Some of the most devastating infectious diseases affect the nervous system and especially the brain and spinal cord. Pathogens capable of causing disease of the nervous system often have virulence characteristics of a special nature to penetrate defenses of the body. As with cardiovascular and lymphatic diseases, the diseases of the nervous system also infect other systems. Most infections affect the central nervous system (brain and spinal cord), and the meninges. The brain is protected by the blood-brain barrier which contains capillaries with a thickened outer layer that severely limits permeability. Oxygen, carbon dioxide, glucose, and the essential amino acids can cross freely, but many toxins and microorganisms cannot. Unfortunately, many antibiotics cannot cross the blood-brain barrier either, which limits treatment of CNS infections when they occur. Even though the CNS has considerable protection, it can still be invaded by microorganisms in several ways. Microorganisms can gain access through trauma, such as a skull or backbone fracture, or through a medical procedure such as a spinal tap. Some microorganisms can also move along peripheral nerves. The most common routes of invasion are the bloodstream and lymphatic system, when inflammation alters permeability of the blood-brain barrier.

There are three most common symptoms of infection:

1. meningitis - inflammation or infection of the protective membranes surrounding the brain (meninges). The normally clear cerebrospinal fluid becomes cloudy with white blood cells attracted to the site of inflammation and swelling around the brain increases pressure inside the skull, causing intense headaches. Inflammation and irritation of the spinal meninges affect nearby muscles, causing a stiff neck. Fever is almost always present. Brain function is usually affected because blood flow to the brain is diminished.

2. encephalitis - inflammation or infection of brain tissue, usually with fever. It affects brain function, causing changes in the state of consciousness or behavior.

3. myelitis - inflammation or infection of the spinal cord which interrupts spinal nerve impulses. Depending on the part of the spinal cord that is affected, interruption of nerve impulses affect different areas of the body.
Bacterial Diseases

Various bacteria can infect the meninges and produce bacterial meningitis. Bacteria that infect nervous tissue do so by means of neurotoxins.

1. Meningococcal Meningitis

   a. causative agent: Neisseria meningitidis

   b. method of transmission: Its only natural reservoir is the human body, and it usually causes life-threatening diseases. They can inhabit the nasopharynx without causing any symptoms. This carrier state can last from several days to several months and provides a reservoir. It is readily transmitted from person to person in respiratory droplets. Outbreaks are particularly likely where large numbers of people are housed under crowded and stressful conditions, such as military barracks, dormitories, and day-care centers.

   c. symptoms: The bacteria colonize the nasopharynx, spread to the blood (bacteremia), and then to the meninges. Acute onset of fever, chills and a headache, and occasionally seizures occur. Most of the symptoms are thought to be caused by an endotoxin produced by the bacteria.

   d. prevention: It usually strikes children age 6 months to 2 years. Children are usually born with maternal immunity and become susceptible as the immunity weakens at about 6 months. The risk can be reduced by prevention of overtiring and overcrowding. Vaccines are available for distinct capsular antigens and are used routinely in the military, but it is not effective in very young children. Administer rifampin to carriers.

   e. treatment: Penicillin, ampicillin or third-generation cephalosporins. Sulfonamides are no longer used because of resistant strains.

2. Haemophilus influenzae Meningitis

   a. causative agent: Haemophilus influenzae - It is a normal flora of the pharynx and is responsible for about two-thirds of bacterial meningitis cases during the first year of life. It is the leading cause of mental retardation in the U.S. and worldwide.
b. **method of transmission:** Humans are exposed early in life and rapidly acquire immunity, so it is rare in adults. Among children, 30 to 50% are carriers, and among adults, only 3%. It is spread by respiratory droplets, especially in day-care centers and is becoming an increasing problem. It occurs mostly in children under 4 years of age and is especially prevalent at 6 months. Maternally-acquired immunity lasts about 2 months. It is usually preceded by a viral infection of the respiratory tract, which opens the way for the bacteria to enter the bloodstream and be transported to the meninges.

**c. symptoms:** Headache, fever, chills, stiff neck. Early diagnosis is essential because it can cause permanent brain damage.

**d. prevention:** A series of vaccinations with Hib vaccine beginning at 2 months of age. In most cases, good immunity is achieved at 6 or 7 months. Rifampin is commonly prescribed for household and day-care contacts.

**e. treatment:** Third-generation cephalosporins. Without treatment it is almost always fatal.

3. **Pneumococcal Meningitis**

a. **causative agent:** *Streptococcus pneumoniae* - It causes about 50% of the cases of meningitis in adults over 40 years of age. About half occur in children ages 1 month to 4 years.

b. **method of transmission:** It is a common resident of the nasopharynx and is transmitted through respiratory droplets. It usually strikes people who have a weakened state of health, such as newborns, people with sickle cell disease, hospitalized elderly, and alcoholics.

c. **symptoms:** Fever, chills, headache, stiff neck. The bacteria usually enter the meninges from the bloodstream, but infection can also spread directly from respiratory sites such as the middle ear or sinuses. Permanent brain damage occurs much more frequently than in *N. meningitidis* or *H. influenzae*.

d. **prevention:** Some protection is available from the vaccine for pneumococcal pneumonia, which is caused by the same microorganism.

e. **treatment:** Penicillin, but about 25% still die.
4. Listeriosis
   a. causative agent: Listeria monocytogenes
   b. method of transmission: It is excreted in animal feces and is widely distributed in water and soil. Foodborne transmission by improperly processed milk, cheese, meat, and vegetables is the most common source of infection. It is one of the few pathogens that is capable of growth at refrigerator temperatures, which can lead to an increase in its numbers during a food’s shelf life. Recovering or apparently healthy individuals shed the pathogen indefinitely in their feces. It mainly affects adults who are immunosuppressed, pregnant, or have cancer, and it has a special affinity for growth in the CNS and the placenta. It is a leading cause of infection in kidney transplant patients.
   c. symptoms: In healthy adults the disease is usually mild and often symptomless. When it infects a pregnant woman, the growth on the placenta leads to a high rate of spontaneous abortion or stillbirth. A surviving newborn may be acutely ill with septicemia and meningitis.
   d. prevention: Better methods of detection of the bacteria in foods.
   e. treatment: penicillin or ampicillin.

5. Tetanus
   a. causative agent: Clostridium tetani
   b. method of transmission: It is a normal flora of the intestinal tract of horses, cattle, and some humans. Endospores are found almost everywhere, but especially in cultivated fields where animal feces are used as fertilizer. Tetanus develops when endospore-containing dirt enters a deep, anaerobic wound or puncture. Endospores can germinate in the decaying umbilical cord and is the route of transmission in newborns. Adults usually become infected through wounds or nonsterile surgical procedures. Handling bedpans, dirty diapers, or other objects contaminated with feces can transmit bacteria to individuals who have breaks in their skin. Boiling for 20 minutes does not destroy the endospores and they can survive for years if not exposed to sunlight.
   c. symptoms: Once inside the bacteria stay at the wound site and release a powerful neurotoxin called tetanospsamin. It enters the CNS by way of peripheral nerves or the blood. After 4 to 10 days’ incubation, symptoms begin with generalized muscle stiffness followed by spasms that affect every muscle. An arched back and clenched fists and jaws (lockjaw), are classic symptoms. Spasms can be violent enough to break bones. Eventually, respiratory
muscles become paralyzed, heart function is disturbed, and, with rare exceptions, the patient dies. Survivors experience a period of sore muscles but suffer no further problems.

d. prevention: Tetanus toxoid vaccine (DPT) given prior to injuries protects against the toxin. A sequence of three doses of toxoid and a booster every ten years. People do not get boosters on schedule and at least 50% of the U.S. population does not have adequate protection. Almost 70% of tetanus cases in the U.S. occur in individuals over 50 years of age.

e. treatment: Immune globulin containing high concentrations of tetanus antitoxin and antibiotics are given to nonimmunized patients when injuries are treated, and respiratory support may be necessary. Damaged tissue should also be removed. Patients should receive toxoid immunization after they recover.

6. Botulism

a. causative agent: Clostridium botulinum

b. method of transmission: It is found virtually everywhere in the environment. Since it is prevalent in soil, spores are often present in food, especially raw agricultural products such as vegetables and honey. Spores in ocean sediment contaminate fish and seafood. In anaerobic environments, such as sealed cans of nonacidic foods (green beans, pepper, mushrooms), the bacteria produce a neurotoxin. The neurotoxin is the most potent known. There are three serological types of toxin: Type A is the most virulent and there have been deaths when food was tasted but not swallowed. It is usually found in the western U.S. Type B is found in the eastern U.S., and Type E is often in marine or lake sediments. Endospores are highly heat resistant, but the toxin can be inactivated by only a few minutes' boiling.

c. symptoms: The neurotoxin is highly specific for the synaptic end of the nerve where it blocks the release of acetylcholine, a neurotransmitter necessary to transmit the impulse across the synapse. Incubation time varies, but symptoms usually occur in a day or two. Nausea, but no fever, general weakness, and difficulty swallowing may precede neurological symptoms. There is a sudden onset and rapidly progressing paralysis called flaccid (limp) paralysis because muscles are paralyzed in a relaxed condition. Nerves that control the head are affected first. Double vision, difficulty speaking and swallowing, are followed by difficulty breathing. Infant botulism is caused by ingesting endospores in soil and other materials, but 30% of the reported cases have been associated with honey. The normal microbiota of infants is not well established so competition does not occur. As the toxin is absorbed, the infant becomes lethargic and loses the ability to suck and swallow, and the disease is often called
"floppy baby" syndrome. Wound botulism is the least common form and as the endospores germinate and multiply in anaerobic wounds, they produce toxin. The toxin enters the blood and circulates throughout the body and causes progressive paralysis about a week after injury.

d. prevention: Careful following of canning procedures, and boiling home-canned foods vigorously before serving would eliminate most foodborne botulism. A vaccine is available for exposed laboratory workers.

e. treatment: Treatment relies heavily on supportive care. Antibiotics are of no use because the toxin is preformed. Antitoxins aimed at the neutralization of A, B, and E toxins are usually administered together. The antitoxins do not affect the toxin already attached to the nerve ends. Recovery requires that the nerve endings regenerate, therefore it proceeds slowly. Extended respiratory assistance may be needed, and some neurological impairment may persist for months.

Viral Diseases

1. Rabies

a. causative agent: rhabdovirus - it contains a single strand of RNA surrounded by a lipid envelope and it is bullet shaped.

b. method of transmission: The virus has worldwide distribution and since it infects all mammals exposed to it the possibilities for reservoir infections are almost limitless. Foxes, coyotes, skunks, raccoons, and bats are highly susceptible. In urban areas, cats and dogs may be infected. Bats are particularly dangerous because they are asymptomatic and shed viruses in their feces, urine, and saliva. Infection may occur by inhalation in caves with dense populations of infected bats. The main mode of transmission is from a bite by an infected animal that is shedding viruses in their saliva.

c. symptoms: When the virus enters a wound it multiplies in skeletal muscle and connective tissue for 1 to 4 days. The virus then migrates to nerves, where it multiplies slowly until it reaches the spinal cord. It progresses rapidly up the spinal cord to the brain. Symptoms appear between 20 and 60 days depending on the distance of the wound from the brain. The first symptoms are headache, fever, nausea, and partial paralysis near the bite site (prodromal phase). These symptoms persist for 2 to 10 days and then worsen until the acute neurological phase occurs in which the individual’s gait becomes uncoordinated as paralysis becomes more general. When the central nervous system becomes involved, the
individual alternates between periods of agitation and calm. 

Hydrophobia (fear of water) occurs as throat muscles undergo painful spasms, especially during swallowing. Aerophobia (fear of moving air) occurs because the skin is hypersensitive to any sensations. Confusion, hyperactivity, and hallucinations also occur. Within 10-14 days of the onset of symptoms, the individual usually goes into coma and dies (paralytic phase).

d. prevention: Avoid animals exhibiting strange behavior. The best means of prevention is to immunize pets. Rabies immunization is recommended for veterinarians and their staff, hunters, who may have contact with wild animals, and technicians who work with the virus.

e. treatment: Thoroughly clean the bite with soap and flushing it with large amounts of water. Human diploid cell vaccine (HDCV) is given intramuscularly in six injections combined with passive immunization with human rabies immune globulins (RIG) (serum containing antibodies against the virus).

2. Poliomyelitis (Polio)

a. causative agent: Three strains of single-stranded RNA, non-enveloped picornaviruses that have an affinity for motor neurons of the spinal cord and brain.

b. method of transmission: Transmitted by the fecal-oral route. They survive for long periods outside the body and are transmitted by food and water contaminated with feces.

c. symptoms: The primary areas of multiplication are the throat and small intestine. The majority of cases are asymptomatic or cause mild symptoms, such as headache, sore throat, fever, and nausea, which are interpreted as mild meningitis or influenza. Asymptomatic or mild cases are most common in the very young. When infection occurs in adolescence or early adulthood, the paralytic form occurs more frequently. The virus replicates in the epithelial cells lining the nose, throat, and intestine and then enters the lymph nodes, where it multiplies. From the lymph nodes it enters the blood and if the viremia is persistent, the virus penetrates the capillary walls and enters the CNS. High fever, back pain, muscle spasms, and partial or complete paralysis in a relaxed state (flaccid paralysis resembling botulism) result from the invasion of and multiplication in the motor neurons. When respiratory muscle are affected, death results.
d. **prevention:** Good sanitation and vaccination. Since there are three different serotypes of the poliovirus, immunity must be provided for all three. The *Salk* vaccine uses viruses that have been inactivated (inactivated polio virus or IPV) by treatment with formalin. They require a series of injections and their effectiveness is 90% against paralytic polio. The antibody levels decline with time and booster shots are needed every few years to maintain immunity. A new enhanced inactivated polio vaccine (E-IPV) has been produced on human diploid cells and is important in the immunization of immunosuppressed individuals. The *Sabin* vaccine contains three living, attenuated strains of the virus and is more popular in the U.S. than the *Salk* vaccine. The immunity achieved resembles that acquired by natural infection.

e. **treatment:** Supportive treatment and individuals with respiratory paralysis are put on mechanical support.

3. **Arthropod-borne Encephalitis**

   a. **causative agent:** arboviruses (a group of RNA viruses). There are strains that cause Eastern equine encephalitis (EEE), Western equine encephalitis (WEE), Venezuelan equine encephalitis (VEE), and St. Louis encephalitis (SLE)

   b. **method of transmission:** Horses and birds are the main reservoirs of infection and it is transmitted to humans by the bite of an infected mosquito.

   c. **symptoms:** The virus multiplies in the skin and then spreads to lymph nodes. Viremia involving large numbers of viruses follows. In a few infections, the viruses invade the CNS where they cause shrinkage and lysis of neurons. The symptoms of WEE are fever and headache, and sometimes convulsions. EEE is a much more serious disease, causing tissue necrosis in the brain. The disease is fatal in 50-80% of cases, and survivors often suffer permanent brain damage. VEE symptoms resemble influenza. SLE causes the most severe symptoms in elderly individuals. Malaise, fever, and chills result from viremia. Anorexia, myalgia (muscle pain), sore throat and drowsiness are common. Some have neurological disorders, altered states of consciousness, and convulsions. Recovery is complete.

   d. **prevention:** Mosquito control and vaccinating horses.

   e. **treatment:** Supportive treatment.