**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
- Form spores
  - Spores are highly resistant
- **Habitats**
  - Intestines: major reservoir
  - Damaged tissue
  - Decaying organic materials
  - Spores persist in soil

**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”, an acute and potentially fatal intoxication
  - In most cases, the bacteria enter the tissue through wounds, particularly “deep penetrating wounds”
C. tetani: toxins

- C. tetani does not actively invade and multiply
  - Pathogenesis relies solely on "toxin production"

- Tetanospasmin (spasmogenic toxin)
  - It blocks neurotransmitter release at CNS synapse
  - Binds irreversibly to gangliosides on nerve cells

- 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

- Tetanus: the Greek "tetanos", meaning "to contract"
  - Intense, painful muscle contractions

- The organism (spore) enters wounds (deep puncture wounds)
  - Often with soil or contaminating bacteria
  - 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 enters the nervous system
  - Contraction of skeletal muscles

C. tetani: tetanus

- Incubation period: one to several weeks
- Localized stiffness at the site of the infected wound develops to generalized stiffness

- Species & susceptibility
  - Horses and humans: highly sensitive
  - Ruminants and pigs: moderately susceptible
  - Dogs: relatively resistant
  - Cats: resistant
  - Carnivores: comparatively resistant
  - Poultry: not susceptible to tetanus

C. tetani: tetanus

- Horses
  - Spasms of masticatory tissues → 'lockjaw'
  - Spasms of the neck and back muscle → Extension of the head and neck
  - Generalized stiffness in horses (Stiffness of leg muscles) → 'saw-horse' stance
  - 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 wounds
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
    - large doses
    - antibiotic is not very effective after the onset of clinical signs
  - Muscle relaxants help to control muscle spasms
- **Vaccination**
  Toxoid administration is routine in humans, horses, and lambs

C. botulinum: General

- **Morphology**
  - Typical large rod
  - Spores former
- **Seven types of C. botulinum**
  - A, B, C, D, E, F, and G
  based on the antigenic properties of the toxins
- **Habitat**
  - The endospores are distributed in soil and aquatic environments (lake and sea sediments)
  - Dead fish, contaminated meat, fruits, vegetables, honey
  → Food poisoning in humans, domestic animals, and waterfowl

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 SNARE proteins
    → 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: Types

- **Types C and D**
  - Cause most outbreaks in domestic animals
  - Outbreaks occur most commonly in waterfowl, cattle, horse, sheep, mink, poultry, farmed fish
- **Type E**
  - The most acute
  - Results in the highest mortality rate
  - Pigs and dogs are relatively resistant
  - Botulism is rare in cats
**C. botulinum: Transmission**

- Ingestion of "preformed toxins" → causes botulism in animals and humans

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

- Human botulism in the US is most often associated with
  - canned vegetables (particularly canned green beans)
  - to a lesser extent with canned meats
  - honey may contain the spores → causing infant botulism

- Forage poisoning in horses due to ingestion of the toxin in poor quality feed

**C. botulinum: Botulism in birds**

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

**C. botulinum**

- Ingestion of preformed toxins
- Transmission
- Infection in wounds
- Soil, manure, windblown spores
- Spore biohazard

**C. tetani & C. botulinum**

<table>
<thead>
<tr>
<th></th>
<th>C. tetani</th>
<th>C. botulinum</th>
</tr>
</thead>
<tbody>
<tr>
<td>Major virulence factor</td>
<td>Toxin (tetanospasmin)</td>
<td>Toxin (A~G)</td>
</tr>
<tr>
<td>Transmission</td>
<td>Entry of the organism (spores) into wounds &quot;deep puncture wounds&quot;</td>
<td>Ingestion of feed contaminated with bacteria or preformed toxins</td>
</tr>
<tr>
<td>Type of paralysis</td>
<td>Stiff muscles</td>
<td>Flaccid muscles</td>
</tr>
<tr>
<td>Animal species</td>
<td>Horses, humans, ruminants, pigs...</td>
<td>Birds, humans, ruminants, horses...</td>
</tr>
<tr>
<td>Treatment</td>
<td>Polyvalent antitoxin is available for use in humans</td>
<td>Cost and availability limit the use of antitoxin in animals</td>
</tr>
<tr>
<td>Treatment</td>
<td>Treatment of ducks and mink with type C antitoxin is often successful</td>
<td>Cost and availability limit the use of antitoxin in animals</td>
</tr>
</tbody>
</table>
Histotoxic Clostridia

Clostridial myonecrosis: Gas gangrene

- **Gas gangrene**
  - Clostridia cause tissue necrosis
  - 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 and produce toxins
  - 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

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

- **Toxins:**
  - $\alpha$-toxin is lethal, necrotizing and hemolytic
  - $\delta$-toxin is a hemolysin
**C. chauvoei: Disease**

- **Blackleg**, necrotizing myositis
  - **Main hosts**
    - Cattle and sheep
    - Usually affects calves (3-24 months)
  - High fever, anorexia, lameness, swelling due to "gas accumulation", sudden death
  - Frequently affected large muscle masses of the limbs, back, and neck
- **Diagnosis**
  - Clinical signs and very characteristic postmortem lesions
  - Fluorescent antibody tests
  - PCR
- **Vaccination**: killed vaccines
- **Treatment**: Penicillin in the early stages

**C. septicum**

- **Braxy**, a hemorrhagic and necrotic abomasitis in sheep
  - Often occur in young sheep
  - Associated with eating frozen grass in winter
  - Frozen food damages localized area in abomasum
  - Spores in abomasum cause disease
  - Edema, hemorrhage, and sometimes necrosis of the abomasum and anterior small intestine
  - 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**

- **Habitats**: Soil, intestinal contents of animals
- **Cause of malignant edema**
  - an acute, generally fatal toxemia in cattle, horses, sheep, and pigs of all ages
  - Organism enters via wounds
  - Fever and soft swelling around wound
  - Swelling rapidly spreads
  - Gelatinous intermuscular exudates are produced with gas (less gas is produced compared to blackleg)
  - The lesion looks dark brown to black
  - Rapid death when lesions are extensive
- **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
**C. novyi: General & Type A**

- **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. speticum*)
    - Sudden death

- **Type B & C**

**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 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

**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; it is called "redwater" disease
- Fatality rate: 90-95%
  - Death is due to anoxemia
**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

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**C. sordellii**

- **Habitat:** Soil and intestine of domestic animals
- **Causes myonecrosis (gas gangrene)** in cattle, sheep and horses
- **Enters via wounds**
  - Flulike symptoms
  - Edema begins locally and spread rapidly
  - Mostly die rapidly
  - Sudden death

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**C. perfringens type A**

- Cause myonecrosis and gas gangrene

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**Histotoxic clostridia**

<table>
<thead>
<tr>
<th>Species</th>
<th>Major hosts</th>
<th>Disease</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>C. chauvoei</em></td>
<td>Sheep, cattle</td>
<td>Blackleg</td>
</tr>
<tr>
<td><em>C. septicum</em></td>
<td>Sheep, cattle</td>
<td>Malignant edema</td>
</tr>
<tr>
<td><em>C. novyi</em> type A</td>
<td>Sheep, goats</td>
<td>Wound infections (Bighhead)</td>
</tr>
<tr>
<td><em>C. novyi</em> type B</td>
<td>Sheep, cattle</td>
<td>Infectious necrotic hepatitis (Black disease)</td>
</tr>
<tr>
<td><em>C. novyi</em> type D (C. haemolyticum)</td>
<td>Cattle</td>
<td>Bacillary hemoglobinuria (Redwater disease)</td>
</tr>
<tr>
<td><em>C. sordellii</em></td>
<td>Sheep, cattle</td>
<td>Myonecrosis, enteritis</td>
</tr>
<tr>
<td><em>C. perfringens</em> type A</td>
<td>All warm-blooded</td>
<td>Myonecrosis, gas gangrene</td>
</tr>
</tbody>
</table>

To be continued tomorrow!