Microbiology/ Clostridium

• In Anaerobic spore, bearing Gram positive, bacilli Spores are wider, than the body giving, spindle shape

- The name derived from word **Kolster meaning spindle**

Genus Clostridium

Clostridium consists of around 100 species that include common free-living bacteria as well as important pathogens . There are four main species responsible for disease

C. perfringens: gas gangrene; food poisoning

C. tetani: tetanus

C. botulinum: botulism

C. difficile: pseudomembranous colitis

Physiology and Structure

Anaerobic.

Large gram-positive rods., The spores are usually wider than the rods, and are located terminally or sub terminally.

Most clostridia are motile by peritrichous flagella.

Clostridia

• Large Gram positive bacilli.

• Straight or slightly curved rods with slightly rounded ends

• Anaerobic bacilli

• Spore bearing

• Spore do not germinate and growth does not normally proceed unless a suitably low redox potential Eh exists

• Many are Saprophytes

SHAPES OF CLOSTIDIA

The shape an position of spores varies in different species and is useful for the identification of Clostridia Central and equatorial in ***Cl.bifermentans***, Sub terminal in ***C.perfringens***, Oval or terminal in ***Cl.tertium***

Spherical and terminal giving drum stick in C.tetani

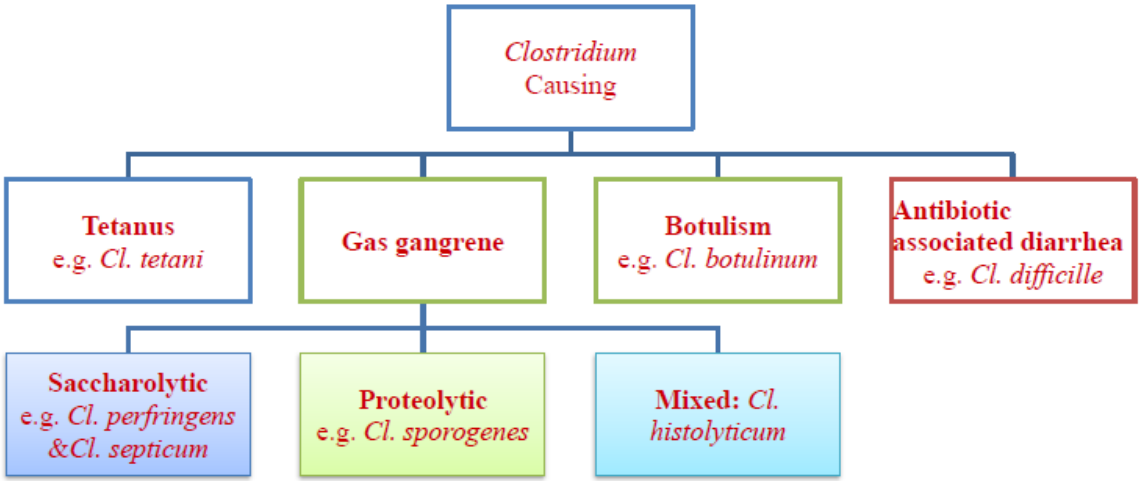
Some are Commensals But Can be Pathogenic

• Some are commensals of the animal & human gut which invade the blood and tissue when host die and initiate the decomposition of the corpse (dead body)

• Causes diseases such as gas gangrene, tetanus, botulism & pseudomembranous colitis by producing toxins which attack the neurons pathways

Clostridia are biochemically active, frequently possessing both saccharolytic and proteolytic properties, although in varying degrees. Many species are highly toxigenic. The toxins produced by the organisms of tetanus and botulism attack nervous pathways and are referred to as neurotoxins.

Clostridia of medical importance



Gram staining

• They are Gram positive, but may appear to be Gram negative. All produce spores, which enable the organisms to survive in adverse conditions, for example

in soil and dust and on skin.

Some Clostridia Produce Gas gangrene

• The organisms associated with gas gangrene attack soft tissues by producing toxins and aggressins, and are referred to as histotoxic. C. difficile and some strains of C. perfringens produce enterotoxins

Clostridium Causing Gas Gangrene

1- Saccharolytic organisms Cl. perfringens, Cl. Septicum
2- Proteolytic organisms, Cl. Sporogenes
3- Mixed saccharolytic & proteolytic Cl. Histolyticum

Clostridium perfringens

• Large Gram-positive bacilli with stubby ends
• **Capsulated**
• **Non motile** Anaerobic
• Grown quickly on selective media
• **Can be identified by** Nagler reaction

• C. perfringens is a relatively large Gram positive bacillus (about 4-6 × 1 µm) with blunt ends. It is capsulate and non-motile. It grows quickly on laboratory media, particularly at high temperatures (approximately 42°C), when the doubling time can be as short as 8 min**.**

– Found in soil, decaying matter and intestinal tract of mammals

• 5 types (A-E)

– Types B and D produce the epsilon toxin

Resistance

• Vegetative bacteria is killed like other bacteria

• Cl.perfringens destroyed by boiling

• Cl, botulinum not killed even at 105 c 0 for less than 100 minutes

• All spores are killed at 121 oc in 20 minutes

• Halogens , Glutaraldehyde are effective on spores

• Metronidazole and Pencillin andChloramphenicol are effective

Virulence Factors

–toxins –

• alpha toxin – causes RBC rupture, edema and tissue destruction

–collagenase

–Hyaluronidase

–DNase

Toxins

• The toxins of Cl. perfringens

– **Alpha toxin** (phospholipase C, lecithinase) is the most important toxin

• Lyses of RBCs, platelets, leucocytes and endothelial cells

• Increased vascular permeability with massive hemolysis and bleeding tissue destruction

• Hepatic toxicity and myocardial dysfunction

– **Beta toxin** is responsible for necrotic lesions in necrotizing enterocolitis

– **Enterotoxin** is heat labile toxin produced in colon → food poisoning

Epsilon Toxin

• Produced as an inactive protoxin

• Activated by trypsin, which removes a 13-residue of N-terminal peptide

• Increases intestinal permeability

• Increases vascular permeability

– Vascular damage and edema in brain, heart, lung and kidneys

Pathology

• Not highly invasive; requires damaged and dead tissue and anaerobic conditions

• Conditions stimulate spore germination, vegetative growth and release of exotoxins, and other virulence factors.

• Fermentation of muscle carbohydrates results in the formation of gas and further destruction of tissue.

C. perfringens

Clinical Diseases

Gas gangrene

Spores germinate vegetative cells multiply, ferment carbohydrates and produce gas in the tissue. This results in distension of tissue and interference with blood supply the bacteria produce necrotizing toxin and Hyaluronidase, which favor the spread of infection tissue necrosis extends, resulting in increased bacterial growth, hemolytic anemia, then severe toxemia and death.

Incubation: 1-7 days after infection.

Symptoms: Crepitation in the subcutaneous tissue and muscle, foul smelling discharge, rapidly progressing necrosis, fever, hemolysis, toxemia, shock, renal failure, and death.

Can be also caused by other Clostridium species.

Mechanism of Clostridial Infections

• When Clostridial infection has been initiated in a focus of devitalized anaerobic tissue, the organisms multiply rapidly and produce a range of toxins and aggressins. These damage tissue by various necrotizing effects, and some have demonstrable lethal effects. They spread into adjacent viable tissue, particularly muscle, kill it, and render it anaerobic and vulnerable to further colonization, with the production of more toxins and aggressins.

Toxic and Enzymatic Mechanisms

Hyaluronidase produced by C. perfringens breaks down intercellular cement substance and promotes the spread of the infection along tissue planes. Collagenase and other proteinases break down tissues and virtually liquefy muscles. The whole of a muscle group or segment of a limb may be affected. α-Toxin, a phospholipase C (lecithinase), is generally

considered to be the main cause of the toxaemia associated with gas gangrene, although other Clostridial species can produce similar manifestations.

Clinical Diseases (Food poisoning)

The enterotoxin causes marked hyper secretion in jejunum and ileum. Enterotoxin: a heat-labile protein produced by some strains of C. perfringens type A. When >108 cells in contaminated meat are ingested and sporulate in the small intestine, enterotoxin is formed. It disrupts ion transport in the enterocytes, and induces antibodies (non-protective) in adults. Symptoms: diarrhea, usually without vomiting or fever. Necrotizing enteritis (pig-bel): a fatal disease (acute necrosis in jejunum attributed to □-toxin) in children in New Guinea caused by type C C. perfringens. Clostridium bacteremia usually occurs in patients with tumors

Treatment

Treatment for Suppurative myositis or myonecrosis:

- Prompt and extensive debridement.
- Antibiotics (penicillin) administration.
- Hyperbaric oxygen may "detoxify" patients rapidly.
- Efficacy of antitoxins is doubtful.
- C. perfringens food poisoning requires only symptomatic care.

Prevention, and Control

- Preventive measures: surgical debridement and prophylactic antibiotics.
- Immediate cleansing of dirty wounds, deep wounds, decubitus ulcers, compound fractures, and infected incisions
- Debridement of disease tissue
- Large doses of cephalosporin or penicillin
- Hyperbaric oxygen therapy
- No vaccines available

Importance of Prompt Antibiotic Treatment

- Antibiotic therapy is started immediately in very high doses. This must take account of the likely coexistence of coliform organisms, Gram-positive cocci and faecal anaerobes. Accordingly, **penicillin, metronidazole and an aminoglycoside** may be given in combination. Alternatively, clindamycin plus an aminoglycoside or a broadspectrum antibiotic, such as meropenem or imipenem, may be considered. Much intensive supportive therapy is needed.

Clostridium tetani

Anaerobic bacteria of the genus species Clostridium it is gram positive, slender bacillus and it has spherical terminal spores giving drum stick appearance. It is non capsulated & motile with peritrichus flagella

It produces a potent biological toxin, tetanospasmin, and is the causative agent of tetanus a disease characterized by painful muscular spasms that can lead to respiratory failure and, in up to 40% of cases, death.

What is the tetanus

An infectious disease caused by contamination of wounds from the bacteria Clostridium tetani, or the spores they produce that live in the soil, and animal feces. Infection follows when spores become activated and develop into gram-positive bacteria that multiply and produce a very powerful toxin (tetanospasmin) that affects the muscles.

Causes

Tetanus spores are found throughout the environment, usually in soil, dust, and animal waste. Tetanus is acquired through contact with the environment; it is not transmitted from person to person. The usual locations for the bacteria to enter the body:

- Puncture wounds (such as those caused by rusty nails, splinters, or insect bites.)
- Burns, any break in the skin, and IV drug access sites are also potential entryways for the bacteria.

Mode of action of tetanospasmin

1. It inhibits the release of acetylcholine thus it interferes with neuromuscular transmission.

2. Inhibition of postsynaptic spinal neurons by blocking the release of an inhibiting mediator

Clostridium Difficile

"C. diff", is a species of Gram-positive bacteria of the genus Clostridium that causes diarrhea and other intestinal disease when competing bacteria are wiped out by antibiotics.

Most common cause of nosocomial diarrhea.

Clostridium difficile is a bacterium that can cause symptoms ranging from diarrhea to life-threatening inflammation of the colon. Illness from C. difficile most commonly affects older adults in hospitals or in long term care facilities and typically occurs after use of antibiotic medication

Habitant

C. difficile bacteria can be found throughout the environment — in soil, air, water, and human and animal feces. A small number of healthy people naturally carry the bacteria in their large intestine. But C. difficile is most common in hospitals and other health care facilities, where a much higher percentage of people carry the bacteria.

Pathogenesis

Disruption of normal colonic flora. Colonisation with C. difficile, Production of toxin A+/- B, Mucosal injury and inflammation

Toxigenic strains produce 2 major toxins:

toxin A (enterotoxin)

toxin B (cytotoxin) , Neutralised by C. sordellii antitoxin

Signs and symptoms

Watery diarrhea three or more times a day for two or more days. Mild abdominal cramping and tenderness . Watery diarrhea 10 to 15 times a day. Abdominal cramping and pain, which may be severe Fever , Blood or pus in the stool. Nausea. Dehydration. Loss of appetite. Weight loss

Closteridium Botulinum

Gram positive, Obligate anaerobic bacillus,

Spores: 1- Resistant to heat, light, drying and radiation

2- Specific conditions for germination: Anaerobic conditions, Warmth (10-50oC), Mild alkalinity

Transmission

Ingestion : Organism, Spores, Neurotoxin

Wound contamination

Inhalation

Person-to-person not documented

Diagnosis

- The symptoms of botulism are similar to those of Guillain-Barré syndrome, stroke,and myasthenia gravis.
- As a result, botulism is probably substantially under-diagnosed.
- Serum electrolytes, renal and liver function tests, complete blood tests, urinalysis, and electrocardiograms will all be normal unless secondary complications occur.

- The incubation period varies according to the mode of transmission, rate of absorption of the toxin, and the total amount and type of toxin.
- Foodborne botulism usually takes 24-36 hours to manifest itself.
- Wound botulism often takes 3 or more days to appear
- Inhalation botulism has occurred very rarely, but incubation times may range from several hours to perhaps days, again depending upon the type and amount of toxin inhaled.
- All four types of botulism result in symmetric descending flaccid paralysis of motor and autonomic nerves always beginning with the cranial nerves. These symptoms are preceded by constipation in cases of infant botulism.

Symptoms include:

- Double or blurred vision
- Drooping eyelids
- Dry mouth

- Difficulty Swallowing
- Muscle weakness
- If left untreated symptoms may expand to include paralysis of respiratory muscles as well as the arms and legs.
- Asphyxiation due to respiratory paralysis is the most common cause of death in botulism cases

Prevention

- Proper food preparation is one of the most effective ways to limit the risk of exposure to botulism toxin.
- Boiling food or water for ten minutes can eliminate some strains of Clostridium botulinum as well as neutralize the toxin as well. However, this will not assure 100% elimination.
- Limiting growth of Clostridium botulinum and the production of botulism toxin is an alternative to their outright destruction.

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