Microbiology

Sheet Slide

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Microbiology

Review:
Talking about adhesion: colonization starts with attachment.

Some bacteria colonize after adhesion and then they may penetrate (invade).

This invasion happens at a very wide spectrum. Despite being very dangerous, some of them are noninvasive at all such as Clostridium tetani.

Noninvasive: it stays at the site of infection only, but the toxins released travel and do all the damage.

-Strep. pneumoniae is highly invasive.

Virulence depends on genetic information which is coding for the different virulence factors like capsules, etc.

Means to help bacteria (increase virulence):

This can happen if the bacteria are ***strep. pyogenes*** which produces **collagenase** and **hyaluronidase** (spreading factors) that break collagen and hyaluronic acid existing in the EC matrix of the connective tissue. On the other hand, **coagulase** produces fibrin clots that wall off the macrophages and the site of infection surrounding the bacteria يعني كأنها بتعمل حجب او تغطية.

In addition, some ***staph. aureus*** strains produce collagenase which is sometimes needed to wall off the site of infection to be able to spread.

IgA protease break down IgA.

Capsule is antiphagocytic -> some cell wall proteins such as **M protein** of strep. pyogenes acts as antiphagocytic

protein A on staph. aureus acts as an anticomplement(complement proteins exist in the serum which is part of our innate immunity and doesn't increase with stimulation).

Parasite bacteria (ATP parasites) -Chlamydia-: Not enough machinery to produce ATP so it requires a host cell.
Some certain bacteria can be grown on a MICROBIOLOGIC MEDIA such as mycobacterium tuberculosis, listeria, legionella, Brucella, fungus histoplasma. In our body, they can survive in

macrophages (**intracellularly**).

Normally 60-70% of the WBC's are **neutrophils** (polymorphonuclear cells family-PMNs). These come to rescue because they can easily move from the blood vessels into the space to the connective tissue to engulf the bacteria.

If the PMNs can't do the job then **macrophages** (existing in the secondary lymphoid organs) come to engulf the organisms. However, intracellular parasites stop the engulfment process by living in the macrophages.

Mechanism: when the organism is engulfed by the macrophage it is called a **phagosome**. Normally this phagosome will fuse with a lysosome forming a **phagolysosome** and the decrease in pH will activate the enzymes that will breakdown the organism and get rid of it. A piece (MHC2) may stay on the surface of the macrophage to activate T cells or other immune cells later.

But in this case, parasites stay in the macrophages and inhibit the acidification and then divide to fill the whole cytoplasm. Eventually, it will lyse the macrophage and spread to other macrophages.

Listeria moves from one cell to another by a sling shot fashion by aggregating actin filaments inside the cytoplasm on its surface and propelling itself to other cells.

All the other bacteria will be phagocytized by the PMNs, if the PMNs couldn't kill them it will die and aggregate (in acute inflammation forming pus) and the macrophage will kill the bacteria (**extracellular parasites**).

*Bacteria kills neutrophils by dividing in it producing **oxygen radicals (toxic).**

Yersinia pestis (Plague) has virulence outer membrane proteins which inhibit phagocytosis by neutrophils and macrophages. They also inhibit cytokinase production by macrophages.

Yop j is a protease which cleaves two signal transduction pathway proteins required for the induction of tumor necrosis factor synthesis. It produces **dam proteins** (DNA adenine methylase) which control the synthesis of many virulence factors.

Some bacteria have **pathogenicity islands** which are a cluster of genes coding for many virulent factors while nonpathogenic bacteria don't have these pathogenicity islands.

Pathogenicity islands don't replicate independently from bacterial chromosome. We can find them in gram negative bacteria such as E.coli, Salmonella, Cholera and in gram positive bacteria like strep. pneumoniae.

Bacteria causes two types of inflammation:

- Acute inflammation.
- Chronic inflammation.

Acute inflammation is caused by **extracellular bacteria** (pus formation by dead neutrophils).

Some gram-negative bacteria also cause acute inflammation like meningitis caused by ***neisseria meningitides*** and gonorrhea caused by ***Neisseria gonorrhoeae***.

Chronic inflammation: intracellular parasite infection. Our body tries to limit it by surrounding macrophages with T cells then fibroblasts surround T cells forming granuloma. In lungs, it is called tubercle (Chronic infection).

So bacteria can cause damage by i**nflammation** or by **invading** or by **toxin production**.

Endotoxins and Exotoxins:

Endotoxins exist in gram negative bacterial outer membrane(all gram negative bacteria have LPS). Even if the bacteria is dead, it has the same effect of toxicity when alive. LPS stimulate macrophages, when activated they will release lots of interleukins most importantly tumor necrosis factor which causes the lowering of blood pressure and other things. Interleukin 1 is called "endogenous pyrogen" which causes fever.
(exotoxins are much stronger than endotoxins)

-The most important symptoms of a septic shock are fever and low blood pressure.

In immunology we have good antigens and poor antigens:

Good antigens stimulate antibodies production and they are proteins.

Proteins are better than carbohydrates or lipids, LPS is not a good antigen, it is poorly antigenic, meaning that it does not induce antibodies production. LPS cannot be destroyed by boiling and it is stable at 100 degrees for 1 hour. LPS is very important in the pathogenesis of Neisseria meningitidis causing meningococcemia **which** is sepsis (septicemia) caused by Neisseria meningitides (a gram negative cocci).

Exotoxins can be produced and secreted either by gram-positive bacteria like clostridium tetani or by gram-negative bacteria like ***Bordetella pertussis*** or ***E coli*** or ***vibrio cholera*****.**

Proteins can be coded by a bacteriophage like ***Corynebacterium diphtheria.*** The genes for diphtheria toxin are actually viral genes whereas the genes for ***vibrio cholerae*** toxins are viral genes coded by a bacteriophage. They can also be coded by plasmids and they are highly toxic; a little amount can be lethal.

Corynebacterium diphtheriae produces a toxin which causes the production of a thick membrane (pseudomembrane) in our throat that can stop our ability to breathe by blocking the airway. While tetanus exotoxin blocks inhibitory neurotransmitter in the CNS causing contraction of muscles (spastic paralysis).

Good antigens produce antibodies that are antitoxins. We're immunized against diphtheria, against tetanus and against pertussis by using a toxoid. Toxins are proteins and toxoids are the treated proteins to make it non-toxic but still immunogenic which means it can induce immune response to produce antibodies. These antibodies bind to the toxin and will be neutralized; so toxoids are used for vaccines since they are proteins. It can be treated with: formalin , heat (the shape of a protein changes in which it loses its toxicity) and genetic engineering.

There are always exceptions: ***staphylococcus aureus*** produces an exotoxin which causes staphylococcus aureus food poisoning that affects our GI. This is why this toxin is called enterotoxin and this toxin is heat stable meaning it is not killed by heat.

Botulism is caused by ***Clostridium botulinum***. Symptoms of botulism are the opposite of tetanus flaccid paralysis. This means we cannot breathe because the diaphragm doesn't move which means we could die because of the inability to breathe. (Bacteria release the exotoxin and then we ingest it and get food poisoning which causes the symptoms).

Many exotoxins have an A subunit (active) and a B subunit (binding). A lot of exotoxins act by adding ADP ribose (ADP ribosylating exotoxins).

Mechanism: it will add ADP ribose to something to inactivate it. Pseudomonas toxin a, diphtheria toxin and exotoxin A both add ADP ribose to elongation factor 2 which is originally used in protein synthesis in translation so it is inactivated causing necrosis.

Diphtheria stays in the pharynx but it releases exotoxins that inhibit protein synthesis so it causes cell death. Necrosis with fibrin deposition produces a pseudomembrane that blocks the airway.

Pseudomonas is dangerous on many people specially those who wear eye contacts. This is because it produces exotoxins that cause necrosis which could lead to blindness in few hours.

Other ADP ribosylating exotoxins like in E.coli and cholera toxins add ribose to a stimulatory protein causing it to be more activated meaning there is an increase in CAMP in the cell which results in a net secretion of water and electrolytes(in vibrio cholera we have massive watery diarrhea).

Pertussis toxin is also ADP ribosylating. G_i inhibitory protein inhibits adenylate cyclase from functioning, so the toxin turns on adenylate cyclase which also increases CAMP and this causes whooping cough (paroxysmal cough) in the respiratory tract.