SHEET NO.

MICROBIOLOGY (Bacteriology)

DOCTOR 2019 | MEDICINE | JU

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SCIENTIFIC CORRECTION :

GRAMMATICAL CORRECTION : Bushra Ghnemat & Nour Maher

DOCTOR :

GRAM POSITIVE RODS

- Divided by their ability to form spores or not
- SPORE forming : Bacillus (AEROBIC) and Clostridium (NON AEROBIC)
- NON SPORE forming :
- Corynebacterium diphtheriae and Listeria monocytogenes

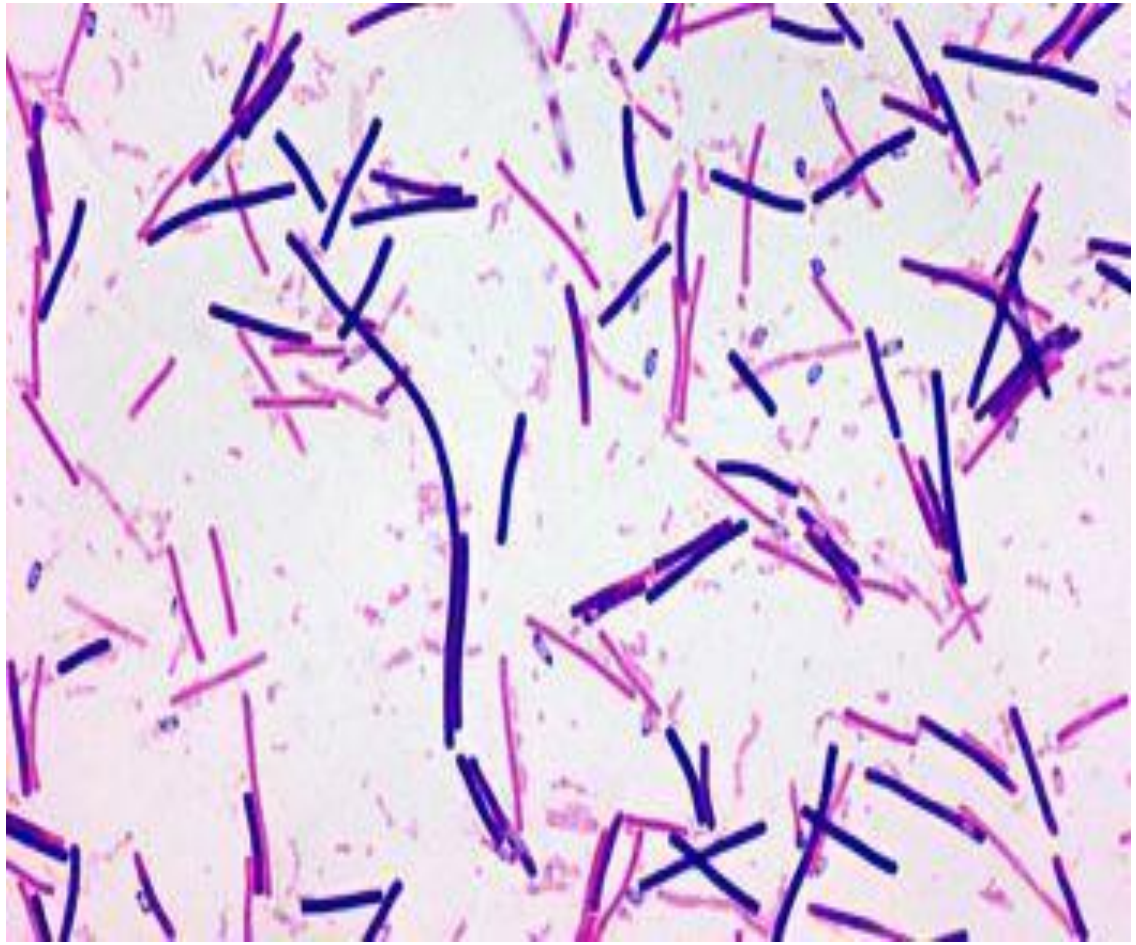
The main mechanism of pathogenesis in gram positive rods is exotoxin production.
listeria doesn't produce exotoxin, it secrets itself.

Growth	Anaerobic Growth	Spore Formation	Exotoxins Important in Pathogenesis
Bacillus	–	+	+
Clostridium	+	+	+
Corynebacterium	–	–	+
Listeria	–	–	–

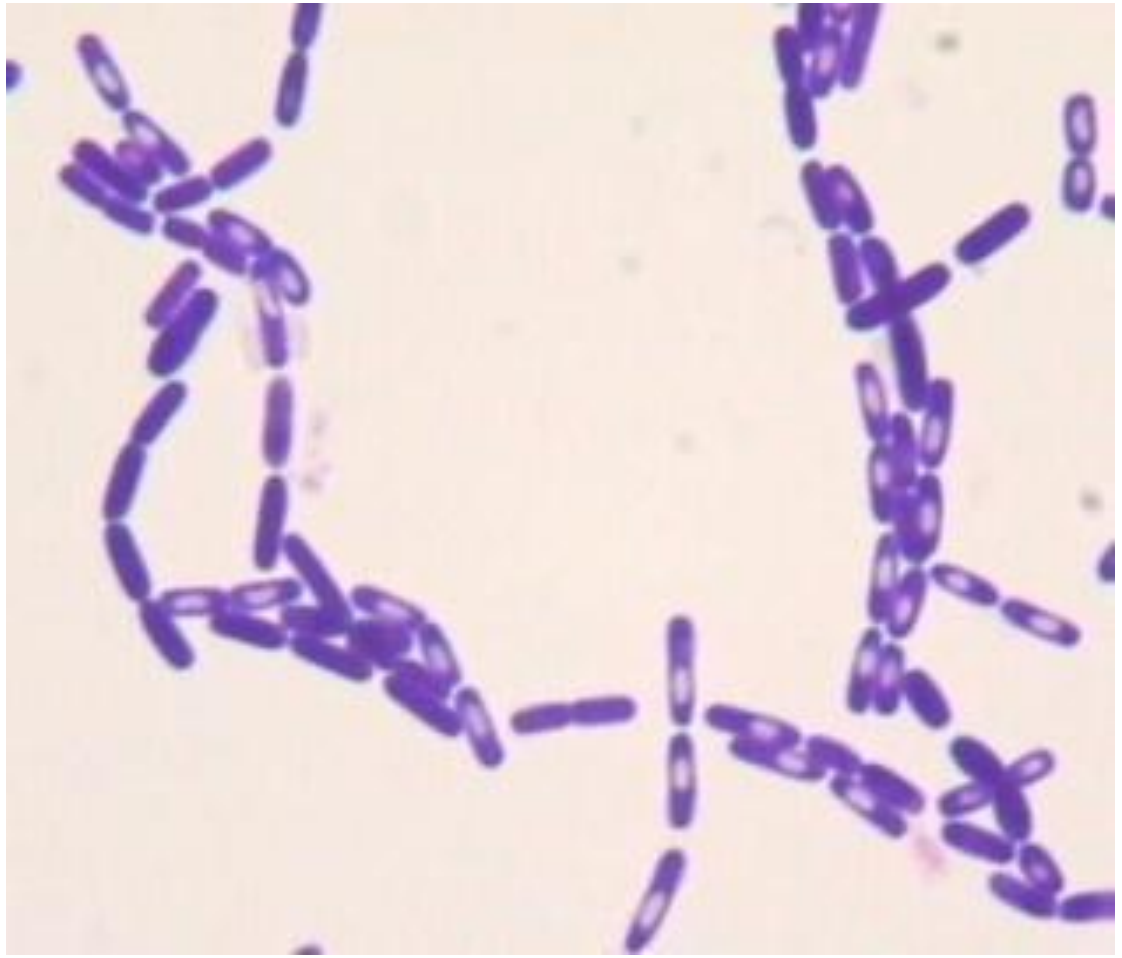
- These two gram-positive rods can also be distinguished based on the appearance (size, stain intensity and spore size/position) on Gram stain.

- Bacillus and Clostridium species are longer and more deeply staining than Corynebacterium and Listeria species.
- Corynebacterium species are club shaped (i.e., they are thinner on one end than the other, the other end contains large granules which makes it look like a club)
  (some bacteria can save its energy sources by making complex molecules when breaking down, they provide energy, so it condenses it on a one side of the cell. When it gets bigger, it will push the boundaries of the rod so it looks like a club)
- Corynebacterium and Listeria species characteristically appear as V- or L-shaped rods.

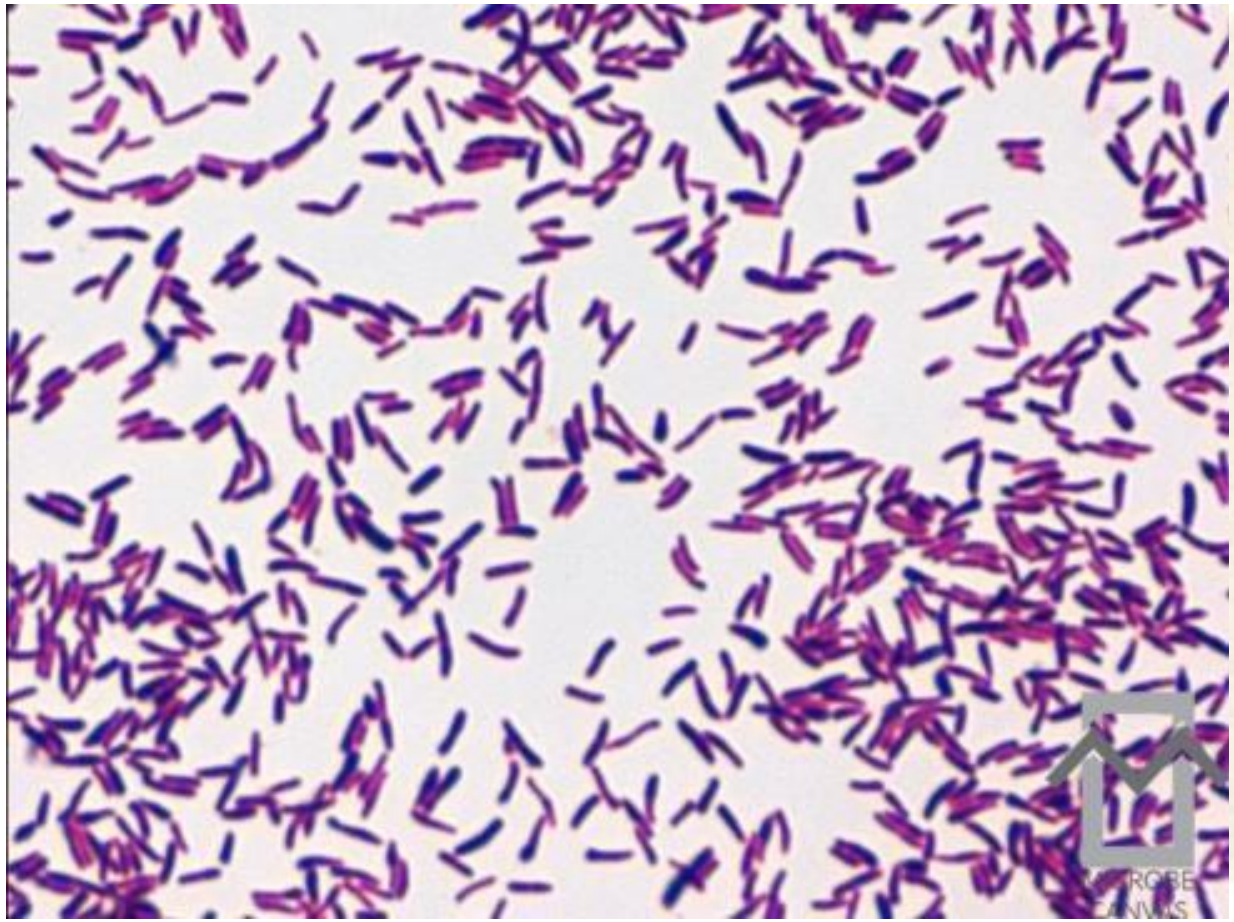
  (the shape is a bit more relaxed than the rigid forms BACILLUS AND CLOSTRIDIUM)

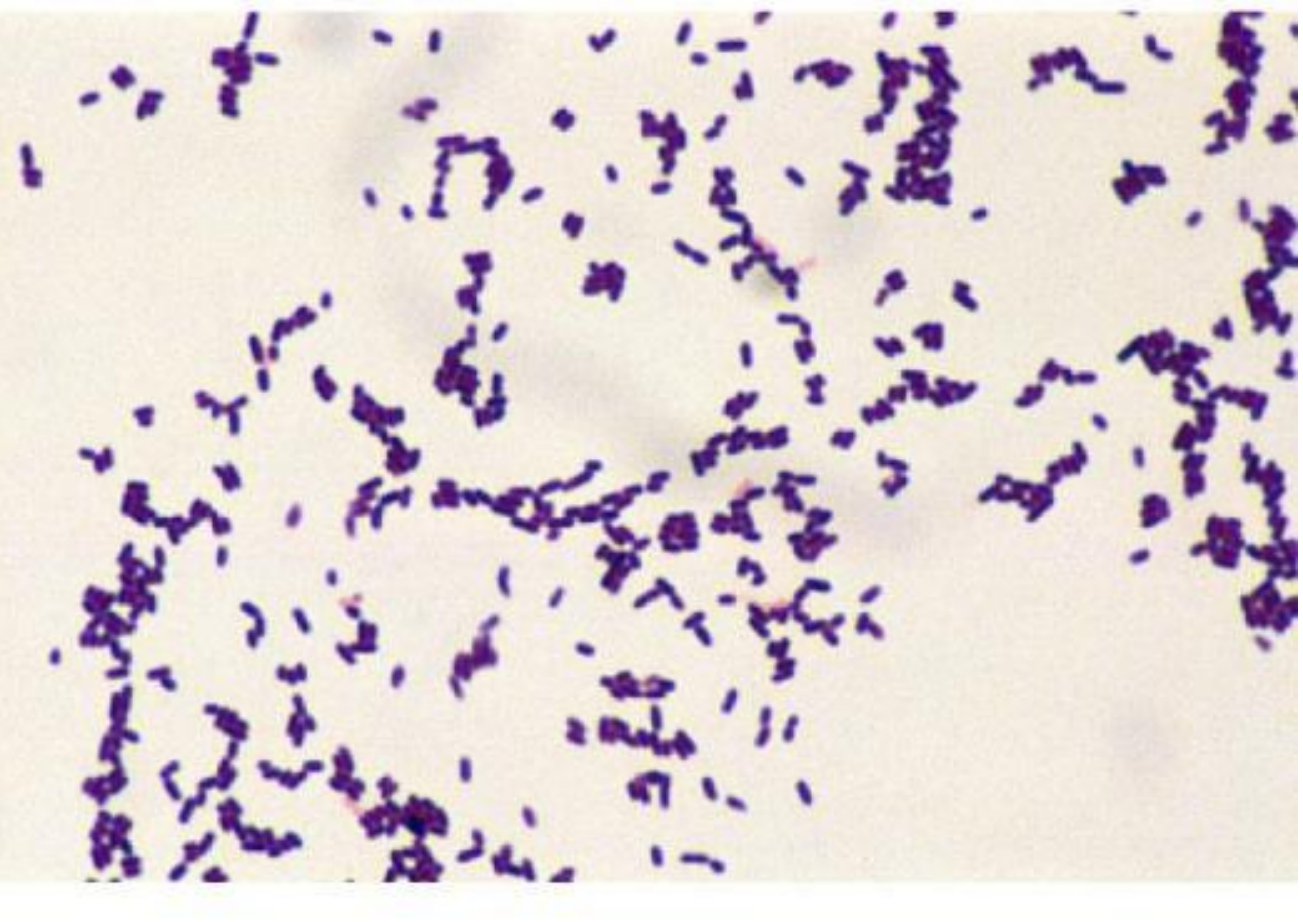


Clostridium difficile
Very deep staining
Very long



Bacillus Cereus
Notice central clearing of the spore
shorter





Corynbacterium

Less deeply staining

The shape is a bit relaxed

The Chinese letter appearance

Listeria

1- BACILLUS species

TABLE 17–2 Important Features of Pathogenesis by *Bacillus* Species

Organism	Disease	Transmission/Predisposing Factor	Action of Toxin	Prevention
B. anthracis	Anthrax	1. Cutaneous anthrax: spores in soil enter wound 2. Pulmonary anthrax: spores are inhaled into lung	Exotoxin has three components: protective antigen binds to cells; edema factor is an adenylate cyclase; lethal factor is a protease that inhibits cell growth	Vaccine contains protective antigen as the immunogen
B. cereus	Food poisoning	Spores germinate in reheated rice, then bacteria produce exotoxins, which are ingested	Two exotoxins (enterotoxins): 1. Similar to cholera toxin, it increases cyclic AMP 2. Similar to staphylococcal enterotoxin, it is a superantigen	No vaccine

Protective antigen → enables the toxin to exert its action.
very prominent edema.

Spores are very hard to get rid of; they can survive in a very extreme situation.

1-Causes a very watery diarrhea ---> larger amount of water into GI tract.

2- causes prominent vomiting and watery diarrhea.

SPORE-FORMING GRAM-POSITIVE RODS

1. Bacillus anthracis

- Disease:

Zoonosis----> sth you get from animal

- *B. anthracis* causes anthrax (Figure 17–1), which is common in animals but rare in humans.
- Human disease occurs in three main forms: cutaneous, pulmonary (inhalation), and gastrointestinal.
- In 2001, an outbreak of both inhalation and cutaneous anthrax occurred in the United States.
- The outbreak was caused by sending spores of the organism through the mail. There were 18 cases, causing 5 deaths in this outbreak.

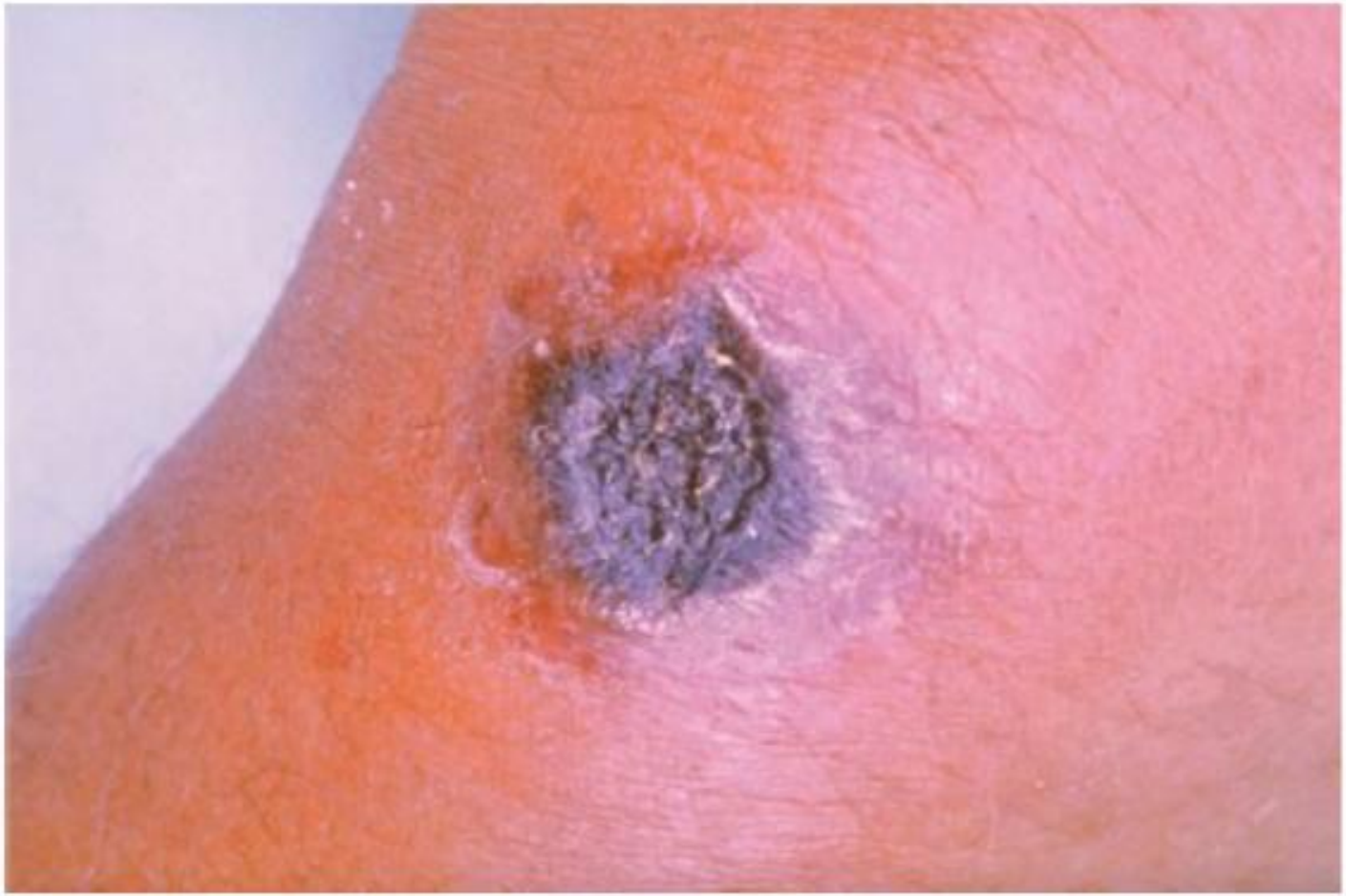
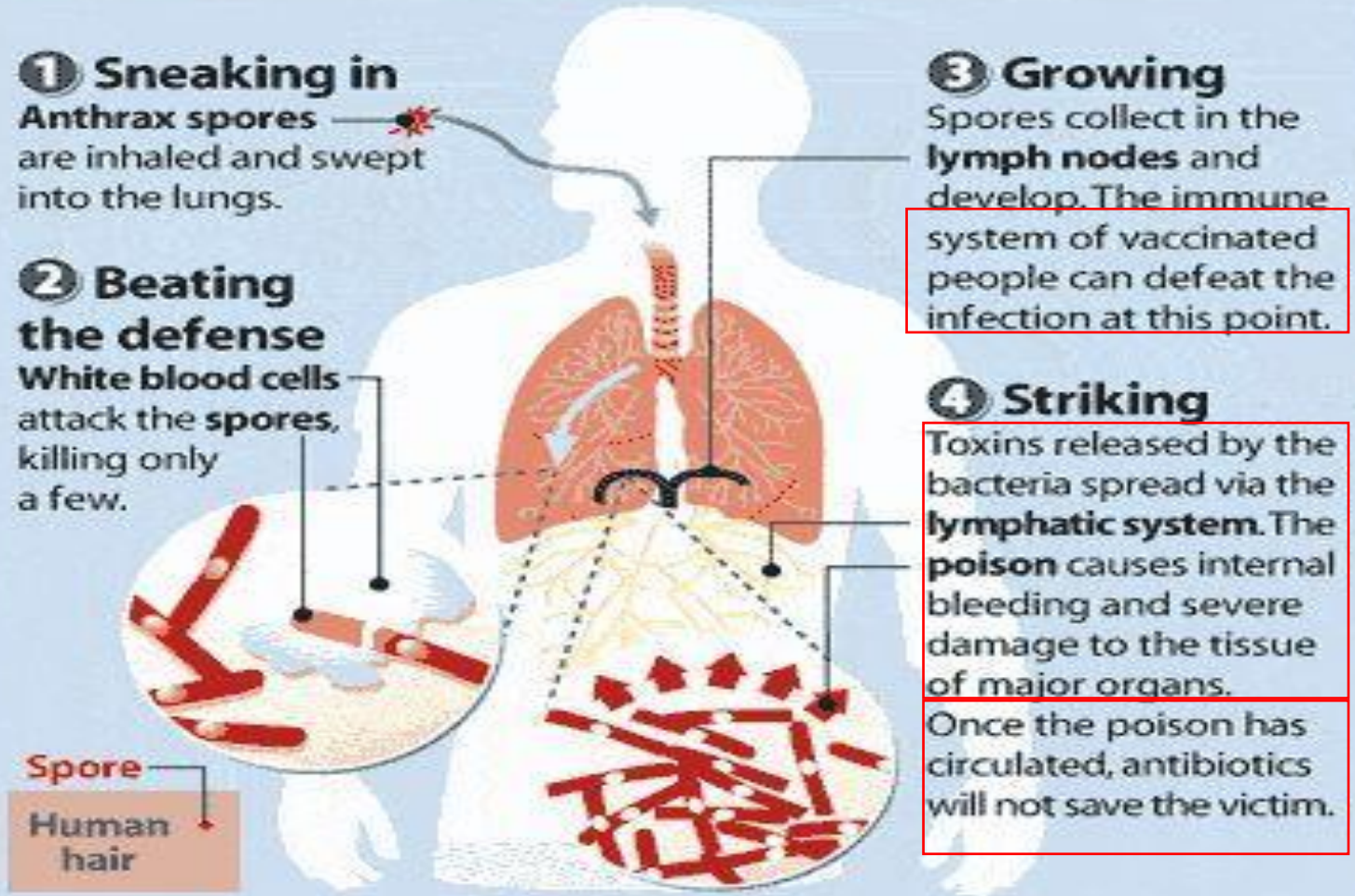


FIGURE 17–1 Skin lesion of anthrax. Note the *black eschar*, a necrotic lesion covered by a crust, caused by lethal factor, an exotoxin produced by *Bacillus anthracis*. Note the area of edema surrounding the eschar, which is caused by another exotoxin called *edema factor*. (Source: Centers for Disease Control and Prevention. CDC # 2033. CDC Provider: Dr. James H. Steele.)

HOW ANTHRAX ATTACKS

Anthrax is a naturally occuring bacterium that plagues farm animals and, occasionally, agricultural workers. An airborne form of the disease, however, can be harnessed as a potent biological weapon.



1 Sneaking in

Anthrax spores are inhaled and swept into the lungs.

2 Beating the defense

White blood cells attack the **spores**, killing only a few.

3 Growing

Spores collect in the **lymph nodes** and develop. The immune system of vaccinated people can defeat the infection at this point.

4 Striking

Toxins released by the bacteria spread via the **lymphatic system**. The **poison** causes internal bleeding and severe damage to the tissue of major organs.

Once the poison has circulated, antibiotics will not save the victim.

Source: "The World's Best Anatomical Charts"; "Zoology"; Anthrax Vaccine Immunization Program; Journal of the American Medical Association

ADRIAN HOLOVATY/Missourian

- Important *Properties B. anthracis* is a large gram-positive rod with square ends, frequently found in chains .
- Its antiphagocytic capsule is composed of D-glutamate/(*This is unique—capsules of other bacteria are polysaccharides.)*
- It is nonmotile, whereas other members of the genus are motile.
- Anthrax toxin is encoded on one plasmid, and the polyglutamate capsule is encoded on a different plasmid.

Bacillus anthracis/Transmission

- Spores of the organism persist in soil for years. The route of entry determines type of disease: Skin/GI/RT
- Skin→ Humans are most often infected cutaneously, at the time of trauma to the skin , humans will get spores to enter and cause disease cutaneously, this source is usually animal hides.
- Lung→ Spores inhaled into the respiratory tract cause Pulmonary (inhalation) anthrax.
- GI → Gastrointestinal anthrax occurs when contaminated meat is ingested
- Inhalation anthrax is not communicable from person to person, despite the severity of the infection after being inhaled into the lung, the organism moves rapidly to the mediastinal lymph nodes, where it causes hemorrhagic mediastinitis.
- Because it leaves the lung so rapidly, it is not transmitted by the respiratory route to others.

Bacillus anthracis/Pathogenesis

- Pathogensis is based on exotoxin production (primarily two exotoxins, which are both collectively known as anthrax toxin).
- edema factor and lethal factor, both these exotoxin are made up of two subunits (A–B subunits).
- The B (binding) subunit in is a protective antigen.
- The A (active) subunit has the enzymatic activity.

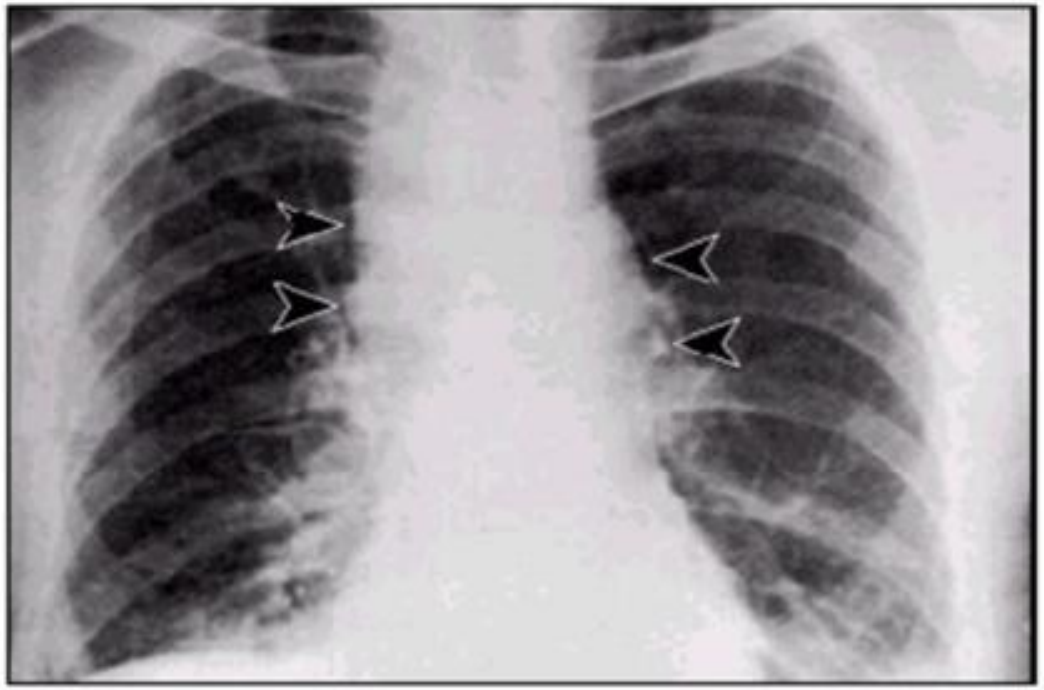
- 1- Edema factor exotoxin:
- increases the intracellular cyclic adenosine monophosphate (cAMP) as it works as an adenylate cyclase.
- This causes an outpouring of fluid (recall *B. pertussis*?) from the cell into the extracellular space, which manifests as edema (this is similar to the mechanism of diarrhea causes by vibrio cholera)
- 2- Lethal factor exotoxin:
- This has a protease activity causes the inhibition of the MAPK signal transduction pathway (mitogen-activated protein kinase). MAPK is the signal pathway that promotes human cell growth, the cleavage of MAPK and inhibition of this pathway thus inhibits cell growth.
- The *Binding antigen causes the formation of small pores on cell membrane of target cells which then allows edema factor and lethal factor exotoxins to enter the cell.*
- The binding antigen is called the protective antigen due to the fact that ABs against this antigen are protective against the disease.

Bacillus anthracis/Clinical Findings

- The typical lesion of cutaneous anthrax is a painless ulcer with a black eschar (crust, scab), with a striking Local edema (usually exaggerated).
- The lesion is called a malignant pustule.
- Skin anthrax → Untreated cases progress to bacteremia and death – the lesions are full of bacteria and we have a small window of treatment before they reach the blood...
- Pulmonary (inhalation) anthrax → also known as "wool-sorter's disease (inhaled from breathing spores present on infected sheep), begins with nonspecific respiratory tract symptoms resembling influenza, especially a dry cough and **substernal pressure**, which then progresses to hemorrhagic mediastinitis, bloody pleural effusions, septic shock, and death.
- Although the lungs are infected, the classic signs and symptoms and Xray features of pneumonia are not present, however mediastinal widening seen on chest X-ray is an important diagnostic criterion. Hemorrhagic mediastinitis and hemorrhagic meningitis are severe life-threatening complications.
- → The symptoms of gastrointestinal anthrax include vomiting, abdominal pain, and bloody diarrhea.

Black eschar , edema

Anthrax: Inhalational



Mediastinum is significantly widens.

No lesions in the lung

Bacillus anthracis/Laboratory Diagnosis

- Smears (microscopy of samples from lesions) show the typical large, gram-positive rods in long chains.
- Spores are usually not seen in smears of exudate because spores form when nutrients are insufficient, and **nutrients are plentiful in infected** tissue.
- Nonhemolytic (gamma) colonies form on blood agar aerobically.
- In case of a bioterror attack, rapid diagnosis can be performed in special laboratories using polymerase chain reaction (PCR)–based assays.
- Another rapid diagnostic procedure is the direct fluorescent antibody test that detects antigens of the organism in the lesion.
- Serologic tests, such as an enzyme-linked immunosorbent assay (ELISA) test for antibodies, require acute and convalescent serum samples and can only be used to make a diagnosis retrospectively.

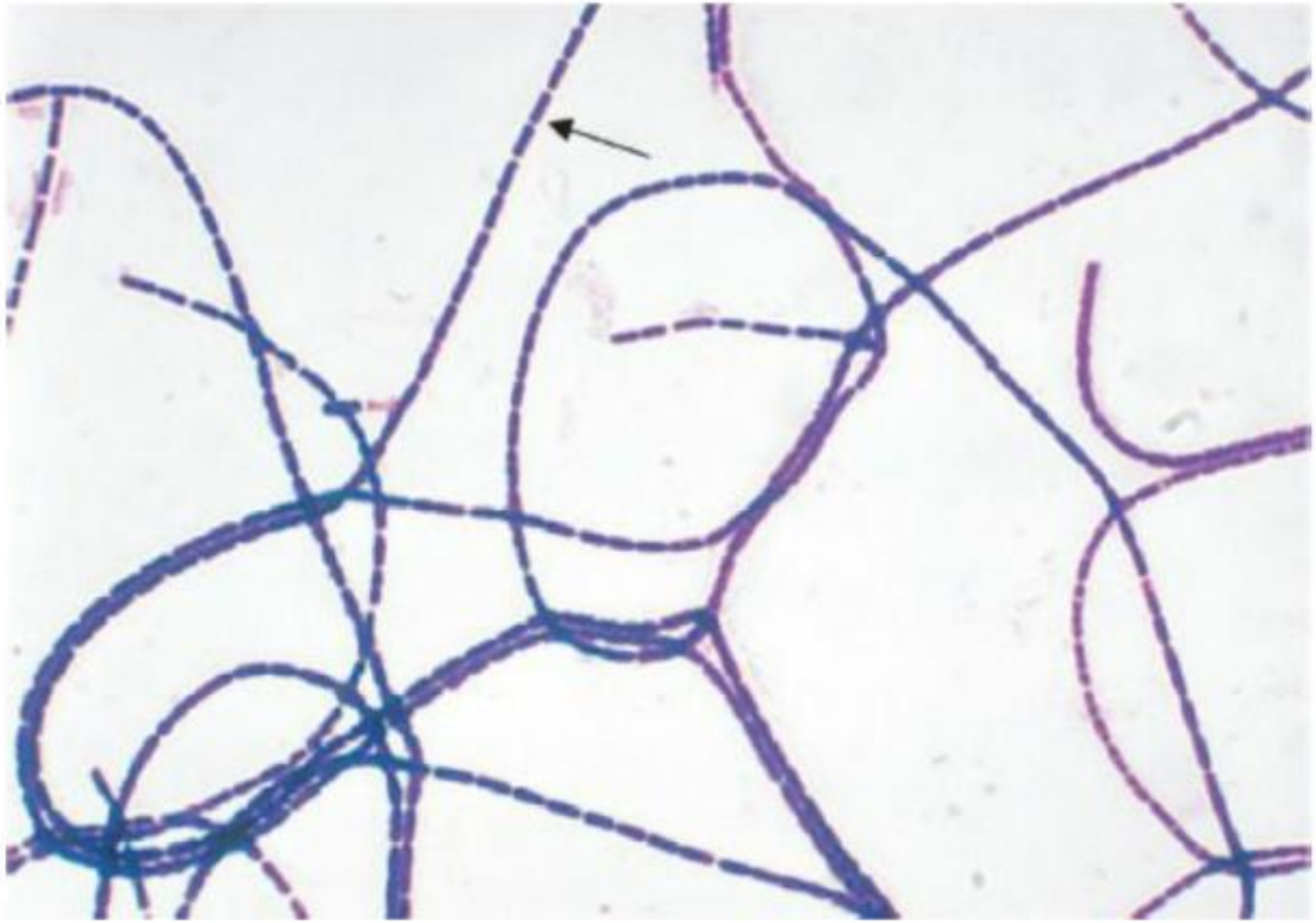


FIGURE 17–2 *Bacillus anthracis*—Gram stain. Arrow points to one large "box car–like" gram-positive rod within a long chain. (Figure courtesy of Public Health Image Library, Centers for Disease Control and Prevention.)

Bacillus anthracis/Treatment and Prevention

- Ciprofloxacin or doxycycline was used as prophylaxis in those exposed during the outbreak in the United States in 2001.
- People at high risk can be immunized with cell-free vaccine containing purified protective antigen as immunogen, the vaccine is weakly immunogenic, and six doses of vaccine over an 18-month period are given. Annual boosters are also given to maintain protection.
- Incinerating animals that die of anthrax, rather than burying them, will prevent the soil from becoming contaminated with spores.
- Antibiotics (Ciprofloxacin + another antibiotic) given IV as treatment, also antitoxins are also given

2. Bacillus cereus

- Disease *B. cereus* causes food poisoning (also toxin mediated!).

- Transmission:
- This is caused by spores that survive heating, the classic food item is **rice** (especially rice that is kept warm for a long time –reheated fried rice- buffets) , **spores survive steaming and quick frying**.

- When the rice is kept warm, the spores germinate , they grow and start producing the exotoxin,

. Bacillus cereus/Pathogenesis

- B. cereus produces two **entero**toxins (enteric targeting toxin).
- one of the enterotoxins is the same as that of cholera toxin (it adds adenosine diphosphate ribose, a process called ADP-ribosylation, to a G protein, which stimulates adenylate cyclase and leads to an increased concentration of cyclic AMP within the enterocyte).

(lots of fluids inside the lumen GI tract)

- The other enterotoxin resembles that of staphylococcal enterotoxin (acts as a superantigen).

. Bacillus cereus/Clinical Findings

- There are two syndromes.
- (1) *One syndrome has a short incubation period (4 hours) and consists primarily of nausea and vomiting, similar to staphylococcal food poisoning*. (recall staph food poisoning has prominent vomiting)

(because it happens in the stomach and it needs 4 hours to empty) --- super antigens

- (2) The other has a long incubation period (18 hours) and features watery, non bloody diarrhea, resembling clostridial gastroenteritis.

(no invasion of toxins, just cyclic AMP)

- No laboratory diagnosis is usually done
- Treatment is only symptomatic/ self limited, once the toxin does its damage, the symptoms are gone, this is due to the fact that **you ingest the toxin and not the bacteria (in sum)**
- Prevention : rice!

(In any diarrheal disease & vomiting, we fear of electrolytes and fluids imbalances)

If you lose a lot of acids, you will undergo metabolic alkalosis.

If you lose a lot of potassium, you will undergo hypokalemia

CLOSTRIDIUM

- There are four medically important species:
- *Clostridium tetani, Clostridium botulinum, Clostridium perfringens* (which causes either gas gangrene or food poisoning), and *Clostridium difficile (pseudomembranous colitis)*.

- All clostridia are anaerobic (unlike Bacillus), spore-forming, Gram-positive rods

1 & 2 ---> affect nerves (affect peripheral nervous system
3 & 4 ----> affect GI tract
3 ---> skin also

acetylcholine causes the muscles to move. If there is a block, this will lead to paralysis.

Organism	Disease	Transmission/ Predisposing Factor	Action of Toxin	Prevention
C. tetani	Tetanus muscle spasms	Spores in soil enter wound	Blocks release of inhibitory transmitters (e.g., glycine)	Toxoid vaccine
C. botulinum	Botulism causes paralysis	Exotoxin in food is ingested	Blocks release of acetylcholine	Proper canning; cook food
C. perfringens	1. Gas gangrene	Spores in soil enter wound	Lecithinase	Debride wounds
	2. Food poisoning	Exotoxin in food is ingested	Superantigen	Cook food
C. difficile	Pseudomembranous colitis	Antibiotics suppress normal flora	Cytotoxin damages colon mucosa	Appropriate use of antibiotics

inhibit the inhibition ---> so there is over activation.

TABLE 7–9 Main Features of Exotoxins and Endotoxins

Property	Comparison of Properties	
	Exotoxin	Endotoxin
Source	Certain species of gram-positive and gram-negative bacteria	Cell wall of gram-negative bacteria
Secreted from cell	Yes With a pump	No
Chemistry	Polypeptide	Lipopolysaccharide
Location of genes	Plasmid or bacteriophage	Bacterial chromosome Because it is essential part
Toxicity	High (fatal dose on the order of 1 µg)	Low (fatal dose on the order of hundreds of micrograms)
Clinical effects	Various effects (see text)	Fever, shock Causes low systemic vascular resistance
Mode of action	Various modes (see text)	Includes TNF and interleukin-1
Antigenicity	Induces high-titer antibodies called antitoxins	Poorly antigenic
Vaccines	Toxoids used as vaccines	No toxoids formed and no vaccine available
Heat stability	Destroyed rapidly at 60°C (except staphylococcal enterotoxin)	Stable at 100°C for 1 hour
Typical diseases	Tetanus, botulism, diphtheria	Meningococcemia, sepsis by gram-negative rods

TNF = tumor necrosis factor.

Bacterium	Disease	Mode of Action	Toxoid Vaccine
Gram-positive rods			
Corynebacterium diphtheriae	Diphtheria	Inactivates EF-2 by ADP-ribosylation	Yes
Clostridium tetani	Tetanus	Blocks release of the inhibitory neurotransmitter glycine by proteolytic cleavage of releasing proteins	Yes
Clostridium botulinum	Botulism	Blocks release of acetylcholine by proteolytic cleavage of releasing proteins	Yes[1]
Clostridium difficile	Pseudomembranous colitis	Exotoxins A and B inactivate GTPases by glucosylation	No
Clostridium perfringens	Gas gangrene	Alpha toxin is a lecithinase; enterotoxin is a superantigen	No
Bacillus anthracis	Anthrax	Edema factor is an adenylate cyclase; lethal factor is a protease that cleaves MAP kinase, which is required for cell division	No
Gram-positive cocci			
Staphylococcus aureus	1. Toxic shock syndrome	Is a superantigen; binds to class II MHC protein and T-cell receptor; induces IL-1 and IL-2	No
	2. Food poisoning	Is a superantigen acting locally in the gastrointestinal tract	No
	3. Scalded skin syndrome	Is a protease that cleaves desmoglein in desmosomes	No
Streptococcus pyogenes	Scarlet fever	Is a superantigen; action similar to toxic shock syndrome toxin of *S aureus*	No
Gram-negative rods			
Escherichia coli	1. Watery diarrhea	Labile toxin stimulates adenylate cyclase by ADP-ribosylation; stable toxin stimulates guanylate cyclase	No
	2. Bloody diarrhea	Shiga toxin inhibits protein synthesis in enterocytes by removing adenine from 28S ribosomal RNA	No
Shigella dysenteriae	Bloody diarrhea	Shiga toxin inhibits protein synthesis in enterocytes by removing adenine from 28S ribosomal RNA	No
Vibrio cholerae	Cholera	Stimulates adenylate cyclase by ADP-ribosylation	No
Bordetella pertussis	Whooping cough	Stimulates adenylate cyclase by ADP-ribosylation; inhibits chemokine receptor	Yes[2]

[1]For high-risk individuals only.

[2]The acellular vaccine contains pertussis toxoid and four other proteins.

1. *Clostridium tetani*, cause of tetanus // Transmission

- **Spores are widespread in soil** (spores and soil are always intimate, not really rusty nails, but soil, rusty nails are usually discarded on soil, and thus have higher potential of containing the spores).
- The portal of entry is usually a wound site (e.g., where a nail penetrates the foot), but the spores can also be introduced during "skinpopping," a technique used by drug addicts to inject drugs into the skin.
- Germination of spores is favored by necrotic tissue and poor blood supply in the wound (why? Less blood = less oxygen). <<because clostridium is anaerobe >>

For example , if there is a wound in the foot and this bacteria(soil) enter the foot. it will cause crush to the foot because the foot is considered low blood supply tissue.

- Neonatal tetanus, in which the organism enters through a contaminated umbilicus or circumcision wound, is a major problem in some developing countries.

Clostridium tetani, cause of tetanus// Pathogenesis

- Tetanus toxin (tetanospasmin) is an exotoxin produced by **vegetative** cells at the **wound site**.
- This polypeptide toxin is carried (retrograde) through the axons of neurons to the central nervous system, where it binds to ganglioside receptors and blocks release of inhibitory mediators (e.g., glycine and γ-aminobutyric acid [GABA]) at spinal synapses- so it inhibits the inhibitors substance= over excitation.
- Tetanus toxin and botulinum toxin (see later, both are clostridial toxins) are among the most toxic substances known.
- Tetanus toxin has one antigenic type (so the vaccine has one antigenic toxoid), unlike botulinum toxin, which has eight.

EXTRA INFORMATION

- **Tetanospasmin** is a neurotoxin **that inhibits the release of γ-aminobutyric acid (GABA)** and results in muscle spasms and rigidity, trismus (lockjaw), dysphagia, tendon rupture, opisthotonus, respiratory difficulty, and death.

- HOW???

(((it binds to ganglioside receptors and blocks release of inhibitory mediators (e.g., glycine and γ-aminobutyric acid [GABA]) at spinal synapses- so it inhibits the inhibitors substance= over excitation.)))

- A muscle **spasm** is a sudden, involuntary movement in one or more muscles.

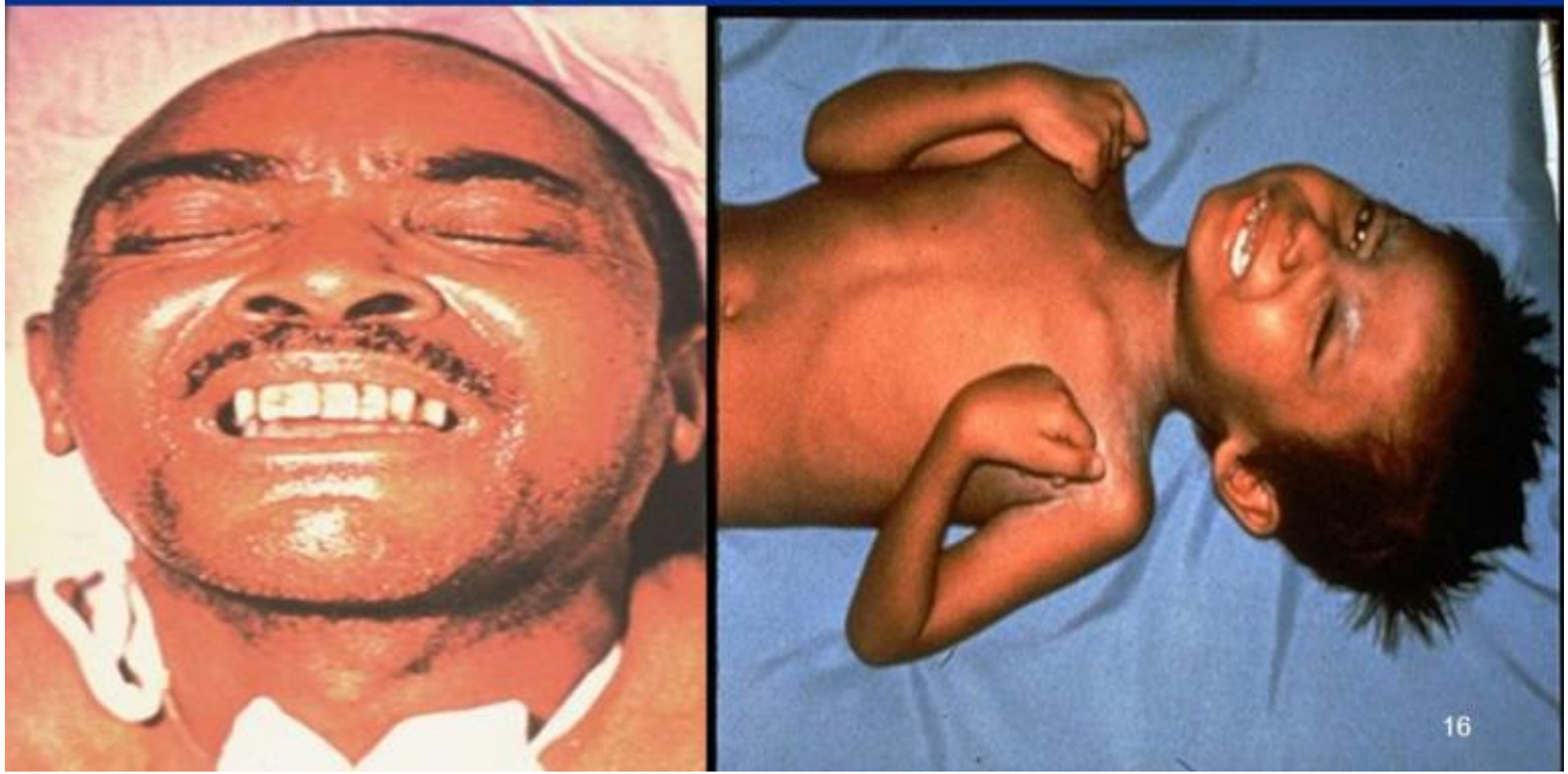
Clostridium tetani, cause of tetanus// Clinical Findings

- Tetanus is characterized by strong muscle spasms (spastic paralysis, tetany).
- Specific clinical features include lockjaw (trismus) due to rigid contraction of the jaw muscles, which prevents the mouth from opening; a characteristic grimace known as risus sardonicus; and **exaggerated reflexes**
- Opisthotonos, a pronounced arching of the back due to spasm of the strong extensor muscles of the back, is often seen (Figure 17–4).
- Respiratory failure ensues
- A high mortality rate is associated with this disease.
- **in tetanus, spastic paralysis (strong muscle contractions) occurs, whereas in botulism, flaccid paralysis (weak or absent muscle contractions) occurs.**

Risus sardonicus

Risus Sardonicus :

Spasm of facial muscles (frontalis & angle of mouth muscles) producing grinning facies



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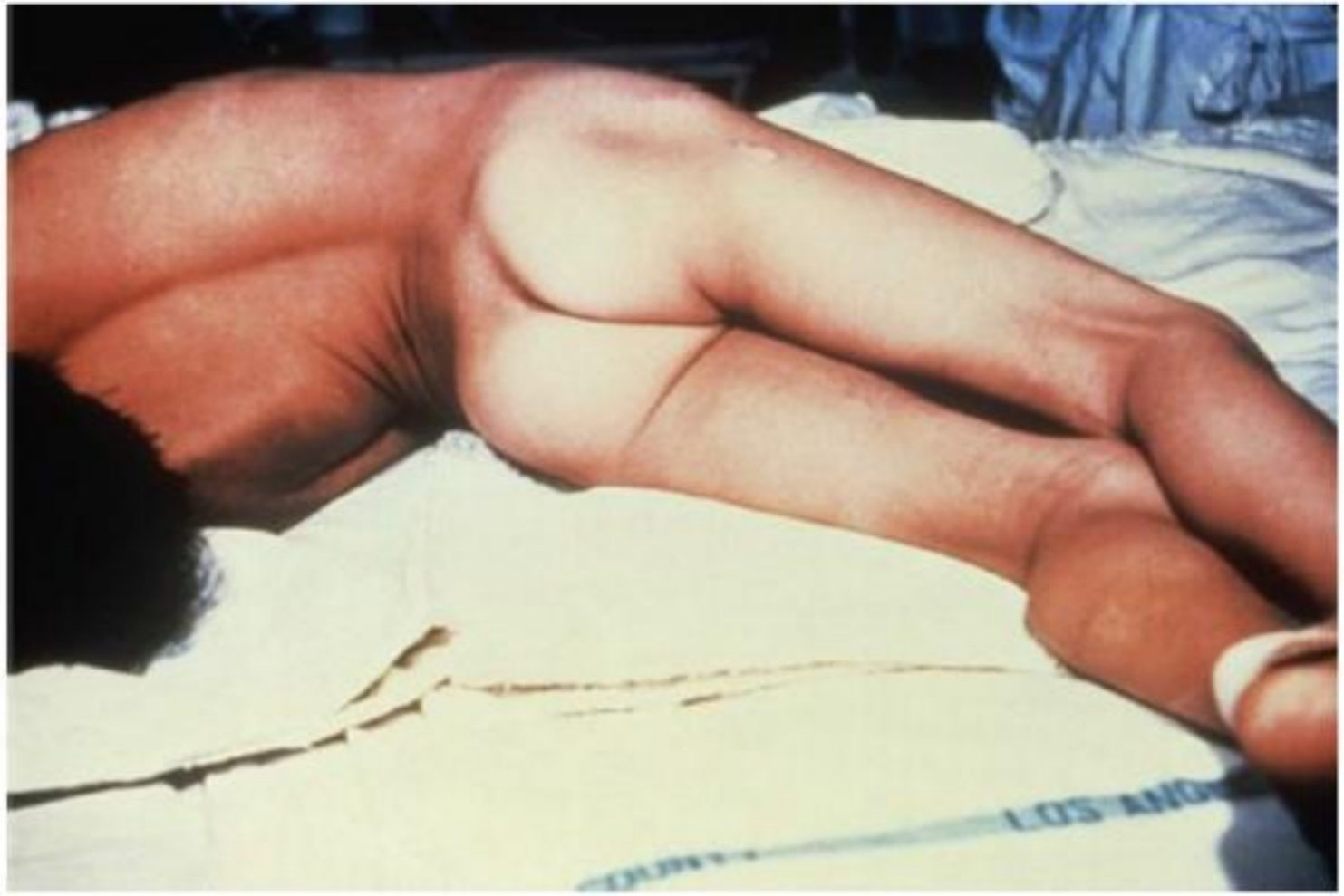


FIGURE 17–4 Tetanus. Note the marked hyperextension of the back, a position called *opisthotonos*, caused by tetanus toxin, an exotoxin that inhibits the release of mediators of the inhibitory neurons in the spinal cord. (Source: Centers for Disease Control and Prevention. CDC # 6373.)

Clostridium tetani, Laboratory Diagnosis and Treatment

- There is no microbiologic or serologic diagnosis (diagnosed clinically, LOCKJAW is the first symptom usually).
- Organisms are rarely isolated from the wound site (again disease is due to toxin production not infection).
- *C. tetani* produces a large terminal spore (spore at the end of the rod), this gives the organism the characteristic appearance of a "tennis racket." see next slide
- Treatment:
- Tetanus immune globulin (**tetanus antitoxin**)<passive> is used to neutralize the toxin, the role of antibiotics is **uncertain**(metronidazole or penicillin G can be given, however not proven to be helpful).to reduce the production of exotoxin
- An adequate airway must be maintained and respiratory support given, with Benzodiazepines (e.g., diazepam [Valium]) to prevent spasms.

The treatment is done by three ways :

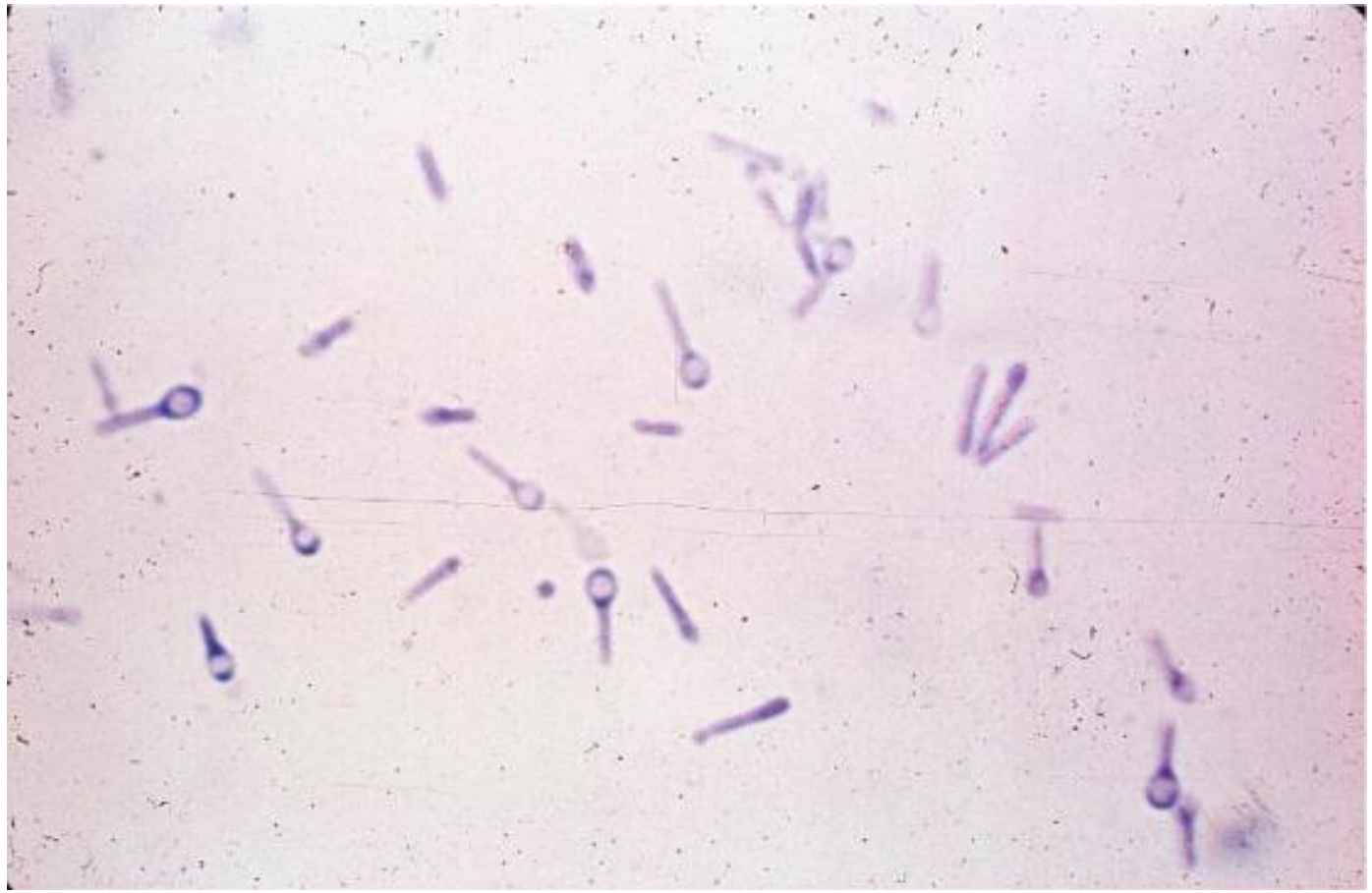
passive immunity is provided when a person is given antibodies to a disease rather than producing them through his or her own **immune** system

active immunity : refers to the process of exposing the body to an antigen to generate an adaptive **immune** response

--Antibiotics are used to **treat** or prevent some types of bacterial infection. They work by killing bacteria or preventing them from reproducing and spreading.

Why the role of antibiotics is uncertain here?

Because antibiotics reach the region of infections by the blood .however, this bacteria is anaerobic, so it lives in low blood supply regions



Large and terminal spore, *C. tetani*

http://classconnection.s3.amazonaws.com/344/flashcards/1212344/jpg/clostridiumtetani1349841271090.jpg

Clostridium tetani/Prevention (important)

- Tetanus is prevented by immunization with tetanus toxoid (formaldehyde-treated toxin) in childhood and every 10 years thereafter.
- Tetanus toxoid is part of the scheduled vaccines that are usually given to children (in combination with diphtheria toxoid and the acellular pertussis vaccine, all three are called –DTaP).
- Clean wound → When trauma occurs, the wound should be cleaned and debrided, and tetanus toxoid (TT) booster should be given (active immunity boost).
- All other wounds (contaminated especially) → tetanus immune globulin the toxoid booster and penicillin administered. (active + passive immunity + chemotherapy-antibiotics-)

Wound management and tetanus prophylaxis

Previous doses of tetanus toxoid*	Clean and minor wound		All other wounds¶	
	Tetanus toxoid-containing vaccine[Δ]	Human tetanus immune globulin	Tetanus toxoid-containing vaccine[Δ]	Human tetanus immune globulin[◊]
<3 doses or unknown	Yes[§]	No	Yes[§]	Yes
≥3 doses	Only if last dose given ≥10 years ago	No	Only if last dose given ≥5 years ago[¥]	No

Appropriate tetanus prophylaxis should be administered as soon as possible following a wound but should be given even to patients who present late for medical attention. This is because the incubation period is quite variable; most cases occur within 8 days, but the incubation period can be as short as 3 days or as long as 21 days. For patients who have been vaccinated against tetanus previously but who are not up to date, there is likely to be little benefit in administering human tetanus immune globulin more than one week or so after the injury. However, for patients thought to be completely unvaccinated, human tetanus immune globulin should be given up to 21 days following the injury; Td or Tdap should be given concurrently to such patients.

* Tetanus toxoid may have been administered as diphtheria-tetanus toxoids adsorbed (DT), diphtheria-tetanus-whole cell pertussis (DTP, DTwP; no longer available in the United States), diphtheria-tetanus-acellular pertussis (DTaP), tetanus-diphtheria toxoids adsorbed (Td), booster tetanus toxoid-reduced diphtheria toxoid-acellular pertussis (Tdap), or tetanus toxoid (TT).

¶ Such as, but not limited to, wounds contaminated with dirt, feces, soil, or saliva; puncture wounds; avulsions; wounds resulting from missiles, crushing, burns, or frostbite.

Δ The preferred vaccine preparation depends upon the age and vaccination history of the patient:

- <7 years: DTaP
- Underimmunized children ≥7 and <11 years who have not received Tdap previously: Tdap. Children who receive Tdap between age 7 and 11 years do not require revaccination at age 11 years.
- ≥11 years: A single dose of Tdap is preferred to Td for all individuals in this age group who have not previously received Tdap. Pregnant women should receive Tdap during each pregnancy.
- Td is preferred to TT for those who received Tdap previously and when Tdap is not available.

◊ 250 units intramuscularly at a different site than tetanus toxoid; intravenous immune globulin should be administered if human tetanus immune globulin is not available.

§ The vaccine series should be continued through completion as necessary.

¥ Booster doses given more frequently than every five years are not needed and can increase adverse effects.

This slide is important , to understand it press here https://youtu.be/GdHxTgqqKgo?t=2418

http://www.uptodate.com/contents/image?imageKey=PEDS/61087

2. *Clostridium botulinum*, cause of botulism

- Transmission Spores:
- Similarly, spores are found in soil but also contaminate vegetables and meats.
- This is especially true with canned food (or vacuum sealed foods),beware of misshapen cans – remember that's an anaerobic condition.
- When foods are canned or vacuum-packed without adequate **sterilization**, spores survive and germinate in the anaerobic environment. (don't eat misshaped canned food)
- Toxin is produced within the canned food and ingested preformed.
- The highest-risk foods
- (1) alkaline vegetables such as green beans, peppers, and mushrooms
- (2) smoked fish.
- The toxin is relatively heat-labile; it is inactivated by boiling for several minutes. Thus, disease can be prevented by sufficient cooking (in essence, don't eat out of the can, don't eat without proper boiling of canned goods, avoid swollen or misshapen cans).

So make sure that the canned food is well cooked

http://www.sasionline.org/prepping/storing-your-canned-goods-safely-how-to-avoid-botulism/

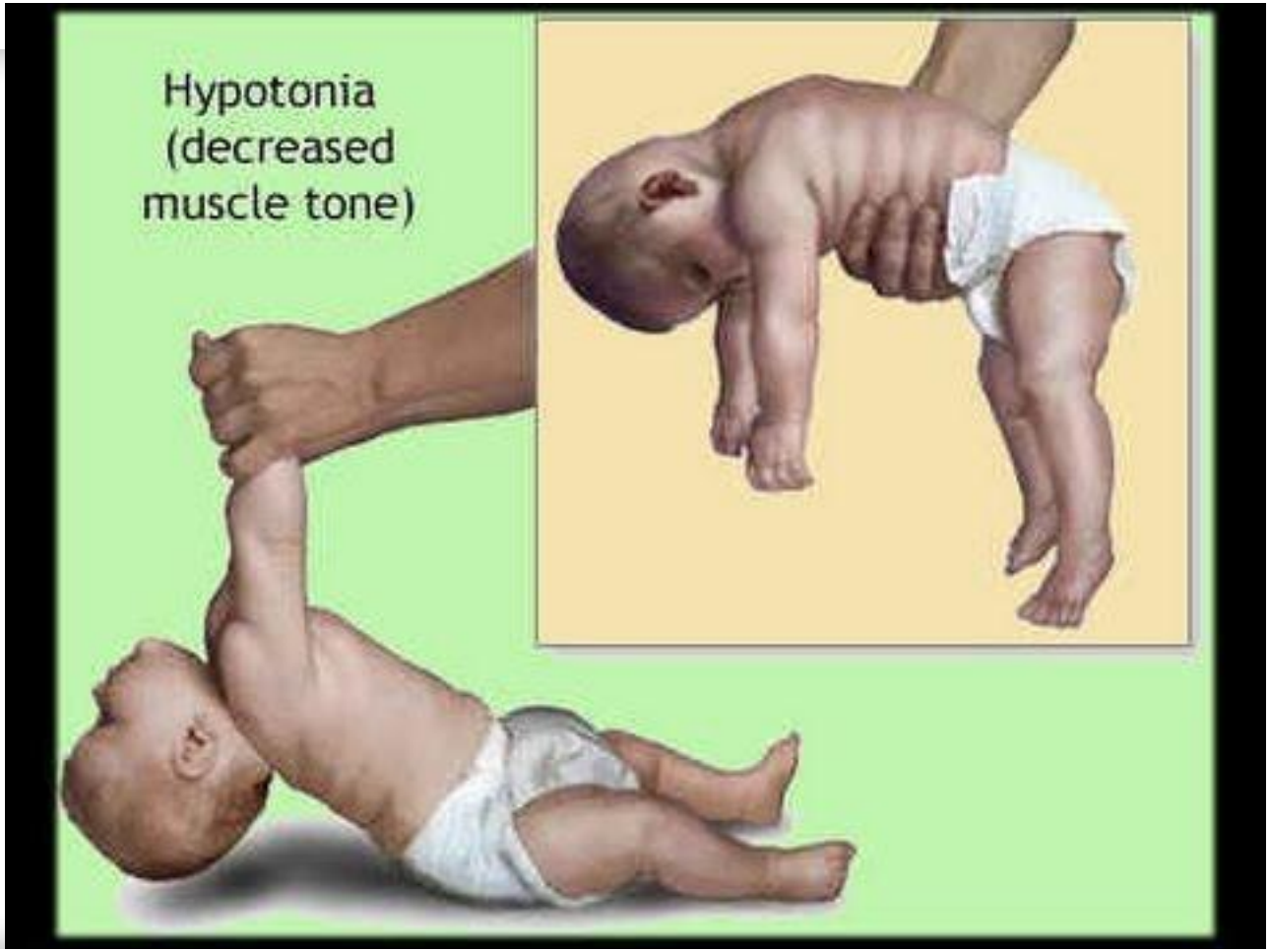
http://www.sciencephoto.com/image/11863/530wm/B2201300-Botulism_bacteria-SPL.jpg

Clostridium botulinum, cause of botulism / Pathogenesis

- The botulinum toxin is absorbed from the gut (once ingested, preformed) and carried **via the blood (unlike Tetanus toxin)** to **peripheral** nerve synapses, where it **blocks release of acetylcholine (blocks the activating neurotransmitter= loss of tone)**.and then flaccid paralysis.
- the toxin acts as protease that cleaves the proteins involved in acetylcholine release.
- The toxin is a polypeptide encoded by a lysogenic phage.
- Along with tetanus toxin, it is among the most toxic substances known.
- *There are eight immunologic types of toxin; types A, B, and E are the most common in human illness*.
- Medical uses:
- In plastic surgery (Botox is a commercial preparation of exotoxin A used to remove wrinkles on the face (induced hypotonia)).
- Minute amounts of the toxin are effective in the treatment of certain spasmodic muscle disorders such as torticollis, “writer’s cramp,” and blepharospasm.

Medical use Vs. disease

https://www.epainassist.com/images/treatment-of-benign-essential-blepharospasm.jpg



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2. *Clostridium botulinum*/Clinical Findings

- Descending muscle weakness and paralysis (descends from head and goes lower)
- (diplopia, dysphagia, and respiratory muscle failure)
- No fever is present.
- In contrast, Guillain-Barré syndrome (post viral syndrome) is an ascending paralysis(starts at legs and goes higher) <<means the paralysis starts rapidly after eating .actually it needs time. It starts with viral symptoms and with time the illness will develop along with paralysis symptoms.>>
- Clinical forms
- (1) Wound botulism, in which spores contaminate a wound, germinate, and produce toxin at the site, associated with drug abuse (skin popping)
- (2) Infant botulism, in which the organisms grow in the gut and produce the toxin there . ex: children must not take aspirin
- Ingestion of honey containing the organism is implicated in transmission of infant botulism, affected infants(under 1 year) develop weakness or paralysis and may need respiratory support but usually recover spontaneously.

Clostridium botulinum/Laboratory Diagnosis

- The organism is usually not cultured. it is antitoxin
- Botulinum toxin is demonstrable in uneaten food and the patient's serum by mouse protection tests *(we give mice a sample from the patient and we see the symptoms develop, we give them antitoxin and they are saved = Dx made).*

Clostridium botulinum/Treatment

- Trivalent antitoxin (types A, B, and E) is given
- respiratory support.
- The antitoxin is made in horses (whereas tetanus antitoxin is made in humans) and serum sickness occurs in about 15% of recipients

Clostridium botulinum/Prevention

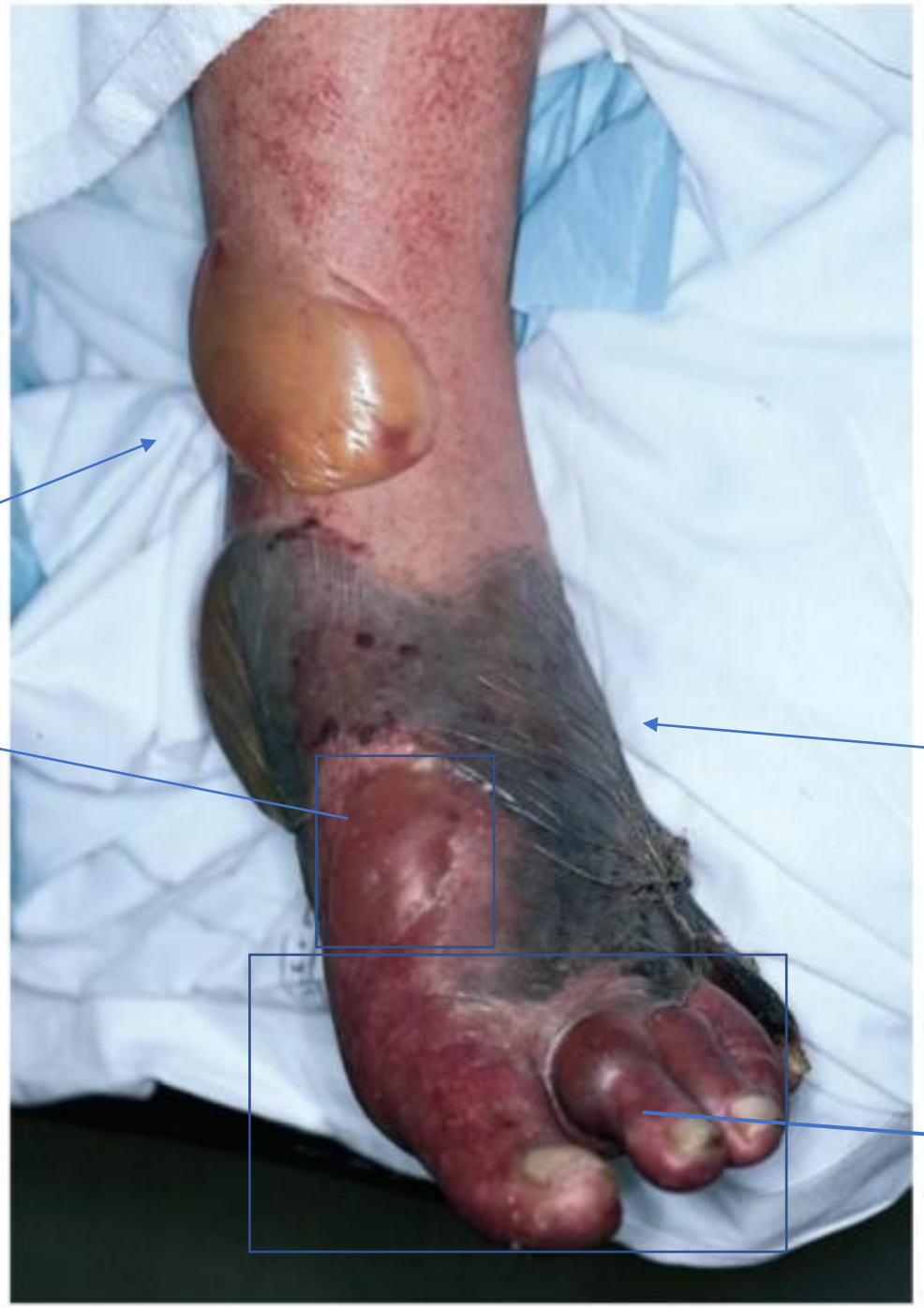
- **Sterilization of food prior to introducing it in anaerobic conditions**.
- **Adequate cooking to inactivate the toxin.**
- Swollen cans must be discarded (clostridial proteolytic enzymes form gas, which swells cans).

3. *Clostridium perfringens*

- *C. perfringens* causes clinical forms,
- In wounds = gas gangrene
- If ingested = food poisoning

1- Gas Gangrene

- **Gas gangrene** (myonecrosis, necrotizing fasciitis) is one of the two diseases caused by *C. perfringens*
- Gas gangrene is also caused by other histotoxic clostridia such as *Clostridium histolyticum, Clostridium septicum, Clostridium novyi*, and *Clostridium sordellii*.
- *C. sordellii* also causes toxic shock syndrome in postpartum and postabortion women.
- Normal—accident –crush blood supply – soil—growth of spores – exotoxin -- Clostridium perfringens -- more destrection of tissue -- gangrene



A large gas- and fluid-filled bulla is seen near the ankle (in an aerobic bacteria)

Bulla (next lecture)

Gas in tissue is a feature of gangrene produced by these anaerobic bacteria

large area of necrosis on lateral aspect of foot. Necrosis is mainly caused by lecithinase produced by Clostridium perfringens.

Loss of blood supply

- *Clostridium perfringens* /Transmission :
- Spores are located in the soil (surprise); HOWEVER = normal vegetative cells part normal flora of the colon and vagina (**also 3% of people carry *C. diff*, but no one should carry tetani or botulism**).
- When C. diff cause disease ? This is not a normal flora but it lives with them normally . When you give antibiotic , you will kill the normal flora and this bacteria level will arise so it causes disease.
- Gas gangrene is associated with **war wounds, road traffic accidents, diabetic foot and septic abortions** (endometritis).
- Pathogenesis :
- Organisms grow in traumatized tissue (especially muscle where oxygen is less!) and produce a variety of toxins (notice so far, all these organisms cause illness by exotoxin production).
- The most important is alpha toxin (lecithinase), which damages cell membranes, including those of erythrocytes, resulting in hemolysis. Degradative enzymes produce gas in tissues

Clostridium perfringens/Clinical Findings

- Pain, edema, cellulitis, and gangrene (necrosis) occur in the wound area
- Crepitation indicates the presence of gas in tissues.
- Hemolysis and jaundice are common, as are blood-tinged exudates.
- Shock and death can ensue.
- Mortality rates are high

Clostridium perfringens/Laboratory Diagnosis

- Microscopy of exudate from wounds will show large Gram-positive rods.
- Spores are not usually seen because they are formed primarily under nutritionally deficient conditions.
- The organisms are cultured anaerobically and then identified by sugar fermentation reactions and organic acid production. *C. perfringens* colonies exhibit a double zone of hemolysis on blood agar.
- Egg yolk agar is used to demonstrate the presence of the lecithinase. Serologic tests are not useful.