Immune System 101

You can view this presentation at: youtu.be/SlyUmBhmTvA

Dr. Michael Levy: [00:00:04] Well, hello everyone. My name is Michael Levy. I'm an associate professor at Harvard Medical School and a neurologist at Massachusetts General Hospital. And I am going to give you an overview of the immune system as it relates to neuro-immunological diseases like NMO, transverse myelitis, and MOG antibody disease. This is real basic, this is a slide set that I adapted from the internet. This is just kind of basic immunology 101 type of information.

[00:00:35] First thing to recognize and understand about the immune system is that it's divided into two parts. There's an innate immune system. That's the part I'm going to talk about first which is the acute reactive part. This is not the thoughtful part of your immune system that considers, “Is this a cancer? Is this a self-tissue?” No. The innate immune system is just I see something bad and I'm going to react to it. And you have to have a very strong innate immune system. There's not a lot that can go wrong with it or else you're going to have really, really bad outcome. So, we've evolved over many tens of thousands of years to have a very good innate immune system. So that's the part I'm going to talk about first.

[00:01:24] Okay. Your innate immune system has physical barriers like skin and mucosa that keeps out organisms. It's not very effective at keeping out organisms. You're exposed to bugs everywhere, germs everywhere. Even if you isolate from other people, you just have it in the air. So, you have a second line of defense in case those organisms try to invade. And that's made up of several different types of cells that are bundled into a group called phagocytes. Phagocytes just means they engulf stuff. Bacteria invades, this cell just surrounds it and swallows it and then breaks it down. There are many different types of those cells. The most numerous are the neutrophils. You'll find that in your white blood cell differential count. You'll see neutrophils are by far the largest number of white blood cells in your bloodstream. They don't live very long, just a few hours at a time and they're just constantly working to get rid of all these bugs. If you lose your neutrophils, you're extremely vulnerable to any sort of infection that comes along at any time.

[00:02:36] Then you have these specialized cells called natural killer cells, and what they're really designed to do is to kill cells that may be infected or cancerous or something else. So, they're not exactly foreign invaders but they need to be destroyed and your natural killer cells will do that.

[00:02:58] Then the other parts of your second line of defense of your innate immune system are not cells, they're chemicals. And many of those chemicals are bundled into a group called cytokines. These are communications between immune cells. So, one immune cell might make a certain type of cytokine that alerts the immune system to be ready. And some other immune cells might secrete a cytokine to make the immune system calm down. So, these are chemicals that alert or suppress the immune system.

[00:03:32] And then you have the complement system. This is a set of proteins that basically are designed to label a cell like a bacterial cell or something like that. And then there's a part of the complement system that blows holes in these organisms. So, you have to have a functioning complement system or else you're vulnerable to many of these infections.

[00:03:57] The innate immune system, innate immune cells, and then I'll talk about the adaptive immune cells, all of your white blood cells come from the bone marrow and then into the blood. Your thoughtful immune system, the adaptive immune system which I'll talk about later has to get trained first and then it's allowed to circulate. But the other ones, the neutrophils, the other phagocytes, they're all just dumped into the circulation and then they get around the body and do their thing. So, when I say that they engulf bacteria, I literally mean they literally will surround a bug and then just gobble it up and then break it down. That's how these phagocytes work. And they're very, very effective at what they do.

[00:04:47] Now, a lot of people have allergies. That's a whole different part of your immune system. That's mediated by these cells called basophils. I have horrible allergies and I take antihistamines which is released by these cells that cause a whole bunch of allergic symptoms, but they're really not linked to the other parts of your immune system that are involved in autoimmune disease. That's why antihistamines don't work for autoimmunity. Just wanted to put that in there. It's part of the innate immune response. These basophils are reacting to things like pollen and causing symptoms but they're not harmful.

[00:05:20] Then you have these other interesting cells called eosinophils. I bring this up because some of my patients have zero in their white blood cell count and that's okay. We've kind of evolved in this clean germ-free society to not really need them. They're useful if you're infected with worms. But for most Americans you can get away with not even having them in your circulation anymore.

[00:05:45] And then NK cells as I mentioned are a little bit on the boundary. They don't kill foreign things. They kill things in your own body that you want to destroy specifically like unhealthy or cancerous cells. And here's an example of a cytokine, one called interferon which is made by an infected cell. So, if you have a cell that's infected, it's going to make these cytokines, it's going to alert the rest of the immune system, "Hey, come kill me and be on alert, there's a virus going around." So that's what is so important about these chemicals.

[00:06:19] And then the complement system is the one that tags different organisms and then also blows holes in them. Literally these complement proteins can stick into a membrane and then form a hole and then the contents of that organism just get leaked out. Pretty amazing. It's like a grenade on the surface of a bacteria.

[00:06:47] Okay. That's the innate immune system. And the second half of this presentation I'll talk about the adaptive immune system. This is the thoughtful, careful part. This is mediated by two main cells T cells and B cells, and then there are a whole bunch of other cells that enable them called antigen-presenting cells.

[00:07:08] There are four specific aspects of adaptive immunity. First is that they're very specific. One T cell reacts to one thing and one B cell reacts to one thing. But you have billions of T cells that react to everything that you need to react to. They're also very versatile. They can recognize many, many different types of organisms and they can learn and then they can unlearn. So, it's a very versatile system. And it also maintains a memory. Once you're infected with something these cells remember and they hang around in case you're infected again.

[00:07:48] And it's really important for these cells to undergo tolerance. Tolerance is where they learn that if they react to something in your body they need to be destroyed or re-educated. That's tolerance. If you're intolerant of your own body, then your own immune system is going to attack it. That's the basis of autoimmunity.

[00:08:09] Now, how do these cells interact with the rest of the world where they don't engulf stuff? That's how the innate immune system works. The adaptive immune system has receptors like feelers, and they go around and things that fit in their receptors, things that fit in their hand can signal to them, can activate them. They can communicate with every cell in your body, and they can communicate with other enablers like antigen-presenting cells that either activate them or tell them to relax.

[00:08:38] And again you have two major cell types, T cells and B cells. On the surface of B cells, you have antibodies called B cell receptors that fit proteins in their cleft here and then on T cells you have T cell receptors that are much more complex than an antibody that also bind certain proteins.

[00:09:01] Now, you hear about this all the time. You heard about this when you're developing a COVID reaction of the vaccine. Antibodies are made when a B cell gets activated. When a B cell receptor which looks like an antibody sticks to its target and gets activated it will then undergo a process of differentiation to produce more and more and more antibodies. It's like an activation system. And then it'll go hide out in the bone marrow and just make antibodies for the next 10 or 15 years and these antibodies stick to their target. You can think of them like bullets and a gun. These bullets will stick to their target and then can do many things.

[00:09:41] NK cells for example that encounter an antibody stuck to something will just take the antibody up with whatever stuck to it and process it. And antibodies stick to all kinds of things and trigger complement formation for example. So, whatever an antibody sticks to, it alerts the immune system, oh, oh, we've got a problem here and then the immune system responds to it.

[00:10:05] Now, you make different types of antibodies and they come in phases. So, the first type of antibody you make is called an IGM. And that's made very early and it's very effective. And then later on you make IGGs that persist for a much longer period of time and that maintains your memory. In case the bacteria comes back you're able to fight it off later.

[00:10:28] T cells don't use antibodies; they use T cell receptors. And I said these are a little bit more complicated than just antibodies. Antibodies can just stick to their protein. But a T cell receptor doesn't just stick to a protein. That protein has to be presented to it through a secret handshake with another cell. Okay. So, the T cell and the other cell they communicate together by touching each other and then that protein is in the cleft in between them. And so, it's not just a secret handshake. It's like there's a message that's being delivered from one cell to the T cell and that tells it what to do. And the type of handshake that it undergoes has some properties about whether it's going to be activated or suppressed. And so, this is a very, very complicated system. But these T cells interact with every cell in your body. And they can go around, and they can introduce themselves to a neuron, brain cells, "Everything okay over here?" And then depending on the type of secret handshake it gets back it'll know if it's infected or if it's doing just fine. So those T cells are very, very complicated types of cells. We don't even know everything about them.

[00:11:45] But we do know that in many diseases like neuromyelitis optica and MOG antibody disease there is a problem with the T cells and that they recognize something that's self and where they should have been educated not to do that or re-educated if they made the mistake to not attack. But there's something that goes wrong in autoimmunity, and it allows these T cells to persist in the circulation even though they're targeting a self-protein.

[00:12:17] So over the period of an immune response, this is typically to an infection, you have different timing of cells and immune processes. I told you that the innate immune response reacts first because it's just going to react no matter what. And that's made up by neutrophils and these natural killer cells. And then you can see they react right away. And then as their reaction starts to wane, you have the rest of the immune system that comes on board. You have the T cells and B cells that are thinking, oh, do I really want to kill this bacteria? Where did it come from? Do I have a memory against it? If I don't, I'm going to make antibodies, so I'll have a memory to it from now on. And so, all of that takes place over the next few days and weeks.

[00:13:02] So there's a timing to an immune response. And we could see the activation patterns here with a long-lived antibody that persists for a long time that maintains memory all the way down to the very earliest reaction by the innate immune response.

[00:13:19] So that's it, folks. In 15 minutes, you've got the basics of all of immunology. Obviously, there's a lot more to it when things go wrong, but that's basically how the immune system works.

