10

Microbiology

Doctor 2017 | Medicine | JU

Sheet ○ Slides

DONE BY

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DOCTOR

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Bacteria are divided into pathogenic, non-pathogenic, and opportunistic pathogenic.

Pathogenic bacteria: Bacteria that cause disease.

Non-pathogenic bacteria: Bacteria that don't cause disease.

opportunistic pathogenic bacteria: Bacteria that cause disease only when there is opportunity to cause disease, so they take advantage of an opportunity not normally available, e.g. a host with a weakened immune system such as in case of cancer patients, patients who undergo chemotherapy, HIV patients in the late stages, or patients who were born with low immunity.

Those divisions are used to describe the most common presentation of a certain bacterial type, because in certain cases, bacteria that is part of the flora and not causing disease (non-pathogenic) can become pathogenic and cause disease if introduced to sterile tissue. For bacteria to cause disease, the sum of a group of factors should be considered, those factors include the virulence of the bacteria, the immune system of the host, and the site of infection.

Pathogenesis of bacterial infection:

Infectious means that bacteria are present in the tissue, replicating and causing disease.

Characteristics of bacteria that are pathogens (Virulence factors):

Virulence factors: refers to the components or structure of microorganism that helps in establishment of disease or infection.

1- Transmissibility

2- Adherence to host cells

3- Persistence

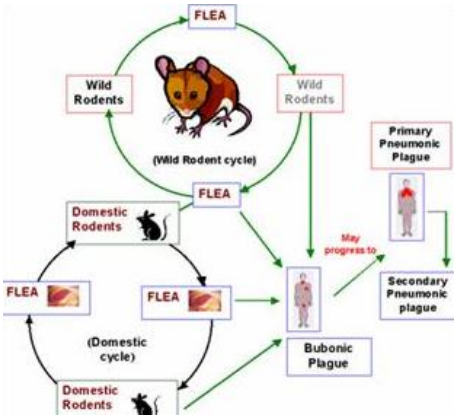
4- Invasion of host cells and tissues

5- Toxigenicity

6- The ability to evade or survive the host's immune system

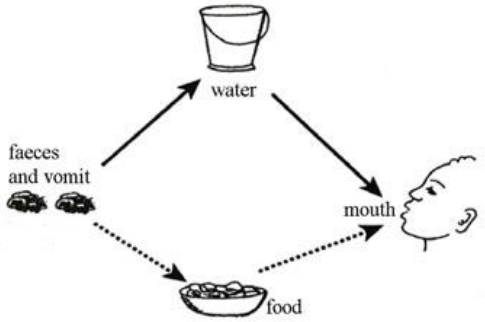
7- Resistance to antimicrobials and disinfectants

1- Transmission:



It takes place depending on what host do bacteria live in usually, sometimes if the bacteria only live in animals it can be transmitted accidentally to humans such as the case in Yersinia pestis (plague) which are usually found in rodents but in some cases a FLEA can bite the rodent and by that FLEA Yersinia pestis can be transmitted to humans.

Another way for transmission is **the clinical manifestation of the disease** which can help in the transmission of the disease.



e.g. Vibrio cholerae can cause voluminous diarrhea, Mycobacterium tuberculosis (tuberculosis) naturally infects only humans; it produces respiratory disease with cough and production of aerosols, resulting in transmission of the bacteria from one person to another.

Note: For the advantage of bacteria is not to cause lethal disease because if the host died quickly it wouldn't be able to transmit to another host and stay alive, so that the most successful bacteria are the ones that cause minor symptoms and can be transmitted from one to another.

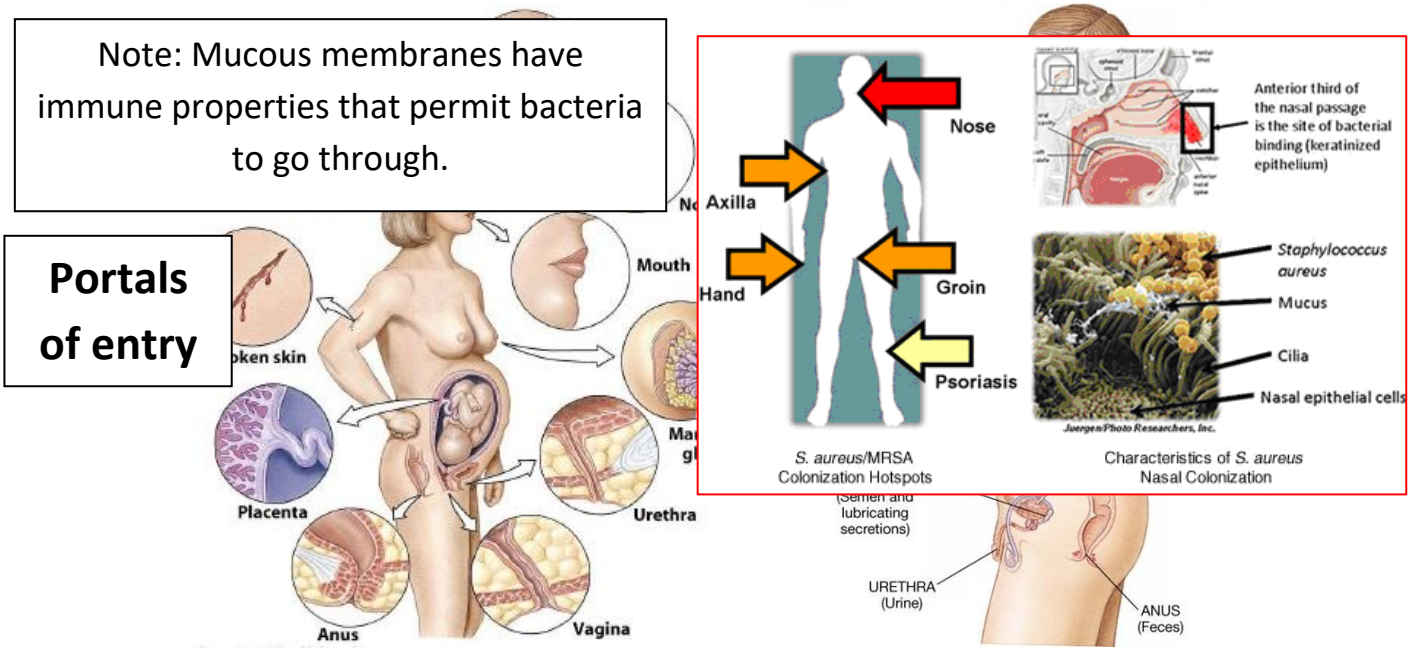
Many bacteria are transmitted from one person to another on hands. A person with S. aureus carriage in the anterior nares may rub his nose, pick up the staphylococci on the hands, and spread the bacteria to other parts of the body or to another person, where infection results.

Portals of entry:

The most frequent portals of entry of pathogenic bacteria into the body are the sites where mucous membranes meet with the skin, which are the respiratory (upper and lower airways), gastrointestinal (primarily mouth), genital, and urinary tracts. Abnormal areas of mucous membranes and skin (e.g, cuts, burns, and other injuries) are also frequent sites of entry.

Note: Mucous membranes have immune properties that permit bacteria to go through.

Portals of entry

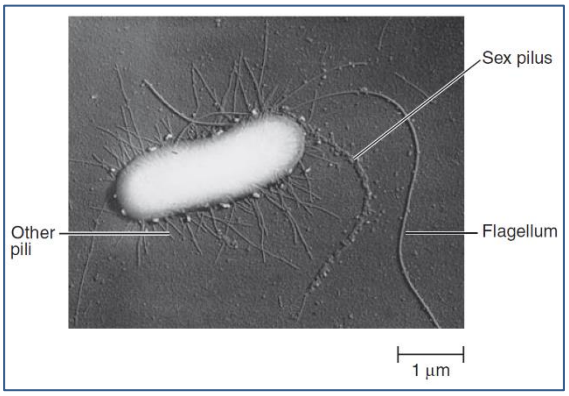


Bacteria can be transmitted from animal to human, from human to human, and also from other sources (e.g. clostridium botulinum and clostridium tetani are found in soil so if you had a dirty wound it can be transmitted into your body and cause tetanus. Usually because it's a harsh environment in the soil, bacteria form spores that can enter the body through wounds).

Sometimes bacteria are found in body but it's not causing any symptoms for humans (10-20% of humans carry staph aureus which is pathogenic only for for people with special immune response)

Skin infections are caused by the compromised skin integrity that some people may have, but generally skin is hard and can't be infected unless it's compromised because it usually provides unsuitable environment for the bacteria.

2- Adherence to host cells



Bacteria also have specific surface molecules that interact with host cells. Many bacteria have **pili**, thick rodlike appendages or **fimbriae**, shorter "hairlike" structures that extend from the bacterial cell surface and help mediate adherence of the bacteria to host cell surfaces.

When bacteria enter the body of the host, they must adhere to cells of a tissue surface. If they did not adhere, they would be swept away by mucus and other fluids that bathe the tissue surface.

Lipoteichoic acid, protein F, and M protein can be found on the fimbriae. The lipoteichoic acid and protein F cause adherence of the streptococci to buccal epithelial cells; this adherence is mediated by fibronectin, which acts as the host cell receptor molecule. M protein acts as an antiphagocytic molecule and is a major virulence factor.

Pili (fimbria):

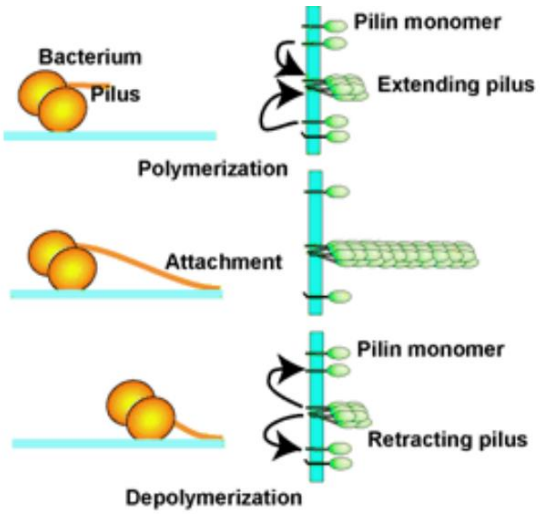
Composed of structural protein subunits termed **pilins**. Minor proteins called **adhesins** are located at the tips of pili and are responsible for the attachment properties.

* Two classes can be distinguished: **ordinary pili**, which play a role in the **adherence** of symbiotic and pathogenic bacteria to host cells, and **sex pili**, which are responsible for .the attachment of donor and recipient cells in bacteria **conjugation**

- Their tips strongly adhere to surfaces at a distance from the cells. Pili then .depolymerize from the inner end, thus retracting inside the cell

- In one group of gram-positive cocci, the streptococci, **fimbriae are the site of the main surface antigen, the M protein.** Lipoteichoic acid, associated with these fimbriae, is responsible for the adherence of group A streptococci to epithelial cells of their hosts.

- Their tips strongly adhere to surfaces at a distance from the cells. Pili then depolymerize from the inner end, thus retracting inside the cell. The result is that the bacterium moves in the direction of the adhering tip. This kind of surface motility is called **twitching** and is widespread among piliated bacteria.

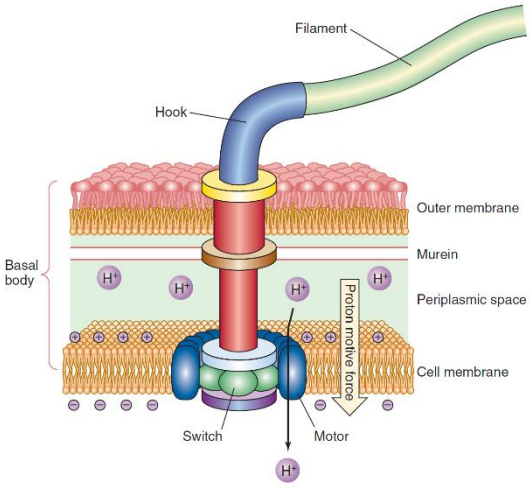


***Pili grow from the inside of the cell outward.**

****Pili inhibit the phagocytic ability of leukocytes**

Flagella:

Bacterial flagella are thread-like appendages composed of a protein subunit called **flagellin**.



Rotation is driven by the flow of protons down the gradient produced by the primary proton pump. Proton gradient will help in rotating the motor either clockwise or counterclockwise and depending on this movement the motor will help the flagella to propel, and this gives the bacteria the ability of **chemotaxis** in seeking for nutrients. Which is also present in immune cells helping them reach the site of infection.

Chemotaxis: the net movement of the cell toward the source (a sugar or an amino acid). Cell behavior brought about in response to a change in the environment is called **sensory transduction**.

Flagella and pili are highly antigenic (H antigens) which means that it has a lot of antigens exposed on its surface so that immune cells can recognize them. Immune responses to infection can be directed against these proteins.

3- Invasion:

Not all bacteria need to internalize, some bacteria just adhere on the surface and keep replicating on the surface. Most commonly, the ones that internalize are the **pathogenic** ones.

* Invasion is the term commonly used to describe the entry of bacteria into host cells and for many disease-causing bacteria, invasion of the host's epithelium is central to the infectious process.

* Invasion can happen through tight junctions of epithelial surfaces or through internalization into epithelial cells (eg, Salmonella species) invade tissues through the junctions between epithelial cells. Other bacteria (eg, Yersinia species, N gonorrhoeae, and Chlamydia trachomatis) invade specific types of the host's epithelial cells and may subsequently enter the tissue.

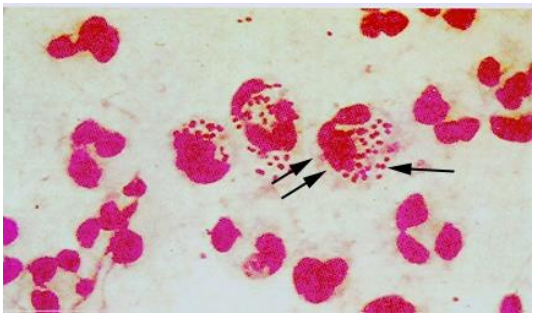
* In-vitro models and knockouts are important. (they're ways of studies; in-vitro means that studies are performed with microorganisms, cells, or biological molecules outside their normal biological context and Knockout organisms or simply knockouts are used to study gene function, usually by investigating the effect of gene loss.)

Note: The sentence between brackets is from Wikipedia just to define the meaning of these terms.

* In many infections, the bacteria produce virulence factors that cause the host cells to engulf (ingest) the bacteria and the host cell can actively undergo polymerization of actin. The host cells play a very active role in the process, so it's not just the bacteria which is working in this process.

* Usually requires actin polymerization.

Invasion will depend on the bacteria and cell type (sometimes immune cells are infected such as the in the case of gonorrhoeae)

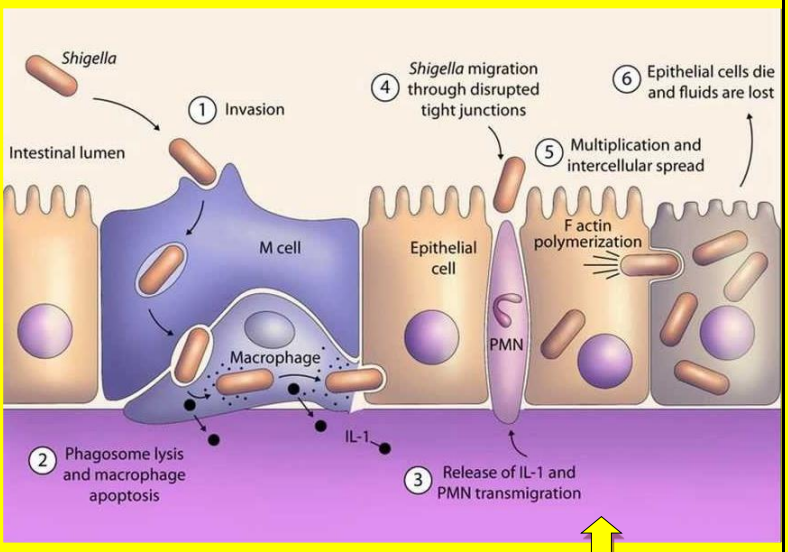


N gonorrhoeae uses pili as primary adhesins and opacity-associated proteins (Opa) as secondary adhesins to host cells. Certain Opa proteins mediate adherence to polymerphonuclear cells.

Shigella invasion:

In the lining of the epithelium we've many types of cells such as epithelial cells and immune cells. M cells usually present the antigen of the bacteria to the macrophage.

"Shigella passes the epithelial cell (EC) barrier by **transcytosis through M cells** and encounters resident macrophages. The bacteria **evade degradation in macrophages by inducing an apoptosis-like cell death**, which is accompanied by proinflammatory signaling. Free bacteria **invade the EC** from the basolateral side, **move into the cytoplasm by actin polymerization, and spread to adjacent cells. Proinflammatory signaling** by macrophages and EC further activates the innate immune response and attracts PMN. The influx of PMN **disintegrates the EC lining**, which initially exacerbates the infection and tissue destruction by facilitating the invasion of more bacteria. Ultimately, PMN phagocytose and kill Shigella, thus contributing to the resolution of the infection."



I missed this image while making the sheet. (Saba)

(This paragraph was written by the doctor 😊)

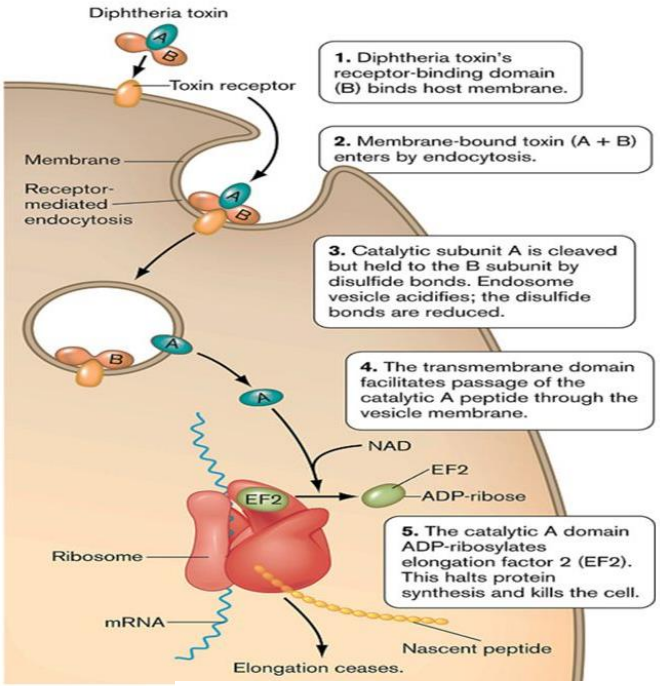
4- Toxigenicity:

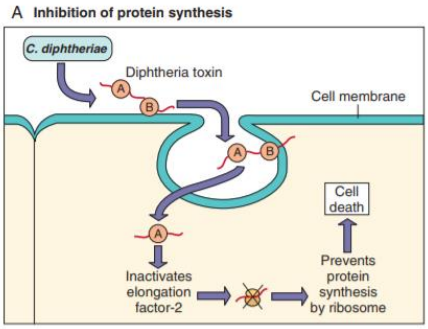
Toxins produced by bacteria are generally classified into two groups: **endotoxin**, which is present in the cell wall, and **exotoxins** which are toxins that are secreted actively, by contact only, or by cell death.

a- Exotoxins:

* Exotoxins are made of A and B subunits. B subunit will help attaching and internalizing into the host cell and when the toxin is internalized the A subunit will do its catalytic activity (toxic effect).

* Exotoxins associated with diarrheal diseases are frequently called **enterotoxins**.





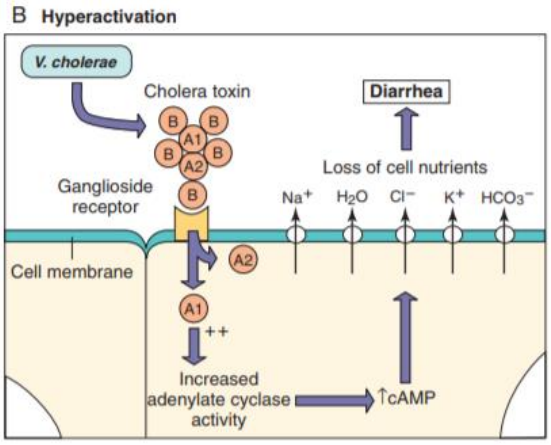
Diphtheria toxin:

Strains of C diphtheriae that carry a lysogenic, temperate corynebacteriophage and produce **diphtheria toxin** (A subunit inhibits peptide elongation so it's affecting protein synthesis) and cause **Diphtheria**.

Table 14-3 Properties of A-B–Type Bacterial Toxins

Toxin	Organism	Gene Location	Subunit Structure	Target Cell Receptor	Biological Effects
Botulinum toxin	*Clostridium botulinum*	Phage	A-B	Polysialogangliosides plus synaptotagmin (co-receptors)	Decrease in peripheral presynaptic acetylcholine release, flaccid paralysis
Cholera toxin	*Vibrio cholerae*	Chromosomal	$A\text{-}B_5$	Ganglioside (GM_1)	Activation of adenylate cyclase, increase in cAMP level, secretory diarrhea
Diphtheria toxin	*Corynebacterium diphtheriae*	Phage	A-B	Growth factor receptor precursor	Inhibition of protein synthesis, cell death
Tetanus toxin	*Clostridium tetani*	Plasmid	A-B	Polysialogangliosides plus 15-kDa glycoprotein (co-receptors)	Decrease in neurotransmitter release from inhibitory neurons, spastic paralysis

Cholera toxin: It is made of 2 subunits A, which is split into two peptides A1 and A2, and B subunit that has 5 identical peptides. The Toxin causes secretion of water and some ions to the lumen of the intestine and decreases reabsorbing of water causing diarrhea.

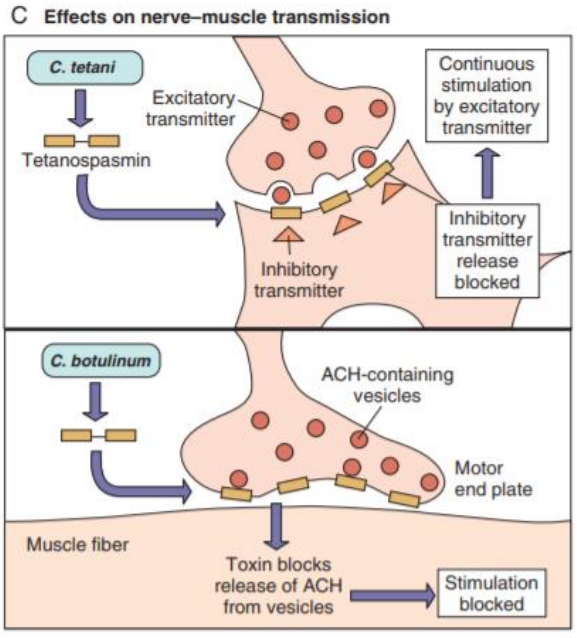


These toxins are often found on mobile genetic ele… (e.g. phage or plasmid) and toxin production can be transmitted from one bacterium to another by these mobile genetic elements. They also have different cell targets and biological effects.

Note: there are more examples in the slides but those are the ones mentioned by the doctor and we need to know.

Tetanus toxin: The Bacteria secrets tetanospasmin which will prevent the release of inhibitory transmitters causing continuous activation and spasm (**spastic paralysis**).

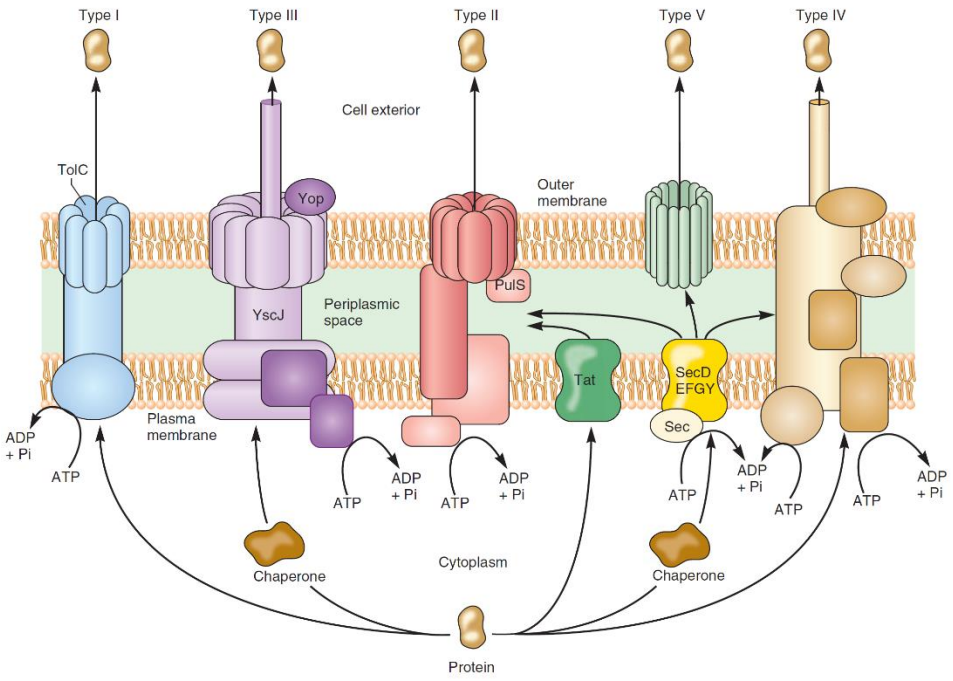
Botulinum toxin: The toxin will prevent the release of Ach. so it decreases stimulation causing **flaccid paralysis**.



* Exotoxins are bases of some vaccines (toxoids):

Exotoxins are inactivated by heat and thus it's called toxoid. So, when the toxin (tetanospasmin) is heated the inactivated toxin **(toxoid)** is formed and thus used to make a vaccine against tetani.

*Secretion systems:



Secretion systems are group of proteins that form a way for a protein that's made in the cytoplasm to be secreted to the cell exterior, some are found in gram positives and some in gram negatives but they're most commonly in gram negative (The type I and IV secretion systems have been described in both gram-negative and gram-positive bacteria, but the type II, III, V, and VI secretion systems have been found only in gram-negative bacteria.)

Gram - → All types **Gram + → I and IV**

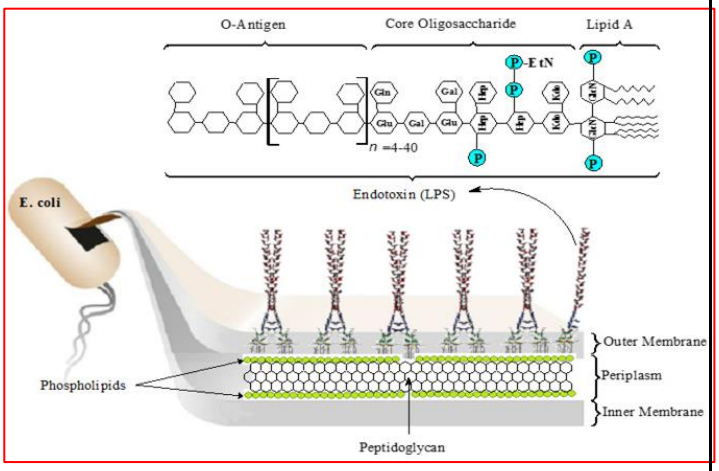
* The type I and type III secretion pathways are sec independent (sec is general secretion pathway) and thus do not involve amino terminal processing of the secreted proteins. Protein secretion by these pathways occurs in a continuous process without the presence of a cytoplasmic intermediate. Type I secretion is exemplified by the a-hemolysin of E coli and the adenylyl cyclase of Bordetella pertussis.

* Type III secretion pathway is a contact-dependent system. It is activated by contact with a host cell, and then injects a toxin protein into the host cell directly.

* Almost all of them depend on ATP and some depend on chaperons.

b- Endotoxins (Part of gram-negative bacterial cell wall):

The LPS (Lipopolysaccharide/ endotoxin) of gram-negative bacteria are bacterial cell wall components that are often liberated when the bacteria lyse.

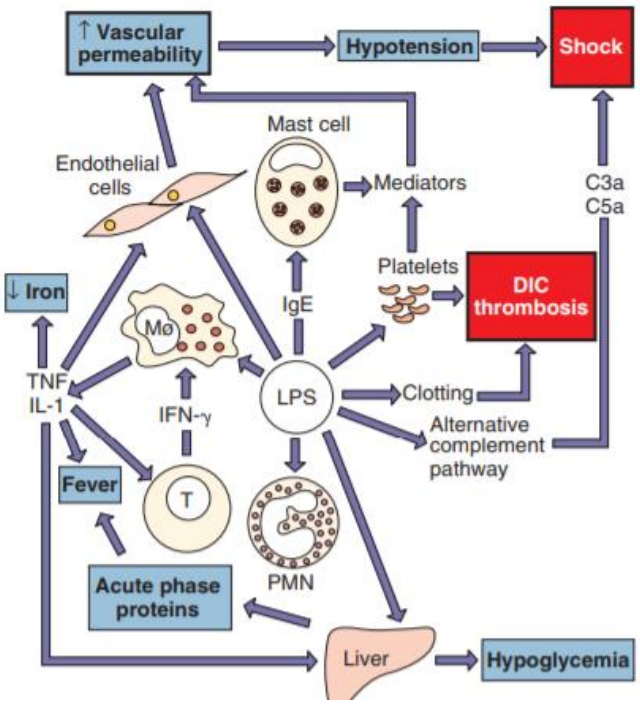


* Endotoxins are heat-stable so it won't be activated by heat like exotoxins.

* It's very toxic for animals even in low dose.

*They're the most pathogenic part in bacteria and triggers the biggest effect on immune response:

LPS in the bloodstream is initially bound to circulating proteins, which then interact with receptors on macrophages neutrophils and other cells of the reticuloendothelial system. Proinflammatory cytokines such as IL-1, IL-6, IL-8 , TNF-α, and other cytokines are released, and the complement and coagulation cascades are activated.



**The following can be observed clinically or experimentally:

Fever, leukopenia, and hypoglycemia; hypotension and shock resulting in impaired perfusion of essential organs (e.g. brain, heart, kidney), intravascular coagulation, and death from massive organ dysfunction.

- On the other hand, peptidoglycan released from gram-positive bacteria can cause similar immune responses, but much less potent than endotoxin (LPS).

Watch the last 5 minutes of lecture 10 for further illustration.

TABLE 9-4 Characteristics of Exotoxins and Endotoxins (Lipopolysaccharides)

Exotoxins	Endotoxins
Excreted by living cell; high concentrations in liquid medium	Integral part of the cell wall of gram-negative bacteria; released on bacterial death and in part during growth; may not need to be released to have biologic activity
Produced by both gram-positive and gram-negative bacteria	Found only in gram-negative bacteria
Polypeptides with a molecular weight of 10,000–900,000	Lipopolysaccharide complexes; lipid A portion probably responsible for toxicity
Relatively unstable; toxicity often destroyed rapidly by heating at temperatures above 60°C	Relatively stable; withstand heating at temperatures above 60°C for hours without loss of toxicity
Frequently controlled by extrachromosomal genes (eg, plasmids)	Synthesis directed by chromosomal genes

There are more characteristics in slides but those are the ones mentioned by the doctor and we need to know

😊 GOOD LUCK 😊