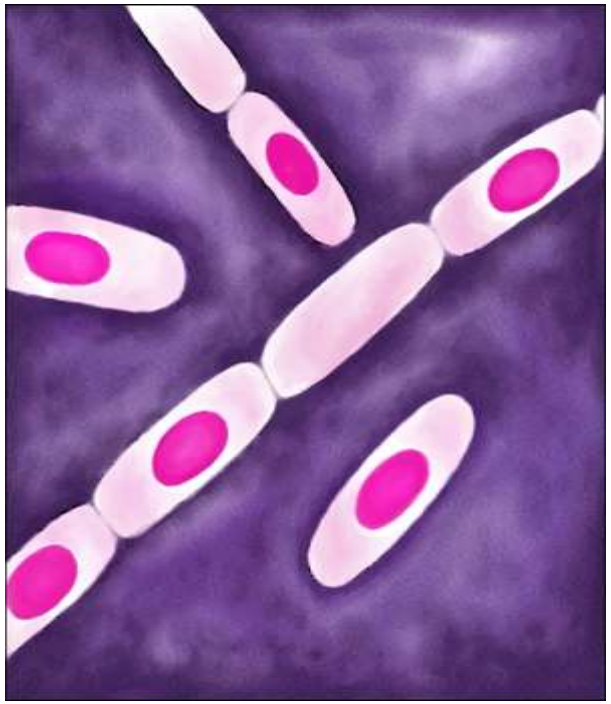
Spore-forming G positive bacilli

- Aerobic (Bacillus)
- Anaerobic (clostridia)

These bacilli are ubiquitous & because they form spores they can survive in the environment for many years. Several species causes important disease in human.

Bacillus

These include large aerobic G positive rods occurring in chains, most of them are saprophytic prevalent in soil, water, air & on vegetation e.g. *B. cereus & B. subtilis*. The location of the spore is either central, terminal, or subterminal according to species. The spores are resistant to environmental changes, dry heat & certain chemical disinfectant & can persist for years in dry soil.



B. anthracis:

It causes the **anthrax**, which is a primarily a disease of animals. Human becomes infected incidentally by contact with infected animals or their products. Soil is contaminated with spores from the carcasses of dead animals & can remain viable for decades. Spores can germinate in soil at PH 6.5 at proper temperature.

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B. anthracis:

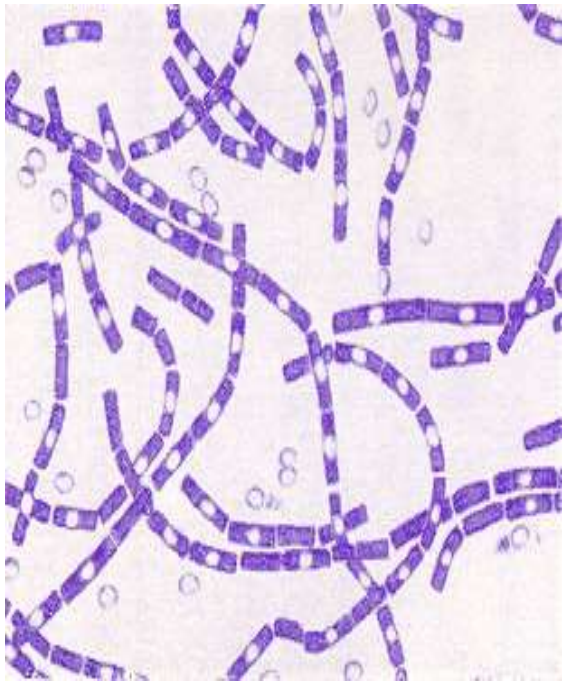
Pathogenesis:

In animals the portal of entry is the mouth & GIT. In human the infection usually acquired by entry of spores through skin wounds (**Cutaneous anthrax**) or rarely through mucous membrane (**Gastrointestinal anthrax**) or through inhalation of spores (**Inhalation anthrax**).

The spores **germinate** in the tissues at the site of entry. Growth of vegetative organism & start secreting the toxin result in formation of gelatinous edema & congestion. Bacilli via lymphatic **recah to** the blood stream. Capsulated *B. anthracis* is only pathogenic & can cause anthrax. The poly D- glutamic acid capsule is antiphagocyric.

Anthrax toxin is composed of three proteins; protective protein (PA), edema factor (EF)& lethal factor (LF).PA bind to specific cell receptors forming a membrane channel that mediate entry of EF & LF into the cell. LF & PA form lethal toxin, which is a major virulence factor.

In inhalation anthrax (**Wool sorter disease**) the spores from dust of wool or hair are inhaled & phagocytosed in the lung & transported to mediastinal LNs where germination occur followed by toxin production & development of hemorrhagic mediastinitis & sepsis that are usually fatal.



Clinical findings:

In human, 95% of cases are cutaneous anthrax & 5% are inhalation anthrax. Cutaneous anthrax generally occur on arms or hands & less frequently on face & neck. A pruritic papule at the site of entry (wound or scratches). The papule rapidly change to vesicle & coalesce & necrotic ulcer develop. The lesion is typically 1-3 cm in diameter with central black eschar. Marked edema & enlargement of LNs with systemic signs & symptoms of fever, malaise & headache may occur.

The early clinical manifestations of inhalation anthrax is marked hemorrhagic necrosis & edema of the mediastinum & substernal pain. Hemorrhagic pleural effusion. Cough is secondary to the effect on trachea. Sepsis occur. Spread to GIT may lead to bowel ulceration & to the meninges causing hemorrhagic meningitis. The fatality rate is 85-90%.

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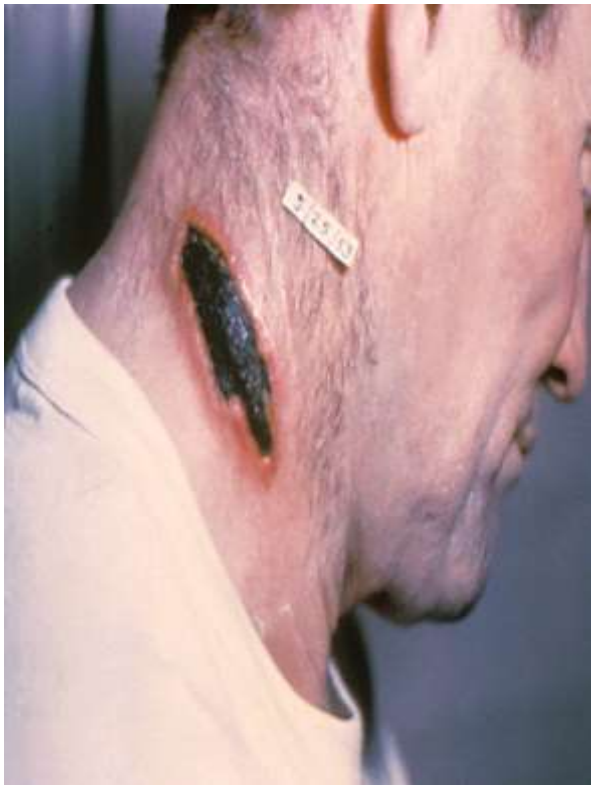
B. anthracis:



Laboratory diagnosis:

1. specimens : fluid or pus from local lesion. Blood, sputum.

2. Gram- stained smear usually revealed chains of large G positive rods. Dried smear may be stained by fluorescent stain.

3. Culture on blood agar yield gray to white non-hemolytic colonies with ground-glass appearance common shaped outgrowth (Medusa head)may project from the colony.

4. Serological tests: ELISA to detect antibodies against edema & lethal toxins.

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B. anthracis:

Colonies of *B. anthracis*

B. cereus is a soil organism that commonly contaminate rice. Food poisoning caused by *B. cereus* has two distinct types; the emetic type associated with fried rice & the diarrheal type associated with meat & sauces. The toxin produced by *B. cereus* caused an intoxication rather than food-borne infection. The emetic type which is manifested by nausea, vomiting, abdominal crumps, it is self-limited, recovery occur within 24 hrs. The diarrheal type (1-24 hrs incubation period) manifested by profuse diarrhea with abdominal crumps & pain.

B. cereus is an important cause of eye infection when the bacterium introduced to the eye with foreign bodies with trauma. *B. cereus* has also been associated with localized & systemic diseases e.g. endocarditis, meningitis, osteomyelitis & pneumonia.

Spore-forming G positive bacilli

B. cereus

Spore-forming G positive bacilli

Clostridia

Cl. botulinum

These are large anaerobic G positive rods. Their natural habitat is the soil & intestine of animals & man.

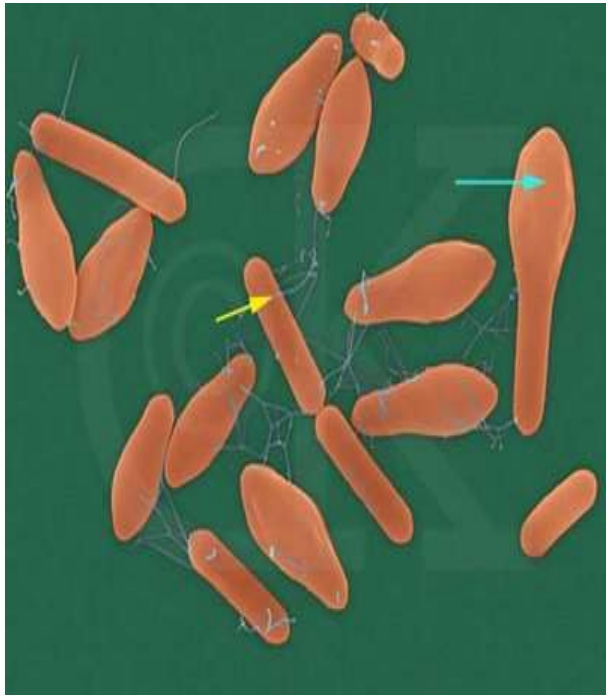
Morphology & identification:

Spores of clostridia are usually wider than the diameter of the rod. They may be centrally, subterminally or terminally located.

Culture: clostridia are strictly anaerobic, some produced large, raised colonies with entire margin (e.g. *Cl. Perfringens*), other produce small colonies (*Cl.tetani*). Many clostridia produce hemolysis (*Cl. Perfringens*).

Cl. botulinum

It is worldwide in distribution, found in soil & occasionally in animal feces. The spores are highly resistant to heat (100 C for 5 min.). *Cl. Botulinum* produces several antigenic types of toxins (A-G). Type A,B & E(and occasionally F) caused human illness. Type A & B are associated with a variety of food. Type E predominantly with fish products.



Spore-forming G positive bacilli

Clostridia

Cl. botulinum

Pathogenesis:

Botulism is an intoxication rather than infection resulted from ingestion of food (Mostly smoked or canned food that are eaten without cooking) contaminated with spores which germinate under anaerobic conditions. Vegetative form grows & produces toxin. The toxin is absorbed from the gut and binds to receptors of presynaptic membrane of motor neurons of PNS & cranial nerves. It inhibits the release of acetylcholine at neuromuscular junction resulting in lack of muscle contraction & flaccid paralysis. *Cl. Botulinum* toxins are among the most highly toxic substance known for human. The toxin can be destroyed at 100 C for 20 min.

Clinically:

Symptoms begin 18-24 hrs. after ingestion of toxic food with visual disturbances, inability to swallow & speech difficulty. Death occurs due to respiratory paralysis or cardiac arrest. The mortality rate is high. Recovered patients do not develop serum antitoxin.

Infant botulism is more common than classical paralysis botulism associated with ingestion of toxin-contaminated food. Infants in the first months of life develop poor feeding, weakness & signs of paralysis (floppy baby). Infant botulism may be one of the causes of sudden infant death syndrome.

Laboratory diagnosis:

1. Toxin can be demonstrated in serum of patients & in the leftover food.
2. Culture of leftover food.
3. Test for toxin production & antigenic type can be identified with specific antitoxin.
4. In infants *Cl. Botulinum* & its toxin may be found in feces but not in serum.

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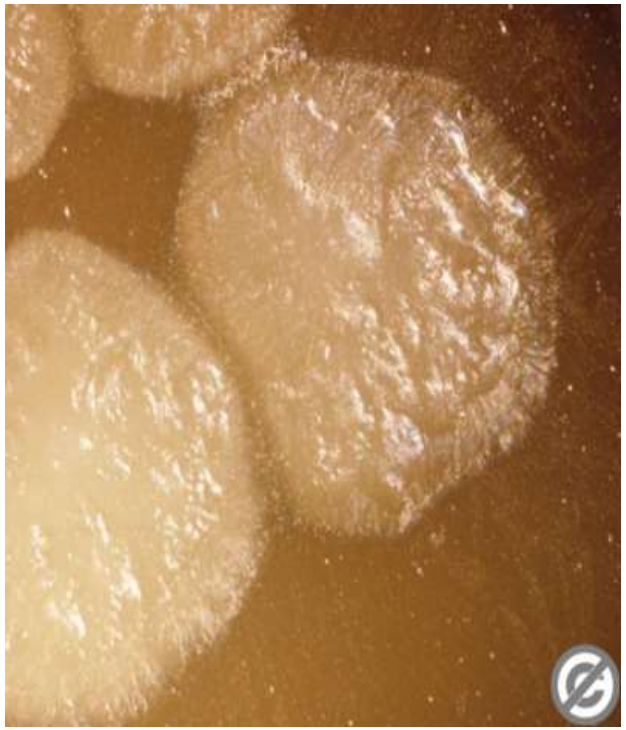
Clostridia

Cl. botulinum



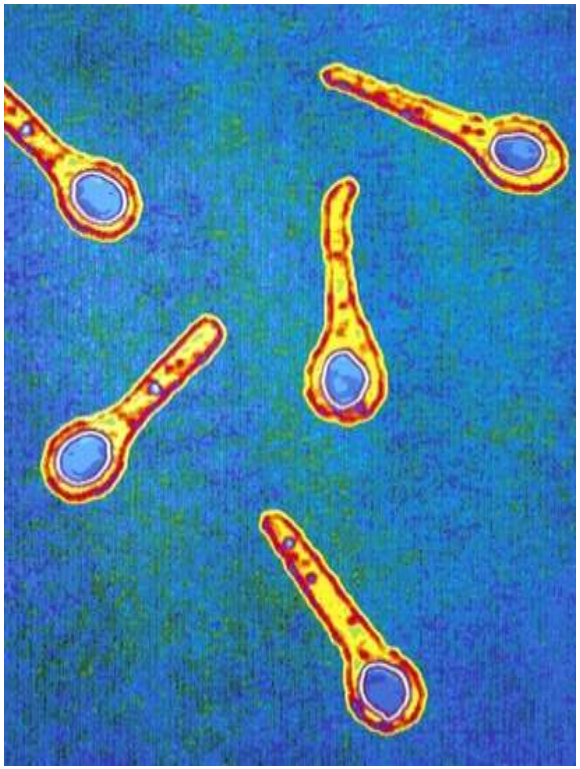
Spore-forming G positive bacilli

Clostridia

Cl.tetani

Cl.tetani that causes **tetanus** is worldwide in distribution in the soil & in the feces of herbivorous animals & man. All types of *Cl.tetani* share common O (somatic) antigen & can be differentiated by specific flagellar antigens. All produce the same antigenic type of neurotoxin (tetanospasmin). Autoclaving (123 C 15 lb/sq inch for 20 min.) can destroy the *Cl. Tetani* spores.

The vegetative cells of *Cl.tetani* produce the tetanospasmin that initially binds to receptors on the presynaptic membrane of motor neurons, then it migrate by the retrograde axonal transport system to spinal cord & brain. Hyperreflexia , muscle spasm & spastic paralysis result.



Pathogenesis:

Cl.tetani is not an invasive organism. The infection remains localized in the area of tissues (wounds burns, umbilical stump, surgical suture) into which the spores have been introduced. Germination of spores & vegetative cells produce toxin. Toxin production are aided by 1. Necrotic tissues 2. Calcium salt 3. Associated pyogenic infections. The toxin reaches the CNS & rapidly become irreversibly fixed to receptors in the spinal cord & brain & exerts it action.

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Clostridia

Cl.tetani

Clinical findings:

The incubation period range from 5 days to many weeks. The disease is characterized by rigidity & spasm of voluntary muscles beginning at the site of injury, followed by the muscles of the jaw (Lockjaw). Gradually, other voluntary muscles are involved result in tonic spasm. Death occurs due to interference with respiration. The mortality rate in generalized tetanus is high.

Tetanus neonatorum is an enormously important medical problem in developing countries. The cause is sepsis of umbilical stump.

Laboratory diagnosis:

1. Gram-stained smear from suspected specimens revealed drum-stick appearance G positive rods.

2. Anaerobic culture of tissues or materials from contaminated wounds.

Detection of *Cl. Tetani* in swabs from surgical or maternity theatres necessitates closure & fumigation of these theatres & reopened only if the subsequent culture is negative.

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Clostridia

Cl.tetani

Prevention:

Passive immunization: prophylactic use of human antitoxin (tetanus immunoglobulin) (I.M. injection of 200-500 units) may gives protection for 2-4 weeks. It neutralizes toxin that has not been fixed to nervous tissues. Active immunization with tetanus toxoid should be given with antitoxin prophylaxis.

Active immunization: with tetanus toxoid should be given to all children during the first year of life. 3 doses followed by a dose at 1 year later. A booster dose is given at school entry. In young children tetanus toxoid is often combined with diphtheria toxiod and pertussis vaccine (**DPT**).

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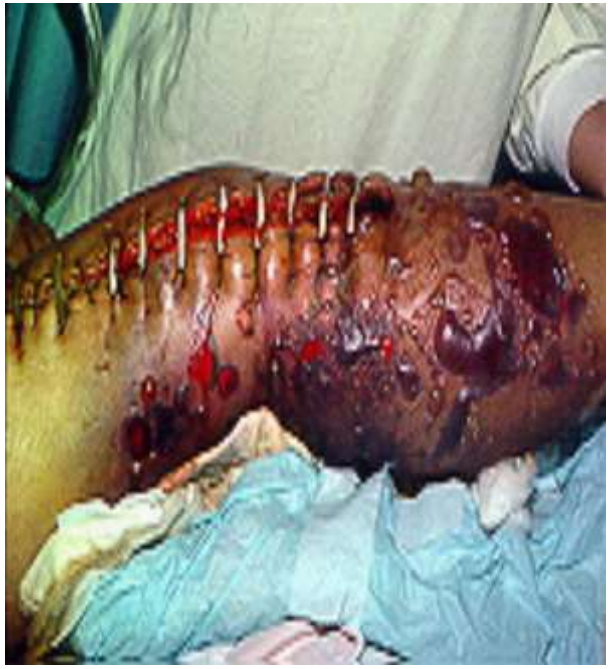
Clostridia

Cl.perfringens

The most common (90%)clostridia causing invasive infection including myonecrosis & gas gangrene when introduced into damaged tissues. The invasive clostridia produce a large variety of toxins & enzymes that resulted in spreading of infection. These toxins may be lethal, necrotizing or hemolytic. The alpha toxin of clostridia is lecithinase (Lecithin is an important constituent of cell membrane) The theta toxin has hemolytic & necrotizing effect. DNAase & hyaluronidase; a collagenase that digest collagen & subcutaneous tissues & muscles. Some strains of *Cl. Perfringens* produce a powerful enterotoxin that can induce diarrhea within 6-18 hrs.



Spore-forming G positive bacilli

Clostridia

Cl.perfringens

Pathogenesis:

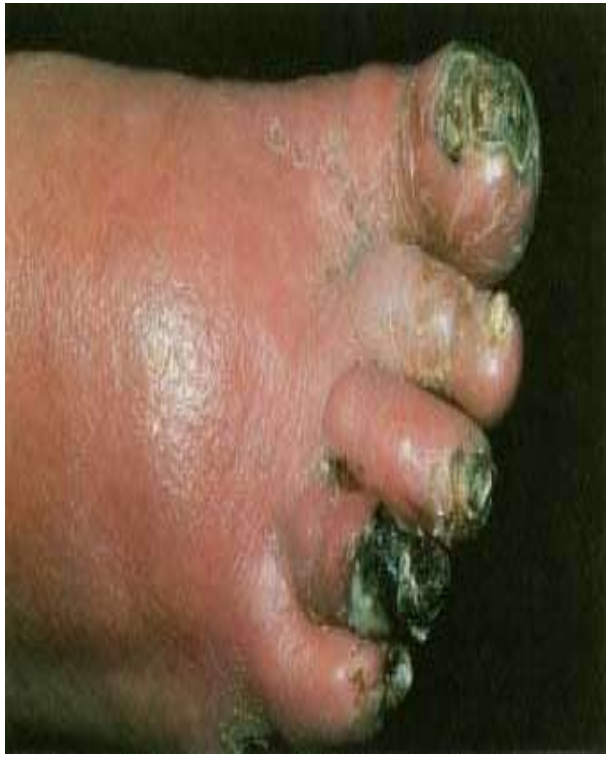
The spores reach tissues either through contamination of area with soil or feces or from the intestinal tract. The spores germinate, the vegetative cells multiply & ferment carbohydrates in tissues producing gas. Distension of tissues & interfere with blood supply together with secretion of necrotizing toxin & hyaluronidase favor the spread of infection. Extension of tissue necrosis increased the bacterial growth result in hemolytic anemia, severe toxemia & death.

Gas gangrene (clostridial myonecrosis) is a mixed infection (Toxogenic & proteolytic clostridia with various cocci & G negative rods). *Cl. Perfringens* occurring in genital tract of 5% of women.

Clinical findings:

From contaminated wounds (Fractures, postpartum uterus) the infection spread in 1-3 days to produce crepitation in the subcutaneous tissue & muscles, foul-smelling discharge, rapidly progressive necrosis, fever, hemolysis, toxemia, shock & death.

Cl.perfringens food poisoning usually follow the ingestion of large number of clostridia. The toxin is produced when the clostridia sporulation in the gut, with onset of diarrhea usually without vomiting or fever in 6-18 hrs. The illness only lasts for1-2 days.



Spore-forming G positive bacilli

Clostridia

Cl.perfringens

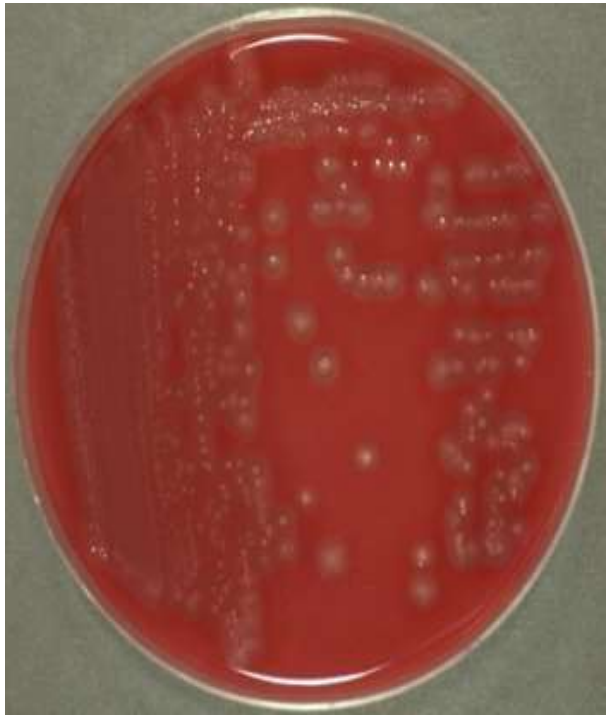
Laboratory diagnosis:

Specimens: Materials from wounds, pus.

Gram-stained smear showed G positive rods.

Culture: on meat-extract medium or thioglycolate medium & on blood agar (Incubated anaerobically). Further identification based on colonial morphology, hemolysis & biochemical reactions.

Identification of toxin production & neutralization with specific antitoxin.



pseudomembranous colitis

Administration of antibiotics result in proliferation of drug-resistant *Cl. difficle* causing watery or bloody diarrhea, sometimes with abdominal crumps, leukocytosis & fever. *Cl.difficile* produce two toxins; toxin A, a potent enterotoxin that may also have cytotoxic activity. It binds to brush border of mucous membrane of the gut at receptor sites. Toxin B is a potent cytotoxin (Both toxins are found in the stool of patients with pseudomembranous colitis).

The most common antibiotics that associated with PMC are ampicillin & clindamycin.

The diagnosis is by detection of one or both *Cl. Difficile* toxins in the stool & by endoscopic observation of pseudomembrane or microabsses.

Antibiotic associated diarrhea:

The administration of antibiotics frequently leads to a mild to moderate form of diarrhea termed AAD. The condition is less severe than PMC. About 25% of AAD is caused by *Cl. difficile*.

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Clostridia

Cl. difficile