
Chapter 14. Anaerobic Infections

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CHAPTER PREVIEW

- *Clostridium* Species
- Non-sporing Anaerobes

The obligate anaerobic bacteria infecting man can be grouped into spore-bearing (e.g. *Clostridium*) and non-sporing anaerobes.

CLOSTRIDIUM SPECIES

Clostridia are gram-positive bacilli with bulging spores, commonly found as saprophytes in soil and commensals in the intestine of man and animals. However, few members can cause a variety of infections in humans.

- *Clostridium perfringens*: causes gas gangrene
- *Clostridium tetani*: causes tetanus
- *Clostridium botulinum*: causes botulism
- *Clostridioides difficile*: causes pseudomembranous colitis.

Clostridium perfringens

It is an intestinal commensal and also a soil saprophyte. It is the causative agent of **gas gangrene**, a rapidly spreading edematous myonecrosis.

Pathogenesis

The pathogenesis is due to its invasiveness and liberation of a variety of toxins including α -toxin (lecithinase), which is the principal virulence factor.

Clinical Manifestations

Clostridium perfringens infections are mostly polymicrobial involving other clostridia species. Various manifestations include:

- **Clostridial wound infections:** It occurs in three stages—(i) simple wound contamination, (ii) anaerobic cellulitis, (iii) anaerobic myositis or gas gangrene

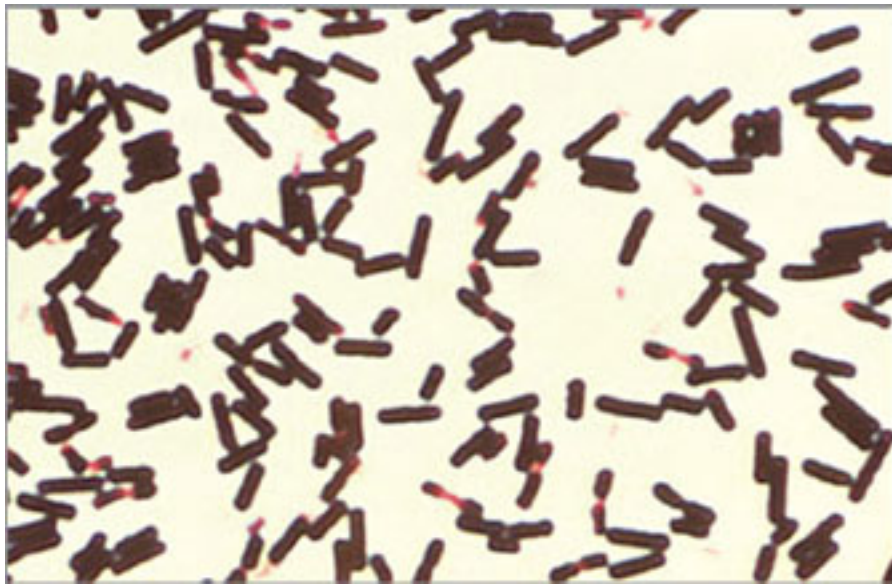
Gas gangrene

It is rapidly spreading, edematous myonecrosis, occurring in association with severely crushed wounds contaminated with pathogenic clostridia:

- **Agents:** *C. perfringens* is the most common causative agent (60%), followed by *C. novyi* and *C. septicum* (20-40%)
- **Predisposing factors:** Crushing injuries of muscles (e.g. road traffic accidents or bullet injuries) lead to interruption in the blood supply and anoxic muscle necrosis.
- **Clinical Manifestations include**—the incubation period is about 10-48 hours. Characterized by sudden onset of excruciating pain at the affected site, rapid development of a foul-smelling thin serosanguineous discharge and gas bubbles (**crepitus**) in the muscle planes.

- **Clostridial enteric infections** such as food poisoning, necrotizing enterocolitis, and gangrenous appendicitis

Fig. 14.1. Gram-stained smear of *Clostridium perfringens*.



Source: Public Health Image Library/ID# 11196, Don Stalons/Centers for Disease Control and Prevention (CDC), Atlanta (with permission).

- Skin and soft-tissue infections
- Bacteremia.

Laboratory Diagnosis

- **Specimen:** Necrotic tissues, muscle fragments, and exudates from deeper parts of the wound
- **Direct microscopy:** Thick, stubby, boxcar-shaped gram-positive bacilli without spore are suggestive of *C. perfringens* (**Fig. 14.1**)

- **Culture:** Culture media such Robertson cooked meat (RCM) broth, egg yolk agar, etc. are used, which are incubated anaerobically by GasPak or Anoxomat, etc.
- **Identification:** *C. perfringens* is identified by:
 - Target hemolysis (double zone of hemolysis)
 - Nagler's reaction: Opalescence surrounding the streak line on egg yolk agar
 - Reverse CAMP test: Positive
 - Automated ID method such as MALDI-TOF is the current method of choice for rapid and accurate identification.

TREATMENT

Gas gangrene

Surgical debridement is the mainstay of treatment. All devitalized tissues should be widely resected to remove conditions that produce an anaerobic environment. Other treatment modalities include:

- Hyperbaric oxygen
- Antibiotics such as penicillin plus clindamycin
- Passive immunization with anti- α -toxin antiserum.

Clostridium tetani

It is the causative agent of 'tetanus'—an acute disease, manifested by skeletal muscle spasm and autonomic nervous system disturbance.

- **Transmission:** Tetanus bacilli enter through wounds (accidents or surgical incision) or neonates through umbilical stumps
- **Pathogenesis:** It produces a powerful neurotoxin *tetanospasmin*, which blocks the release of neurotransmitters glycine and GABA (gamma-aminobutyric acid) from the inhibitory neuron terminals, thereby causing spastic contraction of muscles (**Fig. 14.2A**)
- **Clinical manifestation:** The incubation period is about 6–10 days. Muscles of the face and jaw are often affected first (called trismus or lockjaw) followed by painful muscle spasms → leading to descending spastic paralysis
 - *Abnormal posture:* The patient may develop an opisthotonos position due to generalized spastic contraction of the extensor muscles (**Fig. 14.2B**)
 - *Autonomic disturbance* may occur leading to alerted blood pressure, tachycardia, intestinal stasis, sweating, etc.
- **Laboratory diagnosis:** Excised tissue bits from the necrotic depths of wounds are more reliable than wound swabs
 - *Gram staining* reveals gram-positive bacilli with terminal and round spores (drum stick appearance) (**Fig. 14.2C**)
 - *Culture* using Robertson cooked meat broth, followed by toxigenicity test.
- **Treatment:** The treatment modalities of tetanus include:

Figs. 14.2A to C. A. Lockjaw and facial spasms; B. Patient with opisthotonos seen in tetanus; C. Gram-stained smear of *Clostridium tetani* showing round terminal spore-bearing gram-positive bacilli.



Source: **A.** Wikia/Hoidkempuhtust; **B.** Public Health Image Library, ID# 6373; **C.** ID# 12056/Dr Holdeman/Centers for Disease Control and Prevention (CDC), Atlanta (with permission).

- Passive immunization by tetanus immunoglobulin
- The first dose of TT (if unvaccinated)
- Antibiotics: Metronidazole or penicillin.
- **Vaccine:** The tetanus toxoid (TT) vaccine is the most effective way of prevention of tetanus. TT is given along with DPT vaccine under the childhood immunization program (refer Chapter 13 for details).

Clostridium botulinum

It produces a powerful neurotoxin *botulinum toxin*, which acts by blocking the release of acetylcholine from nerve terminals and thereby causing flaccid paralysis of voluntary muscles. Botulism occurs in three clinical types.

1. **Food-borne botulism:** It results from the consumption of foods (e.g. canned food) contaminated with preformed botulinum toxin
2. **Wound botulism:** It results from contamination of wounds with *C. botulinum* spores
3. **Infant botulism:** It is the most common type; (75%); usually affects infants following ingestion of contaminated food (usually **honey**). Manifestations include floppy neck, and extreme weakness (hence called **floppy child syndrome**). It is usually self-limiting.

Clostridioides difficile Infection (CDI)

Clostridioides difficile (old name *Clostridium difficile*) is an important cause of healthcare-associated infection. It is responsible for a unique colonic disease—**pseudomembranous colitis**, which occurs almost exclusively in association with prolonged antimicrobial use in hospitals; therefore, called as antibiotic-associated diarrhea.

- **Risk factors:** *Clostridioides difficile* is associated with the following risk factors
 - **Prolonged antibiotics use:** Cephalosporins, clindamycin, ampicillin and fluoroquinolones are frequently responsible for this condition

- Advanced age (>65 years)
- Immunosuppression and cancer chemotherapy
- Malignancies and gastrointestinal surgeries.
- **Laboratory diagnosis:** Various methods to detect CDI include:
 - Culture on special media such as CCFA (cycloserine cefoxitin fructose agar)
 - Cell culture cytotoxin neutralization assay
 - Detection of antigen (GDH, toxin A/B) in stool (by rapid test)
 - PCR detecting toxin gene (toxin A/B).
- **Treatment:** Oral vancomycin or metronidazole are given for treatment
- **Prevention (infection control measures)** followed are:
 - Broad spectrum antimicrobials should be stopped at the earliest
 - Infection control measures of contact precaution (see Chapter 38) should be followed such as: strict hand hygiene and patient isolation
 - Ensure proper disinfection of floor, surfaces, toilets and other soiled areas using 1% freshly prepared hypochlorite solution.

NON-SPORING ANAEROBES

Non-sporing anaerobes are often a part of the normal flora of the mouth, GIT, and genital tract of man and animals. Medically important non-sporing anaerobes include:

- Gram-positive cocci: *Peptostreptococcus*
- Gram-negative cocci: *Veillonella*
- Gram-positive bacilli: *Bifidobacterium*, *Propionibacterium*, and *Mobiluncus*
- Gram-negative bacilli: *Bacteroides*, *Prevotella*, *Porphyromonas*, *Fusobacterium*.

Bacteroides fragilis

Bacteroides fragilis is recognized as the most common commensal in the human intestine; it is also the most frequent anaerobe isolated from clinical specimens. It causes peritonitis and intra-abdominal abscess following bowel injury (most common manifestation), pelvic inflammatory disease (PID), brain abscesses, bacteremia, and empyema.

EXPECTED QUESTIONS

1. I. Write short notes on:

1. Gas gangrene.
2. Tetanus.
3. Botulism.

4. Antibiotic-associated diarrhea.

2. II. Multiple Choice Questions (MCQs):

1. Naegler's reaction is positive for?

- a. *Clostridium perfringens*
- b. *Clostridium tetani*
- c. *Clostridium botulinum*
- d. *Clostridioides difficile*

2. Pseudomembranous colitis is caused by__?

- a. *Clostridium perfringens*
- b. *Clostridium tetani*
- c. *Clostridium botulinum*
- d. *Clostridioides difficile*

3. The most common type of botulism?

- a. Food botulism
- b. Infant botulism
- c. Wound botulism
- d. Iatrogenic botulism

4. Which of the following produces a toxin that inhibits release of GABA and glycine neurotransmitters?

- a. *Clostridium perfringens*
- b. *Clostridium tetani*
- c. *Clostridium botulinum*
- d. *Clostridioides difficile*

5. The most effective way of preventing tetanus:

- a. Hyperbaric oxygen
- b. Antibiotics
- c. Tetanus toxoid
- d. Surgical debridement and toilet

Answers

1. a	2. d	3. b	4. b	5. c
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