PROFESSOR: So Chapter 4 discusses immunity, hypersensitivity, allergy, and autoimmune disease. Basically, we talked about the body's defense mechanisms. And we talked about the inflammatory response, and basically that's a generalized response or a nonspecific response. And it involves phagocytosis, a material, foreign proteins that phagocytize by the neutrophils and macrophages.

The acquired immunity. That's what we're talking about where immunity develops after contact with a pathogenic microorganism. It depends on the immune system. It's associated with a stage of altered reactivity to the foreign material or hypersensitivity. The acquired immunity involves basically the lymphocytes. So inflammatory reaction more for the neutrophils or polys. And then the monocytes -- the acquired immunity is going to be primarily dependent on lymphocytes, okay. And it's individual.

Inflammatory reaction, generalized across the board. We all have the same type inflammatory reaction. Acquired immunity is different. It depends on what you've been exposed to. You, as a person, your body then develops immunity to the microorganisms, whether they be viruses, bacteria or even proteins.

So there's two types of acquired immunity. There's the humoral and the cell-mediated. The humoral immunity refers to production of antibodies. And the type of lymphocytes that are involved in humoral immunity are what we called the B lymphocytes. They are the main defense against bacteria and bacterial toxins. Bacterial toxins are proteins that are produced by bacteria.

Now, the B lymphocytes, what they can do is they can -- they know what is -- basically, they are sensitized so that they know what is part of the host and which proteins are foreign. As a result, when they come in contact with foreign protein, whether it be a bacteria or whatever, they then can respond to that foreign protein. They pick it up as foreign and they then will ingest it. They engulf it; they ingest it. These are the B lymphocytes. They then, in response to that ingestion, they break it down and produce antibodies.

Each B lymphocyte, when it engulfs or phagocytizes a specific protein, will then produce an antibody that is specific to that antigen or that protein. Once it meets up with a foreign antigen and responds to that antigen by producing antibody, it then is only capable of producing that type of
antibody. So it's like if a B lymphocyte comes up with Antigen A, okay? Ingests it, reacts to it, produces Antibody B to correspond to Antigen A. Then it can only produce Antibody A. So that six months from now, if it comes in contact with Antigen M, it can't respond to it. It would not respond to it. So when the B lymphocyte comes in contact with the foreign antigen, it then responds to it and produces an antibody specific to that antigen, and will then divide and produce memory cells. These memory cells retain the capability of responding to that antigen that it was sensitized to.

So when the B lymphocyte comes in contact with an antigen and then produces an antibody, it then becomes what we call plasma cells. Plasma cells produce antibodies. Also might have cells that develop into memory cells.

Now, for example, when you guys are vaccinated, say, for hepatitis, okay, what happens? What is the purpose of the vaccination? The purpose of the vaccination is to introduce foreign protein in, okay, kill the antigen. It can cause an infection, but it's specific to the hepatitis virus. The purpose of that is for you to develop an immune response to the hepatitis virus so that six months, a year, two years, ten years later if you come in contact with the hepatitis virus again, those memory cells are capable of responding and producing an immune response right away to prevent you from getting the infection.

So B lymphocytes come contact with an antigen. What do they do? They can produce antibodies and the plasma cells, and then they also develop memory cells, okay? So main defense against bacteria and bacterial toxins.

Cell-mediated immunity is a little different. Question?

STUDENT: So there is -- plasma cells and B lymphocytes stay the same.

PROFESSOR: Yes.

STUDENT: But B lymphocytes become plasma cells.

PROFESSOR: That's right. A plasma cell is a dedicated B lymphocyte. It's a dedicated B lymphocyte. It can only respond to one type of antigen. Now, that process of responding, producing antibody takes seven to ten days.

Cell-mediated immunity. This involves the T lymphocytes, a different classification of lymphocytes. B lymphocytes, T lymphocytes. The T lymphocytes are responsible -- they are a population of lymphocytes that attack and destroy foreign material. They are considered the common defenses against viruses, fungi, parasites, and some bacteria. And they are also the primary mechanism by which the body rejects transplanted organs. What are some of the organs that are transplanted? What is the most common one?

STUDENT: The kidney.

PROFESSOR: The kidney, okay. They do have heart
transplants. They have liver transplants. And the whole concern is that when you transplant an organ, it's a ball, it's a mass of foreign antigen. So you have to control, suppress, the body's immune system so it doesn't go wild and produce an immune response that will destroy the tissue, the organ donation tissue.

So anyway, the cell-mediated immunity is a means of eliminating abnormal cells that arise spontaneously in cell division. So it may be significant in also preventing the development of cancer. This is all the cell-mediated immunity.

The difference between a B lymphocyte and a T lymphocyte besides the name and cellular characteristics, the T lymphocyte cannot respond do a naked antigen, cannot respond to a naked antigen. It has -- the antigen has to be engulfed in the cell cytoplasm, digested, and then what we call presented on the cell membrane. By presenting on the cell membrane, what that means is there is a MHC protein, major histocompatability protein, and there's two types, Type I and Type II. Type I, MHC, is characteristic -- each of us have a MHC Type I protein. That's involved in the immune system recognition of cells and also the immune system recognition of foreign tissue, donor or whatever.

The MHC II protein is specific to certain cells, lymphocytes included. And what happens is for cell-mediated immunity to occur, foreign protein has to be ingested by the lymphocyte process complex with the MHC II protein and placed on the membrane, okay. When it's placed on the membrane, then the T lymphocyte can react to it. It cannot respond to naked antigen like the B lymphocytes.

STUDENT: Type II MHC does what?

PROFESSOR: The MHC, major histocompatibility protein Type II, that is complex with the antigen, and then that complex is pasted on the cell membrane. That process and presentation enables the T lymphocyte to become sensitized to it and to react to it. T lymphocytes do not produce antibodies.

So, in hypersensitivity, what you have is an individual who displays an increased sensitivity to an organism or its products. It usually possesses some degree of immunity as well. Many diseases are associated with the development of acquired immunity without a demonstrable hypersensitivity. Normally a person develops the immune response only against foreign antigens, not self antigens. Because the body has developed a tolerance to self antigens present in the individual cells and tissue. So what we're saying is basically the body recognizes the MHC Type I proteins, recognizes them itself and doesn't respond to them. That's what that statement is. So by recognition of self antigens, it enables the immune system to respond to nonself antigens.

Autoantibodies. In autoimmune disease what happens is a patient forms antibodies against their own cells and tissues. Basically, the antigens on the cells, in the cells or on their
tissues. These antibodies can injure or destroy the patient's cells or a tissue component.

So basically, these are broad definitions. Development of autoantibodies, what we're talking about is autoimmune disease where people develop antibodies against their own tissues. We don't always know why they do it, okay. There may be a gene that's involved in that, more than one gene. They may get an infection with a virus. It could be a low grade virus and they may not even be aware of it. They may develop antibodies or immune response to that virus. And the antigens of that virus are very similar to maybe several of their own or self antigens. As a result the immune response then gets triggers for what we call the cross reactivity.

Autoimmune disease more common in men or women? What is it? Anybody know?

STUDENT: Women.

PROFESSOR: Women, more common in women.

Of course, some of the autoimmune diseases are rheumatoid arthritis, systemic lupus erythematosus, scleroderma. In lupus, I think I mentioned this before, people develop antibodies against nuclear antigens. Depending on which organs, nuclear antigens they develop antibodies against will determine how the disease presents.

When I was teaching Survey a couple of years back one semester, I had two girls in my class, both of them had been diagnosed with lupus within the last year of taking the class. One girl actually had to miss three weeks of school because it affected her bone marrow and production of red blood cells. As a result her hemoglobin hematocrit count went down so low and platelet count went down so slow, she had to be placed on bed rest. She was placed on Prednisone to suppress the immune response. Her count came back and she came back to class. So this can be a very severe illness.

So the acquired immunity, role of lymphocytes. We have a lot of information to cover. Response to foreign antigens. Cytokines are produced by cells. They are chemical messengers and they're involved in immune response. Lymphokines are soluble proteins that are messengers that are produced by lymphocytes. As I said, they're chemical messengers. They exert their effects. They communicate with various cells of the immune system. They increase the immune response.

Interferon is another chemical messenger and that interferes with the multiplication of viruses within the cell. We'll talk about viruses, I believe, in the next chapter, Chapter 5. Viruses will invade a cell. Very often they require part of the host cell mechanisms to produce additional virus particles. Interferons interferes with the multiplication of viruses within the cell. I'm sure that interferon gets very often when a cell is infected with HPV, human papillomavirus.

Interleukin is another chemical messenger that involves
regulatory signals between the cells of the immune system. People who have kidney transplants, they can take medication that suppresses interleukin. Still maintain their immune system, immune response, but suppresses interleukin, which is involved in rejection of kidney transplants.

Tumor necrosis factor. Very interesting. What this does is it destroys foreign or abnormal cells and tumor cells. Tumor necrosis factor.

So let's see now. The lymphatic system. Precursor cells. I told you about T lymphocytes and B lymphocytes. Where do they come from? The T lymphocytes, we think are derived from the thymus. Anybody know where the thymus gland is located?

STUDENT: In the neck.

PROFESSOR: In the neck, okay. And it's largest at birth, and then as the child grows and matures, it shrinks and involutes. It shrinks and becomes a lot, lot smaller.

So the T lymphocytes are virus dependent. They're the precursor cells that migrate from the bone marrow to the thymus, and then they're the circulatory system. From the bone marrow to the precursor cells that remain within the bone marrow. The T and B cells, they need time to be activate and function effectively. There also is a small percentage of lymphocytes that are not B lymphocytes and they are not T lymphocytes, but are called NK cells. They are natural killer cells. They can destroy target cells when they come in contact with them. They do not have to become sensitized. So NK don't require sensitization. T cells, B cells to respond, do.

So before birth you have precursor cells of T and B. They migrate into the spleen, the lymph nodes, other sites, proliferate and they form mature lymphocytes. The lymphocytes, their life spans can vary. They do not remain localized, but they circulate in the bloodstream. So two-thirds of the lymphocyte are probably T lymphocytes, one-third would be B, and then the NK cells, 10 to 15 percent. Fifteen percent may be a little high, but it's a smaller percentage than the T lymphocytes and B lymphocytes. The targets, all right, for the NK cells can be virus infected cells or cancer cells.

So each programmed lymphocytes develops antigen receptors on cell membranes. This allows it to recognize and to respond to a specific antigen. The programming process allows T and B cells to be programmed to recognize and respond to a different antigen. So the response of lymphocytes to foreign antigens, what happens? The foreign antigen enters the body and triggers a chain of events. The chain of event is recognition of foreign antigen, then proliferation of lymphocytes sites that are programmed to respond to the antigen. They form a large clone of cells, and then there's destruction of foreign antigen by the responding lymphocytes. That's why you are vaccinating against hepatitis.

We'll talk about hepatitis B in another chapter, but that's
the whole purpose of the vaccine. The concern about hepatitis B is that it is an STD. It can be transmitted also by exposure to blood and blood products. Ten percent of the people who get hepatitis B become chronic, active carriers. When they become chronic, active carriers, what that means is it's a chronic infection. What's a chronic infection? The body is -- the body's defense mechanisms are unable to eliminate the virus, so it exists in low state. But what that means is there is intact virus particles in the blood in the semen. So exposure to blood or semen or cervical/vaginal secretion can cause further infections of other people. So also ten percent of those people, as I said, become chronic, active carriers. A high percentage of them go on to develop a chronic hepatitis and liver cancer. Liver cancer is not compatible for longevity, so that is the reason for the vaccine against hepatitis B.

Once you get the vaccine, then your immune system responds to and has the memory so that if it gets it exposed to the virus again, it mounts a huge response right away, overwhelms the virus and you do not get a chronic infection. So it's destruction of the foreign antigen by the responding lymphocytes.

All right. Here we go. Here is a diagram and what this diagram does is demonstrates what I've discussed or represented to you guys for the last couple of minutes. You have the antigen present. You see the macrophage. The macrophage meets the antigen and engulfs it, digests it. Then what that macrophage does is it presents itself, presents the digested antigen on the cell membrane. It's complex with the MHC II protein. It's on the cell membrane and macrophage. Then that's what we call processed antigen. The T lymphocyte meets it and responds to it, and therefore becomes an activated T lymphocyte capable of producing lymphokines. Lymphokines augment the inflammatory response. Also, it develops memory cells. The T lymphocyte, when it responds to that process antigen, interacts with the B lymphocyte. The B lymphocyte responds to the naked antigen. It responds to the naked antigen. It becomes a plasma cell capable of producing antibody and also develops into memory cells. Memory cells retain the ability to respond to the antigen.

Any questions on that? This is very significant, guys. Guarantee there's going to be some test questions on this.

So interaction of cell-mediated and humoral immunity. The antigens first have to be processed, displayed on the cell membrane of the antigen processing cell before the immune response can be set in motion. Lymphocytes interact with the antigen they are programmed to recognize. When appropriately stimulated, B lymphocytes proliferate and mature into antibody forming plasma cells. The T lymphocytes proliferate to form a diverse population of cells that regulate the immune response and generate a cell-mediated immune reaction to eliminate the
antigen. How do they do that? They do that through the production of lymphokines, chemical messengers. The initial contact with a foreign antigen is followed by a lag phase of a week or more, seven to ten days, before an immune response is demonstrated.

Another example is -- how many here have had a test for TB? All you guys have? Essentially, what is that test for TB? Anybody know the name of it? What was the name they told you it was? There's several names for it. There's not a right or wrong answer. Anybody know the name?

STUDENT: (Inaudible.)

PROFESSOR: All right. That's one. What else?

STUDENT: PPD.

PROFESSOR: PPD. Good. How many of you didn't know that? So you let people take a needle, inject you, and you don't know what it's called or what it is for? Guys, that's a survey. You have to ask these questions.

So what is a PPD? PPD is killed and it activates TB protein. What do they do? They inject it in the skin. And once they inject it into the skin, what do they look for?

STUDENT: Inflammation.

PROFESSOR: Inflammatory reaction. So if you don't -- it's not all of them. PPD, they may have to read. But don't they give you a card sometimes to describe what the reaction looks like? You designate it and you mail it in. What are they looking for?

STUDENT: Reaction.

PROFESSOR: What type of reaction? What are the characteristics? What are they looking for?

STUDENT: Red skin.

PROFESSOR: Redness, raised. So you inject that TB antigen into the skin, and you get a reaction two days later. It's like hello, what's going on? Normally the initial response takes seven to ten days. So someone who gets a TB test and they get a reaction in one or two days, what can you say?

STUDENT: You've either had a TB vaccine or you've been exposed to it.

PROFESSOR: You've been exposed already because you've developed the immune response which happens very quickly. So that's why when you have a test or a PPD or a mantoux test or whatever, if you don't have a reaction in two days then you haven't been exposed to TB because you'll have memory cells. Memory cells enable the immune response to occur very quickly.

So once the body's immune mechanisms have reacted to a foreign antigen, some lymphoid cells retain the memory of the antigen that induces sensitization. That memory is passed on to succeeding generations. So you have been vaccinated against hepatitis; you have the hepatitis B vaccine. Twenty years from now, you'll still have a population of memory cells that are capable of responding to the hepatitis B. Later on, contact
with the same antigen, therefore, provokes a stronger and faster proliferation of the sensitized lymphocytes or antibody-forming plasma cells.

Now, interesting. T cells. What types of T cells are there? There's the regulator T cells we call the helper T cells or also known as CD4 cells. They regulate the immune system by establishing a balance between promoting and inhibiting the immune response. You have to understand something. The immune response is a balance, okay. If the immune system is too aggressive, it may develop an immune response to host or cell antigens. So it can't be too aggressive. It has to be a balance. If it's not aggressive enough, then the host may become sick because it doesn't fight off foreign antigens. So it is a balance.

The effector T cells are involved in delayed hypersensitivity reactions. Significant here. The AIDS virus attacks and destroys the helper T lymphocyte. So therefore, when -- we'll talk more about AIDS in another chapter, but the AIDS virus attacks the helper T lymphocytes. There is a receptor on the helper T lymphocyte that the AIDS virus can bind to. When it binds to it, the cell opens up. The AIDS virus enters the cell, takes over the host cell mechanisms and is able to produce other viruses that then break out of the cell and infect other cells.

The helper T cell. Therefore, as time goes on, the helper T cell goes down. The CD4 count goes down. As a result the patient, the person, has a compromised immunity. The significance of a compromised immunity is that the AIDS patients will get infections.

Does anybody know the name of these type of -- the general category of infections that these people get or how we categorize them? Anybody want to take a guess?

STUDENT: (Inaudible.)

PROFESSOR: Right. They are opportunistic infections. These are infections that require a special opportunity to cause the disease. What's the opportunity? A reduced helper T cell count, a reduced CD4 count. We'll talk more about that later.

So classification and function of the immune system cells.

Here is a little chart that helps a lot. As far as antigen processing, macrophages are involved in that, B lymphocytes, also dendritic cells. We didn't mention them. They're not that significant. What do they do? They process the antigen and present it to lymphocytes. It's a generalized chart.

Helper T cells, what do they do? They regulate the immune response, they produce cytokines that are involved in the immune system activity.

Cytotoxic T cells. These are the CD8 cells, okay, and they produce -- or that promote a cytotoxic immune response. They produce cytokines that can destroy abnormal cells that display antigen fragments combined with the MHC Class I antigens.
Let's see. Cell type. The T cells, CD4 also are involved also in delayed hypersensitivity. And what do they do? They respond to antigen processing cells, presenting foreign antigens. Combined with the MHC Class II, they produce cytokines. And they stimulate cytotoxic T cells and NK cells.

The NK cells, what do they do? They can destroy antigens with no previous exposure. They are the lowest percentage of the lymphocytes.

All right. Plasma cells. Plasma cells are dedicated B lymphocytes that produce antibodies. They've been lymphocytes that have been exposed to antigens.

So immune response genes. We're not going to go into this too much, but there are immune response genes that are closely related to the HLA complex and chromosome 6. This is discussed in the previous chapter. You guys don't have to know that. I told you.

And the immune response genes may be involved in the regulation of T and B cell proliferation; therefore, they can influence the resistance to infection and tumors. Also, they may be involved in the likelihood of developing an autoimmune disease.

Antibody types. GMADE. Easy to remember, G and then the word made, M-A-D-E. Immunoglobulin G. Immunoglobulin, another name for antibody. IgG is basically Immunoglobulin G or an antibody type G. And the same for IgA, IgM, IgE, IgD. The two most significant ones are IgG and IgM. IgM is produced -- the greatest percentage is produced with the initial response to an antigen. So when you get exposed to a foreign antigen, you measure IgM levels, they are going to be high about seven to ten days after the exposure. You're going to peak high, they start to fall, and then IgG levels start to rise. IgG is the most significant of the antibodies as far as mounting an immune response.

Someone comes to the emergency room, they have got an infection. They have got a bacteria. You have got IgM, IgG levels. If they have high IgG levels, low IgM, that means it's a chronic infection. If they have high IgM levels and low IgG, it means an initial infection. It's just started.

So here is a diagram of an antibody. Now these are the antibodies that are produced by plasma cells, and they can react only with specific antigen that induces its formation. So if you look, you can see that the antibody is composed of four chains: Two what we call heavy chains and two light chains. The antigen binding site is up at the top, okay. It's up at the top, and it's specific for an antigen. The bottom part of the antibody, sometimes we call the tail, and it's comprised just of the heavy chain. When antigen is bound by antibody, in other words, when antibody meets the foreign antigen specific for it and it binds to it, it fits lock and key. It fits lock and key. And then the heavy chains, the tail of the antibody flails out.
When it flails out, that is the change in shape in morphology.
And what did I say gets activated when the antibody changes
shape? Complement. Complement is another way of enhancing the
body's immune response. Complement is a waterfall or cascading
effect. The initial fragment of complement then activates
fragment B. Fragment B, when it's activated, activates fragment
C. Complement is a protein in the blood; it's produced by the
liver.

IgG is a smaller antibody. Principal antibody molecule in
response to a majority of infections. IgM is a larger antibody
very efficient in combining and dealing with fungi. IgE, high
levels of IgE are found in people who have allergies.
Otherwise, it's a very low level immunoglobulin in the blood.
IgA more related to the GI tract. Produced by
antibody-forming cells located in respiratory and GI tract.
When you're breathing air, virus and bacteria can be in the air.
You breathe them in and they come into your system. How come
they don't cause an infection a lot of the times? Because of
the presence of IgA. Same thing with the GI tract. You're
taking food in; it's not sterilized. And you don't get an
infection from it because why? Probably because of the IgA
that's available, the immune response cells present in the GI
tract.

Hypersensitivity reactions, they characterize them here as
Type I, Type II, and Type III. Type I is anaphylactic,
immediate. Cytotoxic and then the immune complex. We'll go
over all three.

Type I, anaphylactic immediate. What happens? There is a
sensitizing antigen that is present, and it circulates
throughout the body, and then it triggers a widespread mediated
release from the immunoglobulin coated mast cells and basophils.
What happens there with the widespread of the release of the
chemical, what happens is you can get an anaphylactic reaction.
An anaphylactic reaction can be a fall in blood pressure,
developmental hives and respiratory distress. Prompt treatment
is required. They give you epinephrine and other agents.

I have to tell you, as a small digression, I did develop an
anaphylactic reaction a couple of years ago. What happens is my
wife and I were moving. We were moving and I said to her at the
end of the day, I said, you know, it's really weird. I said I
must have bumped my thumb or something because it really got
swollen. I don't remember banging it like that that it would be
so swollen.

And the next day there was a pustule there, and I thought
that's really weird. I didn't think anything more about. And
the move was successful and everything.

And then like two months later, I was out walking my dog
and I just had a pair of sandals on. I was walking in the
grass, and I came back in, and I had this itching area on my
foot and it was red and swollen. I thought, wow, they must be
mosquito bites. I noticed the next day I had another small pustule.

A month later, I was out the dogs again and same thing. I came back in, I had a couple pustules, a couple of raised areas that were red on my feet. It's kind of funny because I had a little bit of tingling in my foot and in my lower leg.

The next time, about a month or so later again, I was out with the darn dogs and I saw, you know, a couple of red ants. I walked by a hill and, you know, I had gotten a couple of red ants. With that, I started have tingling in my foot. My foot started to swell. It moved all the way up my leg. I started to have a redness to my leg and my wife -- it was like 7:30 in the morning. My wife was just getting up. I said, listen, I have to go to the emergency room. I feel like my tongue is starting to swell. I really can't take the time for you to get addressed. I said meet me at the emergency room. So I drove myself to the emergency room. It was right at the change of shift. So I come into the emergency room, there is no one at the front desk. There is no one at the triage center. The way these emergency rooms are set up, there's a big wall. So I'm banging on the wall for someone to come because I can't get through the doors. The doors are locked. Someone comes running. I go, listen, I'm a physician, I'm having an anaphylactic reaction. As I'm talking, my tongue is swelling. They can hardly understand me. So they take me right back, start an IV, gave me epinephrine. I was wheezing. I don't have asthma, but I developed wheezing. I was going into respiratory distress. So they gave me some bronchodilators, and it took really several hours for these symptoms to subside. So anaphylactic reaction can occur at any time. Basically, you know, I was developing antigens -- antibodies against the antigens from these darn red ants. It really was pretty severe.

STUDENT: How in the world do you live in Florida, though?

PROFESSOR: What?

STUDENT: How in the world do you live in Florida with so many red ants?

PROFESSOR: What is interesting is that I have -- another digression. People have allergies, right? If they have allergies, what do they do? They go to their allergist and they receive shots to try to reduce their allergic response or sensitivity, right? What are those shots? Those shots are dilute amounts of antigens that they are sensitive to. By injecting them with that, the hope is that you're exposing their immune system to these foreign antigens and they will develop a normal immune response instead of the hypersensitivity.

STUDENT: Do you still have problems with the red ants?

PROFESSOR: It's happened. Because I still have -- like honestly, I was fishing this weekend, you know, the beach and surf. My wife goes, you know what, your toe looks swollen.

I said, oh, it's nothing. But the next day, there was a
pustule there. I fished at night and I know it was a red bite -- it was a red ant bite.

But I've had several since then. The first couple of times, I was really concerned about it because -- I have a EpiPen; I carry it with me. I didn't have an anaphylactic reaction. So I think probably ever since that anaphylactic reaction was treated in the emergency room, I think like maybe once or twice a year, I may have been exposed to a red ant bite. I gradually developed -- my immune system has developed a tolerance for it so I don't have the hypersensitivity reaction. So anyway, enough digression. We'll move on.

Hypersensitivity reactions. Antihistamine drugs often relieve many of the allergic symptoms. Histamine is one of the mediators released from the IgE-coated cells. Of course, histamine being a release, you have increased swelling because of the increased permeability in the capillaries. Later contact with the same antigen triggers release of the mediators, histamine, and also related clinical manifestations such as a localized response. You have hay fever, food allergy to peanuts. I mean, you know, peanut allergies can be very severe. Why don't they serve peanuts on planes anymore? The risk is -- someone with a peanut allergy can have a problem. Systemic response: bee sting, red ants, penicillin allergy.

An atopic person is described as an allergy-prone individual. Eczema can be considered an allergy. Allergen is a sensitizing antigen, something someone responds to. There's certain antigens that are sensitizing. For people who are atopic, who have the potential, greater potential for developing allergies to dust, cat dander, these are all examples of sensitizing antigens.

Cytotoxic, a Type II hypersensitivity reaction, that's where the antibody combines. It binds the cell tissue or antigen resulting in a complement-mediated lysis of cells. Lysis means what? Destruction. Breaks down the cell wall. So that's what complement does. Complement is involved -- I told you augments the response and it can produce lysis of cells or also a bacteria, bacterial membranes.

So an example of this would be an autoimmune hemolytic disease where people develop antibodies against their red blood cells or on their red blood cells. You have lysis of the cell membrane; therefore, the red blood cell count goes down. Lysis, I told you, is destruction. Hemo for blood. So hemolytic destruction of red blood cells. Transfusion reactions, RH hemolytic disease. Sometimes -- let me just see one thing here. Okay, good.

So I want to discuss RH hemolytic disease. RH factor, probably about ten percent of the population is RH negative. RH negative means that you do not have the RH factor antigen on your red blood cells. Of course, the major blood type antigens are A, B, and O, and also RH. It's a separate category. And
what's the concern about the RH factor?

STUDENT: -- additional proteins that are on the red blood cells, and so -- for example, if you're a blood donor, you need to make sure that -- if you have the proteins, I don't believe you can donate.

PROFESSOR: Right. Those are the major antigens. But for the RH factor or being RH negative, especially for women?

STUDENT: If you're pregnant and you have RH negative blood, and your baby doesn't --

PROFESSOR: Right, that's exactly right. For women who are RH negative, what that means is they don't have the RH factor on their red blood cells. If they get pregnant and the father of the child is RH positive, they run the risk of having a baby that is RH positive. So if the baby is RH positive, and they are RH negative, at the time of delivery, whether it's a vaginal delivery or a cesarean section, the mother will be exposed to the fetal blood through the placenta or whatever. As a result she will be exposed to the RH factor and develop antibodies to the RH factor. She then will become what we call sensitized. Her plasma and her B lymphocytes will become sensitized to the RH factor, produce antibodies, and also produce memory cells. So it's a first pregnancy. She has a baby that's RH positive. She takes it home, everything is going great. She is happy, loving being a mother, loving taking care of the child. Unbeknownst to her, her immune system is developing antibodies to RH factor.

Two years later, she gets pregnant again. Maybe the baby is an RH negative. Maybe the blood type is RH negative, and so there is no RH factor present. Great. But if the baby is RH positive, then there is the chance that some of those RH negative -- I'm sorry, RH positive antibodies will cross the placenta. If they cross the placenta, what will they do? What will they bind to? The baby's blood cells. Red blood cells basically will bond to the RH antigen on the red blood cells. When antibody binds to antigen, what happens? Complement gets activated. What does complement do?

STUDENT: Destroys the cell.

PROFESSOR: Destroys the cell wall. So all of a sudden, the baby then can develop a hemolytic anemia. If it's not -- second pregnancy, all right. If it's the first pregnancy after sensitization, you can't quantitate how much of a hemolytic disease occurs. Maybe not much. So she delivers her second baby, and the baby is going to be born with a lower red blood cell count and is going to be jaundiced. Jaundice means what?

STUDENT: Yellow.

PROFESSOR: They are yellow. Why are they yellow? Why does the skin have the appearance of yellow?

STUDENT: (Inaudible.)

PROFESSOR: Because of increased levels of?

STUDENT: Bilirubin.
Where does the bilirubin come from? Break down of hemoglobin.

So gets pregnant one more time. She's already been exposed to the RH factor twice. Those memory cells are really kicking into gear because they had another pregnancy and got exposed to it. She gets pregnant again. Higher levels of IgG against the RH factor, more antibodies cross the placenta at an earlier stage of development. The baby develops a more severe hemolytic disease. And as a result, if the pregnancy goes to term, good chance the baby will not be viable. The baby may die ahead of time, so you have to have an earlier delivery. There's ways to monitor the baby's status in regards to the RH factor.

Now, we don't really have many situations nowadays, year 2012, where pregnancies have to be delivered early because of RH factor disease. Why do we not have that? We still have RH factor babies, RH negative women giving birth to RH positive babies. Why don't we have that problem? We given injections. Injection of what?

STUDENT: Immunosuppressant.

PROFESSOR: No, not immunosuppressant. Anybody? We give them an injection of what they market as Rogan. Rogan is concentrated immunoglobulin specifically against the RH factor. So any woman who has an obstetrical event, and if she is RH negative needs to get a shot of Rogan, whether it be a miscarriage, whether it be a voluntary abortion, whether it be a pregnancy in a tube, second trimester miscarriage or term delivery. No matter what, she should get a shot of Rogan. What does Rogan do? Rogan is antibody directed against the RH antigen, okay. Enters the bloodstream, and what does it do? It binds to the RH antigen that is present in the mother's blood. When it binds to it, it neutralizes the antigen; therefore, it's covered. The immune system is not going to be able to recognize that RH antigen as foreign. If it doesn't recognize it's foreign, it doesn't develop a sensitivity to it. As a result, women can RH negative and have several pregnancies without complication.

Any questions on that? Okay.

So Type III, immune complex. The antigen-antibody immune complexes are deposited in tissues and they activate complement. The polymorphonuclear leukocytes are attracted to the site causing tissue damage. Example of this, the immune complex disease is lupus. Lupus, one of the problems with lupus is that they can develop antibodies to the basement membrane of some of the cells. They also have circulating antigen antibody complexes. If they do, if it's in the blood stream, what organ is responsible for filtering the blood? The kidney. So the kidney then filters the blood. These immune complexes, antigen-antibody complexes, are deposited in the kidney of the basement membrane. And when antibody binds the antigen, what happens? What gets activated? Complement. Complement then
increases the inflammatory response. As a result these people can develop glomerulonephritis.

Type IV, delayed hypersensitivity or cell-mediated hypersensitivity. That is where T lymphocytes are sensitized and they can become activated on a second contact with the same antigen. Lymphokines induce inflammation and activate macrophages. Example would be considered TB, fungal and parasitic infections, contact dermatitis.

So suppression of the immune response, why would you do that? You want to prevent the undesirable effects. So suppression can be directed against the individual's own cells or the tissue components leading to autoimmune diseases. Also, you may want to do it because you want to prevent rejection of transplanted organs or you want to do it to prevent the RH hemolytic disease in newborn infants, which we talked about. So these are all reasons for suppression of the immune response.

So methods of immune suppression. Radiation is one. Immunosuppressive drugs that impede cell division or cell function. Adrenal corticosteroids. Prednisone was mentioned. That is the most common one you can take by mouth. How does Prednisone work? It suppresses the inflammatory reaction. It impairs phagocytosis. It also inhibits protein synthesis.

Occasionally in my practice, we had patients we had to operate on who were -- who had autoimmune disease. Some of them on fairly high levels of Prednisone to suppress their autoimmune disease. As a result, when we did surgery, we had take extra special care and use special types of suture material and put in special deep types of sutures to hold the incision together because the normal healing process was going to be prolonged because the Prednisone that they were on inhibits protein synthesis. Of course, protein synthesis is necessary for healing.

Gamma globulin preparations which contain potent antibodies can prevent the body from responding to corresponding antigen. What are they talking about here? They are talking about the illustration of the RH, the hemolytic disease in the newborn. Giving a women a shot of Rogan, it's a concentrated preparation of potent antibodies that, therefore, will prevent the immune system from responding to the corresponding foreign antigen.

Autoimmune diseases. For pathogenesis, what happens? You have alteration of the patient's own self antigens maybe. So infection may alter the antigens of the host, the self antigens. Therefore, they become antigenic and cause an immune response. Or you have development of cross-reacting antibodies against foreign antigens. So what happens is patients develop antibodies, even if it's a virus or bacteria, and then they cross-react with some of the host antigens. Or you have defective regulation, okay, of the immune response by the regulator T lymphocytes. The regulator T lymphocyte, maybe it augments or increases the immune response so that the immune
response is directed against host antigens. Treatment is going to be basically corticosteroids, sometimes cytotoxic drugs.

Let's see. Examples of autoimmune disease. We have lupus, rheumatic fever, inflammation in the heart and joints. Of course, rheumatic fever is caused by an infection. It's a sequela or consequence of an infection by a specific bacteria. What bacteria are we talking about with rheumatic fever? I think I heard it. What is it?

STUDENT: (Inaudible.)

PROFESSOR: Step. Strep infection. So strep infections to the throat, very serious. We'll talk about them more in the next chapter. If they are not treated properly, patients can go on to develop rheumatic fever. And with rheumatic fever, they have inflammation of the heart, the joints, kidney disease. It also can affect the brain. The inflammation of the heart can require cardiac surgery eventually because it affects the valves.

So autoimmune diseases, anemia, low white count, thrombocytopenia refers to low platelets. I told you about that one patient of mine who had lupus and who, as a result, had to miss class because her bone marrow was depressed. Thyroiditis, inflammation of the thyroid. Also, diffuse toxic goiter, which results in hyperthyroidism.

(End of class.)

CERTIFICATE OF TRANSCRIPTION

I hereby certify that the foregoing transcription is a verbatim account of the recorded proceedings.

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