**Colistiradial diseases**

**Colistradium**:

Anaerobic, Gr +ve, spore forming bacilli

Some are saprophytes in soil, sewage and water.

Others are commensals in intestine of man and animals

**Important members cause disease in man:**

* *Cl. Tetani* causing tetanus.
* *Cl. Perfringens* causing gas gangrene and food poisoning.
* *Cl. Botulism* causing botulism.
* *Cl. Difficile* causing pseudomembranouscolitis (antibiotic associated diarrhoea).

**The ability of clostridia to cause various lesions is due to:**

1. ability to survive adverse environmental conditions through *spore* formation.
2. *rapid growth* in a nutritionally enriched, oxygen-deprived environment.
3. production of numerous *histolytic toxins*, enterotoxins, and neurotoxins.

**Clostridium perfringens**

***Clostridium perfringens:****the agent of Gas Gangrene or Myonecrosis  
C. perfringens* produce one or more major lethal toxins: α, β, ε, and ί (iota)

**Clinical Situations:**

1. **Soft-tissue infections**

**Pathogenesis:**

Soil contaminated deep devitalized wounds by the organism or its spores **🡪** the presence of foreign bodies and decreased blood supply**🡪** lowers oxygen tension**🡪** germination of the spores**🡪** vegetative cells multiply and ferment sugars producing large amount of gas which distend the tissue and interfere with blood supply**🡪**tissue death**🡪** cl. Digest dead tissues **🡪** dark color change and foul odour, with crepitation**🡪** generalized toxaemia shock and multiple organ failure

* **Cellulitis:** Localized edema and erythema with gas formation in the soft tissue; generally nonpainful**.**
* **Suppurative myositis (fasciitis):** Accumulation of pus (suppuration) in the muscle planes without muscle necrosis or systemic symptoms
* **Myonecrosis:** Painful, rapid destruction of muscle tissue 🡪 systemic spread with high mortality

1. ***Gastroenteritis:***

* **Food poisoning:** Rapid onset of abdominal cramps and watery diarrhea with no fever, nausea, or vomiting; short, self-limited duration
* **Necrotizing enteritis:** Acute, necrotizing destruction of jejunum with abdominal pain, vomiting, bloody diarrhea, and peritonitis

**Treatment and Prevention:**

* Rapid treatment is essential for serious infections:

Surgical débridement

High-dose penicillin therapy

The value of hyperbaric oxygen treatment is unproven .

Symptomatic treatment for food poisoning.

**Prevention:** adequate wound cleaning and antisepsis, and proper use of prophylactic antibiotics.

Remember: other members of Clostridia which can cause gas gangrene are:

Clostridium novyi

Clostridium septicum

Clostridium histolyticum

**Tetanus**

***Clostridium tetani:***

* *Clostridium tetani* is the causative agent of **tetanus**.
* The organism is found in soil, and in the intestinal tracts and feces of various animals.
* Contaminated wound are characteristically small and penetrating.

**TETANUS**

* Localized infection, caused by a *C.tetani* toxin
* General muscle spasms-due to neurotoxin

**Tetanospasmin**

* Blocks the muscle relaxation pathway
* Death results from spasms of respiratory muscles
* Released from dead bacterial cells
* Once it attaches to nerves, therapy is usually ineffective

**Types of tetanus:**

I.P – 5-15 days.

1. ***Generalized tetanus:(mild, moderate or severe) :***

* Descending pattern: lockjaw 🡪 stiffness of neck 🡪 difficulty swallowing 🡪later grimacing of the face(risussardonicus) 🡪 rigidity of abdominal and back muscles(opisthotonos).
* Spasms continue intermittently for 3-4 weeks, and recovery can last for months
* Sympathetic over-activity (profuse sweating, hypertension, hyperpyrexia, tachycardia, ventricular ectopics)

1. ***Neonatal tetanus:***

* Form of generalized tetanus that occurs in newborn infants born without protective passive immunity because the mother is not immune.
* Usually occurs through infection of the unhealed umbilical stump, particularly when the stump is cut with an unsterile instrument.

**Uncommon types:**

**3- Local tetanus:**persistent muscle contractions in the same anatomic area as the injury, which will however subside after many weeks; very rarely fatal; milder than generalized tetanus, although it could precede it.

**4- Cephalic tetanus:**occurs with ear infections or following injuries of the head; facial muscles contractions (Risus sardonicus).

**Complication and causes of death:**

1. Bronchopulmonary comlications
2. Bronchopneumonia
3. Pulmonary embolism
4. Fracture spine
5. Arrythmias
6. Coma
7. Infection
8. Respitatory distress

***Methods of diagnosis:***

Based on the patient’s account and physical findings that are characteristic of the disease.

**Tests that may be performed include the following:**

* Diagnostic studies generally are of little value
* Culture of the wound site (may be negative even if tetanus is present)
* Tetanus antibody test
* Other tests may be used to rule out meningitis, rabies, strychnine poisoning, or other diseases with similar symptoms.

**Treatment of tetanus:**

* If treatment is not sought early, the disease is often fatal.
* The **bacteria** are killed with antibiotics, such as penicillin and metronidazole; further toxin production is thus prevented.
* The **toxin** is neutralized with shots of tetanus immune globulin, TIG.
* Other drugs may be given to provide sedation, relax the muscles and relieve pain.
* Due to the extreme potency of the toxin, immunity does not result after the disease.

**Method of prevention – immunization:**

* A person recovering from tetanus should begin active immunization with tetanus toxoid (Td) during convalescence.
* The tetanus toxoid is a formalin-inactivated toxin, with an efficiency of approx. 100%.
* The DTaP vaccine includes tetanus, diphteria and pertussis toxoids; it is routinely given in the US during childhood. After 7 years of age, only Td needs to be administered.
* Because the antitoxin levels decrease over time, booster immunization shots are needed every 10 years.

**What else can be done?**

* Remove and destroy the source of the toxin through surgical exploration and cleaning of the wound (debridement).
* Bed rest with a non stimulating environment (dim light, reduced noise, and stable temperature) may be recommended.
* Sedation may be necessary to keep the affected person calm.
* Respiratory support with oxygen, endotracheal tube, and mechanical ventilation may be necessary.

**Botulism**

***Clostridium botulinum***

**Neurotoxins**

Seven different types: A through G

* Different types affect different species
* All cause flaccid paralysis
* Only a few nanograms can cause illness
* Binds neuromuscular junctions

**Toxin:** Destroyed by boiling, Spores: Higher temperatures to be inactivated

**Transmission**

Ingestion

1. Organism
2. Spores
3. Neurotoxin

Wound contamination

Inhalation

Person-to-person not documented

**Disease in Humans:**

* Three forms

1. Food borne
2. Wound
3. Infant

* All forms fatal and a medical emergency
* Incubation period: 12-36 hours

**Food-borne Botulism:**

* Preformed toxin ingested from contaminated food

**Infant Botulism:**

* Most common form in U.S.
* Spore ingestion:Germinate then toxin released and colonize large intestine
* Infants < 1 year old, 94% < 6 months old
* Spores from varied sources: Honey, food, dust, corn syrup

**Wound Botulism:**

Organism enters wound

* Develops under anaerobic conditions
* From ground-in dirt or gravel
* It does not penetrate intact skin
* Associated with addicts of black-tar heroin

**Adult Clinical Signs**

1. Nausea, vomiting, diarrhea
2. Double vision
3. Difficulty speaking or swallowing
4. Descending weakness or paralysis

Shoulders to arms to thighs to calves

1. Symmetrical flaccid paralysis
2. Respiratory muscle paralysis

**Diagnosis**

* Clinical signs
* Toxin in serum, stool, gastric aspirate, suspected food
* Culture of stool or gastric aspirateTakes 5-7 days
* Electromyography also diagnostic
* Mouse neutralization test Results in 48 hours

**Treatment:**

* Intensive care immediately, Ventilator for respiratory failure
* Botulinum antitoxin: Derived from equine source
* Botulism immune globulin

**Pseudomembranous colitis**

**Consequences of *C. difficile* infection:**

* Excretion
* Asymptomatic colonization of gut
* Diarrhoea
* Colitis
* Pseudomembranous colitis
* Death

**Antibiotic Associated Colitis:**

* 3-5 loose stools per day
* No alternative cause
* Onset during or after antimicrobial administration (Erythromycin stimulates gut peristalsis)
* Wide specturm
* Loose watery stools
* 8-11 days

**Clinical Presentation:**

* Diarrhea within a few days of antibiotic therapy
* Faeces have a distinctive foul odour
* Abdominal pain +/- pyrexia
* Blood if pseudomembranous colitis
* Electrolyte disturbances
* Hypoalbuminaemia
* Paralytic ileus
* Toxic Megacolon/perforation/shock
* Increased WBC

Antibiotic-related risk of *C. difficile* Infection

|  |  |  |
| --- | --- | --- |
| High Risk | Medium Risk | Low Risk |
| Cephalosporins | Macrolides | Aminoglycosides |
| Clindamycin | Co-trimoxazole | Metronidazole |
| Amipicillin/  amoxycillin | Tetracyclines | Anti-pseudomonalpenicillins |
| Fluoroquinolones |  | Rifampicin |
|  |  | Vancomycin |

ANTIBIOTIC THERAPY

**↓**

ALTERATION OF COLONIC MICROFLORA

**↓**

C. DIFFICILE EXPOSURE AND COLONIZATION

**↓**

RELEASE OF TOXINS A AND B

**↓**

BINDING TO ENTEROCYTE RECEPTORS

**↓**

COLONIC MUCOSAL INJURY AND ACUTE INFLAMMATION

**↓**

DIARRHEA AND COLITIS

**Microorganisms Which Inhibit the Growth of *C. difficile***

1. Lactobacillus species
2. Group D Streptococci
3. *Staphylococcus aureus*
4. Bacteroides species
5. Bifidobacteria

**Diagnosis of C. difficile Associated Diarrhea:**

1. The cytotoxicity assay using cultured fibroblasts remains the gold standard for testing for C.difficile toxin, with sensitivity exceeding 90%. However, the test is costly and requires 2–3 days for completion.
2. less-expensive enzyme-linked immunosorbent assays (ELISAs) for stool C difficile toxin, less sensitive but provide a result within 1 day.
3. endoscopy

**Treatment of *C. difficile* Associated Colitis**

* Discontinue preciptitating antibiotics
* Oral Vancomycin 250-500 mg/ 6hs for 7-10 d
* Oral Metronidazole 400-500 mg tds for 7-10d (Recent reports of resistance to metronidazole)