




Gram-positive and spore-forming bacterial infections of the gastrointestinal tract

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- Gram-positive bacteria cause several important GI syndromes, ranging from rapid toxin-mediated food poisoning to inflammatory colitis.
 - Some act through **preformed toxins**, or through **toxin production after ingestion**, and others through **invasion and inflammation**.
 - Foodborne disease is a major global public-health problem and prevention depends heavily on hygiene, temperature control, and safe food handling
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Learning objectives

Classify

Classify the main Gram-positive GI pathogens by food intoxication, enteritis, and colitis/enterocolitis.

Recognize

Recognize the major clinical patterns caused by *Staphylococcus aureus*, *Bacillus cereus*, *Clostridium perfringens*, *Clostridium botulinum*, *Clostridioides difficile*, and *Listeria monocytogenes*.

Explain

Explain the pathogenesis and common food or healthcare associations of each organism.

Propose

Propose preventive measures based on organism biology and transmission.

- Gram-positive foodborne and GI pathogens are especially important because many illnesses are **preventable** through correct food handling, storage, and infection-control practices.
- These pathogens also represent infection principles such as toxin-mediated disease, spore survival, and dysbiosis-associated colitis.

https://www.who.int/news-room/fact-sheets/detail/food-safety?utm_source=chatgpt.com
<https://www.who.int/activities/promoting-safe-food-handling>



Home / Activities / Promoting safe food handling



Promoting safe food handling

1. Keep clean
2. Separate raw and cooked
3. Cook thoroughly
4. Keep food at safe temperatures
5. Use safe water and raw materials

These are “Five keys to safer food”, which were developed to educate safe food handling behaviours to all consumers and food handlers.

Each year, 1 in 10 people get ill by eating unsafe food. While food safety is a shared responsibility, individual consumers and food handlers play a huge role in preventing foodborne diseases. “Five keys to safer food” messages were therefore developed, and validated by an independent body of international scientists in 2001, to empower all consumers worldwide with a simple and applicable set of actions to prevent foodborne diseases.

The poster with the Five Keys messages has been translated into 88 languages (as of October 2019) and are [available online](#).



Food safety

4 October 2024

Key facts


- Food safety, nutrition and food security are inextricably linked.
- An estimated 600 million – almost 1 in 10 people in the world – fall ill after eating contaminated food and 420 000 die every year.
- US\$ 110 billion is lost each year in productivity and medical expenses resulting from unsafe food in low- and middle-income countries.
- Children under 5 years of age carry 40% of the foodborne disease burden, with 125 000 deaths every year.
- Foodborne diseases impede socioeconomic development by straining health care systems and harming national economies, tourism, and trade.
- Food safety is a shared responsibility among different national authorities and requires a multisectoral, one health approach.





Clinical syndrome classification

- **Food intoxication:** toxin is already present in the food before ingestion.
 - **Enteritis:** disease mainly affects the small intestine and often causes watery diarrhea and cramping.
 - **Colitis:** disease mainly affects the colon and is more associated with inflammation, abdominal pain, and toxin-mediated mucosal injury.
 - **Enterocolitis:** both small intestine and colon are involved.
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- Rapid onset after a meal suggests **preformed toxin**.
 - Watery diarrhea without marked inflammation suggests **small-bowel involvement**.
 - More severe abdominal pain, inflammatory diarrhea, or pseudomembranous disease suggests **colitis**.
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Organisms of relevance

- *Staphylococcus aureus*
 - *Bacillus cereus*
 - *Clostridium perfringens*
 - *Clostridium botulinum*
 - *Clostridioides difficile*
 - *Listeria monocytogenes*
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Organism	Gram stain / morphology	Spore former	Main GI pattern	Main mechanism
<i>Staphylococcus aureus</i>	Gram-positive cocci in clusters	No	Food poisoning	Preformed enterotoxin
<i>Bacillus cereus</i>	Gram-positive rod	Yes	Food poisoning or enteritis	Preformed emetic toxin or toxin produced in gut
<i>Clostridium perfringens</i>	Gram-positive anaerobic rod	Yes	Enteritis	Toxin produced after ingestion
<i>Clostridium botulinum</i>	Gram-positive anaerobic rod	Yes	Foodborne intoxication	Preformed neurotoxin
<i>Clostridioides difficile</i>	Gram-positive anaerobic spore-forming rod	Yes	Colitis	Toxin-mediated mucosal injury after dysbiosis
<i>Listeria monocytogenes</i>	Gram-positive rod	No	Enteritis or invasive infection	Invasive foodborne infection



Spore forming bacteria

- Spores are resistant dormant forms that can survive environmental stress and sometimes survive cooking conditions better than vegetative bacteria.
 - If cooked food is cooled slowly or stored improperly, spores may germinate and multiply.
 - This is central to the epidemiology of ***B. cereus***, ***C. perfringens***, ***C. botulinum***, and ***C. difficile***.
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Staphylococcal Food Poisoning

- Staphylococcal food poisoning, is an **intoxication** rather than an infection.
- Common food source are **processed meats** such as ham and salted pork, **custard-filled pastries, potato salad, and ice cream.**
- Staphylococcal food poisoning results from contamination of the food by a human carrier with no animal reservoir involved (asymptomatic nasopharyngeal colonization in half of infections).
- *Staphylococci* introduced into the food (sneeze or contaminated hands) grow and multiply when food left at room temperature or warmer (danger zone 40°F and 140°F).
- Subsequent heating kills the bacteria but doesn't inactivate the heat stable enterotoxin.



Staphylococcal Food Poisoning

EXPLORE THIS TOPIC ▾

SEARCH

Preventing Staphylococcal (Staph) Food Poisoning

For Everyone
APRIL 22, 2024

KEY POINTS

- You can take steps to prevent Staph food poisoning.
- Always wash your hands before preparing or serving food.
- Keep food out of the "danger zone" between 40°F and 140°F.
- Refrigerate perishable food after 2 hours (or 1 hour if in 90°F or hotter temperatures).



https://www.cdc.gov/staph-food-poisoning/prevention/index.html?utm_source=chatgpt.com



Clinical features, diagnosis and treatment

- The onset of disease is abrupt and rapid, with a mean incubation period of 4 hours, lasting for less than 24 hours.
 - **Severe vomiting, diarrhea, and abdominal pain** or nausea are characteristic symptoms; sweating and headache may occur, but **fever is not seen**.
 - The **diarrhea is watery and non-bloody**, and dehydration may result from the considerable fluid loss.
 - The toxin-producing organisms can be cultured from the contaminated food if still viable during food prep.
 - Contaminated food can be tested for the heat stable enterotoxin.
 - Diagnosis of food poisoning is primarily clinical.
 - Treatment is symptomatic (hydration and pain killers), **antibiotic therapy is not indicated**.
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Immunity and Staphylococcal Enterocolitis

- **Neutralizing antibodies** against enterotoxins may provide some protection but **limited cross-protection** among related enterotoxins.
- Immunity is short lived and recurrence can occur (different enterotoxin serotypes).
- Certain strains of ***S. aureus*** can also cause **staphylococcal enterocolitis**, resulting from **active growth of the organism in the colon**.
- Enterocolitis usually occurs in patients who have received **broad-spectrum antibiotics (dysbiosis)**.
- Clinical features include **watery diarrhea, abdominal cramps, and fever**.
- Diagnosis is considered after excluding more common causes such as ***Clostridium difficile* colitis**, with confirmation by finding **abundant *S. aureus* in stool**.
- **Fecal leukocytes** and **white colonic plaques with ulceration** may be found.

Bacillus cereus

- **B. cereus** is a Gram-positive, aerobic or facultative, spore-forming rod found widely in the environment.
- Gastroenteritis caused by *B. cereus* is mediated by one of two enterotoxin:
 1. The heat-stable, proteolysis-resistant enterotoxin causes **the emetic** form of the disease,
 2. and the heat-labile enterotoxin causes the **diarrheal form** of the disease.
- The heat-labile enterotoxin stimulates the adenylate cyclase– cAMP system in intestinal epithelial cells, leading to profuse watery diarrhea.

TABLE 20.2 *Bacillus cereus* Food Poisoning

Disease Features	Emetic Form	Diarrheal Form
Implicated food	Rice	Meat, vegetables
Incubation period (hours)	<6 (mean, 2)	>6 (mean, 9)
Symptoms	Vomiting, nausea, abdominal cramps	Diarrhea, nausea, abdominal cramps
Duration (hours)	8-10 (mean, 9)	20.36 (mean, 24)
Enterotoxin	Heat stable	Heat labile

Clinical disease

- In most patients, the **emetic form** of disease results from consumption of contaminated rice.
- Bacteria are killed during cooking but spores survive and germinate if the rice is not refrigerated, and heat stable toxin is released when the rice is reheated.
- Emetic form is an intoxication, incubation period is short (1-6 hours), and the duration of illness is <24hours.
- Symptoms consists of vomiting, nausea, and abdominal cramps. Fever and diarrhea are generally absent

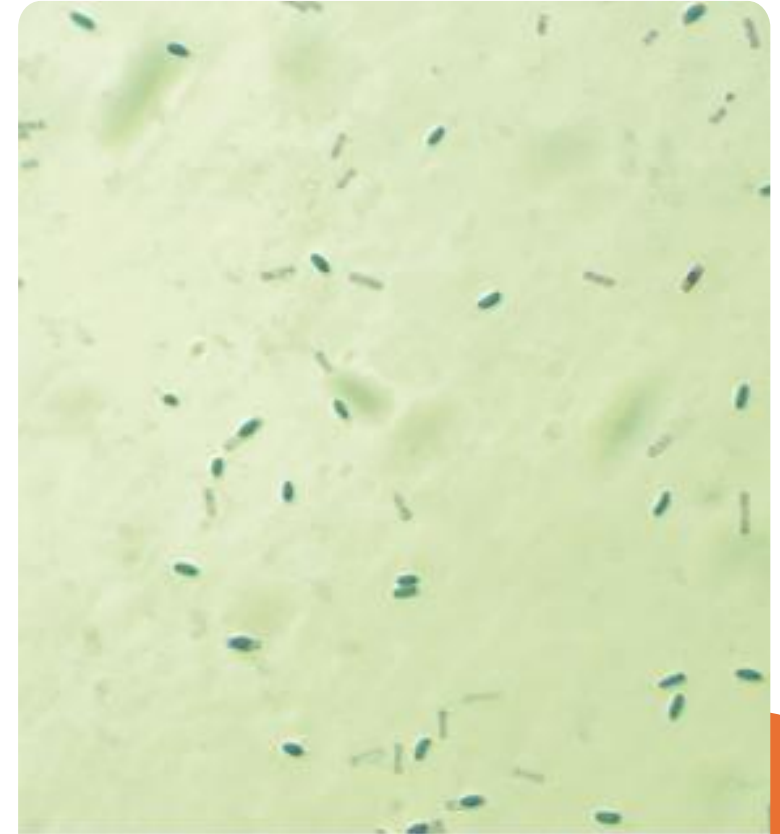



Fig. 20.5 *Bacillus cereus*. Spores retain the malachite green dye in this special spore stain, and the vegetative cells are gray or colorless.

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- The **diarrheal** form of *B. cereus* food poisoning is a true infection resulting from ingestion of the bacteria in contaminated meat, vegetables, or sauces.
 - The organism multiplies in the intestinal tract and release heat labile enterotoxin.
 - Incubation period is longer, and symptoms include diarrhea, nausea, and abdominal cramps generally lasting 1 day or longer.
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Lab diagnosis, treatment and prevention

- Implicated food (rice, meat, vegetables) can be cultured to confirm foodborne disease; diagnosis is mainly clinical.
 - Neither cultures nor tests to detect the heat-stable or heat-labile enterotoxins are commonly performed.
 - The course of *B. cereus* gastroenteritis is short and uncomplicated, symptomatic treatment is adequate.
 - Rapid consumption of foods after cooking and proper refrigeration of uneaten foods can prevent food poisoning.
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Clostridium perfringens

- *C. perfringens* is a large rectangular, gram-positive spore forming rod.
- In the lab, *C. perfringens* colonies are spreading and beta hemolytic.
- One or more “major lethal” toxins is produced by *C. perfringens* (alpha, beta, epsilon, and iota toxins) subdividing it into five types (A through E).
- *C. perfringens* produces **enterotoxin** (a superantigen) primarily by **strain A**.
- The enterotoxin binds the brush border of intestinal epithelium in the ileum and jejunum leading to altered membrane permeability and loss of fluids and ions.





Gastrointestinal disease

- Type A *C. perfringens* commonly inhabits the intestinal tract of humans and animals and is widely distributed in nature (soil and water).
 - **Clostridial food poisoning** has a short incubation period (8-12 hrs), presenting with abdominal cramps and watery diarrhea but no fever, nausea, or vomiting, lasting for less than 24 hours.
 - Disease results from ingestion of meat products (e.g., beef, chicken, turkey, gravy) contaminated with strain A (10^8 to 10^9 organisms).
 - Holding contaminated foods at temperatures less than 60°C allows spores to germinate and multiply to high numbers.
 - Reheating the food to 74°C can destroy the heat-labile enterotoxin.
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- **Necrotizing enteritis is** characterized by acute abdominal pain, vomiting, bloody diarrhea, ulceration and perforation of the small intestine.
- Beta toxin produced by *C. perfringens* type C is responsible for this disease; mortality approaches 50%.
- Results from consumption of both undercooked contaminated pork and sweet potatoes.
- Recovery of more than 10⁵ organisms per gram of food or more than 10⁶ bacteria per gram of feces collected within 1 day of the

Clostridium perfringens

Soft-Tissue Infections

Cellulitis: localized edema and erythema with gas formation in the soft tissue; generally nonpainful

Suppurative myositis: 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

Gastroenteritis

Food poisoning: rapid onset of abdominal cramps and watery diarrhea with no fever, nausea, or vomiting; short duration and self-limited

Necrotizing enteritis: acute, necrotizing destruction of jejunum, with abdominal pain, vomiting, bloody diarrhea, and peritonitis



Diagnosis and treatment

- Food poisoning is documented by the recovery of more than 10^5 organisms per gram of food or more than 10^6 bacteria per gram of feces collected within 1 day of the disease.
 - Culture and immunoassays are available; but the diagnosis is primarily clinical.
 - Clostridial food poisoning is managed by oral rehydration and in severe cases intravenous fluids and electrolytes; antibiotics are not recommended.
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Clostridioides difficile

- *C. difficile* is a large anaerobic rod that freely forms spores in vivo and in culture.
- *C. difficile* is part of the normal intestinal flora in a small number of healthy people and hospitalized patients (asymptomatic carriage).
- It is associated with a history of exposure to a health care facility.
- The disease develops in individuals taking antibiotics altering the normal enteric flora; permitting overgrowth of *C. difficile* or disrupting colonization resistance (e.g., ampicillin, clindamycin, fluoroquinolones).

The infographic features a blue header with the title "Assess Your Patient's Risk For *C. diff* Infection Before Prescribing an Antibiotic". To the right is the "BE ANTIBIOTICS AWARE" logo with the tagline "SMART USE, BEST CARE". Below the header are five risk factors, each with an icon in a blue circle: "Antibiotic exposure" (pills), "Previous history of *C. diff*" (bacteria), "Older age" (65+), "Extended stay in healthcare settings (examples: hospitals, nursing homes)" (hospital building), and "Immunocompromising conditions" (shield with gear). The CDC logo and ID "CS321425C" are in the bottom right.

Assess Your Patient's Risk For *C. diff* Infection Before Prescribing an Antibiotic

BE ANTIBIOTICS AWARE
SMART USE, BEST CARE

- Antibiotic exposure
- Previous history of *C. diff*
- Older age (65+)
- Extended stay in healthcare settings (examples: hospitals, nursing homes)
- Immunocompromising conditions

CDC
CS321425C

<https://www.cdc.gov/c-diff/hcp/resources/assess-patient-risk.html>



Pathogenesis and Immunity

- *C. difficile* produces two toxins: an enterotoxin (toxin A) and a cytotoxin (toxin B).
 - The enterotoxin produces cytopathic effect resulting in increased permeability of intestinal wall and diarrhea; cytotoxins lead to destruction of the cellular cytoskeleton.
 - Production of one or both toxins alone does not appear to be sufficient for disease (e.g., carriage of *C. difficile* and high levels of toxins are common in young children, although disease is rare)
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Clinical disease

- Toxin-producing *C. difficile* is the most common cause of antibiotic-associated GI diseases.
- ranging from a relatively benign, self-limited diarrhea to severe, life-threatening pseudomembranous colitis.
- *C. difficile* virulence it is attributed to multiple virulent phenotypes.

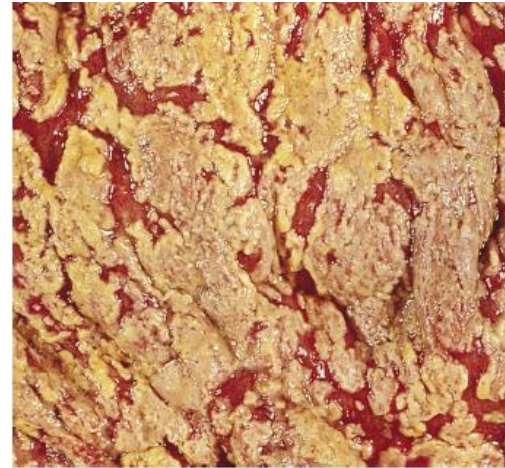


Fig. 30.1 Antibiotic-associated colitis: gross section of the lumen of the colon. Note the white plaques of fibrin, mucus, and inflammatory cells overlying the normal red intestinal mucosa.

BOX 30.1 Clostridial Diseases: Clinical Summaries

Clostridium difficile

Antibiotic-associated diarrhea: acute diarrhea generally developing 5 to 10 days after initiation of antibiotic treatment (particularly clindamycin, penicillins, cephalosporins, fluoroquinolones); may be brief and self-limited or more protracted

Pseudomembranous colitis: most severe form of *C. difficile* disease, with profuse diarrhea, abdominal cramping, and fever; whitish plaques (pseudomembranes) over intact colonic tissue seen on colonoscopy



Diagnosis

- Disease is suspected in hospital acquired diarrhea 48-72 hours after admission
 - Testing for *C. difficile* infection (CDI) in hospitalized patients is indicated for new-onset, unexplained diarrhea, defined as three or more loose/unformed stools within 24 hours.
 - Isolation of the *C. difficile* in stool culture documents colonization but not disease.
 - Detection of the enterotoxin or cytotoxin or detection of the *C. difficile* toxin A and B genes in stool by nucleic acid amplification techniques is confirmatory (loose stool is tested).
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Treatment and prevention of *C. difficile* infection

- Discontinuation of the implicated antibiotic is generally sufficient to alleviate mild disease; **metronidazole**, **fidaxomicin** or **vancomycin** is necessary for severe diarrhea or colitis.
- Relapse could occur due to persistence of spores.
- Fecal transplant has been used for recurring infection.
- Prevention includes **antibiotic stewardship**, appropriate infection control, hand hygiene, and environmental cleaning in healthcare environments .

Listeria monocytogenes

- *L. monocytogenes* is the most significant human pathogen in the listeria genus.
- It is a short nonbranching, gram-positive, facultatively anaerobic rod capable of growth at a broad temperature range (1° C to 45° C) and in a high concentration of salt.
- The organism is motile at room temperature (less at 37 ° C), exhibiting end over end tumbling motility in broth, and is weakly beta hemolytic on sheep blood agar.

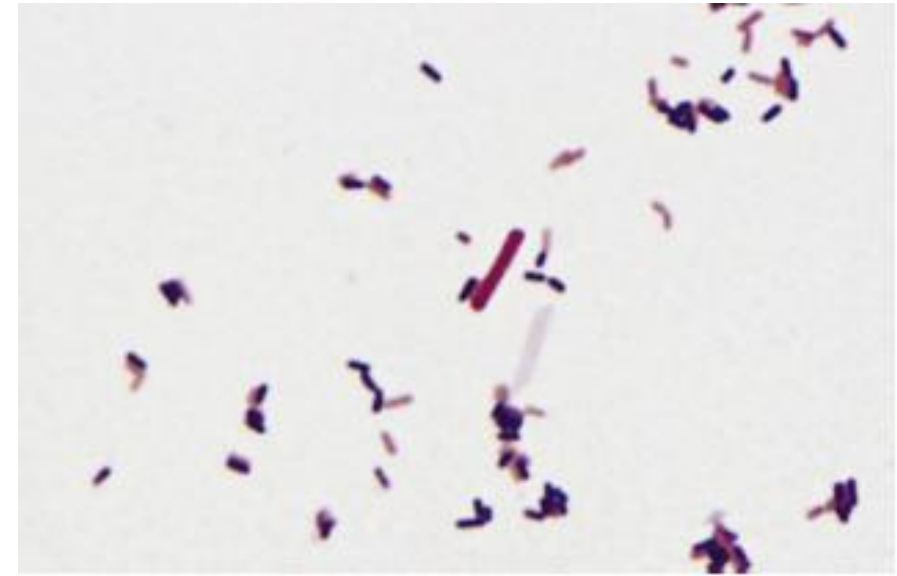


Fig. 21.1 Gram stain of *Listeria monocytogenes* in culture. *Listeria* appear as small gram-positive rods; some readily decolorize and appear gram-negative. The much larger gram-negative rod in the center of the photograph is *Escherichia coli*.

Pathogenesis

- *L. monocytogenes* is a facultative intracellular pathogen.
- The organism **has internalins A+B** for adherence to host cells, pore-forming cytolysin (**listeriolysin O**) to escape the phagolysosome, and **ActA** which coordinates assembly of actin to mediate intercellular directional movement.
- Cellular immunity manages *L. monocytogenes* because these bacteria can replicate in macrophages and move within cells escaping antibody-mediated clearance.

Epidemiology

- *L. monocytogenes* is isolated from a variety of environmental sources and from the feces of mammals, birds, fish, and other animals.
- The primary source of infection is consumption of contaminated food: undercooked processed meat (e.g., turkey franks, cold cuts); unpasteurized or contaminated milk or cheese; and unwashed raw vegetables.
- Listeria can grow in a wide pH range and at cold temperatures, foods with small numbers of organisms can become heavily contaminated during prolonged refrigeration.

Clinical disease

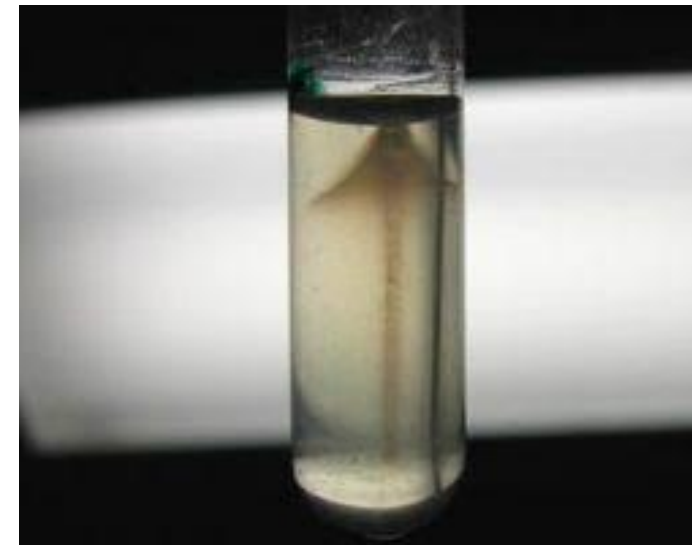
- Most infections in healthy adults are asymptomatic; listeriosis is more severe in certain risk groups (elderly, neonates, pregnant women) and immunocompromised.
- *Listeria* infections can result in neonatal disease (granulomatosis infantiseptica), abortions, meningitis and bacteremia
- An acute self-limited gastroenteritis develops in some patients, characterized by a 1-day incubation period followed by 2 days of symptoms, including watery diarrhea, fever and myalgias.

TABLE 21.2 Human Disease Associated with *Listeria* and Related Bacteria

Organism	Diseases
<i>Listeria monocytogenes</i>	Neonatal disease (spontaneous abortion, disseminated abscesses and granulomas, meningitis, septicemia); influenza-like illness in healthy adults; bacteremia or disseminated disease with meningitis in pregnant women and patients with cell-mediated immune defects

Diagnosis, treatment and prevention

- Can be detected in gram stain (intracellular and extracellular gram-positive coccobacilli) and culture of clinical specimens (CSF and blood).
- Cold enrichment of specimens enhances detection.
- Umbrella motility is observed in semisolid agar.
- Treatment of mild gastrointestinal disease is supportive; **gentamicin with either penicillin or ampicillin** is the treatment of choice for serious infections.
- *Listeria* are naturally resistant to cephalosporins, and resistance to macrolides, fluoroquinolones, and tetracyclines has been observed.
- People at high risk of infection should avoid eating raw or partially cooked foods of animal origin, soft cheeses, and unwashed raw vegetables.



Clostridium botulinum

- *C. botulinum* is an anaerobic, Gram-positive, spore-forming rod that produces a potent neurotoxin.
- The spores are heat-resistant and can survive in foods that are incorrectly or minimally processed.
- Botulism is caused by a potent neurotoxin formed during growth of *C. botulinum*, resulting in flaccid paralysis of muscles, including those of the respiratory tract
- Three major types of botulism are known: foodborne botulism , infant botulism and wound botulism.
- Children under 1 year old should never be fed honey, which has been linked to infant botulism.



Foodborne botulism

- Is a severe type of food poisoning caused by ingestion of foods containing the toxin produced by *C. botulinum*.
- Develops after consumption of improperly processed and inadequately cooked home preserved foods and canned food (e.g. canned corn, and vegetables, lobster, smoked salted fish etc.).
- Onset of symptoms in adults 18 to 36 hours after toxin ingestion.
- Botulinum toxin blocks peripheral cholinergic neurotransmission at the neuromuscular junction and autonomic nervous system.
- Symptoms are neurologic (flaccid muscle weakness, double vision etc..).
- Constipation after a period of normal development is often the first sign of infant botulism.

Diagnosis and treatment

- Botulinum toxin can be detected serum, feces or food by mouse neutralization test; diagnosis is mainly clinical.
- Recommended treatment for foodborne botulism includes early administration of botulinum antitoxin and intensive supportive care, including mechanical breathing assistance.
- Antimicrobial therapy is not recommended, due to concerns about increased toxin release.

References

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