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Clostridium perfringens

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Epidemiology

C. perfringens is a non-motile, encapsulated, short and thick bacillus with blunt ends. Subterminal ovoid spores are produced. Strains are divided in five toxicological types (A to E) based on four major toxins (α, β, ε, and ι). Types A and C are the only ones associated with human gastroenteritis; type A also causes gas gangrene. Most heat resistant strains of *C .perfringens* are killed at 100ºC for a few minutes but some may surviving boiling temperature for hours. *C. perfringens* is demanding for its nutrition (several amino-acids and growth factors), and therefore prefers protein-rich foods (meat dishes).

C. perfringens (formerly *Clostridium welchii*) is **ubiquitous** throughout the natural environment, commonly encountered in soils, foods (frequently in raw meat and poultry), dust and intestinal tracts of humans (10% to 30% of adults), and domestic animals (30% to 60% in beef meat, 30% to 50% in pork, 40% to 80% in poultry). It can be isolated in almost any soil throughout the world. It is the most frequent clinical isolate of *Clostridium.* Under still poorly understood conditions, *C. perfringens* will form spores that are highly resistant to environmental stresses such as radiation, desiccation and heat.

Clostridium perfringens Food Poisoning

Vegetative cells of *C. perfringens* can multiply very rapidly in food. The heat resistance of its spores allows *C. perfringens* to survive incomplete cooking of food, with the surviving bacteria then able to cause food poisoning. *C. perfringens* has a predilection for meat or poultry that has been boiled, stewed or roasted, or meat with sauces, gravies, pies, salads, casseroles and dressings. The food is almost invariably held at room temperature or refrigerated in large masses for several hours.

Because many *C. perfringens* cells are killed by exposure to stomach acidity after ingestion, cases of *C. perfringens* food poisoning usually develop only when heavily contaminated food (i.e., food containing greater than one million to ten million *C. perfringens* vegetative cells per gram of food) is consumed. The spores germinate and multiply during cooling and holding at room temperatures. The toxin is a **heat-labile toxin** produced in vivo by *C. perfringens* type A. The enterotoxin produced by the organisms in the lower intestine is responsible for symptoms. Beef, poultry, gravies and dried or precooked foods are common sources. Infection usually is acquired at banquets or institutions (e.g. schools and camps) or from food caterers or restaurants where food is prepared in large quantities and kept warm for prolonged periods.

Illness is not transmissible from person-to-person.

The incubation period is six to 24 hours, usually eight to 12 hours.

Clinical Description

Food poisoning is characterized by a sudden onset of watery diarrhea and moderate to severe, crampy, midepigastric pain. Vomiting and fever are uncommon. While everyone appears to be susceptible to *C. perfringens* food poisoning, the illness tends to be more severe in elderly or debilitated individuals.

The absence of fever in most patients differentiates *C. perfringens* foodborne disease from shigellosis and salmonellosis. The infrequency of vomiting and longer incubation period contrast with the clinical features of foodborne disease associated with heavy metals, *Staphylococcus aureus* enterotoxins and fish and shellfish toxins. Diarrheal illness caused by *Bacillus cereus* enterotoxin may be indistinguishable from that caused by *C. perfringens*.

Illness related to of *C. perfringens* usually spontaneously resolve within 12 to 24 hours. In the elderly, ill or debilitated individuals, serious complications have led to death.

Diagnosis

C. perfringens is nonmotile and generally has a distinctive "boxcar" appearance on Gram stain of clinical material or subcultures. On blood agar, the colonies are typically surrounded by a "double zone of hemolysis": an inner zone of complete hemolysis that is due to θ-toxin and a larger outer zone of incomplete hemolysis that is due to α-toxin.

Because the fecal flora of healthy persons frequently includes *C. perfringens*, counts of at least one million *C. perfringens* spores per gram of feces obtained within 48 hours of onset of illness are required to support the diagnosis in ill persons. Stool rather than rectal swabs should be collected.

The most reliable method to diagnose *C. perfringens* toxi-infection is the direct detection of *C. perfringens* enterotoxin in stool by commercially available kits. The Reverse Passive Latex Agglutination Test (RPLA) is commonly used. Polystyrene latex particles are coated with rabbit anti-entero toxin A antibodies. In presence of stools containing *C. perfringens* entero-toxin A, an agglutination is observed. The sensitivity is 2 ng/mL of stools.

To confirm *C perfringens* as the cause, the concentration of organisms should be at least 100,000 per gram in the epidemiologically implicated food. Although *C. perfringens* is an anaerobic bacteria, special transport conditions are unnecessary because the spores are durable. Identification of enterotoxin in food is not successful as most of the enterotoxins are produced, not in the food, but in the human gut after ingestion of food where *C. perfringens* was allowed to grow in large numbers.

Surveillance

Clostridium perfringens is reportable as food poisoning.

Case Management - Treatment

Usually no treatment is required. Oral rehydration or, occasionally, intravenous fluid and electrolyte replacement may be indicated for patients with severe dehydration. Antibiotics are not indicated.

Hospital precaution and isolation: Standard precautions are recommended.

Control Measures:

Preventive measures depend on limiting proliferation of *C. perfringens* in foods by maintaining food warmer than 60°C (140°F) or cooler than 7°C (45°F). Meat dishes should be served hot shortly after cooking. Foods should never be held at room temperature to cool, but should be refrigerated after removal from warming devices or serving tables. Foods should be reheated to at least 74°C (165.2°F) or higher

before serving. Roasts, stews and similar dishes should be divided into small quantities for cooking and refrigeration to limit the time such foods are at temperatures at which *C. perfringens* replicates.

Wound *C. perfringens* Infection

When clinical signs of clostridial infection (eg, gas, myonecrosis) are present, rapid, aggressive intervention is mandatory. Thorough drainage and debridement are as important as antibiotics; both should be instituted rapidly. Penicillin G is the drug of choice; 1 to 2 million units IV q 2 to 3 h should be given immediately for severe cellulitis and myonecrosis.

Addition of clindamycin: 600 mg IV q 6 h is beneficial. If gram-negative organisms are seen or suspected, a broad-spectrum antibiotic: ticarcillin plus clavulanate, ampicillin plus sulbactam, piperacillin plus tazobactam) should be added. If penicillin-allergic patients have a life-threatening infection, desensitization to penicillin is required (see Desensitization).

Hyperbaric O_2 therapy may be helpful in extensive myonecrosis, particularly in the extremities, as a supplement to antibiotics and surgery. Hyperbaric O_2 therapy may salvage tissue and lessen mortality and morbidity if it is started early, but it should not delay surgical debridement.

For extensive myonecrosis, consider hyperbaric O_2 therapy, but do not let it delay surgical treatment

Clinical

Enteritis Necroticans

Necrotizing enteritis (enteritis necroticans, or pigbel) is caused by β toxin produced by type C strains of *C. perfringens* following ingestion of a high-protein meal in conjunction with trypsin inhibitors (e.g., in sweet potatoes) by a susceptible host who has limited intestinal proteolytic activity. This disease has been reported among children and adults in New Guinea.

Suppurative Deep Tissue Infections

Clostridia are frequently recovered from various suppurative conditions in conjunction with other anaerobic and aerobic bacteria but can also be the only organisms isolated. These suppurative conditions, which exist with severe local inflammation but usually without the characteristic systemic signs induced by clostridial toxins, include intraabdominal sepsis, empyema, pelvic abscess, subcutaneous abscess, frostbite with gas gangrene, infection of a stump in an amputee, brain abscess, prostatic abscess, perianal abscess, conjunctivitis, infection of a renal cell carcinoma and infection of an aortic graft.

Clostridia are isolated from approximately two-thirds of patients with intraabdominal infections resulting from intestinal perforation.

Clostridia have been isolated from suppurative infections of the female genital tract, particularly tuboovarian and pelvic abscesses. The major species involved has been *C. perfringens*. Most of these are mild suppurative infections without evidence of uterine gangrene. *C. perfringens* has been isolated from as many as 20% of diseased gallbladders at surgery.

Clostridia are among the many organisms found in empyema fluid or isolated by transtracheal aspiration from patients with lung abscesses. *C. perfringens* has been reported as a cause of empyema arising from aspiration pneumonia, pulmonary emboli and infarction. However, the majority of cases of clostridial empyema are secondary to trauma.

Skin and Soft Tissue Infections

Various categories of traumatic wound infections due to clostridia have been described: simple contamination, anaerobic cellulitis, fasciitis with or without systemic manifestations and anaerobic myonecrosis.

Gas Gangrene (Clostridial Myonecrosis)

Gas gangrene is characterized by rapid and extensive necrosis of muscle accompanied by gas formation and systemic toxicity and occurs when bacteria invade healthy muscle from adjacent traumatized muscle or soft tissue. The infection originates in a wound contaminated with clostridia. Although more than 30% of deep wounds are infected with clostridia, the incidence of clostridial myonecrosis is quite low. These infections occur in both military and civilian settings. An essential factor in the genesis of gas gangrene appears to be trauma, particularly involving deep muscle laceration.

Bacteremia and Clostridial Sepsis

The relatively common entity of transient clostridial bacteremia can arise in any hospitalized patient, but is most common with a predisposing focus in the gastrointestinal tract, biliary tract, or uterus. Fever frequently resolves within 24 to 48 hours without therapy. Despite the finding of clostridial bacteremia following septic abortions and the frequent isolation of clostridia from the lochia, most of the patients involved do not have evidence of sepsis.

Clostridial sepsis is an uncommon but almost invariably fatal illness following clostridial infection - primarily that of the uterus, colon, or biliary tract. This entity must be differentiated from transient clostridial bacteremia, which is much more common. *C. perfringens* causes the majority of cases of both sepsis and transient bacteremia.

Diagnosis

Early suspicion and intervention are essential; clostridial cellulitis responds well to treatment, but myonecrosis has a mortality rate of ≥ 40% with treatment and 100% without treatment.

Although localized cellulitis, myositis, and spreading myonecrosis may be clinically distinct, differentiation often requires surgical exploration. In myonecrosis, muscle tissue is visibly necrotic; the affected muscle is a lusterless pink, then deep red, and finally gray-green or mottled purple and does not contract with stimulation. X-rays may show local gas production, and CT and MRI delineate the extent of gas and necrosis.

Wound exudate should be cultured for anaerobic and aerobic organisms. Because of their short generation time, anaerobic cultures of *Clostridia* may be positive in as little as six hours. However, other anaerobic and aerobic bacteria, including members of the *Enterobacteriaceae* family and *Bacteroides, Streptococcus*, and *Staphylococcus* spp, alone or mixed, can cause severe clostridia-like cellulitis, extensive fasciitis, or myonecrosis (see Necrotizing Subcutaneous Infection). Also, many wounds, particularly if open, are contaminated with both pathogenic and nonpathogenic *Clostridia* that are not responsible for the infection.

The presence of *Clostridia* is significant when

- Gram stain shows them in large numbers.
- Few PMNs are found in the exudates.
- Free fat globules are demonstrated with Sudan stain.

However, if PMNs are abundant and the smear shows many chains of cocci, an anaerobic streptococcal or staphylococcal infection should be suspected. Abundant gram-negative bacilli may indicate infection with one of the *Enterobacteriaceae* or a *Bacteroides* spp (see Mixed Anaerobic Infections).

Detection of clostridial toxins in the wound or blood is useful only in the rare case of wound botulism

Treatment

When clinical signs of clostridial infection (eg, gas, myonecrosis) are present, rapid, aggressive intervention is mandatory. Thorough drainage and debridement are as important as antibiotics; both should be instituted rapidly. Penicillin G is the drug of choice; 1 to 2 million units IV q 2 to 3 h should be given immediately for severe cellulitis and myonecrosis.

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Tissue Gas

Tissue gas is the name given to the action of the bacteria Clostridium perfringens (formerly known as C. welchii) in dead bodies. Its effect on the deceased is that of an extremely accelerated decomposition. It is only halted by embalming the body and special additive chemicals must be employed. It most commonly occurs in the bodies of people who have died of gangrene, large decubitus ulcers, necrotising fasciitis or who have had soil, faeces or water forced into wounds.