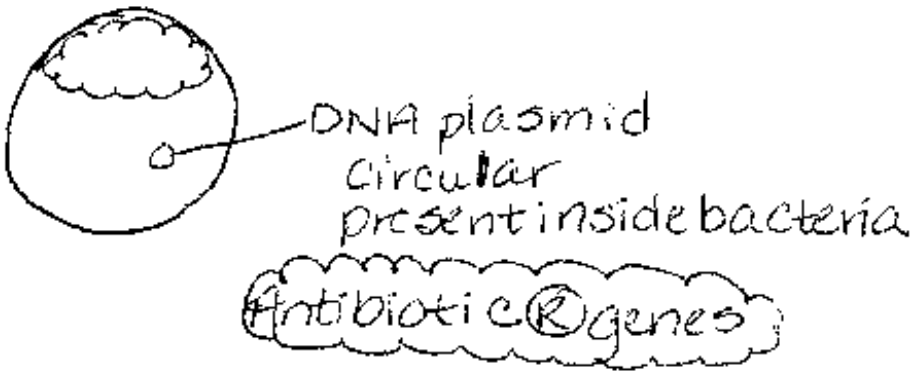
Micro notes part 4
Chapter 15
What makes organisms harmful to us?

Virulence – The degree of pathogenicity (disease-causing) of a microorganism.

What increases their virulence?

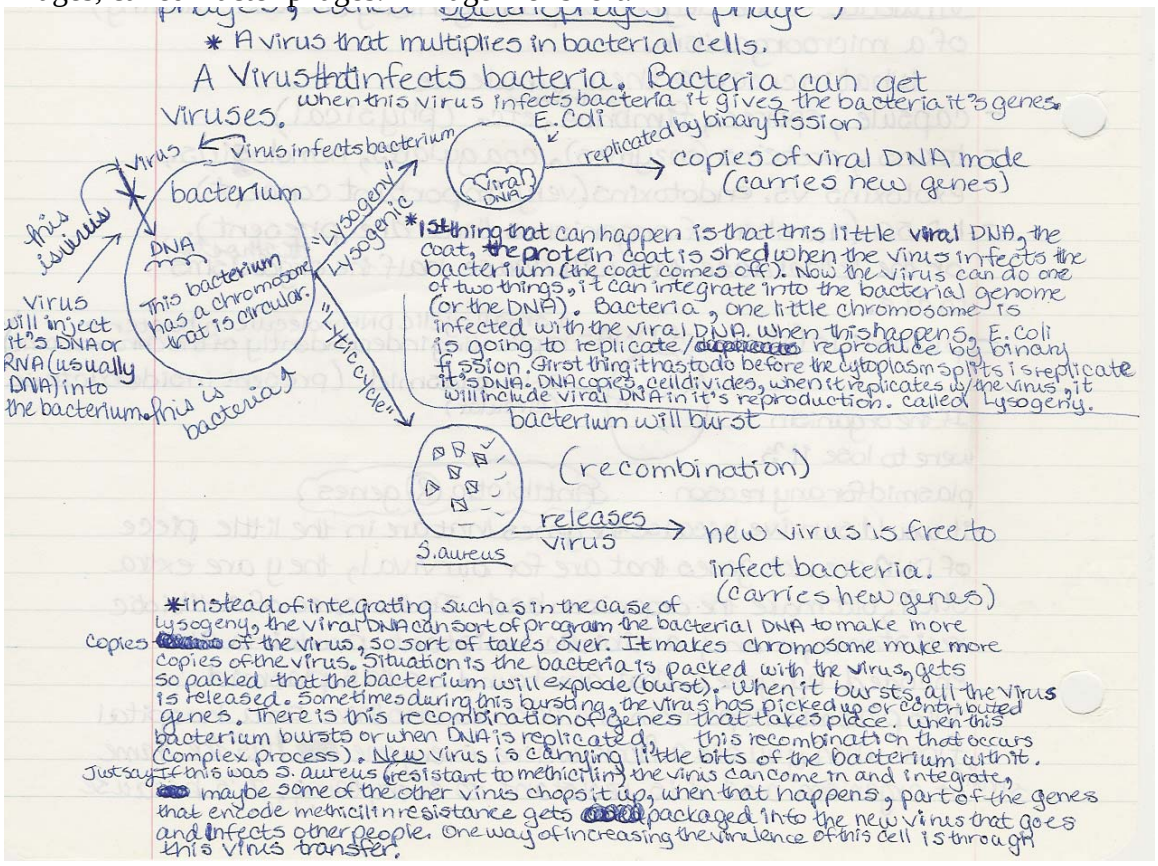
- Capsule, spores, fimbriae (adherence), etc. *physical.
- Toxins, proteins (enzymes), coagulates, hemologins, exotoxins vs. endotoxins (very important concept).
- LD50 (number of organisms that are present) or the lethal dose that will cause half of the organisms (Test hosts) to die.
- Plasmids - piece of DNA. (A small cyclic DNA molecule in bacteria replicating independently of the chromosome).



If the organism were to loose it's plasmid for any reason it would survive because the genes that are in the little piece of DNA are not genes that are for survival, they are extra stuff, but make the organism bad. In the case of antibiotic resistance, many antibiotic resistant proteins are encoded by genes that are found on this plasmid. This plasmid hops from one case to another. On a hospital floor when you see a floor where everyone has the same strain of organism and it is resistant to everything, it's because this little plasma is jumping and replicating through each patient.

This is why people who have MRSA – Methicillin R resistant S. aureus – patients that have this and other nosocomial organisms (An infection that develops over the course of a hospital stay and was not present at the time the patient was admitted) have to be kept in isolation. Why? Because you want to try to stop the plasmid from hopping around. That's why these people are in isolation. Just one example of nosocomial problems.

- Phages, called Bacteriphages. "Phage" for short.



Both copies of viral DNA mode (Lysogeny) and the new virus is free to infect bacteria (Lytic cycle) can carry new genetic information and when that happens, you can end up with things like antibiotic resistance from patient to patient. Simply using a virus to transmit this information.

Lysogeny – A state in which phage DNA is incorporated into the host cell without lysis.

Lytic cycle – A sequence for replication of phages that result in host cell lysis.

Need to know that ways of virulence for organisms include little plasmids and include viruses that give them special genes.

Page 401 Figure 15.5 Some cytopathic effects of viruses.

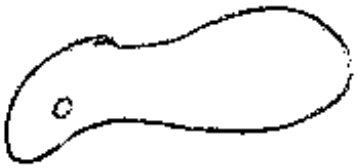
Virulence of viruses – "Cytopathic effect" (CPE). Tissue deterioration caused by viruses.

When viruses infect, say animal cells, (including humans not different from bacterial) the cause cytopathic effects. Very clinically significant. In real life you will encounter CPE usually in cases of cultivating the viruses.

Her example: Suppose you have a patient, you're working for an OB-BYN, and you have a woman that is ready to deliver a baby. She has a history of genital herpes. If she is in active herpes, and she has a vaginal delivery, she will pass it onto the baby. So, you want and try to prevent this. You will want to find out if she is inactive herpes. If she is in active herpres, a c-section will have to be performed. What you can do is you can take a genital culture from this woman prior to her going into labor, but it has to be close enough (can get a little crazy) to going into labor, so it's at the right time. If you do it too early, she may not be in active herpes at that time. You have to do it close enough to the time of delivery. You take a genital culture either cervical or vaginal and you inoculate cells that you can buy from biological supply houses and these cells are used for viral cultures. You can't grow viruses on agar so you have to grow inside a living cell. You can buy these cells (Called cell lines) from bacterial supply houses. Take your patient and inoculate these cells with the patient's specimen.

This takes 2-3 days to get results. Will either get positive CPE, she is in active herpes, or negative CPE which means she is not in active herpes.
Genital culture → cell lines
(cannot wait until woman is in labor, because test takes so long)

Just say this is a normal cell  , a cell infected with genital herpes might look like this:



This change is due to the infection of the virus is known as cytopathic effects (CPE). Her definition – change in cells due to viral infection.

Page 401 – various types of CPE.

All kinds of viral cultures: Rodovirus in children look for CPE.

Clinically important.

<u>Virulence of Algae and Fungus</u>

Algae and fungus can also be virulent.
<u>Algae</u>: certain algae can produce toxins which can be harmful. Algae blooms. Water (in ocean) in completely red, recommendation is not to swim in it. Algae contributes toxins that can get into the fish and other sea life. No regulation on seafood. No USDA regulation at all for seafood. Algae toxins and wastes in fish.

Dioxin levels

Acceptable levels (safe for consumption):
ppb – parts per billion
Fish from Newark Bay, off coast of Sandy Hook have been found with dioxin levels of
ppm – parts per million (significantly higher).

Dioxin – known carcinogen (causes cancer)
Fungus:
Found in: grass and grain crops, wheats, ryes, peanuts / soybean – aflatoxin (#1 toxin commercially)
Aspergillus sp. A carcinogen (causes cancer). Spores can be inhaled by people with AIDS and kill them.

Most fungal toxins are carcinogenic (cancer causing). Theory that those Salem witches baked bread and got the disease called Ergot – disease of plants, cause effects similar to LSD.

Chapter 16 – Nonspecific Host Defenses

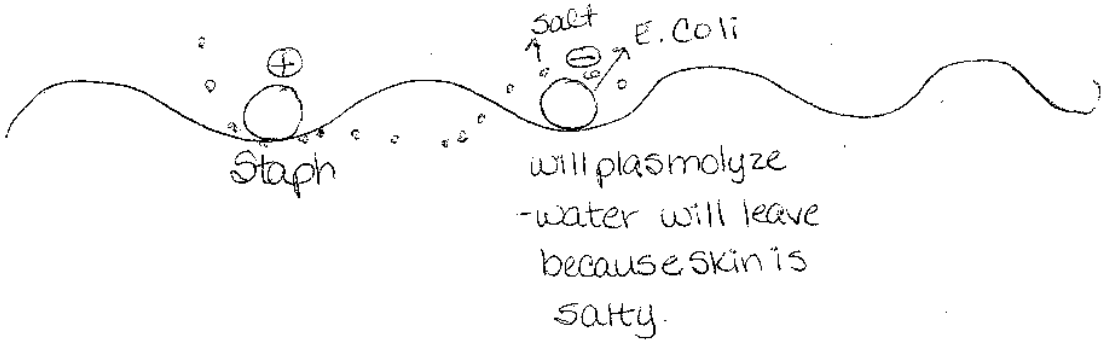
What do humans have to do to fight off infection?

Antibodies (is specific) – a protein produced by the body in response to an antigen and capable of combining specifically with that antigen, usually leading in vivo to its destruction or inactivation.

Non specific:

1. Physical barriers / chemicals

- Skin #1 place where organism will be stopped. # 1 preventer of organism. Skin has a pH level of 5-6, bacteria prefers 6-8; keratin (water-proofing protein that is on the skin that prevents organisms from entering); salt (osmotic lyses); S + S + C (Staph + Strep + Corynebacterium) Gram positive C protects against osmotic lyses; sebum (oil in skin). Organism trapped in oil.



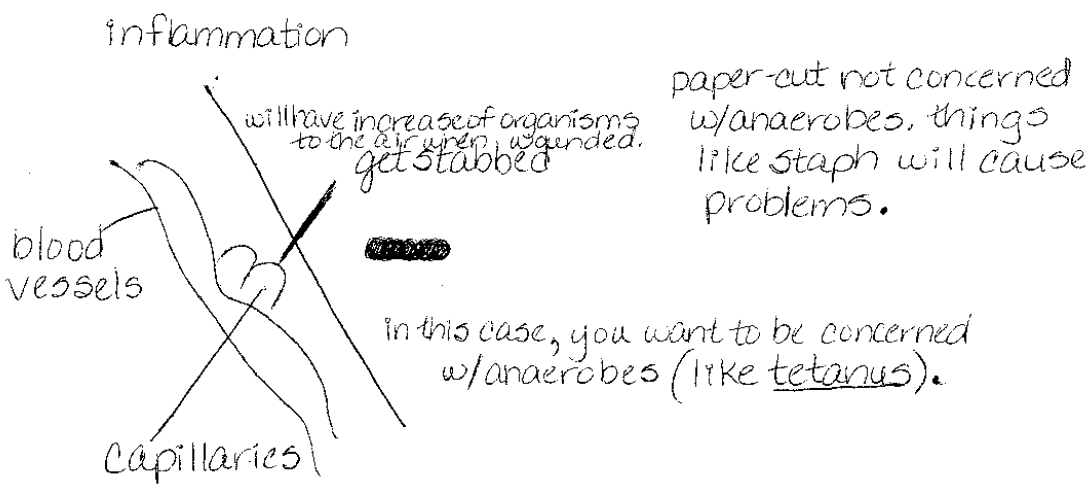
  P. acnes – thrives in sebum
- Cilia (when you smoke, it destroys them).
- Mucous membranes – capillary beds.
  Saliva, antibodies
  Close proximity to blood vessels. All port of entries have something to protect

them. Ex. Eyes have eyelashes, cilia in respiratory tract, hair in nose. Babies are susceptible to second hand smoke.

- Flow – urine / sweat / tears. All prevents organisms from gaining entry. Tears – important chemical protein called lysozyme – it destroys cells' walls in Gram + cells. Protects against Staph, Strep, and Corynebacterium that causes things like styes. Pink eye is usually cause by a Gram – cell like Hemopholis.

2. Phagocytosis (inflammatory response). The ingestion of solids by cells.

Page 415 – Figure 16.9 The process of inflammation



Most common dialator histamine released by white blood cells.

1st step in inflammation is vasodilation – dilation or enlargement of blood vessels. Cause blood vessels to open up so phagocytes can come and start doing their job. Blood vessels dialate from histamine. Symptoms: redness, red eyes.

2nd step – Diapedesis – The process by which phagocytes move out of blood vessels. Migration of white blood cells into tissue.

3rd step – Phagocytosis – 4 steps

- Chemotaxis – attracting phagocytes to the area. Chemotactic factors: Interleukin – chemicals that cause T-Cell proliferation. Things which attract other cells to the area.
- Chemotaxis – motion in response to the presence of a chemical.
- Neutrophils – also called polymorphonuclear leukocyte; a highly phagocytic granulocytic.
- White blood cells go through capillaries to injured tissue.

White blood cells – Leukocytes. Will do their job, they are going to eat the microorganisms, engulf them and destroy them.

Two groups (types) of white Blood Cells:

Granulocytes – a leukocyte with visible granules in the cytoplasm; includes neutrophils, basophils, and eosinophils.

- Neutrophils – 1st phagocyte to respond (polymorphonuclear / PMNs / "polys"). Mostly found in blood – highest %. When you have a high amount of polys in your blood, exceeding 80% (depending upon your normal population), it is a normal indication that you are dealing with a bacterial infection rather than a viral one. There should be no white blood cells in your spinal fluid. If there is white blood cells in your spinal tap, will take a look at a gram stain of spinal fluid if there is white blood cells, there is a problem. (No time to do culture). If doctor sees neutrophils in abundance, it is quite critical, generally there is a bacterial infection. If when he does the spinal fluid, he does a gram stain and sees an increase of either lympocytes or monocytes, the general rule (not all the time, but generally) that this is viral meningitis. A trick of the trade.
- Basophils – release histamine. A granulocyte that readily takes up a dye. Acts as as vasodilator.
- Eosinophils – a granulyte whose granules take up the stain eosin. Very low percentage in blood. Sometimes you will have an elevation in people who have allergies, parasite infections, or taking medications.

These next pages may be confusing. The professor was bouncing back and forth and I had a hard time keeping up both in class and listening to my tape.

Agranulocytes

- Monocytes – tissue macrophages – a phagocyte that is the precursor of a macrophage. Clean up debri.
- Lymphocytes – T and B cells (specific). A white blood cell involved in specific immune responses. Have nothing to do with phagocytosis.

In phagocytosis, neutrophils are first to respond, and they have a high degree of phagocytic activity. After about 20 minutes go by, 2nd type of white blood cell that will be attracted to the area are monocytes. These are known as tissue macrophages, that are very big and they eat tissue macrophages. Sort of a clean up all the mess that has gone on.

Page 413: Figure 16.8 The mechanism of phagocytosis in a phagocyte.

Here is the picture that the following notes refer to:

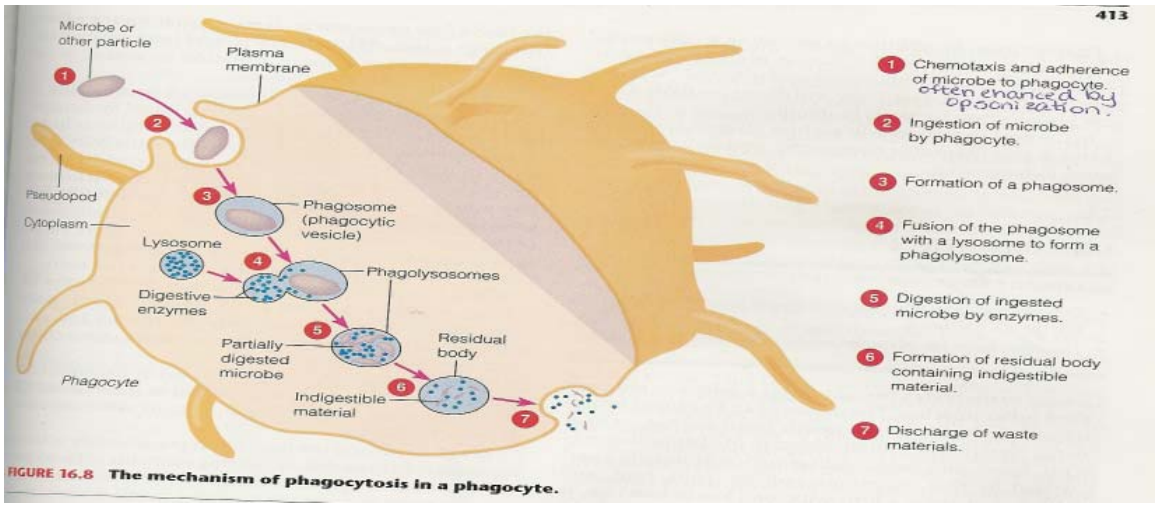


FIGURE 16.8 **The mechanism of phagocytosis in a phagocyte.**

Neutrophils respond very quickly but they can not do the bulk of the phagocytic work. The monocytes really clean up.

(On tape she is going back and forth, I apologize for the confusion and am including it all in case there is things that may be important).

1st step of phagocytosis is:
Chemotaxis – this is the chemical attraction of either the other white blood cells to come help out or it can be between the phagocyte and other organism. Chemotaxis is simply a term that refers to an attraction that is the result of a chemical stimulant.
First you have chemotaxis, phagocytes come to the area. Then you have engulfment. By the picture on 413, you see first the particle (organism) has to adhere to the surface of the phagocyte, then the phagocyte takes it in. This adherence is quite important or enhanced by:
Process called opsonization – causes adherence to rise. The enhancement of phagocytosis by coating microorganisms with certain serum proteins (opsonins). We say a microbe is oxidized when it is coated with proteins. So chemicals will coat the organism and this advances chemotaxis between the phagocyte and the organism. Once organism is opsonized (coated), adherence can take place between the phagocyte and the organism.

Once adherence takes place, engulfment is the next step. Organism is taken away in by a vacuole called a phagosome. This fuses with the lysosome. The lysosomes have digestive enzymes. The two vacuoles fuse together and the lysosomes digests the bacteria. A lysosome is an organism containing digestive enzymes.

Digestion and release.

Fever. Fever is NOT a cardinal sign of inflammation, it is a result of the inflammatory process. Result of inflammation.
Four cardinal signs of inflammation:

- Redness – comes from dialated blood vessels.

- Swelling – fluid builds up from phagocytosis.
- Pain – nerve endings in area will be affected.
- Local heat (not fever) – pressure from the increase of pus or beta dialation.

When you have a fever, it is a good thing. It is your body's way of trying to destroy the organism by resetting the temperature. How fever occurs? Page 398.

Fever is a systemic response to the inflammatory process, and it usually (not always) is caused by a Gram – bacterial infection. Bacterial infections can cause high fevers. Viruses can cause fevers but they will be lower. Reason why bacterial infections cause high fevers is because of the process on 398.

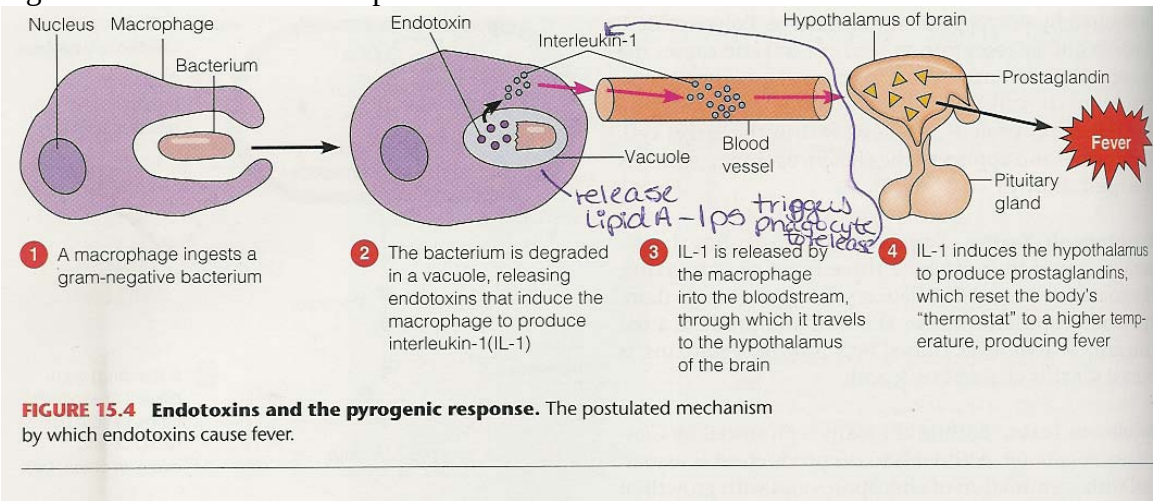


FIGURE 15.4 Endotoxins and the pyrogenic response. The postulated mechanism by which endotoxins cause fever.

Assume that it is a Gram – organism. It's opsonized (means it is coated). The organism is being engulfed by the phagocyte. A vacuole will form and the lysosome will start breaking the organism down. The break down of the organism will release LPS (Lipid A) endotoxins. Lipid A triggers the phagocytes to release interleukin (a chemotactic factor). Attract other cells to the area. So, the phagocyte eat the organism, Lipid A is released (part of the cell membrane). That in turn, stimulates the phagocytes to release interleukin.

Interleukin does a number of things. One of the things it does is travel to the brain (hypothalamus). In the hypothalamus it will stimulate the synthesis of prostaglandins (hormone like substances that are synthesized in many tissues and circulate in the blood, the exact function which is not known).

When you give a patient an aspirin, you are actually competively inhibiting the enzyme that produces prostaglandins.

What you need to know is prostaglandins is synthesized when interleukin goes to the hypothalamus. Once prostaglandin is synthesized, it sort of resets the body's thermostat, your body tries to meet the new setting by shivering, by trying to meet the raised temperature. The only way you are going to lower a fever, you can give aspirin which is

going to inhibit prostaglandin synthesis, or you can try to get rid of interleukin, which is not going to happen until the organism is completely eaten up.

Septicemia – Gram – septicemia may cause death (intestinal rupture). Fever, shock, often death. Will always be treated with immediate antibiotics and immediately do a blood culture.

Interleukin can stimulate other cells. Possible cure for diseases such as HIV or AIDS. Because when it is given, chemotactic factor will boost the immune response. Interleukin is caused by a cytokine, in the family where it attracts other things. Causes T-cells to rise.

Antigen – Any substance that, when introduced into the body, causes antibody formation and reacts only with its specific antibody.

Antibody – A protein produced by the body in response to an antigen and capable of combining specifically with that antigen, usually leading in vivo to its destruction or inactivation.

Complement – a group of serum proteins involved in phagocytosis and lysis of bacteria. Very effective. Non-specific defense.

- Series of serum proteins
- Activated in a "cascade" effect. Reactive together, one protein turns on another. Very complex. Very important to the patient.
- Classical pathway of activation
  Antigen – anything foreign, combine together. Ag-Ab complex. Turns on these proteins.
  Antibody
- Alternate pathway – antigen alone (viral / fungal).
- When proteins are turned on, 3 basic things that they do.
- Effects:
  1. Increase (enhancement) the inflammatory response. Increase the blood vessels, permeability, chemotaxis with the phagocytes coming into the area.
  2. Proteins that coat the bacteria to make it more attractive to the phagocytes, called opsonization.
  3. Cytolysis – directly destroying the bacterial cell by actually puncturing it. Sit on the membrane and drill a hole right into the membrane. Direct killing of the organism.

Non specific component called Interferon. An antiviral protein produced by certain animal cells in response to a viral infection.

Page 420
Cancer patients. Looking into for cancer treatments. Antiviral in it's action (virus invasion).

Interferon (or signal message) – a protein
+
AVP (antiviral protein) – inhibits viral replication. Doesn't kill virus, stops it from being made.

**Need to be infected for interferon to produce but only works on uninfected cells.

Interferon – chemical substance that will travel, is produced by an already infected cell that will travel to an uninfected neighbor. The neighbor has not seen the virus, it has to be virus-free. It is species-specific, only humans can produce human interferon.

Four cardinal signs of inflammation:

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Source: class notes and
Tortora, Gerard J., Funke, Berdell R., Case, Christine L.
Microbiology: An introduction, Fifth edition. Redwood City, CA. The Benjamin/Cummins Publishing Co., Inc., 1995