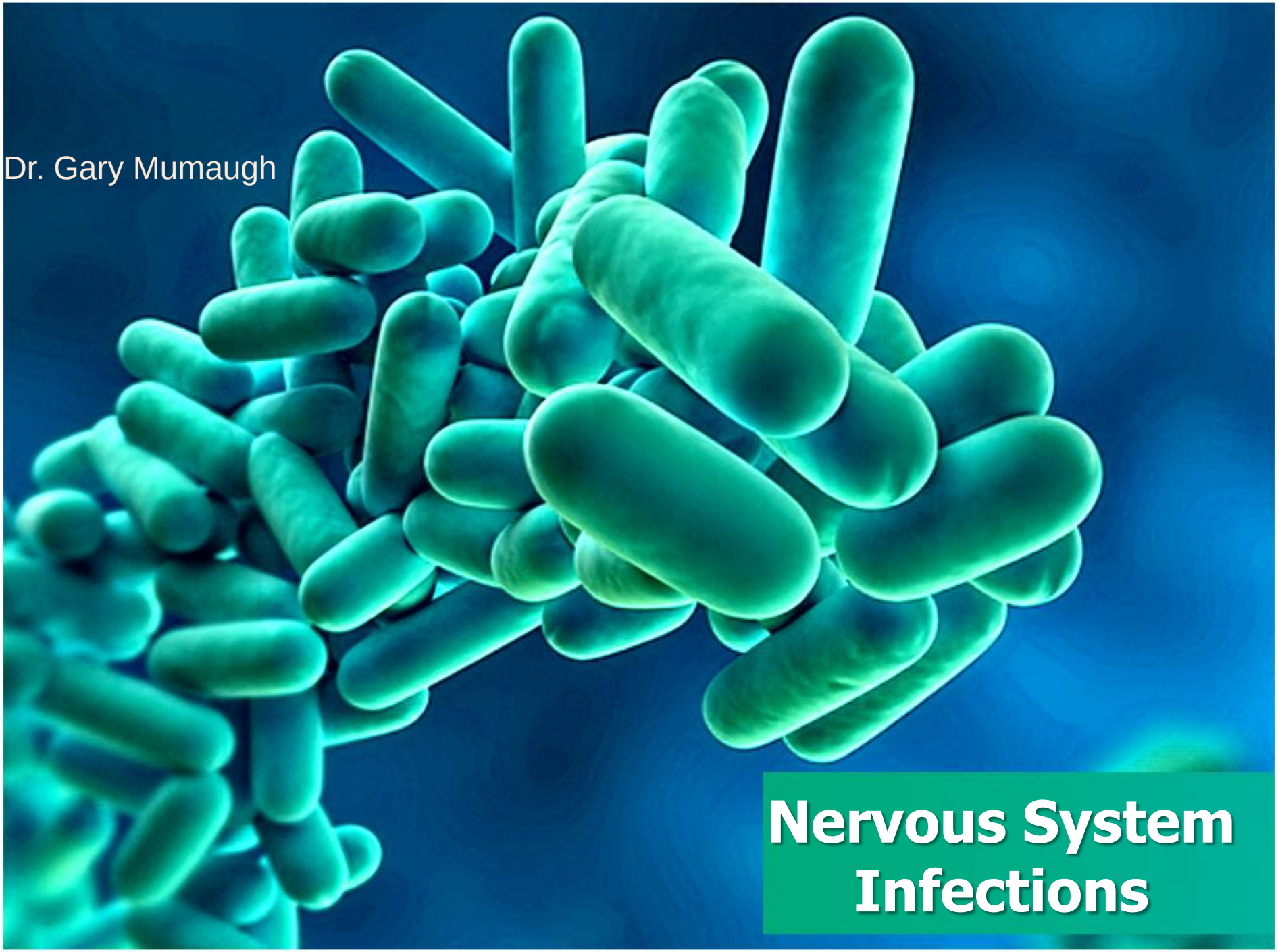
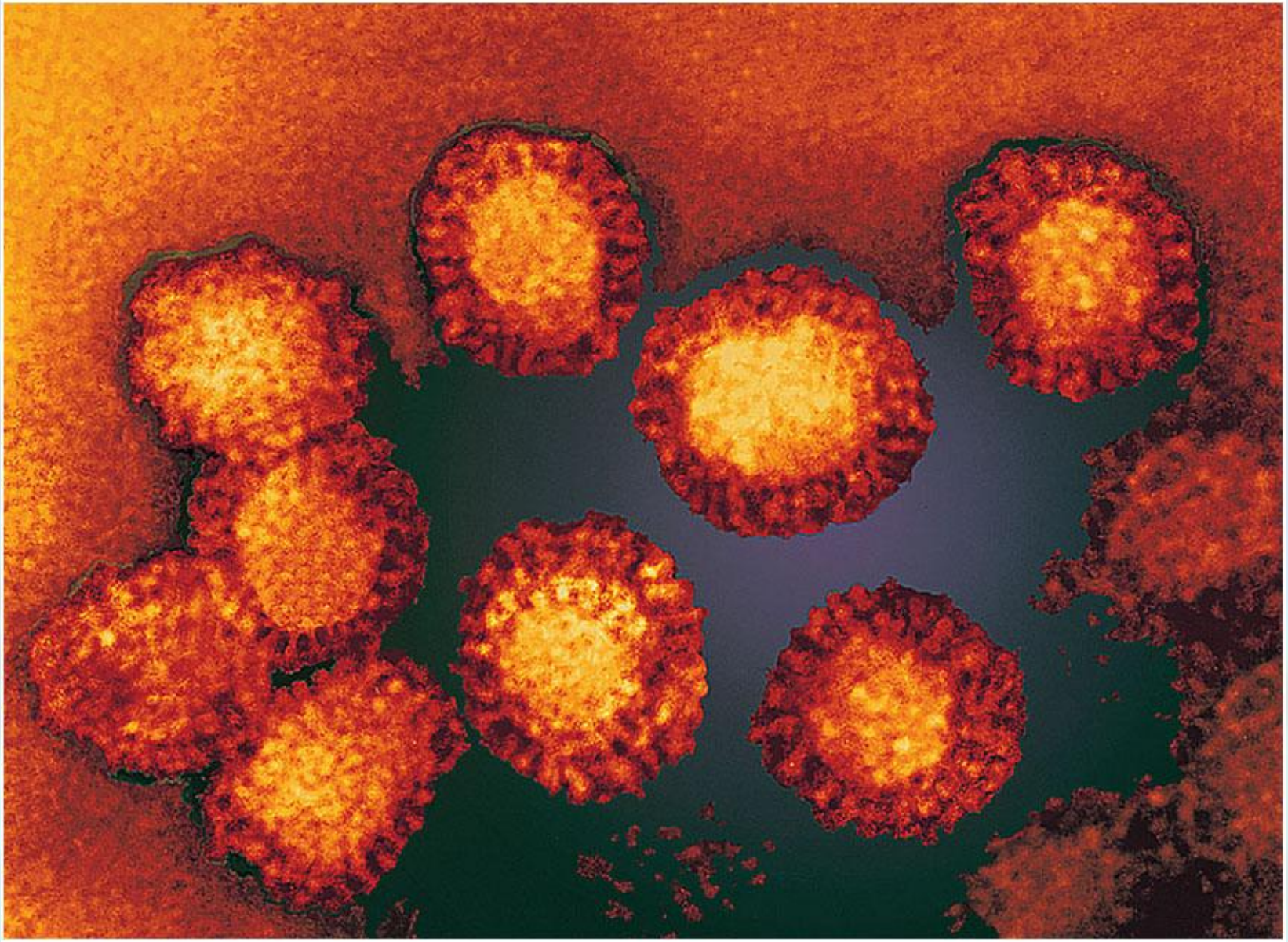

Dr. Gary Mumaugh
Nervous System Infections



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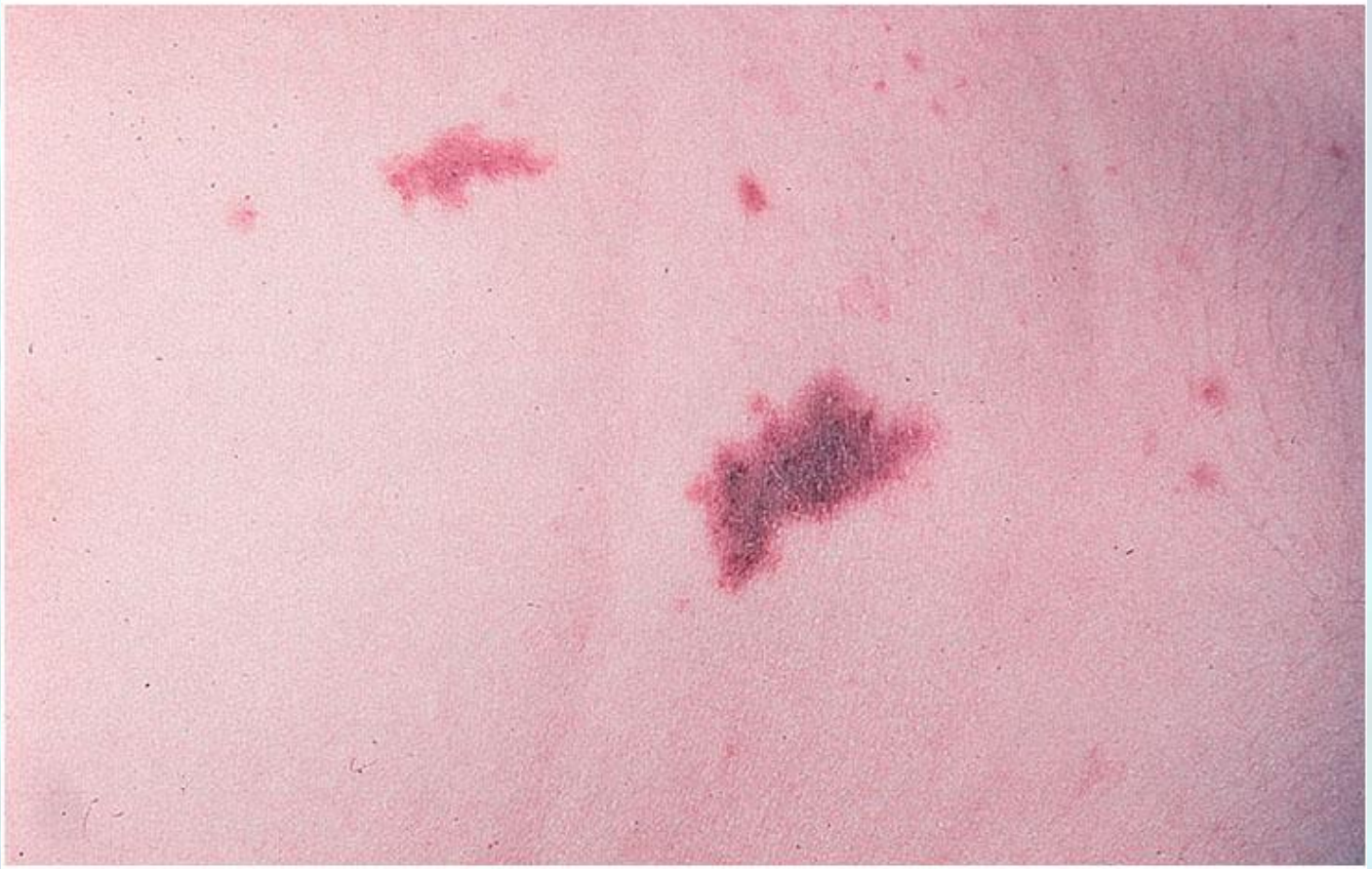
Meningococcal Meningitis

- Symptoms
  - Mild cold followed by onset of throbbing headache
  - Fever
  - Pain and stiffness of neck and back
  - Nausea and vomiting
  - Deafness and alteration in consciousness may appear progressing to coma
- Small hemorrhages called petechiae may appear on skin
- Infected person may develop shock and die within 24 hours
  - Usually progression of disease is slower allowing time for treatment

Meningococcal Meningitis



Meningococcal Meningitis

- Pathogenesis
  - Acquired by inhaling infected respiratory droplets
  - Bacteria adhere to mucous membranes
  - Invade bloodstream by passing through respiratory epithelium
    - Bloodstream carries organisms to CSF
  - Inflammation causes swelling and infarcts to brain tissue
    - Can also cause obstruction of outflow of CSF
      - Causes brain to squeeze against skull
  - Release of endotoxin causes drop in blood pressure leading to shock

Meningococcal Meningitis

- Causative agent - *Neisseria meningiti*
- Epidemiology
  - *N. meningitis* more prone to cause epidemics
  - Can spread rapidly in crowded stressed places
  - Human only source of infection
  - Transmission can occur with disease or asymptomatic carrier
    - Organism recovered from 5% - 15% of healthy individuals

Meningococcal Meningitis

- Prevention and Treatment
  - Vaccine is available
    - Used to control epidemics
    - Not given routinely due to ineffectiveness in children less than 2 years of age
    - Effect is not long lasting
  - Mass prophylaxis with antibiotics helpful at controlling epidemics in small populations
  - Can usually be cured unless brain injury or shock present
    - Mortality is less than 10% in treated populations

TABLE 27.1 Meningococcal Meningitis

① *Neisseria meningitidis* inhaled, infects upper airways.

② Bacteria enter the bloodstream and are circulated throughout the body.

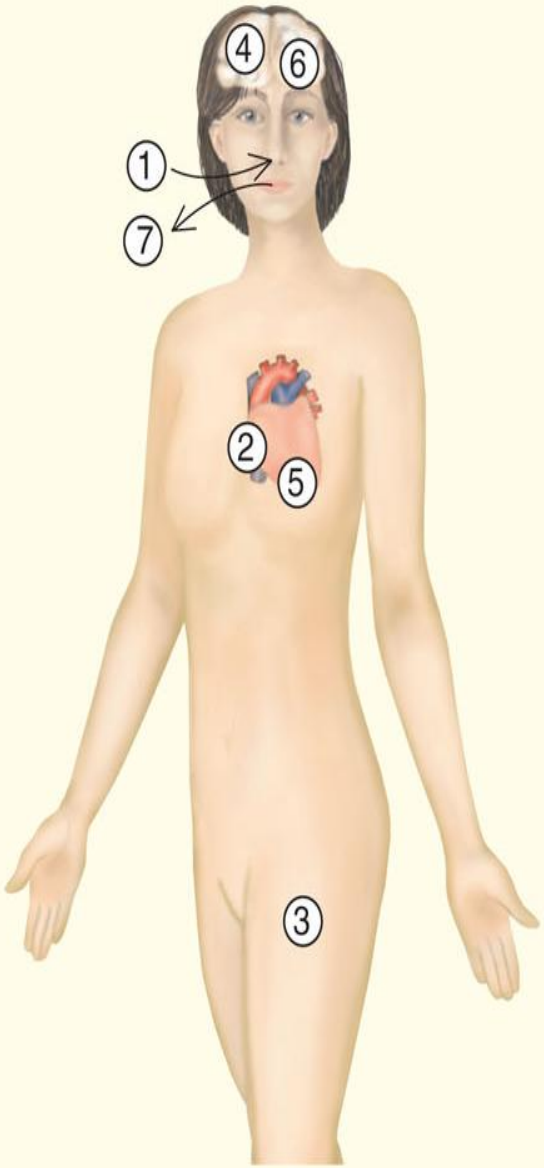
③ The bacteria lodge in the skin and cause petechiae.

④ Bacteria on the meninges causes meningitis.

⑤ Lysing bacteria in the circulation release endotoxin, producing shock.

⑥ Inflammatory response in meninges can damage nerves of hearing causing deafness and obstruct the flow of cerebrospinal fluid causing increased pressure inside the brain.

⑦ Bacteria exit with respiratory secretions.



Symptoms	Mild cold followed by headache, fever, pain, stiff neck and back, vomiting, petechiae
Incubation period	1 to 7 days
Causative agent	*Neisseria meningitidis,* the meningococcus; a Gram-negative diplococcus
Pathogenesis	Meningococci adhere by pili, colonize upper respiratory tract, enter bloodstream; carried to meninges and spinal fluid; inflammatory response obstructs normal outflow of fluid; increased pressure caused by obstructed flow impairs brain function; damage to motor nerves produces paralysis; endotoxin release causes shock.
Epidemiology	Close contact with a case or carrier; inhalation of infectious droplets; crowding and fatigue predispose to the disease.
Prevention and treatment	Conjugate vaccine against serogroups A, C, W135, and Y used to immunize ages 11–55 years; rifampin given to those exposed. Penicillin, ceftriaxone, for treatment.

Listeriosis

- Symptoms
  - Most cases asymptomatic
  - Symptoms include
    - Fever and muscle aches
    - Sometimes nausea and diarrhea
    - 75% of cases coming to medical attention have meningitis
      - With typical symptoms of meningitis
  - Pregnant women who become infected often miscarry or deliver terminally ill infants

Listeriosis

- Causative agent - *Listeria monocytogenes*
- Pathogenesis
  - Mode of entry usually generally thought to enter through GI tract
  - Bacteria penetrate intestinal mucosa then enter the bloodstream
    - Leads to bacteriemia
  - Organism can cross the placenta
    - Produces abscesses in fetal tissues
    - Babies usually develop meningitis after 1-4 week incubation period

Listeriosis

- Epidemiology
  - Widespread in natural waters and vegetation
  - Can be carried asymptomatically in animals and humans
  - Pregnant women, elderly and immuncompromised at highest risk
    - Advised to refrain from soft cheeses and reheat leftovers
  - Epidemics have resulted from contaminated foods
    - Organism can survive in commercially prepared foods and at refrigeration temperatures

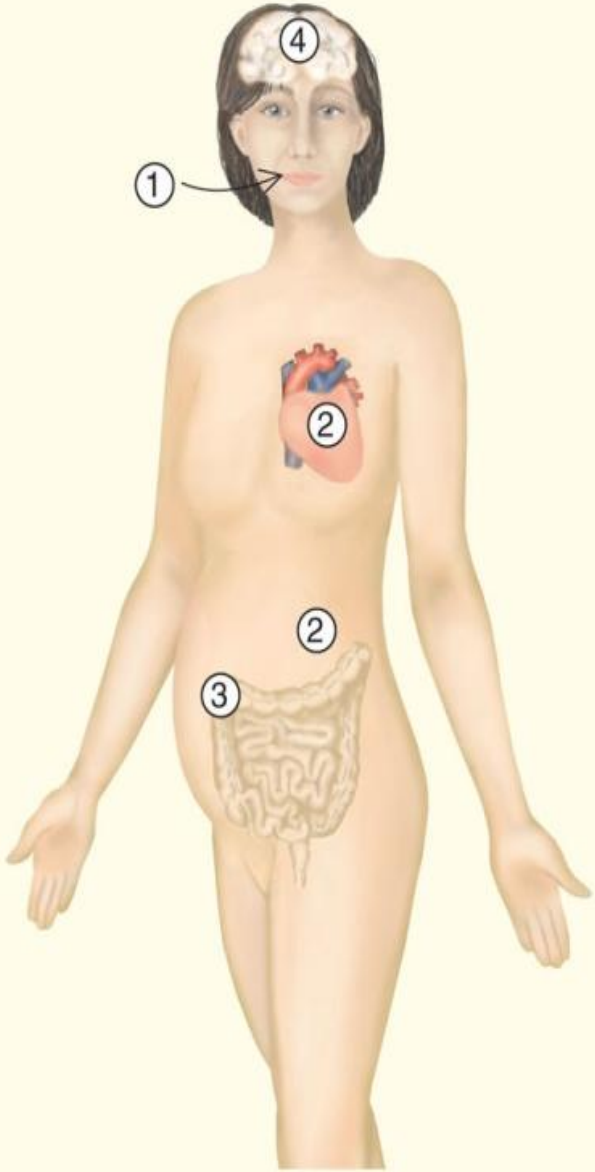
TABLE 27.2 Listeriosis

① Causative organism *Listeria monocytogenes* is ingested with food such as Mexican cheese, soft cheeses, non-pasteurized milk, hot dogs, or coleslaw.

② The bacteria rapidly penetrate the intestinal epithelium and establish bacteremia, especially in pregnant women, the elderly, and the immunodeficient.

③ In pregnant women, circulating *L. monocytogenes* crosses the placenta and fatally infects the fetus or bacteria transmitted to the baby at birth cause meningitis in one to four weeks. The mother usually does not have a serious illness.

④ In older people and those with underlying diseases *L. monocytogenes* attacks brain and meninges, causes meningitis, brain abscesses.



Symptoms	Fever and muscle aches, with or without gastrointestinal symptoms; headache and stiff neck mark the onset of meningitis
Incubation period	A few days to 2 to 3 months; in newborn babies, 1 to 4 weeks
Causative agent	*Listeria monocytogenes,* a non-spore-forming Gram-positive rod able to grow at 4°C
Pathogenesis	Ingested *L. monocytogenes* penetrate the intestinal epithelium and enter the bloodstream; the resulting bacteremia seeds the meninges, causing meningitis.
Epidemiology	Epidemics from contaminated soft cheeses, non-pasteurized milk, coleslaw, hot dogs. Pregnant women get bacteremia, fetal infection, miscarriage. Infants contract infection at birth, develop meningitis in the first month of life. Elderly and those with immunodeficiency, cancer, and diabetes also at high risk.
Prevention and treatment	Care in handling, cooking of raw meats; thorough washing of vegetables; reheating of cold cuts, hot dogs, and refrigerated leftovers. Antibacterial medications such as penicillin, given promptly, are effective treatment.

TABLE 27.3 Main Causes of Acute Bacterial Meningitis Compared

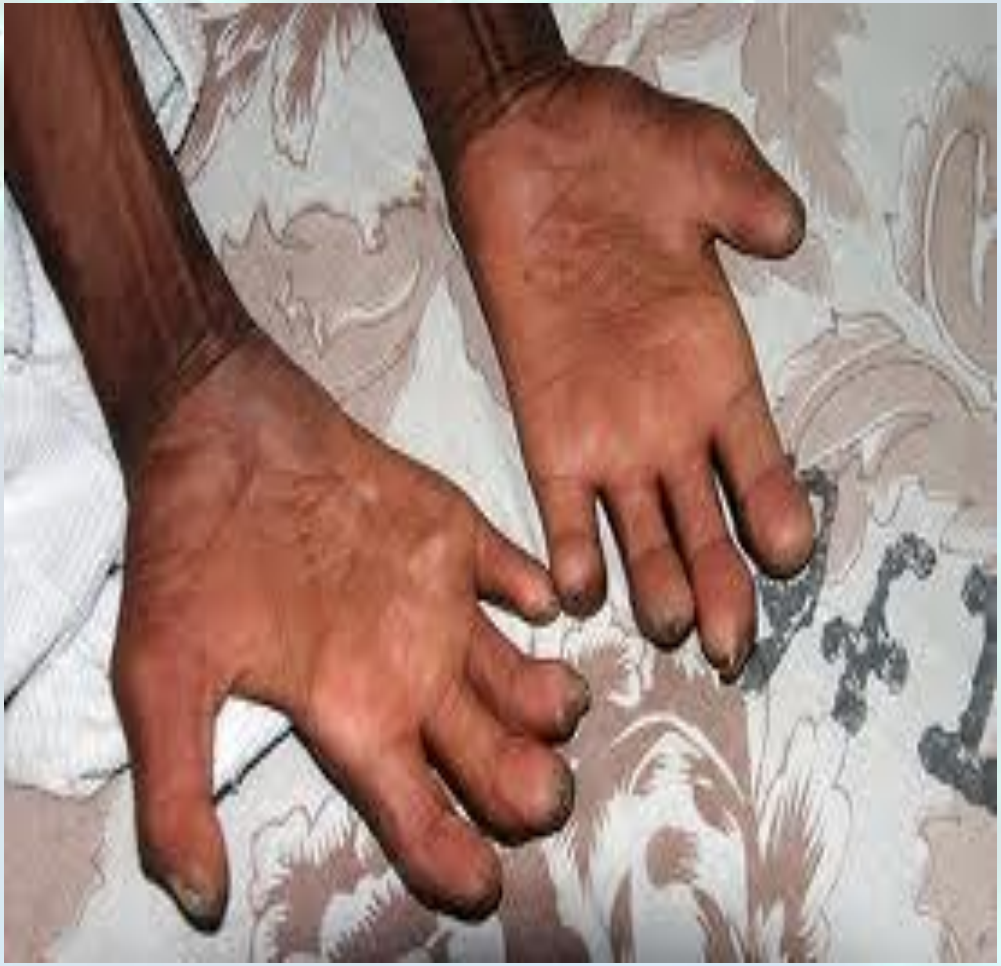
Agent	Characteristics	Source	Vaccine ?	Usual Victims
H. influenzae	Tiny, Gram-negative coccobacilli	Human respiratory system	Yes, type b	Young children
N. meningitidis	Gram-negative diplococci	Human respiratory system	Yes, four types	Mostly ages 2–20 years; can cause epidemics
S. pneumoniae	Encapsulated, Gram-positive diplococci	Human respiratory system	Yes, multiple types	Mostly late teens and adults
S. agalactiae	Gram-positive cocci in chains	Bowel, vagina	No	Mostly neonates; others with underlying diseases
E. coli	Gram-negative rods; usually a specific encapsulated type	Bowel	No	Mostly neonates
L. monocytogenes	Gram-positive motile rods; multiply at refrigerator temperatures	Environment; contaminated cheeses, coldcuts, other foods	No	Pregnant women, neonates; elderly

Hansen's Disease (Leprosy)

- Symptoms
  - Begins gradually
    - Usually with onset of increased or decreased sensation in certain areas of skin
    - These areas usually have changes in pigmentation
  - Affected areas later enlarge and thicken
  - Loss of hair, ability to sweat and sensation
  - Nerves in extremities visibly enlarge
    - Usually accompanied with pain that proceeds to numbness, muscle wasting, ulceration
      - Loss of fingers and toes follows
  - Changes most obvious in face
    - Thickening of nose and ears with deep wrinkling

Hansen's Disease (Leprosy)

- Causative agent - *Mycobacterium leprae*



Hansen's Disease (Leprosy)

- Pathogenesis
  - Earliest detectable findings in humans is infection of small nerves of skin
  - Only know human pathogen to preferentially attack peripheral nerves
  - Grows slowly
  - Disease may spontaneously stop progressing
    - Nerve damage although permanent doesn't progress

Hansen's Disease (Leprosy)

- Epidemiology
  - Transmission via direct human-to-human contact
    - Disease develops in small number of people
      - Controlled by body defenses
  - Natural infections occur in wild armadillos and mangabey monkeys
    - Armadillos not a source of human infection

Hansen's Disease (Leprosy)

- Prevention and Treatment
  - No proven vaccine
  - Dapsone and rifampin used to arrest tuberculoid leprosy
    - Treated for 6 months to 2 years
  - Combination therapy required to control resistance

TABLE 27.4 Hansen's Disease (Leprosy)

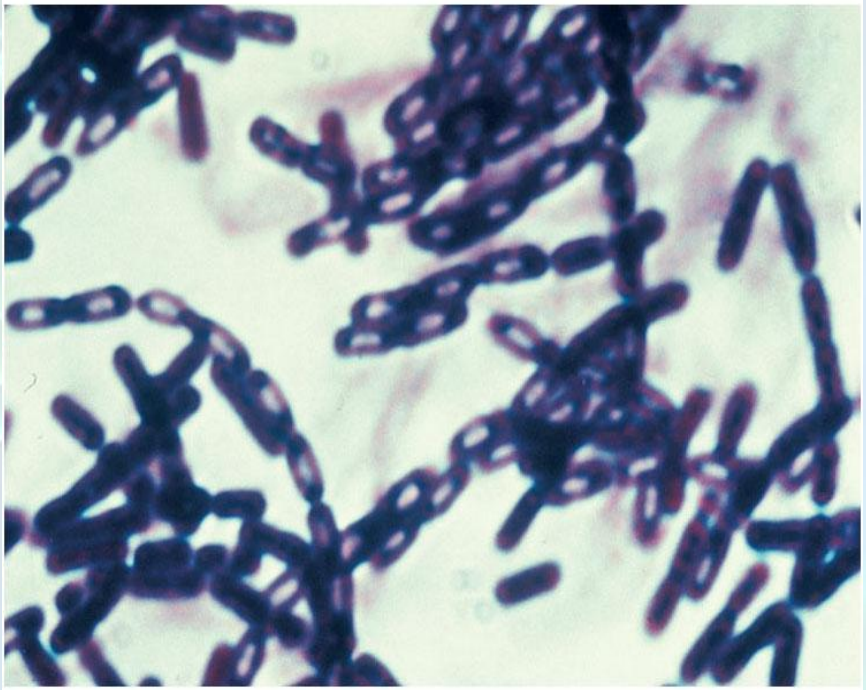
Symptoms	Skin lesions that lack sensation, deformed face, loss of fingers or toes
Incubation period	3 months to 20 years; usually 3 years
Causative agent	*Mycobacterium leprae,* an acid-fast, non-culturable rod
Pathogenesis	Invasion of small nerves of skin; multiplication in macrophages; course of disease depends on immune response of host; activated macrophages limit growth of bacterium; attack of immune cells against infected nerve cells produces nerve damage, leading to deformity; in lepromatous leprosy, lymphocytes fail to react to the bacteria, allowing unrestrained growth of *M. leprae.*
Epidemiology	Direct contact with *M. leprae* from mucous membrane secretions.
Prevention and treatment	No vaccine. Treatment: dapsone plus rifampin for months or years; clofazimine added for lepromatous disease.

Botulism

- Symptoms
  - Begins 12 to 36 hours post ingestion of contaminated foods
  - Begins with dizziness, dry mouth and blurred vision
  - Abdominal symptoms include pain, nausea, vomiting and diarrhea or constipation
  - Progressive paralysis ensues
    - Paralysis of respiratory muscles most common cause of death
    - Paralysis distinguishes botulism from other forms of food poisoning

Botulism

- Causative agent
  - *Clostridium botulinum*
  - Endospores generally resist boiling for hours
    - Killed by autoclaving
  - Produces toxin



Botulism - Pathogenesis

- Spores germinate in favorable environment
  - Bacterial growth results in toxin release
    - Toxin resists digestion and is absorbed by small intestine
    - Toxin can circulate in blood stream for 3 weeks or more
- Toxin is neurotoxin
  - Acts against nervous system
  - One of most powerful poisons known
  - Toxin attaches to motor nerves blocking function of neurotransmitter and causes paralysis

Botulism

- Epidemiology
  - Widely distributed in soils and aquatic sediments
  - In early 20th century food-borne outbreaks common
    - Strict controls on commercially canned foods decreases incidence
  - Intestinal botulism more common than food-borne
    - Intestinal occurs in small children to 6 months of age
      - Results in mild disease ranging from mild lethargy to respiratory insufficiency

Botulism

- Prevention and Treatment
  - Prevention depends on proper sterilization and sealing of canned food
  - Heating food to 100°C for 15 minutes just prior to eating generally makes food safe to eat
    - Can’t rely on smell, taste or appearance to detect contamination
  - Treated by intravenous administration of antitoxin ASAP
    - Antitoxin only neutralizes circulating toxin
    - Affected nerves recover slowly
  - Gastric washing and surgical removal of tissues removes unabsorbed toxin
  - Artificial respiration may be required for prolonged periods

TABLE 27.5 Botulism

Symptoms	Blurred or double vision, weakness, nausea, vomiting, diarrhea; generalized paralysis and respiratory insufficiency
Incubation period	Usually 12 to 36 hours
Causative agent	*Clostridium botulinum,* an anaerobic, Gram-positive, spore-forming, rod-shaped bacterium
Pathogenesis	*Clostridium botulinum* endospores germinate in food and release neurotoxin. Toxin is ingested, survives stomach acid and enzymes, is absorbed by the small intestine, and is carried by the bloodstream to motor nerves; toxin acts by blocking the transmission of nerve signals to the muscles, producing paralysis; *C. botulinum* can also colonize intestine or wounds, and cause generalized weakness or paralysis.
Epidemiology	Ingestion of contaminated, often home-canned, non-acid food that was not heated enough to kill *C. botulinum* spores. Spores widespread in soil, aquatic sediments, and dust. Can result in colonization of the intestine of adults and infants with deficiencies in normal microbiota, and wounds containing dirt and dead tissue, including those caused by injected-drug abuse.
Prevention and treatment	Education in proper home-canning methods; heating food to boiling for 15 minutes just prior to serving. Treatment: enemas and stomach washing to remove toxin, cleaning infected wounds of dirt and dead tissue, intravenous administration of antitoxin, and artificial respiration.

Viral Meningitis

- Symptoms
  - Typically abrupt in onset
  - Characterized by
    - Fever
    - Severe headache above or behind eyes
    - Stiff neck with increased pain on forward flexion
    - Sensitivity to light
    - Nausea and vomiting
    - May have sore throat, chest pain, swollen parotid gland and skin rash
      - Depends on causative agent

Viral Meningitis

- Pathogenesis
  - Begins with infection of throat and intestinal epithelium
    - Progresses to lymphoid tissue in the bloodstream
  - Viremia results in meningeal infection
    - May also be responsible for rash and chest pain
- Causative agent
  - Member of the enterovirus subgroup of picornavirus family
  - Responsible for at least half of viral meningitis cases
    - Most common offenders are Coxsackie virus and echovirus

Viral Meningitis

- Epidemiology
  - Relatively stable in environment
    - Can survive in chlorinated water
  - Infected often eliminate virus in feces
    - Often for weeks
  - Transmission via fecal-oral route
  - Mumps virus transmitted via respiratory droplets

Viral Meningitis

- Prevention and Treatment
  - Handwashing and avoidance of crowded swimming pools
    - When aseptic disease present in community
  - No vaccine against Coxsackie virus and echoviruses
    - Mumps virus controlled via immunization

TABLE 27.6 Viral Meningitis

Symptoms	Abrupt onset, fever, severe headache, stiff neck, often vomiting; sometimes sore throat, large parotid glands, rash, or chest pain
Incubation period	Usually 1 to 2 weeks for enteroviruses, 2 to 4 weeks for mumps
Causative agents	Most cases: small non-enveloped RNA enteroviruses of the picornavirus family, usually coxsackie or echoviruses. Mumps virus common in unimmunized populations
Pathogenesis	Viremia from primary infection seeds the meninges. Fewer leukocytes enter cerebrospinal fluid than with bacterial infections, and many are mononuclear, usually no decrease in CSF glucose.
Epidemiology	Enteroviruses transmitted by the fecal-oral route, mumps by respiratory secretions and saliva. Enteroviruses transmission mainly summer and early fall; mumps in fall and winter.
Prevention and treatment	Handwashing, avoiding crowded swimming pools during enterovirus epidemics; mumps vaccine for mumps prevention. No specific treatment.

Viral Encephalitis

- Symptoms
  - Onset usually abrupt
  - Characterized by
    - Fever
    - Headache
    - Vomiting
    - One or more nervous system abnormalities
      - Disorientation, localized paralysis, deafness, seizures or coma

Viral Encephalitis

- Causative agent
  - Arboviruses
    - Arthropod borne viruses
  - Transmitted by insects, mites and ticks
  - Viruses enveloped single-stranded RNA viruses

Viral Encephalitis

- Pathogenesis
  - Knowledge of pathogenesis incomplete
  - Viruses multiply at site of bite and in local lymph nodes
    - Produces viremia
  - Virus crosses blood-brain barrier
    - Mechanism unknown
  - Causes extensive damage to brain tissue in severe cases
  - Progression of disease halted with appearance of neutralizing antibody
  - Mortality ranges from 2% to 50% depending of type of infecting agent
  - Disabilities often present in those who recover

Viral Encephalitis

- Epidemiology
  - Only minority infected develop encephalitis
    - Other develop viral meningitis
  - Disease are all zoonoses
    - Maintained naturally in birds and rodents
      - Humans are accidental hosts

Viral Encephalitis

- Prevention and Treatment
  - Animals often used to identify emergence of disease
    - Equine encephalitis generally infects horses 1 – 2 weeks before first human case seen
  - Prevention directed towards
    - Avoiding outdoor activities at night when mosquito populations highest
    - Make sure windows and porches properly screened
    - Use insect repellents and insecticides
  - No proven antiviral therapy

TABLE 27.7 Epidemic Viral Encephalitis

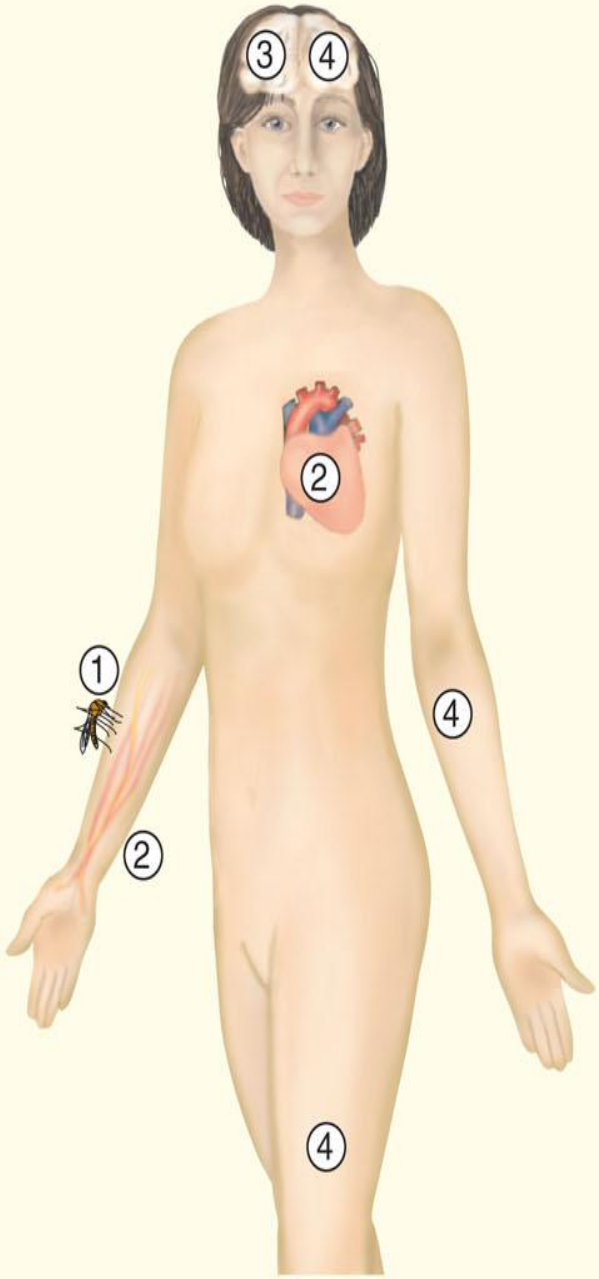
① Infected mosquito introduces encephalitis virus.

② Virus multiplies locally, establishes brief low-level viremia.

③ Virus crosses blood-brain barrier and preferentially attacks the brain.

④ Destruction of brain tissue causes death or permanent disabilities such as emotional instability, mental retardation, paralysis of face, arm, leg.

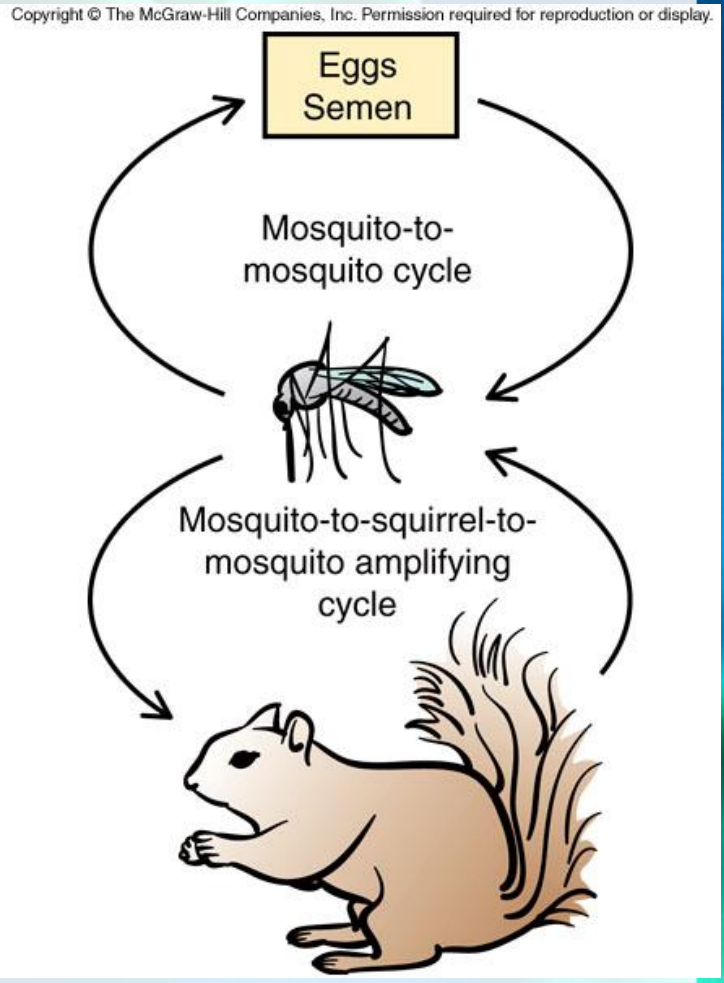
⑤ Due to brief viremia, there is no exit for the virus, thus humans are the final host.



Symptoms	Abrupt onset, fever, headache, vomiting, disorientation, paralysis, seizures, deafness, coma
Incubation period	First symptoms within a few days; encephalitic symptoms often within the first week
Causative agent	Usually caused by one of four arboviruses, LaCrosse, St. Louis, western equine, or eastern equine
Pathogenesis	Replication of virus at the site of the mosquito bite, further replication in lymph nodes, then viremia that seeds brain tissue. Nerve cells in the brain invaded, destroyed. Process halted by neutralizing antibody.
Epidemiology	Viruses transmitted to humans from birds or rodents by mosquitoes.
Prevention and treatment	Chicken sentinels to warn of arbovirus epidemics. Insecticides and other anti-mosquito preventive measures. No accepted treatment for arboviral encephalitis.

Infantile Paralysis, Polio

- Symptoms
  - Usually begins with symptoms of meningitis
  - Pain and spasm of muscles generally occur usually followed by paralysis
  - Paralyzed muscles shrink and bones do not form normally
  - In severe cases respiratory muscles become paralyzed
    - Artificial respiration is required
  - Some recovery if patient survives acute stage



Infantile Paralysis, Polio

- Causative agent – Poliovirus
- Pathogenesis
  - Enter body orally
    - Virus infects the throat and intestinal tract then moves to bloodstream
  - Immune system conquers infection in most people
    - Viruses enters nervous system of small percentage of people
      - Virus attacks motor nerves
  - Infected cells are destroyed upon cell release
  - Post-polio syndrome
    - Development of muscle weakness and pain many years after acute disease

Infantile Paralysis, Polio

- Pathogenesis
  - Enter body orally
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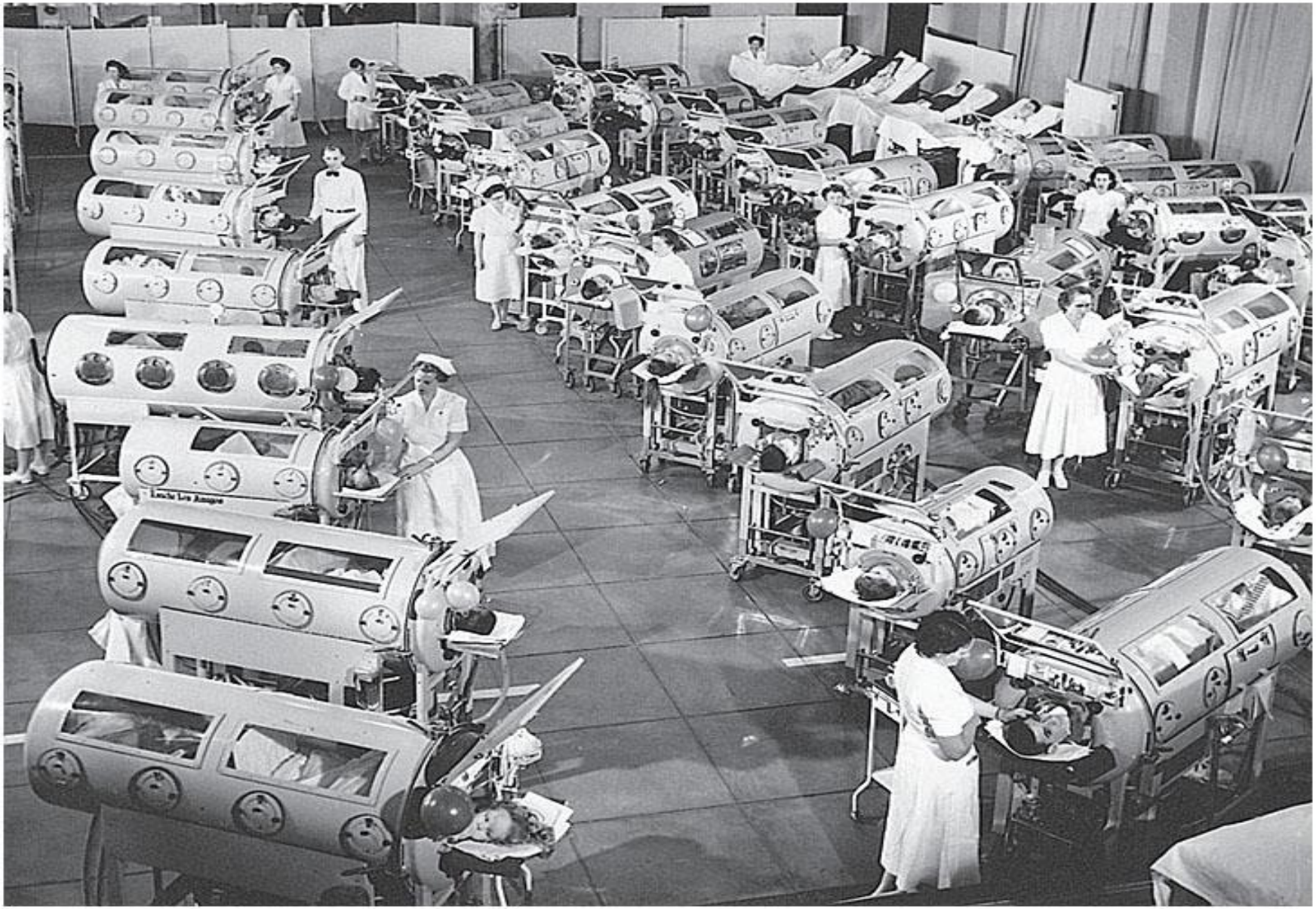

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Infantile Paralysis, Polio

- Epidemiology
  - Virus widespread in areas where sanitation is poor
    - Virus usually spread via fecal-oral route
  - In endemic areas people generally do not escape childhood without contracting disease

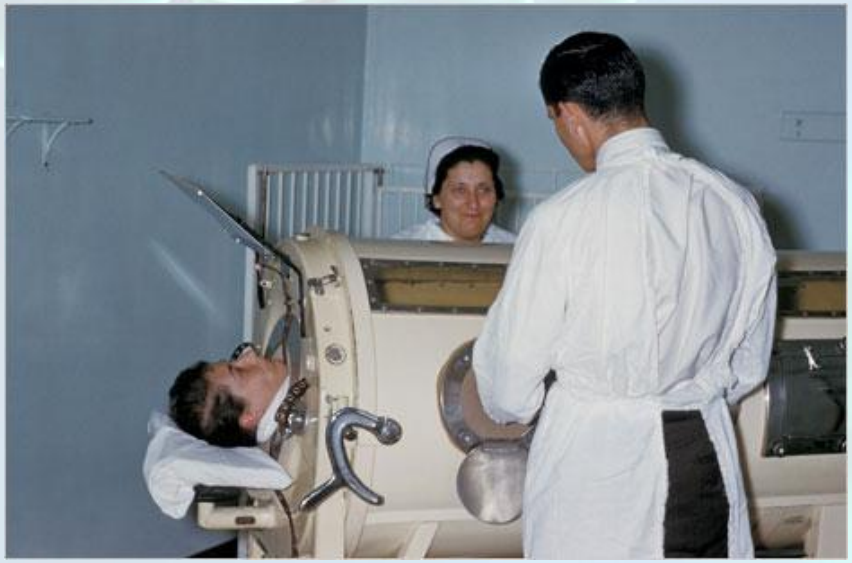
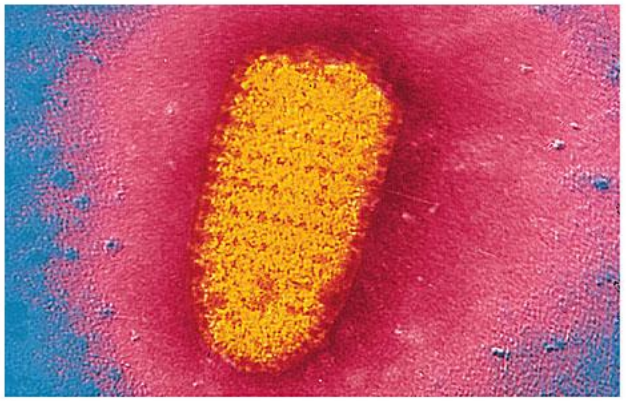


TABLE 27.8 Poliomyelitis

Symptoms	Headache, fever, stiff neck, nausea, pain, muscle spasm, followed by paralysis
Incubation period	7 to 14 days
Causative agents	Polioviruses 1, 2, 3, members of the picornavirus family
Pathogenesis	Virus infects the throat and intestine, circulates via the bloodstream, and enters some motor nerve cells of the brain or spinal cord; infected nerve cells lyse upon release of mature virus.
Epidemiology	Spreads by the fecal-oral route; asymptomatic and nonparalytic cases common.
Prevention and treatment	Prevented by injecting Salk's inactivated vaccine, or by Sabin's orally administered attenuated vaccine in areas of epidemic or endemic disease. Treatment: artificial ventilation for respiratory paralysis; physical therapy and rehabilitation.

Rabies

- Symptoms
  - Fever/Fatigue
  - Head and muscle ache
  - Sore throat
  - Nausea
  - Tingling/twitching at site of viral entry



(a)

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Rabies

- Early symptoms begin 1 to 2 months post infection
  - Progress rapidly to secondary symptoms of
    - Encephalitis, agitation, confusion, hallucinations, seizure, increased sensitivity to light and touch
  - Body temperature rises with increased salivation and difficulty swallowing
    - Results in frothing of mouth
  - Hydrophobia occurs in 50% of cases
  - Coma develops
  - About 50% of patients die within 4 days

Rabies

- Causative agent - Rabies virus
- Pathogenesis
  - Mode of transmission primarily via saliva of rabid animal
    - Usually due to bite or abrasion
    - Can be contacted via inhalation
  - Virus reaches brain via infected nerve
    - Virus multiplies extensively in brain

Rabies

- Epidemiology
  - Widespread in wild animals
    - 5,000 cases reported annually in United States
  - Skunks, raccoons and bats considered chief reservoir
    - Raccoons most infected
    - Almost all human cases due to contact with infected bats

Rabies

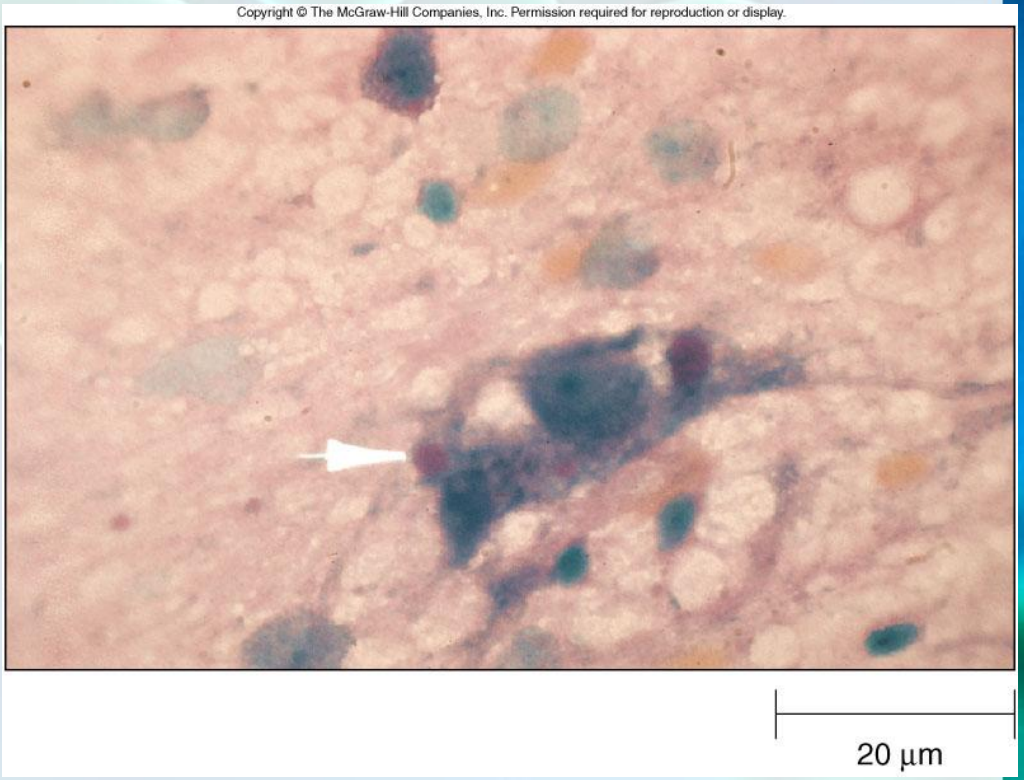
- Prevention and Treatment
  - Wash wound immediately and thoroughly
    - Use soap and water and apply antiseptic
  - Risk of developing rabies from bite of rabid dog is approximately 30%
    - Risk can be lowered considerably if vaccine is administered as soon as possible after exposure
      - Presumably vaccine provokes better immune response
  - Bitten individual should receive series of 5 injections at wound site and intramuscularly
    - Shots should be given even if biting animal presumed to be rabid
  - No effective treatment for rabies
    - Only six known survivors of disease

Cryptococcal Meningioencephalitis

- Symptoms
  - Develop gradually in healthy individuals
  - Generally consist of
    - Difficulty thinking
    - Dizziness
    - Intermittent headache
    - Slight or no fever
  - Slow progression of disease results in other symptoms
    - Vomiting
    - Weight loss
    - Paralysis
    - Seizures
    - Coma

Cryptococcal Meningioencephalitis

- Causative agent
  - Yeast form of *Filobasidiella neoformans* fungus



Cryptococcal Meningioencephalitis

- Pathogenesis
  - Fungus becomes airborne in dust
    - Enters body via inhalation and establishes infection first in lung
      - Infection often eliminated by body defenses
  - Organism multiplies and enters bloodstream
  - Capsule inhibits phagocytosis and neutralizes opsonins
  - Organisms typically cause thickening of meninges
    - This can often impede the flow of CSF
    - Also invade brain tissue producing abscesses

Cryptococcal Meningioencephalitis

- Epidemiology
  - Distributed worldwide in soil and vegetation
    - Numerous in soil where pigeon droppings accumulate
  - For every one case of disease millions are infected with organism
  - Symptomatic infection often the first indicator of AIDS
  - Person-to-person spread does not occur

Cryptococcal Meningioencephalitis

- Prevention and Treatment
  - No vaccine or other preventative measures
  - Treatment with amphotericin B is effective
    - Often given concurrently with flucytosine or itraconazole
    - Amphotericin B does not reliably cross blood-brain barrier
      - Drug administered through tube inserted through the skull into lateral ventricle

TABLE 27.10 Cryptococcal Meningoencephalitis

Symptoms	Headache, vomiting, confusion, and weight loss; slight or no fever; symptoms may progress to seizures, paralysis, coma, and death
Incubation period	Widely variable, few to many weeks
Causative agent	*Cryptococcus neoformans,* an encapsulated yeast
Pathogenesis	Infection starts in lung; encapsulated organisms multiply, enter bloodstream, and are carried to various parts of the body; phagocytosis inhibited and opsonins neutralized; meninges and adjacent brain tissue become infected.
Epidemiology	Inhalation of dust containing dried pigeon droppings contaminated with the fungus; other sources; most people resistant to the disease.
Prevention and treatment	No preventive measures. Treatment; amphotericin B with flucytosine or itraconazole.