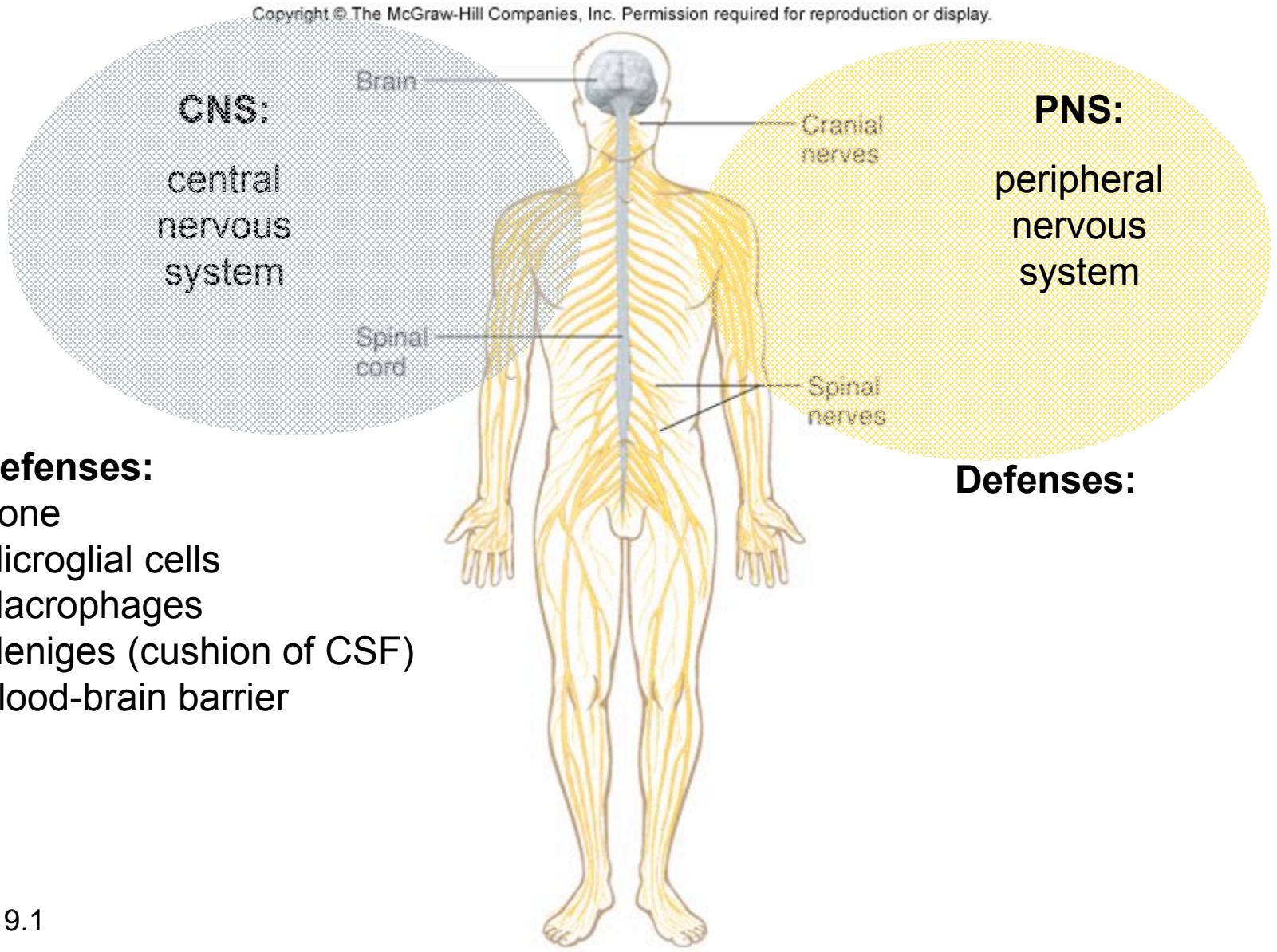
Infectious Diseases Affecting the Nervous System

The Nervous System and its Defenses

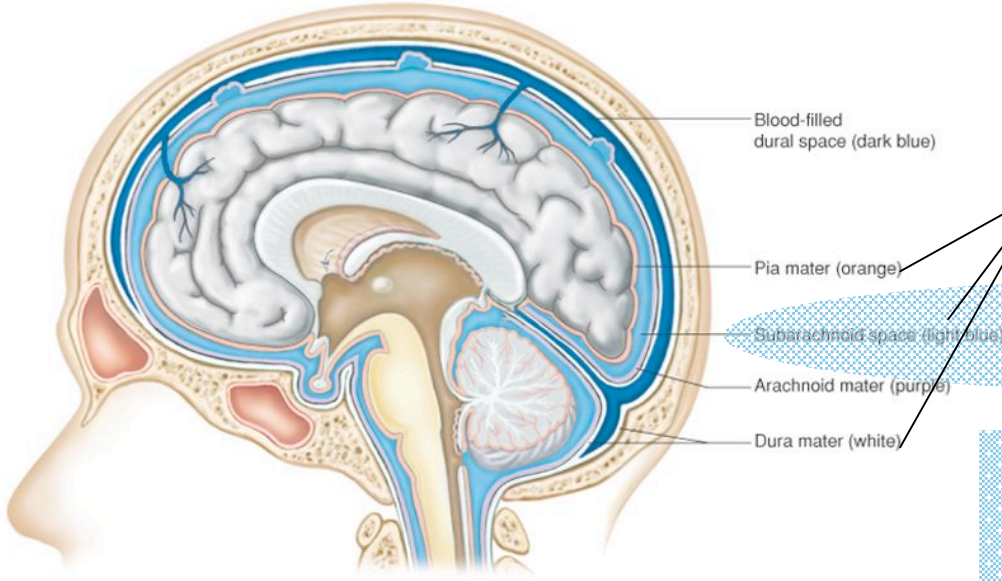


Defenses:
Bone
Microglial cells
Macrophages
Meniges (cushion of CSF)
Blood-brain barrier

Defenses:

Figure 19.1

The meninges



meninges

Filled with CSF: cerebral spinal fluid

Provides defense:
cushioning
protection
Provides nutrition

Also can be site of infection

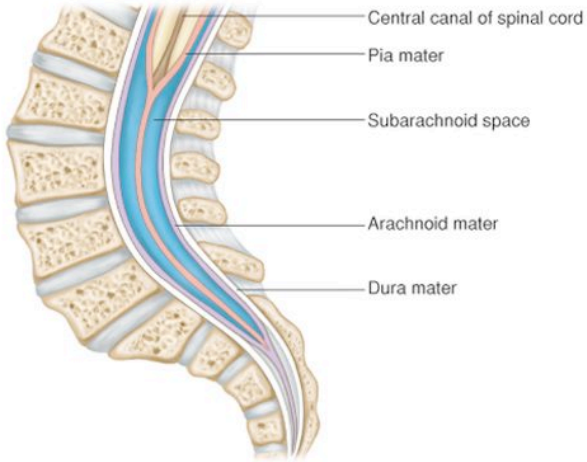


Figure 19.2

Normal Biota of the Nervous System

none

Who “wins” from nervous system infections?

In almost all cases, neither the host nor the pathogen.

Meningitis

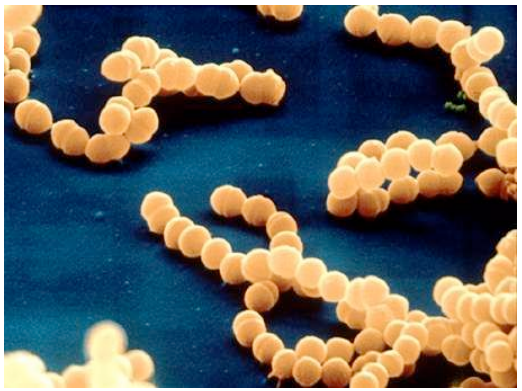
- Inflammation of the meninges
- Many microorganisms can cause meningitis
- More serious forms caused by bacteria
- If it is suspected, lumbar puncture is performed to obtain CSF
- *Typical symptoms: headache, painful or stiff neck, fever, and usually an increased number of white blood cells in the CSF*

CHECKPOINT 19.1 Meningitis

Causative Organism(s)	*Neisseria meningitidis*	*Streptococcus pneumoniae*	*Haemophilus influenzae*	*Listeria monocytogenes*	*Cryptococcus neoformans*	*Coccidioides immitis*	Viruses
Most Common Modes of Transmission	Droplet contact	Droplet contact	Droplet contact	Vehicle (food)	Vehicle (air, dust)	Vehicle (air, dust, soil)	Droplet contact
Virulence Factors	Capsule, endotoxin, IgA protease	Capsule, induction of apoptosis, hemolysin and hydrogen peroxide production	Capsule	Intracellular growth	Capsule, melanin production	Granuloma (spherule) formation	Lytic infection of host cells
Culture/ Diagnosis	Gram stain/ culture of CSF, blood, rapid antigenic tests	Gram stain/ culture of CSF	Culture on chocolate agar	Cold enrichment, rapid methods	Negative staining, biochemical tests, DNA probes	Identification of spherules, cultivation on Sabouraud's agar	Initially, absence of bacteria/fungi/ protozoa, followed by viral culture or antigen tests
Prevention	Conjugated vaccine; rifampin or tetracycline used to protect contacts	Two vaccines: Prevnar (children), and Pneumovax (adults)	Hib vaccine	Cooking food, avoiding unpasteurized dairy products	–	Avoiding airborne spores	–
Treatment	Penicillin G or Cefotaxime	Cefotaxime check for resistance (add vancomycin in that case)	Cefotaxime	Ampicillin, trimethoprim-sulfamethox-azole	Amphotericin B and fluconazole	Amphotericin B or oral or IV itraconazole	Usually none unless specific virus identified and specific antiviral exists)
Distinctive Features	Petechiae, meningo-coccemia	Serious, acute, most common meningitis in adults	Serious, acute, less common since vaccine became available	Asymptomatic in healthy adults, meningitis in neonates, elderly and immuno-compromised	Acute or chronic, most common in AIDS patients	Almost exlusively in endemic regions	Generally milder than bacterial or fungal

Neisseria meningitides

- Gram-negative diplococcic lined up side by side



- Commonly known as meningococcus
- Often associated with epidemic meningitis
- Causes most serious form of acute meningitis

Causes of meningitis

N. meningitidis transmission and dissemination

Normal transmission:

- does not survive long in environment
- normally lives in human nasopharynx
- often asymptomatic
- 3-30% of adults are carriers
- sporatic or epidemic in late winter / early spring

Dissemination to meninges:

- unusual situation: spread to meninges through infection of roof of nasal cavity (see figure)
- host and microbial contributors to meningitis
- can be fast progressing and deadly
- is a transmission dead-end for the bacterium

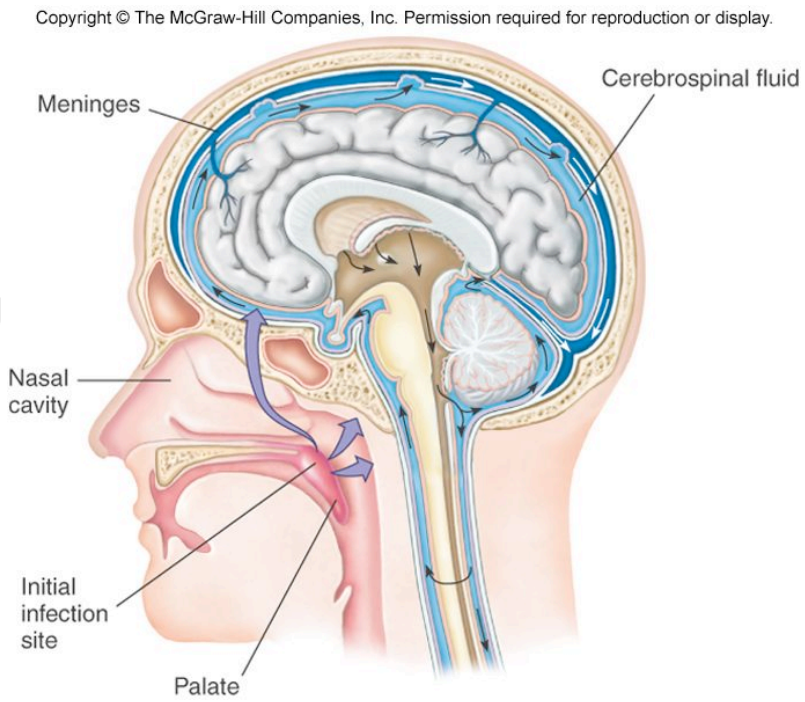


Figure 19.4

Meningitis caused by *N. meningitidis* must treated *FAST*

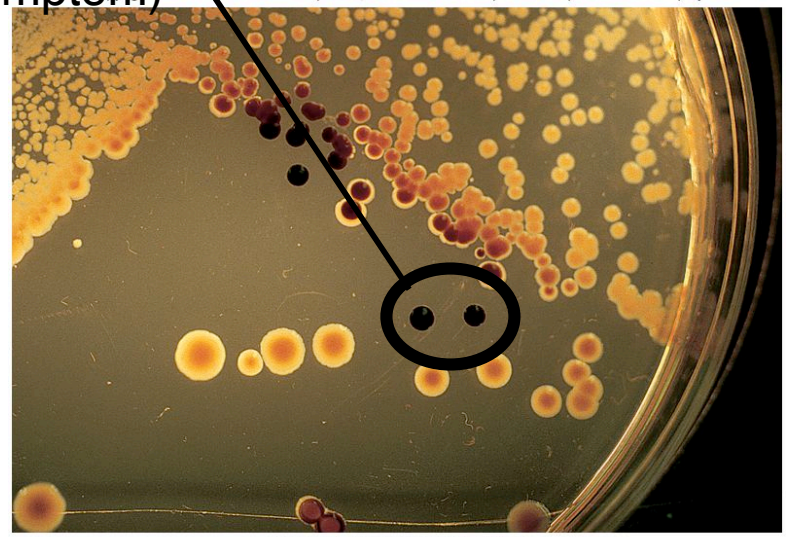
Diagnosis:

First priority: rule out or identify *N. meningitidis*

- gram negative
- rapid tests for capsular polysaccarides
- oxidase testing (*N. meningitidis* is oxidase positive)
- need to differentiate from *N. gonorrhoeae*
- causes **petechiae** (diagnostic symptom)

Treatment:

Penicillin G (high dose, IV)

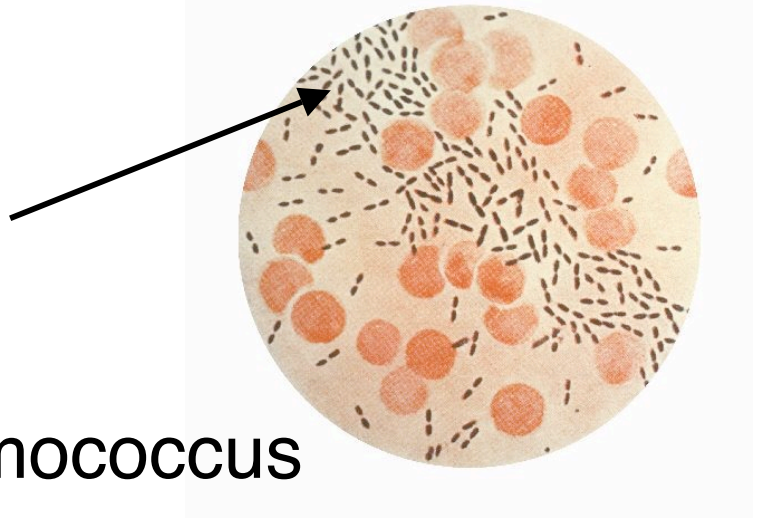


Petechiae: small red or purple spots on skin

Figure 19.5

Streptococcus pneumonia

- Small gram-positive flattened cocci in end-to-end pairs



- Commonly called pneumococcus
- Does not cause petechiae
- Most frequent cause of community-acquired meningitis
- Very severe

Causes of meningitis

S. pneumonia diagnosis and treatment

Diagnosis:

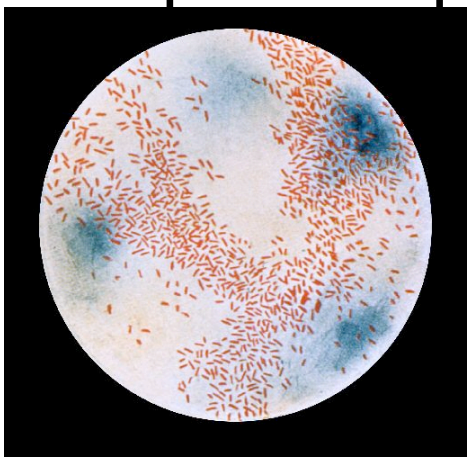
- Also major causes of bacterial pneumonias
- Often accompanied by pneumococcal pneumonia
- Usually enters meninges through bloodstream (via lungs)

Treatment:

- Drug resistance common: susceptibility must be tested
- Two vaccines available

Haemophilus influenza

- **Tiny** gram-negative pleomorphic rods



- **Fastidious:** sensitive to drying, temperature extremes, disinfectants
- Causes severe meningitis
- Symptoms: similar to *N. meningitidis*-caused meningitis

Causes of meningitis

H. influenza diagnosis and treatment

Diagnosis:

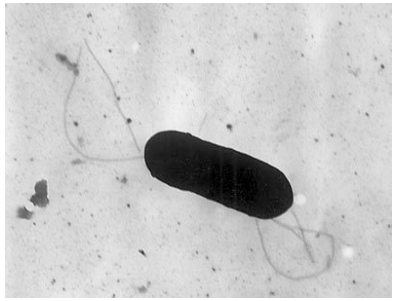
- Like meningococcus, part of normal nasopharyngial flora
- Meningitis most common in children 3-5 years
- Rarely epidemic (instead is sporatic)

Treatment:

- Vaccine recommended for all children over 2 months
- Even with treatment 33% suffer residual damage

Listeria monocytogenes

- Gram-positive, ranges in morphology from coccobacilli to long filaments in palisades formation



- **Not fastidious:** resistant to cold, heat, salt, pH extremes, and bile
- Reservoir unknown: *environmental, foodborne*

Causes of meningitis

L. monocytogenes diagnosis and treatment

Symptoms:

• In normal adults- mild infection with nonspecific symptoms of fever, diarrhea, and sore throat

• In elderly or immunocompromised patients, fetuses, or neonates can affect the brain and meninges

•***Diagnosis:***

• Difficult to isolate: use of cold enrichment

• Recently: rapid non-culture based techniques

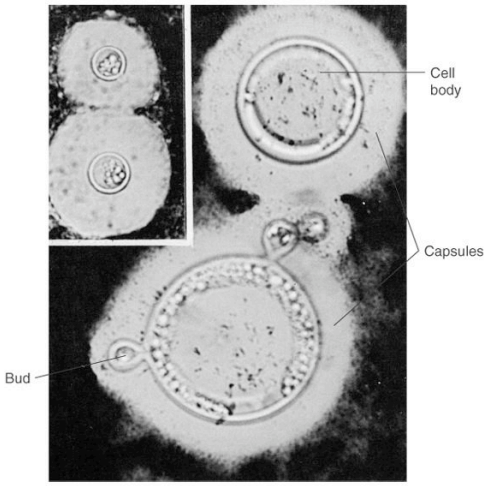
Treatment:

• Prevention via pasteurization, cooking of foods

• Antibiotic treatment

Cryptococcus neoformans

- Fungus with spherical to ovoid shape and a large capsule

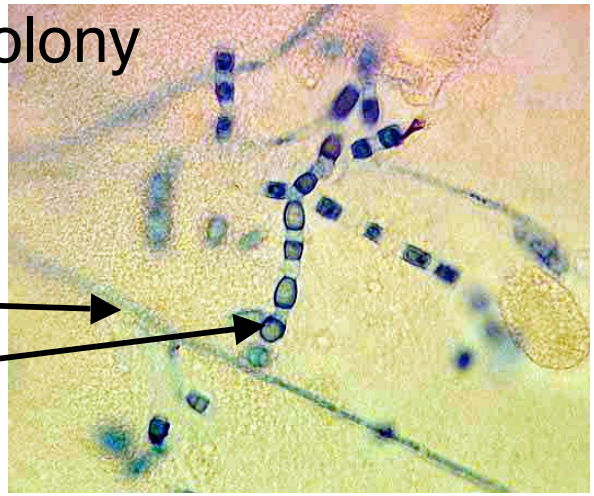


- More chronic form of meningitis, gradual symptom onset
- Headache- most common symptom; also nausea, stiff neck
- ***Environmental*** *- common in human habitats*

Causes of meningitis

Coccidioides immitis

- At 25°C forms a moist white to brown colony with abundant, branching, septate hyphae



- Hyphae fragment into **arthroconidia (asexual spores)** at maturity
- Source: environmental. Infection usually begins in the lungs

Causes of meningitis

Coccidioides immitis infection process

Dormancy in winter/spring
Growth in summer/fall

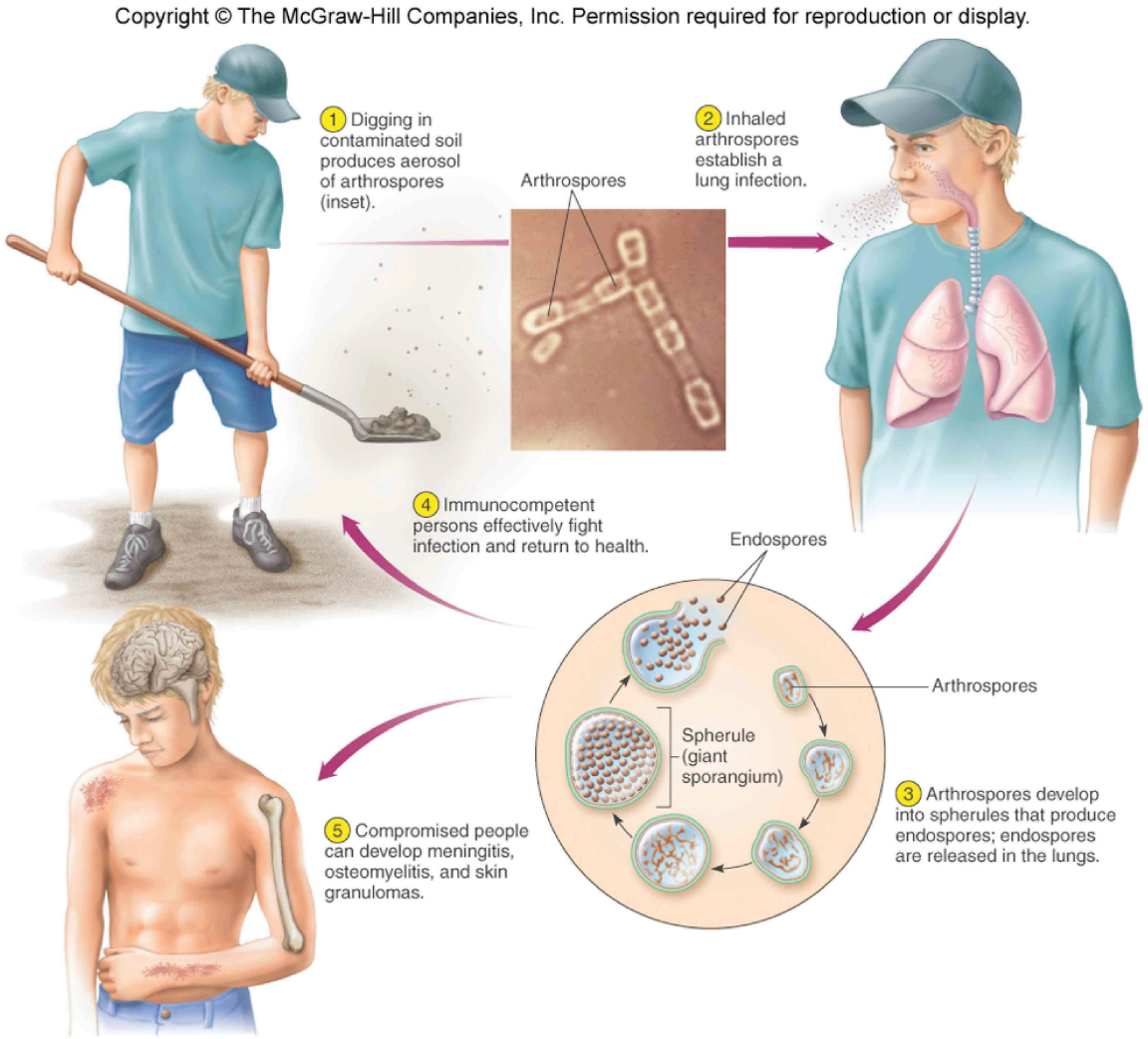


Figure 19.9

Coccidioides immitis distribution

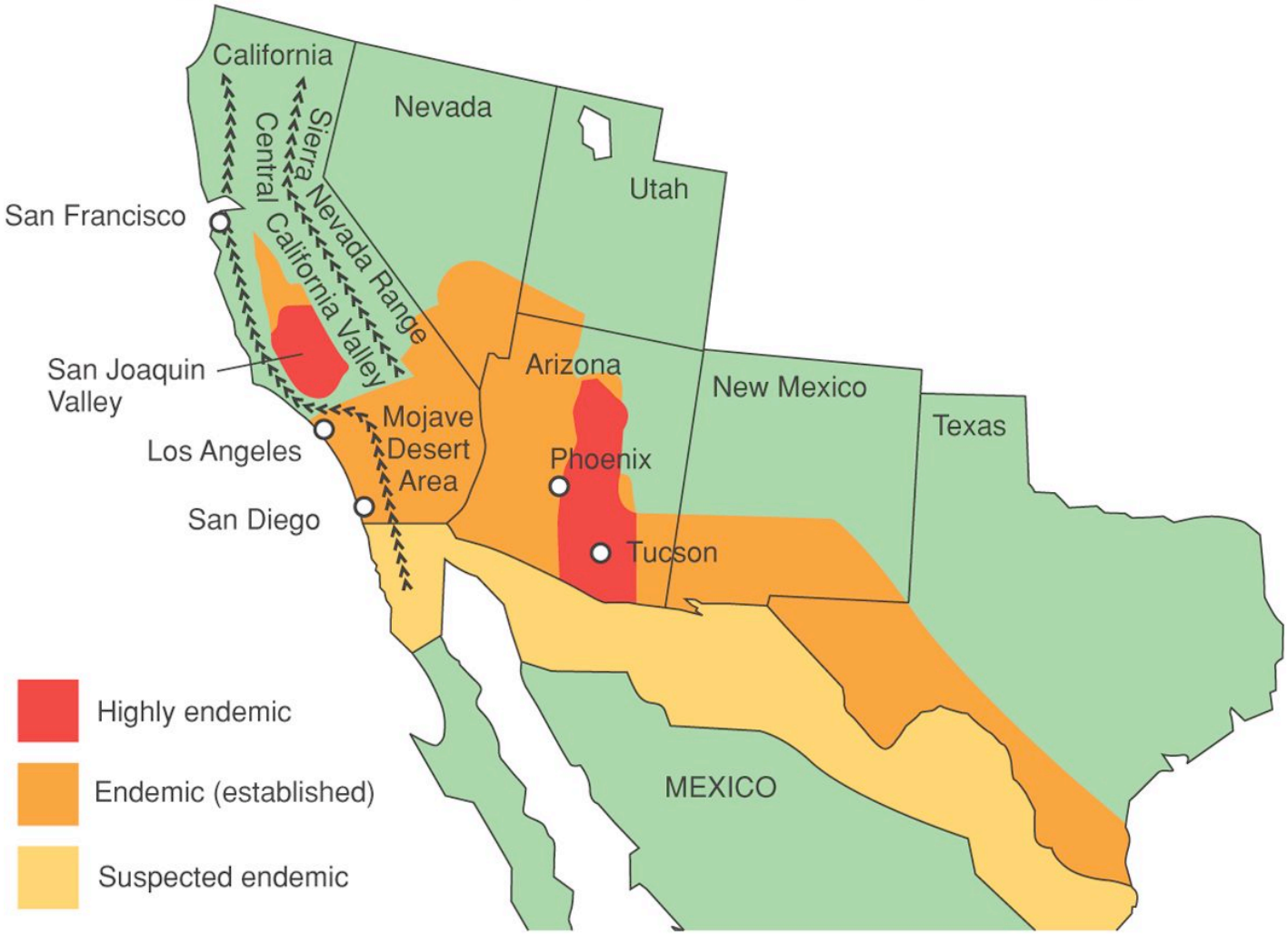


Figure 19.10

Viruses

- Aseptic meningitis
- Majority of cases occur in children
- 90% caused by enteroviruses
- Generally milder than bacterial or fungal meningitis

Causes of meningitis

Neonatal Meningitis

- Almost always a result of infection transmitted by the mother, either in utero or during passage through the birth canal

CHECKPOINT 19.2 Neonatal Meningitis

Causative Organism(s)	*Streptococcus agalactiae*	*Escherichia coli*, strain K1	*Listeria monocytogenes*
Most Common Modes of Transmission	Vertical (during birth)	Vertical (during birth)	Vertical
Virulence Factors	Capsule	–	Intracellular growth
Culture/Diagnosis	Culture mother's genital tract on blood agar; CSF culture of neonate	CSF Gram stain/culture	Cold enrichment, rapid methods
Prevention	Culture and treatment of mother	–	Cooking food, avoiding unpasteurized dairy products
Treatment	Penicillin G plus aminoglycosides	Cefotaxime plus aminoglycoside	Ampicillin, trimethoprim-sulfamethoxazole
Distinctive Features	Most common; positive culture of mother confirms diagnosis	Suspected if infant is premature	Suspected if infant is premature

Meningoencephalitis

- **Encephalitis**: inflammation of the brain

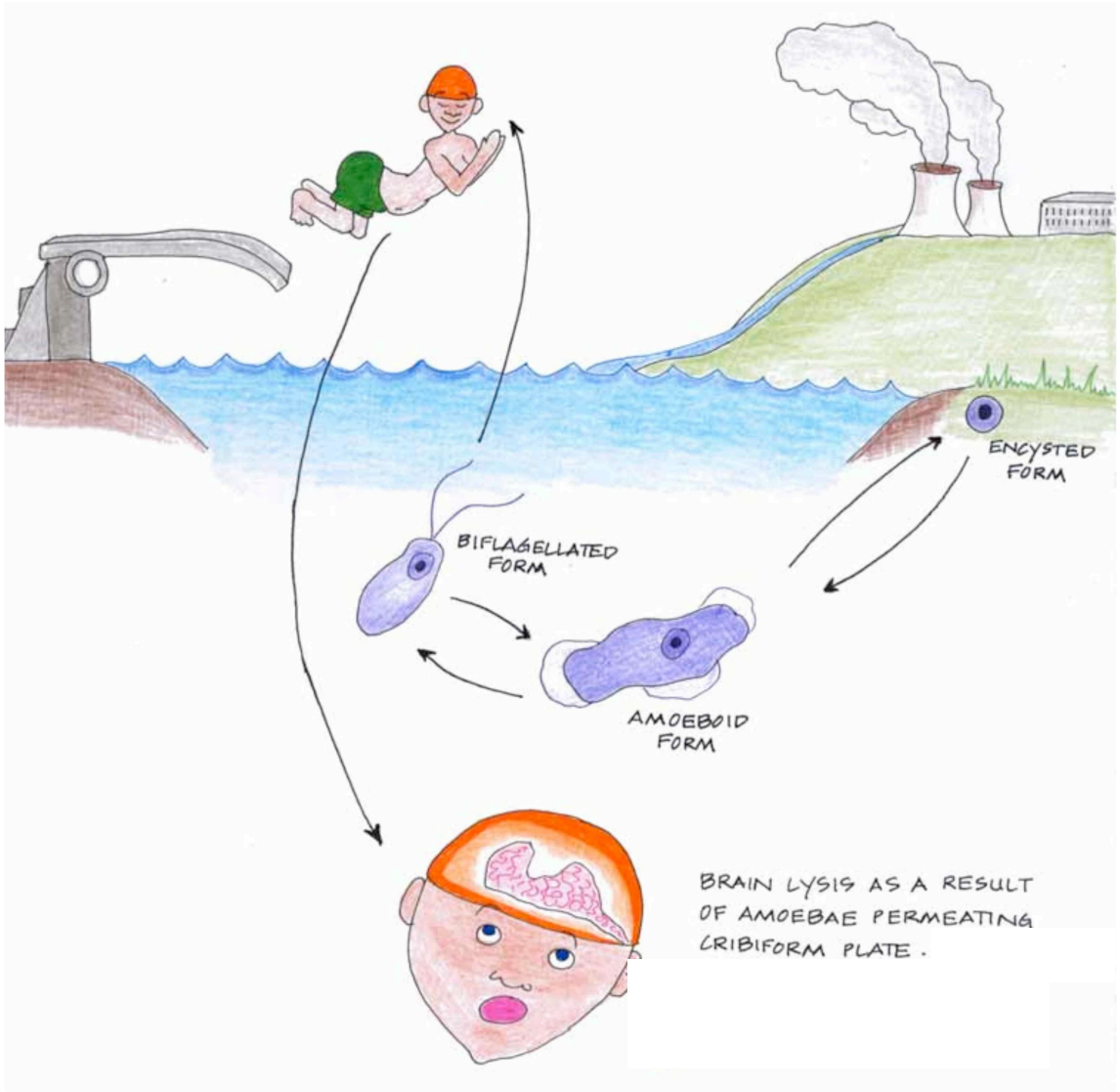
- Two microorganisms cause meningoencephalitis (both amoebas)
  - *Naegleria fowleri*
  - *Acanthamoeba*

Naegleria fowleri

- Causes primary amoebic meningoencephalitis (PAM)
- Small, flask-shaped amoeba
- Forms a rounded, thick-walled, uninucleate cyst
- Resistant to temperature extremes and mild chlorination

Causes of meningoencepalitis

Naegleria fowleri in the environment



- Very common - may children are carriers, and disease is extremely rare
- Infection begins when amoebas are forced into human nasal passages as a result of swimming, diving, or other aquatic activities
- Amoeba burrows in to the nasal mucosa, multiplies, and migrates into the brain and surrounding structures
- Fatal within a week, treatment usually futile

Acanthamoeba

- Granulomatous amoebic meningoencephalitis (GAM)
- Large, amoeboid trophozoite with spiny pseudopods and a double-walled cyst
- Invades broken skin, the conjunctiva, and occasionally the lungs and urogenital epithelia
- Course of disease slower

Encephalitis

- Encephalitis can present as **acute** or **subacute**
- Always a serious condition
- ***Acute:*** almost always caused by viral infection

  Acute encephalitis signs and symptoms vary but may include behavior changes, confusion, decreased consciousness, seizures

- ***Subacute:*** can be caused by protozoans, viruses, prions

  Asymptomatic at first, thereafter symptoms and signs vary, often less striking

Arborviruses

- Borne by insects feeding on the blood of hosts
- Most common outcome: acute fever, often accompanied by rash

Western equine encephalitis (WEE)

Eastern equine encephalitis (EEE) (high case fatality)

California encephalitis (may include two viruses)

St. Louis encephalitis (SLE) (most common US viral cause)

West Nile encephalitis

Causes of acute encephalitis

Herpes Simplex Virus

- Can cause encephalitis in newborns born to HSV-positive mothers
- Prognosis is poor

Causes of acute encephalitis

JC Virus

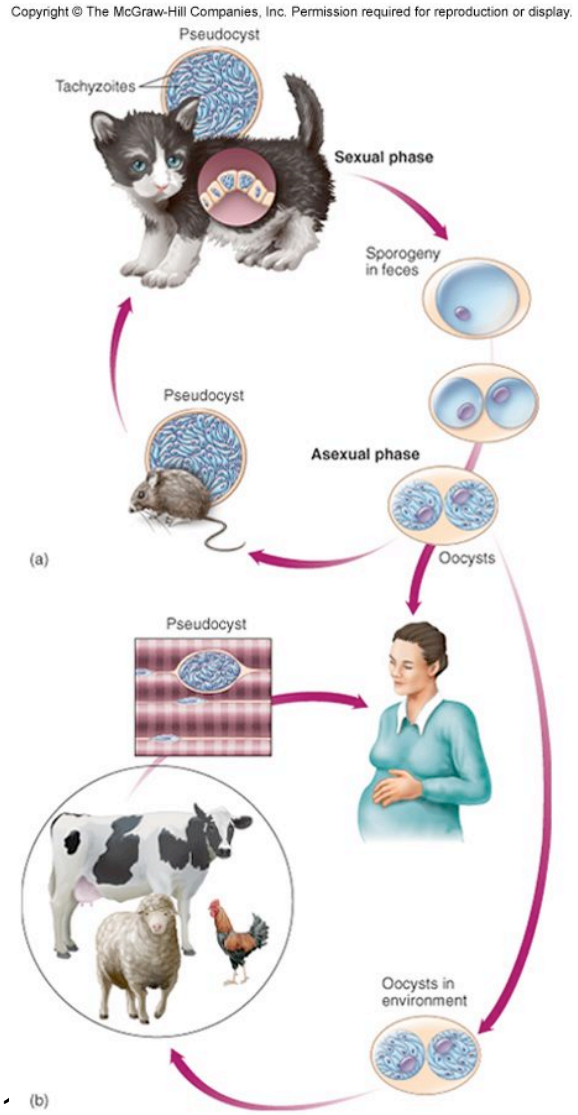
- Infection is common, pathology rare
- In patients with immune dysfunction, cause **progressive multifocal leukoencephalopathy (PML)**- uncommon but generally fatal

Toxoplasma gondii

- Flagellated parasite
- Most common cause of **subacute** encephalitis
- Most cases go unnoticed
- In the fetus and immunodeficient people, severe and often fatal
- Asymptomatic or marked by mild symptoms such as sore throat, lymph node enlargement, and low-grade fever

Causes of subacute encephalitis

T. gondii life cycle



Normal life cycle

Atypical life cycle: note that it ends with the infected human.

Figure 1.

Measles Virus: **Subacute Sclerosing Panencephalitis (SSPE)**

- Occurs years after an initial measles episode
- Seems to be caused by direct viral invasion of neural tissue
- Reason for persistence of the virus in some people is unclear

Causes of subacute encephalitis

Prions

- **Transmissible spongiform encephalopathies (TSEs)**: neurodegenerative diseases with long incubation periods but rapid progression once they begin
- Proteins with “contagious” altered structure
- Highly resistant to chemicals radiation and heat
- Human TSEs
  - **Creutzfeldt-Jakob disease (CJD)**
  - Gerstmann-Strussler-Scheinker disease
  - Fatal familial insomnia

Causes of subacute encephalitis

Effects of prions on brain tissue

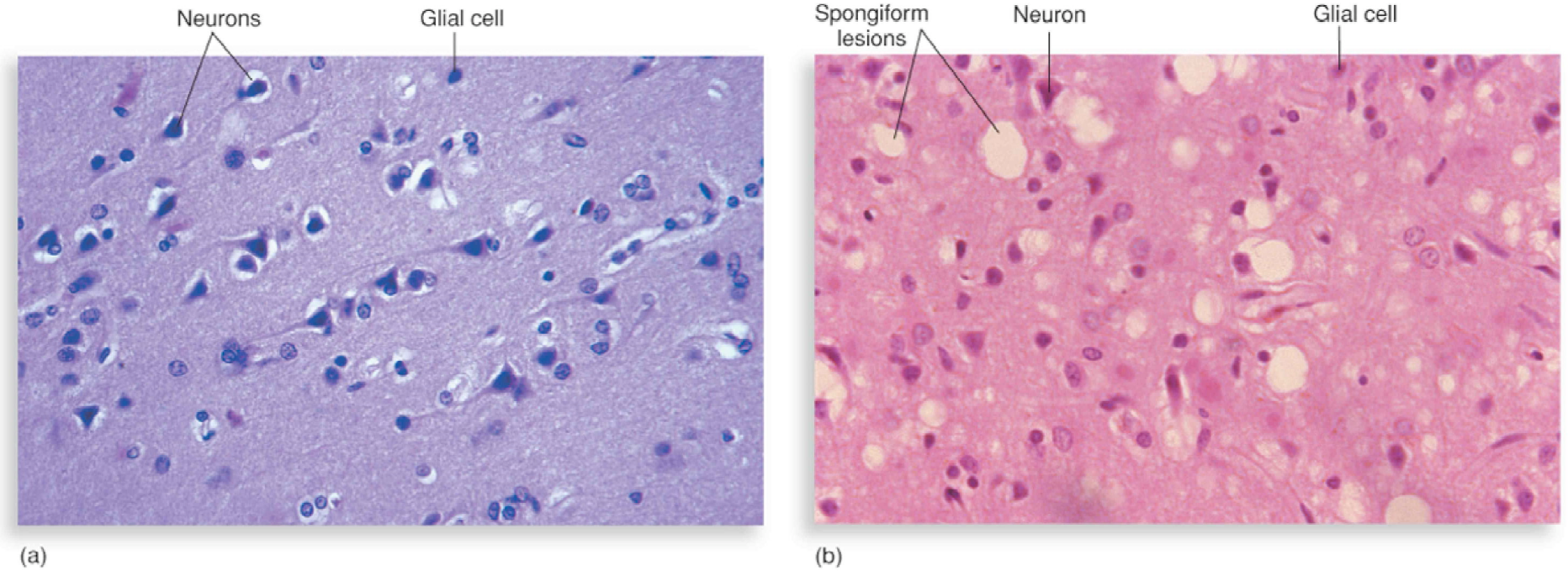


Figure 19.14

Other Disease of the Nervous System

- Rabies (caused by rabies virus)
- Poliomyelitis (caused by poliovirus)
- Tenanus (caused by bacterium *Clostridium tetani)*

  Toxin causes spasms

- *Botulism* (caused bacterium *Clostridium botulinum*)

  Toxin causes flaccid paralysis

- African Sleeping sickness (caused by protozoan *Trypanosoma brucei*)

Rabies

- Exception to “no one wins” rule: normally a nervous sytem disease of mammals
- Slow, progressive zoonotic disease characterized by fatal encephalitis
- Average incubation time: 1-2 months or more
- Prodromal phase begins with fever, nausea, vomiting, headache, fatigue, and other nonspecific symptoms
- Furious rabies
  - Periods of agitation, disorientation, seizures, and twitching
  - Spasms in the neck and pharyngeal muscles lead to hydrophobia
- Dumb rabies
  - Patient is not hyperactive but is paralyzed, disoriented and stuporous
- Both forms progress to the coma phase, resulting in death, unless vaccination precedes symptoms.

Rabies virus is related to VSV

It's an enveloped negative sense RNA virus.

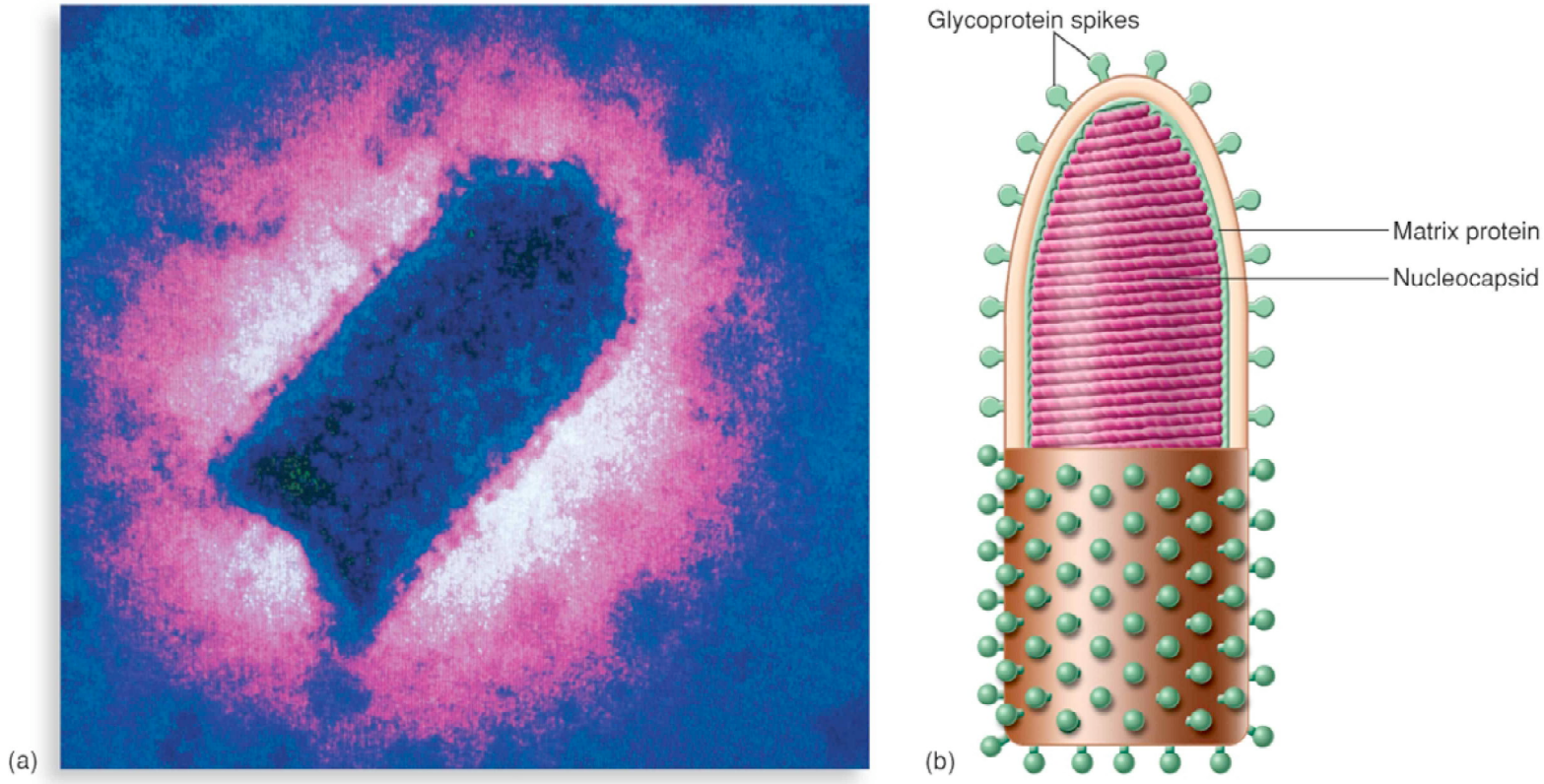
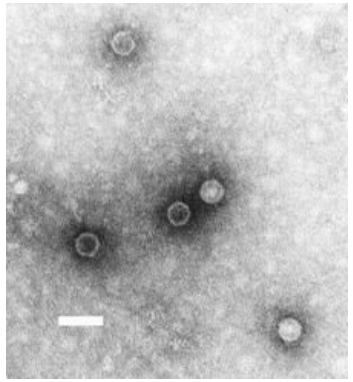
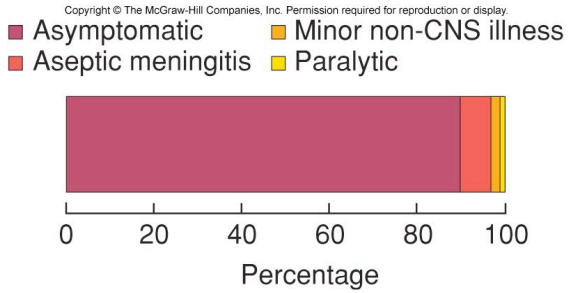


Figure 19.15

Poliomyelitis

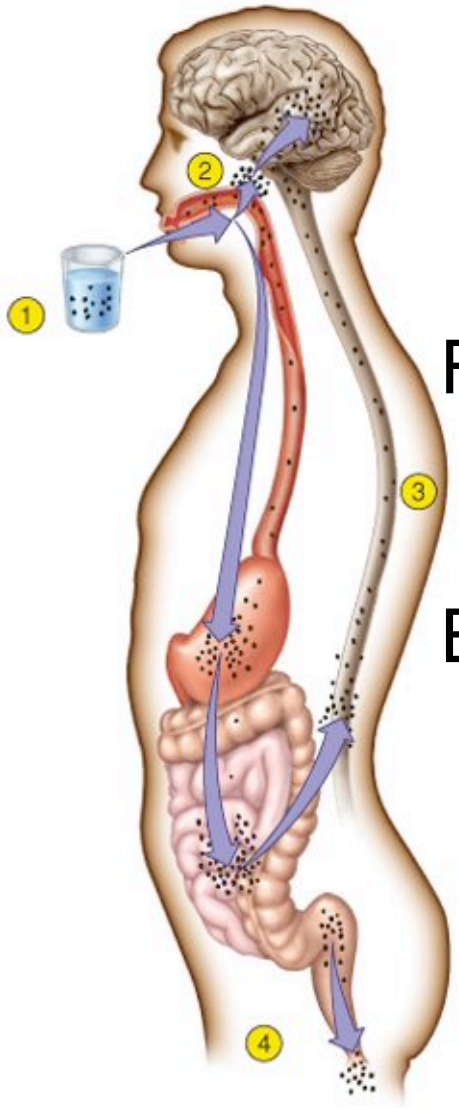


- Acute enteroviral infection of the spinal cord
- Can cause neuromuscular paralysis
- Often affects small children
- Most infections are contained as short-term, mild viremia
- Some develop mild nonspecific symptoms of fever, headache, nausea, sore throat, and myalgia



- Then spreads along specific pathways in the spinal cord and brain
- *Neurotropic:* the virus infiltrates the motor neurons of the anterior horn of the spinal cord
- *Nonparalytic:* invasion but not destruction of nervous tissue
- Paralytic: various degrees of flaccid paralysis
- Rare cases: bulbar poliomyelitis

Poliovirus transmission

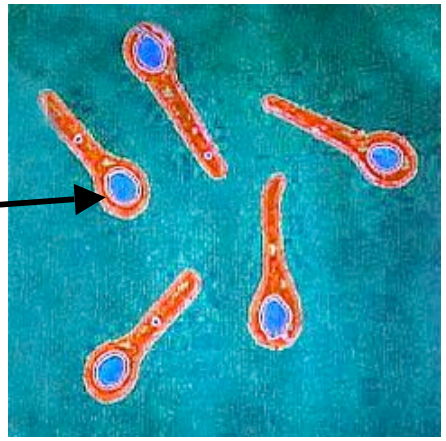


Fecal-oral transmission

Escape into the nervous system

Figure 19.18

Tetanus



- Also known as lockjaw
- Caused by *Clostridium tetani*
- Gram-positive, spore-forming rod
- Releases a powerful neurotoxin, tetanospasmin, that binds to target sites on peripheral motor neurons, spinal cord and brain, and in the sympathetic nervous system
- Toxin blocks the inhibition of muscle contraction
- Results in spastic paralysis
- First symptoms : clenching of the jaw, followed in succession by extreme arching of the back, flexion of the arms, and extension of the legs
- *Risus sardonicus* (sustained spasm of facial muscles)

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- Soil-borne
- Entry of bacterium into (anaerobic) wound is required

  Neonatal tetanus associated with ash or mud on ubilical stump
- Effective vaccine available
- Treatment with antibiotics and passive TIG (tetanus immune globulin)

Figure 19.21

Botulism

Cause: spore forming bacterium *Clostridium botulinum*

Three major forms

- **Food-borne botulism (not an infection)**
  - Ingestion of preformed botulinum exotoxin from bacteria growing in an anaerobic environment (e.g. canned foods)
  - Results in an intoxication affecting neuromuscular junctions
- **Infant botulism (true infection)**
  - Entrance of botulinum toxin into the bloodstream after spore enters the gut and establishes infection
- **Wound botulism (true infection)**
  - Entrance of **botulinum** toxin into the bloodstream after anaerobic infection of a wound from environmental source

- Symptoms: double vision, difficulty in swallowing, dizziness; later symptoms include descending muscular paralysis and respiratory compromise

Mechanism of toxin's effect

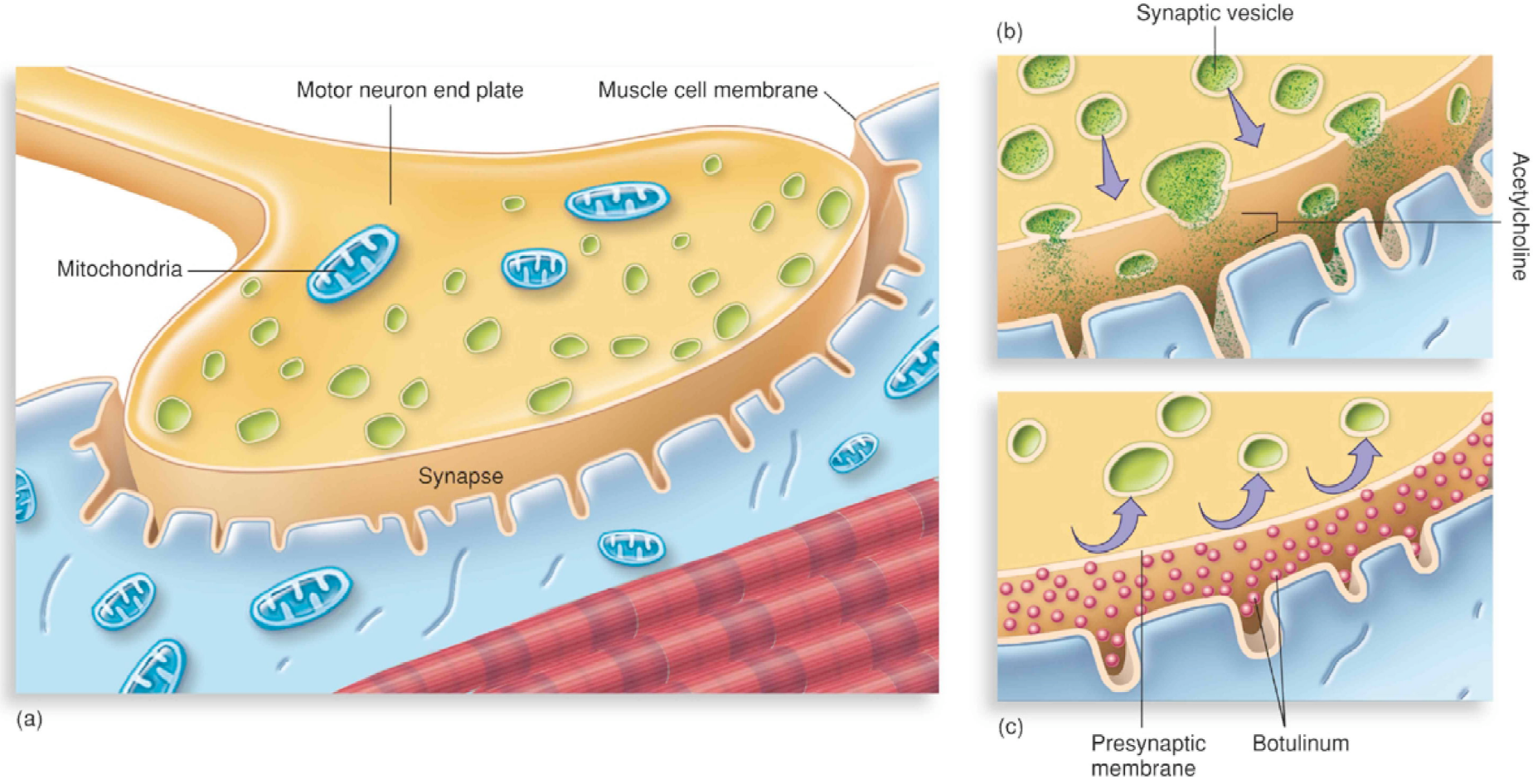


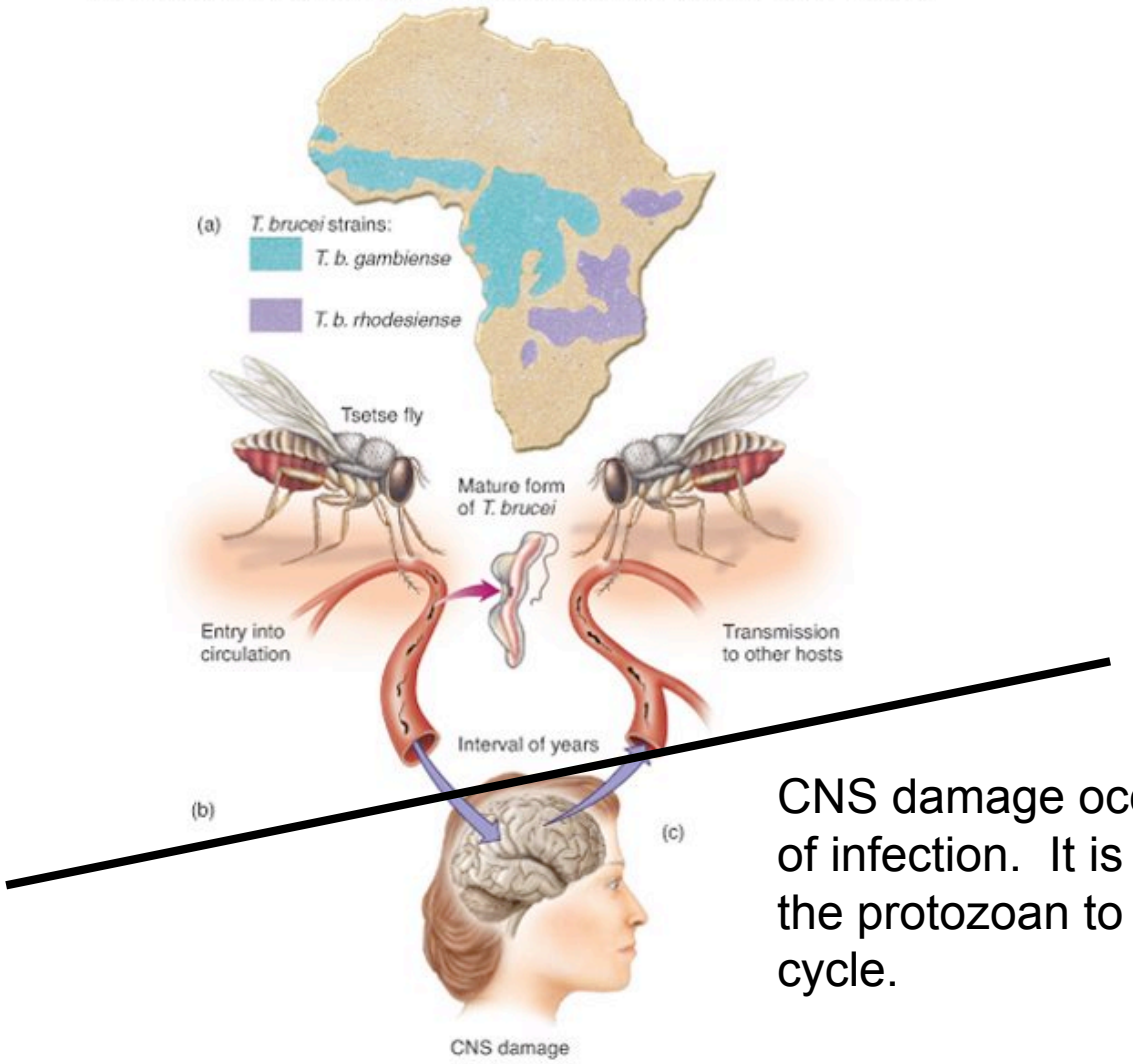
Figure 19.23

African Sleeping Sickness

- Caused by *Trypanosoma brucei protozoan*
- Also called **trypanosomiasis**
- Escape of immune system by *antigenic shift*

- Affects the lymphatic system and areas surrounding blood vessels
- Usually a long asymptomatic period precedes onset of symptoms
- Symptoms include intermittent fever, enlarged spleen, swollen lymph nodes, and joint pain
- Central nervous system is affected with personality and behavioral changes that progress to lassitude and sleep disturbances

T. brucei infection cycle



CNS damage occurs over years of infection. It is not required for the protozoan to complete its life cycle.

Figure 19.24