Microbial Diseases of the Nervous System

Chapter 22
I. STRUCTURE AND FUNCTION OF THE NERVOUS SYSTEM

• 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.
I. STRUCTURE AND FUNCTION OF THE NERVOUS SYSTEM

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.
The CNS is covered by three layers of membranes called meninges: the dura mater, arachnoid, and pia mater. Cerebrospinal fluid (CSF) circulates between the arachnoid and the pia mater in the subarachnoid space.
I. STRUCTURE AND FUNCTION OF THE NERVOUS SYSTEM

• 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 to allow entry of organisms.

• F. An infection of the meninges is called meningitis. An infection of the brain is called encephalitis.
Lumbar puncture. The CSF is obtained by inserting a long, sterile, hollow needle into the spinal subarachnoid space in the lower (lumbar) back.
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.
BACTERIAL DISEASES OF THE NERVOUS SYSTEM

1. *Hemophilus influenzae*

   - *H. influenzae* is part of the normal throat microbiota.
   - *H. influenzae* requires blood factors for growth: X and V; there are six types of *H. influenzae* based on capsule differences.
   - *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 blood stream and then invade meninges.
   - Now have vaccine = Hib. A conjugated vaccine directed against the capsular polysaccharide antigen.
Direct smear of CSF from a child, showing abundant gram-negative, pleomorphic coccobacilli characteristic of H. influenzae. The background shows degenerating inflammatory cells. Gram stain, High-power view.
Example of H. influenza growing on Chocolate agar. Notice the gray, mucoid colonies characteristic of encapsulated strains.
II. BACTERIAL DISEASES OF THE NERVOUS SYSTEM

– 2. Neisseria meningitidis

• *N. meningitidis* causes meningococcal meningitis.
  – This bacterium is found in the throats of healthy carriers.

• The bacteria probably gain access to the meninges through the bloodstream.
  – The bacteria may be found in leukocytes in CSF.

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

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

• Some types cause widespread epidemics in US (type C) Africa (type A).
Neisseria meningitidis attached to epithelial cells of the pharyngeal mucous membrane
Direct smear of CSF from a high-school student showing clusters of gram-negative diplococci consistent with N. meningitidis within polymorphonuclear leukocytes. Note the increased cellularity of the smear in this cytocentrifuge preparation. Gram stain. High-power view.
Petechial lesion in meningococcemia.
II. BACTERIAL DISEASES OF THE NERVOUS SYSTEM

3. *Streptococcus pneumoniae*

- *S. pneumoniae* is commonly found in the nasopharynx (70% healthy carriers).
- Gram Pos encapsulated diplococci.
- Elderly patients and young children (1mo to 4yr) are most susceptible to *S. pneumoniae* meningitis. It is rare but has a high mortality rate.
- The vaccine for pneumococcal pneumonia may provide some protection against pneumococcal meningitis.
- Antibiotic resistant strains are common.
Direct smear of acute bacterial meningitis in an adult showing the lancet-shaped gram-positive diplococci characteristic of *S. pneumoniae*. The polysaccharide capsule produces a prominent "halo" around organisms. Gram stain. Non-cyto centrifuge preparation. High-power view
Streptococcus pneumoniae colonies on blood agar. The colonies demonstrate a characteristic mucoid appearance.
II. BACTERIAL DISEASES OF THE NERVOUS SYSTEM

— 4. *Listeria monocytogenes*

- *Listeria monocytogenes* causes meningitis in newborns (via pregnant women).
  - L. monocytogenes can cross the placenta and cause spontaneous abortion and stillbirth.
- Adult meningitis: the immunosuppressed, and cancer patients.
- Proliferates within macrophages where it avoids the immune system.
- GPR can grow in refrigerator temperature.
- Acquired by ingestion of contaminated food, it may be asymptomatic in healthy adults. A well recognized animal pathogen.
Cell to cell spread of *L. monocytogenes*. 

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Figure 22.5
II. BACTERIAL DISEASES OF THE NERVOUS SYSTEM

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

• *Broad spectrum cephalosporins may be administered before identification of the pathogen.*

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

• *Cultures are usually made on blood agar and incubated in an atmosphere containing increased CO$_2$.*
II. BACTERIAL DISEASES OF THE NERVOUS SYSTEM

— 6. **Tetanus — Clostridium tetani**

- *Tetanus is caused by a localized infection of a wound by Clostridium tetani endospores. 1 million cases worldwide each year.*
- *Obligate anaerobic spore forming GPR found commonly in soil, esp. those contaminated with animal waste.
- *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.*
- *Opposing muscles contract simultaneously so joints become ‘locked’.*
  - Normally, the opposing muscle receives an inhibitory neurotransmitter (GABA) signal to relax.
- *C. tetani is an anaerobe that will grow in deep, unclean wounds and wounds with little bleeding.*
- *Acquired immunity results from DPT immunization in childhood that includes tetanus toxoid.*
- *Following an injury, an immunized person may receive a booster of tetanus toxoid. An unimmunized person may receive tetanus immune globulin (human).*
- *Debridement (removal of tissue) and antibiotics may be used to control the active infection.*
Figure 22.6

Advanced case of tetanus
Infectious Diseases - Tetanus - The disease is due to the action of toxin (tetanospasmin) produced by *Clostridium tetani* on synapses within the central nervous system. The characteristic clinical manifestations are trismus (“lockjaw”) and generalized muscle spasms. Risus sardonicus, the “sardonic smile”, is caused by spasm of the facial muscles and is a feature of tetanus in older children and adults. Opisthotonus, due to intense contraction of the paravertebral muscles, is seen most commonly in neonatal tetanus. Arching of back, heels bend back on legs, arms and hands to flex rigidly at the joints.
Fig. 84

Microbiology of Infectious Disease - Gram stained appearance of *Clostridium tetani* showing thin gram positive rods with terminal drum stick spores. It is an anaerobe. The spores are especially resistant to desiccation and on implantation germinate and produce powerful toxin.
II. BACTERIAL DISEASES OF THE NERVOUS SYSTEM

– 7. Botulism – *Clostridium botulinum*

- Botulism is caused by an exotoxin produced by *C. botulinum* growing in foods.
- Obligate anaerobic spore forming GPR.
- Serological types of botulinum toxin vary in virulence, with type A being the most virulent and found in the Western US. Type E most common in Alaska.
- The toxin is a neurotoxin that inhibits the transmission of nerve impulses by preventing the release of ACh at the synapse.
- Blurred vision occurs in 1-2 days; progressive flaccid paralysis follows for 1-10 days, possibly resulting in death from respiratory and cardiac failure.
- *C. botulinum* will not grow in acidic foods or in an aerobic environment.
- Endospores are killed by proper canning. The addition of nitrites to foods inhibits growth after endospore germination.
- The toxin is heat labile and is destroyed by boiling (100 C) for 5 minutes.
- Infant botulism results from the growth of *C. botulinum* in an infant's intestines.
- Wound botulism occurs when *C. botulinum* grows in anaerobic wounds.
- For diagnosis, mice protected with antitoxin are inoculated with toxin from the patient or foods.
- This toxin can be diluted (Botox) and used in local injections as a cosmetic aid to eliminate wrinkles in the face and prevent arm pit sweating! Can also be used to treat excessive muscle contractions.
*Clostridium botulinum* showing spore production
Diagnosis of botulism by identification of toxin type. Inject mice with filtrate of food and check for symptoms within 72 hours. Protect some mice with anti toxin: A, B, E to see which are protected this identifying the toxin type.
BACTERIAL DISEASES OF THE NERVOUS SYSTEM

8. Leprosy – *Mycobacterium leprae*

- *Mycobacterium leprae* causes leprosy, or Hansen's disease.
- Only organism that grows primarily in peripheral nervous system tissue.
- *M. leprae* has never been cultured on artificial media. It can be cultured in armadillos and footpads of mice.
- The tuberculoid form of the disease is characterized by loss of sensation in the skin surrounded by nodules. The lepromin skin test is positive.
- Laboratory diagnosis is based on observations of acid-fast rods (AFB) in lesions or fluids and the lepromin test.
- In the lepromatous form, disseminated nodules and tissue necrosis occur. The lepromin test is negative.
- Leprosy is not highly contagious and is spread by prolonged contact with exudates and nasal secretions.
- Untreated individuals often die of secondary bacterial complications, such as tuberculosis.
- Patients with leprosy are made noncommunicable within 4-5 days with sulfone drugs and then treated as outpatients.
- Leprosy occurs primarily in the tropics. 500K new cases reported each year in these areas.
Leprosy lesions. a) depigmented area of skin surrounded by border or nodules is typical of tuberculoid (neural) leprosy. b) When the immune system fails to control the infection, the result is lepromatous (progressive) leprosy. Typical of the late stage of the disease, progressive damage occurs especially in the cooler parts of the body.
Infectious Diseases - Leprosy (Hansen’s Disease) The neuropathy of lepromatous leprosy leads to ulceration, loss of tissue and eventually to gross deformity. Acid-fast bacilli are seen in skin snips of biopsies.
- *M. leprae* from a skin biopsy from a patient with lepromatous leprosy (acid-fast smear stained with Ziehl-Nielsen stain).
III. VIRAL DISEASES OF THE NERVOUS SYSTEM

– 1. Poliomyelitis - Poliovirus
  • *The symptoms of poliomyelitis are usually headache, sore throat, fever, stiffness of the back and neck, and occasionally paralysis (less than 1% of cases).*
  • *Poliovirus is found only in humans and is transmitted by the ingestion of water contaminated with feces.*
  • *Poliovirus first invades lymph nodes of the neck and small intestine. Viremia and spinal cord involvement may follow. The virus attacks motor neurons, especially in the upper spinal cord.*
  • *Post-Polio Syndrome – Muscle weakness in middle aged adults due to previous infection in childhood. Progresses slowly.*
  • *Diagnosis is based on isolation of the virus from feces and throat secretions.*
  • *The Salk vaccine (an inactivated polio vaccine, or IPV) involves the injection of formalin-inactivated viruses and boosters every few years.*
    – *Vaccine of choice where wild virus is no longer present as is case currently in US.*
  • *The Sabin vaccine (an oral polio vaccine, or OPV) contains three live, attenuated strains of poliovirus and is administered orally.*
    – *Vaccine of choice in areas with wild virus.*
  • *Through vaccination, the WHO plans to eliminate polio by the year 200?*. 
Polio patients in an iron lung machines. Used to assist in breathing by alternately creating a negative and positive atmospheric pressure outside of the body.
III. VIRAL DISEASES OF THE NERVOUS SYSTEM

2. Rabies – Rabies virus

- Rabies virus (a rhabdovirus) causes an acute, usually fatal, encephalitis called rabies.
- 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.
- Encephalitis occurs when the virus moves along peripheral nerves to the CNS.
- Symptoms of rabies include spasms of mouth and throat muscles followed by extensive brain and spinal cord damage and death.
  - Hydrophobia: paralysis in pharynx makes swallowing difficult, so fear of water. Foaming of mouth due to saliva accumulation.
- Laboratory diagnosis may be made by direct immunofluorescent tests of saliva, serum, and CSF or brain smears.
- Reservoirs for rabies in the U.S. include skunks, bats, foxes, and raccoons. Domestic cattle, dogs, and cats may get rabies. Rodents and rabbits seldom get rabies.
- The Pasteur treatment for rabies involved multiple subcutaneous injections of rabies virus grown in rabbit spinal cord tissue.
- Current post-exposure treatment includes administration of human or human rabies immune globulin (RIG) along with multiple intramuscular injections of human diploid cell vaccine (HDCV).
- Unique in that incubation is long enough to immunize after exposure.
- Pre-exposure immunization consists of injections of HDCV.
Pathology of rabies infection.
Left: Areas of US where rabies dominates on certain wildlife species. Right: Reported cases of rabies in animals, 2003 CDC. Note: rabies infected bats were found in 47 out of 48 of the contiguous lower 48 states.

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III. VIRAL DISEASES OF THE NERVOUS SYSTEM

3. Arboviral Encephalitis

- Cases range from subclinical to severe with symptoms of encephalitis: chills, headache, fever, and eventually coma.
- Many types of arboviruses transmitted by mosquitoes cause encephalitis.
- The incidence of encephalitis increases in the summer months when mosquitoes are most numerous.
- Horses are frequently infected by EEE, WEE, West Nile viruses.
- Diagnosis is based on serological tests.
- Control of the mosquito vector is the most effective way to control encephalitis.
Cytocentrifuge preparation of CSF in a case of "aseptic" meningitis. Lymphocytes are present, and in this case the background is bloody. No organisms are seen. Wright stain. Most of these viral infections are diagnosed with serological (antibody) tests or CPE
### DISEASES IN FOCUS: Types of Arboviral Encephalitis

<table>
<thead>
<tr>
<th>Disease</th>
<th>Pathogen</th>
<th>Mosquito vector</th>
<th>Reservoir</th>
<th>U.S. distribution</th>
<th>Epidemiology</th>
<th>Mortality</th>
</tr>
</thead>
<tbody>
<tr>
<td>Western equine encephalitis</td>
<td>WEE virus</td>
<td>Culex</td>
<td>Birds, horses</td>
<td><img src="image1" alt="Map" /></td>
<td>Severe disease; frequent neurological damage, especially in infants</td>
<td>5%</td>
</tr>
<tr>
<td>Eastern equine encephalitis</td>
<td>EEE virus</td>
<td>Aedes, Culiseta</td>
<td>Birds, horses</td>
<td><img src="image2" alt="Map" /></td>
<td>More severe than WEE; affects mostly young children and younger adults; relatively uncommon in humans</td>
<td>&gt;30%</td>
</tr>
</tbody>
</table>

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Types of arboviral encephalitis by region of the US. Types are named after location where first identified, whether they are common causes of disease there or not. See next slide for rest of arboviral types.
## Diseases in Focus: Types of Arboviral Encephalitis

<table>
<thead>
<tr>
<th>Disease</th>
<th>Pathogen</th>
<th>Mosquito Vector</th>
<th>Reservoir</th>
<th>U.S. Distribution</th>
<th>Epidemiology</th>
<th>Mortality</th>
</tr>
</thead>
<tbody>
<tr>
<td>St. Louis encephalitis</td>
<td>SLE virus</td>
<td>Culex</td>
<td>Birds</td>
<td>Mostly urban outbreaks; affects mainly adults over 40</td>
<td>20%</td>
<td></td>
</tr>
<tr>
<td>California encephalitis</td>
<td>CE virus</td>
<td>Aedes</td>
<td>Small mammals</td>
<td>Affects mostly 4- to 18-year age groups in rural or suburban areas; La Crosse strain medically most important. Rarely fatal; about 10% have neurological damage</td>
<td>1% of those hospitalized</td>
<td></td>
</tr>
<tr>
<td>West Nile encephalitis</td>
<td>WN virus</td>
<td>Primarily Culex and Aedes</td>
<td>Primarily birds, assorted rodents, and large mammals</td>
<td>Most cases asymptomatic, otherwise symptoms vary from mild to severe; likelihood of severe neurological symptoms and fatality increases with age</td>
<td>4-18% of those hospitalized</td>
<td></td>
</tr>
</tbody>
</table>
An example of a mosquito vector that can pass some of the arboviruses.
Cases of reported California encephalitis virus in the US. Note the seasonal variation.
III. FUNGAL DISEASES OF THE NERVOUS SYSTEM
(Rarely invaded by fungi.)

1. Cryptococcus neoformans meningitis (Cryptococcus)
   • Cryptococcus neoformans is an encapsulated yeastlike fungus that causes meningitis.
   • The disease may be contracted by inhalation of dried infected pigeon (or other bird) droppings.
   • The disease begins as a lung infection and may spread to the brain and meninges.
   • Immunosuppressed individuals are most susceptible to Cryptococcus neoformans meningitis.
   • Diagnosis is based on latex agglutination tests for cryptococcal antigens in serum or CSF.
Cryptococcus neoformans showing a well developed capsule made visible with India ink.
India ink preparation is used primarily to examine cerebrospinal fluid for the presence of the encapsulated yeast *Cryptococcus neoformans*. This is an India ink preparation from an exudate containing encapsulated budding yeasts.
Cytocentrifuge preparation of CSF showing a single yeast with narrow-based budding and prominent surrounding capsule characteristic of Cryptococcus neoformans. Cryptococcal meningitis in partially immunocompetent hosts may show only rare organisms mixed with an inflammatory background of lymphocytes, monocytes, and eosinophils. Wright stain. High-power view.
Cryptococcus neoformans on Sabourds agar.
Microbiology of Infectious Disease - Gram stain of *Cryptococcus neoformans*.
III. FUNGAL DISEASES OF THE NERVOUS SYSTEM (Rarely invaded by fungi.)

- 2. *Coccidioides imitis*- San Joaquin Valley fever
  - Valley fever is acquired by respiratory exposure to dry soil with spores of *Coccidioides imitis*.
  - A respiratory infection may progress to systemic disease including meningitis.
Ⅳ. Protozoan Diseases of the Nervous System

– 1. African Trypanosomiasis

• *African trypanosomiasis is caused by the protozoa Trypanosoma brucei gambiense and T. b. rhodesiense and transmitted by the bite of the tsetse fly (Glossina).*

• One million people in Africa affected – 20,000 new cases/year.

• *The disease affects the nervous system of the human host, causing lethargy and eventually coma. It is commonly called sleeping sickness.*

• 2-4 year course of disease as the organism goes from blood to CNS.

• *Vaccine development is hindered by the protozoan’s ability to change its surface antigens.*
Infectious Diseases - African trypanosomiasis - *Trypanosoma gambiense* (West Africa) and *Trypanosoma rhodesiense* (East Africa). This is a blood smear from a patient from West Africa. Note the free flagellum and undulating membrane.
Life cycle of the etiologic agents of sleeping sickness (Trypanosoma gambiense and T. rhodesiense.)
How trypanosomes evade the immune system where one clone replaces another over time. As the parasites are practically eliminated by the immune system, another antigenic variant arises to replace them.
African Trypanosomiasis - During the acute phase of the illness organisms are found in the blood and lymph nodes, and a helpful diagnostic sign is enlargement of nodes in the posterior cervical triangle (Winterbottom’s sign).
African Trypanosomiasis. In both forms of African trypanosomiasis a meningoencephalitis results and causes much of the morbidity and mortality of this disease. In both forms, the final stage of the encephalitis is a profound stupor.
V. NERVOUS SYSTEM DISEASES CAUSED BY PRIONS

1. Prions: abnormally folded proteins that mimic an infectious disease
   - Diseases of the CNS that progress slowly and cause spongiform degeneration are caused by prions. Symptoms progress to loss of motor control and death.
   - Sheep scrapie and bovine spongiform encephalopathy (BSE) are examples of diseases caused by prions that are transferable from one animal species to another.
   - Creutzfeldt-Jacob disease and kuru are human diseases similar to scrapie. Kuru occurs in isolated groups of cannibals who eat brains.
   - Prions are proteins that can induce a shape change in a normal protein causing them to clump leading to cell death.
   - Heating and irradiation have no effect on the prions. Autoclaving is not reliable.
a) Spongiform effect of the prions on brain tissue. b) Fibrils produced in the brain due to prion disease. Prions themselves are not visible.
GENE ID: 5621 PRNP | prion protein (p27-30) (Creutzfeldt-Jakob disease, Gerstmann-Strausler-Scheinker syndrome, fatal familial insomnia) [Homo sapiens] (Over 100 PubMed links)

Score = 339 bits (870), Expect = 9e-92, Method: Compositional matrix adjust. Identities = 226/254 (88%), Positives = 243/254 (95%), Gaps = 1/254 (0%)

Query 1
MANLGYWLLALFVT TCTDVGLCKKR PKPGGWNTGGSR PQGSPGNRYPQGSGTGWQP 60
MANLG W+L LFV T +D+GLCKKR PKPGGWNTGGSR PQGSPGNRYPQGSGTGWQP

Sbjct 1
MANLGCWMLVLFATWSDLGLCKKR PKPGGWNTGGSR PQGSPGNRYPQGSGTGWQP 60

Query 61
HGGGWQPGPHGGGWQPHGGGWQPHGGGWQPHGGGWQPHGGGWQPGGGWQGGGTHQWNKPSKPTNKLKHVAGAA AAGA 120
HGGGWQPGPHGGGWQPHGGGWQPHGGGWQPHGGGWQPGGGWQGGGTHQWNKPSKPTNKLKHVAGAA AAGA

Sbjct 61
HGGGWQPGPHGGGWQPHGGGWQPHGGGWQPHGGGWQPGGGWQGGGTHQWNKPSKPTNKLKHVAGAA AAGA 120

Query 121
VVGGLGGYMG LSAMS RPLHFGND WE DRYRE YREN MRYNPQVYR PVDOYSQNNNFVHDCV 180
VVGGLGGYMG LSAMS RPLHFGND WE DRYRE YREN MRYNPQVYR PVDOYSQNNNFVHDCV

Sbjct 121
VVGGLGGYMG LSAMS RPLHFGND WE DRYRE YREN MRYNPQVYR PVDOYSQNNNFVHDCV 180

Query 181
NITIKQHTVT TTTKGENF TEDV KMMERVQE MQCVT QY QE S AYY YDGRRSSAVLFSSPP 240
NITIKQHTVT TTTKGENF TEDV KMMERV EQM C+TQY++ESQAYY R SS VLFSPP

Sbjct 181
NITIKQHTVT TTTKGENF TEDV KMMERV EQM C+TQY++ESQAYY R SS VLFSPP 240

Query 241
VILLISFLIFLIVG 254
VILLISFLIFLIVG

Sbjct 240
VILLISFLIFLIVG 254

Mouse v human

GENE ID: 5621 PRNP | prion protein (p27-30) (Creutzfeldt-Jakob disease, Gerstmann-Strausler-Scheinker syndrome, fatal familial insomnia) [Homo sapiens] (Over 100 PubMed links)

Score = 504 bits (1299), Expect = 2e-143 Identities = 231/262 (88%), Positives = 248/262 (94%), Gaps = 11/262 (4%)

Query 4
SHIGSWILLFVAMWDSDLGLCKKR PKPGGWNTGGSR PQGSPGNRYPpqgppqgggwq 63
+++ G W+L LFV A WSD+GLCKKR PKPGGWNTGGSR PQGSPGNRYPpqgppqgggwq

Sbjct 2
ANLGOWMLVLFATWSDLGLCKKR PKPGGWNTGGSR PQGSPGNRYPpqgppqgggwq 59

Query 64
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Sbjct 64-------PHGGGWQPHGGGWQPHGGGWQPHGGGWQPHGGGWQPHGGGWQPHGGGWQPHGGGWQPHGGGWQPHGGGWQPHGGGWQ 111

Query 123
vagaaagavqgglggYMLGSAMS RPLIHFGDYEDRYRE YREM HRYNPQVYR PVDOYSN 182
+AGAAAGAVGGLGGYMLGSAMS RPLIHFGDYEDRYRE YREM HRYNPQVYR PVDOYSN

Sbjct 123
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Query 183
QNNFVHDCV Ntvk ehtvtt ttgtgenf tedDIKM M KRV EQM C ITQY QE S AYY YQRGAS 242
QNNFVHDCV NtvK+H+TV TTTT KGENF TED+K+M M+R VE QM C ITQY QE S AYY YQRGAS+S

Sbjct 183
QNNFVHDCV NITIK QHTVT TT TTT KGENF TED V KMMERV EQM C ITQY QE S AYY YQRGAS+S 231

Query 243
VILFS sppvillissflivG 264
++LFSPPVILLISFLIFLIVG

Sbjct 232
MVLFSSPPVILLISFLIFLIVG 253

Cow vs human
Rendering of a cow in a tissue digester. Reduces animal tissue to a noninfectious slurry.
<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Classic CJD</th>
<th>Variant CJD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median age at death (yr)</td>
<td>68 (range 23–97)</td>
<td>28 (range 14–74)</td>
</tr>
<tr>
<td>Median duration of illness (mo)</td>
<td>4 to 5</td>
<td>13 to 14</td>
</tr>
<tr>
<td>Clinical presentation</td>
<td>Dementia; early neurologic signs</td>
<td>Prominent psychiatric and behavioral symptoms; delayed neurologic signs</td>
</tr>
<tr>
<td>Genotype*</td>
<td>Methionine/methionine</td>
<td>Other amino acid combinations</td>
</tr>
</tbody>
</table>

*Victims are homozygous at codon 129, that is, both of their PrP genes (one from each parent) have methionine coded at this position. This is characteristic of only about 37% of Caucasians. Other members of this population have different amino acid combinations at this position—and no one with these genotypes has contracted vCJD to date.

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<table>
<thead>
<tr>
<th>Pathogen</th>
<th>Portal of Entry</th>
<th>Method of Transmission</th>
<th>Treatment</th>
<th>Prevention</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Bacterial Diseases</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><em>Haemophilus influenzae</em> meningitis</td>
<td>Respiratory tract</td>
<td>Endogenous infection; aerosols</td>
<td>Cephalosporin</td>
<td>Capsular Hib vaccine</td>
</tr>
<tr>
<td><em>Neisseria meningitidis</em> Meningococcal meningitis</td>
<td>Respiratory tract</td>
<td>Aerosols</td>
<td>Cephalosporin</td>
<td>Capsular vaccine against A, C, Y, W-135</td>
</tr>
<tr>
<td><em>Streptococcus pneumoniae</em> Pneumococcal meningitis</td>
<td>Respiratory tract</td>
<td>Aerosols</td>
<td>Cephalosporin</td>
<td>Polysaccharide vaccine</td>
</tr>
<tr>
<td><em>Listeria monocytogenes</em> Listeriosis</td>
<td>Mouth</td>
<td>Foodborne infection</td>
<td>Penicillin G</td>
<td>Pasteurizing and cooking food</td>
</tr>
<tr>
<td><em>Clostridium tetani</em> Tetanus</td>
<td>Skin</td>
<td>Puncture wound</td>
<td>Tetanus immune globulin; antibiotics</td>
<td>Toxoid vaccine (DTaP, Td)</td>
</tr>
<tr>
<td><em>Clostridium botulinum</em> Botulism</td>
<td>Mouth</td>
<td>Foodborne intoxication</td>
<td>Antitoxin</td>
<td>Proper canning of foods; infants should not have honey</td>
</tr>
<tr>
<td><em>Mycobacterium leprae</em> Leprosy</td>
<td>Nasal mucosa</td>
<td>Probably prolonged contact with contaminated secretions</td>
<td>Dapsone, rifampin, clofazimine</td>
<td>Possibly BCG vaccine</td>
</tr>
<tr>
<td>Pathogen</td>
<td>Portal of Entry</td>
<td>Method of Transmission</td>
<td>Treatment</td>
<td>Prevention</td>
</tr>
<tr>
<td>--------------------------</td>
<td>-----------------</td>
<td>-------------------------------------------------------------</td>
<td>--------------------------------</td>
<td>------------------------------------------------</td>
</tr>
<tr>
<td>Poliovirus</td>
<td>Mouth</td>
<td>Ingesting contaminated water (fecal–oral route)</td>
<td>Mechanical breathing aid</td>
<td>Inactivated polio vaccine (E-IPV)</td>
</tr>
<tr>
<td>Lyssavirus, including rabies virus</td>
<td>Skin</td>
<td>Animal bite</td>
<td>Postexposure treatment: rabies immunoglobulin + vaccine</td>
<td>Human diploid cell vaccine for high-risk individuals; vaccination of domestic animals</td>
</tr>
<tr>
<td>Arboviruses</td>
<td>Skin</td>
<td>Mosquito bite</td>
<td>None</td>
<td>Insect repellent; protective clothing; remove standing water (mosquito breeding)</td>
</tr>
</tbody>
</table>

Table 22.2 (2 of 4)
<table>
<thead>
<tr>
<th>Pathogen</th>
<th>Portal of Entry</th>
<th>Method of Transmission</th>
<th>Treatment</th>
<th>Prevention</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Fungal Diseases</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cryptococcosis</td>
<td><em>Cryptococcus neoformans</em></td>
<td>Respiratory route</td>
<td>Inhaling soil contaminated with spores</td>
<td>Amphotericin B, flucytosine</td>
</tr>
<tr>
<td><strong>Protozoan Diseases</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>African trypanosomiasis</td>
<td><em>Trypanosoma brucei rhodesiense, T. b. gambiense</em></td>
<td>Skin</td>
<td>Tsetse fly</td>
<td>Suramin; pent-amidine</td>
</tr>
<tr>
<td>Primary amebic meningoencephalitis</td>
<td><em>Naegleria fowleri</em></td>
<td>Mucous membranes</td>
<td>Swimming</td>
<td>Amphotericin B</td>
</tr>
<tr>
<td>Granulomatous amebic encephalitis</td>
<td><em>Acanthamoeba spp.; Balamethia mandrillaris</em></td>
<td>Mucous membranes</td>
<td>Swimming</td>
<td>Amphotericin B</td>
</tr>
<tr>
<td>Pathogen</td>
<td>Portal of Entry</td>
<td>Method of Transmission</td>
<td>Treatment</td>
<td>Prevention</td>
</tr>
<tr>
<td>---------------------------</td>
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</tr>
<tr>
<td><strong>Prion Diseases</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Creutzfeldt-Jakob disease</td>
<td>Prion</td>
<td>Injection; mouth</td>
<td>Inherited; ingested; transplants</td>
<td>None</td>
</tr>
<tr>
<td>Kuru</td>
<td>Prion</td>
<td>Mucous membranes</td>
<td>Contact or ingestion</td>
<td>None</td>
</tr>
</tbody>
</table>

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