Transcription of Presentation
HSC 4551, Survey of Human Disease
Week 1, Chapter 3: Inflammation and repair.

PROFESSOR: All right, guys, this should come on in a
minute.

So today's Chapter is Chapter 3 and what we're going to be
doing is discussing the inflammatory reactions, first of all.
Inflammatory response is a nonspecific response to any
agent that causes cell injury. Okay? So the agents that can
cause cell injury can be physical, such as hot or cold. Okay?
Anybody who's had a burn, whether it be hot water on your skin,
whether it be frostbite, are examples of physical agents which
can cause cell injury.

Another agent is going to be chemical. Anybody who's done
chemistry, worked in the chemistry lab, is concerned about
strong bases and acids that can cause injury.
And, of course, we have the biologic, bacteria or viruses.
Last Tuesday we mentioned splinter, if you had a splinter, you
can get an infection if it is not removed because you will get
bacteria associated with that.

So inflammation. What happens when inflammation occurs?
There are several things that happen. Number one, there's going
to be capillary dilatation. Let me just go ahead with one
thing.

Let's look at this slide first. So we have the physical
agent, the chemical agent, and we have pathogenic or
microorganism that can act as an agent to cause tissue injury.
When tissue injury happens, there are mediators of inflammation
that occur. These are nonspecific, in that everybody has the
same type of response to these agents; right? Everybody is
susceptible to frostbite, can have the same reaction. Everybody
is susceptible to a burn from acid or lye; okay? If you are
exposed to it, you have the same type of reaction.

So why are the reactions always the same? Because the
medias of inflammation are the same. Now, at the very bottom
when you look at the screen, you see heat, you see redness, you
see tenderness, swelling and pain. These are the characteristic
hallmarks of inflammation. All right? We think of it once
again because if you get a splinter in your finger, what
happens, if it is there for a couple of days, it gets warm, red,
tender, swollen, and becomes painful. Okay?

So why does that happen? Well, the redness and the heat,
tenderness and swelling and pain can be due to the medias of
inflammation. What do they cause? Capillary dilatation. The
capillary, smallest blood vessels in the body, when they
dilate -- "dilate" means to open up -- they carry more blood
flow, so you will have more blood into the area.

Redness -- inflammation -- there will be increased
capillary permeability. That means that it's easier for fluid
and cells to leave the capillaries and go into the surrounding tissue, the interstitial tissue. So there's extravasation of fluid. When you have increased fluid into that area, there's going to be increased swelling, and with capillary dilatation there will be increased redness and heat. Then also, as part of the process of inflammation there's going to be attraction of leukocytes. "Leuko" means what? Anybody? White blood cells. Good.

White blood cells are going to be attracted. What's going to happen is they are going to leave the capillaries, and they are going to go into the surrounding tissue of the capillaries. They are attracted to the tissues that are injured. So they are going to be attracted to that. The increased capillary permeability allows leukocytes to leave capillaries and go to the site of injury. All right? And then the body may respond with a fever, but it will respond also with leukocytosis, increase in the number of white blood cells.

The swelling that occurs at the site of inflammation puts pressure on the nerve endings, and as a result you will have pain. So these are the effects of inflammation. Okay?

So once again, we will go back to that slide with local effects. You have capillary dilatation, increased blood flow, increased warmth and redness to that area. Also, increased capillary permeability, leading to extravasation of fluid, fluid leak out of the capillaries, causing swelling, and there's going to be attraction of white blood cells. These white blood cells migrate to the site of injury. Initially they will stick to the endothelium of the small blood vessels. The endothelial cells are the flat squamous cells we talked about last lecture. They line the blood vessels, the veins, the arteries and the capillaries.

All right. So signs of inflammation. We have heat and redness, swelling, tenderness and pain.

SLIDE: Here's some examples, acute inflammation of the ear. What causes it? Maybe a contact dermatitis. We see extensive blistering on the buttocks on the next slide here.

SLIDE: And as far as the inflammatory process, you have the polymorphonuclear leukocyte cell involved in the inflammatory process. Now, leukocytes I told you are white blood cells. There are further subdivisions of white blood cells. One type of white blood cell is called the polymorphonuclear leukocyte, abbreviated as poly's. It's called polymorphonuclear leukocyte because when you look at that cell underneath the microscope it looks like it has more than one nucleus. Actually what has happened is, there's only one nucleus, but there's segmented lobes of the nucleus, so there's a swelling and a narrow area of swelling, so it looks like there is more than one area of nucleus, but there's not. They are called poly's. They are phagocytic cells -- they are actively phagocytizing. Does anybody know what "phagocytize" means?
"Phago" means "to eat." "Cytic" means basically to kill. So they are a cell that is involved in picking up debris. All right? They engulf debris, foreign protein.

The other important cell in the inflammatory process is the mononuclear cells, monocytes. Monocytes are another type of white blood cell. Okay? Another type of leukocyte. When they leave the vascular tree, when they leave the capillaries and go to the surrounding tissue, they become macrophages. And macrophages are garbage cells. You see P-H-A-G-E, phage, means to eat. Okay? And they clean up the tissue, debris.

All right. So with the severe inflammatory process, what happens is sometimes systemic effects become more evident. You can become ill and develop a fever. What happens is also, response. Bone marrow increases the production of leukocytes, resulting in increased levels in the bloodstream. And the liver may produce certain proteins such as C-reactive protein, which are involved in the inflammatory response.

Now, going back, the mild inflammatory response is what you call self-limiting. It doesn't progress to something else. It subsides with some tissue resolution, and -- okay. For example, when you put your hand into hot water -- not scalding water so it blisters, but just hot water -- that would be a self-limiting, mild inflammatory process; and very often with the severe inflammatory process you are going to have some tissue damage. And the tissue damage then requires replacement of damaged cells, and in the process of healing, there may be scarring. Okay? The mild inflammatory process really does not have scarring.

Outcome of inflammation. What can happen? There is going to be resolution of the inflammation. There may be repair. The areas of destruction could be replaced by a scar. There are mediators involved in the process of inflammation that can intensify the inflammatory process, and sometimes what happens is the mediators end up generating even more mediators.

Now, exudate. When there is an inflammatory process, what happens? An exudate may form wherein -- I showed you that one slide of the person who had blistering on the buttocks. There was severe injury there, and there developed fluid, which consists mostly of protein, white blood cells, some tissue debris. And the amount of protein that's present in the exudate or fluid when the inflammatory cells are present can vary. And we have three types of exudate basically, serous, purulent and fibrin.

Serous is made up of fluid with a little bit of protein. If you ever popped a blister, the fluid that comes out is serous. It may be straw-colored. It is basically clear. If you leave the splinter in too long, what happens is you develop an exudate. However, it's not going to be serous. It's not going to be clear. It's going to be a little bit pussy. The reason for that is that the pus is basically -- the cloudy
purulent nature is determined by the presence of white blood cells. So basically, pus is an exudate, a purulent exudate, with a large concentration of white blood cells.

The last type of exudate is fibrinous exudate. It is rich in fibrinogen. We'll talk about fibrinogen in another lecture, but fibrinogen helps coagulate, which produces fibrin, a sticky film on the surface of inflamed tissue. It is involved in the formation of a scab. Okay? Scabs are made up of fibrin, and platelets, and other proteins.

Now, sometimes what happens then is, adhesions can form after a tissue injury. Adhesions are bands of fibrins that form.

We use hemorrhagic to refer to an increased number of red blood cells.

Now, we talked about chemical mediators. What are they? They are chemical agents that intensify the inflammatory process. So there are cell-derived mediators, mediators that come from cells. They are: Histamines, serotonin, prostaglandins, leucocytes.

So let's look at mast cells first -- specialized connective tissue cells. These are cells that are in connective tissue; these are tissues that are directly underneath our skin, in between the epithelial cells, the epithelium, and the muscle and fascia; and they contain granules that are rich in histamine; and histamine is a vasodilator, so it encourages the vessels to dilate.

Now this is significant. Small digression, for people who have allergies. What is the typical or the most common medicine that is given to people over the counter when they have symptoms of hay fiver and allergic rhinitis, which is basically nasal stuffiness, itchy eyes, that kind of thing? What is the name of it?

STUDENT: Benadryl.

PROFESSOR: Benadryl. That is an antihistamine. What does it do? It counteracts the effect of histamine. So people who have allergic rhinitis due to allergies, they have nasal stuffiness and congestion, that's due to the release of histamine. You take Benadryl, Benadryl counteracts the effects of histamine. It is an antihistaminic agent. So instead of causing vasal dilation, it causes vasal restriction. What happens is, there is less permeability and as a result, there is less nasal stuffiness. All right?

So mast cells contain -- basically they are within connective tissue cells, and they contain histamine. Histamine and serotonin are also in blood platelets. Platelets will stick to an area of tissue injury. Prostaglandins also mediate inflammatory response.

What is the common medication you can buy over the counter that inhibits the actions of prostaglandins? Anybody know? No one? And I am sure you have taken them all. All of you have
taken them. Advil. All right? Advil is an antiprostaglandin agent.

So now that I have told you one, what are some of the other ones? What's the same category as Advil? Motrin, good. What else? What? What did you say? Ibuprofen, right. What else? Aleve, Anaprox -- all of those inhibit the synthesis of prostaglandins. All right.

Prostaglandins. For example, when you get an injury such as a sports injury, whether you sprain an ankle, have tendinitis, what is the first line of drug that the orthopedic doctor or trainer will recommend? They will recommend antiprostaglandin agents -- Motrin, Advil, Nuprin. The reason, this agent inhibits the synthesis of prostaglandins, so the fewer prostaglandins reduces the inflammation that can occur from the injury.

Leukotrienes -- synthesized from arachidonic acid.

SLIDE: Also bradykinin, which is present in blood plasma, can mediate complement. Complement is very interesting. It is a protein that is produced by the liver. It gets activated by the binding of antibody to antigen. All right? And we will talk about this in the next Chapter.

But, let me say that when antibody binds to antigen, the antibody chain changes the shape or configuration. That change in configuration activates complement. Complement is a series of proteins produced by the liver, and so complement fragment A gets activated by the binding of antibody A. After complement fragment A gets activated, it activates complement fragment B. When complement fragment B gets activated, it activates complement fragment C. It is a cascade effect. It reduces the process of inflammation. It is also used to destroy bacteria, which we will discuss in another chapter. Okay?

Yes? Yes, mediates inflammation, increases it.

So here is a diagram. And the mediators are released from cells. They stimulate the kinins in plasma and also stimulate the mediators from complement. Complements stimulate the mediator by kinins and the mediators released from cells. So that's how mediation can increase the inflammatory process.

SLIDE: Now, I mentioned lysosomes also in the last lecture. Okay? And lysosomal enzymes, basically what they do is break down protein. And the enzymes are in vacuoles that are in the cytoplasm of cytophilic (cytositic?) cells. Primarily, cytophilic cells will be neutrophils. We have polys, we have neutrophils, we have leukocytes. Same cell type, three different names. Unfortunately, they will be used interchangeably throughout this semester. You need to understand that. Polys, neutrophils, they are the same.

So anyway, the cytoplasm on these cytositic cells have enzymes that can digest the protein material. The lysosomal enzymes are contained in lysosomes, in the plasm.

Also the antigen-antibody reaction activates complement.
Activated complement increases the inflammatory response.

Now, what are the harmful effects of inflammation? Obviously, inflammation is important because it is part of the healing process. How can it be harmful? It can result in severe tissue injury. Okay? And an example for that is, how many people have had poison ivy in this class, besides me? Okay. So poison ivy is an allergic reaction to a substance on the leaf of the plant, and you end up with little pustules, blisters, severe itching. And then, if it's really severe, it's a progressive type of thing; it can become secondarily infected because these little blisters break. The doctor may place you on adrenal corticosteroids, usually called -- anybody know the name of the most common corticosteroid that is administered by prescription by mouth? Yes. Prednisone, right. And to treat something-like poison ivy, they put you on a prednisone Dosepak for seven days. Highest dose is the first day, and it reduces over the 7 days. Anybody else have had that? Okay, you guys have had that. For poison ivy or something similar? Yep.

So that's an example where adrenocorticosteroids are used to suppress an inflammatory reaction. Also, later on we will talk about autoimmune disease, where people develop antibodies to their own antigen. When that happens, they will use prednisone to cut down the inflammatory response to reduce the side effects that occur from the autoimmune disease.

So infection refers to inflammatory process caused by disease-producing organisms. I mentioned last lecture the suffix "itis" refers to inflammation. We mentioned tendinitis, bursitis, hepatitis, bronchitis. We have peritonitis, appendicitis. All these terms refer to inflammation.

Inflammation of what? Inflammation of the organ. It's the root word, whether it's going to be the appendix or the liver.

Okay? So the word, cellulitis, what that refers to is an infection basically of the skin. And cellulitis can be a side effect of poison ivy.

So also there's a term, abscess. Abscess is an infection associated with the breakdown of tissue, formation of pus. So it's a collection of pus. And it usually refers to a deeper collection, not a superficial collection of skin, but a little deeper. Okay?

Now, the term septicemia. Septicemia refers to a large -- they use the word "overwhelming." It's kind of scary, but it's a severe infection of bacteria basically in the bloodstream. You have heard the phrase "septic." That refers to someone who is sick, basically has a bacterial infection and is in the bloodstream.

"Pathogenic" refers to being capable of producing disease. All bacteria are not necessarily pathogenic. They are not all pathogenic.

Virulence refers to a measure of the severity of the disease. And also it refers to the measure the severity of the
bacteria in causing the disease. There are virulent bacteria. And if they are considered virulent bacteria, it doesn't take a large number of bacteria to cause an infection. If bacteria has low virulence, then it's going to take a greater number of bacteria to cause an infection.

The word "host" refers to the affected individual that has the bacteria.

SLIDE: So anybody know -- anybody know what that is over on the top left? It is an appendix that was removed. It's infected.

There you see a finger with the cellulitis.

SLIDE: Infection involves the relationship between the invading organism and the defenses of the body. So the course of infection is going to be determined by the balance between the virulence and dosage of the bacteria and the body's defenses. If it's an extremely virulent bacteria, large exposure, exposure to large numbers of the bacteria, the infection could progress. If it's a low virulent bacteria, the dosage or exposure to the numbers is low, then the body's defenses will take over and protect the body. Okay?

So basically, you have either progression of disease, on the left side, or resolution and healing, depending on which is larger. If it's a stalemate, then you end up with chronic infection. Chronic infection refers to infection that is low-grade but persistent. An example sometimes of a chronic infection might be TB. People can have TB for years and not know it; they are really not that symptomatic. We will talk about TB in another Chapter. But that's an example of an infection that may be present for a while, and people really are not even knowing it. The body is not able to ward it off, but it doesn't -- it's not extremely virulent in its course.

All right. So factors influencing the outcome, virulence of organism, numbers of invading organisms, and the host resistance.

SLIDE: Chronic infection. State in which the pathogenic organism and the host are evenly matched. So as a result, it's a relatively quiet, smoldering inflammation, and it is associated with repeated attempts of the body at healing. So the body tries to heal it. Defenses of the body, defense mechanisms, are not strong enough to overwhelm it, so it persists at a low-grade level.

Predominant cells involved in a chronic infection are going to be lymphocytes, plasma cells, and monocytes.

Now, lymphocytes. Lymphocytes are another type of white blood cell. All right? So we have talked about neutrophils; we have talked about lymphocytes and monocytes. All of these are three types of white blood cells that are present in the blood. The most common is going to be the neutrophil or the poly. The next common is going to be lymphocyte. After that, probably the monocyte.
The other two white blood cells I have not mentioned, I will mention them for the sake of completion, so you guys know all five. The eosinophils, which tend to be related to allergy, and basophils. The terms eosinophils and basophils were names derived from their characteristic appearance underneath the microscope when they are stained with special dye.

(End)(28 minutes.)

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