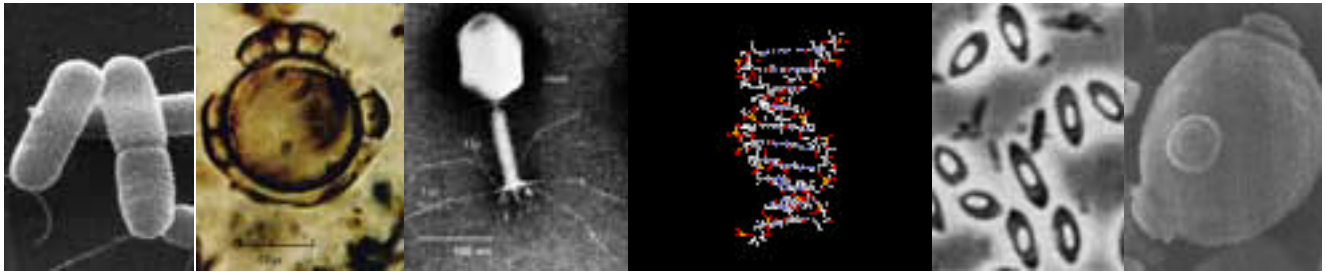


# General Microbiology

## Cañada College – Spring 2003

**Instructor: Tamas Torok, Ph.D.**

**http://www-esd.lbl.gov/ESD_staff/torok/torok_lectures.html**

# Topics of the day

- Structure and function of the nervous system
- Bacterial diseases of the nervous system
- Fungal and protozoan diseases of the nervous system
- Diseases caused by prions

# Structure and function of the nervous system

- Central nervous system (CNS)
  - the main information-processing organs of the nervous system, consisting of the brain, spinal cord, and meninges
    - meninges
      - dura mater
      - arachnoid
      - pia mater
      - subarachnoid space with 100–160 ml cerebrospinal fluid (CSF)
        - «low levels of complement, circulating Abs, few phagocytes
  - blood-brain barrier
    - inflammation alters permeability
  - meningitis/encephalitis
- Peripheral nervous system (PNS)
  - the nervous system outside of the brain and spinal cord

# Bacterial diseases of the nervous system

- Bacterial meningitis
  - serious infection of the fluid in the spinal cord and the fluid that surrounds the brain
  - most cases caused by
    - Haemophilus influenzae type b
    - Neisseria meningitidis
    - Streptococcus pneumoniae
  - can be treated with antibiotics
  - ~50 bacterial species were reported as opportunistic pathogens

# Listeriosis

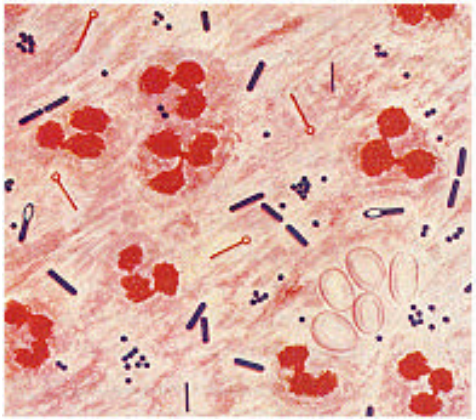
- Stillbirth and neurological disease caused by Listeria monocytogenes
  - widely spread environmental microbe
  - infects mostly immuno-suppressed, pregnant adults or cancer patients
  - grows in CNS and placenta
  - human outbreaks are food related that is stored at refrigeration temperature

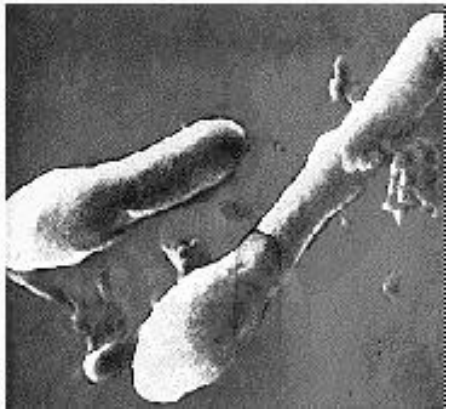
# Pathogenic clostridia

- Clostridia are relatively large, Gram-positive, rod-shaped bacteria
- All species form endospores and have a strictly fermentative mode of metabolism
- Most clostridia will not grow under aerobic conditions and vegetative cells are killed by exposure to $O_2$
- Spores are able to survive long periods of exposure to air
- Clostridia live in virtually all of the anaerobic habitats of nature where organic compounds are present, including soils, aquatic sediments and the intestinal tracts of animals
- Clostridia play an important role in nature in biodegradation and the carbon cycle
- In anaerobic clostridial infections extracellular enzymes play a role in invasion and pathology

# Pathogenic clostridia (cont.)

- Only a few environmental clostridia are pathogenic to humans
- Clostridium tetani and C. botulinum produce the most potent biological toxins known to affect humans
- They owe their virulence almost entirely to their toxigenicity
- Other clostridia are highly invasive under certain circumstances





# Clostridium tetani – the causative agent of tetanus

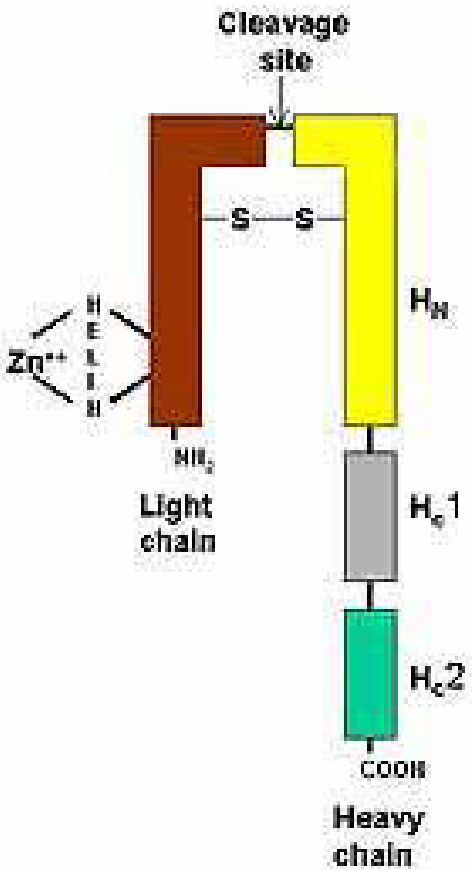
- Found in soil, especially heavily-manured soils, and in the intestinal tracts and feces of various animals, carrier rates in humans vary from 0 to 25%
- Mortality rates reported vary from 40% to 78%
- Neurotoxin (tetanus toxin or tetanospasmin) produced when spores germinate and vegetative cells grow
- Painful spasms and rigidity of the voluntary muscles, death results from interference with the mechanics of respiration
- Neonatal tetanus accounts for about half of the tetanus deaths in developing countries
- 11 strains of C. tetani distinguished primarily on the basis of flagellar antigens and their ability to produce tetanus toxin encoded on a plasmid
- Tetanospasmin initially binds to peripheral nerve terminals, is transported within the axon and across synaptic junctions until it reaches the central nervous system, becomes rapidly fixed to gangliosides at the presynaptic inhibitory motor nerve endings, and is taken up into the axon by endocytosis
- Toxin blocks the release of inhibitory neurotransmitters
- Even a lethal dose of tetanospasmin is insufficient to provoke an immune response

# C. botulinum

- Widely distributed in soil, sediments of lakes and ponds, and decaying vegetation
- Seven immunologically distinct botulinum toxins (A, B, C1 , D, E, F, and G)
- Lysogenic phages encode toxin serotypes C and D, type G toxin is thought to be plasmid encoded
- In food-borne botulism, toxin is ingested with food in which spores have germinated and the organism has grown
- Clinical symptoms of botulism begin 18-36 hours after toxin ingestion, neurologic features soon develop: blurred vision, inability to swallow, difficulty in speech, descending weakness of skeletal muscles and respiratory paralysis
- Infant botulism is an infection in infants 5 – 20 weeks of age that have been exposed to solid foods, presumably the source of infection (spores)

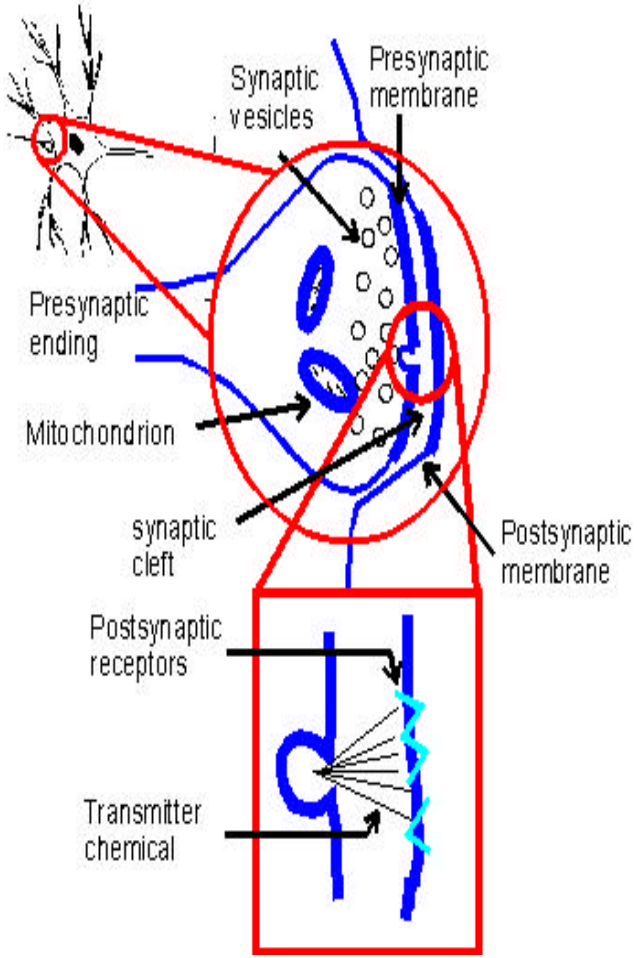
# Botulinum toxin

- Binds to the neuron and prevents the release of acetylcholine across the synaptic cleft
- Zinc-dependent endopeptidase that cleaves a set of proteins, synaptobrevins found in synaptic vesicle of neurons, the vesicles responsible for release of neurotransmitters



# Synapses

- Specialized junctions at which a neuron communicates with a target cell
- Impulses are transmitted from neuron to neuron by the release of a transmitter chemical across synaptic clefts
- Transmitter chemical is stored in synaptic vesicles of the presynaptic ending



# Leprosy – Hansen's disease

- Chronic granulomatous infection caused by Mycobacterium leprae
- Granulomatous lesions are manifested in the skin, the mucous membranes, and the peripheral nerves
- Tuberculoid leprosy
  - few lesions, peripheral nerves involved, rare source of infection
- Progressive form
  - chronic communicable infection

# Viral diseases of the nervous system

- **Poliomyelitis**
  - acute infectious disease of humans, particularly children, caused by any of three serotypes of human poliovirus
  - central nervous system, primarily the spinal cord, may be affected, leading to rapidly progressive paralysis
  - encephalitis may occur
  - virus replicates in the nervous system, and may cause significant neuronal loss, most notably in the spinal cord
  - vaccination

# Viral diseases of the nervous system (cont.)

- Rabies
  - acute infectious disease of the central nervous system affecting almost all mammals, including humans caused by a rhabdovirus and usually spread by contamination with virus-laden saliva of bites inflicted by rabid animals
  - almost always results in fatal encephalitis
  - long incubation period – immunity can develop from post-exposure vaccination

# Fungal diseases of the nervous system

- Cryptococcosis
  - meningeal inflammation caused by Cryptococcus neoformans
  - majority of people with cryptococcal meningitis have immune systems that are damaged by disease
  - yeast-like fungus with an unusually thick capsule
  - treatment : amphotericin B in combination with flucytosine
  - mortality ~30%

# Diseases caused by prions

- Transmissible agent is not a virus
  - no nucleic acid identified
  - chemical and physical procedures ineffective
- Prion (proteinaceous infectious particle) diseases are caused by mutations in the PRNP gene
  - $PrP^{Sc}$ (the abnormal one) induces $PrP^{C}$ (the normal counterpart) to change into $PrP^{Sc}$
  - it acts as the transmissible agent causing further conversion of $PrP^{C}$ to $PrP^{Sc}$

# Diseases caused by prions (cont.)

- Prion-caused diseases of animals
  - scrapie in sheep and goats
  - transmissible mink encephalopathy
  - chronic wasting disease of mule deer and elk
  - feline spongiform encephalopathy
  - bovine spongiform encephalopathy ("BSE")

# Prion-caused diseases of humans

- Kuru
  - found only among the Fore tribe in Papua New Guinea
  - eliminated since the cessation of the ritual handling and eating of the brains of deceased relatives
- Predominantly hereditary disorders
  - Gerstmann-Straussler-Scheinker disease
  - fatal familial insomnia
- Alpers syndrome (prion diseases in infants)
- Creutzfeldt-Jakob Disease ("CJD")
  - rare, fatal brain disorder
  - results from sporadic occurrence, can be hereditary, or through infection
  - microscopic vacuoles in neurons that appear "sponge-like"
  - affects both men and women of diverse ethnic backgrounds usually between the ages of 50 to 75 years
  - occurs worldwide (one case per million people each year)

# Prion-caused diseases of humans (cont.)

- Since 1996, causal relationship between BSE outbreaks in Europe and new variant Creutzfeldt-Jakob disease (nvCJD)
- Both disorders are
  - invariably fatal brain diseases
  - with unusually long incubation periods measured in years
  - caused by an unconventional transmissible agent
- nvCJD predominantly affects younger people
- BSE resulted from feeding scrapie-containing sheep meat-and-bone meal to cattle
- BSE has not been detected in the United States
- As of April 2, 2002, a total of 125 cases of vCJD had been reported in the world: 117 from the United Kingdom, six from France, and one each from Ireland and Italy