# Immune System, Part 2: Crash Course A&P #46Transcript

What’s true in World of Warcraft is also true in your immune system: To defeat your enemy, you have to know your enemy. Uncover its weaknesses. Learn how to see it, before it sees you.

We’ve already talked about how your innate defense system keeps out, or quietly neutralizes, pathogens without much too much fuss. But sooner or later, a threat’s gonna come along that’s stronger than what the first-responders can handle. That’s when it’s time for the adaptive, or acquired immune system to step in.

While your innate system takes its zero-tolerance policy very seriously, and tries to toast any foreign microbe that it encounters, your adaptive system does things differently. It has to be expressly introduced to a specific pathogen, and recognize it as a threat, before it will attack.

As its name suggests, you’re not born with a working adaptive immune system -- it’s slow to act, in part because it takes time for it to shake hands with so many pathogens and get to know them. These introductions may be organic -- like touching a dirty faucet in the bathroom or walking into a sneeze cloud. Or they may be premeditated, which is why vaccination is pretty much the greatest thing to happen to medicine ever.

But once it’s been introduced to a potential threat, your adaptive defenses never forget it. And this ability to remember specific pathogens is one of the key differences between the adaptive and innate defenses.

Another main difference is that adaptive immunity is systemic -- rather than being restricted to a particular infection in, say, a sinus or a sliced finger, your adaptive system can fight throughout your whole body at once. And it does this by deploying one or both of its separate, but cooperating, defenses-- your humoral immunity and your cellular defenses.

Your humoral immunity -- which you might not have heard of before -- works by dispatching important proteins that I’m sure you have heard of: antibodies. They’re made by special white blood cells, and they patrol the body’s “humors” or fluids like blood and lymph, where they combat viruses and bacteria moving around the interstitial space between your cells. Much of what you know, or have heard about, or think of, when your immune system comes up actually has to do with your humoral immunity. It’s why, if you had mumps as a kid, you probably don’t have to worry about getting it again for the rest of your life. It’s also why doctors and nurses and patients who have been infected with the ebola virus-- a disease once thought to be incurable -- have lived to tell about it. And it’s why vaccinations work.

Whether you’re protecting yourself from infections or playing an MMO, one of the first steps in any good defensive strategy is to be able to tell your friend from your foe. And in the case of your immune system, that means being able to identify antigens. An antigen could be an invader from the outside world, like a bacterium, virus, or fungus. Or it could be a toxin or a diseased cell within your own body. But in any case, antigens are large signalling molecules not normally found in the body, and they act as flags that get the adaptive immune system riled up.

So let’s say a flu virus gets inside of you, and it’s floating around trying to find a good host cell to start multiplying inside of. Before it finds that cell, hopefully it will be paid a visit by one of the stars of your humoral response -- a B lymphocyte. Like all blood cells, these guys originate in your bone marrow. But unlike other white blood cells, they also mature in the bone marrow too. And as a B cell matures, it develops the ability to determine friend from foe, developing both immunocompetence -- or how to recognize and bind to a particular antigen -- as well as self-tolerance, or knowing how to NOT attack your body’s own cells.

Once it’s fully mature, a B lymphocyte displays at least 10,000 special protein receptors on its surface -- these are its membrane-bound antibodies. All B lymphocytes have them, but the cool thing is, every individual lymphocyte has its own unique antibodies, each of which is ready to identify and bind to a particular kind of antigen. That means that, with all of your B lymphocytes together, it’s like having 2 billion keys on your immune system’s keychain, each of which can only open one door. So, part of your immune system’s strategy is just to win with overwhelming odds: The more unique antibodies your lymphocytes have, the more likely it is that one will eventually find, bind to, and mark a particular antigen.

Once they’ve matured, B cells colonize or “seed” your secondary lymphoid organs, like your lymph nodes, and start roaming around in your blood and lymph. At this point they’re still naive and untested, and they won’t truly be activated until they meet their perfect enemy match.

Which brings us back to the flu virus. When the right B cell finally bumps into an antigen it has antibodies for -- usually in a lymph node or in the spleen -- and recognizes it, it binds to it. This summons the full power of the humoral immune response, and the cell basically goes into berserker mode. Once activated, the B cell starts cloning itself like crazy, quickly producing an army of similar cells, all with the instructions for the exact same antibodies that are designed to fight that one particular antigen. Most of these clones become active fighters, or effector cells. But a few become long-lived memory cells that preserve the genetic code for that specific, successful antibody. This ensures that, if and when the antigen returns, there will be a prepared secondary immune response that’s both stronger and faster than the first.

This is key to why vaccinations are so brilliant and important, which I’ll come back to in a minute. But while the memory cells are just there to hang back and record things, the effector, or plasma cells, are packed with extra amounts of rough endoplasmic reticulum, which acts as an antibody factory. These cells can mass-produce the same antibodies over and over for that particular invader, spitting them out into the humor at a rate of around 2,000 antibodies per second for four or five days until they die.

And the antibodies they make work the same way that the membrane-bound ones do; they’re just free-floating. So they ride the tides of blood and lymph, binding to all the antigens they can find, and marking them for death.

Now, antibodies can’t really do the killing themselves, but they do have a few moves that could make it hard for intruders to take hold. One of their most effective and common strategies is neutralization, where antibodies physically block the binding sites on viruses or bacterial toxins, so they can’t hook up to your tissues. And because antibodies have more than one binding site, they can bind to multiple antigens at the same time, in a process called agglutination. The resulting clumps can’t get around easily, which makes it easier for macrophages to come and gobble them up.

And not only that, but while all this is going on, antibodies are also ringing a chemical dinner bell, calling in phagocytes from the innate immune system, and special lymphocytes from the adaptive system, to destroy these messy little antigen-antibody clumps.

So, the point of all this in the short term is to keep you healthy. But in the long term, this process also adds to your overall immunity. The humoral response allows your body to achieve immunity by encountering pathogens either randomly or on purpose. Active humoral immunity is what we were just talking about -- it’s when B cells bump into antigens and start cranking out antibodies. This can occur naturally, like when you catch the flu or get chickenpox or pick up some nasty bacterial infection, or it can happen artificially -- particularly through vaccination.

Most vaccines are made of a dead or extremely weakened pathogen. And they work on the premise that, because a secondary immune response is more intense than a primary response, by introducing a pathogen into your body, you’re priming it to fight hard and fast should that antigen show up again.

In the case of typically non-fatal infections, like the common flu, this immunity should at least spare you from some of the most severe symptoms. But in the case of more serious diseases, like polio, smallpox, measles, and whooping cough, vaccinations can be truly life-saving.

Now, some antigens -- like those for mumps or measles -- don’t really change much over time, so a few immunizations will leave you set for life. But others, like influenza, are constantly evolving and changing their surface antigens. So immunity to last year’s flu probably doesn’t work against this year’s flu.

Still, acquired immunity doesn’t have to be active. Babies, for example, naturally obtain passive humoral immunity while still in the womb. They receive readymade antibodies from their mothers through the placenta, and later on through breast milk. And that works pretty well for a few months, but the protection is temporary, because passively obtained antibodies don’t live long in their new body. And they can’t produce effector cells or memory cells, so a baby’s own system won’t remember an antigen if it gets infected again.

You can also acquire this kind of temporary passive immunity artificially, by receiving exogenous antibodies from the plasma of an immune donor. This is what recently saved some doctors and nurses who had contracted the ebola virus from infected patients. A serum was made from the blood plasma of other medical workers who had been infected, and survived. The antibodies helped defend the patients from the virus before their own active immunity could identify that particular antigen and start creating their own antibodies. It’s not the same as a vaccine, which immediately engages your B cells, but it can buy a patient some crucial, life-saving time against an infection that would otherwise quickly kill.

But B cells and antibodies are only part of the immunity equation. There are plenty of pathogens that quickly worm their way right inside your cells, where they’re safer from the humoral response and free to multiply as much as they’d like. Luckily, your immune system has yet another game plan and new set of players ready to fight that final battle with cell to cell combat. Make sure you catch our final episode next week and learn all about this epic battle royale.

But as for today, in our second-to-last episode, you learned how the adaptive immune system’s humoral response guards your extracellular terrain against pathogens. We looked at how B cells mature, identify antigens, and make antibodies, and how antibodies swarm pathogens and mark them for death. We also talked about active and passive humoral immunity, and how vaccines work.

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