Anaerobic Infections

- A large majority of the bacteria that make up the normal human microbiota are anaerobes.

- Certain characteristics are suggestive of anaerobic infections:

  (1) They are often contiguous with a mucosal surface.

  (2) They tend to involve mixtures of organisms.

  (3) They tend to form closed-space infections, either as discrete abscesses (lung, brain, pleura, peritoneum, and pelvis) or by burrowing through tissue layers.

  (4) Pus from anaerobic infections often has a foul odor.

  (5) Most of the pathogenically important anaerobes except *Bacteroides* and some *Prevotella* species are highly susceptible to penicillin G.

  (6) Anaerobic infections are favored by reduced blood supply, necrotic tissue, and a low oxidation-reduction potential

**Clostridia**
The clostridia are large, spore-forming, Gram-positive bacilli. They are able to survive for years in the environment and return to the vegetative form when placed in a favorable conditions. The shape of the cell and location of the spore varies with the species, but the spores themselves are rarely seen in clinical specimens. The medically important clostridia are potent producers of one or more protein exotoxins.

Other groups of anaerobic bacteria

- **Peptostreptococcus**: Positive cocci, NF. in Mouth and intestine, cause Oropharyngeal infections, brain abscess
- **Propionibacterium**: gram Positive rods, small pleomorphic bacilli, are among the most common bacteria in the normal flora of the skin.
- **Bacteroides**: B. fragilis group, gram negative rods (coccobacillary), mostly isolated from anaerobic infection, The lipopolysaccharide (LPS) in its outer membrane have a much lower lipid content and thus lower toxic activity than that of most other Gram-negative bacteria. Virtually all B. fragilis strains have a polysaccharide capsule and are relatively oxygen tolerant through production of superoxide dismutase.
- **Fusobacterium**: Negative rods (elongated)
- **Prevotella**: Negative rods
- **Porphyromonas**: Negative rods
- Except for infections with some environmental clostridia, anaerobic infections are almost always endogenous with the infective agent(s) derived from the patient’s normal flora.

**PATHOGENESIS**

- The anaerobic flora normally lives in a commensally relationship with the host. However, when displaced from their niche on the mucosal surface into normally sterile tissues these organisms may cause life-threatening infections. This can occur as the result of
  - **Trauma** (eg, gunshot, surgery)
  - **Disease**
  - **Isolated events** (eg, aspiration).
  - **Host factors such as malignancy**
  - **Impaired blood supply**

- All increase the probability that the dislodged flora eventually produce an infection.

- The organisms involved are anaerobes normally found at the mucosal site adjacent to the infection.

- The relationship between normal flora and site of infection may be indirect. For example, aspiration pneumonia, lung abscess, and empyema typically involve anaerobes found in the oropharyngeal flora.

- In contaminated open wounds, clostridia can come from the **intestinal flora** or from **spores surviving in the environment**.

Additional virulence factors are needed for anaerobes to produce infection. Classical virulence factors such as **toxins** and **capsules** are known only for the
toxigenic clostridia and B. fragilis, but a feature such as the ability to survive brief exposures to oxygenated environments can also be viewed as a virulence factor. Anaerobes found in human infections are more likely to produce catalase and superoxide dismutase

- The great majority of anaerobic infections are mixed; that is, two or more anaerobes are present, often in combination with facultative bacteria such as Escherichia coli. In some cases the components of these mixtures are believed to synergize each other’s growth either by
  - providing growth factors
  - Lowering the oxidation-reduction potential.
- Bacteroides, Fusobacterium, and peptostreptococci, alone or together with other facultative or obligate anaerobes, are responsible for the majority of localized abscesses within the cranium, thorax, peritoneum, liver, and female genital tract.
- Foul-smelling pus and crepitation (gas in tissues) are signs associated with anaerobic infections.

**Clostridium perfringens**

- *C. perfringens* is a large, Gram-positive, nonmotile rod with square ends.
➢ It grows overnight on blood agar medium under anaerobic conditions, producing colonies surrounded by a double zone of hemolysis.

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➢ In broth containing fermentable carbohydrate, produce large amounts of hydrogen and carbon dioxide gas, which can also be produced in necrotic tissues; hence the term gas gangrene.

➢ *C. perfringens* produces multiple exotoxins that serve as the basis for classification.

➢ Type A is by far the most important in humans and is found consistently in the colon and often in soil.

- The most important exotoxin is the **α-toxin**, a phospholipase that hydrolyzes lecithin and sphingomyelin, thus disrupting the cell membranes of various host cells, including erythrocytes, leukocytes, and muscle cells. The α-toxin alters capillary permeability and is toxic to heart muscle. The bacterium produces at least 11 exotoxins that have hemolytic or other cytotoxic and necrotic effects.
- *C. perfringens* produces a wide range of wound and soft tissue infections. The most important is “Gas Gangrene” begins as a wound infection but progresses to shock and death in a matter of hours.

- Gas gangrene develops in traumatic wounds with muscle damage when they are contaminated with dirt, clothing, or other foreign material containing *C. perfringens*. The clostridia can come from the patient’s own intestinal flora or spores in the environment.

- Compound fractures, bullet wounds, or the kind of trauma seen in wartime are prototypes for this infection.

**Pathogenesis of Gas Gangrene (Myonecrosis)**

- Spores germinate in open wounds, such as those caused by GI tract surgery, burns, puncture wounds, and war wounds, and produce cytotoxic factors.

- Fermentation of organic compounds in host tissues causes formation of gas bubbles.

- If the oxidation–reduction potential in a wound is sufficiently low, *C. perfringens* spores can germinate and can multiply, elaborating toxins.

- The process passes along the muscle bundles, producing rapidly spreading edema and necrosis as well as conditions that are more favorable for growth of the bacteria.

- Very few leukocytes are present in the myonecrotic tissue. As the disease progresses, increased vascular permeability and systemic absorption of the toxin and inflammatory mediators leads to shock.
Clinical aspects of Gas Gangrene

- Gas gangrene usually begins 1 to 4 days after the injury but may start within 10 hours.
- The earliest reported finding is severe pain at the site of the wound associated with a sense of heaviness or pressure. The disease then progresses rapidly with edema, tenderness, discoloration and hemorrhagic bullae.
- The gas is apparent as crepitance in the tissue, but this is a late sign.
- Systemic findings are those of shock with intravascular hemolysis, hypotension, and renal failure leading to coma and death.
**Anaerobic Cellulitis** is a clostridial infection of wounds and surrounding subcutaneous tissue in which there is marked gas formation (more than in gas gangrene) but in which the pain, swelling, and toxicity of gas gangrene are absent. This condition is much less serious than gas gangrene.

**Endometritis:** If *C. perfringens* gains access to the uterus, it may multiply and infect the endometrium. Necrosis of uterine tissue and septicemia with massive intravascular hemolysis due to -toxin may then follow.

**DIAGNOSIS**

- Specimen, preferably pus or fluid aspirated directly from the infected site. Swabs are not used since cotton fibers are detrimental. Tissue samples should be digested and put in degasses sealed container.
- The specimen needs to be taken quickly to the microbiology laboratory and protected from oxygen exposure while on the way.
- A direct Gram-stained smear of clinical material demonstrating Gram-negative and/or Gram-positive bacteria of various morphologies is highly suggestive, often even diagnostic of anaerobic infection.
- Because of the typically slow and complicated nature of anaerobic culture, the Gram stain often provides the most useful information for clinical decision-making.
- The simple anaerobic jar is sufficient for isolation of the clinically significant anaerobes.
The use of media that contain reducing agents (cysteine, thioglycollate) and growth factors needed by some species further facilitates isolation of anaerobes.

The polymicrobial nature of most anaerobic infections requires the use of selective media to protect the slow growing anaerobes.

Once the bacteria are isolated, identification procedures including morphology, biochemical characterization, Nagler reaction, and metabolic end-product detection by gas chromatography may begin.

**BACTEROIDES FRAGILIS**

The *B. fragilis* group constitutes the most common opportunistic pathogens of the genus Bacteroides. These are

- Pale-staining
- Capsulate
- Gram-negative rods
- Form colonies overnight on blood agar medium.
- Has surface pili
  - The LPS endotoxin in the *B. fragilis* outer membrane is less toxic than that of most other Gram-negative bacteria, possibly due to modification or absence of the lipid A portion.

**EPIDEMIOLOGY** Like the other Gram-negative anaerobes, *B. fragilis* infections are endogenous, originating in the patient’s own intestinal flora. It is typically mixed with other anaerobes and facultative bacteria.

**PATHOGENESIS**
- Its pili have adhesive properties, and the polysaccharide capsule confers resistance to phagocytosis and inhibits macrophage migration.
- The most distinguishing pathogenic feature of the organism is its ability to cause abscess formation. The capsule stimulates abscess formation.
- *B. fragilis* and other Bacteroides species produce a number of extracellular enzymes (*collagenase*, *fibrinolysin*, *hyaluronidase*) that may also contribute to the formation of the abscess.

**IMMUNITY** Although it has been demonstrated that antibody to capsular polysaccharide facilitates classical complement pathway killing, there is no evidence that this confers immunity to reinfection. In contrast, there is some evidence that cell-mediated immunity may be protective.

**Clinical aspects manifestations**
- There is no evidence the organism is invasive on its own.
The local effects of the developing abscess include **abdominal pain** and **tenderness**, often with a **low-grade fever**.

The subsequent course depends on whether the abscess remains localized or ruptures through to other sites such as the peritoneal cavity. This may cause several other abscesses or peritonitis.

Spread to the bloodstream is more common with **B. fragilis** than any other anaerobe.

**TREATMENT**: Drainage of abscesses and debridement (العلاج بالتنظير) of necrotic tissue