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## Editorial

Botulism is a rare and potentially fatal illness caused by a toxin produced by the bacterium *Clostridium botulinum*. The disease begins with weakness, blurred vision, feeling tired, and trouble speaking. This may then be followed by weakness of the arms, chest muscles, and legs. Vomiting, swelling of the abdomen, and diarrhea may also occur. The disease does not usually affect consciousness or cause a fever.

Botulism can be spread in several different ways. The bacterial spores which cause it are common in both soil and water. They produce the botulinum toxin when exposed to low oxygen levels and certain temperatures. Foodborne botulism happens when food containing the toxin is eaten. Infant botulism happens when the bacteria develops in the intestines and releases the toxin. This typically only occurs in children less than six months old, as protective mechanisms develop after that time. Wound botulism is found most often among those who inject street drugs. In this situation, spores enter a wound, and in the absence of oxygen, release the toxin. It is not passed directly between people. The diagnosis is confirmed by finding the toxin or bacteria in the person in question.

Prevention is primarily by proper food preparation. The toxin, though not the organism, is destroyed by heating it to more than 85 °C (185 °F) for longer than 5 minutes. Honey can contain the organism, and for this reason, honey should not be fed to children under 12 months. Treatment is with an antitoxin. In those who lose their ability to breathe on their own, mechanical ventilation may be necessary for months. Antibiotics may be used for wound botulism. Death occurs in 5 to 10% of people. Botulism also affects many other animals. The word is from Latin, *botulus*, meaning sausage. Early descriptions of botulism date from at least as far back as 1793 in Germany. Read all about this serious condition under "DISEASE DIAGNOSIS".

Since the big article is on AAEROBES, so are the lesser mortals but equally important. Flip over to absorb the essence of "TROUBLESHOOTING" and "INTERPRETATION", these two are also related to anaerobes. Somewhere in between, you will find "THE BOUQUET".



## DISEASE DIAGNOSIS

### BOTULISM

#### Practice Essentials

Botulism is an acute neurologic disorder that causes potentially life-threatening neuroparalysis due to a neurotoxin produced by *Clostridium botulinum*. The 3 main clinical presentations of botulism are as follows:

- Infant botulism
- Foodborne botulism
- Wound botulism

#### Signs and symptoms

More than 90% of patients with botulism have 3-5 of the following signs or symptoms:

- Nausea
- Vomiting
- Dysphagia
- Diplopia
- Dilated/fixated pupils
- Extremely dry mouth unrelieved by drinking fluids

Generally, botulism progresses as follows:

- Preceding or following the onset of paralysis are nonspecific findings such as nausea, vomiting, abdominal pain, malaise, dizziness, dry mouth, dry throat, and, occasionally, sore throat
- Cranial nerve paralysis manifests as blurred vision, diplopia, ptosis, extraocular muscle weakness or paresis, fixed/dilated pupils, dysarthria, dysphagia, and/or suppressed gag reflex
- Additional neurologic manifestations include symmetrical descending paralysis or weakness of motor and autonomic nerves
- Respiratory muscle weakness may be subtle or progressive, advancing rapidly to respiratory failure

The autonomic nervous system is also involved in botulism, with manifestations that include the following:

- Paralytic ileus advancing to severe constipation
- Gastric dilatation
- Bladder distention advancing to urinary retention
- Orthostatic hypotension
- Reduced salivation
- Reduced lacrimation

Other neurologic findings include the following:

- Changes in deep tendon reflexes, which may be either intact or diminished
- Incoordination due to muscle weakness
- Absence of pathologic reflexes and normal findings on sensory and gait examinations
- Normal results on mental status examination

See Clinical Presentation for more detail.

#### Diagnosis

A mouse neutralization bioassay confirms botulism by isolating the botulinum toxin. Toxin may be identified in the following:

- Serum
- Stool



- Vomitus
- Gastric aspirate
- Suspected foods

*C botulinum* may be grown on selective media from samples of stool or foods. Note that the specimens for toxin analysis should be refrigerated, but culture samples of *C botulinum* should not be refrigerated. Wound cultures that grow *C botulinum* suggest the presence of wound botulism.

#### Electromyography

Characteristic electromyographic findings in patients with botulism include the following:

- Brief, low-voltage compound motor-units
- Small M-wave amplitudes
- Overly abundant action potentials

An incremental increase in M-wave amplitude with rapid repetitive nerve stimulation may help to localize the disorder to the neuromuscular junction.

See Workup for more detail.

#### Management

Rigorous and supportive care, including use of the following, is essential in patients with botulism:

- Meticulous airway management - Of paramount importance, since respiratory failure is the most important threat to survival in patients with botulism
- Cathartics and enemas - Administered to patients with bowel sounds to remove unabsorbed botulinum toxin from the intestine
- Stress ulcer prophylaxis - A standard component of intensive care management
- Nasogastric suction and intravenous hyperalimentation - Helpful if an ileus is present; if no ileus is present, tube feeding can be used for nutritional supplementation
- Foley catheter - Often used to treat bladder incontinence; the catheter must be monitored conscientiously and changed regularly
- Antibiotic therapy - Useful in wound botulism, but has no role in foodborne botulism

Magnesium salts, citrate, and sulfate should not be administered, because magnesium can potentiate the toxin-induced neuromuscular blockade.

Wound botulism requires the following:

- Incision and thorough debridement of the infected wound
- Antitoxin therapy
- High-dose intravenous penicillin therapy

#### Prevention of nosocomial infections

Measures to reduce the risk of nosocomial infections include the following:

- Close observation for hospital-acquired infections - Especially pneumonia (particularly aspiration pneumonia); precaution against aspiration is also necessary
- Close observation for urinary tract infection
- Meticulous skin care - To prevent decubital ulcers and skin breakdown

Careful attention to peripheral and central intravenous catheters with regular site rotation to reduce the risks of thrombophlebitis, cellulitis, and line infections should be part of the patient's supportive care.

See Treatment and Medication for more detail.

#### Background

Botulism is an acute neurologic disorder that causes potentially life-threatening neuroparalysis due to a neurotoxin produced by *Clostridium*

*botulinum*. The toxin binds irreversibly to the presynaptic membranes of peripheral neuromuscular and autonomic nerve junctions. Toxin binding blocks acetylcholine release, resulting in weakness, flaccid paralysis, and, often, respiratory arrest. Cure occurs following sprouting of new nerve terminals. **The 3 main clinical presentations of botulism** include infant botulism (IB), foodborne botulism (FBB), and wound botulism (WB). Additionally, because of the potency of the toxin, the possibility of botulism as a bioterrorism agent or biological weapon is a great concern. For more information, see CBRNE – Botulism. **Infant botulism is caused by ingested *C botulinum* spores** that germinate in the intestine and produce toxin. These spores typically come from bee honey or the environment. Most infants fully recover with supportive treatment; the attributed infant mortality rate is less than 1%. Improperly canned or home-prepared foods are common sources of the toxin that can result in foodborne botulism. Wound botulism results from contamination of a wound with toxin-producing *C botulinum*. Foodborne botulism and wound botulism occur predominantly in adults and are the focus of this article. ***C botulinum* is an anaerobic gram-positive rod** that survives in soil and marine sediment by forming spores. Under anaerobic conditions that permit germination, it synthesizes and releases a potent exotoxin. Microbiologically, the organism stains gram-positive in cultures less than 18 hours old. The organism may stain gram-negative after 18 hours of incubation, potentially complicating attempts at diagnosis. On a molecular weight basis, botulinum toxins are the most potent toxins known. **Eight antigenically distinct *C botulinum* toxins** are known, including A, B, C (alpha), C (beta), D, E, F, and G. Each strain of *C botulinum* can produce only a single toxin type. Types A, B, E, and, rarely, F cause human disease. Toxins A and B are the most potent, and the consumption of small amounts of food contaminated with these types has resulted in full-blown disease. During the last 20 years, toxin A has been the most common cause of foodborne outbreaks; toxins B and E follow in frequency. In 15% of *C botulinum* infection outbreaks, the toxin type is not determined. Toxins C and D cause disease in various animals. Type G toxin has been associated with sudden death but not with neuroparalytic illness. It was isolated from autopsy material from 5 patients in Switzerland in 1977.

### Pathophysiology

The mechanism of action involves toxin-mediated blockade of neuromuscular transmission in cholinergic nerve fibers. This is accomplished by either inhibiting acetylcholine release at the presynaptic clefts of the myoneural junctions or by binding acetylcholine itself. Toxins are absorbed from the stomach and small intestine, where they are not denatured by digestive enzymes. Subsequently, they are hematogenously disseminated and block neuromuscular transmission in cholinergic nerve fibers. The nervous, gastrointestinal, endocrine, and metabolic systems are predominantly affected. **Because the motor end plate responds to acetylcholine**, botulinum toxin ingestion results in hypotonia that manifests as descending symmetric flaccid paralysis and is usually associated with gastrointestinal symptoms of nausea, vomiting, and diarrhea. Cranial nerves are affected early in the disease course. Later complications include paralytic ileus, severe constipation, and urinary retention. **Wound botulism results when wounds are contaminated** with *C botulinum* spores. Wound botulism has developed following traumatic injury that involved soil contamination, among injection drug users (particularly those who use black-tar heroin), and after cesarean delivery. The wound may appear deceptively benign. Traumatized and devitalized tissue provides an anaerobic medium for

the spores to germinate into vegetative organisms and to produce neurotoxin, which then disseminates hematogenously. The nervous, endocrine, and metabolic systems are predominantly affected. Symptoms develop after an incubation period of 4-14 days, with a mean of 10 days. The clinical symptoms of wound botulism are similar to those of foodborne botulism except that gastrointestinal symptoms (including nausea, vomiting, diarrhea) are uncommon.

### Frequency International

Human botulism is found worldwide. Spores from *C botulinum* strains that produce type A or B toxins are distributed widely in the soil and have been found throughout the world. Toxin type B is commonly found in Europe. Toxin G was originally isolated in Switzerland.

### Mortality/Morbidity

Mortality rates vary based on the age of the patient and the type of botulism. Foodborne botulism carries an overall mortality rate of 5-10%. Wound botulism carries a mortality rate that ranges from 15-17%. The risk of death due to infant botulism is usually less than 1%. **The recovery period from botulism** is often prolonged (30-100 d). Some patients demonstrate residual weakness or autonomic dysfunction for 1 year after the onset of the illness. However, most patients achieve full neurologic recovery. Permanent deficits may occur in those who sustain significant hypoxic insults.

### Sex

Wound botulism is more common in males. Foodborne botulism has no sexual predilection.

### Age

Foodborne botulism and wound botulism predominately occur in adults. The mean age of infant botulism is 3 months.

### Botulism Clinical Presentation

#### History

Following the onset of symptoms, botulism quickly progresses over several days. The magnitude of the neuromuscular impairment can advance hourly. Persons who survive this phase eventually stabilize and then recover over a period of days to months. The mechanism of recovery is not fully understood but requires the generation of new presynaptic axons and the formation of new synapses, as the original synapses are permanently affected. As with tetanus, recovery from botulism does not confer long-term immunity. Rare reports have described a second episode in the same patient.

#### Foodborne botulism

Foodborne botulism should be suspected in patients who present with an acute gastrointestinal illness associated with neurologic symptoms. Symptoms usually appear within 12-36 hours following consumption of contaminated food products. The severity of the illness varies from mild to severe, but death can occur within 24 hours. **The incubation period is usually 18-36 hours**. Depending on toxin dose, the incubation period ranges from 2 hours to 8 days. The onset of symptoms can be abrupt or can evolve over several days.

#### Wound botulism

Patients with wound botulism typically have a history of traumatic injury with wounds that are contaminated with soil. **Since 1994, the number of patients with wound botulism** who have a history of chronic intravenous drug abuse has increased dramatically. In most cases, black-tar heroin has been the implicated vehicle. A study by Yuan et al followed 17 heroin

users who had recurrent botulism after using black-tar heroin. Physicians need to be alert to recognize botulism, especially in patients who use black-tar heroin or in those with a history of injection drug-associated botulism. [Rare cases of wound botulism](#) after cesarean delivery have been documented. [Aside from a longer incubation period](#), wound botulism is similar to foodborne botulism. The incubation period of wound botulism ranges from 4-14 days, with a mean of 10 days. Unlike foodborne botulism, wound botulism causes no gastrointestinal symptoms. Patients may be febrile, but this is more likely due to the wound infection rather than the wound botulism. In many cases, the wound appears benign.

#### Adult intestinal toxemia

Adult intestinal toxemia results from enteric colonization with *C botulinum* that progresses to toxin production. The pathophysiology of the changes in the gastrointestinal flora that facilitate colonization is unclear.

#### Iatrogenic botulism due to accidental overdose of botulinum toxin (Botox)

Cases of botulism due to Botox overdosage have been reported. Symptoms vary and can include dysphagia, ptosis, and diplopia, as well as more severe presentations of systemic weakness or muscle paralysis.

#### Physical

More than 90% of patients with botulism have 3-5 of the following signs or symptoms: nausea, vomiting, dysphagia, diplopia, dilated/fixed pupils, and an extremely dry mouth unrelieved by drinking fluids.

Generally, botulism progresses as follows:

- Preceding or following the onset of paralysis are nonspecific findings such as nausea, vomiting, abdominal pain, malaise, dizziness, dry mouth, dry throat, and, occasionally, sore throat. Except for nerves I and II, the cranial nerves are affected first.
- Cranial nerve paralysis manifests as blurred vision, diplopia, ptosis, extraocular muscle weakness or paresis, fixed/dilated pupils, dysarthria, dysphagia, and/or suppressed gag reflex. Additional neurologic manifestations include symmetric descending paralysis or weakness of motor and autonomic nerves.
- Respiratory muscle weakness may be subtle or progressive, advancing rapidly to respiratory failure. Progressive muscle weakness occurs and often involves the muscles of the head and neck, as well as intercostal diaphragmatic muscles and those of the extremities.

The autonomic nervous system is also involved. Manifestations of this include the following:

- Paralytic ileus advancing to severe constipation
- Gastric dilatation
- Bladder distention advancing to urinary retention
- Orthostatic hypotension
- Reduced salivation
- Reduced lacrimation

Other neurologic findings include the following:

- Changes in deep tendon reflexes, which may be either intact or diminished
- Incoordination due to muscle weakness
- Absence of pathologic reflexes and normal findings on sensory and gait examinations
- Normal results on mental status examination

Many patients with foodborne botulism and wound botulism are afebrile.

#### Causes

##### Wound botulism

Causes of wound botulism have been associated with traumatic injury involving contamination with soil, chronic abuse of intravenous drugs (eg, black-tar heroin), and cesarean delivery. Wound botulism illness can occur even after antibiotics are administered to prevent wound infection.

##### Foodborne botulism

Foodborne botulism results from the ingestion of preformed neurotoxins; A, B, and E are the most common. On average, 24 cases of foodborne botulism are reported annually. [High-risk foods include home-canned or home-processed](#) low-acid fruits and vegetables; fish and fish products; and condiments, such as relish and chili peppers. [Commercially processed foods](#) and improperly handled fresh foods are occasionally associated with botulism outbreaks. [Outbreaks of foodborne botulism in restaurants](#), schools, and private homes have been traced to uncommon sources, such as commercial pot-pies, baked potatoes, beef stew, turkey loaf, sautéed onions, chopped garlic in oil, and cheese sauce.

#### Diagnostic Considerations

##### Botulism Differential Diagnoses

The diseases most frequently confused with botulism are those that produce generalized weakness. Differentiating botulism from other diseases is essential for early initiation of therapy. Botulism should be considered in patients who are afebrile and mentally intact and who have symmetric descending paralysis without sensory findings. The diagnosis should be suspected on clinical grounds in the context of an appropriate history. Other conditions often confused with botulism include the following:

- Guillain-Barré syndrome
- Fisher variant of Guillain-Barré syndrome
- Myasthenia gravis
- Lambert-Eaton syndrome
- Poliomyelitis
- Tick paralysis
- Cerebrovascular disease of the brainstem
- Basilar artery stroke
- Encephalitis
- Diphtheria
- Neurasthenia
- Progressive external ophthalmoplegia
- ☹ Intracranial mass lesions
- Drugs, penicillamine
- Aminoglycosides: Very large doses can induce neuromuscular blockade.
- Poisonings by atropine, scopolamine, organophosphate insecticides, shellfish, amanita mushrooms, carbon monoxide, methyl alcohol, methyl chloride, and sodium fluoride
- Congenital neuropathy or myopathy

##### Differential Diagnoses

- Familial Mediterranean Fever
- Hypermagnesemia
- Hyperthyroidism and Thyrotoxicosis

#### Botulism Workup

##### Laboratory Studies

Laboratory tests are not helpful in the routine diagnosis of botulism. [WBC counts and erythrocyte sedimentation rates](#) are normal.

Cerebrospinal fluid is normal, except for occasional mild elevations in protein concentration. A mouse neutralization bioassay confirms botulism by isolating the botulism toxin. Toxin may be identified in serum, stool, vomitus, gastric aspirate, and suspected foods. *C botulinum* may be grown on selective media from samples of stool or foods. Note that the specimens for toxin analysis should be refrigerated, but culture samples of *C botulinum* should not be refrigerated. Because intestinal carriage is rare, identifying the organism or its toxin in vomitus, gastric fluid, or stool strongly suggests the diagnosis. Isolation of the organism from food without toxin is insufficient grounds for the diagnosis. Only experienced personnel who have been immunized with botulinum toxoid should handle the specimens. Because the toxin may enter the blood stream through the eye or via small breaks in the skin, precaution is warranted. Wound cultures that grow *C botulinum* suggest of wound botulism.

### Imaging Studies

Imaging studies are generally not useful in the diagnosis of botulism. The only potential role for imaging studies (eg, CT scan, MRI) would be to rule out CNS pathology, such as intracranial mass lesions, cerebrovascular disease of the brainstem, or basilar artery stroke, in patients in whom the presentation is atypical or vague.

### Other Tests

Patients with botulism may have mild nonspecific abnormalities on electrocardiography. Results from nerve conduction studies are normal, and electromyography (EMG) reveals reduced amplitude of compound muscle action potentials. EMG may be useful in establishing a diagnosis of botulism, but the findings can be nonspecific and nondiagnostic, even in severe cases. Characteristic findings in patients with botulism include brief low-voltage compound motor-units, small M-wave amplitudes, and overly abundant action potentials. An incremental increase in M-wave amplitude with rapid repetitive nerve stimulation may help to localize the disorder to the neuromuscular junction. Single-fiber EMG may be a more useful and sensitive method for the rapid diagnosis of botulism intoxication, particularly in the absence of signs of general muscular weakness. The results of the edrophonium chloride, or Tensilon, test for myasthenia gravis may be falsely positive in patients with botulism. If positive, it is typically much less dramatically positive than in patients with myasthenia gravis.

## Botulism Treatment & Management

### Medical Care

On March 22, 2013, the FDA approved the first botulism antitoxin that can neutralize all 7 known botulinum nerve toxin serotypes. The heptavalent antitoxin is derived from horse plasma and is the only drug available for treating botulism in patients older than 1 year, including adults. It is also the only available drug for treating infant botulism that is not caused by nerve toxin type A or B. Rigorous and supportive care is essential in patients with botulism. Meticulous airway management is paramount, as respiratory failure is the most important threat to survival in patients with botulism. Patients with symptoms of botulism or known exposure should be hospitalized and closely observed. Spirometry, pulse oximetry, vital capacity, and arterial blood gases should be evaluated sequentially. Respiratory failure can occur with unexpected rapidity. Intubation and mechanical ventilation should be strongly considered when the vital capacity is less than 30% of predicted, especially when paralysis is progressing rapidly and hypoxemia with

hypercarbia is present. Many patients require intubation and ventilatory support for a few days to months. Tracheostomy may prove necessary to manage secretions. Patients with bowel sounds are administered cathartics and enemas to remove unabsorbed botulinum toxin from the intestine. Magnesium salts, citrate, and sulfate should not be administered because magnesium can potentiate the toxin-induced neuromuscular blockade. Stress ulcer prophylaxis is also a standard component of intensive care management. If an ileus is present, nasogastric suction and intravenous hyperalimentation are very helpful supportive measures. If no ileus is present, tube feeding can be used for nutritional supplementation. A Foley catheter is often used to treat bladder incontinence. This must be monitored conscientiously and changed regularly.

Measures to reduce the risk of nosocomial infections include the following:

- Close observation for hospital-acquired infections, especially pneumonia (particularly aspiration pneumonia), is necessary, as is precaution to prevent aspiration. Aggressive pulmonary toilet with clearance of secretions, ventilatory support, and incentive spirometry are typically used.
- Close observation for urinary tract infection is essential. Foley catheters should be changed on a regular basis.
- Meticulous skin care is required to prevent decubital ulcers and skin breakdown.
- Careful attention to peripheral and central intravenous catheters with regular site rotation to reduce the risks of thrombophlebitis, cellulitis, and line infections should be part of the supportive care.
- Deep venous thrombosis (DVT) prophylaxis is also a standard component of intensive care management.

### Surgical Care

Wound botulism requires incision and thorough debridement of the infected wound, antitoxin therapy, and high-dose intravenous penicillin therapy.

### Consultations

A nutritionist should be consulted for hyperalimentation and tube-feeding recommendations and monitoring. Physical and occupational therapists are needed to work on range-of-motion exercises and assisted ambulation, as tolerated. A psychiatrist and/or a psychologist is recommended for counseling, as needed; patients with prolonged hospitalization, slow recovery, and complications from the disease or from extended hospitalization are at increased risk for depression. Pastoral care is recommended, as needed. Physical medicine and rehabilitation specialists may be helpful in coordinating long-term rehabilitation planning once sustained recovery has begun.

### Diet

Nasogastric suction and intravenous hyperalimentation are important when an ileus is present. If no ileus is present or when the ileus resolves, tube feeding can be used for nutritional supplementation.

Oral intake should be reinstated gradually under the following conditions:

- Respiratory status is stable without mechanical ventilation.
- Swallowing safety has been assessed and confirmed with a swallowing study, as appropriate.
- Ileus has resolved.

### Activity

- Bedrest is initially required.
- Increase activity as tolerated.

### Medication Summary

Antibiotics are useful in wound botulism, but they have no role in foodborne botulism.

#### Antibiotics

##### Class Summary

When botulism develops following a wound infection, antibiotic therapy and meticulous debridement of the wound are essential.

Antibiotics

Penicillin G

Chloramphenicol (Chloromycetin)

Clindamycin (Cleocin)

Antitoxins

##### Class Summary

These agents are essential in the treatment of foodborne botulism and wound botulism. Heptavalent antitoxin (toxins A through G) is available at the Centers for Disease Control and Prevention (CDC). The CDC phone number is (770) 488-7100. Twenty percent of patients experience some degree of serum sickness or hypersensitivity reaction, and anaphylaxis can also occur. Patients who react to a test dose must be desensitized. Because of the risk of adverse reactions, prophylactic antitoxin is not recommended in patients who are exposed to botulism toxin but who have no symptoms. These patients may undergo gastric lavage or induced vomiting in an attempt to eliminate the toxin prior to absorption. **Botulinum antitoxin**, heptavalent (HBAT)

### Botulism Follow-up

#### Further Outpatient Care

The most significant improvements in ventilatory and upper airway muscle strength occur over the first 12 weeks, and, in some patients, recovery may not be complete for as long as a year. Close follow-up is crucial.

#### Further Inpatient Care

Recovery of ventilatory and upper airway muscle strength in patients who develop respiratory failure is most significant over the first 12 weeks. The time for recovery typically ranges from 30-100 days. Artificial respiratory support may be required for months in severe cases.

#### Inpatient & Outpatient Medications

When botulism develops following a wound infection, antibiotic therapy and meticulous debridement of the wound are essential. **Penicillin is the drug of choice**. **Clindamycin and chloramphenicol** are reasonable second-line agents.

#### Transfer

Transfer is indicated if the patient's condition continues to deteriorate or if the initial hospital is unable to manage the complexities involved.

#### Deterrence/Prevention

Prompt notification of public health authorities regarding a suspected case of botulism may prevent further consumption of a contaminated home-canned or commercial food product. **Foodborne botulism is best prevented** by strict adherence to recommended home-canning techniques. High-temperature pressure cooking is essential to ensure spore elimination from low-acid fruits and vegetables. Although boiling

for 10 minutes kills bacteria and destroys the heat labile botulism toxin, the spores are resistant to heat and can survive boiling for 3-5 hours. Food contaminated by botulism toxins usually has a putrefactive odor; however, contaminated food may also look and taste normal. Hence, terminal heating of toxin-containing food can prevent illness and is an important preventive measure. **Wound botulism due to intravenous drug abuse** can be prevented by cessation of drug use. **Wound botulism is best prevented** by prompt thorough debridement of contaminated wounds. Prophylactic use of antibiotics after trauma cannot be relied on to prevent wound botulism.

### Complications

#### Nosocomial infections

Hospital-acquired pneumonia, especially aspiration pneumonia, can occur. Atelectasis and poor secretion clearance also increase the risk of hospital-acquired pneumonia. **Urinary tract infection can occur** from indwelling Foley catheters. **Skin breakdown** and decubitus formation can occur. **Thrombophlebitis, cellulitis, and line infections can occur**. These patients often have peripheral and central intravenous catheters for prolonged periods. **Fungal infections can occur**; the predisposing factors include prolonged hospitalization, parenteral nutrition, and central venous catheters. DVT prophylaxis is essential to reduce the risk of these potential complications. DVT and pulmonary embolism (PE) are potential complications because patients can be bedridden for weeks to months. **Stress ulcers can occur** and are common in the intensive care unit setting. Stress ulcer prophylaxis is essential to reduce the risk of this potential complication.

#### Other potential complications

Other potential complications include the following:

- Hypoxic tissue damage can lead to permanent neurologic deficits.
- Death

### Prognosis

Botulism due to type A toxin is generally more severe than that caused by type B or E. **Mortality rates vary based on the age of the patient** and the type of botulism. Foodborne botulism carries an overall mortality rate of 5-10%. Botulism carries a higher mortality rate in patients older than 60 years than in younger patients. Wound botulism carries a mortality rate that ranges from 15-17%. The risk of death due to infant botulism is usually less than 1%. **The recovery period ranges from 30-100 days**. Artificial respiratory support may be required for months in severe cases. Full neurologic recovery usually occurs. Hypoxic insults, although infrequent, can result in permanent deficits. Some patients experience residual weakness and autonomic dysfunction for as long as a year after disease onset.

Mortality is due to the following:

- Delayed diagnosis and respiratory failure
- Hospital complications such as nosocomial infections (usually pneumonia)

#### Patient Education

When preserving food at home, kill *C botulinum* spores by pressure cooking at 250°F (120°C) for 30 minutes. The toxin can be destroyed by boiling for 10 minutes or cooking at 175°F (80°C) for 30 minutes. Do not eat or taste food from bulging cans. Discard food that smells bad. **Cessation of intravenous drug use** prevents wound botulism due to this vehicle.

## INTERPRETATION

### Bacterial Wound Culture

#### Reference Range

Bacterial wound cultures, together with clinical examination, are used to determine the presence of infection in wounds.

The reference range for a negative bacterial wound culture result depends on the method, as follows:

**Qualitative wound culture:** No growth of any pathogenic organism or growth of normal skin flora.

**Semiquantitative wound culture:** Less than 4+ growth.

**Quantitative wound culture:** Less than 100,000 organisms per gram (if tissue specimen is used), per milliliter (if fluid collection is used), or per swab (if swab is used).

#### Interpretation

Wound cultures commonly serve as an adjunct to clinical examination, and both should therefore be interpreted concurrently. Interpretation of a qualitative bacterial wound culture requires determination of whether the isolated organism is the cause of the infection or is a contaminant/part of normal skin flora. Quantification by semiquantitative and quantitative methods is used to further determine whether the isolated pathogen is a true infection by standard cutoff values for wound bacterial burden as outlined in Reference Range.

In general, qualitative cultures are useful in identifying pathogenic bacteria. Organisms that are commonly part of normal skin flora and that are not usually pathogenic include the following:

- *Staphylococcus epidermidis* or other coagulase-negative staphylococci
- *Corynebacterium* species and other diphtheroids
- *Brevibacterium* species
- *Propionibacterium acnes*
- *Pityrosporum* species
- Alpha or gamma streptococci
- *Neisseria* species (except *Neisseria meningitidis* or *Neisseria gonorrhoeae*)
- *Bacillus* species (except *Bacillus cereus* or *Bacillus anthracis*)

Growth of aforementioned organisms usually represents contamination, except for coagulase-negative *Staphylococcus* species, which could represent either contamination or true infection.

The most common pathogenic bacteria isolated in acute and chronic wound infections are as follows:

- *Staphylococcus aureus*
- *Pseudomonas aeruginosa*
- Enterococci
- Beta-hemolytic streptococci
- Coliform bacteria, including *Escherichia coli*, *Enterobacter* species, and *Klebsiella pneumoniae*
- Coagulase-negative staphylococci
- Pigmented gram-negative anaerobes (*Prevotella* and *Porphyromonas* species)
- Nonpigmented gram-negative anaerobes (primarily *Bacteroides*, *Prevotella*, and *Fusobacterium* species)
- *Peptostreptococcus* species

#### ● *Clostridium* species

Quantitative cultures obtained via biopsy are considered the criterion standard among wound culture techniques. Growth of more than 100,000 or 10 organisms per gram of tissue or per milliliter of fluid aspirate is considered positive for wound infection. For semiquantitative cultures, blood agar plates are streaked 3 times on one quadrant and then 3 times on each remaining quadrant using a sterile loop for each quadrant. This is thought to create dilutions of the original swab in each quadrant. Growth of more than 30 colonies in a quadrant is read as 4+ growth and is considered positive for infection. Semiquantitative cultures are considered to have good correlation with quantitative cultures for detection of wound sepsis, with a positive predictive value of 100% and a negative predictive value of 93.7%.

#### Collection and Panels

The 3 most common methods of collecting specimen for wound culture include wound tissue biopsy, needle aspiration of fluid, and swab.

##### Wound tissue biopsy

Container: Sterile tube or container

Normal volume: 0.005-0.2 g of involved tissue or 3-4 mm punch biopsy

Procedure: A tissue biopsy is obtained aseptically via either a punch biopsy instrument or excision using a scalpel. Other accepted techniques include curettage of superficial devitalized tissue, most commonly used in diabetic foot ulcers, and a dermabrasion procedure for deep tissues without being too invasive. For optimum recovery, the specimen should be sent to the laboratory within 60 minutes.

##### Needle aspiration

Container: Sterile tube or container

Normal volume: 0.5-2 mL

Procedure: This is the best procedure for wounds involving focal fluid collections or abscesses. The area should be prepared aseptically. Multiple aspirations around the wound are performed using a 22-gauge needle attached to a 10-mL syringe. The syringe containing the specimen may be capped or the specimen can be transferred onto a sterile container and sent to the laboratory within 60 minutes after collection.

##### Swab

Normal amount: 1 swab

Procedure: Swabbing, which is probably the most common method of collecting specimen for culture, is usually performed on open wounds. Because surface organisms can easily contaminate wounds, it is essential to clean and irrigate the surface of the wound with saline until it is free of drainage, necrotic debris, eschar, or purulent material.

The Z-stroke technique involves rotating a swab between the fingers as the swab is moved in a zigzag fashion across the wound. The wound edges should be avoided. The Levine technique involves rotating the swab over a 1 cm area with sufficient pressure to express fluid within the wound. As above, wound edges should be avoided. This technique is found to be superior to the Z-stroke technique for identifying infected wounds, largely because of the technique's ability to express pus from the wound.

#### Background

##### Description

Bacterial wound cultures, together with clinical examination, are used to

determine the presence of infection in wounds. Additionally, cultures are used to identify the specific organism or organisms and to guide specific antimicrobial therapy.

#### Indications/Applications

Bacterial wound culture is indicated for surgical and nonsurgical wounds, both acute and chronic, suspected of being infected. [It is also indicated for hospital](#) or local surveillance protocols to monitor drug-resistant microorganisms.

#### Considerations

Tissue biopsy is considered the criterion standard in collecting wound

culture specimens. Culture of viable but potentially infected tissue is preferred over necrotic tissue. [Swab cultures may be unreliable](#) because they usually indicate contamination. When appropriate, perform tissue biopsy or aspiration to collect specimens. [Ideally, specimens should be collected](#) before starting antibiotics. [Clinical examination of the wound](#) and how it is progressing should always carry more weight than culture results. Cultures are best used to confirm clinical impression of infecting pathogen(s), to suggest an unanticipated pathogen if the wound is not improving, and to guide alternative antimicrobials (via susceptibility testing), as indicated. [Serial wound cultures to evaluate response](#) to treatment is discouraged.

## TROUBLESHOOTING

### Anaerobic bacteria culture

#### Definition

An anaerobic bacteria culture is a method used to grow anaerobes from a clinical specimen. Obligate anaerobes are bacteria that can live only in the absence of oxygen. Obligate anaerobes are destroyed when exposed to the atmosphere for as briefly as 10 minutes. Some anaerobes are tolerant to small amounts of oxygen. Facultative anaerobes are those organisms that will grow with or without oxygen. The methods of obtaining specimens for anaerobic culture and the culturing procedure are performed to ensure that the organisms are protected from oxygen.

#### Purpose

Anaerobic bacterial cultures are performed to identify bacteria that grow only in the absence of oxygen and which may cause human infection. If overlooked or killed by exposure to oxygen, anaerobic infections result in such serious consequences as amputation, organ failure, sepsis, meningitis, and death. Culture is required to correctly identify anaerobic pathogens and institute effective antibiotic treatment.

#### Precautions

It is crucial that the health care provider obtain the sample for culture via aseptic technique. Anaerobes are commonly found on mucous membranes and other sites such as the vagina and oral cavity. Therefore, specimens likely to be contaminated with these organisms should not be submitted for culture (e.g., a throat or vaginal swab). Some types of specimens should always be cultured for anaerobes if an infection is suspected. These include abscesses, bites, blood, cerebrospinal fluid and exudative body fluids, deep wounds, and dead tissues. The specimen must be protected from oxygen during collection and transport and must be transported to the laboratory immediately.

#### Description

Anaerobes are normally found within certain areas of the body but result in serious infection when they have access to a normally sterile body fluid or deep tissue that is poorly oxygenated. Some anaerobes normally

live in the crevices of the skin, in the nose, mouth, throat, intestine, and vagina. Injury to these tissues (i.e., cuts, puncture wounds, or trauma) especially at or adjacent to the mucous membranes allows anaerobes entry into otherwise sterile areas of the body and is the primary cause of anaerobic infection. A second source of anaerobic infection occurs from the introduction of spores into a normally sterile site. Spore-producing anaerobes live in the soil and water, and spores may be introduced via wounds, especially punctures. Anaerobic infections are most likely to be found in persons who are immunosuppressed, those treated recently with broad-spectrum antibiotics, and persons who have a decaying tissue injury on or near a mucous membrane, especially if the site is foul-smelling.

#### Some specimens from which anaerobes are likely to be isolated are:

- blood
- bile
- bone marrow
- cerebrospinal fluid
- direct lung aspirate
- tissue biopsy from a normally sterile site
- fluid from a normally sterile site (like a joint)
- dental abscess
- abdominal or pelvic abscess
- knife, gunshot, or surgical wound
- severe burn.

#### Some of the specimens that are not suitable for anaerobic cultures include:

- coughed throat discharge (sputum)
- rectal swab
- nasal or throat swab
- urethral swab
- Voided urine

#### Specimen collection

The keys to effective anaerobic bacteria cultures include collecting a contamination-free specimen and protecting it from oxygen exposure. Anaerobic bacteria cultures should be obtained from an appropriate site without the health care professional contaminating the sample with

bacteria from the adjacent skin, mucus membrane, or tissue. Swabs should be avoided when collecting specimens for anaerobic culture because cotton fibers may be detrimental to anaerobes. Abscesses or fluids can be aspirated using a sterile syringe that is then tightly capped to prevent entry of air. Tissue samples should be placed into a degassed bag and sealed, or into a gassed out screw top vial that may contain oxygen-free prereduced culture medium and tightly capped. The specimens should be plated as rapidly as possible onto culture media that has been prepared.

### Culture

Cultures should be placed in an environment that is free of oxygen, at 95°F (35°C) for at least 48 hours before the plates are examined for growth. [Gram staining is performed on the specimen](#) at the time of culture. While infections can be caused by aerobic or anaerobic bacteria or a mixture of both, some infections have a high probability of being caused by anaerobic bacteria. These infections include brain abscesses, lung abscesses, aspiration pneumonia, and dental infections. Anaerobic organisms can often be suspected because many anaerobes have characteristic microscopic morphology (appearance). For example, *Bacteroides* spp. are gram-negative rods that are pleomorphic (variable in size and shape) and exhibit irregular bipolar staining. *Fusobacterium* spp. are often pale gram-negative spindle-shaped rods having pointed ends. *Clostridium* spp. are large gram-positive rods that form spores. The location of the spore (central, subterminal, terminal, or absent) is a useful differential characteristic. The presence of growth, oxygen tolerance, and Gram stain results are sufficient to establish a diagnosis of an anaerobic infection and begin antibiotic treatment with a drug appropriate for most anaerobes such as clindamycin, metronidazole, or vancomycin.

### Gram-negative anaerobes and some of the infections they produce include the following genera:

- *Bacteroides* (the most commonly found anaerobes in cultures; intra-abdominal infections, rectal abscesses, soft tissue infections, liver infection)
- *Fusobacterium* (abscesses, wound infections, pulmonary and intracranial infections)
- *Porphyromonas* (aspiration pneumonia, periodontitis)
- *Prevotella* (intra-abdominal infections, soft tissue infections)

### Gram-positive anaerobes include the following:

- *Actinomyces* (head, neck, pelvic infections; aspiration pneumonia)
- *Bifidobacterium* (ear infections, abdominal infections)
- *Clostridium* (gas, gangrene, food poisoning, tetanus, pseudomembranous colitis)
- *Peptostreptococcus* (oral, respiratory, and intra-abdominal infections)
- *Propionibacterium* (shunt infections)

The identification of anaerobes is highly complex, and laboratories may use different identification systems. Partial identification is often the goal. For example, there are six species of the *Bacteroides* genus that may be identified as the *Bacteroides fragilis* group rather than identified

individually. Organisms are identified by their colonial and microscopic morphology, growth on selective media, oxygen tolerance, and biochemical characteristics. These include sugar fermentation, bile solubility, esculin, starch, and gelatin hydrolysis, casein and gelatin digestion, catalase, lipase, lecithinase, and indole production, nitrate reduction, volatile fatty acids as determined by gas chromatography, and susceptibility to antibiotics. The antibiotic susceptibility profile is determined by the microtube broth dilution method. Many species of anaerobes are resistant to penicillin, and some are resistant to clindamycin and other commonly used antibiotics.

### Diagnosis/Preparation

The health care provider should take special care to collect a contamination-free specimen. All procedures must be performed aseptically. The health care professional who collects the specimen should be prepared to take two samples, one for anaerobic culture and one for aerobic culture, since it is unknown whether the pathogen can grow with or without oxygen. In addition, health care professionals should document any antibiotics that the patient is currently taking and any medical conditions that could influence growth of bacteria.

### Aftercare

In the case of vein puncture for anaerobic blood cultures, direct pressure should be applied to the vein puncture site for several minutes or until the bleeding has stopped. An adhesive bandage may be applied, if appropriate. If swelling or bruising occurs, ice can be applied to the site. For collection of specimens other than blood, the patient and the collection site should be monitored for any complications after the procedure.

### Risks

Special care must be taken by the health care team obtaining, transporting, and preparing the specimen for anaerobic culture. Poor methodology may delay the identification of the bacterium, may allow the patient's condition to deteriorate, and may require the patient to provide more samples than would otherwise be required. Patients may experience bruising, discomfort, or swelling at the collection site when tissue, blood, or other fluids are obtained.

### Results

Negative results will show no pathogenic growth in the sample. Positive results will show growth, the identification of each specific bacterium, and its antibiotic susceptibility profile.

### Patient education

A health care team member should explain the specimen collection procedure to the patient. If the patient is seriously ill, the team member should explain the procedure to the patient's family members. The patient and his or her family should understand that because bacteria need time to grow in the laboratory, several days may be required for bacterium identification.

## BOUQUET

## In Lighter Vein

The Teacher says to the class: Who ever stands up is stupid



\*Nobody stands up\*

Teacher: I said who ever stands up is STUPID!

\*Little Johnny stands up\*

Teacher: Johnny, do you really think that you are stupid?

Little Johnny: No Mrs, I just thought that maybe you are lonely being the only one standing.

Teacher: Who answers my next question, can go home.

One boy throws his bag out the window.

Teacher: Who just threw that?

Boy: Me and I'm going home now.



A husband tells his wife, "Since it is your birthday, remember that yellow Lamborghini that you really wanted?". The wife screams in joy and starts crying tears of joy. Then the husband says, "Well I got you a toothbrush, same color".

Teacher: What makes you see?

Bobyjack: My eyes, my nose and my ears.

Teacher: True for the eyes but why for your ears and nose?

Bobyjack: It's to hold my glasses!!!



## Wisdom Whispers by Gautama Buddha



"No one saves us but ourselves. No one can and no one may. We ourselves must walk the path."

"Holding on to anger is like grasping a hot coal with the intent of throwing it at someone else; you are the one who gets burned."

"Purity or impurity depends on oneself, No one can purify another."

"It is a man's own mind, not his enemy or foe, that lures him to evil ways."

## Brain Teasers

- What steps does one PCR cycle consist of?
  - Denaturation
  - Annealing
  - Extension
  - All of the above.
- What kinds of PCRs exist in clinical practice?
  - Reverse transcriptase
  - Real time
  - Nested and differential
  - All of the above.
- In relation to immunoassays what does R stand for in RIA?
  - Rapid
  - Radio
  - Resonance
  - Real.
- What is usual normal reference range given for TSH in  $\mu\text{IU/ml}$ ?
  - 0.3–6.2
  - 0.8–2.0
  - 1.4–4.2
  - 10–20.

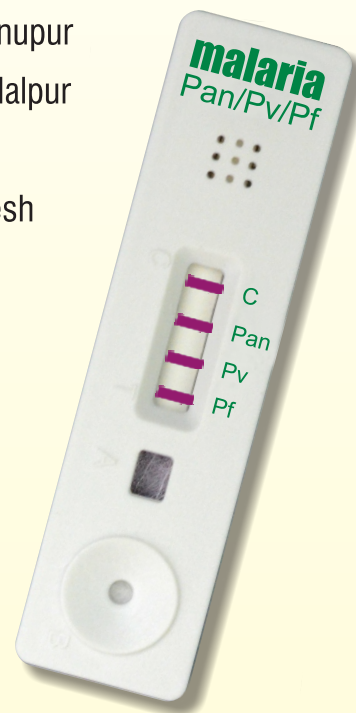
ANSWER: 1. D, 2. D, 3. B, 4. A

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