the synapse.
e) Blurred vision occurs in 1-2 days; progressive flaccid paralysis follows for 1-10 days, possibly resulting in death from respiratory and cardiac failure.
f) C. botulinum will not grow in acidic foods or in an aerobic environment.
g) Endospores are killed by proper canning. The addition of nitrites to foods inhibits growth after endospore germination.
h) The toxin is heat labile and is destroyed by boiling (100 C) for 5 minutes.
i) Infant botulism results from the growth of C. botulinum in an infant’s intestines.
jk) Wound botulism occurs when C. botulinum grows in anaerobic wounds.
k) For diagnosis, mice protected with antitoxin are inoculated with toxin from the patient or foods.

8. Leprosy – Mycobacterium leprae

a) Mycobacterium leprae causes leprosy, or Hansen’s disease.
b) Only organism that grows primarily in peripheral nervous system tissue.
c) *M. leprae* has never been cultured on artificial media. It can be cultured in armadillos.

d) The tuberculoid form of the disease is characterized by loss of sensation in the skin surrounded by nodules. The lepromin skin test is positive.

e) Laboratory diagnosis is based on observations of acid-fast rods (AFB) in lesions or fluids and the lepromin test.

f) In the lepromatous form, disseminated nodules and tissue necrosis occur. The lepromin test is negative.

g) Leprosy is not highly contagious and is spread by prolonged contact with exudates and nasal secretions.

h) Untreated individuals often die of secondary bacterial complications, such as tuberculosis.

i) Patients with leprosy are made noncommunicable within 4-5 days with sulfone drugs and then treated as outpatients.

j) Leprosy occurs primarily in the tropics. 500K new cases reported each year in these areas.

**B. VIRAL DISEASES OF THE NERVOUS SYSTEM**

1. Poliomyelitis - Poliovirus
   a) The symptoms of poliomyelitis are usually headache, sore throat, fever, stiffness of the back and neck, and occasionally paralysis (less than 1% of cases).
   b) Poliovirus is found only in humans and is transmitted by the ingestion of water contaminated with feces.
   c) Poliovirus first invades lymph nodes of the neck and small intestine. Viremia and spinal cord involvement may follow.
   d) Post-Polio Syndrome – Muscle weakness
   e) Diagnosis is based on isolation of the virus from feces and throat secretions.
   f) The Salk vaccine (an inactivated polio vaccine, or IPV) involves the injection of formalin-inactivated viruses and boosters every few years. The Sabin vaccine (an oral polio vaccine, or OPV) contains three live, attenuated strains of poliovirus and is administered orally.
   g) Through vaccination, the WHO plans to eliminate polio by the year 200?.

2. Rabies – Rabies virus
a) Rabies virus (a rhabdovirus) causes an acute, usually fatal, encephalitis called rabies.
b) Rabies may be contracted through the bite of a rabid animal, by inhalation of aerosols, or invasion through minute skin abrasions. The virus multiplies in skeletal muscle and connective tissue.
c) Encephalitis occurs when the virus moves along peripheral nerves to the CNS.
d) Symptoms of rabies include spasms of mouth and throat muscles followed by extensive brain and spinal cord damage and death.
e) Hydrophobia: paralysis in pharynx makes swallowing difficult so fear of water. Foaming of mouth due to saliva.
f) Laboratory diagnosis may be made by direct immunofluorescent tests of saliva, serum, and CSF or brain smears.
g) Reservoirs for rabies in the U.S. include skunks, bats, foxes, and racoons. Domestic cattle, dogs, and cats may get rabies. Rodents and rabbits seldom get rabies.
h) The Pasteur treatment for rabies involved multiple subcutaneous injections of rabies virus grown in rabbit spinal cord tissue.
i) Current post-exposure treatment includes administration of human rabies immune globulin (RIG) along with multiple intramuscular injections of human diploid cell vaccine (HDCV).
j) Unique in that incubation is long enough to immunize after exposure.
k) Pre-exposure immunization consists of injections of HDCV.

3. Arboviral Encephalitis

a) Symptoms of encephalitis are chills, headache, fever, and eventually coma.
b) Many types of arboviruses transmitted by mosquitoes cause encephalitis.
c) The incidence of encephalitis increases in the summer months when mosquitoes are most numerous.
d) Horses are frequently infected by EEE, WEE, West Nile viruses.
e) Diagnosis is based on serological tests.
f) Control of the mosquito vector is the most effective way to control encephalitis.

C. FUNGAL DISEASES OF THE NERVOUS SYSTEM (Rarely invaded by fungi.)

1. Cryptococcus neoformans meningitis (Cryptococcus)

a) Cryptococcus neoformans is an encapsulated yeastlike fungus that causes meningitis.
b) The disease may be contracted by inhalation of dried infected pigeon (or other bird) droppings.
c) The disease begins as a lung infection and may spread to the brain and meninges.
d) Immunosuppressed individuals are most susceptible to Cryptococcus neoformans meningitis.
e) Diagnosis is based on latex agglutination tests for cryptococcal antigens in serum or CSF.

2. Coccidioides imitis- San Joaquin Valley fever
   a) Valley fever is acquired by respiratory exposure to dry soil with spores of Coccidioides imitis.
   b) A respiratory infection may progress to systemic disease including meningitis.

D. Protozoan Diseases of the Nervous System

1. African Trypanosomiasis
   a) African trypanosomiasis is caused by the protozoa Trypanosoma brucei gambiense and T. b. rhodesiense and transmitted by the bite of the tsetse fly (Glossina).
   b) One million people in Africa affected – 20,000 new cases/year.
   c) The disease affects the nervous system of the human host, causing lethargy and eventually coma. It is commonly called sleeping sickness.
   d) 2-4 year course of disease as the organism goes from blood to CNS.
   e) Vaccine development is hindered by the protozoan’s ability to change its surface antigens.

E. NERVOUS SYSTEM DISEASES CAUSED BY PRIONS

1. Prions: abnormally folded proteins that mimic an infectious disease
   a) Diseases of the CNS that progress slowly and cause spongiform degeneration are caused by prions. Symptoms progress to loss of motor control and death.
   b) Sheep scrapie and bovine sprongiform encephalopathy (BSE) are examples of diseases caused by prions that are transferable from one animal species to another.
   c) Creutzfeldt-Jacob disease and kuru are human diseases similar to scrapie. Kuru occurs in isolated groups of cannibals who eat brains.
   d) Prions are proteins that can induce a shape change in a normal protein causing them to clump leading to cell death.
   e) Heating and irradiation have no effect on the prions. Autoclaving is not reliable.
F. DISEASES CAUSED BY UNIDENTIFIED AGENTS

1. Chronic Fatigue Syndrome