

## ***Lec12- B- Strict anaerobic – Genus Clostridium .***

Clostridia are large gram-positive rods, the obligate anaerobic, blunt-ended rods. They **form endospores**; the position of the developing spore within the vegetative cell is useful in identifying the species. Most species are motile. These organisms also synthesize some of the most potent exotoxins. Clinically significant species of *Clostridium* include *C. perfringens*, which causes (gas gangrene) and food poisoning; *C. difficile*, which causes pseudomembranous colitis associated with antibiotic use; *C. tetani*, which causes tetanus and *C. botulinum*, which causes botulism.

### ***A. Clostridium perfringens***

It is ubiquitous in nature, with its vegetative form as part of the normal flora of the vagina and gastrointestinal (GI) tract. Its spores are found in soil. *C. perfringens* can cause anaerobic cellulitis, and myonecrosis (gas gangrene). Some strains cause a common form of food poisoning.

### **Pathogenesis:**

*C. perfringens* secretes a variety of exotoxins, enterotoxins, and hydrolytic enzymes that facilitate the disease process.

**1. Exotoxins:** *C. perfringens* elaborates at least 12 exotoxins. The most important of these required for virulence in tissue, is alpha toxin. Alpha toxin is a lecithinase that degrades lecithin in mammalian cell membranes, causing lysis of endothelial cells, as well as RBC, WBC and platelets.

**2. Enterotoxin:** a small protein, acts in the lower portion of the small intestine, and causes loss of fluid and intracellular proteins.

**3. Degradative enzymes:** it produces hydrolytic enzymes, including proteases, DNases, hyaluronidase, and collagenases, which liquefy tissue and promote the spread of infection.

## Clinical significance

The disease processes initiated by *C. perfringens* result from a combination of infection with the production of exotoxins and/or enterotoxins and degradative enzymes.

**1. Myonecrosis (gas gangrene):** Clostridial spores are introduced into tissue, for example, by contamination with infected soil, or by endogenous transfer from the intestinal tract. Severe and open wounds are a prime predisposing condition. Alpha toxin and other exotoxins are secreted and extensive cell killing ensues. Production of enzymes that break down ground substance facilitates the spread of infection. Fermentation of tissue carbohydrates yields gas, and an accumulation of gas bubbles in the subcutaneous spaces produces a crinkling sensation on palpation; hence, the name gas gangrene.

The exudates are copious and foul smelling. As the disease progresses, increased capillary permeability leads to the exotoxins being carried by the circulation from damaged tissue to other organs, resulting in systemic effects such as shock, renal failure, and intravascular hemolysis. Untreated clostridial myonecrosis is uniformly fatal within days of the initiation of gangrene.

**2. Anaerobic cellulitis:** This is a clostridial infection of connective tissue (Necrotizing processes).

**3. Food poisoning:** *C. perfringens* is a common cause of food poisoning. The symptoms; nausea, abdominal cramps, diarrhea occurs 8 to 18 hr. after eating contaminated food.



**Laboratory identification:**

When cultured its anaerobically on blood agar, *C. perfringens* grows rapidly, producing colonies with double zone of hemolysis, large gram-positive rods with endospores.

**Treatment and prevention:**

The key to both prevention and treatment of gas gangrene is immediate and thorough removal of foreign material and dead tissue, and exposure of the wound to O<sub>2</sub>. Hyperbaric oxygen chambers increase the tissue O<sub>2</sub> tension in the affected part and probably inhibit the pathologic process. This bacterium is sensitive to penicillin.

***B. Clostridium botulinum***

*C. botulinum* causes botulism, which occurs in several clinical forms. Botulism is caused by the action of a neurotoxin that is one of the most potent poisons known. It causes a flaccid paralysis.

**Pathogenesis:**

There are several types of botulinum toxin, designated A through G, but human disease is almost always caused by types A, B, or E. The botulinum serotypes and tetanus toxin constitute a homologous set of proteins whose neurotoxicity arises from proteolytic cleavage of specific synaptic vesicle peptides, causing subsequent failure of neurotransmission. In contrast to tetanus toxin, which causes constant contraction, botulinum toxins affect peripheral cholinergic synapses by blocking the neuromuscular junction and inhibiting release of the neurotransmitter, acetylcholine, preventing contraction and causing flaccid paralysis.

**Clinical significance:**

- 1. Infant botulism:** or a cause of floppy baby syndrome. *C. botulinum* colonizes the large bowel of infants 3 to 24 weeks of age; the toxin produced is slowly absorbed. Constipation, feeding problems, lethargy, and poor muscle tone are common early signs. The condition is possibly a cause of sudden infant death syndrome, but recovery is the usual outcome, following symptomatic treatment that may be prolonged.
- 2. Wound botulism:** A rare form of botulism occurs when a wound becomes contaminated with the organism, and toxin is absorbed from that site.

**Laboratory identification:**

The organism can be cultured and identified by standard anaerobic.

**Treatment and prevention:** Antitoxin, which neutralizes unbound botulinum toxin,

***C. Clostridium tetani***

The introduction of tetani spores into even small wounds via contaminated soil is probably a common occurrence. But a combination of the extreme O<sub>2</sub> sensitivity of vegetative *C. tetani* and widespread immunization against its exotoxin, make the resulting disease, tetanus, rare in developed countries. Growth of *C. tetani* is completely local, but it produces a powerful neurotoxin that is transported to the central nervous system, where it causes spastic paralysis.

**Pathogenesis:**

Tetanus toxin, called tetanospasmin, is an extremely potent toxin. It is transported from an infected locus by retrograde neuronal flow or blood. The heavy fragment (B) mediates binding to neurons and cell penetration of the light fragment (A). The A fragment blocks neurotransmitter release

at inhibitory synapses, and thus causes severe, prolonged muscle spasms. The A fragment has been shown to be a protease; it cleaves a small synaptic vesicle protein (synaptobrevin) and abolishes the flow of inhibitory neurotransmitters.

### **Clinical significance:**

Tetanus has an incubation period varying from four days to several weeks. A shorter period is usually associated with more severe disease and wounds closer to the brain. Tetanus presents as a spastic paralysis, in which muscle spasms often first involve the site of infection. In the early stages of the disease, the jaw muscles are affected, so that the mouth cannot open (trismus). Gradually, other voluntary muscles become involved, and any external stimulus (for example, noise or bright light) precipitates a painful spasm, and sometimes convulsions. Death, which occurs in fifteen to sixty percent of cases, is usually the result of paralysis of chest muscles leading to respiratory failure.



**Laboratory identification:** is rod with terminal spore (drum stick), and characteristic swarming growth on anaerobic blood agar.

**Treatment:** Treatment with human hyperimmune globulin (tetanus immune globulin). The organism is sensitive to penicillin.

**Prevention:** Active immunization with tetanus toxoid prevents tetanus. It is usually administered to children as a triple vaccine with diphtheria toxoid and pertussis antigens (DPT).