Clostridium

## Clostridium: General

- Obligate anaerobes
- Catalase (-) and oxidase (-)
- Gram-positive (except *C. piliforme*, which is Gram-negative)
- Majority are motile: *C. perfringens* is non-motile
- Large, usually straight rods
- Over 100 species described, and less than 20 are pathogenic
- Forms pores
  - Spores are highly resistant

**Habitats**
  - Intestines: major reservoir
  - Damaged tissue
  - Decaying organic material
  - Spores persist in soil
**Clostridium Groups**

Three Clostridium Musketeers

**Neurotoxic Clostridia**
- *C. tetani*
- *C. botulinum*
**C. tetani**

● **Morphology**
  - Usually a slender rod and single
  - Spores are terminal bulging the cell: look like drumstick or badminton racket
  - Motile

● **Habitat:** Soil, intestinal tracts, fecal material

● **Infection**
  - Cause of “tetanus” - acute and potentially fatal intoxication
  - In most cases, the bacteria enter the tissues through wounds, particularly “deep puncture wounds”

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**C. tetani: toxins**

● *C. tatan*i does not actively invade and multiply
  → Pathogenesis rely solely on “toxin production”

● **Tetanospasmin** (spasmogenic toxin)
  - It blocks neurotransmitter release at CNS synapse
  - The toxin binds to gangliosides almost irreversibly

● **Hemolysin**
  - Produces local necrosis and thereby stimulates the growth of the organism

● **Non-spasmogenic toxin**
  - Binds to the neuromuscular junction but its function is unknown
C. tetani: tetanus

- The organism (spore) enters wounds (deep puncture wounds) often with soil or contaminating bacteria in wounds
  → May cause necrosis in the surrounding tissues
  → Reduce the oxygen tension (blood can’t come)
  → Allow the germination and growth of C. tetani
  → Autolysis of bacterial cells (bacterial death)
  → Toxin is released from the bacteria (toxin is a protease)
  → Toxin is absorbed
    1. Ascending tetanus
       - Toxin is absorbed by the motor nerve
       → moves to the CNS
    2. Descending tetanus (usual type in horses and humans)
       - Too much toxins for the surrounding nerves to take up
       → Toxin disseminates to the bloodstream → CNS

C. tetani: tetanus

- Incubation period: one to several weeks
- Localized stiffness at the region of the infected wound
  → General stiffness

- **Species affected**
  - Horses and humans: highly sensitive
  - Ruminants and pigs: moderately susceptible
  - Dogs: relatively resistant
  - Cats: resistant
  - Poultry: quite resistant

Are you scared horsey!
C. tetani: tetanus

- Horses
  - Generalized stiffness in horses (Stiffness of leg muscles) → ‘saw-horse’ stance
  - Spasms
    - Spasms of masticatory tissues → 'lockjaw'
    - Spasms of the neck and back muscle
      - Extension of the head and neck
      - Spasms disturb circulation and respiration
        → increase heart and respiratory rates
- Sheep, goats, and pigs: Often fall to the ground
- Dogs and cats: localized tetanus near a wound

C. tetani: Treatment

- Diagnosis
  - Clinical signs
  - Detection of toxins in the affected animals
  - If the wound is apparent → gram staining of bacteria
- Treatment
  - Antitoxin
  - Penicillin: In large doses. Antibiotic is not very effective after the onset of clinical signs
  - Muscle relaxants help to control the muscle spasms
- Vaccination
  Toxoid administration is routine in humans, horses, and lambs
**C. botulinum: General**

- **Morphology**
  - Typical large rod
  - Spores former

- **Habitat**
  - Soils, lake and sea sediments
  - but different bacterial types are distributed in various habitats
    - Type A & B: soil
    - Type C & D: appear to be obligate parasites of animals
    - Type E: sea or lake sediments (bacteria grow in dead fish)
  - Food: dead fish, contaminated meat, fruits and vegetables, honey

- Food poisoning in humans, domestic animals, and waterfowl
- Over half the cases of human botulism in the U.S. are in infants

**C. botulinum: Botulism**

- Botulinum toxin
  - The most potent biological toxin known
  - Bacterial cell lysis
    - Release of the toxin
    - The toxin is absorbed into the blood and lymph
    - Carried to the peripheral nervous system
    - Hydrolysis of synaptobrevins
    - Irreversible interference with the release of neurotransmitter (acetylcholine)
    - Flaccid paralysis

- Clinical signs
  - Vision disturbance
  - Paralysis of muscles
  - Death results from paralysis of respiratory muscles
C. botulinum: Toxin

- Types C and D
  - Cause most outbreaks in domestic animals
  - Transmitted by bacteriophages

- Type E
  - The most acute
  - Results in the highest mortality rate

- Most of the toxins are readily destroyed by boiling 3 min or heating to 80°C for 5 minutes
**C. botulinum: Botulism**

- **Limberneck**
  - A term used to describe botulism in birds
  - Ducks and other aquatic birds that feed on the vegetation at the bottom of ponds and lakes
  - They develop flaccid paralysis of the neck
  - The buried carcass is rediscovered and ingested by chickens → there are occasional multiple deaths
  - Affected birds may recover without treatment
  - Antibiotic treatment: bacitracin or streptomycin → not successful

![Flaccid Paralysis](image)

**C. botulinum: Transmission**

- Ingestion of “preformed toxin” → causes botulism in animals and humans

- Toxin may be produced in:
  - Decaying carcasses
  - Improperly preserved foods

- Human botulism in the U.S. is most often associated with canned vegetables (particularly green beans) and to a lesser extent with canned meats

- Forage poisoning in horses due to ingestion of the toxin in poor quality feed or animals
  - e.g. Rabbits killed in the mowing process → The organism multiplies in the carcass → Toxin is produced
C. botulinum

- **Vaccination**
  - Toxoid is used in high risk populations
  - Have to have the toxoid specific for the type of toxin that produces disease
  - Immunization of cattle with types C and D toxoid has proved successful

- **Diagnosis**
  - Demonstrate the toxin in serum, intestinal contents and feed

- **Treatment**
  - Polyvalent antitoxin is available for use in humans
  - Treatment of ducks and mink with type C antitoxin is often successful
  - Antitoxin is rarely used in cattle

Histotoxic Clostridia
**Clostridial myonecrosis: Gas gangrene**

- **Gas gangrene**
  - Tissue necrosis always caused by microorganisms particularly Clostridia
  - Entry of the organisms into wounds or damaged tissues with foreign objects such as soil
  - Tissue necrosis reduces blood (oxygen) supply:
    - low oxygen promotes germination of the spores
  - The bacteria multiply
  - The toxin tends to travel along muscle planes and thus spreads to adjacent tissues
  - Clostridia accumulate “gaseous metabolic byproducts” in necrotic tissues
  - thus, called “gas gangrene”
C. chauvoei: General

- **Morphology**
  - Typical large rod
  - Usually singly or in short chains
  - Motile

- **Natural habitat**
  - Intestines of cattle and sheep
  - Exists in the soil as spores

- **Transmission**
  - Tissues and wounds are seeded with spores

- **Toxins:**
  - α-toxin is lethal, necrotizing and hemolytic
  - δ-toxin is a hemolysin

- **Disease:**
  - Blackleg in young ruminants especially young cattle

C. chauvoei: Disease

- **Blackleg**, necrotizing myositis
  - **Main hosts**
    - Usually affects calves (3-24 months) but may affect older animals
    - Sheep
  - High fever, anorexia, lameness, swelling due to “gas accumulation”, sudden death
  - The large muscle masses of the limbs, back and neck are frequently affected: swelling usually occur in hind limb

- **Diagnosis**
  - Clinical signs and very characteristic postmortem lesions
  - Culture • FA

- **Vaccination:** killed vaccines

- **Treatment:** Penicillin in the early stages
**C. septicum: Malignant edema**

- **Habitats:** Soil, intestinal contents of animals (including humans)
  
- **Cause of malignant edema**
  - an acute, generally fatal toxemia in cattle, horses, sheep, and pigs of all ages
  - Organism enters via wounds or umbilicus
  - Fever and soft swelling around wound → Swelling rapidly spreads
  - There are gelatinous intermuscular exudates with gas (little or no gas is produced unlike blackleg)
  - The lesion looks dark brown to black
  - Rapid death (within 24 hours)

**C. septicum: Braxy**

- **Braxy** is a hemorrhagic and necrotic abomasitis in sheep
  - Often occur in young sheep
  - Edema, hemorrhage, and sometimes necrosis of the abomasum and anterior small intestine
  - Spores in abomasum cause disease
  - Associated with eating frozen grass
    : frozen food damages localized area in abomasum
  - High mortality, but rare in Canada and US

- **Toxins**
  1. α-toxin: oxygen-stable hemolysin associated with malignant edema
  2. β-toxin: DNase, leukocidin /
  3. γ-toxin: hyaluronidase
  4. δ-toxin: oxygen-labile hemolysis
**C. septicum: Diagnosis & Treatment**

- **Diagnosis**
  - Culture of the organism can be done
  - Fluorescent antibody testing of the tissues is rapid and efficient

- **Vaccination**
  - Killed vaccines

- **Treatment:** Penicillin, Tetracycline early

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**C. novyi: General & Type A**

- **General**
  - One of the largest clostridia
  - More oxygen sensitive than other clostridia

- **Habitats:** soil and intestinal tract of herbivores

- **Type A**
  - **Bighead**
    - Rams that fight and get head wounds
    - The organism enters via wounds
    - Edema rapidly spreads in the head and neck

  - **Gas gangrene**
    - Cattle, sheep, and humans
    - The organism enters via wounds
    - Legions are similar to those of malignant edema (*C. septicum*)
    - Sudden death
**C. novyi: Type B & C**

- **Type B**
  - **Black disease** (Infectious necrotic hepatitis)
    - Sheep and occasionally in cattle
    - Characterized by darkening of the underside of the skin due to venous congestion
    - Fatal
  - Dormant spores germinate in liver tissues
    → disseminate α, β-toxins (cardiotoxic, histotoxic & hepatotoxic)
    → produce edema, focal hepatic necrosis
  - Liver fluke (*Fasciola hepatica*) predisposes the disease
    (see type D)
  - Vaccination: Killed vaccines
  - Treatment: Penicillin may be of help in cattle but the disease course is very rapid once clinical signs occur
- **Type C**: avirulent

**C. novyi type D = C. haemolyticum**

- *C. novyi* type D is also called *C. haemolyticum*
- Pathogenesis is similar to type B
  - Hepatitis, intravascular hemolysis, hemorrhage
  - Causes bacillary hemoglobinuria (“redwater disease”)
  - Cattle, deer, and sometimes sheep
- Occasionally seen in western Canada

Decolorized urine by hemoglobinuria

Redwater, AB, Canada
C. haemolyticum: Pathogenesis

- Spores of the organism originate in the intestine, migrate to the liver and remain there in a dormant state.
  - The liver fluke (Fasciola hepatica) migrates through the liver and creates a favorable environment (necrosis) for the germination of the spores already present.
  - The organisms multiply and produce β-toxin.
  - The toxin causes hepatic necrosis and is absorbed into the blood.
  - Cause massive intravascular hemolysis and capillary damage (lysis of 40-50% of the RBC).
  - Fever, hemoglobinuria (hemoglobin is passed in the urine); it is called “redwater” disease.
- Fatality rate: 90-95%; Death is due to anoxemia (abnormal reduction in the oxygen content of the blood).

C. haemolyticum: Diagnosis & Treatment

- **Diagnosis:**
  - Culture and toxin demonstration in the liver.
  - Inoculation of Guinea pigs with the liver tissue → death in 1-2 days.

- **Vaccination:**
  - Killed multivalent vaccines.

- **Treatment:**
  - Antiserum and large doses of intravenous penicillin.
  - But, no effective treatment for C. novyi infections.
C. sordellii

- Habitat: Soil and intestine of domestic animals
- Causes myonecrosis (gas gangrene) in cattle, sheep and horses
- Sometimes found in the intestines of cattle with “sudden death syndrome”
- Enters via wounds
  - Flulike symptoms
  - Edema begins locally and spread rapidly
  - Mostly die rapidly

C. perfringens type A

- Cause myonecrosis and gas gangrene
- Type A is mostly involved

C. perfringens will start later!
## Histotoxic clostridia: Summary

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<td>All warm-blooded</td>
<td>Myonecrosis, gas gangrene</td>
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