



Dr. David Stukus: Hello and welcome to Conversations from the World of Allergy, a podcast produced by the American Academy of Allergy, Asthma & Immunology. I'm your host Dave Stukus. I'm a board certified allergist and immunologist and serve as a social media medical editor for the Academy. Our podcast series will use different formats to interview thought leaders from the world of allergy and immunology. This podcast is not intended to provide any individual medical advice to our listeners. We do hope that our conversations provide evidence-based information. Any questions pertaining to one's own health should always be discussed with their personal physician. The Find an Allergist <http://allergist.aaaai.org/find/> search engine on the academy website is a useful tool to locate a listing of board-certified allergists in your area. Finally, use of this audio program is subject to the American Academy of Allergy, Asthma & Immunology terms of use agreement which you can find at <http://www.AAAAI.org>. Today's edition of our "Conversations from the World of Allergy" podcast series has been accredited for continuing medical education credit. The American Academy of Allergy, Asthma & Immunology is accredited by the Accreditation Council for Continuing Medical Education to provide continuing medical education for physicians. Information about credit claiming for this and other episodes can be found at <https://education.aaaai.org/podcasts/podcasts>. Credit claiming we will be available for one year from the episode's original release date. We are pleased to welcome Dr. Vivian Hernandez-Trujillo to today's episode. Dr. Hernandez-Trujillo is the director of the division of allergy and immunology at Nicklaus Children's Hospital and works at Allergy and Immunology Care Center South Florida and Miami Lakes Florida. She has a long track record of service to the American Academy of Allergy, Asthma & Immunology as well as the Immune Deficiency Foundation. In addition to clinical and research interests surrounding food allergy and anaphylaxis Dr. Hernandez-Trujillo has a strong interest in primary immune deficiency in children with recurrent infections which is the topic of today's episode. Dr. Hernandez-Trujillo serves as a consultant, advisory board member and speaker for CSL Bearing and is a consultant on the advisory board for Shire. I do not have any relevant relationships to disclose. Dr. Hernandez-Trujillo thank you so much for taking the time to join us today. And welcome to our show.

Dr. Vivian Hernandez-Trujillo: Thank you so much. I'm very excited to be here today.

Dr. David Stukus: Well, I'm also looking forward to our conversation because this is a topic that, you know, we hear a lot about especially as pediatricians and allergists and immunologists. And as a parent and pediatrician I can attest that young children just seem to constantly have runny noses, congestion and cough. What would be considered a normal pattern and type of infections for healthy children?

Dr. Vivian Hernandez-Trujillo: So this is an important question that many parents ask especially at the time of the first visit. And, especially, during this time of year that we're preparing for back to school and many children will be starting a daycare it's a very relevant question. So the average child will have eight to ten respiratory infections per year. And if you round that off it's about every six weeks. If there's older siblings in the home or if they're in daycare the number may increase from ten to twelve and the mean

duration may be approximately eight days. I can see that as a pediatrician and parent of twins when they first went to school it was every three weeks someone had-- they were battling a URI. And upper respiratory infections are not only common, I think the red flag and the time to worry would be if every infection requires antibiotic or if the child requires hospitalization.

Dr. David Stukus: Okay. We're going to definitely get into that some more. So what you're saying is that we would expect healthy children to essentially be sick almost half the year on average. Does that sound about right?

Dr. Vivian Hernandez-Trujillo: That's exactly the number.

Dr. David Stukus: Wow. We expect most of these to be viral ailments and, as you mentioned, they're going to be sick for one to two weeks at a time. What are some other factors in the history? You mentioned antibiotics and hospitalization. But when should suspicion be raised that other factors may be contributing?

Dr. Vivian Hernandez-Trujillo: The Immune Deficiency Foundation has a campaign really that says is it just an infection? And I like the way that it's characterized because the key things to really raise a red flag would be are the infections severe? Are they persistent or unusual? And then the other factors would be are they recurrent infection? Then, obviously, if it runs in the family? Those are all kind of red flags that would make us pause and say, all right, is there something else going on? Is it just not that the child is getting these frequent, which would be normal otherwise in a child, especially, very young and life that's starting school or has just started daycare.

Dr. David Stukus: And do you think that the pattern of the infections is an important component to consider as well?

Dr. Vivian Hernandez-Trujillo: The pattern and the severity because a recurrent infection that it's a cold and it doesn't complicate into something like asthma or it doesn't lead to an ear infection or pneumonia. If the pattern is that the child has an upper respiratory infection and then every time they're either having an ear infection or it results in pneumonia and then, again, it requires that they are hospitalized that's where I would be more concerned.

Dr. David Stukus: Okay. Now, my daughter she had six episodes of strep throat this past school year. And we were told that once she hit seven and seven was the cutoff, that's when we would consider removing her tonsils. Can we say that in regards to any number of infections that equals an immune deficiency? Is there some clear cutoff or black-and-white picture that we can use?

Dr. Vivian Hernandez-Trujillo: We really need more studies to determine cutoff. I consider the Jeffrey Modell Foundation has what we call the 10 warning signs and that's used as a guide that has been helpful but it's not all-inclusive. So I'll give you some examples: four or more new ear infections within one year; or two or more serious sinus infections within a year; or two or more months on antibiotics with little effect; two or more pneumonias within a year. For me, as a pediatrician, I always step back and I look is this

child failing to gain weight? Is it an infant that's just not thriving? Are they having recurrent or deep skin or organ abscesses? Or persistent thrush especially beyond a year of age? Needing IV antibiotics, for me, is obviously a red flag and that's part of the warning signs. And then two or more deep-seated infections including sepsis. And then, obviously, again, what we come back to is there a family history? But that's not true in every case. So the reality is we need more studies but if a child has fewer infections than what I said in these warning signs and they're just clinically not thriving that would be a sign to evaluate their immune system. And as an immunologist, a pediatric immunologist my threshold is, obviously, going to be lower. But I think that medical professionals need to just be aware of the possibility and considered an immune workup.

Dr. David Stukus: Okay. And you touched upon some of the important details within the clinical history to focus on. And I'm going to ask you if you're willing to expand upon that a little bit. So how do you take a history when you see a new patient who has concerns for recurrent infection? What details about their reported infections do you really delve into? And what do you focus on?

Dr. Vivian Hernandez-Trujillo: That's actually a really important question. I think for children, especially, as a pediatrician I'm always looking at their growth parameters even before I walk in the room. If I have a height and weight I want to look at the curve. And if I have the possibility to look at the curve over time from their general pediatrician that's very helpful. Then I'll sit with the family and then I ask about not only infections, we're focusing on recurrent infections today, but if the child is thriving or having, for example-- are they having recurrent diarrhea, just chronic diarrhea without explanation? Are they having recurrent episodes of thrush or skin lesions that aren't improving? That someone may have thought, "Well, this is eczema," but it's not responding to appropriate treatment. Does the child have-- even early in life children can have an autoimmune disease? That's another thing that I would ask specifically while I'm talking to the family about history. And then, for me, family history is, obviously, important. But the child him or herself is the most important. So whether or not-- if there's no family history that doesn't really help. If there is, obviously, that's a more helpful piece of information. But, I think, by focusing on those type-- and then we already mentioned, you know, how many infections. Is there a pattern to the infections? Do they need antibiotics? Do they need more than one course of antibiotics? Do they need to have IV antibiotics? Have they been hospitalized? Those are all key points and elements of the history that we need to obtain.

Dr. David Stukus: How do you specifically ask about family history because I think that's a tricky question. I'm glad you brought that up. How do you actually phrase that when you ask families?

Dr. Vivian Hernandez-Trujillo: So when I ask about family history I don't necessarily only ask about primary immune deficiency because the answer is very frequently no. It may be, do you have any children who have died early in life without an explanation? Or from a severe infection? Do you have any children that have recurrent infections and are frequently in the hospital? Is there anyone in the family, because you want to open it up to adults as well, who may require IV antibiotics to clear an infection? Those are the types of questions I ask because many people don't understand what a primary immunodeficiency is. And they also may not have a diagnosis. Is there a family member that has recurrent sinusitis and pneumonia who just is not doing well? And you'd be surprised how many times somebody says, "Yes. The mom's brother. Or the grandfather." Those are important.

Dr. David Stukus: That's interesting. That's great. Thank you for that. How often do you find yourself having to go through medical records? As you know parents aren't always the best historians and maybe some of the important details may be lacking when you try to obtain history. Do you think that that's an important component of evaluation especially when you first meet somebody of going through whether it's admissions or culture data or things like that?

Dr. Vivian Hernandez-Trujillo: Absolutely. And that's especially if you're questioning whether the family may have all the information available to you or if they hesitate when you ask the question, asking for records not only from the pediatrician, yes, but, exactly looking at labs that have previously been done. Any cultures so you can see what the organism responsible was. And then, obviously, if they've been hospitalized looking at the details of that hospitalization.

Dr. David Stukus: We're going to talk about testing in a little bit here but before we even consider testing it sounds like you're spending an extensive time really going through the important details of the clinical history and medical record.

Dr. Vivian Hernandez-Trujillo: Absolutely.

Dr. David Stukus: Okay. Now, what you do when we have these children referred who have already received multiple courses of antibiotics? Does that alone just sort of indicate a more serious underlying condition? Or what are some of the more common reasons why you see all of these multiple courses of antibiotics being prescribed so often?

Dr. Vivian Hernandez-Trujillo: So this really depends on the clinical scenario. If you have a child, for example, with older siblings or a little one that started daycare recently they're more likely to have the recurrent upper respiratory infections that can lead to recurrent ear infections. If you have a young child especially early in life within the first year that required tympanostomy tubes because of the recurrent ear infections, or if the first infection is very early in life, for example, from four to six months when infants are losing antibodies from their mothers and the antibodies are decreasing, if their own body is not producing they're more likely to have an infection, that's when I would be more suspicious of a possible primary immunodeficiency. I think the challenge for us especially in this day and age-- you know, since we're in a society where parents often will ask for antibiotics. And the medical team needs to take the time to explain that it's not always necessary. And it's, also, not always in the best interest of the patient. We know that overuse leads to resistance. And this is a big problem not only for all of us but for your own patient and taking the time to explain that to the parent is very, very important.

Dr. David Stukus: I'm sure that's challenging especially when somebody has received antibiotics every time they get an upper respiratory infection. So like you said it's important to really figure out the reason why and why it keeps getting prescribed so often. What do you do with patients who have say recurrent strep throat? Or if it's more urinary tract infections? Are those conditions where they receive frequent antibiotics? For those that you'd say oh, maybe, this is less likely to be a primary immunodeficiency? Or where do you kind of characterize those?

Dr. Vivian Hernandez-Trujillo: Recurrent strep is very interesting to me because I think I've helped many families. The recurrent strep may just be that they're in a carrier state and they need treatment for that. Right? So that's the most common presentation that we see. So frequently that's a question that is raised-- before, like you were talking about your daughter before that you would, obviously, just want to be sure that when the challenge is asymptomatic, not having any problems that you have a negative culture. For urinary tract infections I might be a little bit less concerned. However, I truly listen to the whole history because usually if a child comes in with a history of recurrent UTI, for example, and there could be parts of the complement pathway that could be involved there if they're not very common but many of our diseases are not common. I think just listening to the whole history and eliciting parts of the history and, obviously, the physical may not be as helpful in that case. But just listening to the whole history in determining where I should be focusing is very, very important. And we'll talk a little bit more about that when we get to diagnostics.

Dr. David Stukus: Great. Okay. Now, you touched upon this earlier about the normal healthy child is expected to have multiple different viral upper respiratory infections throughout the year. That's just a normal expectation of life. And that they can have increased frequency based upon attendance at daycare and with siblings and things like that. But let's start to dive into your sort of thought process and differential diagnosis. What are some other comorbid conditions that you see contributing to the frequency or duration of infections?

Dr. Vivian Hernandez-Trujillo: When the child presents to me initially I like to say I go into the room with an open mind. So I try to actually be a general pediatrician and not an allergist/immunologist because if I do that I'm going to close off the possibility of really thinking about these other differential diagnoses. So if I have a child that may present with recurrent pneumonia a few things come to mind. If they've had four different chest x-rays and they've had four episodes of pneumonia I want to look at those because I want to know if it's in the same area. So could this be an anatomic problem in the lungs? Or has it been in different parts of the lung? I also consider cystic fibrosis. Cystic fibrosis can result in failure to thrive and recurrent infections especially sinopulmonary infections. So I consider the diagnosis of cystic fibrosis. We have the advantage of newborn screening but not all patients are diagnosed with newborn screening. Also, ciliary dysfunction. We've helped several families. And ciliary dysfunction can be primary or secondary. In some cases the child is the one that's first diagnosed and then it's actually the parents that benefit because they also have been battling, for example, recurrent sinusitis and we have seen that. We're also in the-- we have the advantage as allergists and immunologists to care for patients with asthma. And passive smoke exposure is something that we always have to consider. We always ask in our history but a child with asthma and passive smoke exposure and even a child with passive smoke exposure alone will have the likelihood of having more recurrent infections. So those are the types of conditions that I really think about when I'm thinking about the differential in a patient with recurrent infections.

Dr. David Stukus: Okay. And do you spend time talking about the indoor air quality or environmental triggers inside the home that may also be contributing as well?

Dr. Vivian Hernandez-Trujillo: Absolutely. So every child we talk about the home where we ask our common questions as allergists. So we're asking about exposure to any pets. We're asking about other factors. So if a child has severe dust allergy and they have wall-to-wall carpeting and curtains and fans and they're not changing the air conditioning filters, obviously, we would ask all those questions and just help guide our workup.

Dr. David Stukus: Okay. Now, when you do determine that there are factors inside the home such as cigarette smoke that may be contributing to the pattern of infections, you know, this can be a challenging conversation for any of us to have with families. Do you have any tips on how you have this important conversation?

Dr. Vivian Hernandez-Trujillo: This can be challenging. I actually-- when I have a history, when I have a child that comes in and the parents-- especially when the parents are very concerned and the parents actually admit and they say, "I'm a smoker but I smoke outside." So, again, I feel as an allergist and immunologist I have the opportunity to address many factors that can contribute. And when the parents, you know, raise the question and they admit, "Well, I smoke but I smoke outside," I really pause and I take the time to talk to them. The first thing I asked him is do you want to quit? And almost always they'll say yes. And I'll say this is great. We're here to support you. And the first thing I'll say is I truly recommend changing your behavior because-- meaning if you're used to getting up in the morning and you have your coffee and a cigarette, I need you to change that because that changing behavior is the most important and the most difficult part. And you'd be surprised how many people are open to it. And then you can say there's other options. There's treatment options. But just opening the door to that conversation albeit difficult at times it's amazing how many people you can help.

Dr. David Stukus: I agree. And thanks for sharing that. I've had similar experiences. I think that if you just approach it in a reasonable way and you have the conversation and you let them know that this is a factor that's likely contributing I also find that most people are very receptive to that conversation. Now, let's get back to we're approaching probably the halfway point of our conversation here and we haven't even really talked about primary immune deficiency yet. So for these kids that have recurrent infections there's a whole host of other things to consider before you even really think about the underlying immune system. So let's delve into that. And you mentioned before but I'd like for you to summarize as we kind of get into that aspect of it what are some red flags that really catch your attention right out of the gate that says, "Uh-oh I believe this child likely has an underlying immune deficiency"?

Dr. Vivian Hernandez-Trujillo: So early in life and even as they're toddlers and older failure to thrive in any child for me is the biggest red flag. A child that has chronic diarrhea, we have many children that present with mild failure to thrive but the parents say, "He or she has never had normal bowel movements." That's a concern. That's definitely red flag. Again, a child with recurrent skin lesions that just aren't getting better that's been diagnosed with eczema in the first year of life but they're on appropriate treatment it's not getting better. It may not be eczema. It might be something more. So those, just in general terms, those are really the biggest red flags that I would look for. A child that has been diagnosed with autoimmune disease or early in life this is something that we never really talked about before but autoimmune disease especially more than one would be a reason to look at the immune-- to properly

evaluate the immune system because it may be that there's a primary immunodeficiency responsible for everything.

Dr. David Stukus: How would you characterize antibiotic-resistant organisms? Does that also fall in this category of automatic suspicion? Or is that sort of a different entity when you think about this?

Dr. Vivian Hernandez-Trujillo: For me it's a different entity. I think, again, we live in a society right now where because of the overuse of antibiotics we really have kind of put ourselves into a bad situation with that respect. But, again, here as allergists we have the opportunity for things like removing labels from penicillin allergy which I think is incredibly important because if we're using less broad spectrum antibiotics I think that that's going to be very helpful in the long run.

Dr. David Stukus: Yes. I agree as well. All right. Now, I want to pick your brain. And I think our listeners would love to hear your input on this as well. How do you think about the immune system? I mean it's this overwhelmingly complex system that we all have. Do you compartmentalize it in any way when you think through this in evaluating patients? How do you do so?

Dr. Vivian Hernandez-Trujillo: I really think there's different ways to think about the immune system. And I will be the first to tell you if you simplify it in your mind and you simplify it in your differential it's not going to look as complex and as overwhelming. So I think that's really important. I'm going to go through-- today I'm going to talk about just how I compartmentalize based on the type of infection because you can do it by age of onset. There are many ways to do this. But for me-- and as I'm teaching fellows and we're talking I say, okay, let's talk about the type of infections. So you have a child that's presenting with sinopulmonary infections. They're having pneumonias, otitis. They're having sinusitis. We have to consider that there could be a problem with antibody production or antibody function. So that's the first. Then I think about, well, if they're coming in with recurrent viral or fungal infections I'm going to think more about a T-cell problem either in production, again, or in its function. With failure to thrive or a child that has had all kinds of infections, bacterial, viral, fungal I think more about a combined immunodeficiency. An example, obviously would be SCID. As far as patients with recurrent infections that are associated with or due to staph or Aspergillus or someone that has a liver abscess, you need to think more about your phagocytic and your neutrophil disorders. And then the next that I would think about is, you know, a child with recurrent or has had one episode of meningococcal meningitis we need to consider at that very first time whether there could be a terminal complement problem. So that's the way I compartmentalize so that it helps in guiding the type of workup I do because when evaluate any child you really want to have more of a guided workup. I don't like to just throw everything up and see what comes back because then that is not always helpful.

Dr. David Stukus: Thank you. That's great. I'm hearing from you, really, it all starts with the details, the detailed clinical history. What are the types of infections, the pattern of infections? And then you take that and compartmentalize essentially into five different categories B-cell, T-cell, combined, innate immunity and then complement. I think that's a great way to go about it.

Dr. Vivian Hernandez-Trujillo: And, obviously, there's infections that are not going to fall into those and we're learning more and more and immunology is really at a time of rapid growth and explosion. But these are just the five general categories. And then anything that may fall outside then we may have to consider a different workup depending on the presentation.

Dr. David Stukus: Now, this is a loaded question but bear with me and I'd love to hear your take on it. But can you give us a broad overview of the types of immune deficiencies within these categories and including those that are the most common that we're going to see among children?

Dr. Vivian Hernandez-Trujillo: Absolutely. If we start with antibody disorders, disorders like transient hypogammaglobulinemia of infancy is common and will often resolve by the age of four. Selective IGA deficiency which is one of the more common immunodeficiencies. And in those patients they may be completely asymptomatic or they may have recurrent sinopulmonary infections. X-linked agammaglobulinemia or Bruton's agammaglobulinemia, which is also known as XLA, is less common than the previous two but very important especially to be able to identify as early in life as possible. And then in the second decade of life children with common variable immunodeficiency will also have sinopulmonary infections. When we shift a little bit towards T cells disorders like 22q11 deletion or DiGeorge syndrome will have-- they can have problems with rash or candida infections. And then the combined immunodeficiencies we all know about SCID which is some severe combined immunodeficiency. I think right now we are at a time which is very exciting because all 50 states in the US are actually screening newborn screening in some form for SCID and that will help us identify these patients earlier than ever and really help improve their prognosis long-term because it can lead to earlier treatment and things like bone marrow transplant; so that is very exciting. There are forms of hyper IGM which can be combined as well. And those patients will frequently have Sino pulmonary infection and those patients will frequently have sinopulmonary infections. Some of them will have enlarged lymph nodes. When we shift to neutrophil disorders-- so chronic granulomatous disease is the most, I think, commonly discussed but it is very important because these are the patients that have problems with staph, with Aspergillus, very strange. Any fungal infection that doesn't seem to improve or they have different fungi and then liver abscess. So these are the patients the present in that way. And then shifting to the complement disorders if a child has meningococcal meningitis and I tell our pediatric residents and our fellows if you come once with meningococcal meningitis you need to consider terminal complement deficiency and you really have to order the CH50 because that's going to be life-changing. Nobody really deserve to have to have more than one episode to have that test ordered. So we could talk about this for a long time but I think in general terms that is a broad review of the more common immunodeficiencies that we see.

Dr. David Stukus: Yeah. That's great. And, I agree, each one of those could probably be a podcast episode in itself and I look forward to having you back on to delve into a couple of those in more detail. And for the listeners we're going to put some links on the website after the CME credit that will give you some sort of information regarding those as well. But that's a great overview. Now, over the last decades we've really seen a huge increase in the number of different tests that can be obtained including genetic testing for potential mutations. Do you think that most patients who present with the history of recurrent

infections should have a huge number of tests ordered initially? Or is there are more streamlined approach that you recommend?

Dr. Vivian Hernandez-Trujillo: So here it's really going to depend on a clinical scenario. If you have a child that's acutely ill in the intensive care unit it probably is going to be more helpful to order as many tests as possible to get to the root of the problem at that moment. If you have a child that comes to your office with recurrent infections but is otherwise thriving you have more of an opportunity to order some screening tests and then follow or observe if it's likely you're going to have the opportunity to do that over time. Again, I don't like to just have one thing that I order on everybody. I really think it's going to depend on the patient and their presentation. And I think that that's the most helpful for most patients. Not every patient is going to need all of the tests that you would order on a child who is acutely ill in the intensive care unit, for example.

Dr. David Stukus: I think this is the fourth or fifth time where I've heard you really mention the importance of using the specific clinical history to guide the rest of the evaluation. Yeah. I agree 100 percent. I can't emphasize that enough. And what would you say is the downside in ordering as many tests surrounding the immune system as possible. What kind of bad things happen when that occurs?

Dr. Vivian Hernandez-Trujillo: Okay. There's many things. First of all, due to the small size of many children we're limited in the number of tests. So that's one thing that sometimes we have to remind the parents but we really can't just get every test that you would want to do in adult because the reality is they're small. More importantly, running tests that are not consistent with their presentation may give you abnormal values that not only are not helpful but it's more confusing because then you may have to explain okay why is this test coming back when it doesn't have anything to do with the clinical presentation? And that, we all know, we don't like to run tests unless there's a reason to run them because you can have abnormal values that mean absolutely nothing and they confuse you and don't help you and may actually guide you along the wrong path. So those are really the big reasons that I don't like to just order as many tests as possible. I don't think that that's helpful for anybody.

Dr. David Stukus: Do values on some of these tests change according to age?

Dr. Vivian Hernandez-Trujillo: Absolutely. So we have age normal values and that's one thing I would recommend for any clinician. If you have a test that comes back especially I will say if I have a very high index of suspicion and everything looks normal I like to just make sure that the reference values, the normals are correct because they need to be according to the age of the patient. And those are well published and those are available. So it's important to make sure that you're looking at apples and apples and not apples and oranges.

Dr. David Stukus: Yeah. And in your experience do the laboratories always provide the proper reference range according to age? Or is that something that needs to really be looked at very carefully?

Dr. Vivian Hernandez-Trujillo: They don't. So I gave you the example of someone you have a high index of suspicion, ensuring that those normals are correct. But I will give you the opposite side. If you get

back an abnormal and then it turns out well they used the wrong age reference well that's important and that happens, as well. So I will tell you I tend to double check especially if I'm getting back abnormal maybe when I'm not as highly suspicious but definitely if I'm getting normal values when I'm very suspicious about a particular disorder.

Dr. David Stukus: Okay. And how often in your experience do you think you're looking at the same piece of paper and the same information as somebody else who ordered the test and yet you come up with a completely different sort of interpretation of that.

Dr. Vivian Hernandez-Trujillo: It may be five to ten percent of the time but that's not a small number. I think that it's worth taking the time and really looking.

Dr. David Stukus: Sure. Okay. Now, let's go back to sort of a more specific example. And you mentioned that one of the more common presentations of immunodeficiency would be recurrent sinopulmonary infections. What would be a good baseline starting points in regards to the diagnostic evaluation for that type of patient?

Dr. Vivian Hernandez-Trujillo: I would start with probably the simplest test that almost everybody gets which is a CBC with this. And here I really do look not only overall at their white blood cell count but I'm looking at the absolute lymphocyte number, that is very important and very helpful. You can also have just total immunoglobulin so your serum IGG, A, M and E because that can be helpful. And this isn't a test but, again, going back to looking at the height and weight and how the child is growing. I think that as a screen those are really important. As we move on we can look more specifically at their response to vaccines. We can look at the lymphocytes that we can take a good look at the numbers of B cells, of the T cells, of NK cells. And those all will help guide us on whether or not there's a need for further evaluation. But the specific antibody to vaccines tells us about antibody function which is important. The lymphocyte numbers tell us about the numbers. And if the numbers are very low then the function and the quantity of the total immunoglobulins may not have a chance to be normal. So I feel like every piece is important but for screening purposes a CBC with diff, total immunoglobulins, and taking a good look at the growth of the child are a good starting point.

Dr. David Stukus: And what vaccines do you typically evaluate or which antigens do you look at in regards to response?

Dr. Vivian Hernandez-Trujillo: For response to antigens you can look at especially in the younger children below the age of two tetanus, diphtheria and Haemophilus influenza. You can look at those same in people-- patients of any age as well as pneumococcal. And if you are concerned especially in this day and age of what's happening with measles in our country you can look at the levels of measles, mumps and rubella to make sure that the patients that have been immunized have proper protection.

Dr. David Stukus: And what if somebody isn't immunized? Is there any practical way that you can assess immunoglobulins function in those patients?

Dr. Vivian Hernandez-Trujillo: It's a little bit more of a challenge but it's not impossible. If the blood type of the child is not AB you're actually able to measure isohemagglutinins to the blood group antigens if they're positive it's helpful, if it's negative it may not be as helpful. In these patients I recommend obtaining at least total immunoglobulins. And then if the family is agreeable and they have an open mind you know you can challenge them with giving them vaccines with tetanus, diphtheria, depending on the age with HIB. And then we have different pneumococcal vaccines that are also possible to administer the vaccine and then retest and see if there was a proper response four to eight weeks later.

Dr. David Stukus: Okay. So you need to wait at least four weeks or so to allow them to mount the response to the vaccine?

Dr. Vivian Hernandez-Trujillo: Absolutely. That's very important.

Dr. David Stukus: Okay. Now, when your suspicion based upon the clinical history and your evaluation takes you down the path of consideration for T-cell immune deficiencies where's a good starting point in regards to the diagnostic testing that people should think about for those patients?

Dr. Vivian Hernandez-Trujillo: So if you're concerned about T-cells I usually start with the lymphocyte subsets so I'm looking at the numbers of T-cells, the total T-cells and then specifically at CD4s and CD8s. That will give you the quantity. I will tell you that early on in my career, as a young immunologist, we had a patient present with HIV in her teens and it was actually congenital. So those are the patients that really kind of leave the mark on you. I have never forgotten that patient. My primary immunodeficient patients are really what I trained most in and I feel most comfortable with but I never forget the secondary immunodeficiencies. And HIV is something to keep in the back of your mind. So I think that's looking at the T-cell numbers can help guide you not only for primary immunodeficiency patients but also secondary immunodeficiency patients. And then we can also look at function of T-cells by ordering response to mitogens. And I think that also can give valuable information.

Dr. David Stukus: Great. And then you mentioned the CH50 assay, what part of the immune system does that evaluate?

Dr. Vivian Hernandez-Trujillo: So that's looking for any terminal complement disorder and that's important because when that's deficient, again, the patients can present with meningococcal meningitis which is not something we want anyone to have to have especially more than once.

Dr. David Stukus: And then for completeness sake when you're concerned about innate immunity or phagocytic dysfunction what kind of tests would people think about?

Dr. Vivian Hernandez-Trujillo: So there is oxidative burst to look at neutrophil function. The gold standard now is dihydrorhodamine 123 and that's a flow assay that actually looks at the function of neutrophils.

Dr. David Stukus: And something as we talk about this it popped in my head, do you see any changes to these laboratory values and the patient who's acutely ill? So say they're in the hospital setting and they're battling an infection acutely and you try to obtain these. Are you going to get a different result than if they're otherwise at a healthy point?

Dr. Vivian Hernandez-Trujillo: That's a really good question. Obviously, if it's possible it's better to have an opportunity to study them when they're healthier because when a child is very, very critically ill or even dying and we see these things can really-- it can affect your immune labs. But I always say I start-- you're in a situation. You have to start where you are and then if something doesn't seem right or it's very off you may need to repeat it and this is very common. This is not uncommon. So you just repeat the test and see is it still consistent? Or have things improved? The child is healthier now. Or vice versa, when you had the first lap they did-- they were not very abnormal but now they're coming and they're very, very sick. You may see the opposite. So it's just following over time. I think when I first meet families I tell them today is our first visit but this is going to be probably a long relationship. And I'm going to follow you over time and observe and see how things change because our patients don't come with a neon sign that says their diagnosis. It takes time. But if you have the option, obviously, it would be better to have the opportunity to study them when they're healthier but that's not always possible.

Dr. David Stukus: And when do you think about these more involved genetic tests? And before you order those is there anything special that needs to be done such as genetic counseling?

Dr. Vivian Hernandez-Trujillo: Yes. And that's really-- that's a great question. I think every immunologist will have their own response to this but I do believe that if I'm going to have genetic studies ordered or I'll order them then I really want them to have the opportunity to discuss this with a genetic counselor because once I have confirmation-- let's say that I have a patient that the labs are abnormal and it's leading me towards more of a genetic cause or I have a high suspicion but the lab tests aren't helping me, I may order those tests. But I like for them to have the opportunity to discuss them because once you get the test back it can be very daunting for the family. It can be very confusing. And it's important for them to have as much information as possible especially when you're talking about a family who may consider having more children or a late teen patient who may be considering starting a family, you really want to have as much information available to them as possible so that they can make informed decisions.

Dr. David Stukus: Unfortunately, due to time constraints, we're not going to be able to delve into the issues surrounding treatments of the various immune deficiencies and that's a really complicated aspect as well but we'll make sure that we put some information and links on the website as well. Now, before we conclude this wonderful conversation I'd like to revisit a topic that you just brought up a few minutes ago and that's in regards to measles resurgence and vaccine hesitancy which, as you know, has been listed as a top 10 global health threat by the World Health Organization for 2019. And we're seeing a resurgence of vaccine preventable infections. I'd like to have you discuss how this really impacts those children or individuals who have underlying immunodeficiency and who cannot receive vaccines because they're at risk of having infection from those? So what impact does this vaccine hesitancy and decreased rates of immunization have on that cohort of patients with underlying immunodeficiency?

Dr. Vivian Hernandez-Trujillo: Yeah. This is, again, near and dear to my heart. I think as a pediatric immunologist first of all I truly believe in the safety and the efficacy of the vaccines that we have available. As parents and medical professionals we have the responsibility to protect our own children from infections that are preventable. And we also have the responsibility to help protect those who cannot receive the vaccine. So whether it's the young infant who is not old enough and is exposed to pertussis because somebody wasn't vaccinated I think that it's very important for the parents and grandparents. And then nowadays we are asking them to receive boosters. Whether it's the immunocompromised patients, such as my patients with primary immunodeficiency or even patients that are undergoing chemo for cancer, anyone that's immunocompromised the herd immunity aspect is so important to protect us all. I will share that when my brother was 18 months old he had pneumococcal meningitis. This was long before we had the vaccines available. And he came very close to death. And I feel not only from my experience as a professional but what we went through with my brother we had the opportunity to receive the vaccines that will prevent these types of diseases. And we owe it to ourselves and to our children and, obviously, to the other people and all the patients who may not be able to receive vaccines we're really relying on this herd immunity. I think that the return of measles really is a call for all of us to come back and as medical professionals take the time and address the need for vaccination. I think this is really important. And it's something that if we're not changing this path there's going to be other diseases that will return. There's no doubt about that.

Dr. David Stukus: Yeah. Okay. Well, thank you for your thoughts on that. I think it really hits home when you have the personal aspect of it and you take care of these patients as well or have family members who can't receive the vaccines. Well, this was fantastic. And I can attest for our listeners I think this was a wonderful conversation. We covered a whole host of territory and different aspects of this. This really was a great primer in regards to thinking through recurrent infections and when to evaluate the immune system and how to do so. So, thank you again, for taking the time to be with us today. Is there anything else you'd like to add?

Dr. Vivian Hernandez-Trujillo: No. I think just as a pediatrician and parent I think it's important to have open and honest conversations and communication with not only our healthcare professionals and our medical team but whenever as a physician or a clinician you think about a child that presents with infections that don't seem right or the child is not thriving or the parents are just overly concerned please keep in mind the possibility of a primary immune deficiency because they're really not as rare as we all believe. And the patients will not only benefit but you can save their lives.

Dr. David Stukus: Great. Thank you. Thank you, again, for joining us.

Dr. Vivian Hernandez-Trujillo: Thank you so much.

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