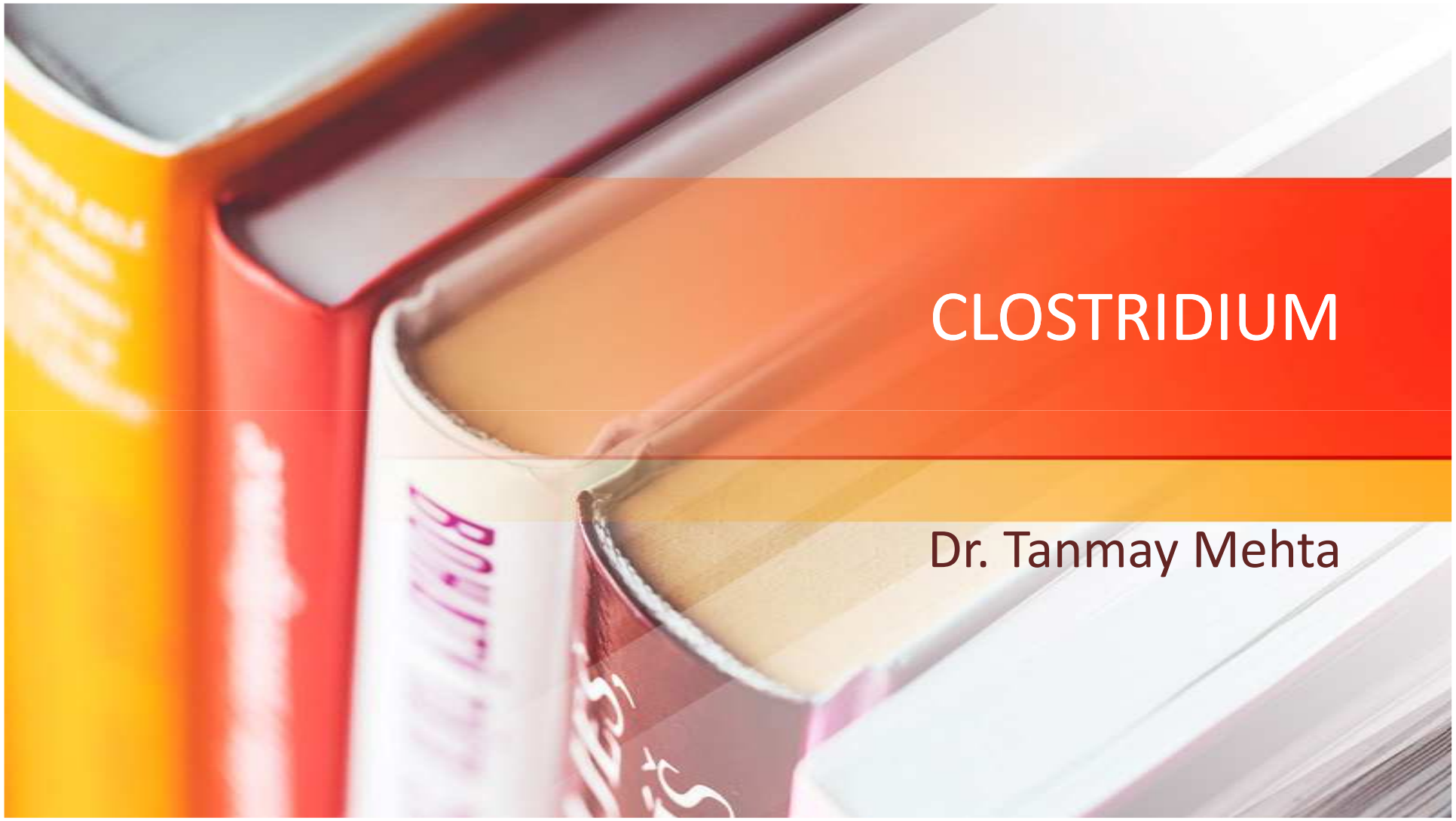


CLOSTRIDIUM

Dr. Tanmay Mehta

Learning objectives

At the end of the session, the students will be able to

- Describe morphology and antigens
- Describe Pathogenesis & Clinical features
- Choose appropriate lab diagnosis and interpret the results
- Describe prevention and treatment

Ananerobes

- Anaerobic bacteria do not have cytochrome system for oxygen metabolism and hence are unable to neutralize toxic oxygen metabolites
- Classification
- **Obligate anaerobes:** Cannot tolerate O2. Completely lack superoxide dismutase and catalase enzymes
- **Aerotolerant anaerobes:** Do not utilize oxygen forgrowth, but tolerate its presence. Possess small amounts of superoxide dismutase and peroxidase (but lack catalase)

Special requirements to grow Anaerobes

- **Anaerobic condition:**

- McIntosh and Filde's anaerobic jar
  - GasPak system
  - Anoxomat system
  - Anaerobic glove box
  - Pre-reduced anaerobically sterilized (PRAS) media.

- **Medium with low redox potential:** By adding reducing substances -unsaturated fatty acid, ascorbic acid, glutathione, cysteine, glucose, sulfites and metallic iron

CLOSTRIDIUM

- Gram-positive bacilli, having bulging spores
- Saprophytes found in soil, fresh water, marine water, decaying vegetation, animal matter and sewage
- Harbored in intestine of vertebrates and invertebrates
- **Human Pathogens:**

- *C. perfringens: Gas gangrene*
- *C. tetani: Tetanus*
- *C. botulinum: Causes botulism*

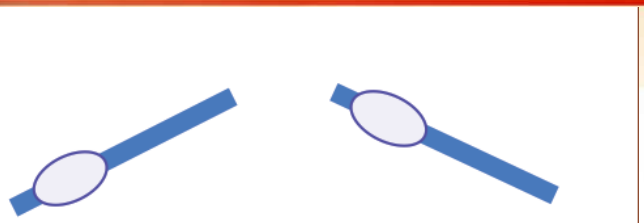
- *C. difficile: Causes pseudomembranous colitis.*

Spore of Clostridia

- Wider than the vegetative bacteria → swollen or spindle-shaped appearance
- Most of the clostridia bear a sub-terminal spores except
- C.bifermentans – Central & oval
- C.perfringens – subterminal & oval
- C.tetani – terminal & spherical (drumstick)
- C.tertium – terminal & oval (tennis racket)

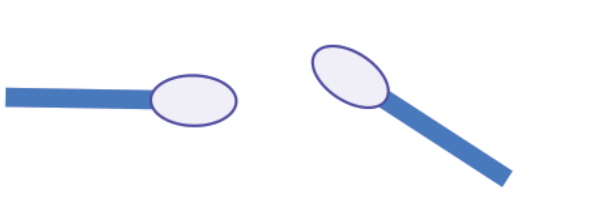
Spores of Clostridia

Oval and central spores
(e.g. *Clostridium bifermentans*)



Subterminal spores
(e.g. *Clostridium perfringens*)

Spherical and terminal spores
(e.g. *Clostridium tetani*)

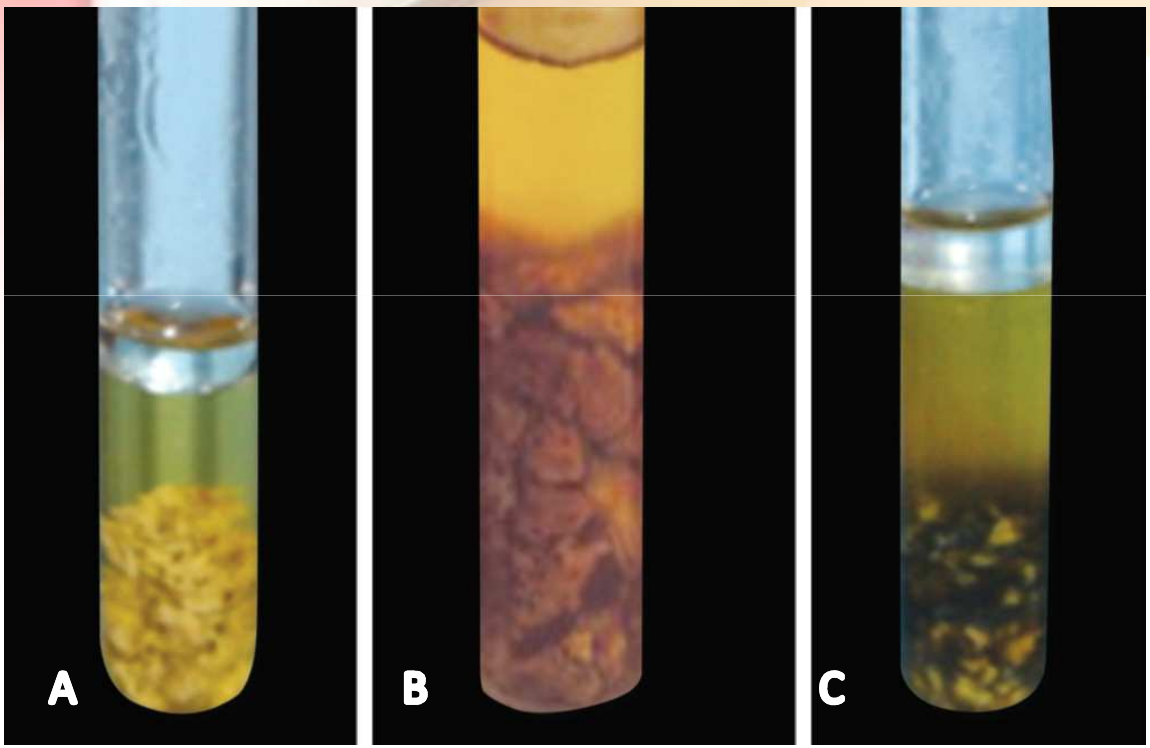


Oval and terminal spores
(e.g. *Clostridium tertium*)

Cultivation

- Clostridia grow well in common anaerobic media
- **Robertson's cooked meat (RCM) broth**
- Chopped meat particles → glutathione and unsaturated fatty acids which take up oxygen
- Proteolytic - turn the meat black and produce foul odor, e.g. *C. tetani, C. botulinum A, B and F.*
- Saccharolytic species - turn the meat pink, e.g. *C. perfringens, C. difficile and C. botulinum C, D and E.*

Robertson cooked meat broth: A. Uninoculated;
B. Pink and turbid (*C. perfringens*); C. Black and turbid (*C. tetani*)



CLOSTRIDIUM PERFRINGENS

CLOSTRIDIUM PERFRINGENS

- *C. perfringens (previously, C. welchii)* - commensal in human animals large intestine and environmental saprophyte
- Capsulated, non-motile, gram-positive bacillus
- Sub-terminal bulging spores, NO spores in tissues or in culture media (especially the gas gangrene strains)
- Invasive and toxigenic.

Major Toxins of *C.difficile*

Toxin	Biological activity
Alpha (α)	Lethal, lecithinase (phospholipase C) Hemolytic, Requires Ca^{+2} ion
Beta (β)	Lethal, necrotizing, trypsin labile
Epsilon (ε)	Lethal, permease, trypsin activatable
Iota (ι)	Lethal, dermonecrotic, Binary, has 2 fragments • A-ADP ribosylating • B- Binding
Alpha (α)	Lethal, lecithinase (phospholipase C) Hemolytic, Requires Ca^{+2} ion

Minor Toxins of *C.difficile*

Toxin	Biological activity
Gamma(γ)	Not defined
Delta(δ)	Hemolysin
Lamda (λ)	Protease
Kappa (κ)	Collagenase and gelatinase
Theta (θ)	Hemolysin (O_2 labile) Cytolysin
Eta(η)	Not defined
Mu(μ)	Hyaluronidase
Nu(υ)	Deoxyribonuclease

Classification of *C.perfringens*

Type	Major Toxin produced	Disease
A	Alpha	Gas gangrene, Food poisoning
B	Alpha, beta and epsilon	Lamb dysentery
C	Alpha and beta	Enteritis necroticans in humans
D	Alpha and epsilon	Enterotoxemia and pulpy kidney disease in sheep
E	Alpha and iota	Possible pathogen of sheep and cattle

Clinical Manifestations

- Mostly polymicrobial involving other clostridia species
- **Clostridial Wound Infection** *(*MacLennan Classification*)*
- **Simple wound contamination:** wound surface contamination, without invasion of underlying tissue, as occurs in absence of devitalized tissue
- **Anaerobic cellulitis:** Involves fascial plane with minimal toxin release, without muscle invasion
- **Anaerobic myositis (gas gangrene):** Muscle invasion occurs, which leads to gas in the muscle compartment with abundant toxin release

Clostridial Enteric Infection

- **Food poisoning:** *C. perfringens type A* enterotoxin (

- Improperly cooked contaminated meat

- Diagnosis: By detection of enterotoxin in feces by enzyme immunoassay

- **Enteritis necroticans (gas gangrene of the bowel/ Bigbel/ Darmbrand):** life-threatening condition - ischemic necrosis of the jejunum and gas in the tissue plane

- Caused by *C. perfringens type C strains, producing*β toxin

- **Necrotizing enterocolitis:** associated with *C. perfringens type A*

- **Gangrenous appendicitis.**

Other Clostridial Infections

- **Bacteremia:** *C. perfringens followed by C. tertium and C.septicum*
- **Skin and soft-tissue infections:** *C. perfringens, C.histolyticum, C. septicum, C. novyi, and C. sordellii*
- Endometritis leading to toxic shock - *C. sordellii*
- Meningitis and brain abscess
- Panophthalmitis (due to *C. sordellii or C. perfringens).*

Gas Gangrene

- Rapidly spreading, edematous myonecrosis, in association with severely crushed wounds contaminated with pathogenic clostridia, particularly with *C. Perfringens*
- **Etiological agents -** always polymicrobial

- Established agents: *C. perfringens (60%)* & *C.novyi and C.septicum (20–40%)*

- **Probable agents:** less commonly implicated — *C.histolyticum, C.sporogenes, C.fallax, C.bifermentans, C.sordellii, C.aerofoetidum and C.tertium.*

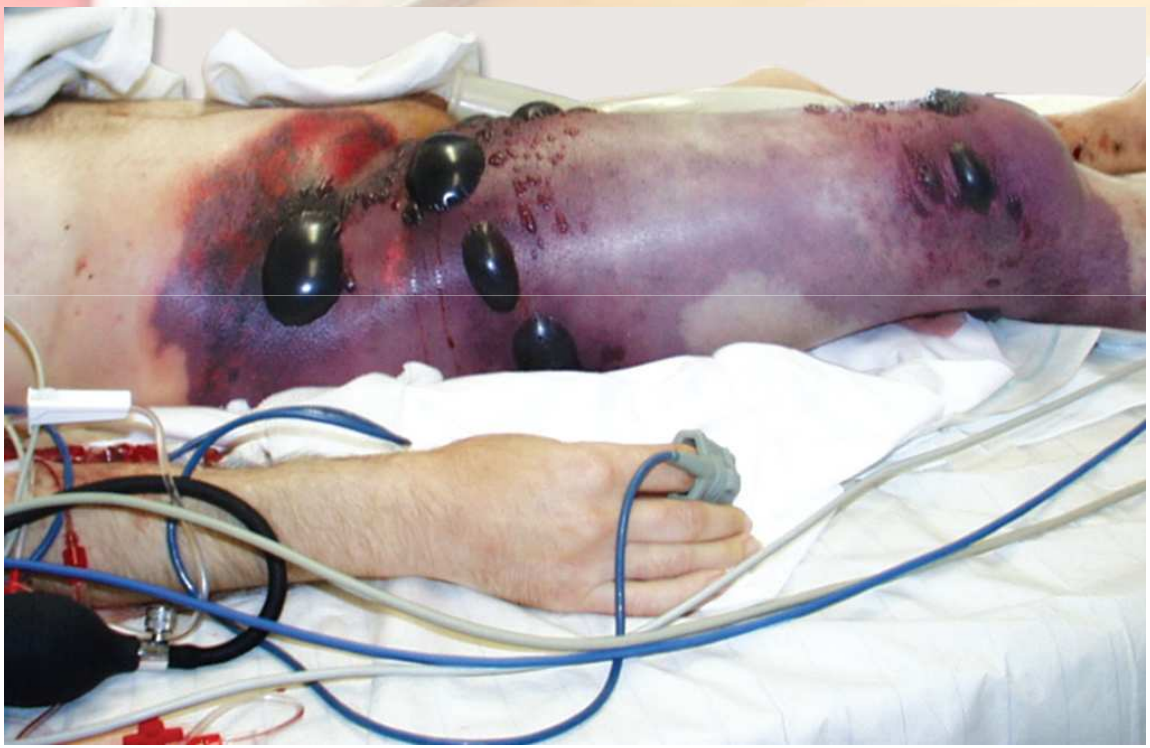
Pathogenesis

- **Anaerobic environment:** Crushing injuries of muscles, open fractures of long bone, foreign bodies, devitalized tissues → interruption in the blood supply → tissue ischemia
- **Contamination of wound with clostridial spores** present in the soil (during war or road traffic accident) or clothes
- N**on-traumatic gas gangrene -** rare via hematogenous seeding of normal muscle with bowel clostridia (e.g. colonic malignancy).

Virulence Factors Mediating Gas Gangrene

- **Toxins produced by *C. Perfringens***
- α **toxin** - phospholipase C and sphingomyelinase activities → aggregates of platelets and neutrophils in the bloodvessels causing occlusion
- α toxin directly suppresses myocardial contractility → reduction in the cardiac output →hypotension
- **θ toxin** - marked vasodilation by activating mediators (e.g. prostacyclin, platelet-activating factor).

Gas gangrene



Clinical Manifestation of Gas Gangrene

- **incubation period-** 10 hrs to 7 days, depending upon nature of injury, amount of wound contamination and type of clostridial species involved
- **Clinical manifestations:** Mortality rate (50%)

- Excruciating local **pain** , sudden
- foul-smelling thin serosanguineous discharge
- Gas bubbles **(crepitus)** in muscle planes
- Brawny edema and induration →gangrene & liquefication
- Shock and organ failure

Laboratory Diagnosis of Gas Gangrene

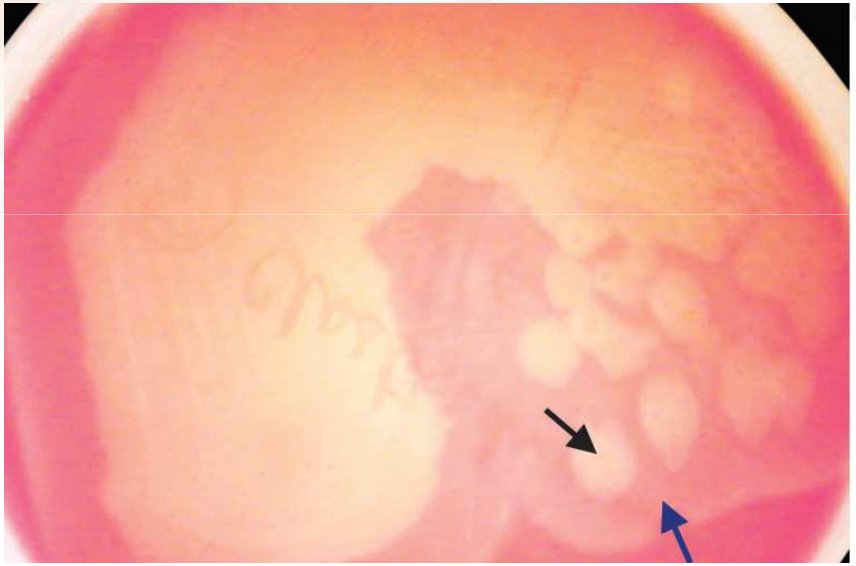
- Treatment to be started early Based on the clinical diagnosis. Laboratory diagnosis has role only for Confirmation of the clinical diagnosis & Species identification
- **Specimen**
- **Ideal samples - Necrotic tissues, muscle fragments and exudates from deeper part of the wound**
- Blood culture if bacteremia is suspected
- **Swabs** rubbed over the wound surface or soaked in exudates are **not satisfactory**
- Transport immediately in Robertson's cooked meat broth

Direct Microscopy

- Absence of neutrophils characteristic feature
- Thick, stubby, boxcar-shaped, gram-positive bacilli without spore— *C. perfringens*
- Spore bearing gram-positive bacilli suggest other clostridia
- Citron bodies - *C.septicum*
- Large rods with oval sub-terminal spores— *C. novyi.*

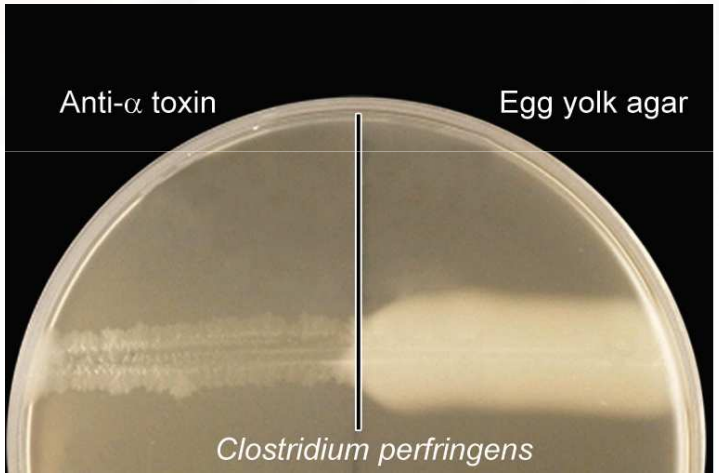
Target hemolysis

- Double zone hemolysis
- Blood agar - inner narrow zone of complete hemolysis (due to θ toxin), surrounded by a much wider zone of incomplete hemolysis (due to the alpha toxin)



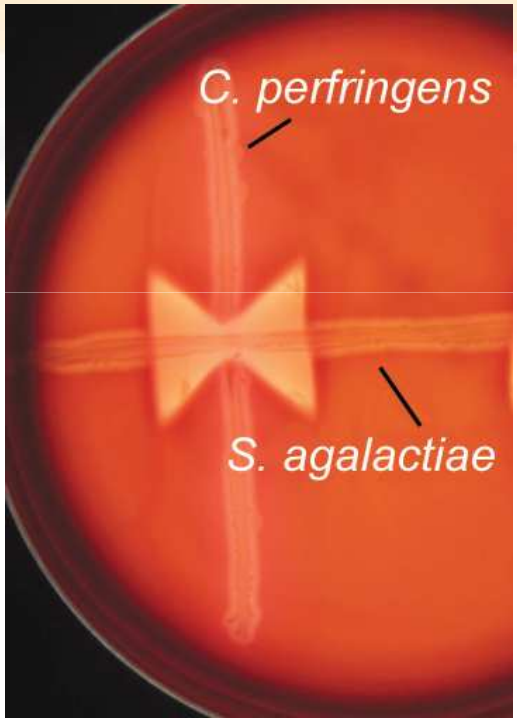
Nagler's reaction

- **Lecithinase activity of α toxin**
- **Opalescence** surrounding streak line on egg yolk agar or media containing 20% human serum
- Opalescence inhibited by anti-α toxin if added in medium
- **Positive** – C.perfringens, *C. Bifermentans,C. baratti and C. sordellii*



Reverse CAMP test

- ***C.perfringens*** is streaked over the center of blood agar plate and **Streptococcus agalactiae** is streaked perpendicular to it
- Presence of **enhanced zone of hemolysis** (arrow-shaped) pointing towards C.perfringens indicates the test is positive



Other tests

- **Heat tolerance:**
- *C. perfringens* can grow when RCM broth is incubated at 45°C for 4–6 hours. This differentiates it from other organisms in the specimen

- **litmus milk-** *C.perfringens* produces ***"stormy clot* reaction"** due to fermentation of lactose producing acid and vigorous gas

Treatment Gas gangrene

- **Early surgical debridement is the most crucial step -** All devitalized tissues widely resected. Closure of wounds delayedfor 5–6 days until the sites are free from infection
- **Antibiotics:** Combination of penicillin and clindamycin is recommended for 10–14 days
- **Hyperbaric oxygen:** may kill the obligate anaerobic clostridia such as *C. perfringens; H*as no effect onaerotolerant clostridia (*C. septicum)*
- **Passive immunization with anti-α-toxin antiserum.**

CLOSTRIDIUM TETANI

CLOSTRIDIUM TETANI

- Obligate **anaerobic, gram-positive bacillus** with terminal round spore (drum stick appearance)
- Causes '**tetanus**'—skeletal muscle spasm and autonomic nervous system disturbance
- *C. tetani* is **ubiquitous in nature**, widely distributed in soil, hospital environment and intestine of man and animals.

Virulence Factors

- **Tetanolysin:** Heat labile, oxygen labile hemolysin. No role in pathogenesis of tetanus
- **Tetanospasmin (or tetanus toxin): neurotoxin** responsible for tetanus
- Prevents the presynaptic release of inhibitory neurotransmitters glycine and GABA, which leads to spastic muscle contraction
- Antigenic. Toxoided by formaldehyde
- Plasmid coded

Mode of Transmission

- Tetanus bacilli enter through:
- **Injury** (superficial abrasions, punctured wounds, road traffic accidents)
- **Surgery** done without proper asepsis
- **Neonates:** Following abortion/delivery, due to **unhygienic** practices
- **Otitis media** (otogenic tetanus)
- Noninfectious: There is no person-to-person spread

Clinical Manifestations

- Incubation period - 6–10 days. Shorter the incubation period, graver is the prognosis. Muscles of the

- Face and jaw are often affected first

- **First symptom: T**rismus or lock jaw, → muscle pain and stiffness, back pain, and difficulty in swallowing

- Neonates - difficulty in feeding

Clinical Manifestations

- **Painful muscle spasm -**

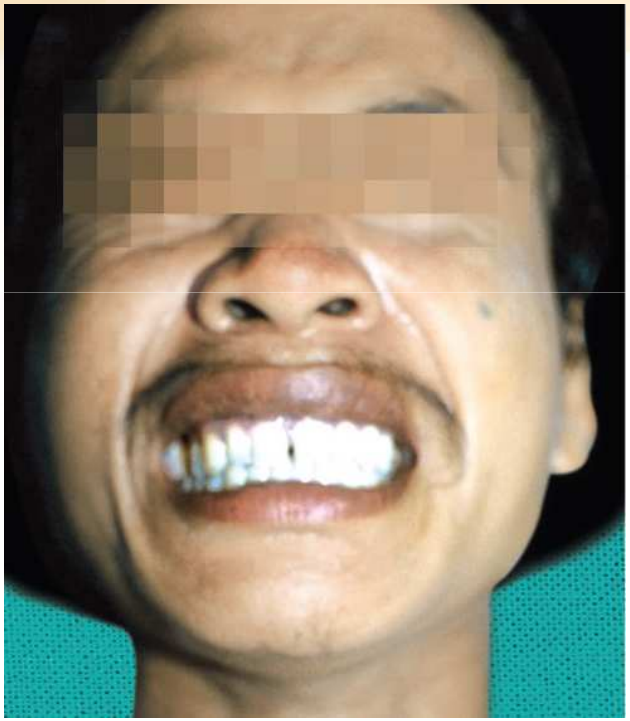
- **Localized:** Involves the affected limb

- **Generalized** painful muscle spasm → leads to descending spastic paralysis

- **Autonomic disturbance** - low or high blood pressure, tachycardia, intestinal stasis, sweating, increased tracheal secretions and acute renal failure.

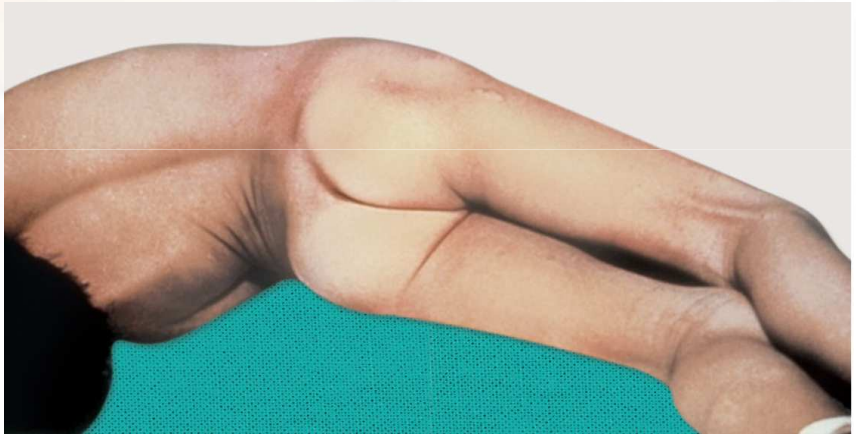
Complications

- R**isus sardonicus:** abnormal, sustained spasm of the facial muscles that appears to produce grinning



Complications

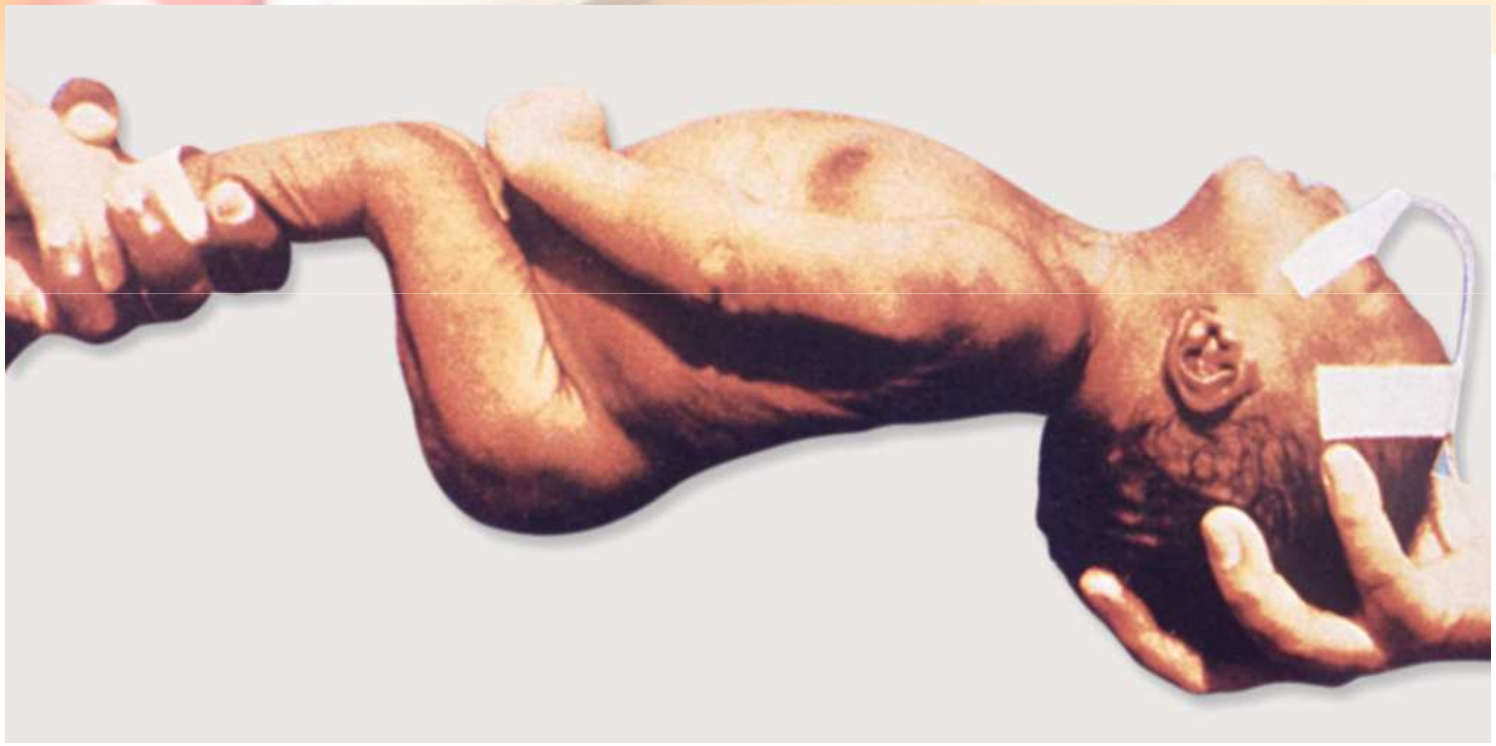
- **Opisthotonos position:** abnormal posture of the body, occurs due to generalized spastic contraction of the extensor muscles
- Respiratory muscles spasm



Neonatal Tetanus

- **Neonatal tetanus (WHO definition) -** 'an illness occurring in a child who loses ability to suck and cry between day 3 and 28 of life and becomes rigid and has spasms'
- Also known as**"8th day disease" as the symptoms usually start after 1 week** of birth
- **Most common reason:** Unhygienic practices during deliveries such as infected umbilical stumps due to application of cow dung, rarely by circumcision or by ear-piercing
- **Seasonal:** More common in July, August and September months

Neonatal tetanus



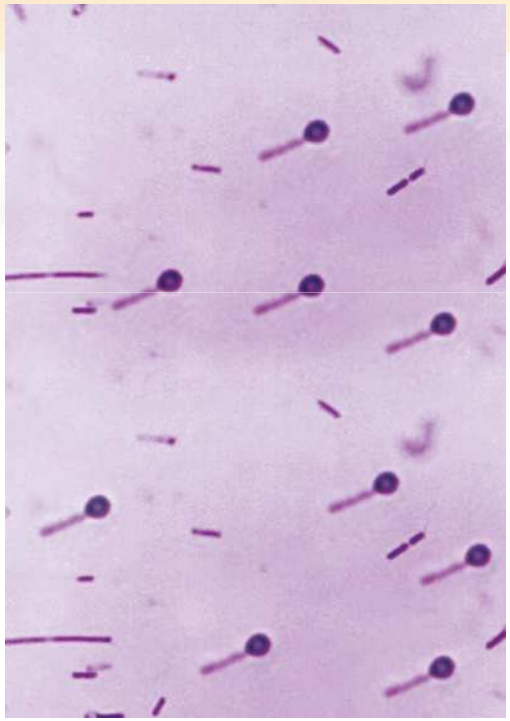
Epidemiology

- Tetanus is more common in developing countries including India due to:
- Warm climate
- Rural area with fertile soil
- Unhygienic surgeries or deliveries.
- Incidence decreasing due to widespread immunization of infants and pregnant mothers

Laboratory Diagnosis

- Treatment started immediately based on clinical diagnosis. Laboratory diagnosis – only supportive
- **Specimen**
- Excised tissue bits from the necrotic depths of wounds
- **Gram Staining**

- Gram-positive bacilli with terminal and round spores (drum stick appearance)



Culture

- Culture is more reliable than microscopy
- **Robertson cooked meat broth:** *C. tetani, being proteolytic* turns the meat particles black and produces foul odor
- **Blood agar with polymyxin B:** These plates are incubated at 37°C for 24–48 hours under anaerobic condition.
- *C. tetani produces characteristic* **swarming growth**

Toxigenicity Test

- ***In vitro hemolysis inhibition test:*** indicates the production of only tetanolysin but not tetanospasmin
- ***In vivo mouse inoculation test:*** growth suspension injected in **root of tail** of mouse. Animal develops **stiffness** which begins with the tail and progresses to involve the hind limbs on the inoculated side → the other limb → trunk →forelimbs.
- **Death** within two days. This test indicates the production of tetanospasmin.

Treatment Tetanus

- **Passive immunization (tetanus immunoglobulin) -** Treatment of choice

1. HTIG (Human tetanus immunoglobulin)
2. ATS (Antitetanus serum, equine derived).

- **Dosage: 250 IU of HTIG or 1500 IU of ATS single** IM
- **Duration of protection:** Effect of HTIG and ATS last for 30 days and 7–10 days respectively

Treatment

- **Combined Immunization** (Both active and passive immunization) - in nonvaccinated person
- **Antibiotics:** Minor role as they cannot neutralize the toxins
- They are useful:

- Early infection, before expression of the toxin (<6 hours)
- To prevent further release of toxin
- Metronidazole - drug of choice. (400 mg rectally or 500 mg IV every 6 hourly for 7 days)
- Penicillin - alternatively

Other measures:

- **Symptomatic treatment**: Antispasmodic (benzodiazepines)can be given
- **Entry wound** should be identified, cleaned and debrided of necrotic material, so as to remove the anaerobic foci of infection
- Patient should be **isolated in a separate room** as any noxious stimulus can aggravate the spasm

Prevention

- *Active Immunization (Vaccine)* - most effective
- **Tetanus toxoid (TT)**

- **Monovalent vaccine:**
- Plain formal toxoid (or fluid toxoid): prepared by exposing to formalin
- Adsorbed: Formol toxoid is adsorbed on to alum
- **Combined vaccine**: DPT (Diphtheria toxoid, Pertussis whole cell killed preparation and Tetanus toxoid)

Prevention

- **Primary immunization of children: Tetanus toxoid**
- 3 doses of Pentavelent vaccine (DPT, Hib HBV) at 6, 10 and 14 weeks of birth → 2 booster doses of DPT at 16–24 weeks and 5 years → two additional doses of TT at 10 years and 16 years
- **Adult immunization:** If primary immunization is not administered in childhood- Four doses of TT; 2 doses at 1 month interval → 2 booster doses at 1 year and 6 years
- **Site:** deep intramuscular route at anterolateral aspect of thigh (children) and in deltoid (adults)
- **Protective titer:** antitoxin titre is ≥0.01 unit/mL.

Prevention of Tetanus after Injury

- Surgical toilet →immunization which depends on the wound type and immunization status of the individual

Type	Major Toxin produced	Disease
A	Alpha	Gas gangrene, Food poisoning
B	Alpha, beta and epsilon	Lamb dysentery
C	Alpha and beta	Enteritis necroticans in humans
D	Alpha and epsilon	Enterotoxemia and pulpy kidney disease in sheep

Prevention of Neonatal Tetanus

- Promoting **hospital or attended deliveries**

- Aseptic **clean practices are followed during** deliveries—clean hand, clean surface, clean blade for cutting cord, clean cord tie, clean cord stump, cleantowel and clean water

- TT (2 doses) - to all pregnant women

- **Neonatal tetanus elimination is based on:**

- Neonatal tetanus rate: 1/1000 live births in every district

- TT coverage to pregnant women >90%

- Attended deliveries >75%

CLOSTRIDIUM BOTULINUM

CLOSTRIDIUM BOTULINUM

- *Clostridium botulinum* produces botulinum toxin and causes botulism
- Latin word *botulus* - sausage (as poorly cooked sausages were formerly associated with food poisoning)
- Anaerobic Gram-positive Bacillus with subterminal spore
- Ubiquitous in nature, saprophyte in soil, animal manure, vegetables and sea mud

Pathogenesis- Botulinum toxin

- Non-invasive
- Pathogenesis is due to production of **powerful neurotoxin 'botulinum toxin' (BT)**
- **Serotype:** Eight serotypes—A, B, C1, C2, D, E, F and G
- Serotypes A, B, E commonly cause human disease; most severe being serotype A
- All serotypes produce neurotoxin; except C2 which produces an enterotoxin
- BT types C and D are bacteriophage coded

Pathogenesis- Botulinum toxin

- Produced intracellularly, **not secreted** and appears outside only after autolysis of bacterial cell
- Synthesized initially as a nontoxic protoxin → trypsin or other proteolytic enzymes convert it into active form
- **Mechanism of Action of Botulinum Toxin (BT)**

  Entry (ingested, inhaled, from wound) → via **blood** to peripheral cholinergic nerve terminals (**neuromuscular junctions**, postganglionic parasympathetic nerve endings, and peripheral ganglia)→ bind to **Ach receptors** at neuromuscular junction →**blockage of release of Ach → Flaccid paralysis**

Botulinum toxin

- Also produced by *C. butyricum , C. baratti and C. argentinense*
- **Recovery:** Blocking of Ach receptor is permanent, but the action is short lasting as the recovery occurs in 2–4 months, once the new terminal axons sprout
- Spores do not produce toxins. Toxin production requires spore germination, which occurs in anaerobic atmosphere
- Spores do not normally germinate in adult intestine, however may germinate in the intestine of infants
- **Therapeutic uses:** Spasmodic conditions such as strabismus, blepharospasm and myoclonus

Clinical Manifestations

- Diplopia, dysphasia, dysarthria
- Descending symmetric **flaccid paralysis of voluntary** muscles
- Decreased Deep tendon reflexes
- Constipation
- Respiratory muscle paralysis, may lead to death
- No sensory or cognitive deficits

Types of Botulism

- **Food-borne botulism:** foods contaminated with preformed botulinum toxin
- Most common source: Homemade canned food
- Mostly sporadic; outbreaks are rare
- **Wound botulism:** Contamination of wounds with *C. botulinum spores*
- Presents like foodborne botulism except for absence of gastrointestinal features

Types of Botulism

- **Infant botulism:**

- Ingestion of contaminated food with spores of *C. botulinum in* children ≤1 year of age

- Manifestations - inability to suck and swallow, weakened voice, ptosis, floppy neck, and extreme weakness (**floppy child syndrome)**

- Self-limiting → Rarely generalized flaccidity, respiratory failure and sudden death. - Management - supportive care

- **Adult intestinal botulism:** suppressed normal flora, colonized clostridial spores may germinate producing toxin
- **Iatrogenic botulism:** injection of overdose of the toxin while used for therapeutic purpose

Laboratory Diagnosis

- **Microscopy of Food/feces**
- Gram-positive, non-capsulated bacilli with subterminal, oval, bulging spores
- Motile by peritrichate flagella
- **Isolation:**
- **RCM broth:** Turbidity occurs with meat particles turning:
- Black and production of foul odor: *C. botulinum A,* B, F (proteolytic)
- Pink: *C. botulinum C, D, E (saccharolytic).*
- **Blood agar:** Irregular, hemolytic with fimbriated border

Toxin Demonstration (Mouse Bioassay)

- Mere presence of bacilli in food or feces is of less significance. **Toxin demonstration is more meaningful**
- **Specimens** - serum, stool, sterile water or saline enema, gastric aspirates, wound material or foods samples
- Specimens injected into mouse → paralysis in 48 hours; which can be inhibited by prior administration of specific antitoxin

Treatment of *Clostridium botulinum*

- Meticulous intensive care support
- **Botulinum antitoxin: A**dministered immediately on clinical suspicion, without waiting for laboratory confirmation. However, once toxin binds to nerve endings, antitoxin has no role
- **Wound botulism** - debrided and drained promptly
- **Antibiotics:** Susceptible to penicillin*;* role of antibiotics has not been established.

CLOSTRIDIOIDES DIFFICILE

CLOSTRIDIOIDES DIFFICILE

- Obligate anaerobic, Gram-positive, spore-forming Bacillus
- Responsible for **pseudomembranous colitis** - in association with prolonged antimicrobial use
- Named due to **unusual difficulties in isolation** of *C.difficile.*
- Taxonomically, it is recently placed into a separate genera, *Clostridioides difficile*

Pathogenesis

- Major cause of hospital-acquired infection mainly in the Western world
- **Risk factors:**
- **Prolonged hospital stay:** Spores in hospital environment colonize colon of patients
- **Prolonged antimicrobial use:** Disruption of normal colonic flora → enhances *C. difficile* infection

- Cephalosporins (e.g. Ceftriaxone) – More common
- Others - Clindamycin, Ampicillin and fluoroquinolones

Toxin production

- Only toxigenic strains are pathogenic
- Two **powerful exotoxins—toxin A (enterotoxin) & toxin B (cytotoxin)**

- Both toxins secreted in intestine → glycosylate GTP binding proteins that regulate the cellular actin cytoskeleton → disruption of the cytoskeleton → loss of cell shape, adherence, and disruption of epithelial cell barrier → diarrhea & pseudomembrane formation

- **Infants** - asymptomatic infection as they lack suitable mucosal toxin receptors

Toxin production

- **Host immune response determine the outcome**

- Strong IgG response to toxin A— become asymptomatic carriers

- Inadequate IgG response to toxin A— develop disease

- **Other risk factors:**

- Suppression of normal flora, Advanced age (>65 years)

- Immunosuppression & malignancy, Gastric acid suppressant medications, Use of electronic rectal thermometer

- **Hypervirulent epidemic strain: BI/NAP1/027** - produces higher levels of toxins and causes severe infection

Clinical Manifestations

- **Diarrhea** – MC manifestation

- Others - abdominal pain and leukocytosis, Blood in stool rare

- **Pseudomembrane:**

- Composition: necrotic leukocytes, fibrin, mucus & cellular debris
- Attaches to the underlying mucosa
- whitish-yellow plaque , 1–2 mm to large enough to spread over the entire colonic mucosa

- Relapse after treatment - 15–30% of cases.

Laboratory Diagnosis

- **Isolation:**
- **Stool culture:** Anaerobic culture on selective
- CCFA (cefoxitin cycloserine fructose agar)
- CCYA (cefoxitin cycloserine egg yolk agar)
- Sensitive and specific
- Since *C.difficile* can be a GIT colonizer the GIT, only isolation is not enough to establish the infection. Toxin demonstration is more meaningful

Laboratory Diagnosis

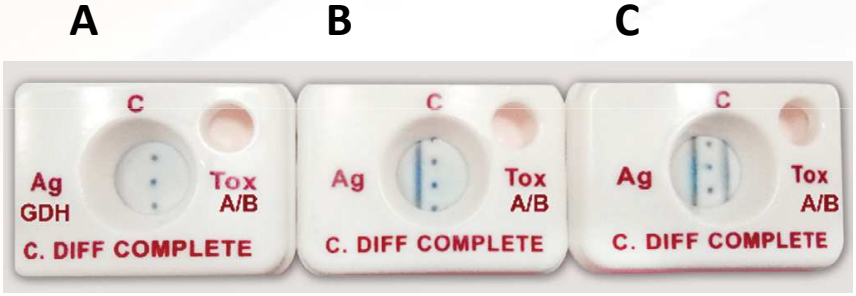
- **Cell culture cytotoxin neutralization assay: Highly** specific but not very sensitive & has long turnaround time
- **Toxin detection:**
- **Toxin and Glutamate dehydrogenase (GDH) detection:** GDH is common antigen present in both toxigenic and non-toxigenic strains
- Enzyme immunoassay or rapid tests

Laboratory Diagnosis

A. **All negative**: Rules out presence of *C. difficile* in stool

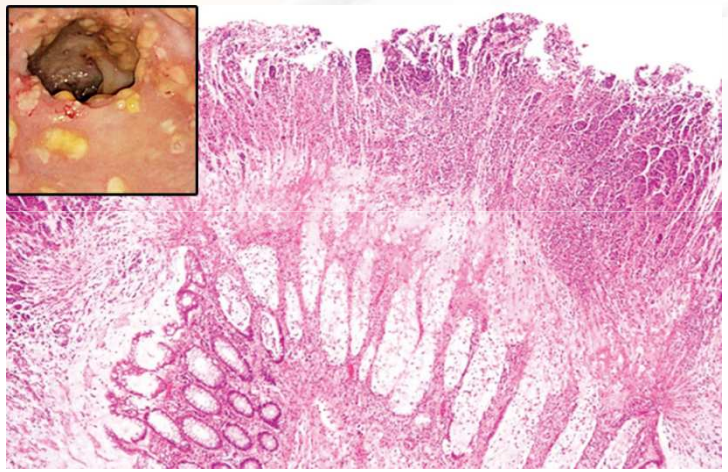
B. **Positive for GDH only**: Confirms presence of nontoxigenic strain of *C.Difficile*

C. **Positive for toxin A and GDH:** Confirms *C. Difficile* expressing either toxin A or toxin B



Laboratory Diagnosis

- **Molecular methods:** PCR, real time PCR, gene Xpert targeting gene coding for *C. Difficile* toxins in stool
- **Colonoscopy:** It is highly specific if pseudomembranes sensitivity is low
- **Histopathology:** highly specific but sensitivity is very



Treatment *Clostridium difficile*

- **<u>Antimicrobial therapy:</u>**
- **Initial episode, mild to moderate cases: Oral metronidazole** (500 mg TID 10–14 days)
- **Recurrent episodes or severe cases: Vancomycin** (500 mg, QID 10–14 days)
- **Severe complicated or fulminant infection:** Vancomycin (via nasogastric tube and by retention enema) plus IV metronidazole

Treatment *Clostridium difficile*

- **<u>Other modalities of treatment:</u>**
- **Intravenous Immunoglobulin:** Passively provide antibodies to neutralize the *C. difficile toxins, primarily toxin A*
- **Fecal transplant:** It involves replenishing of the gut flora with donated feces from a screened healthy donor
- **Fidaxomicin:** It is a macrolide antibiotic, can be used in cases of relapse and also against hypervirulent strains

Prevention (Infection Control Measures)

- Broad spectrum antimicrobials should be stopped at the earliest.
- Infection control measures of contact precaution:

- Strict hand hygiene with chlorhexidine 4% hand wash
- Isolation of patient
- Ensure proper disinfection of floor, surfaces, toilets and other soiled areas using 1% freshly prepared hypochlorite solution