



## Spore forming Gram positive rods

### Clostridia

Clostridia are large gram-positive rods, the obligate anaerobic, motile rods. Clinically significant species of *Clostridium* include *C. perfringens* (non motile , 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.

### *Clostridium tetani*

#### General properties

- 1- Formation of **terminal spore** gives drumstick appearance (tennis racket).
- 2- Habitats spores in soil, gastrointestinal tracts of animals (sheep, cattle, dogs' chickens, horses, rates, guinea pigs) in the feces of the animals. Endospores prevalent in manure treated soils.
- 3-Heat resistant (can survive autoclaving at 121 for 10 – 15 min), antiseptic resistant.
- 4-Transmission spore is widespread in soil. the portal of entry is usually a wound site (e.g. where nail penetrates the foot). Neonatal tetanus in which the organism enters trough a contaminated umbilicus or circumcision wound.



## Tetanus Pathogenesis :-

C. tetani usually enters the body through a wound



In the presence of anaerobic conditions , the spores germinate.



Germinate under anaerobic conditions and being vegetative cell multiply and produce Tetanospasmin also referred to as tetanus toxin.



Toxins are produced and disseminated via blood and lymphatics.



Toxin binds in central nervous system , Interferes with neurotransmitter.

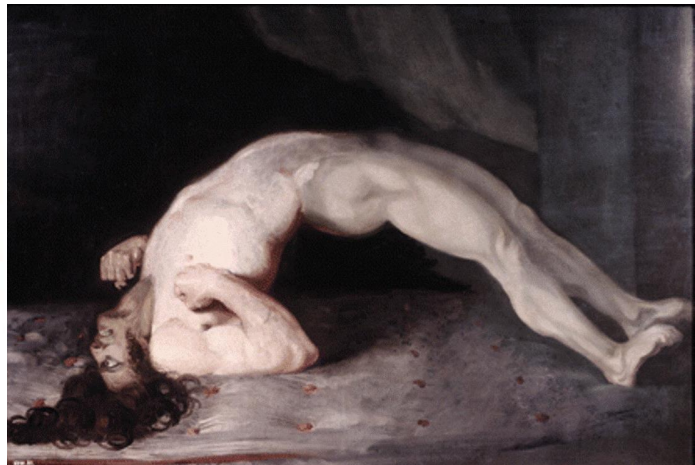


Leads to muscle contraction and spasm.



## Clinical significance:

- The incubation period may range from 5 days up to 3 weeks.
- The disease is characterized by **strong muscle spasms** (**spastic paralysis**).
- Specific clinical features include **lockjaw** (trismus) due to rigid contraction of the jaw muscles, which prevents the mouth from opening a characteristic grimace known risus sardonicus.
- **Opisthotonos** spasm of the muscles causing backward arching of the head, neck, and spine, as in severe tetanus.
- Other symptoms include fever, headache, feeding difficulties, breathing problems.
- The neonate is unable to suck and cry, is rigid, and develops spasms.
- A high mortality rate is associated with this disease.





## Prevention and treatment:-

- ✓ Tetanus can be prevented by vaccination with tetanus toxoid. The CDC recommends that adults receive a **booster vaccine** every ten years.
- ✓ In children under the age of seven, the tetanus vaccine is often administered as a combined vaccine, DPT/DTaP vaccine, which also includes vaccines against diphtheria and pertussis.
- ✓ For adults and children over seven, the Td vaccine (tetanus and diphtheria) or Tdap (tetanus, diphtheria, and pertussis) is commonly used.
- ✓ Antibiotic therapy to reduce toxin production. The antibiotic of choice is **metronidazole**. It can be given as intravenous, by mouth, or by rectum.
- ✓ Benzodiazepines can be used to control muscle spasms.

## *Clostridium botulinum*

### General properties

1- *C. botulinum* causes **botulism**, which occurs in several clinical forms. Botulism is caused by the action of a neurotoxin. It causes a **flaccid paralysis**.

2- Found in soil, sediments of lakes, ponds, coastal waters and occasionally in animals feces.

3- Intestinal tracts of birds, mammals and fish. Gills, viscera of crabs and shellfish.



- 4- Spore of the organism are highly resistant to heat , resistance is diminished at acid ph. or high salt concentration.
- 5- Neutral or low acid environments.
- 6- Usually seen in canned alkaline foods.
- 7- Seven toxigenic subtypes of the organism A, B, C, D, E, F and G.
- 8- Botox is commercial preparation of exotoxin A used to remove wrinkles on the face. Biological warfare (world war II).

### Clinical significance:

#### Three special clinical form occur:-

**1- Food – borne :** ingestion from foods that spores have germinated and grown in , considered an intoxication, most **common form.** food with out cooking , spore of *C. botulinum* germinate that under anaerobic condition ,vegetative forms grow and produce toxin.

**2- Infant botulism: or a cause of floppy baby syndrome.** *C. botulinum* colonizes the large bowel of infants 3 to 24 weeks of age. Ingestion of honey containing the organism is implicated in transmission of infant botulism. The vegetative cells produce toxin. Affecting infants develops weakness or paralysis and a cause of sudden infant death syndrome. most **common form.**



**3- Wound botulism:** a **rare form** of botulism occurs when a wound becomes contaminated with the organism , and produce toxin at the site.

**Symptoms :-**

Symptom begin 18-24 hr. after ingestion of toxic food.

- weakness ,dizziness , dryness of the mouth , nausea and vomiting.
- blurred vision ( diplopia = double vision ).
- inability to swallow (dysphagia).
- difficulty in speech.
- descending weakness of skeletal muscles and respiratory muscles ( failure ) , flaccid paralysis (permanent damage) leading the death.





## Diagnosis:-

The organism is usually not cultured. Toxin demonstrated in serum or leftover food. *C. botulinum* may be grown from food remains and tested for toxin production. Toxin may be demonstrated by ELISA.

## Note:-

That in tetanus , **spastic paralysis** ( strong muscle contraction ) occurs , whereas in botulism , **flaccid paralysis** ( weak or absent muscle contraction ) occurs .

### *Clostridium perfringens*

- ✓ Gram positive, rod shaped, **non-motile**, anaerobic.
- ✓ Can cause gas gangrene also known as myonecrosis.
- ✓ Is one of the most common causes of food poisoning.
- ✓ *C. perfringens* secretes a variety of **exotoxins, enterotoxins**.
- ✓ **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.
- ✓ **Enterotoxin** responsible from food poisoning, when these bacteria contaminate food and allowed to grow they secrete enterotoxin.

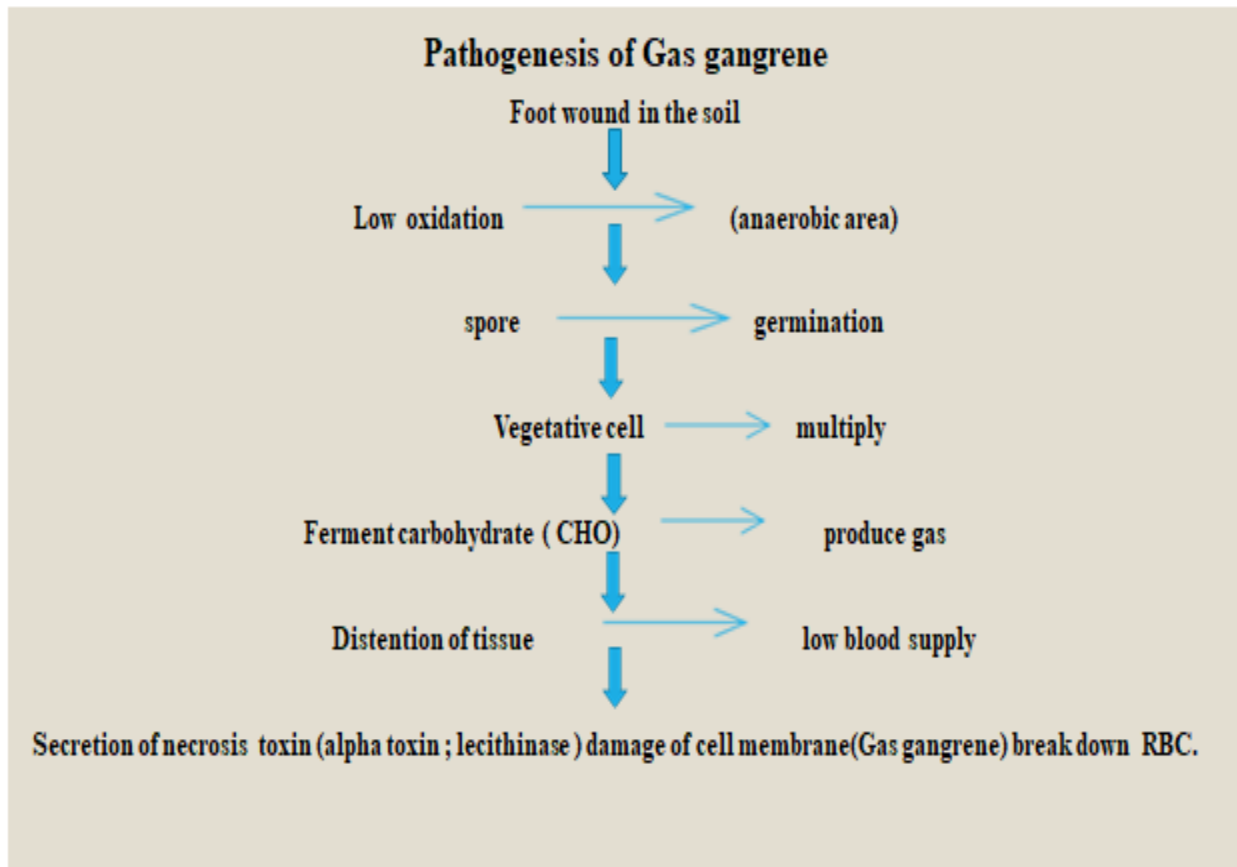


## Gas gangrene:-

Gas gangrene also known as clostridial myonecrosis is a condition of necrotic damage, specific to muscle tissue.

### Symptoms include:

- ✓ Skin discoloration.
- ✓ Foul, smelling discharge from lesions formed on skin.
- ✓ Necrosis.
- ✓ Fever.
- ✓ Pain at site of trauma.
- ✓ Rapid heart rate.
- ✓ Air in subcutaneous tissues (crepitus).
- ✓ Swelling.

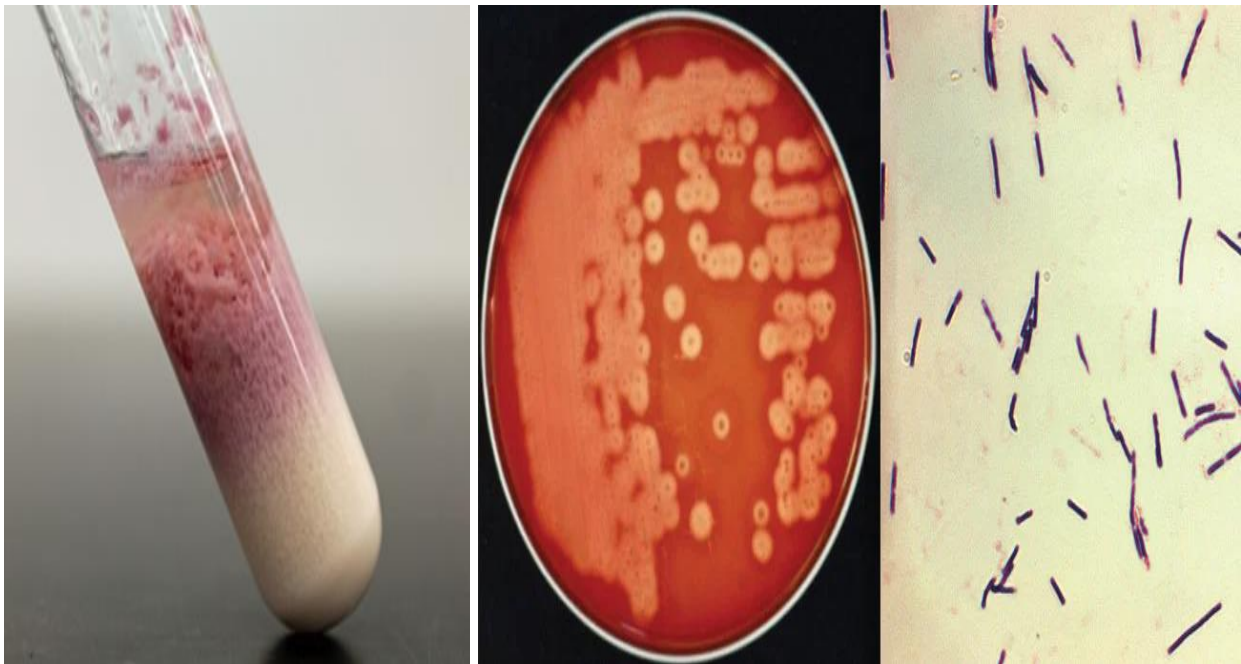


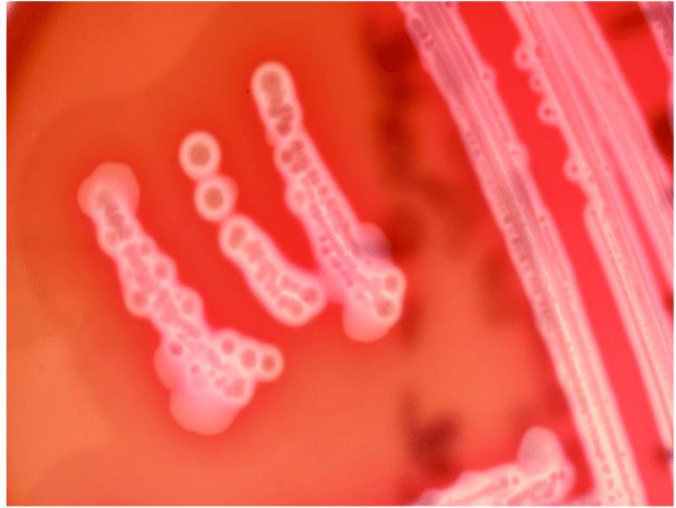
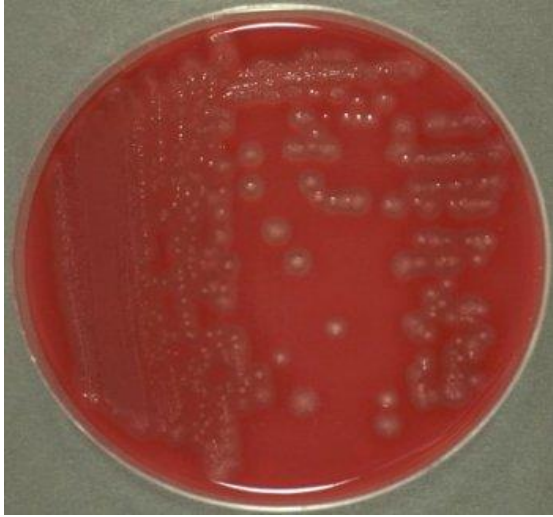




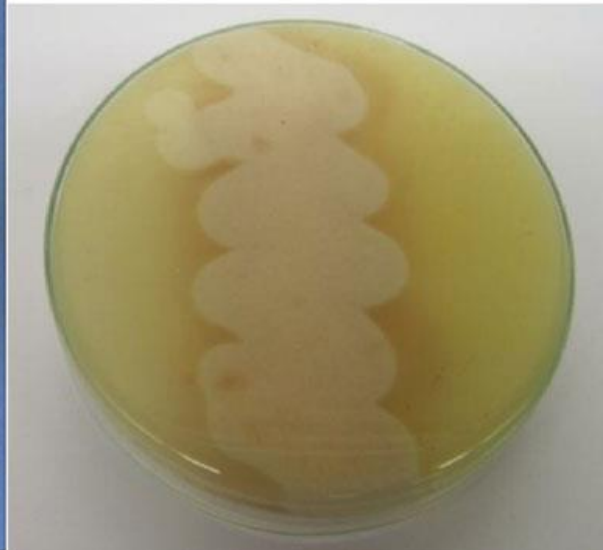
## Diagnosis:-

- ✓ Sample from wound, pus, tissue.
- ✓ Smears show gram positive rods. Sample transferred in thioglycollate broth, culture into blood agar plates anaerobically. On the blood agar Large translucent grayish colonies surrounded a double zone of hemolysis.
- ✓ growth transferred into milk (stormy fermentation). A clot torn by gas.
- ✓ Lecithinase activity (Naglers test ). Lecithin is a normal component of the egg yolk. Microorganisms that possess the enzyme lecithinase break down lecithin which results in a white opaque zone of precipitation that spreads beyond the edge of the colony. Such an opaque halo, surrounding the colony when grown on the egg yolk agar medium .





## Egg Yolk Agar





## ***Clostridium Difficile* ( opportunistic disease)**

- ✓ *C. difficile* is the most common nosocomial (hospital – acquired) cause of diarrhea.
- ✓ *C. difficile* causes antibiotic associated pseudomembranous colitis.
- ✓ the organism colonizes the large intestine of approximately 3 % of general population and up to 30% of hospitalized patient.
- ✓ *C. difficile* is transmitted by the fecal-oral route. The hands of hospital personal are important intermediaries.
- ✓ The pathological mechanism is based on formation of two toxins.
- ✓ **Toxin A** is an enterotoxin (diarrhea).
- ✓ **Toxin B** is a cytotoxin that damages the mucosa of the colon (pseudomembranes).
- ✓ The clinical course includes fever, abdominal cramping pain , watery diarrhea associated with pseudomembrans colitis (yellow – white plaques) on the colonic mucosa. The diarrhea is usually not bloody.
- ✓ Coloscopy reveals edematous changes in the colon mucosa, which is also covered with yellowish-whitish.



*Artist rendition of colonoscopy doing a biopsy of a polyp.*



### Laboratory diagnosis:-

involves culturing the pathogen from patient stool. Both toxins are usually found in the stools. Toxins A and B can also be detected with enzyme-linked immunosorbent assay kits (ELISA tests) . On the blood agar colonies appear yellowish-greenish in color.