Microbes enter the nervous system via:

- Skull or backbone fractures (trauma)
- Medical procedures
- Along peripheral nerves
- Blood stream or lymphatic system

The Nervous System

Define central nervous system and blood-brain barrier.

- Central nervous system: brain and spinal cord
- Peripheral nervous system: nerves branching from CNS
- CNS covered by 3 membranes – dura mater, arachnoid, pia mater
- Cerebrospinal fluid circulates between arachnoid and pia mater

Microbial Diseases of the Nervous System

Differentiate meningitis from encephalitis.

- Bacteria can grow in the cerebrospinal fluid in the subarachnoid space of the CNS
- The blood brain barrier (capillaries) prevents passage of some materials (such as antimicrobial drugs) into the CNS
- Meningitis
  - Inflammation of meninges
  - Caused by viruses, bacteria, fungi, protozoa
  - Nearly 50% of opportunistic bacteria can cause meningitis.
- Encephalitis
  - Inflammation of the brain

The Meninges and Cerebrospinal Fluid

Three major causes of bacterial meningitis

<table>
<thead>
<tr>
<th>Bacterium</th>
<th>Percentage of Cases</th>
<th>Mortality Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Streptococcus pneumonia</td>
<td>30-50</td>
<td>19-46</td>
</tr>
<tr>
<td>Neisseria meningitidis</td>
<td>15-40</td>
<td>3-17</td>
</tr>
<tr>
<td>Haemophilus influenza</td>
<td>2-7*</td>
<td>3-11</td>
</tr>
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Other bacteria causing meningitis account for 6-8% of cases.

*Before introduction of Hib vaccine, H. influenza accounted for about 45% of cases of bacterial meningitis; about 75% of these cases occurred in children under age 5.

Bacterial Meningitis

Explain how bacterial meningitis is diagnosed and treated.

- Fever, headache, stiff neck
- Followed by nausea and vomiting
- May progress to convulsions and coma
- Diagnosis by Gram stain and serological tests of CSF
- Cultures made on blood agar and incubated in reduced oxygen
- Treated with cephalosporins

Haemophilus influenzae Meningitis

Discuss the epidemiology of meningitis caused by H. influenzae, S. pneumoniae, N. meningitidis, and L. monocytogenes.

- H. influenzae normal part of throat microbiota
- Requires blood factors for growth
- Type b occurs mostly in children (6 months to 4 years)
- Gram-negative aerobic bacteria, normal throat microbiota
- Capsule antigen type b
- Prevented by Hib vaccine (conjugated vaccine directed against capsular polysaccharide antigen)

Other bacteria causing meningitis account for 6–8% of cases.

**Table 22.1**

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*Before introduction of Hib vaccine, H. influenzae accounted for about 45% of cases of bacterial meningitis, about 70% of these cases occurred in children under age 5. SOURCE: Adapted from E.J. Phillips and A.E. Simor, “Bacterial Meningitis in Children and Adults,” Postgraduate Medicine 103 (3):104 (1998).

Decline in incidence due to increased vaccination

Neisseria Meningitis, Meningococcal Meningitis

- N. meningitidis – probably gain access to meninges through bloodstream, most often in young children
- Gram-negative aerobic cocci, capsule
- 10% of people are healthy nasopharyngeal carriers
- Begins as throat infection, rash – symptoms due to endotoxin
- Serotype B is most common in the U.S.
- Vaccine against some serotypes is available
- Military recruits vaccinated with purified capsular polysaccharide to prevent epidemics in training camps

N. meningitidis in clusters attached to mucous membrane of pharynx
**Streptococcus pneumoniae** Meningitis, Pneumococcal Pneumonia

- Gram-positive diplococci
- 70% of people are healthy nasopharyngeal carriers
- Most common in children (1 month to 4 years) and hospitalized patients
- Mortality: 30% in children, 80% in elderly
- Prevented by vaccination (some protection)

**Listeria monocytogenes**

- Meningitis in newborns, immunosuppressed, pregnant women, cancer patients
- Gram-negative aerobic rod
- Usually foodborne, can be transmitted to fetus
- Can cross the placenta causing spontaneous abortion and stillborns
- Asymptomatic in healthy adults
- Reproduce in phagocytes

**Listeriosis – spread by pseudopod**

**Tetanus**

*Discuss the epidemiology of tetanus, including mode of transmission, etiology, disease symptoms, and preventive measures.*

- *Clostridium tetani*
- Gram-positive, endospore-forming, obligate anaerobe
- Grows in deep wounds as localized infection
- Tetanosporamin neurotoxin released from dead cells blocks relaxation pathway in muscles
- Spasms, contraction of jaw muscles and respiratory muscles
- Prevention by vaccination with tetanus toxoid (DTP) and booster (DT)
- Treatment with tetanus immune globulin for unimmunized person
- Debridement tissue removal and antibiotics help control infection

**Botulism**

*State the causative agent, symptoms, suspect foods, and treatment for botulism.*

- Diagnosis by inoculating mice protected by antitoxin with toxin from patients or food for differential diagnosis
- Treatment: supportive care and antitoxin
- Infant botulism results from *C. botulinum* growing in intestines
- Wound botulism results from growth of *C. botulinum* in wounds.
Botulism

- *Clostridium botulinum*
- Gram-positive, endospore-forming, obligate anaerobe
- Serological types vary in virulence, type A the worst
- Intoxication due to ingesting botulinic toxin, an exotoxin growing in food (heat labile, destroyed by boiling for 5 minutes)
- Botulinal toxin blocks release of neurotransmitter causing flaccid paralysis
- Blurred vision in 1-2 days, progressive flaccid paralysis, follows for 1-10 days, possibly resulting in cardiac or respiratory failure
- Prevention:
  - Proper canning (not grow in acid foods or aerobic)
  - Nitrites prevent endospore germination in sausages

Botulism

- Type A
  - 60-70% fatality
  - Found in CA, WA, CO, OR, NM
- Type B
  - 25% fatality
  - Europe and eastern U.S.
- Type E
  - Found in marine and lake sediments
  - Pacific Northwest, Alaska, Great Lakes area

Diagnosis

- Diagnosis of botulism
- If mouse dies within 72 hours, evidence of toxin (poor mouse!)
- Mice are vaccinated against 3 types of botulism, providing differential diagnosis

Leprosy (Hansen’s disease)

*Discuss the epidemiology of leprosy, including mode of transmission, etiology, disease symptoms, and preventive measures.*

- *Mycobacterium leprae* – never cultured on artificial media, but on armadillos and mouse footpads
- Acid-fast rod that grows best at 30°C (diagnosed in lesions or fluids and lepromin test)
- Grows in peripheral nerves and skin cells
- Transmission requires prolonged contact with an infected person (not highly contagious)
- Tuberculoid (neural) form: Loss of sensation in skin areas; positive lepromin test
- Lepromatous (progressive) form: Disfiguring nodules over body; negative lepromin test
- Made noncontagious within 4-5 days with sulfone drugs
- Can die of secondary infections like tuberculosis

Leprosy

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- Can die of secondary infections like tuberculosis

Poliomyelitis

*Discuss the epidemiology of poliomyelitis, rubies, and arboviral encephalitis, including mode of transmission, etiology, and disease symptoms.*

- Poliovirus – diagnosis by isolation of virus from feces and throat secretions
- Transmitted by ingestion of water contaminated with feces
- Initial symptoms: sore throat and nausea, headache, fever, stiffness of back and neck
- First invades lymph nodes of neck and small intestine
- Viremia may occur; if persistent, virus can enter the CNS; destruction of motor cells and paralysis occurs in <1% of cases
- Prevention is by vaccination (Salk vaccine injected with inactivated polio vaccine, Sabin vaccine orally with 3 live attenuated strains)
Iron Lungs in 1950’s

Poliomyelitis

Figure 22.10

Compare the Salk and Sabin vaccines.

Figure 22.11

Rabies virus (Rhabdovirus)

Compare preexposure and postexposure treatments for rabies.

• Transmitted by animal bite, inhalation of aerosols, invasion through minute skin abrasions
• Virus multiplies in skeletal muscles and connective tissue, then brain cells causing encephalitis (acute and often fatal)
• Virus moves along peripheral nerves to CNS (next slide)
• Initial symptoms may include muscle spasms of the mouth and pharynx and hydrophobia
• Diagnosis by direct FA (fluorescent antibody) tests of saliva, serum, CSF
• Furius rabies: animals are restless then highly excitable
• Paralytic rabies: animals seem unaware of surroundings
• Preexposure prophylaxis: Infection of human diploid cells vaccine
• Postexposure treatment: Vaccine + immune globulin

Arboviral Encephalitis

Explain how arboviral encephalitis can be prevented.

• Arboviruses are arthropod-borne viruses that belong to several families of viruses.
• Symptoms are chills, headache, fever, coma
• Increase in summer months when mosquitoes numerous
• EEE – Eastern equine encephalitis
• WSE – Western equine encephalitis, etc.
• Diagnosis based upon serological tests (antigen-antibody reactions in blood serum)
• Prevention is by controlling mosquitoes
Arboviral infections in the central nervous system

Seasonal occurrence of disease

<table>
<thead>
<tr>
<th>Year</th>
<th>1990</th>
<th>1995</th>
<th>2000</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cases</td>
<td>15</td>
<td>20</td>
<td>25</td>
</tr>
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</table>

Arboviral Encephalitis

<table>
<thead>
<tr>
<th>Disease</th>
<th>Vector</th>
<th>Host</th>
<th>M. S.</th>
<th>Location</th>
</tr>
</thead>
<tbody>
<tr>
<td>Eastern equine encephalitis (EEE)</td>
<td>Mosquitoes</td>
<td>Horses, cattle</td>
<td>Encephalitis</td>
<td>Eastern United States</td>
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<tr>
<td>Western equine encephalitis (WEE)</td>
<td>Mosquitoes</td>
<td>Birds, horses</td>
<td>Encephalitis</td>
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<tr>
<td>St. Louis encephalitis (SLE)</td>
<td>Mosquitoes</td>
<td>Birds, mammals</td>
<td>Encephalitis</td>
<td>Throughout the year</td>
</tr>
<tr>
<td>California encephalitis (CE)</td>
<td>Mosquitoes</td>
<td>Small mammals, birds, New York</td>
<td>Encephalitis</td>
<td>Throughout the year</td>
</tr>
</tbody>
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Cryptococcus neoformans Meningitis (Cryptococcosis)

Identify the causative agent, vector, symptoms, and treatment for cryptococcosis.

- **Encapsulated yeastlike fungus**
- **Soil fungus associated with pigeon and chicken dropping (inhalation)**
- **Transmitted by the respiratory route; spreads through blood to the CNS (brain and meninges)**
- **Diagnosis by latex agglutination tests in serum or CSF**
- **Mortality up to 30%**
- **Treatment: amphotericin B and flucytosine**

Cryptococcus neoformans Meningitis (Cryptococcosis)

African Trypanosomiasis – Sleeping sickness

Identify the causative agent, vector, symptoms, and treatment for African trypanosomiasis and Naegleria meningoencephalitis.

- **Protozoan Trypanosoma brucei gambiense infection is chronic (2 to 4 years)**
- **T. b. rhodesiense infection is more acute (few months)**
- **Transmitted from animals to humans by tsetse fly**
- **Affects nervous system causing lethargy and coma**
- **Prevention: elimination of the vector**
- **Treatment: Eflornithine blocks an enzyme necessary for the parasite**
- **Parasite evades the antibodies through antigenic variation (surface antigens), complicating vaccine development**

African Trypanosomiasis

Evading the immune system by stages of infection
Protozoan infects nasal mucosa from swimming in water, invades brain
Almost always fatal

Transmissible Spongiform Encephalopathies

- Chronic fatigue syndrome (CFS) may be caused by unknown infectious agent

Naegleria fowleri

Transmissible Spongiform Encephalopathies

- Caused by prions (self-replicating proteins with no detectable nucleic acid)
  - Prions transferable animal to animal
    - Sheep scrapie
    - Bovine spongiform encephalopathy
  - Prions transmitted between humans
    - Creutzfeldt-Jakob disease
    - Kuru
  - Transmitted by ingestion or transplant or inherited
  - Chronic (progresses slowly), fatal causing spongiform degeneration

Table 22.3: Microbial Diseases of the Nervous System

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Transmissible Spongiform Encephalopathies

List the characteristics of diseases caused by prions.

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