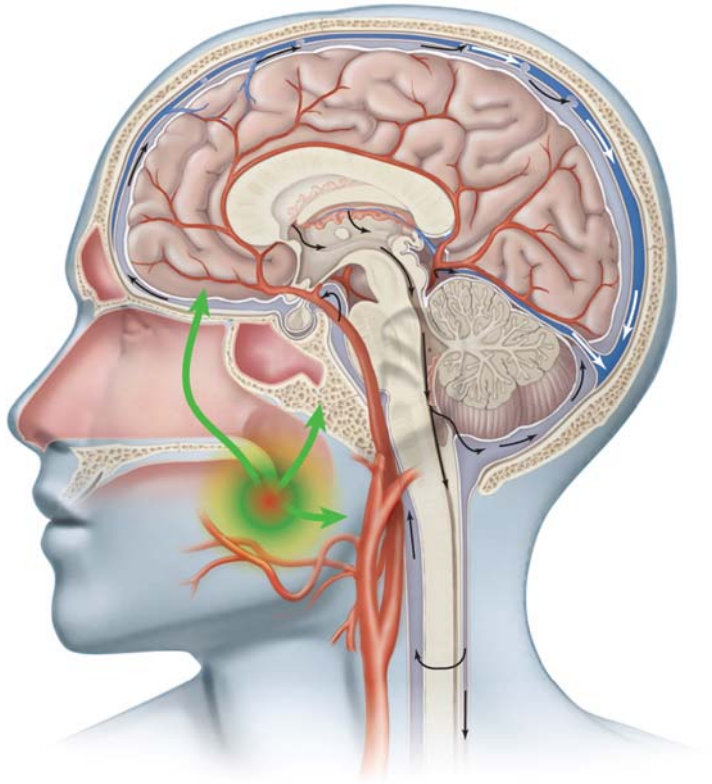
Infectious Diseases Affecting the Nervous System

Chapter 22

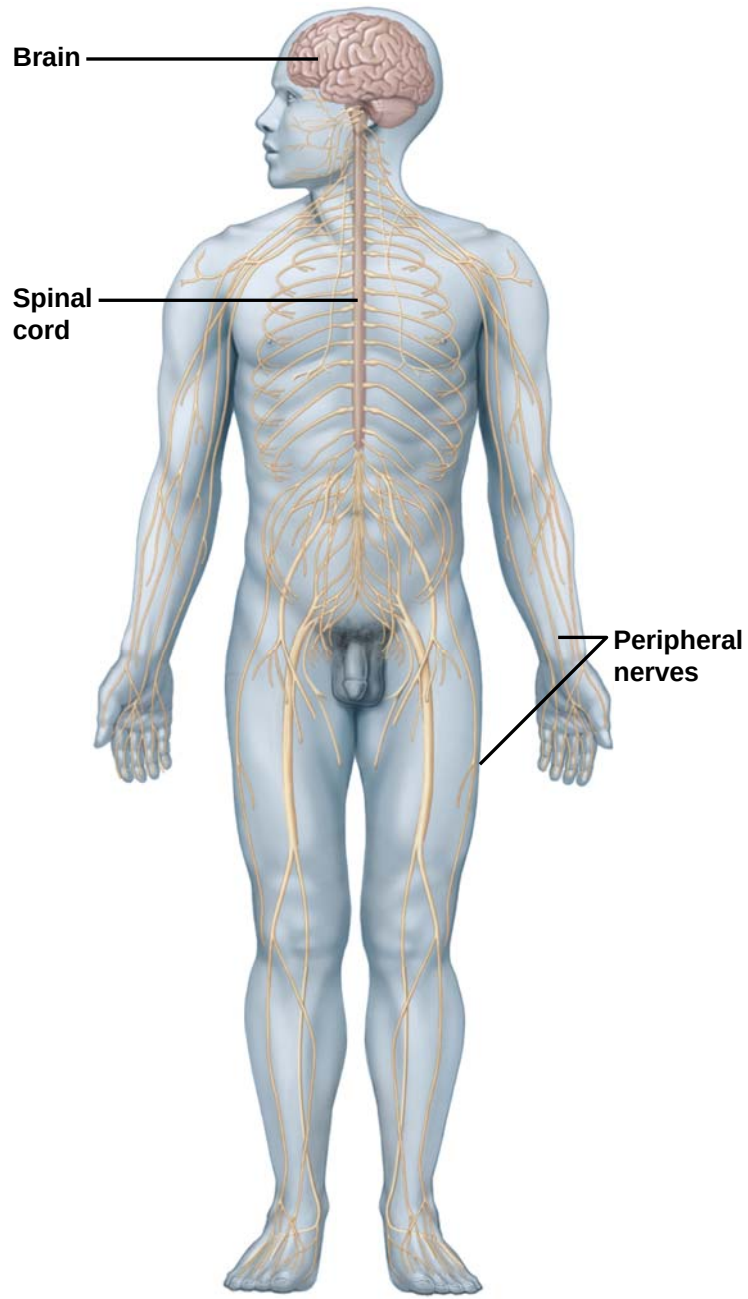


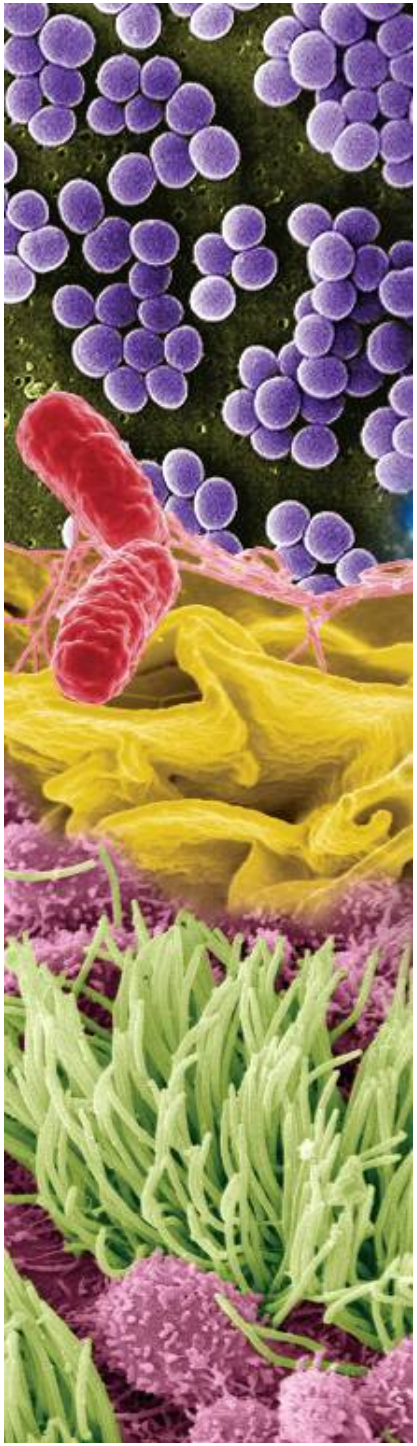
The Nervous System and Its Defenses

Component parts of the nervous system

Central nervous system (CNS): consists of the brain and spinal cord

Peripheral nervous system (PNS): contains nerves that emanate from the CNS to sense organs and periphery of the body



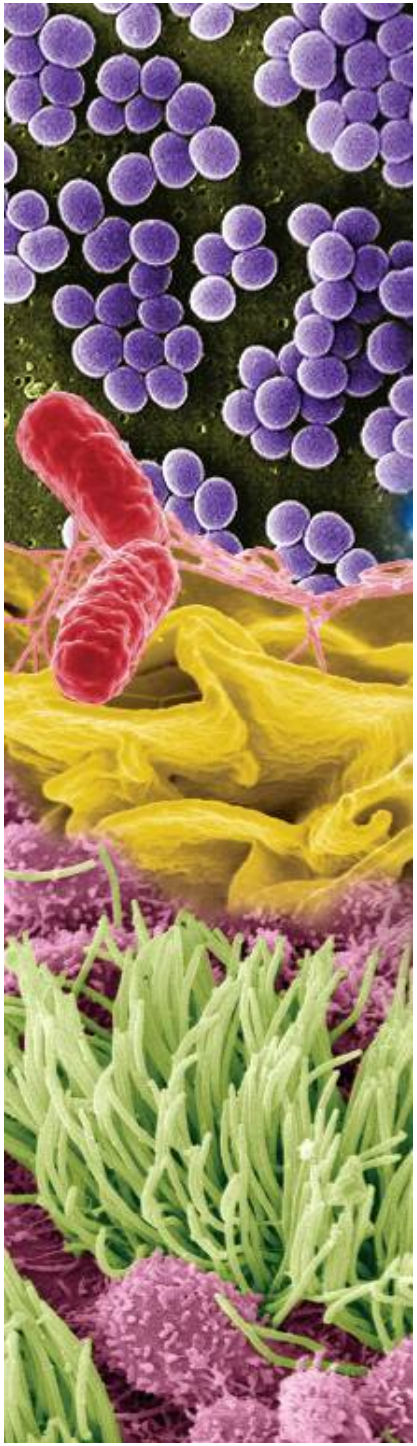


PNS consists of cranial and spinal nerves

nerves: bundles of axons that receive and transmit nerve signals

axons and dendrites of adjacent neurons communicate with each other across a synapse

neurotransmitters are released from one cell and act on the next cell in a synapse



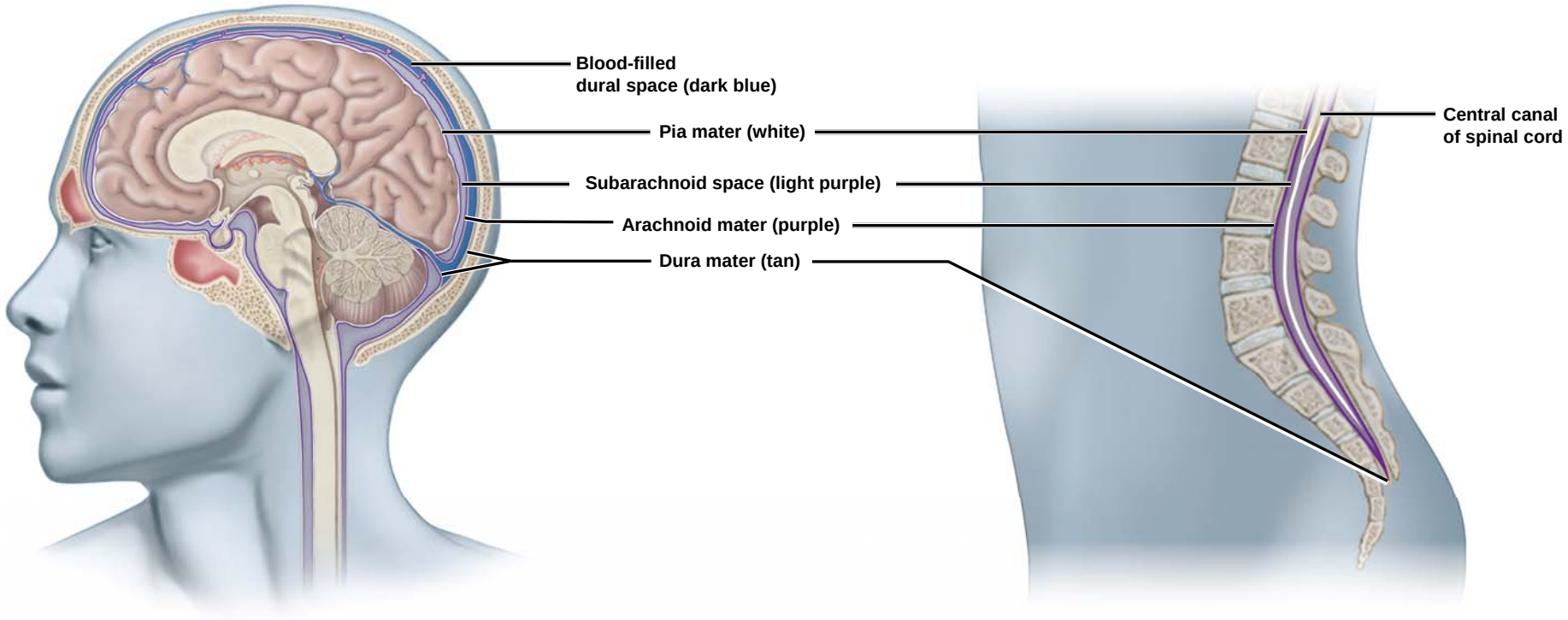
Three important functions

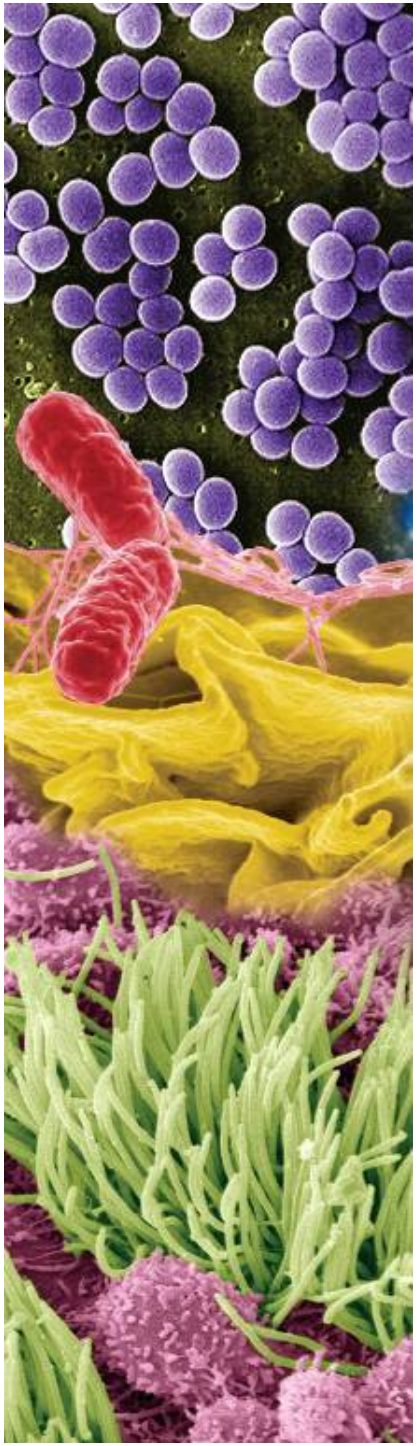
sensory: fulfilled by sensory receptors at the ends of peripheral nerves that generate nerve impulses that are transmitted to the CNS

integrative: translates sensation into thought

motor: receives signals from the CNS in muscles and glands

Detailed Anatomy of the Nervous System





Neurons = dense structures that make up the brain and spinal cord (grey mater)

Brain situated inside the skull // spinal cord lies within the spinal column surrounded by vertebrae

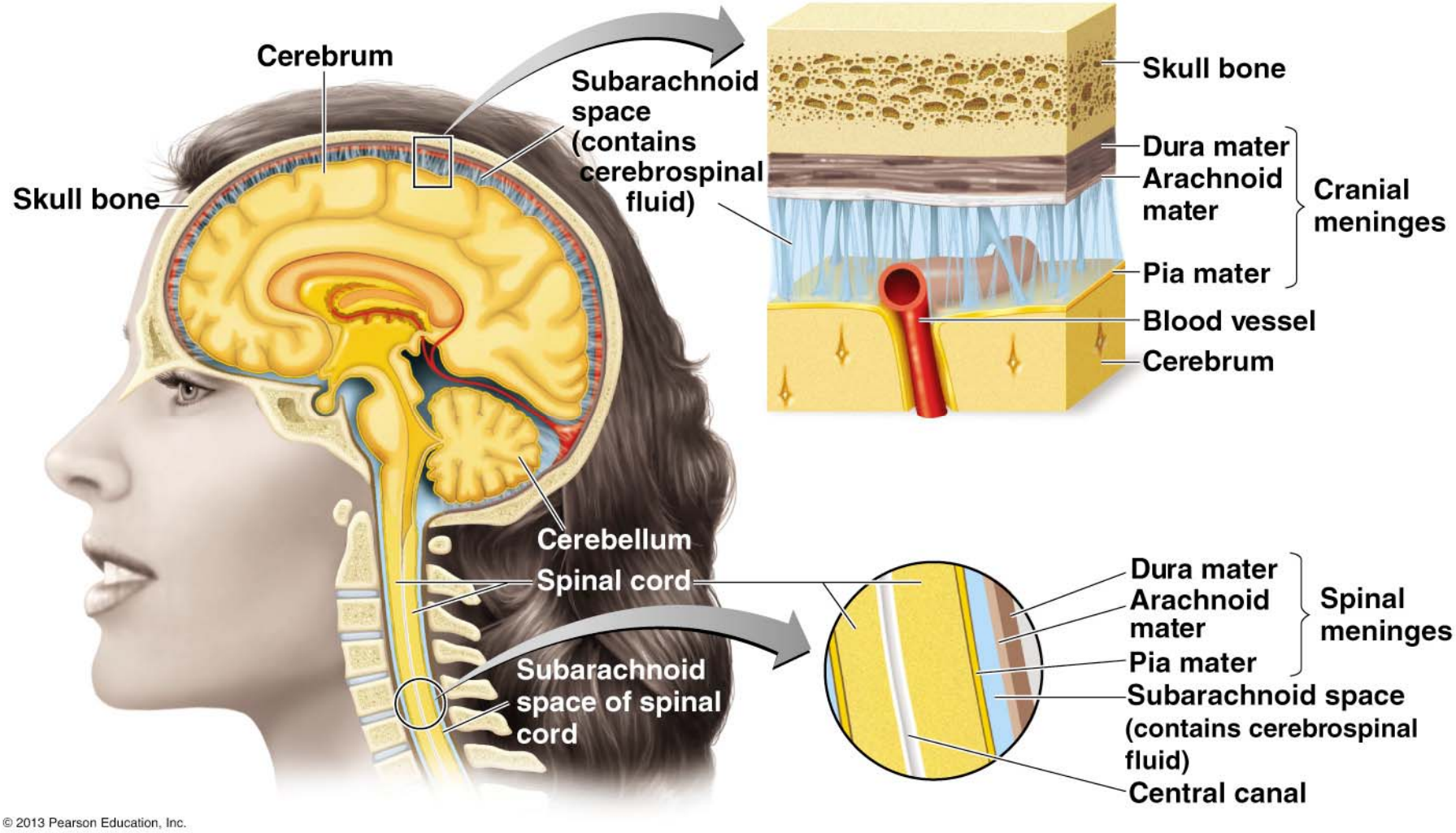
soft tissue encased within three connective tissue layers called the **meninges**

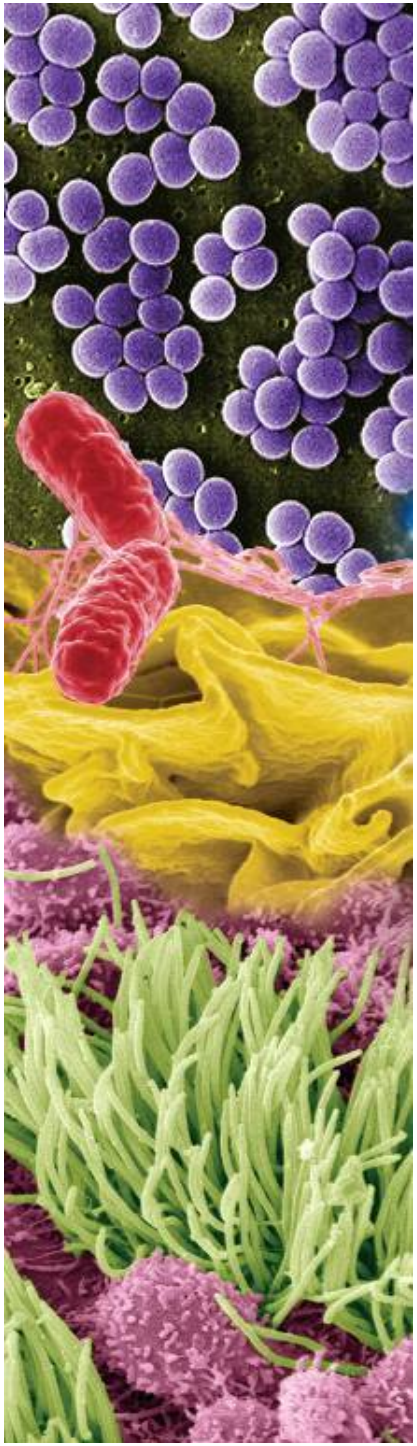
dura mater: outermost layer

arachnoid mater

pia mater

subarachnoid space between the arachnoid and pia mater is filled with cerebrospinal fluid





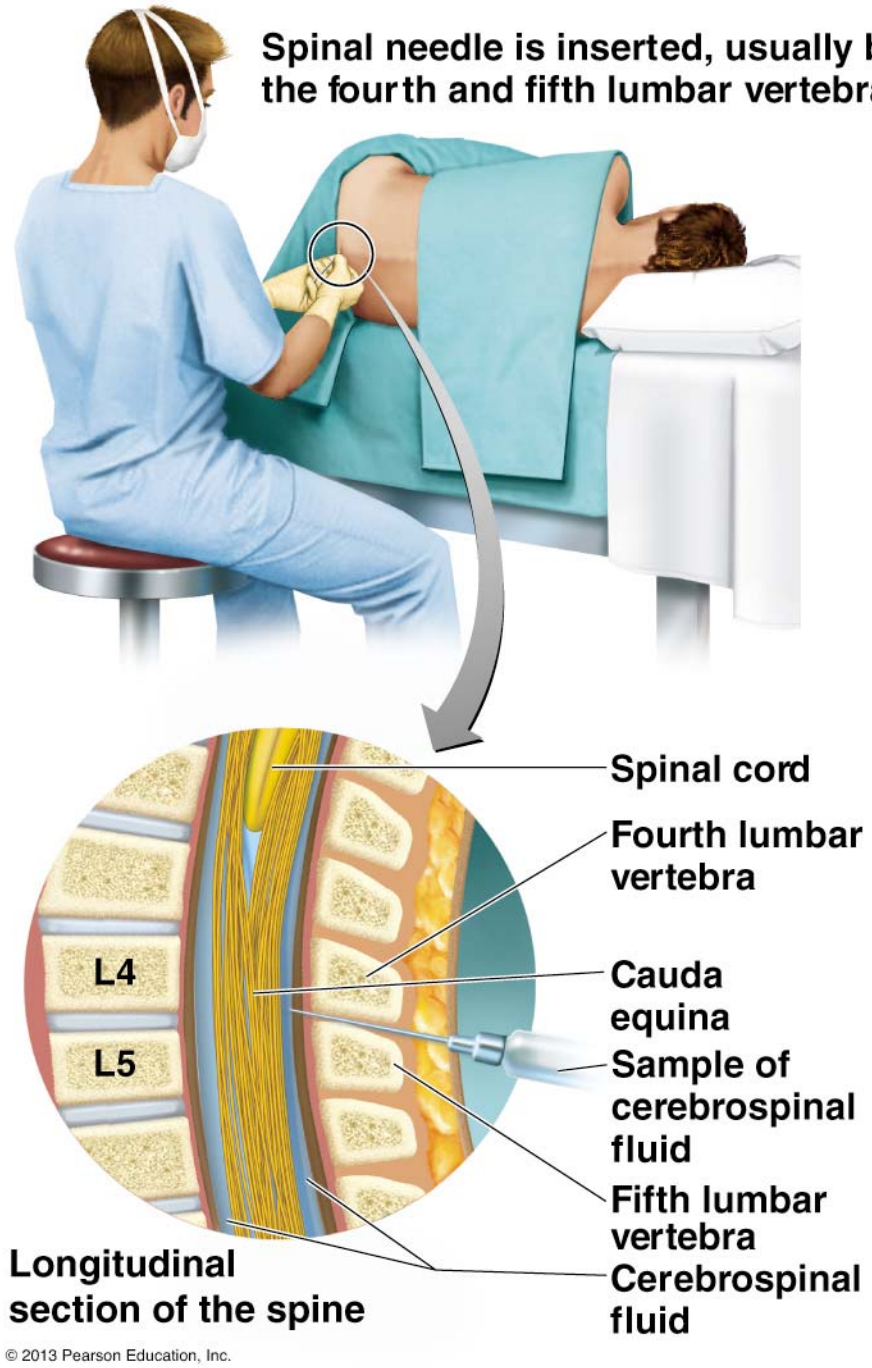
Cerebrospinal fluid (CSF)

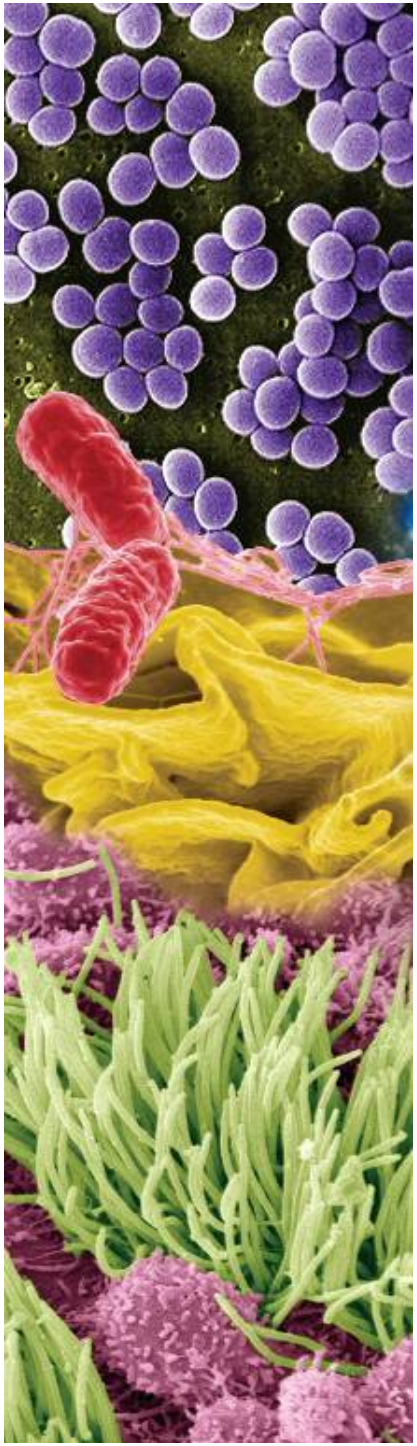
provides nutrition to the CNS

also provides a liquid cushion for the brain and spinal cord

microorganisms can be found within the CSF when meningitis occurs

Meningitis = infection and inflammation of the meninges

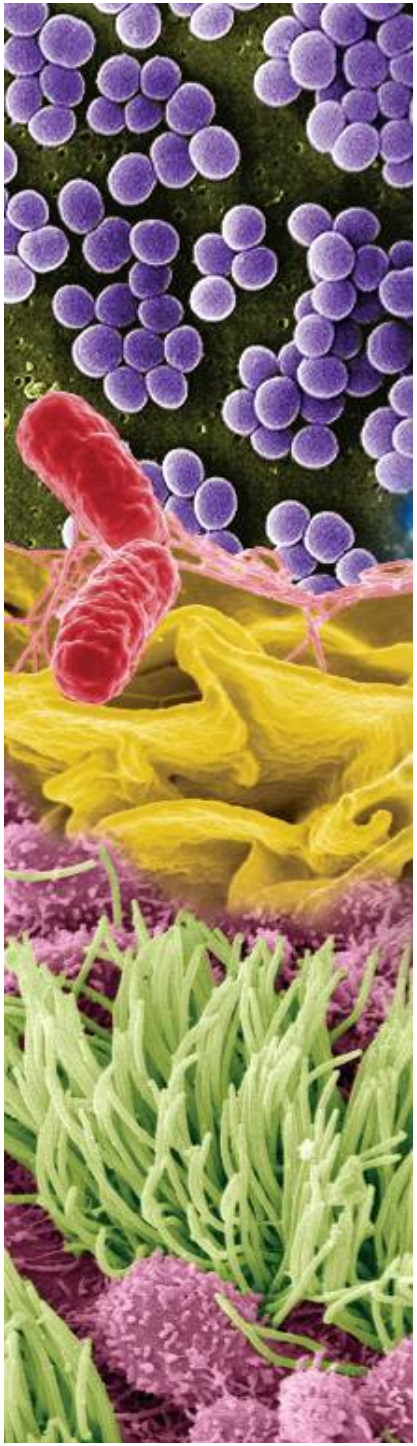




Defenses of the nervous system are *mainly Structural*

Bony casings of the brain and spinal cord protect them from traumatic injury

CSF provides a buoyancy and cushioning function

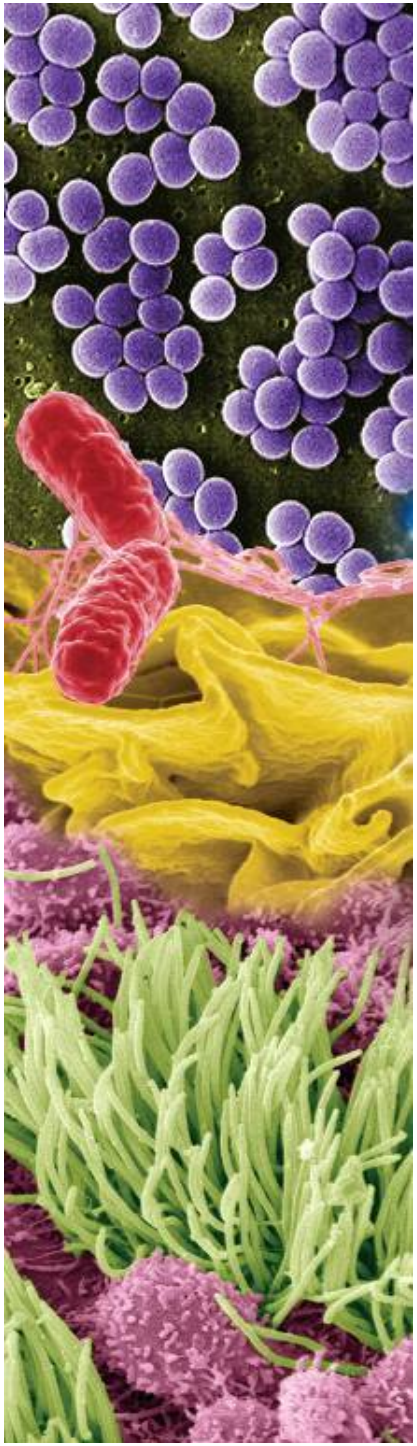


Blood-brain barrier

vascular interface between the blood vessels serving the brain and the brain itself

cells that make up blood vessels only allow a few molecules to pass through

prohibits most microorganisms and most antibiotics from entering the nervous system



CNS is "immunologically privileged"

only able to mount a partial defense, or different immune response when exposed to an immunological challenge

CNS functions are so vital that even temporary damage that could result from normal immune responses could be detrimental

Microglia = brain macrophages

have phagocytic capabilities

activity is reduced when compared to phagocytic cells in other parts of the body

Normal Biota of the Nervous System

It is still believed that there is no normal biota in either the CNS or PNS

finding microorganisms of any type in these tissues represents deviation from the healthy state

herpes viruses live in a dormant (latent) state in the nervous system

not considered normal microbiota

the Human Microbiome Project is not sampling this system at the present time

Meningitis = Inflammation of the meninges

This is an anatomical syndrome: physical trauma can cause inflammation

Many different microorganisms can cause an infection of the meninges

Any infection causes the same constellation of symptoms (triad = fever, headache, and stiff neck)

Entrance to the CNS facilitated by co-infection or previous infection with *respiratory viruses*

These infections make BBB permeable to bacteria and virus

Meningitis = Inflammation of the meninges

Meningitis in neonates is most often caused by microorganisms that differ from those causing disease in children and adults

Encephalitis = inflammation of the brain

Meningoencephalitis = inflammation of both meninges and brain tissue

Most serious forms of acute meningitis are caused by bacteria // less acute caused by virus, fungi, and protozoa

Viral meningitis more common and more mild // enteroviruses common in throat and intestine

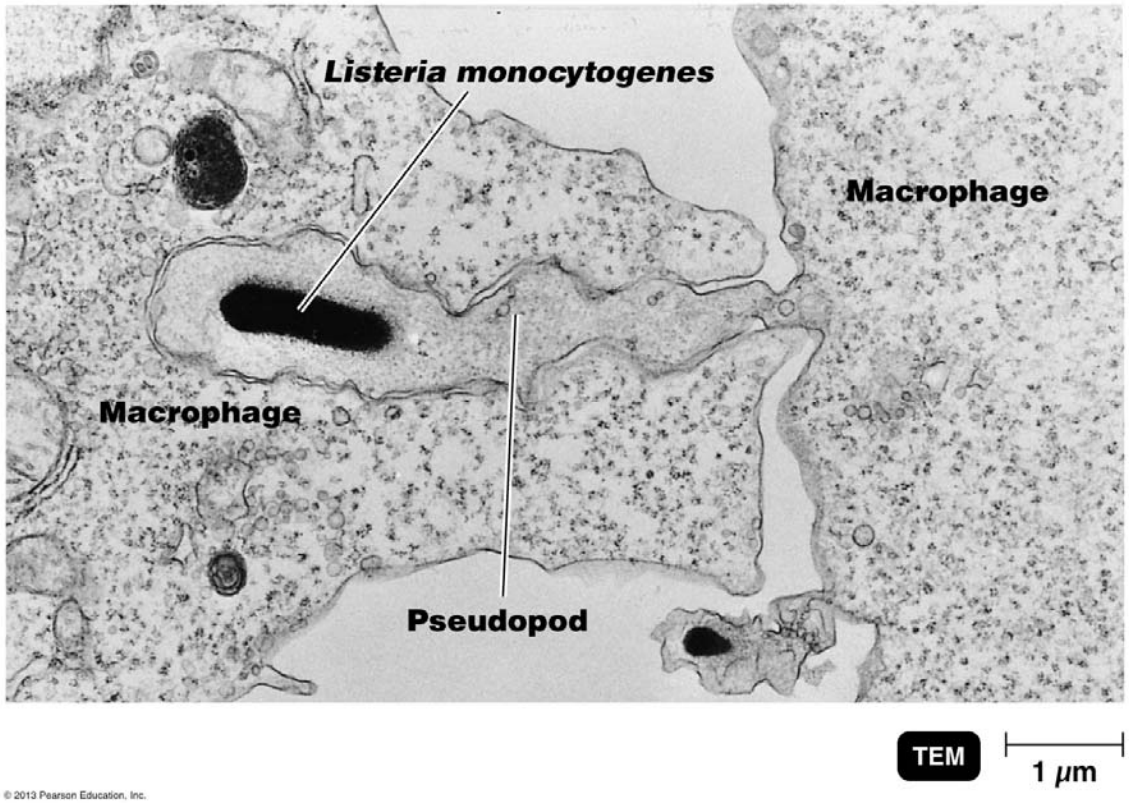
Bacterial Meningitis

- Three bacterial species cause most cases // Haemophilus influenzae type B – Neisseria meningitidis – Streptococcus pneumoniae
- All three have capsule which resist phagocytosis // once in blood rapidly multiply
- Inflammatory event dilates BBB // allow bacteria to enter CSF
- Death occurs within hours after onset of fever, vomiting, and stiff neck // bacteria in CSF always medical emergency // associated with photophobia

Listeriosis

- Listeria monocytogene // gram positive rod – excreted in animal feces – widely distributed in soil and water
- Not destroyed by macrophage // actually grow inside phagocytes
- Recovering and apparent healthy individuals thought to shed L. monocytogene in feces indefinitely
- Infected pregnant women // crosses placenta to cause aborted pregnancy or stillborn infants // may infect fetal CNS – brain injury

Listeriosis



L. monocytogenes = one of few pathogens able to grow at refrigerator temperatures

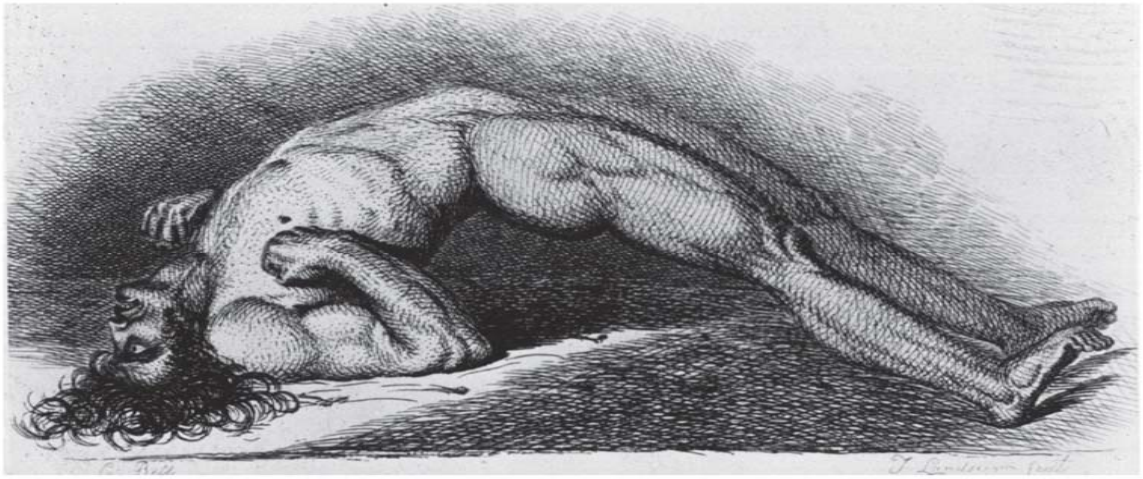
Common outbreaks seen as food borne // ice cream

Tetanus

- Clostridium tetani = obligate anaerobic, endospore-forming gram positive rod

- Produce potent neurotoxin = tetanospasmin // blocks reciprocal inhibition of antagonist in skeletal muscle contraction

- Jaw muscles affected early // lock jaw – clench teeth and unable to open jaw // death from spasms of respiratory muscles



Tetanus

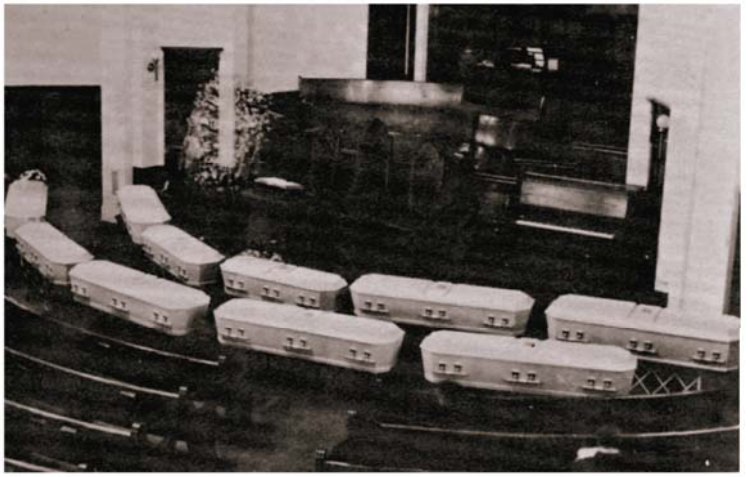
- Infective endospore must be in an anaerobic wound
- Vaccine available since 1940 // standard DTaP (diphtheria, tetanus, and pertussis) childhood vaccination program
- Tetanus vaccine is a toxoid // booster required every 10 years
- Tetanus immune globulin (TIG) // antibody containing serum
- Doctor decides on use of TIG depending on depth of wound and immunizaiton history of patient

Botulism

- Clostridium botulinum // obligetely anaerobic, endospore forming gram positive rod // soil and aquatic sediment

- Sealed cans with endospore allow vegetative growth which results in exotoxin

- Causes flaccid paralysis lasting 1 to 10 days// blocks release of acetylcholine at neuromuscular junction // double or blurred vision, weakness, difficulty swallowing – possible death from respiratory failure



Botulism

- Botulinal toxins not formed in acidic food below pH 4.7
- Botulinal toxins destroyed if food heated to boiling point.
- Infants at risk from endospores // stomach pH not low enough to kill endospores // never recommended to feed honey to infants – why?
- Many therapeutic uses // chronic headaches / relax painful muscle contractions associated with cerebral palsy, Parkinson disease, and multiple sclerosis / control involuntary eye twitching / prevent arm pit sweating / eliminate forehead wrinkles

Leprosy (Hasen's Disease)

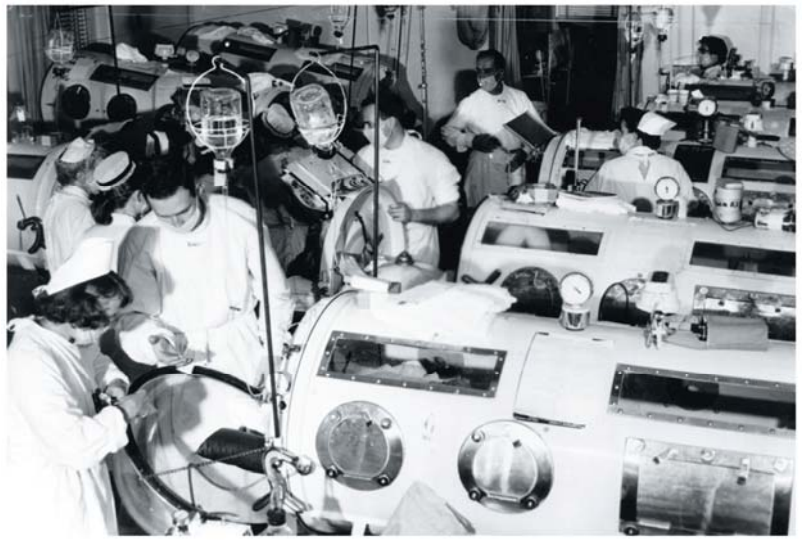
- Mycobacterium leprae // bacillus
- Optimum growth temperature 30 C // why it grows in the extremities
- Able to live inside Macrophage // move from macrophage into peripheral nerves where bacteria live
- Tuberculoid (neural) form // nerve damage from cell-mediated immune response // causes neuropathy – similar to diabetic nerve damage // treated with sulfone drugs // vaccine available

(b) Lepromatous (progressive) leprosy

- Lepromatous (progressive) form // skin cells are infected
- Patients with least effective cell-mediated response develop progressive form

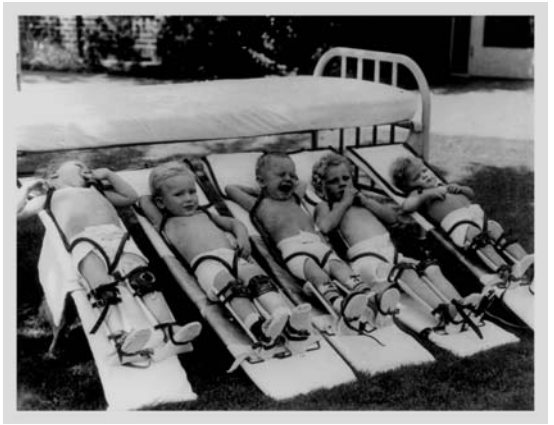
Poliomyelitis

- Poliomyelitis (polio) best known cause of paralysis
- Only 1% infected become paralytic // most cases asymptomatic
- First US outbreak 1894 // summertime outbreaks
- Death from paralysis of respiratory muscle // iron lung developed to keep alive thousands



Poliomyelitis

- Historically – because of poor sanitation // newborn were exposed early in life to virus while still protected by maternal antibodies
- Infants contracted asymptomatic case of polio and acquired lifelong immunity
- Improved sanitation caused delay in infant exposure to virus
- Maternal antibodies no longer providing passive immunity
- Exposure now more likely to cause paralytic polio

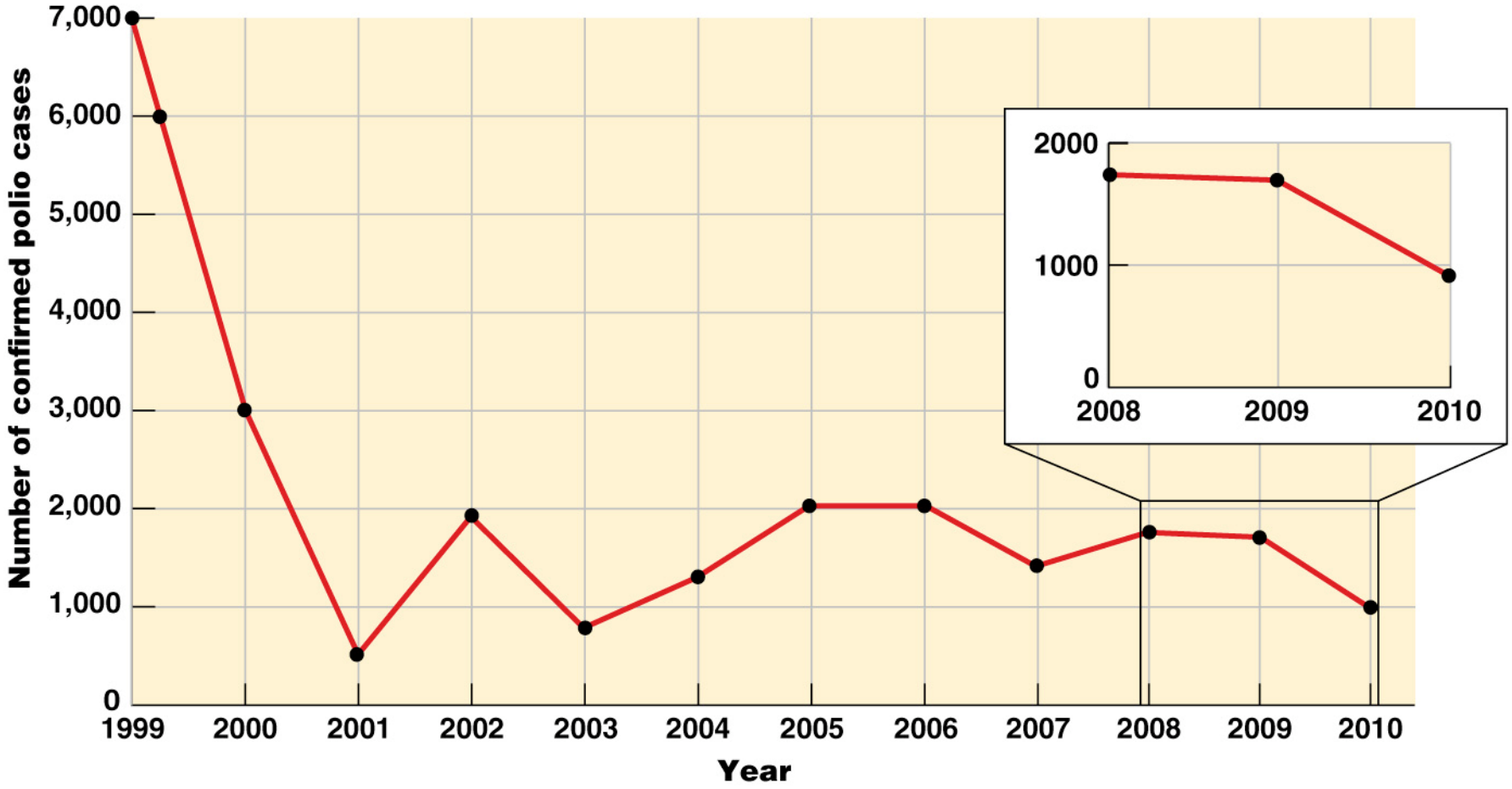


Poliomyelitis Pathway of Infection

- Polio virus portal of entry is throat and/or small intestines // sore throat and nausea
- Virus next invade tonsils and lymph nodes of neck and ileum
- From lymph nodes virus moves to blood // viremia if persistent will pass capillaries of blood brain barrier to enter CNS
- Virus has high affinity for neurons – specifically motor neurons // do not infect peripheral nerves
- Motor cells died resulting in paralysis

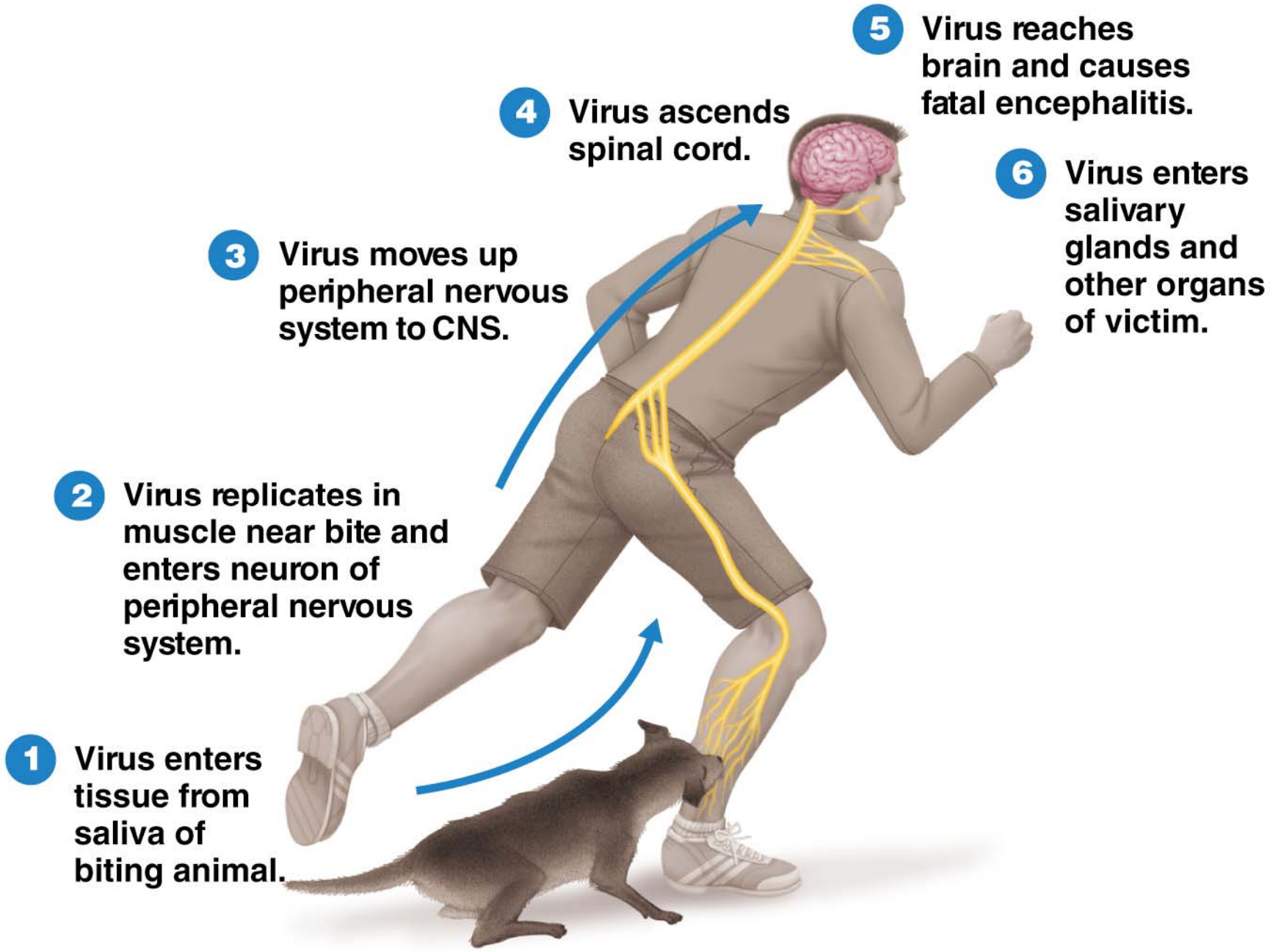
Polio Vaccine

- Three serotypes of poliovirus (type 1,2,3)
- Two type of vaccines developed
- 1955 Salk vaccine // formalin used to inactivate virus // called inactivated polio vaccine (IPV)
- 1963 Sabin vaccine // contains attenuated (weakened) active virus – mimics actual infection and provides active immune response // less expensive easier to administer // known as the oral polio vaccine – helped to eliminate polio in US
- Occasionally, the OPV can result in shedding of active virus and result in disease // now we only use IPV



Rabies

- Rabies virus almost always results in fatal encephalitis // genus Lyssavirus – single stranded RNA
- Rabies is Latin for rage or madness
- Rabies often contracted from bite from infected animal // virus accumulates in salivary glands
- Virus enters PNS then travels to CNS at rate of 15mm to 100 mm per day // once in nervous tissue virus not accessible to immune system // when reaches CNS nearly always fatal – only two or three documented cases not fatal
- In humans virus able to replicate in epithelial cells first then move into PNS // long incubation period from days to months



Rabies Signs & Symptoms

- Early symptoms mild and varied // typical of mild infections
- Reach CNS periods of agitation and intervals of calm
- Patient feels air drafts, swallows, or even the thought of water will trigger muscle spasms in mouth and pharynx // where term hydrophobia becomes associated with Rabies
- Two forms:
- Furious (classical) rabies – first restless then highly excitable and bites at anything – active virus in saliva
- Paralytic (dumb or numb) rabies – minimal excitability seen more in cats but might snap at if handled

Rabies Prevention & Treatment

- High risk workers may receive vaccine before exposure // laboratory workers, animal control workers, and veterinarians
- If non vaccinated person bitten by infected animal // post exposure prophylaxis (PEP)
- Immediately receive series of anti-rabies vaccine and immune globulin injections
- Once CNS symptoms occur – little can be done to save individual // only five survivors known with PEP
- Milwaukee protocol // used successfully to save two people without prior PEP treatment // induce extended coma and administer antiviral drugs

Arboviral Encephalitis

- Caused by mosquito-borne virus
- Arboviral stands for arthropod-borne virus // these diseases increases in summer months
- Symptoms range from sub-clinical to severe // fever, chills, headache, flu like symptoms // including death
- Survivors may have lasting neurological conditions

Culex mosquito engorged with human blood.

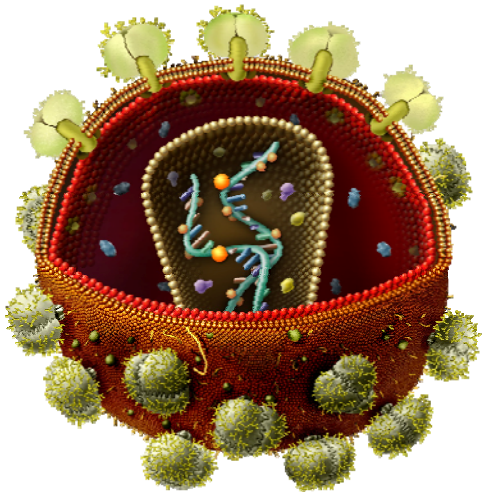
Arboviral Encephalitis Types

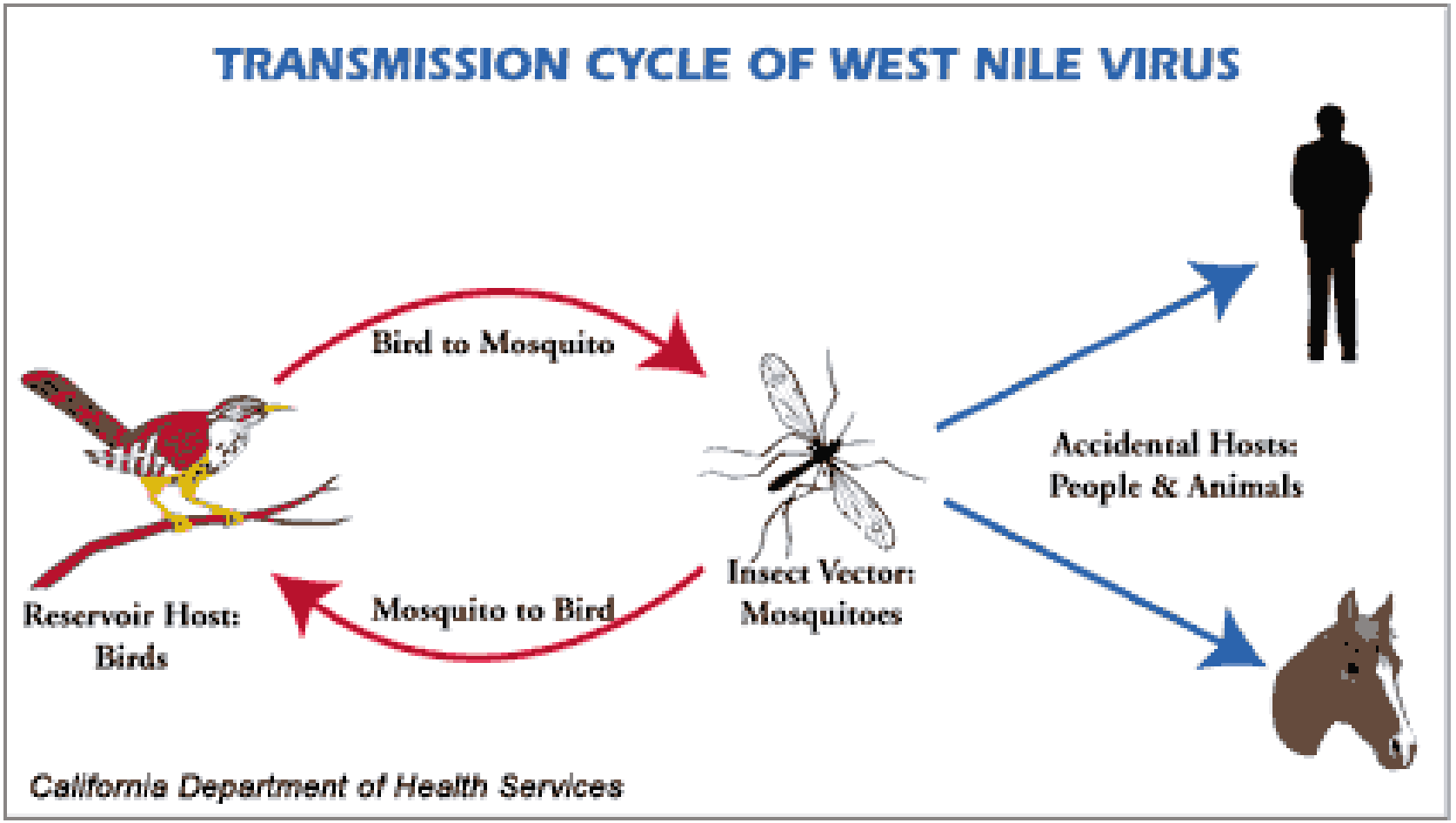
- Western (WEE) and eastern equine encephalitis (EEE) // effects horses and humans – EEE more severe with mortality rate of 30%

- St. Louis encephalitis (SLE) mostly in central and eastern US // only 1% infected show symptoms however - mortality rate in symptomatic patients 20%

- West Nile encephalitis (WNV) – US in 1999 // maintained in bird-mosquito-bird cycle // in Culex mosquito species // most cases subclinical however may cause polio-like paralysis and fatal encephalitis

Culex mosquito engorged with human blood.




TRANSMISSION CYCLE OF WEST NILE VIRUS
Bird to Mosquito
Mosquito to Bird
Reservoir Host:
Birds
Insect Vector:
Mosquitoes
Accidental Hosts:
People & Animals
California Department of Health Services

Crytococcosis

- Emerging fungal disease caused by crytococcus neoformans and C. grubii // disease is known as Crytococcus neoformans meningitis
- Distributed by bird droppings and humans contract fungus by dust inhalation
- People with weakened immune systems at risk
- C. gatti becoming more common in Northern California and Vancouver Island in Canada // fungus finding niche in decay hollows of trees
- Fungus also grows in lungs and found in marine animals, dogs, and also humans

Amebic Meningoencephalitis

- Two protazoa may cause this condition – both found in fresh water // Naegleria fowleri and Acanthamoeba

- Naegleria fowleri - many people carry antibodies but few show symptoms // children who swim in warm ponds and streams at greatest risk

- N. fowleri enters nervous tissue via olfactory nerve in nasal mucosa

- Fatality rate is nearly 100% // death in few days after first symptoms // diagnosis made at autopsy

Cases reported after using Neti Pots

Prion Disease

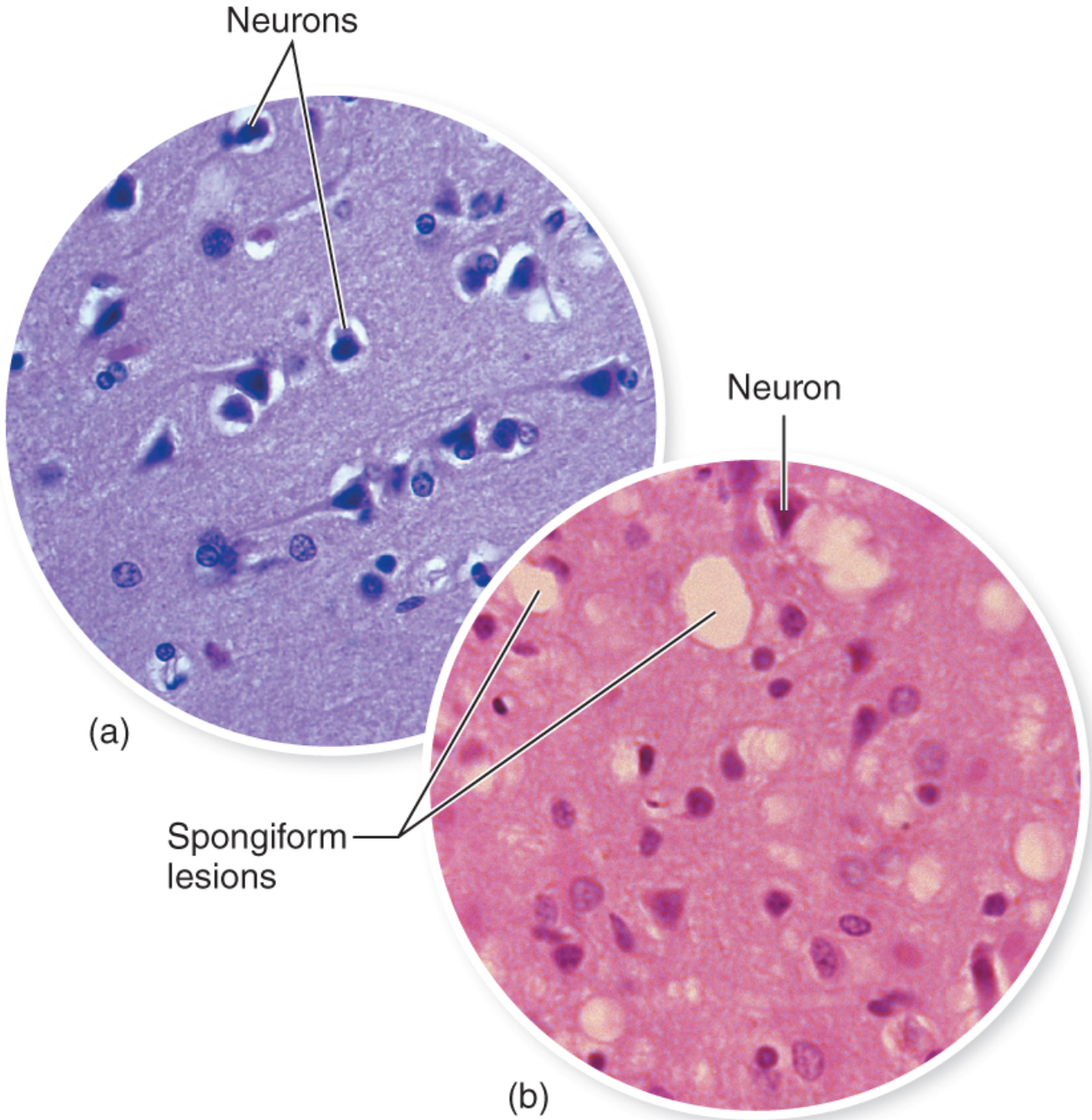
Proteinaceous infectious particles // disease contains no genetic material // / form of sub-acute encephalitis

Cause transmissible spongiform encephalopathies (TSEs)

neurodegenerative diseases with long incubation periods but rapid progressions

human TSEs: Creutzfeldt-Jakob Disease (CJD) and Gerstmann-Strussler-Scheinker disease

animal TSEs // scrapie, transmissible mink encephalopathy, bovine spongiform encephalopathy (BSE, or “mad cow” disease)



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Prions: Signs and Symptoms

Altered behavior, memory loss, impaired senses, delirium, premature senility

Uncontrollable muscle contractions continue until death // usually within a year of diagnosis

causes *transformation of a normal host protein (PrP)* that functions in normal brain development

mutation causes a structural change in the protein, making PrP catalytic and able to convert other normal PrP proteins into the abnormal form

Prions: CJD // Causative Agent

Abnormal PrP proteins start a self-propagating chain that creates a massive accumulation of altered PrP

plaques form in the brain, causing spongiform damage and severe loss of brain function

Prions are considered **transmissible agents**

PrP proteins can be acquired through transmission

genetic mutations of the PrP gene can also be passed on as heritable traits

Prions are hardy "pathogens" // resistant to chemicals, radiation, heat, and prolonged autoclaving (more resistant than endospores!!!!)

Prions: Transmission and Epidemiology

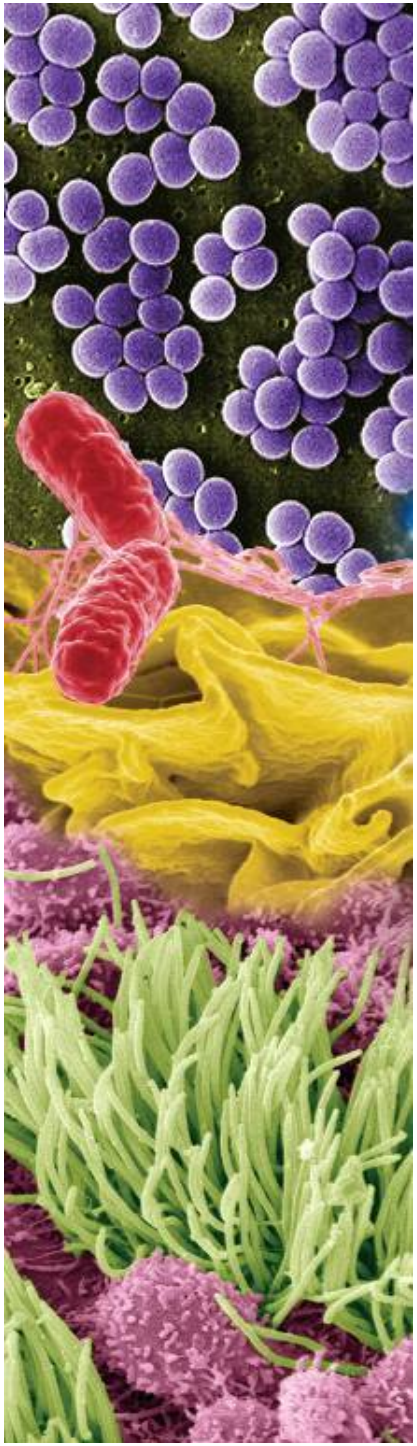
In the late 1990s, humans contracted vCJD after ingesting meat from cattle that had been afflicted with bovine spongiform encephalopathy

meat products had been contaminated with fluid or tissues infected with the prion

cases were centered around Great Britain, where many cows were found to have BSE

median age at death of patients with vCJD is 28 years

median age at death of patients with other forms of CJD is 68 years



Prions: Transmission and Epidemiology

Health care professionals should be aware of the possibility of CJD in patients

cases have been reported of transmission of CJD via contaminated surgical instruments

normal disinfection and sterilization procedures are not sufficient to eliminate the agent from instruments and surfaces

latest CDC guidelines for handling CJD patients in a health care environment should be consulted