So we're going to start by talking about this story. This is a famous moment in the treatment of infectious diseases and the prevention of infectious diseases. This is the first human vaccination, at least the first purposeful human vaccination where the famous British doctor, Edward Jenner, is vaccinating a child for the prevention of smallpox, a devastating disease at that time and for centuries before that time which would wipe out literally millions of people due to its very aggressive nature. Not everybody who died or was infected by smallpox would die from it, but a lot of people did. And it was an important infectious agent throughout the world, actually brought, for example, by colonizing troops in Mexico and wiped out Native peoples there, used purposely as a biological agent in warfare. Smallpox was used by the British to suppress Native Americans in warfare. In fact, the town of Amherst, Massachusetts was named after Jeffrey Amherst, I think, who was an officer in the British Army whom ordered that smallpox infected blankets, or blankets from smallpox infected individuals be sent as a gift to Indian tribes in the region so as to spread the disease to them thereby limiting their ability to fight in an oncoming war. So this is an important agent, and this is an important moment in the treatment and prevention of this particular agent. So I want to tell you this story because it illustrates some important points about immunology. Edward Jenner, who as you see, was doing this work in the late 1700s, made two important observations. One was that milkmaids, people who got milk from cows, milkmaids had smooth skin. And that was unusual in the time, because most people had been infected by this agent smallpox, developed the smallpox disease which led to a pocking of their skin if they survived. So most people did not have smooth skin, but milkmaids had surprisingly smooth skin. One wonders what was behind this observation by Jenner, but it doesn't really matter. He also noticed that milkmaids had previously been exposed, in many instances, to a related disease of cows called cowpox. And this was manifested on their hands, they developed sores on their hands, but it didn't progress into a disease that looked like smallpox. And so Jenner made a hypothesis that prior exposure to cowpox, whatever the agent was that caused cowpox, prior exposure to cowpox protected against smallpox. And this was the suggestion of a phenomenon known as immunological memory. And it was well known by then that you only got a disease once. You only got exposed, if you got exposed to a disease and developed symptoms and recovered, you were protected against getting that disease in the future. And this is a phenomenon of immunological memory, which we now understand in some detail, and I'll tell you how it all works. But that was known already by then. And so what Jenner said was that maybe you develop immunological memory to your cowpox exposure which then protects you against smallpox. Well, so that was the hypothesis. He needed to do an experiment. And the experiment is illustrated up there. He started with a milkmaid by the name of Sarah Nelms who had a cowpox sore on her hand. He took that cowpox sore from her hand and injected it into James Phipps -- -- who was a clueless neighbor's boy. He just happened to live in the neighborhood wandering by one day and where Jenner invited him in for some cocoa or something and said, by the way, since you're here, let me just inject you with some of this stuff. [LAUGHTER] And that's exactly what's depicted here. Sarah Nelms is holding the boy and Jenner is injecting him with some cowpox stuff. He then waited three weeks, and he injected him with smallpox. A known lethal agent. He then waited six weeks and injected him again. [LAUGHTER] Then he waited and waited and waited. And the kid was disease-free. He had, in fact, protected the boy against the development of smallpox. The first purposeful vaccination. It's called vaccination, by the way, because cowpox, which is the agent used to vaccinate the boy, is caused by a virus known as vaccinia. So in honor of that, the whole field, the whole approach is called vaccination. So this is an example of introducing an agent which the body then responds to. And based on the body's response to that agent, the body is protected against further disease. Now, this works because the agent that was used to vaccinate the boy, vaccinia is very similar to the agent that causes smallpox. It's not identical but it's sufficiently similar that the body's response to that agent is compatible with a response to the dangerous agent. This is called a heterologous vaccine. And I'll briefly mention other vaccine strategies towards the end. Jenner succeeded in doing this with a number of patients directly after that. And he actually published his paper, or he tried to publish a paper on this finding in the early 1800s. He was actually blocked from doing so. People didn't want to believe it. People were extremely nervous about this approach. It lead to editorials in local magazines such as shown here. This is a cartoon of Jenner with young James Phipps and a bunch of people getting vaccinated with this cow thing. And the consequence, as you might be able to see, is that these people are sprouting cows out of their arms, out of their faces, out of their butts. And there was general nervousness about tinkering with the natural species in the world in this deliberate way. But it was generally accepted, used extensively in Europe and actually in the United States. And now it's sufficiently successful, has been sufficiently successful over the last couple of centuries that smallpox is no longer a problem. It's been eradicated through proper vaccination using this approach. So there is no longer smallpox out there, although there are vials of smallpox sitting in freezers which have been a concern to governments in the sense that bioterrorists might get their hands on it. And there have actually been efforts to bring back smallpox vaccination as a protective against the potential use of the smallpox agent for some sort of bioterrorism. Do you have a question? OK. Now, as you know, vaccinations against viral agents and other pathogens are commonplace. You've all been vaccinated against lots of things. They've changed the course of human history in a dramatic way. This was not very long ago, 1952, a bunch of children who were infected with polio virus. It led to deaths of many kids and paralysis of many more. And this is a picture in a hospital ward of children in iron lungs, which is how they were kept alive because of their paralysis. Many of them survived this early phase but then went on to develop paralysis in their extremities. And it was a very devastating disease. Fortunately, both Drs. Sabin and Salk in the early 1950s developed vaccines using the principles laid out by Jenner 150 years before. And these were successful. And so kids were treated with polio vaccines for the next 30 or so years. And polio itself was wiped out. So there are no, or very, very few examples of active polio outbreaks these days. And, in fact, kids are not vaccinated with polio vaccines in this country because it's not a threat. It's not that it's not a threat worldwide. In fact, last year when I was teaching this course we read that there were some

that it's not a threat to humans. In fact, last year when I was teaching this course we read that there were some new outbreaks of polio. So it's not that the virus is gone. It hasn't been fully eradicated. But it's very, very uncommon thanks to these kinds of efforts. And we think about this also again to protect against deliberate use of pathogens. Here, Anthrax, I've shown you this slide before. So there are now efforts to develop vaccines against Anthrax. In case somebody were to use it as an agent, you could protect people from getting exposed to Anthrax. And pathogens are important out there. Many of the diseases that have been scourges of humanity over the millennia are due to pathogens. It's been a constant battle between humans and pathogens, viruses, bacteria, other single-cell organisms. And our greatest hope against controlling these infections is to protect them through vaccination. Where that's worked it's been extremely successful. Where it hasn't worked, like in the case of HIV, it's been much more problematic. So vaccination in general, immunological response, immunological memory are extremely important. OK. So to understand what's happening with respect to vaccination and immunological memory, you have to think about what happens in an infection and how your body responds to it. So if you plot a time course of infection where this might be the very earliest stages. When you get exposed to a pathogen, virus, bacterium, it enters your body and it begins to reproduce itself. It will build up. And it might peak in its concentrations at about a week or so, maybe two weeks. And it's at this stage where you're developing symptoms. And those symptoms might be sufficiently severe that it can cause death. But if you live then you observe typically that the pathogen concentrations drop and can be eliminated all together within two or three weeks. The reason that they drop is because your body is making defense mechanisms against it in two forms, antibodies and specialized cells called T cells that are built to eradicate the agent. And so if you plot the concentration of antibodies and T cells that are active against this agent, you find that initially there's a delay. And then the concentrations of these antibodies and T cells rises. And as they do they are acting on either the agent itself or the cells that the agent has infected. And a combined activity then leads to the elimination of those agents. Concentrations stay up and then they fall, but they don't go to zero. They stay around. You have low levels of these specific antibody-producing cells or T cells that are directed against this agent that stay in your blood forever such that if you get a second infection, even years later, these cells are already there set aside such that the response to that agent is very rapid and the concentrations of the agent never rise very high. So you're able to control it before the amounts of the agents build up and cause symptoms or death. And that's why you don't develop secondary infection. This process is called immunological memory. And, as I said, it's the setting aside of cells that are specific to the thing that's causing the disease. And we'll talk about how that happens in a moment. So this phase, I should have said, is called recovery. OK. Now, I mentioned two cell types that are important in this process. There are B cells and T cells, and they are the ones that I'm going to focus on. But it's important for you to know that they are not the only cells of your immune system. The body produces a whole series of cells shown here in addition to B cells and T cells and a specialized form of B cells called plasma cells. And these cells also contribute to your immune response. They're part of what's called the innate immune response. And they act in a way that is nonspecific. So they recognize classes of agents, viruses as a class or bacteria as a class. They recognize things that are common to all viruses or most or all bacteria or most. And they're very important in the early phases of an infection. And, in fact, in this first phase where you're ramping up the antibody producing cells in the T cells, it's those cells that are acting to help suppress the proliferation of the agent. And so this is where the innate immune response is taking place. And Claudette will review for you some of those cell types in the next lecture. We're going to focus on B cells and T cells. And they fall into what's called the adaptive or specific immune response. And that can be broken down, as I said, into these two cell types. There are T cells which are T lymphocytes. And the T lymphocytes constitute what's called cell-based immunity. It's the cells themselves that are participating in the eradication of the agent. And then there are B lymphocytes, and they participate in what's called humoral which is also liquid phase immunity. And what that means is that they're producing something that gets secreted into the bodily fluids, blood or whatever. And it's that which is participating in the eradication of the agent. In particular, what that is, is antibodies, as we'll talk about. These cells have these names, B cells and T cells, because where they mature. So both B lymphocytes and T lymphocytes start off in the bone marrow, or I should say the precursors of these cells start off in the bone marrow. The precursors to B lymphocytes make their way either to the spleen or they stay in the bone marrow, and that's why they're called B cells. And they go on to make B lymphocytes, including these cells called plasma cells, which produce antibodies. A separate precursor called the T cell precursor makes its way to the thymus which is a lymphoid organ in your chest, and there the cells mature into two types of T cells, cytotoxic T cells, otherwise known as CTLs, or TC cells, and helper T cells or TH cells. OK? And because they go to the thymus they're called T cells. Now, these cells are distinguishable based on the types of protective molecules that they produce. This slide just shows you an overview of the lymphoid system in your body emphasizing the points I just made. The bone marrow is important based on the origin of the cells, as well as it's where B cells mature. B cells also mature in the spleen. And here's the thymus where T cells mature. And in green here you see the lymphatic system. These are the vessels that carry your lymph fluids where many of these cells move to get to the sites of infection. And what's not so obvious to see are lymph nodes, which is again where many of these cells mature and turn into fully blown antibody producing cells or matured T cells. I also want to point out that the handout that you have has the wrong numbers. I was looking at least year's book when I took these numbers down. So the figures are what I'm showing you here. And on the Web, the version that's on the Web has been corrected, so you might want to pay attention to that. Now, what the antibodies that are produced by B cells and the molecules on the surface of T cells are recognizing are things called antigens. Antigens are one of a number of different types of molecules, lipids, carbohydrates, proteins, that are specific to the pathogen. And your body makes antibodies produced by T cells, produced by B cells, as well as proteins on the surface of T cells that will specifically recognize these antigens. And that's why it's called a specific immune response, because the protein that the lymphocytes are producing specifically recognizes the antigen, whether it be a lipid antigen, a carbohydrate antigen or a protein antigen. And that's illustrated on this side where you have a virus particle here or a secreted protein that might be floating around in the blood. And you can see

that there are bound to it these colored structures. These are antibodies. And the different colors are recognizing different antigens. So this orange colored antigen is being recognized by that orange colored antibody. The purple colored antigen is being recognized by the purple antibody. Your body has an amazing ability to generate tremendous diversity in the structures, these antibodies or T cell receptors that recognize particular antigens. B cells, B lymphocytes start off by producing on their surface antibody molecules. These antibody molecules are heterotetromers. They have two heavy chains and two light chains. And we'll talk about how those produced in a moment. B cells mature and they turn into plasma cells. And plasma cells secrete the antibody into the bodily fluids. OK? T cells have on their surface a protein called the T cell receptor. And likewise it is very specific. Just like antibodies, as depicted up here, have a particular sequence at the end, which is the antigen binding site. And no two antibodies produced by different B cells would be the same with respect to their antigen binding site. Likewise, this region of the T cell receptor is unique. And, again, that's what gives specificity to the immune system. There are B cells that produce particular antibodies that recognize particular antigens. And T cells that have on their surface T cell receptors that are specific to particular antigens compared to other T cells. This is a detail from your book which shows again an antibody molecule. You can see that it's a heterotetromer, two heavy chains, two light chains, and at the very tips, both of these arms are these antigen binding sites. And, again, this is where the diversity comes from. This antibody, with its particular structure, will bind to this particular antigen because that antigen fits into the pocket formed by that antigen binding site specifically. Likewise, on the surface of T cells there are T cell receptor proteins. They're composed of two chains, an alpha chain and a beta chain. And the coming together of the alpha chain and the beta chain produces, again, an antigen binding site that is unique to that particular T cell receptor. OK. So this is interesting. And it raises an important question, an important problem. There are lots of pathogens. There are lots and lots and lots of things out there that can get into your body and cause you harm. And, therefore, in order to effectively fight those things you need many different antibodies -- -- and many different T cell receptors. It's actually estimated that there are ten to the seventh distinct B cells and T cells in your body at any time. So you've got ten million different B cells and T cells that make different antibodies or different T cell receptors on the surface. So where does that diversity come from? How do you get ten million different B cells or T cells in your body? Well, one possibility would be that there are ten million different genes. That there are ten million different antibody genes or ten million different alpha genes and beta genes in the T cell receptor. Is that the likely explanation? How do you know it's not true? Because I've already told you that there are only 30, 00 genes total throughout your genome. So there sure as hell aren't ten to the seventh different antibody genes. So that answer is wrong. It could have been from alternative splicing. Maybe there are genes with many, many exons. And depending on how those exons get joined together, through a process of alternative splicing, you could produce diverse antibodies or T cell receptors. That could be true. And we actually think a lot of diversity in biology does come from alternative splicing of complex genes, but that's not the answer here. Instead, the answer has to do with a process known as DNA rearrangement. This is a process that was discovered, in the context of the immune system, by Susumu Tonegawa who was a professor in the Cancer Center at MIT. And, actually, he won the Nobel Prize for that discovery some years ago. We now know that the generation of all of these different antibodies and all of these different T cells is due to complex rearrangements of a very small number of complex genes. And I want to go through that with you now. And it is a little complicated. And so I warn you that I'm going to show you slides which come directly out of your book. And we'll walk through them. But then I advise you to read your book which I think does a good job explaining how this rearrangement process takes place. And hopefully together that will solidify the concepts for you. So, again, immunological diversity means that each B cell produces particular antibodies, as I've said. And these are the product of uniquely rearranged heavy chain genes and a uniquely rearranged light chain gene. And, likewise, each T cell, each distinct T cell has a specific T cell receptor on its surface which is the product of a uniquely rearranged T cell alpha genes and a uniquely rearranged T cell beta gene. And you can kind of think about the process that we're going to talk about like a roulette wheel that in roulette, as you know, one wheel spins and a particular object shows up and the next wheel spins and a different object shows up or the same one, and likewise the third way. And you end up with a unique combination of objects. The same is true is here. And there are lots of different combinations that can come up. Actually, last year when I was talking about this, I realized that an even better analogy is Mr. Potato Head. And I thought to bring this morning the Mr. Potato Head thing from my three-year-old daughter, but she threw herself across the door. So I actually was unable to bring Mr. Potato Head with me, but hopefully you remember Mr. Potato Head. It's a bland head, and you can put a different mouth or a different nose or a different pair of eyes or hair. And based on the combination that you choose you get a very different looking face. The same thing is true in the generation of antibodies and T cell receptors. It's a choice at different positions, and based on the choice that's made you make a unique looking antibody or T cell receptor. So this is illustrated here. What we're looking at is a piece of DNA that constitutes the un-rearranged heavy chain gene of antibodies. And you can see that there are different regions colored differently. There's a region called the V region which has several segments, several bits, which are similar but a little bit different. There might be a hundred or so of these V segment exons clustered together here. Next door is another set of segments called the D segments, and there are about 30 of those. And then next to them are the J segments, and there are about six of those. Next door is another set of segments called the constant region exons. These actually get used in a slightly different way. They don't come together by DNA rearrangement but rather by splicing, but this also adds to the diversity. When this rearrangement process is done you can choose a different exon down here by alternative splicing. So you can maybe get a sense, if we're going to pick one of these and then randomly one of these and then randomly one of these we can generate a lot of diversity. This happens, as I said, through an ordered process of DNA rearrangement. Our goal is to take an immature B cell, B cell precursor and then sequentially rearrange the heavy chain gene and the light chain gene. And then finally, when that's all done, that mature B cell is going to be sticking on its surface a specific antibody molecule which will have

this structure here. And the region of the antigen binding site will be the unique product of the coming together of those V segments, D segments and J segments. So the first step that happens is, with respect to the heavy chain gene, rearrangements take place. There are enzymes that get turned on in the immature B cell which specifically recognizes sequences next door to these segments. The first segments that recombine together involve the D region and the J region. So randomly one of the D region segments and one of the J region segments gets chosen, and the enzyme comes along and clips the DNA right next door to that segment and right upstream of that segment looping out the stuff in the middle, getting rid of it and joining together that particular pair of segments. So now you have a unique new piece of DNA which joins one of the D segments with one of the J segments. Next, one of the V segments is chosen which then gets clipped, and this region up here also gets clipped such that the middle piece gets taken away and the two pieces get joined together. And the product of that is a new piece of DNA that has a unique V region joined to a D region joined to a J region. OK? So there's a series of cut and paste reactions that produces a unique combination of V, D and J. Once that process is done then an RNA is produced from that locus. The RNA gets spliced, as I said, to allow the VDJ segment to get joined to one of the constant region segments. That mRNA product then gets translated into the heavy chain. Once you make the heavy chain you more or less go ahead and do the exact same thing with the light chain. You do a VDJ recombination. Join it up with a constant region. Now that cell is able to produce both a heavy chain and a light chain which is unique. Those come together to form a unique specific antibody molecule. So, again, that's complicated stuff. I don't expect that those of you who haven't heard it before will understand it from what I've just said, but all of what I told you is in the book. And there's an animation, which is where this comes from. So I advise you to read your textbook. OK? The important point is that recombination of these individual segments, random joining together of these distinct segments gives tremendous diversity. It allows you to produce ten to the seventh different T cells, sorry, B cells. The exact same process happens in the rearrangement of the alpha genes and the beta genes in the T cell receptor. So you get, again, tremendous diversity in that way. Now, I'm just going to mention this but I don't expect you to know it for life. Well, you might know it for life but you don't need to know it for a test. There are still other mechanisms that the body uses to add even more diversity. It turns out that this process of joining is actually intentionally messy so that the joints that occur between these segments are not all the same from one cell to another. Even if the cells were to rearrange the same two or three segments, they wouldn't necessarily produce the exact same antigen binding site because the process is inherently sloppy in order to even make more diversity. OK? But you don't really need to know about that specific aspect of it. OK. So through this process of rearrangement, through this process of rearrangement we are able to make, in the case of B cells, lots and lots and lots of distinct unique B cells that are circulating throughout your body. They're different from one another because they have on their surface, initially in the case of B cells they have on their surface these antibody molecules which are different from one another in these regions. So these antigen binding sites -- -- are unique. This one is different from this one. And I should have mentioned I wanted to emphasize that because of this rearrangement process the DNA of this cell is different from the DNA of that cell. I point that out because we've emphasized in the past that the genome that you get when you're first fertilized is stable and exactly the same in all of your cells. That's actually clearly not true in the case of B cells and T cells because they purposely rearranged the genome in the production of antibodies in T cell receptor genes. So the genome actually is a little bit different, at least in the case of the lymphoid cells. So these cells then are produced and they're quietly circulating in your blood. So how do you mount an immune response? You're now infected by some pathogen. How do you build up the concentrations of one of these particular B cells or T cells that can recognize that pathogen? How do you mount an immune response? Well, the way you do it through a process of clonal selection. And, again, this comes right out of your book. These cells which are floating around in the blood and not doing very much in terms of making more of themselves, they're not proliferating, can respond through the exposure to the antigen. So if floating around the blood along with these cells is a particular antigen, and it's able to bind to that antibody molecule which is sitting on the surface, that sends a signal to that cell it's time to divide. There's something in the environment that we like so that we need to make more of ourselves in order to fight off whatever that thing is. This induces a rapid and impressive proliferation. So you go from one or a small number of these cells to many, many of these cells, particularly these cells. These cells don't proliferate because they're not binding to the antigen. These cells do proliferate. They make many, many more of themselves, and when they get to a certain point they differentiate. They begin to make the material they need to secrete really well. They actually change their shape dramatically. They become very efficient secretory cells. And so these B cells that have the antibody on their surface then become secretory cells, these plasma cells. And the plasma cells then secrete the antibody into the bodily fluids allowing the antibody to then go off and bind to the antigen whether it is itself circulating or it's on the surface of the pathogen like a virus or a bacterium. So this process of clonal selection then allows for the cells to build up and, in this case, to differentiate into antibody-secreting cells. Now, these are the cells and the antibodies that are going to fight the infection. These are the cells that are building up right here producing, in this case, the antibody. The same exact thing happens with respect to T cells which you'll learn about in detail next time. However, after the infection is cleared most of those cells go away. They're no longer being stimulated and they actually die off. But importantly not all of them go away. Some of them are set aside as these memory cells. And if these memory cells that just kind of hang around in higher concentrations than they were at the very beginning of this process but it's still relatively low concentrations, and it's the presence of those memory cells that when you're infected again they kick into action quickly. They've already matured to a very great extent, as you can see here. They're on the edge. They're poised to make a lot of antibody or be an effective T cell. They build up very quickly and they suppress the immune response, they suppress the infection. So this process of clonal expansion is the early phase. The setting aside of the memory cells is the late phase. And it allows us to effectively respond in a second infection. And it's also the reason that you can respond once vaccinated. Vaccination is the exact same process except you're exposed to something that is not inherently

vaccination. Vaccination is the exact same process except you're exposed to something that is not inherently dangerous. In the case of an active infection, you're infected with the pathogen, the active pathogen, and it builds up and then you respond to it. But there's this dangerous phase where you might actually die. In the case of vaccination, you get exposed to something that is like the antigen, like the pathogen, but it's not otherwise dangerous. But, still, the same stuff happens. You build up antibody producing cells. You build up T cells. They then get set aside in the process of immunological memory. And when you're exposed to the real thing, if you're exposed to the real thing later on, like James Phipps was exposed to smallpox, you already have those cells set aside and you can respond effectively to the agent. So I want to now just mention in closing the various vaccine strategies that are used. And they all rely on this same phenomenon of exposing you to a related agent or antigen allowing you to make T cells or B cells and then fight them effectively. So the first one that I mentioned is cowpox for smallpox and I used the term heterologous vaccine. A heterologous vaccine is an organism which is very similar to the organism that causes the disease cowpox virus versus smallpox virus. And it's so similar that the antigens that it produces direct the development of antibodies or T cells that will also work against the dangerous pathogen. That's a great one if you can have it, but there aren't very many of them. There are very few examples of heterologous vaccines. It's just coincidence or luck that it worked in the case of cowpox and smallpox. A more common one is the attenuated vaccine. In this case, you take the active agent like polio virus and the Sabin polio vaccine is. You take that active agent and you grow it in the laboratory for a long time under conditions in which it changes. It adapts to the laboratory conditions and it's no longer dangerous to a person. If infected with this you will not get polio, but it's sufficiently similar to the original virulent pathogen but it has the same antigens so you mount a proper immune response. This is an effective strategy. It's used all the time. It's a little bit dangerous because if the attenuation process isn't good enough and there's still a little bit of active pathogen in there it could cause disease. And this happens every once in a while with attenuated vaccines. Another way is to just take the agent, whatever it is, and kill it. Mix it with a chemical that will crosslink its genome or heat it up really high so its DNA will be destroyed. That's an agent which cannot reproduce itself in your body. Its genome has been destroyed, but it still has in it the antigens. It still has on its surface the antigens. Your body will still recognize it, make antibodies and, therefore, if you were ever exposed to the live thing you will be protected. This is also very effective. This is the Salk polio vaccine. But every once in a while the killing process isn't perfectly effective. And so there's a little bit of live virus or whatever in there and people get disease. Another strategy is component vaccines. Nowadays, we can purify from the pathogen virus or bacteria a piece of it. You can purify some protein from the virus or from the bacterium and just use that as the antigen. That's not dangerous because it cannot replicate on its own inside you, but your body makes antibodies against it. And, therefore, you'll be protected at some later time against the real thing. And, increasingly, we're using recombinant vaccines. Using molecular biology, genetic engineering, we can actually build new agents that carry the genes of dangerous pathogens. And, actually, a commonly used one is vaccinia itself. So if you take vaccinia, the cowpox virus, take some of its genes out and put in the genes of a dangerous virus like polio virus, now that cowpox virus will get into you. It will replicate a little bit and it will start making those antigens. Your body will recognize that with antibodies and T cells. You'll clear up that infection because it's not a dangerous agent. But you will have made antibodies and T cells that can recognize those other antigens such that if you were infected at a later time you would be protected. So these are examples of vaccines, again extremely effective. They rely entirely on immunological memory, the generation of immunological diversity. Now, importantly, and this is something that you'll pay attention to next time, not all of these vaccines are created equal when it comes to producing a B cell or a T cell response. Some will produce both. Some will only produce a B cell response. And you'll see why that is in Monday's lecture.