Medical Bacteriology- Lecture 10

Clostridia

Clostridium

- large, Gram-positive- rodshaped - All species form **endospores**
- strictly fermentative type of metabolism (**Most clostridia will not grow under aerobic conditions and vegetative cells are killed by exposure to O_2, but their spores are able to survive long periods of exposure to air**)
- live in all of the **anaerobic habitats** of nature, including soils, aquatic sediments and the intestinal tracts of animals.
- Clostridia are able to ferment a wide variety of organic compounds. They produce end products such as butyric acid, acetic acid, butanol & acetone, and large amounts of gas (CO_2 and H_2) during fermentation of sugars.
- A variety of foul smelling compounds are formed during the fermentation of amino acids and fatty acids.
- The clostridia produce a wide variety of extracellular enzymes to degrade large biological molecules (e.g. proteins, lipids, collagen, cellulose, etc.) in the environment. Hence, the clostridia play an important role in nature in biodegradation and carbon cycle. In anaerobic clostridial infections, these enzymes play a role in invasion and pathology.
- Most of the clostridia are saprophytes
- a few are pathogenic for humans; *Clostridium perfringens, C. difficile & C. tetani (*saprophytic in nature and, in a sense, are opportunistic pathogens.
- *Clostridium tetani* (tetanus) & *Clostridium botulinum* (food-borne botulism) produce the most potent biological toxins known to affect humans.
- Other clostridia, however, are highly invasive under certain circumstances.

Clostridium perfringens

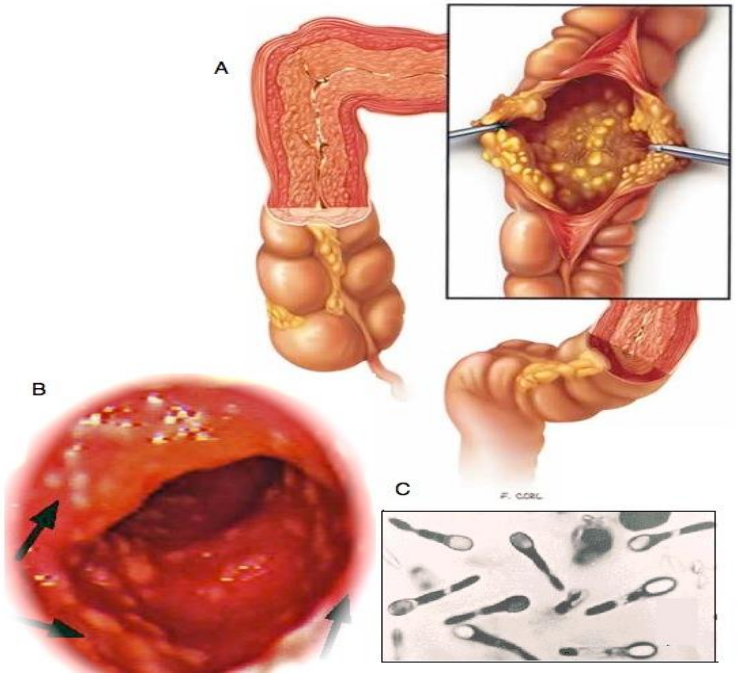
- ***C. perfringens*** produces a huge array of invasins & exotoxins
- causes **wound** and **surgical infections** that lead to **gas gangrene**, in addition to severe **uterine** infections. Clostridial hemolysins and extracellular enzymes such as proteases, lipases, collagenase & hyaluronidase, contribute to the invasive process.
- *C. perfringens* also produces an enterotoxin as an important cause of **food poisoning** (Usually in improperly sterilized (canned) foods in which endospores have germinated).

- **Food poisoning:** *C. perfringens* is classified into 5 types on the basis of its ability to produce one or more of the major lethal toxins. Enterotoxin (CPE)- type A is the most common food poisoning agents worldwide.

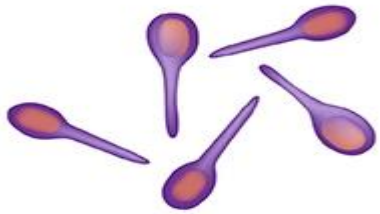
- **Gas gangrene:** occurs at the site of a recent surgical wound. Patients who develop this disease often have underlying blood vessel disease, diabetes.
- *C. perfringens* produces many different toxins, 4 of which (alpha, beta, epsilon, iota) can cause potentially deadly syndromes. The toxins cause damage to tissues, blood cells, and blood vessels.
- Gas gangrene is marked by a high fever, brownish pus, gas bubbles under the skin, skin discoloration, and a foul odor.

Clostridium difficile

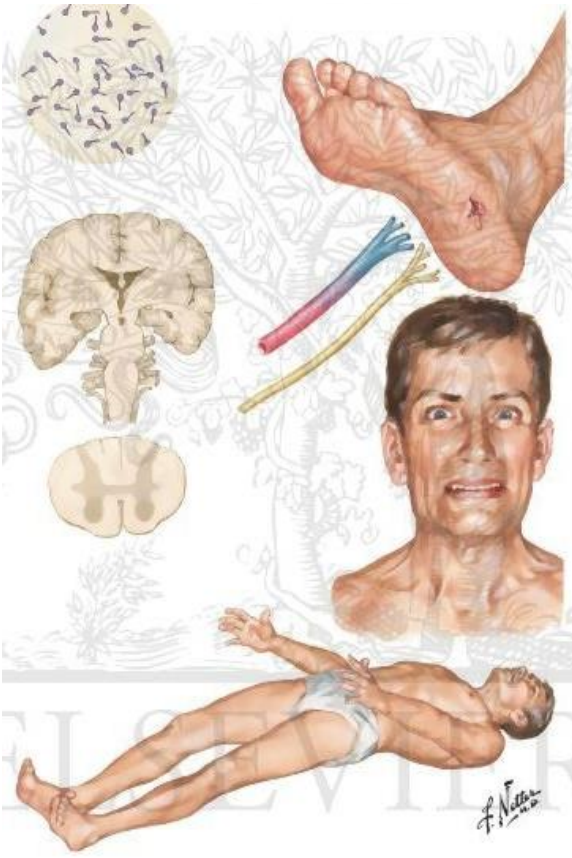
- *C. difficile* causes **antibiotic-associated diarrhea (AAD)** and more serious intestinal conditions such as **pseudomembranous colitis** in humans.
- These conditions generally result from overgrowth of *Clostridium difficile* in the colon, usually after the normal intestinal microbiota flora has been removed by antimicrobial chemotherapy.
- Healthy persons usually do not get *C. difficile* disease. Individuals who have other conditions that require prolonged use of antibiotics, immunocompromised. gastrointestinal surgery.
- *C. difficile* produces two toxins: **Toxin A** is referred to as an enterotoxin because it causes fluid accumulation in the bowel. **Toxin B** is an extremely lethal (cytopathic) toxin.
- *C. difficile* infections can usually be treated successfully with a 10-day course of antibiotics including vancomycin (administered orally).



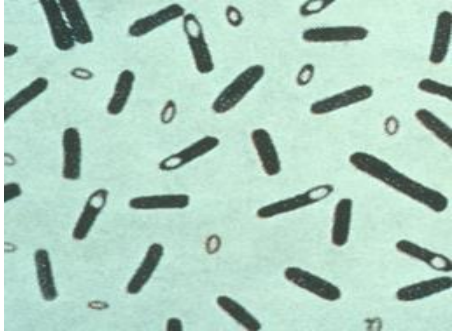
Clostridium tetani



- *C. tetani* is the causative agent of **tetanus**.
- Tetanus is a highly fatal disease of humans.
- The organism is found in soil, the intestinal tracts & feces of animals.
- The organism produces **terminal spores (distinctive drumstick).**
- Most cases of tetanus result from small puncture wounds which become contaminated with *C. tetani* spores that germinate and produce toxin.
- The disease not from invasive infection but from a potent **neurotoxin** (**tetanus toxin** or **tetanospasmin**) produced when spores germinate and vegetative cells grow after gaining access to wounds.
- The infection remains localized. The organism multiplies locally and symptoms appear remote from the infection site.
- The toxin is produced during cell growth. **It migrates along neural paths from a local wound to sites of action in the central nervous system.** The clinical pattern of tetanus consists of **severe painful spasms and rigidity of the voluntary muscles**. The characteristic symptom of **"lockjaw"** involves **spasms of the masseter muscle**. **Spasms of the pharyngeal muscles cause difficulty in swallowing. Death usually results from interference with the mechanics of respiration.**
- Most cases occur over age 60 (waning immunity is a significant risk factor).
- the widespread use of the **tetanus toxoid** for prophylactic immunization.



Clostridium botulinum



- *C. botulinum* is a large anaerobic bacillus that forms **subterminal endospores.**
- It is widely distributed in soil, sediments of lakes.
- the intestinal tracts of birds, mammals and fish may occasionally contain the organism.
- 7 toxigenic types of botulinum toxin. type A is the most significant cause of botulism.
- Not all strains of *C. botulinum* produce the botulinum toxin.
- **Food-borne Botulism: the botulinum toxin is ingested with food in which spores have germinated and the organism has grown.**

  The toxin is absorbed by the upper part of the gastrointestinal tract (GI) tract and passes into blood stream by which it reaches the neuromuscular synapses.

  The toxin binds to the presynaptic stimulatory terminals and **blocks the release of the neurotransmitter acetylcholine which is required for a nerve to simulate the muscle.**

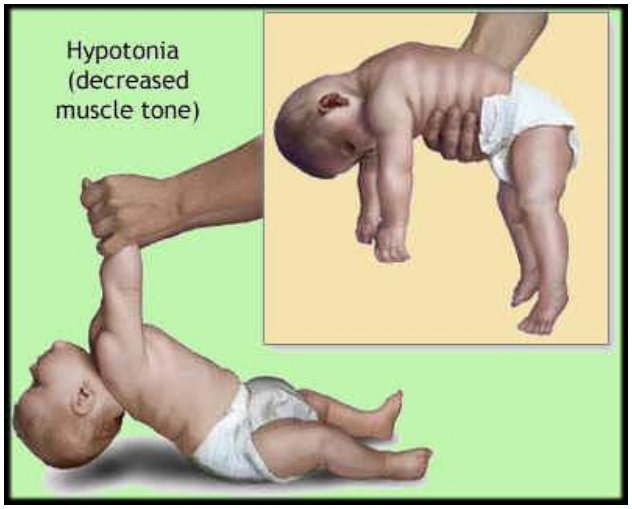
  intoxication infection (results from the ingestion of foods that contain clostridial toxin).

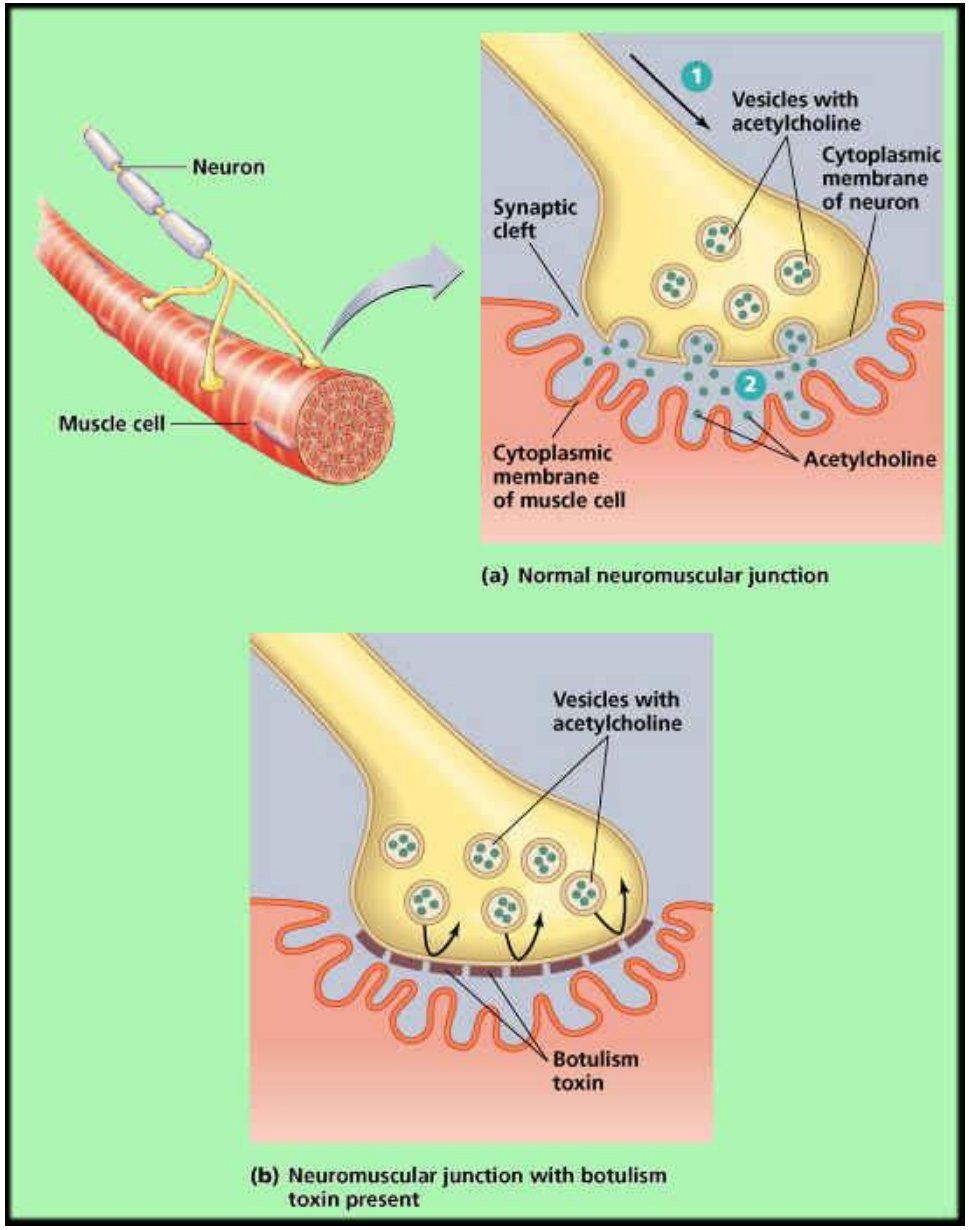
  it resembles staphylococcal or *B. cereus* food poisoning.

  C. botulinum spores are heat resistant & may survive the improper canning procedures.
- Clinical symptoms of botulism muscular paralysis begin 18-36h after toxin ingestion with **weakness, dizziness & dryness of the mouth. Nausea & vomiting may occur. Neurologic features including blurred vision, inability to swallow, difficulty in speech, weakness of skeletal muscles and respiratory paralysis.**

Infant Botulism

- occurs in infants 5 - 20 weeks of age.
- **It is characterized by paralysis, constipation and weak sucking ability and generalized weakness. Flat facial expression, A weak, feeble cry, Muscle weakness and decreased movement. Poor head control, Breathing problems and respiratory failure.**
- **Infant botulism is caused by consuming the spores of the botulinum bacteria, which germinateand then grow in the intestines and release botulinum toxin within the infant's large intestine.**
- *C. botulinum* can apparently establish itself in the bowel of infants at a critical age before the establishment of competing intestinal flora. Production of toxin by bacteria in the GI tract induces symptoms. This "infection-intoxication" is restricted to infants. *C. botulinum* organisms, as well as toxin, can be found in the feces of infected infants. Almost all known cases of the disease have recovered. The possible role of infant botulism in "sudden infant death syndrome-SIDS" has been suggested but remains unproven.




Neuron
Muscle cell
1
Vesicles with acetylcholine
Cytoplasmic membrane of neuron
Synaptic cleft
2
Cytoplasmic membrane of muscle cell
Acetylcholine
(a) Normal neuromuscular junction
Vesicles with acetylcholine
Botulism toxin
(b) Neuromuscular junction with botulism toxin present

Review Questions

- Write the Latin name of the bacteria that cause:
- A. Botulism B. Tetanus C. Gas gangrene D. Antibiotic associated diarrhea (pseudomembranous colitis)
- Compare between adult botulism and Infant botulism?
- Some *Clostridium* species can cause food poisoning. Give two species?
- What is the mode of action of botulism toxins and tetanus toxins?
- What is the symptoms of gas gangrene, tetanus?