Transcription for: PI and Cancer

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Emma Mertens: Alright. Good evening, everyone, and welcome. We are so excited to bring you another session in the immune deficiency foundations decoding PI series. Tonight, we are joined by Dr.
Charlotte Cunningham Rundles, who will be leading a discussion on the relationship between PI and cancer. My name is Emma Martens, and I'm the Program Manager for Education at the Immune Deficiency Foundation. On behalf of IDF, we thank you for tuning in to this virtual event. Throughout this series, guest presenters will provide a deep dive into clinically advanced topics from the world of PI. In offering these programs, we aim to engage and empower the PI community through education.
If time permits, the session will be followed by an audience Q and A with our presenter. During portions of tonight's talk, we will offer audience polls. When a question pops up on your screen, you may submit a response by clicking one of the presented option Also, a reminder that closed captioning is available. This webinar is made possible by our wonderful sponsors. It is reached with our partnership and contributions that we can provide programs like this for the PI community.
Please join me in thanking our sponsors. Before we get started, a brief disclaimer. Please remember that information presented during this meeting is not intended to be a substitute for medical advice, diagnosis, or treatment. We are here today as a trusted source and friend provide you with information. Always seek the advice of your physician or other qualified healthcare provider with questions concerning a medical condition.
Never disregard professional medical advice or delay seeking it based on information presented during an educational event. We're going to kick things off tonight by asking you to answer a quick question using the Zoom polling feature. So everyone should see the pretest that just popped up on your screen. We'll give it about thirty seconds for everyone to answer. And our opening question is, which best describes your understanding of how primary immunodeficiency relates to cancer?
Alright. Thank you so much everyone for answering our poll. Alright. So now I am so pleased to introduce our presenter for this evening. Charlotte Cunningham Rentals is the David S. Gottesman Professor of Immunology, Professor of Medicine and Pediatrics at the Icahn School of Medicine at Mount Sinai in New York. She established and currently directs the immune deficiency program at Mount Sinai. A leading referral service to evaluate and treat infants, children, and adults with a variety of primary immune deficiencies. She serves on the medical advisory board of both IDF and the Jeffrey Modell Foundation and is a longstanding member and officer of the Expert Committee of Inborn Errors of Immunity of the International Union of Immunological Sciences. Thank you so much for joining us, and

welcome Dr.
Cunningham Rundles.

Dr. Cunningham-Rundles: Thank you very much, Emma, and thank you very much for the invitation to join. Let us see whether we can get the slides up in the appropriate way. Are you bringing my slides up now?

Emma Mertens: I can were you gonna share them on your end? I can pull them up as well if that's easier.

Dr. Cunningham-Rundles: I'm going to see what we can do to get mine the way we had them the full before.

Emma Mertens: Okay. Sure thing. Looking good. Perfect.

Dr. Cunningham-Rundles: That's good. Thank you very much.

Emma Mertens: Thank you.

Dr. Cunningham-Rundles: So this is a tough topic because we are going to talk about something for which we don't really know every single piece of information, but I'll tell you what we do know. First of all, just I really want to give you any disclosures. These are companies that I've thought about and worked with previously. And they are really not pertinent to anything I'm going to talk about today. So in what circumstance are we talking about cancer and why are we even talking about it?
Well, for one thing, for the last fifty or so, sixty years, it's been known that people who have an immune deficiency of various sorts are more likely develop cancers. And how do we know that? Well, we know that from organ and for example stem cell transplantation, we knew about that. And we knew it from the standpoint of immune suppression in general, in other words, anyone getting chemotherapy. And third place is that we also knew this also from people who had an HIV infection, but the place where it became much more obvious I think was from the congenital immune deficiencies or the primary immune deficiencies we're talking about today.
So why are we talking about it? Well, we're talking about it because unfortunately we do see it. And the question is, well, why? Why do we see it? What's the problem?
And the other thing I'd like to bring up is, what are the difficulties in diagnosis? Why does sometimes it becomes rather difficult to be sure what you're looking at? The other thing is that unfortunately, we do see a fair number of lymphomas. And the question is, well, why why lymphomas? Why why does the immune system say, I don't want to do the right thing, but I sure don't mind my enolymphoma.
It's a big question. Why does lymphoma occur? The next one is really, like, why well, what have we learned about that? What do we what do we now understand better? And then, of

course, everyone would really like to know if cancer does occur, you know, first of all, how is it treated, but mostly okay?
How does it work? Does it work okay? Do people do well with the therapies that are normally given, or is there more difficulty? So one of the things to mention, first of all, is We know that, for example, patients with primary immune deficiency have more cancers than age matched controls. We are really quite convinced of that and this data was pulled together by several different investigators who were working with the immune deficiency foundations USID net data at that time.
And this data continues to be the same. This was published in two thousand eighteen, but what it says is that we do expect cancer to occur in men and women at a certain age. You know, they We do realize there is a background of that, but cancer was diagnosed more commonly in USID net men and women, as you can see by the colored lines here. It also gives you an idea of the fact that it occurs from the age range of five to nine all the way up to, you know, the more advanced age of eighty five or better. And so it occurs in all ages, and you can see the numbers here in each of those age groups, which is another interesting, you know, phenomenon to say, well, when do they occur?
And what is it more likely? I'm trying to advance. There we go. So how do we understand this? How do we understand these cancer risks?
And I think you'd like to also know, well, okay, who's at risk? So one thing about the immune system, and this is a picture that we have made for the International Union of Immunological Sciences, which is that you think about the immune system in sort of departments. In other words, the antibody making department or the B cell department is different from the T cell department, and that's different from the natural killer cell department. And there's another set of cells that are called the innate lymphoid cells, which have an entirely different purpose. And then, of course, the myeloid cells and eosinophils, which are involved in allergy and neutrophils, which are responsible for chewing up bacteria.
It's useful to think about these things in departments partly because that's the way an immunologist always looks at the immune system when you're first meeting a doctor for their first time, they're going to be thinking, what are where is the difficulty here? Is it going to be in the B cell or in the T cells? Is it going to be, for example, in the monocytes or exactly which of the departments of the immune system is giving us the difficulty? And if you then break it down, there's sort of ten ways that we think about the immune system The first set that the first group there, number one, is the group that's called the severe combined immune deficiency group, where there's really the T cells and the B cells are really not functioning quite normally. The second set is also a combined efficiency, but it has some additional features.
And so in this particular department would be something like Wiscot Aldwych syndrome,

for example, that would be in that area because there's some additional features that really distinguish it from the straight forward severe combined immune deficiencies. Number three, where I spend a lot of my time, of course, isn't what we call the predominantly antibody deficient part of the immune system. And then moving on down, you can see there's diseases of the phagocytes, that's the neutrophils. And moving on down, you can see that there's different ways of looking at it. Why are we making a point about dividing the immune system because it sort of matters about exactly how you look at these particular, you know, immune deficiencies and what you're going to concentrate on Now before I do that, remember that I did show you the study from the United States, but this is not just the United States' point of view.

This happens to be a very large study that was pulled together in Sweden from an international study just to say Alright? So there's more immune deficiency, but what is the most important immune deficiency? Which are the ones that we see the most of? And if you look at the numbers, you can see that the hematologic types of cancers are the ones that are the most common. Now those are the ones that are called lymphoma and leukemia and Hodgkin's disease and other ailments that have to do with that section of the immune system.

We do see other diseases too. There's a little bit of breast cancer, for example, some gastrointestinal cancer, and then you can look along this line and see that there are others as well, but there are really two that kind of matter much more than the others do. This is just another figure from exactly the same paper that just make the same point, which is that hematologic cancers or the blood cancers are really the largest group. Now notice though that the second largest group here is either a multilocation, which is one thing, but then the digestive or the gastrointestinal system, is actually rather a target as well. And I'm just going to mention that in particular because we have, of course, seen quite a few cancers in that particular area.

If we go back to that breakdown a moment ago that I told you, well, where are the cancers? I mean, who is it most at risk? And I think people who are listening are are knowing that they fall into one or more of these categories, For example, either severe combined immune deficiency or maybe the Wiscot Aldridge Syndrome or perhaps number three is mostly the antibody problems. And I'll come to that to break that out on a moment. The ones that I've shaded here, are the ones that are most likely to be developing cancers, and that was the data from the United States.

And by the way, it's also the data from that international study. So these are the categories of immune deficiencies that would be the ones that we are the most suspicious when a patient has something wrong that we think, okay, we better be sure that that's not a cancer. So we spend a little bit more time working on those particular ailments, I would say. Now, this one again goes back to the study that was published from the United States USID

network as well, which is in the United States then fine. You had cancers, but what were they?

And if you take another look, you can see that again Hodgkin's lymphoma, again, was a big one. Hodgkin's disease lymphoma of other types is another way of looking at it. And then leukemia, myelogenous leukemia, and then, of course, other areas of the immune system having to do mostly with the hematologic system, in other words, the blood system or the bone marrow system. It's true that there are other studies as well, the ones that are in the shaded areas are the solid tumors, you know, the breast cancer, skin cancer, colon cancer, bladder cancer, and so forth. Those are a little bit less common than the hematologic cancer.

So everyone is really coming down to the same conclusions. Whether we're looking in the United States or we're looking elsewhere in the world. Now if we're talking about antibody deficiency, this is another way of looking at the antibody system I don't know if you can see my cursor or not, but this is the way that B cells develop. In other words, they develop in the bone marrow, and they move over, and then they commit themselves to the production of B cells. And then those those b cells then mature, then they develop what's called the B cell receptor.

And then the B cell receptor then is going to again be incited by some vaccine or something else in the environment like a virus or a bacteria, and then they will begin to develop and eventually form what we call plasma cell. Plasma cell is a cell which is kind of going to stay on your bone marrow for a very long period time. And it's going to be the one that's going to produce the antibodies to tetanus, to measles, to mumps, to rubella. And I I think of them as kind of the tenured faculty. They they do their job, they only do the one job, and they live in the bone marrow for a very long period of time.

If you look and say, well, tell me more about what those names of those diseases are, these would be the a gamma globulinemia. In other words, the antibody making B cells could never really complete the job. In fact, in some cases, there are no B cells whatsoever, and that would be the X linked or a gamma globulinemia versions. And then other versions called the hyper IgM, which means the job can be partially done, but the job can never be really finished. And then, of course, the very large category called select the common variable immune deficiency or antibody deficiency group, and then a last one, of course, is IG-eight deficiency.

So these are the categories, I would say, of the antibody deficiency diseases. And the reason for talking about these more, of course, is this moment I was telling you a moment ago, is that these are the ones that are the commonist in terms of the cancers. And how do we know that? Again, this is the USID data registry, again, is that for common variable immune deficiency, there were quite a few my lymphomas in both the male and the female population and a number that would be expected in the same group of number of patients

from just US statistics and cancer statistics. It means it was about eight times more than you would have thought was likely to have occurred by just chance alone, just normal every day male or female in the United States.
And for lymphomas, for females, it was again something on the order of seven times more than one would have expected. So we do spend a lot of time thinking really about lymphoma and and what we need to know more about those cells. And it causes a lot of problem, and as you could imagine, now this, in this particular case, this is not USID net data. This comes from the European Society of Immunity, and this is the registry of data that comes from Europe. And it says pretty much the same thing.
So in other words, it's not a US problem. It's really the problem of the diagnosis. So this data was put together. And as you can see, lymphoma was increased and solid tumor was also very much increased And these were what we call the comorbidities or the mortality. Things that actually will cause that person to not do very well in the one hand and on the other hand, perhaps even pass away.
I think that slide is redundant. So I want to tell you a little bit about the data from Mount Sinai because we followed so very many patients over time. So this is the Mount Sinai data. This happens to be the Mount Sinai campus in New York City. You can't really see the building that I'm working in, but it does really front on central park.
It's a very large hospital, but it's very consolidated fortunately for me, because my laboratory and the hospital offices are very, very close in proximity. Now over time, we have followed eight zero one patients with common variable immune deficiency. And over this period of time, we've had thirty three patients with cancers in various organs. Not going into all the tremendous numbers, but that's about four percent we have had. We've also had sixty six patients or eight percent of these patients that have had one or the other form of hematologic cancer, which again is pretty much what I was mentioning a moment ago, which is that the hematologic cancers are the ones that we spent a lot more time thinking about.
Now that's predominantly lymphoma, but we also do see some Hodgkin's disease and also some leukemia And if you know the name, some of these are called marginal zone lymphomas or small lymphomas. And again, I'm just going to put them into the lymphoma category because again, those antibody making cells have made their own decision and they really are lymphomas, they really are not making antibody the way they're supposed to, but they're hematologically abnormal, and they are clonal, and they're really going to be causing difficulty. Now when you talk about the sixty six lymphomas and the eight hundred and one subjects, first of all, it was a little bit more on the women than it was on the men. And the average age at which that diagnosis of lymphoma was made was anywhere between one year old and seventy seven years old. As you can see, it was really diagnosed with lymphoma at a very, very wide range, but the lymphoma was diagnosed between the

ages of eleven and eighty one.
So really a long, long time. Now most of these lymphomas are not in lymph nodes. So I know that those people who are maybe listening realize that in people who have common variable immune deficiency, lymph nodes and spleen are oftentimes enlarged. But the lymphoma doesn't necessarily occur in this location. It may be an entirely different location.
For example, we've seen quite a few in the lung. In other words, not in the lymph node, but in the lung itself. Sometimes in lymph nodes, but we've also seen them in the gastrointestinal tract. And we've seen it sometimes in a diffuse way or even in the pelvic nodes. We've had one or two in the parotid gland and also the abdomen liver spleen and if you go down the list, you can see that you don't find them in the places where you think you should find them People think of lymphomas being always in a lymph node, but in fact, that's actually not the case when it comes down to common variable immune deficiency. They don't seem to want to stay in that one location. Now one of the questions that always comes up and we've tried to look at this and it's not been very easy, which is that were these more common in the patients that already had some kind of inflammatory features And the answer was sometimes yes and sometimes no. So the answer was not completely clear, but Tanisha Smith who is now in San Diego put together the data that we could a few years ago and I haven't updated this slide But at the time that we did this, those who had lymph gland increases or a larger spleen than normal, that would be spleenomegaly, or those who had some GI enteropathy with or without some degree of malabsorption of nutrients lung disease and bronchiectasis. You can see that in some cases, the answer was yes. But in many cases, we would find it in people who did not have any of these particular issues.
So it wasn't as if the previous history gave me a clue that I should look a little harder or not look a little harder. It wasn't easy to make that final decision. So I guess one of the big question is, why do patients with a loss of antibody function develop more cancer? And you can go back and say, well, there's a couple of reasons for that. And one of the big ones is, of course, that there are actually many, many more patients with antibody deficiency.
In anyone's medical practice than there is any other primary immune deficiency. It's just much more common than any other immune defect. So antibody deficiencies are somewhere around seventy percent of all the immune deficiencies And so in a way, because there's many, many, many more patients with these deficiencies, it's not too surprising that we might see more cancers. And there's another factor too, which is that most patients with antibody deficiency actually do rather well. On gamma globulin, go to work, go to school, go on vacation, do all the usual things, have families.
In other words, the life expectancy of a patient with an antibody deficiency is actually quite good. And that means there's actually a lot more time for that lymphoma too have actually

developed. So we can really look over the ages and just say, well, that's why we're seeing people at sixty, seventy, and perhaps even older. Developing a lymphoma because in fact they had a chance to make it to that age group. So I don't think it's easier to say that there's a increased propensity two cancers and antibody deficiency is just these two facts really are overwhelming.

But I'm going to tell you about a couple of our patients here. And so one of my patients She is actually sixty two years old now, but she was diagnosed with a lymphoma at the age of forty four, but I had known her for the twenty years before that because she was first diagnosed at the age of twenty four. And you can see her IgG, her IgA, and her IgM are incredibly tiny. She really had almost no gamma globulin. She had kind of a late diagnosis and reason why was she had a chronic cough and she was a smoker.

And everyone kept thinking, oh, you know, you're a smoker. So yes, sure you have a cough. But in fact, she actually had a cough because she actually had lung damage. So at the age of forty four, then she had a oncoscopy, then she had some follicular bronchialitis, which is just an inflammation of the lungs. And then finally, her lung functions were stable on gamma globulin, but at the age of forty four, then she developed an area of a mass above left kidney, and it was found really by accident because we were looking at her lungs on the x-ray, but what happened is that the x-ray cut took a little bit of the edge of the area of the kidney, so you could see, oh gosh, what's that?

An area of a mass was there. And so when that was done, it was like, oh, dear, what is that? So she had lymph nodes in the abdomen, and then that was biopsied, and that actually was a lymphoma. And she then had lymphomas infiltrate. It was called a marginal zone B cell lymphoma.

She was treated with conventional chemotherapy, the usual therapy, and she also got Rituxan, which is a way of kicking off all the B cells that are abnormal, good ones and bad ones, by the way. And she just is is she's fine. Now it's almost twenty years later, and she's fine. And I recently saw her and we do not expect a recurrent civil lymphoma. She actually has gotten over this lymphoma with the treatment that she was given.

This is another patient to mine a forty five year old man with common variable since the age of twenty. Again, extremely low levels of gamma globulin in his case as well. He was put on gamma globulin And here it is, twenty three years later, he had weight loss and an abdominal mass on the jeuneum, which is part of the gastrointestinal tract, and it was resected. He had some surgery. He was given the usual chemotherapy.

That's the CHOP, CHOP, that's what a chemotherapy regimen. He also got rituxan, and he's now fifty nine years old. But quite a bit of time later, he's now doing extremely well with no difficulties. And Again, I saw him recently. So, again, conventional chemotherapy, the one that everyone should be on, usually including rituxan, is really a wonderful treatment.

Now, I won't say that's true for every single person. This is another patient of mine. The heat

had IT at the age of eleven. He was very low on gamma globulin. He had almost no B cells at all.
He's put on gamma globulin. When he was forty one years old, then finally, after, you know, three decades worth of gamma globulin, He was having some diarrhea, and he had Giardia, which is a common bacterial substance in the GI tract, but it didn't really clear up with a metronidazole, any abdominal pain, and then some obstruction. And with that, then he finally had a CT scan of the mass That's a pet scan over on the right hand side and that just shows you it's an area of the active lymphoma which was present in the jeuneum which is part of the GI tract. And again, he had plasma, blastoid lymphoma, again, hematologic cancer. He had quite a bit of chemotherapy, but he did not survive.
This was a very, very severe cancer, and he did not survive. So lymphoid malignancy and CVID do occur in about four percent to six percent of patients. Almost always, it's those antibody making cells that did not make immunoglobulin, but they became malignant instead. And we don't have good answers for that, but I've always assumed that what they were doing is they were being activated and they just simply could not finish that job, they couldn't do their normal job, and they began to develop some mutations. But the diagnosis and the accurate diagnosis actually turns out to be rather challenging.
And I'm going to tell you why that's the case, because it matters. It matters really a lot. So because you can have this lymphoid hyperplasia, as I mentioned a moment ago, and so many people with antibody deficiency having a large spleen and lots of lymph nodes, you know, there's always a worry that that person may have lymphoma. And so, yes, we do biopsy frequently and we do check when we need to when things have changed. And so the problem is that it's a little bit difficult to tell the difference between the non malignant lymphoproliferative disorder and the overt lymphoma.
It's a little bit hard to recognize on occasion, and that's why you really have to biopsy and be absolutely sure which why it would be the case. I'll tell you a little bit more about that, and that's what it looks like when you look under the pathology. In other words, the lungs over here on the left hand side are really crammed with antibody making B cells, and that's what the brown stain is. Those are B cells. They're in the lung and they are not malignant, but they've gone to the lung because there's some bacteria there and the antibody making B cells are attracted to that location.
In the lower area there, those are T cells which have decided they are going to the lung as well. For the same reason, they're being called there because there's some area of inflammation and that's what the T cells job is going to be doing. Over on the right hand side, you can see that there's lymphocytes in the liver and there's there's collections of of lymphoid aggregates in the abdomen. That's where that arrow is or in the spleen. That's what the spleen is.
Those little white marks across the spleen, each and every one of those is a lymphoid

follicle or in the lymph nodes. So one of the things that's confusing in hypogammaglobulinemia is the lymphocyte sometimes go to the organs where they are not malignant. On the other hand, they are rather immature looking. And this has tells you the same story. I don't know if you've ever seen a can't scan of the abdomen or fore before, but these are pictures of I two guys and one lady who have very, very large spleen.

And I can tell you right off the bat that the middle one is actually a detective on the police force at New York City, and he goes to work with a very large spleen. Just exactly as this large hair. We don't really like to take out spleen ins and so we have the spleen and it's simply there. On the other hand, if you go to a physician, they'll be saying, oh my goodness, the spleen is huge. Maybe it's got a malignancy.

For CBID, generally, that is not the case. The spleen is generally just enlarged because it's under pressure to actually expand and do even more of a job, but it does not make it malignant. These are all very immune deficient subjects, but none of these have cancer. And so this makes it difficult for the physician, makes it difficult for hematologist, to be honest with you. And the reason why I'm making that point is that although we've had the lymphomas that we've had, we also have had six patients who were diagnosed with lymphoma on very careful biopsying with expert advice, it's actually not lymphoma.

Now a couple of these patients were actually given chemotherapy even though it was not a lymphoma. If you look down the list, see course of chemotherapy, you can see several of them either got Rituxan or other you know, chemotherapy agents. But in fact, that was not the final diagnosis. The final diagnosis with just reactive lymphoid hyperplasia. So it matters to try to get the diagnosis as right as you possibly can And that's going to mean looking at expert advice.

It's going to be really having that study re read by somebody who's used to looking at common variable immune deficiency. So I think confirmation of the diagnosis when you think it's lymphoma is really essential That's because these large nodes and larger than normal spleen are going to be common in this aortic, that's not cancer. And the other thing to mention is that the expanded number of these cells, sometimes they're even called clonal which usually means cancer. On the other hand lymphocytes are also commonly clonal, income and variable immune deficiency. And that's not just my opinion, that's the view of everyone who studied those cells they don't really expand normally and therefore they look just way too similar and that would be a clonal look.

So that's the reason why it's so important to kind of get this right because nobody wants to get chemotherapy when that's not the issue. So detection and accurate diagnosis is actually sometimes rather challenging. And if there is lymphoid hyperplasia, then you really, in most cases, are going to have to do a biopsy to say, okay, let's check that. Why not? Let's just be sure.

And then accurate histologic diagnosis has to be done as well. The other reason why it's

difficult is the classifications of lymphoma was established for immune competent patients It was never really established for those who have common variable immune deficiency. So they can look somewhat abnormal even though they are technically really not malignant. And that's just one of those things to really remember. And the other thing to mention that little last point on that slide is that the PET scan can look abnormal too because remember that the lymphocytes are always being activated.
That's what a PET scan does. It looks for activation. It looks for the use of oxygen and for metabolic activity. But if you have an antigen in your system or there's a bacteria a little bit in the system, the immune system hasn't taken care of it completely, then a pet scan can act should be lit up even though it's really not a lymphoma. So the reason why, we do believe it's true, but the question is, okay, well, tell me why.
Well, there's lots of reasons why. One is, of course, the t cells do not work normally. Cell mediated immunity, which control cancer, is not entirely normal. There's really not enough of the cytotoxic t lymphocytes that could recognize a tumor cell they don't really recognize the abnormal cell, and so they don't get rid of it. And the other thing is we all understand that chronic infections can lead to persistent inflammation, so the immune system is always coping with extra drive to do some chore.
And the other thing is remember that there are a few things that on their own are a little bit oncogenic. In other words, they would lead towards the development of cancer. And one of them is the bacteria called helicobacter. Which has been associated very much with stomach cancer. And then, of course, those oncogenic viruses, which is going to be Epstein Barr virus, which drives lymphoma in some, and then papillomavirus, which can also drive in lymphoma can drive cancers as well.
So those things are all true, and we understand that. And the last component to mention, of course, is there may be some genetic mutations. In other words, if you have a DNA repair defect, in other words, if that's the reason why there's an immune deficiency is because the DNA damage repair defect is present, that may also mean that you can't really repair the damage of anything in which case that would lead to cancer. Cell death defects, cell cycle checkpoints that would be for an ailment called cartilage hair hyperplasia, and then cell division defects so the genetics alone could actually, in some cases, kind of, predict that that might be a person who's more likely to have a cancer. So if you sort of look down the chain of command here, you could say DNA repair isn't normal.
Genetic defects can contribute, and then you have chronic bacterial infections with things that may be driving towards cancer. The T cells are exhausted because they're so readily dealing with antigens and viruses and bacteria that you may have inflammation that just can't be controlled, and then defective checkpoints, impaired cell growth, and impaired death. And in a way, it's surprising we don't see cancer much more commonly. But these are some of the many reasons that have been used as reasons for cancer in patients with

primary immune deficiency, and they they're all true. They all hold water, and they're all true, and they all contribute.
So if we're gonna talk about genetics, let's talk about genetics a moment. I concentrated a little bit more on the B cell deficiencies just because those are the ones in which lymphomas are more common. And I'd like to say that B cell deficiency diseases contributing towards antibody deficiency have turned out to be many surprises because it turns out there's at least sixty different genes that can give you a B cell deficiency disease. And it's very strange because some of them really operate what should have really taken away the ability to make any antibody making cells or B cells at all actually just impair the way that they are formed. And so the way that these are lined up is according to those that work in the early ages of B cell development all the way through the middle ranks of B cell development.
And all the way up to the final act in which you're trying to make an antibody memory b cell or a plasma cell that will last a lifetime, and sometimes that's where the error is. So the error can be anywhere along this entire spectrum of immune defects. And it's extremely challenging, actually, we spend a lot of time thinking about the antibody defects. Some of them are making are true because the B cell itself has the abnormality. But in some cases, it's just because the cell is really not getting their stimulation from another cell in the environment, but all of them will end up contributing towards the same lack of antibody.
Now, there is one gene defect that we do know is more likely developed with lymphoma than any other And that happens to be this one, which is the PI3 kinase of the delta version, and this is a characteristic picture, a patient of mine, twenty year old girl, followed from the age of five with hypogammaglobulinemia, also some intraopathy, She had interstitial lung disease, dexamaglia and lymphadenopathy. And over time, as we got to know her and DNA testing became available, we found that she had a mutation in this PI3 kinase gene. And so she had the ailment that we have now termed APDS. It's pretty uncommon. I would say we've only got four or five of those patients in all the patients that I've ever seen, and so it's not the commonest cause, but it does say that when this is all when this is the case, the chances of developing a lymphoma are certainly increased, and that is exactly what happened with this young lady and she ended up having a bone marrow transplant and she did not survive.
So this is the only gene that we can really put our finger on and say this is the one that gives us difficulty. So although I showed you the slide a moment ago, back on the other slide that was, you know, this one here, the only one that we can really say, has got something to do with lymphoma is this one. And that's really, unfortunately, a rather limited number. But we have actually done quite a bit of genetic studies So these are the gene variants that we found in four hundred and five of our patients who developed either cancer of one sort or the other. In some cases, it was not lymphoma, but it was a cancer of an organ, for

example, esophagus or bladder or the mouth cancer, ovarian cancer, gallbladder cancer or rectal cancer.
These were some of the genes that we had found in those circumstances and then other genes that we found in lymphoma and leukemia. But it doesn't mean that everyone who has a mutation in this gene or the set of gene is likely to develop a cancer. It just means that we are always searching for additional reasons for understanding what to do next and also reasons to really know understand more about why the immune system is not really accomplishing the tasks that we want. So what's the best treatment for the cancer? And how do patients do?
And when a cancer is diagnosed first and then treated, how can you know if there was a primary immune deficiency in the beginning? How can you know that? And both issues are difficult. First of all, the standard treatment is that which is the one we always suggest. There's only one caveat to that, which is that if there is a patient who has a radio sensitive mutation, and that is, in particular, a DNA repair defect or a taxi telangectasia, then radiation is something which is either going to either be only accomplished by great reduction of dosage or emission of the alkylating agents and also emission of radiation.
In other words, those methods of treatment would not be used under that circumstance because the immune system really will have some deleterious abnormalities results from that particular therapeutic method. Other than that, standard recommendation is the one that works. The only other thing to mention, of course, is that if you are doing immune suppression, it will predispose to infections. And so in some cases, using antibiotic prophylaxis is important And the other thing, which of course is, you can understand, is readily, completely essential. If you have a chemotherapy that's going to take away your antibody production, it's going to impair the antibody production or if there is already an antibody deficiency state, you have to be absolutely convinced that you are giving adequate replacement of the gamma globulin.
It's really critical to be sure about that. Now in some cases, in some cases, it actually works quite well to think about using a stem cell transplant. And some patients with common variable immune deficiency with lymphoma have had a stem cell transplant, and it actually has really proved to be successful in really not a small number of cases. But I think the general overall view here is that when there is a cancer, it's going to be treated by all the things that would be done if it was your neighbor. In other words, it's going to be the same therapy given to anyone depending on what the nature of the therapy is and what is the best practice that's currently under undertaken.
Now, I think there's one last question and this is just about the end of what I wanted to mention. Which is that when the lymphoma or the cancer comes first, and chemotherapy leads to immune suppression. How can you decide if the patient actually has a primary immune deficiency? And it's difficult to know because you may not be able to tell if you

have a history of very significant infections in the previous moments. In other words, somebody says, oh, yes.
Right. I had a bad pneumonia when I was fifteen or twenty or twenty five and had to be in the hospital. Oh, yeah, I had I had meningitis or I had a bone infection or I had some significant recurring infections, then you can be a little bit suspicious. If there's a history that the spleen has always been enlarged or the lymph glands have been enlarged and the patient says, oh, yeah, I've been told that before, and my spleen is big. Then again, you know, it might be a little bit more likely that person has an immune deficiency.
And of course, if you do have a genetic mutation that's found that suggests immune deficiency, then, of course, that would be another way of being a little bit more sure that cancer was found in the presence of an immune deficiency, or maybe if there was perhaps a family history, that would be the only clues that I can think of that really help. It's something which can be quite important because sometimes you actually don't know whether it's the case or not. It's very hard to be sure, and this particular woman is really characteristic of that, which is she's forty three when I met her, And she'd had profound a fatigue diary of abdominal pain and a cat scan showed that she had a mass on her left kidney, and then she had a partial removal of her kidney because it was a motley lymphoma, which is a a mucosal associated lymphoid tissue lymphoma. She got Rituxan in two thousand and twelve, and then by the time anyone checked, she had an IgG in two thousand and thirteen. She was IgA and IgG and IgM deficient.
At that point she was diagnosed with common variable immune deficiency, but remember that Rituxan can really lower your gamma globulin levels. And sometimes it does that for many, many years and maybe even permanently And so for that reason, she was diagnosed with CVID, but she wondered whether she really had CVID in the beginning or not, and we actually had a difficult time trying to think about it. She had a pet scan, showed some positive lymph nodes. She was then treated again with Bendamustine and Rituxan, and then she had more symptoms of itching and bruising, and then she had more lymph nodes. She had night sweats.
She had lymph node biopsy, and it showed there's some granuloma. She was treated with trucks and again, but now she's forty nine. And the question is, does she really have CVID from the beginning or she does not? Well, she's healthy now. I said she was forty nine when I made the slide.
I think she's now fifty five. And she's working as a teacher and she's actually fine. She is on gamma globulin because she is immune deficient. But did she start with IVIG? She doesn't have any history before two thousand and eleven.
Number one, she has no family history. And the last component is we don't find any genetic reason to understand why she might be having CBID or even an immune deficiency either, so in a way it remains a mystery. So we honestly can't determine if she had the immune

effect before she had the lymphoma. We don't know. Does it matter?
Maybe it doesn't matter because if she's immune deficient and she has low gamma globulins, then you know, we're going to give her gamma globulin anyway. It's not going to alter our treatment now, but it makes a bit of confusion I must admit. So conclusions.
Unless patients with immune deficiency do have an increase in cancers overall, And that's due to a number of reasons, which is defective immune surveillance, reduced clearance of abnormal cells, and to some extent, genetic defects, which we honestly don't completely understand as of yet. Patients with antibody deficiency have an increased incidence of lymphoma.
We are clear about that. Most of those are B cell and type. Very few of them are actually Epstein Barr virus positive. That's just the way that our cancers have been looking.
Lymphoma certainly leads to more morbidity and more mortality.
It's possible that they're a little bit more likely in subjects with other inflammatory conditions In other words, if you know the spleen is big, if you know that the lymph glands are swollen, it might be a little bit more likely, and we're a little bit more inclined to observe those patients very more carefully. Genetic defects are found in only about thirty percent of cbID subjects. But aside from the PI3 kinase catalytic domain gene, none of them are clearly associated with lymphoma. And then as I said a moment ago, the lymphoma is noticed first and then treated with chemotherapy. Sometimes it can be quite difficult or maybe even impossible to decide if the patient has had a real underlying CVID to begin with.
But I think I'd like to make the point that patients that I, in my experience, and remember, we've seen eight hundred and one now, do actually very well with chemotherapy. And I think Rituxan has been a tremendous help to us It's really helped us because it's a way of just getting rid of the abnormal cell and doing very little else as well. But that's my last slide, and I have many wonderful collaborators at Mount Sinai, Rockefeller University, University of again Stanford University, the Carolinsk Institute, and then my friend in Barcelona, Spain. So thank you very much for the chance to talk to you today about this topic.

Emma Mertens: Thank you so much, Dr. Cunningham Rundle. That was incredible. So to our audience, we now do have some time set aside for Q and A. Please know that we will get through as many questions as we can.
But I do just wanna let everyone know. We have a pretty decent audience tonight, which is wonderful, but we may not get to every single question. So we definitely appreciate your patience. And again, we'll get through as many as we can time permitting. Alright.
So if you can just give me one moment, we're gonna go ahead and get started.

Dr. Cunningham-Rundles: Really stop sharing here?

Emma Mertens: I just stopped it and okay. There we go. We're all set to go.

Dr. Cunningham-Rundles: Alright. Good.

Emma Mertens: Alright, everybody. So we're gonna go ahead and start with the Q and A. Okay. Alright. So this first question, this individual says great lecture.
Thank you. From your perspective, should people who have a PI adhere to a standard screening schedule for cancer? Is this different for specific types of cancer such as gastric or gynecological?

Dr. Cunningham-Rundles: I think standard, you know, things, but on the other hand, suppose that some symptom, you know, comes about in the meantime. In other words, some gastric upset, for example, or a lymph gland appears, or a little nodule appears. You know, I think that would be the time to say, listen, let's just go and check this out. Because, again, it's usually easy to do some small checkups just to say, is this a problem? You know, just give me just tell me that.
I don't believe in people walking around being a little bit concerned about themselves. You know, if there's a little bit of difference, you know, just check it out. I think makes sense to me.

Emma Mertens: Certainly. Thank you so much. All right. This next individual asks, they say I have hypogamoglobulinemia and primary myelofibrosis which they shared is a rare blood cancer. Is there any reason to believe they are related, both are conditions related to deficiencies in the blood marrow?

Dr. Cunningham-Rundles: I think we end up having to conclude the answer would be yes. I think the immune system is always trying very hard to come up with a solution for its problem. In other words, if it's not doing the correct thing, oftentimes, there will be more fibrosis or more inflammation which can occur. So I make the conclusion that those things are inevitably linked between each other. I don't see how I could separate them, to be honest.

Emma Mertens: Sure. Thank you. All right. Next question. Dr.
Cunningham Rundles, I think you did cover this earlier, but someone asked, so I just want to drive the point home. Would immunotherapy treatment for cancer work in someone with CVID?

Dr. Cunningham-Rundles: So the question is what immunotherapy are we talking about? Are we talking about something which then is going to, for example, CAR T cells, which you may have heard about? It actually works quite well because in a way what you're doing is you're just eliminating the abnormal cell which has not made the right decision. It's done the wrong thing. On the other hand, it can be eliminated.

So in many cases, the immunotherapy can work just extremely well in a patient with an immune deficiency. And I would not say that it would not.

Emma Mertens: Thank you. All right. This next individual asks, how can I find a clinician who has expertise in both cancer and primary immunodeficiency? They say that feels like finding a unicorn. I wouldn't even know where to begin.
This is actually the first time I've ever seen this topic covered.

Dr. Cunningham-Rundles: : That's interesting. Yes. What we what we have done when we needed to and in fact, this is not uncommon to get a slide re read at another institution. For example, of the National Cancer Institute, for example, Foundation Medicine, for example, Sloan Kettering, for example, Many pathologists are very capable of sending a slide with an abnormal tissue to another institution to say, please give me the second opinion. Tell me what you think about this.
And I do know that the National Cancer Institute is actually a little bit aware of this problem. And so I would suggest that you get it read by a secondary authority, actually. And and pathologists can do that. They don't have to know that person. They can submit it as a second as a request.

Emma Mertens: That is great advice. Thank you. Alright, this next individual says, to clarify a point from earlier, does having a PI make it more challenging to get an accurate cancer diagnosis?

Dr. Cunningham-Rundles: I would say yes. Unfortunately, yes. Partly because if your spleen is bigger than normal, that may be just the way a person with an antibody deficiency is. Hyper IgM syndrome, it could happen to be that's just the way your system is because it's trying really hard to help you. Mhmm.
That's the way I look at it anyway.

Emma Mertens: Thank you so much. Alright. This next individual shares, I have c v I c v I d and am a breast cancer survivor. Anecdotally, I feel like I know a lot of people with PI who have also had breast cancer.

Dr. Cunningham-Rundles: Yeah.

Emma Mertens: Are there any plans or future studies to examine that potential correlation?

Dr. Cunningham-Rundles: I think the only way that we can do that is using the big studies, the national studies, and USID, net studies, for example, we did see a fair amount of breast cancer. On the other hand, you have to think good number of women have CVID, and those women may get breast cancer just because they may get breast cancer.

Emma Mertens: Sure.

Dr. Cunningham-Rundles: I mean, the VRCA locus, you know, would be something which could be checked out as well just to say, is there any connection between that and this particular patient? Just to see that would be an added negative. Let's put it that way. Family history would be another additive negative, but I don't think there's a close association between thinking that. It just does occur in women and women who have CVID generally do live to be fifty, sixty, seventy years old, so it's not too surprising that you're going to see breast cancer.
So I don't think it's going to I don't think I know the numbers to be enhanced. Let's put it that way.

Emma Mertens: Sure. Sure. Thank you. Alright. Our next question, this individual says, I know this may vary, but what is the approximate number of days to separate IVIG and Rituxan infusions?
How far should we space them out?

Dr. Cunningham-Rundles: That's very difficult. We do find that problem ourselves when we're giving Rituxan. They're not supposed to be given closely together if you can, but if you're getting Rituxan once per week for four weeks, and you're supposed to be getting your IVIG every four weeks, every three weeks, you know, it's gonna be difficult on the calendar to figure that out. So generally, what we try to do is to separate them at least by one week. We sometimes, we don't have a choice to separate it further, but ideally, a little further is better.
Because, you know, you don't want to mix those two therapies up. It's true. You don't want to give them on the same day. That is positively correct. They're right about that.

Emma Mertens: Sure.

Dr. Cunningham-Rundles: That's great as much as you can.

Emma Mertens: Thank you. Alright. This next individual asks if permanent a gamma globulinemia is caused by something like rituximab to all the risks that come with a true CVID diagnosis still apply, for example, increased risk of cancer, GI issues, etcetera. Or are low globulins the only thing to worry about?

Dr. Cunningham-Rundles: That's a very, very, very, very good question. And I congratulate the person to ask that one because it's a difficult one. We don't know the answer honestly. And especially if we don't know that that person has an innate immune deficiency, we don't know that. But I would assume that the major thing is to continue to get the gamma globulin up to normal, make it as reasonable as it possible to keep good levels into the blood, and then do the normal cancer screening that one might do and be a little bit on the

lookout just in case.
There's no good answer to that question.

Emma Mertens: That was a tough one for sure.

Dr. Cunningham-Rundles: Yeah.

Emma Mertens: Alright, next question. If someone has a certain type of PI like CBID, but not cancer, is there anything that they can do to reduce their chances of developing cancer at some point in life?

Dr. Cunningham-Rundles: We don't honestly know of anything. I I do, every once in a while, want to think to myself, you know, please do wear your sunblock. I do have patients who have some I know that there's an immune deficiency of some sort, and then I see them walking in, you know, with no sunblock on and playing baseball outside, you know, it makes me worry a little bit. But but that's the only, you know, thing I can think of that you can do to diminish your risk there is no other aortement. There's no other reason that I can think of that you can diminish it.
:

Emma Mertens: So just taking sort of common sense precautions.

Dr. Cunningham-Rundles: The common ones in checking the usual physical examination things, if there's a little bit of a lump or a node that seems unusual. You know, get it checked.

Emma Mertens: Sure thing. Alright. Next question. What symptoms typically raise alarm bells for screenings, specifically in PI patients in your experience you mentioned just now if you have a lump or some sort of irregularity, but what what else?

Dr. Cunningham-Rundles: Swallowing difficulty. I've seen every single thing. Mhmm. Swallowing problems. I mean, so many of the cancers that I've seen have been found almost by accident, like the lady that we were looking at her lungs and it turned out it was in her kidney.
Mhmm. But it doesn't mean that I want to get everyone to do CAT scans yearly. I don't think I would plan to do that.

Emma Mertens: Yeah. Thank you.

Dr. Cunningham-Rundles: That's a tough one.

Emma Mertens: It is. It is.

Dr. Cunningham-Rundles: Yeah.

Emma Mertens: Alright. Next question. Due to cancer treatments, how are primary and secondary PIs determined after treatments are completed. So this is sort of a chicken and the egg situation type of question. Could I have had a PI before my cancer diagnosis?

Dr. Cunningham-Rundles: Yeah. The chances are that that could have been the case I know that that's being worked on quite a bit by several investigators to see if there's any tip offs. And the honest truth is the tip offs that I gave are the only ones that really work. In other words, a genetic mutation to family history, early history of infections, early history of, for example, shingles, somebody who told me they had shingles when they were twenty five, I'm thinking, well, you probably didn't have any antibody either. You know, so it's little chip offs that think something's not quite okay.
We knew that. We sort of knew that.

Emma Mertens: Thank you. Alright, next question. So other than certain, you know, having a certain PI like you mentioned, APDS is more prone to developing lymphoma. Other than having a certain PI and genetics, are there other factors that could increase my chance of developing cancer? Having to do with blood or tumors?

Dr. Cunningham-Rundles: I don't think we know with any other one factor that's going to increase that. I suppose family history must weigh in in some fashion. In other words, the family history of some particular cancer, you know, would be probably pushing one towards a little bit more surveillance. But other than that, no, I don't think so.

Emma Mertens: Thank you. Next question, are PET scans held helpful in people with CVID or does it just tend to lead to more questions?

Dr. Cunningham-Rundles: That's an excellent question. And the answer is it can also lead to a lot more questions because the spleen is going to always light up. L lymph nodes are always going to light up. And then that makes everyone very scared and nervous because they think, okay, gosh, that's got to be a cancer, but the answer is no. That's the immune system working hard.
And so the answer is difficult. That's that's we that's why pet scans really have to be used carefully in people with common variable immune deficiency because those lymph nodes are going to always be bright. That's just the way they are. Thank

Emma Mertens: you. All right, next question. This individual shares they have CVID and have had four different cancers so far. Is your preference for radiationSBRT where possible over systemic chemotherapy due to immunosuppression?

Dr. Cunningham-Rundles: I'm not sure I got the question.

Emma Mertens: I think they're asking having had four cancers and having had CVID. Mhmm. Would you recommend radiation over systemic chemo due to immunosuppression?

Dr. Cunningham-Rundles: It depends entirely on the nature of the cancer. In other words, it depends on what is going to be the recommended treatment for that particular cancer. You know, if either radiation is going to be useful for some and not for others entirely, and I would go by the usual recommendations. Because the idea is to is to do the best job you know how to do. Thank

Emma Mertens: you. Alright, next question. What is the next big step in genetics needed for payers to be able to use as a screening tool when PI is suspected?

Dr. Cunningham-Rundles: Well, it in few, you know, payers don't always really actually want to even cover genetics at all as you probably realize we still do have that problem. Mhmm. And it's not useful to be a screening tool either because, as far as cancer is concerned, because so few of them are so clearly associated. We scarred Alderich, for example, and cartilage -hair hypoplasia, and some of the DNA repair defects, are associated with more cancer, no question about it. And so if the family history is there, I think one could make the case that one needs that in a certain family member, just to be sure that that was or was not going to be the case for that particular member.
But it's a little hard to make the case for some of the other mutations that simply tell you, okay, that's part of the CVID picture. And if kappa b one, and if kappa b two, we have no reason to think they're associated with cancer one way or the other.

Emma Mertens: Sure.

Dr. Cunningham-Rundles: I would have a hard time making that argument with an insurance company.

Emma Mertens: Thank you. All right, next question. This individual wants to know, do you have any more specific information for someone living with WHIM syndrome? Do you know of any WHIM patients or have you treated any patients with WHIM and Lymphoma?

Dr. Cunningham-Rundles: I have not had a patient with WHIM who has had a lymphoma. We've had – it's a relatively rare diagnosis at the moment. We've had several different families. We made the diagnosis recently and a small child. It is associated with lymphoma in statistical sense, but those were with large patient groups.
For example, the NIH patient group has seen a few. But I don't think it's something which has been characteristic of that ailment.

Emma Mertens: Thank you.

Dr. Cunningham-Rundles: Yeah.

Emma Mertens: Alright. A few more questions. Questions are slowing down. So we have a couple more we're gonna go through. And then we're gonna move on.
These have been great questions, so everybody. Thank you so much.

Dr. Cunningham-Rundles: We ought to write these down. They're terrific questions.

Emma Mertens: I know. I know. Our audience is really nosed really nosed a great question. So I

Dr. Cunningham-Rundles: don't know. They really do. I'm impressed. I mean, they're that they're slippers. Which is what is important.

Emma Mertens: Yep, definitely. Alright. This next individual shares, I had an IgG level of one thousand years before I was ever diagnosed with lymphoma. Does this rule out a previous CVID diagnosis? And they say, I know you can't exactly speak to my situation, but every bit of advice helps.
Thank you.

Dr. Cunningham-Rundles: It would speak against it. Yes, especially if the IGM were normal. So take a look at the other numbers, not just the IgG, but it would speak against it. Yes.

Emma Mertens: Thank you. Alright. And then I think we're going to have time for about two more questions I've study. Alright. This next person shares, they have a thirteen year old son who has CVID.
Is there an age in which typical screenings should occur specifically for PI patients? So speaking of like colonoscopies, mammograms, etcetera. Specifically, in relation to children, do the ages at which we start screening change? Or are there any sort of more in-depth specific tests that we should request for our children with PI?

Dr. Cunningham-Rundles: Not in particular, but one would pay attention to swelling or lymph glands. And perhaps if a person has some symptom, for example, gastrointestinal symptom or cough or some other area that points to some some some alteration than than you would than you would go further, other than that you would not.

Emma Mertens: Alright. Sure thing. Thank you so much. Okay. I'm gonna give it a few more moments just to see if any more come through.
And, actually, someone asked something earlier that I thought might make you chuckle, not to put you on the spot, but we did have someone ask if you were taking new patients. So I thought I would just throw that one out there while we're here.

Dr. Cunningham-Rundles: Oh, I saw new patients today.

Emma Mertens: So yes. So the answer is yes, I think. Right? That'll I'm I'm sure that'll make whoever asked that question very happy. Alright.
We're gonna give it just a few more minutes to see if any more come through, but I think we are slowing down.

Dr. Cunningham-Rundles: Okay. Everyone wants dinner.

Emma Mertens: Yeah. I know. Definitely. Alright. Let me see.
Okay. You know what? It's looking like we have gotten through all of our questions that we can ask tonight.

Dr. Cunningham-Rundles: Yes, ma'am. I hope you wrote them down. You you have them recorded. So

Emma Mertens: We do.

Dr. Cunningham-Rundles: I I think they're the ones that everybody wants the answer to.

Emma Mertens: Yes. Exactly. Exactly. Sure. Yeah.
Exactly. But this was amazing. Doctor Cunningham Rundle, thank you so much. This was such a needed and requested topic for our community. So

Dr. Cunningham-Rundles: It's a tough one. It's a tough one, and we need it. We do.

Emma Mertens: Definitely. Definitely. And you can see by the numbers of folks who joined us tonight that it's a in demand topic and people are craving the information really needing it. So thank you so much for joining us tonight, for sharing your time, and your expertise with us. We are so appreciative.

Dr. Cunningham-Rundles: Absolutely. I'm just copying down some of these questions because Sure. So many good questions. Yeah. Online.

Emma Mertens: Yes. We we learn the most from our community. So everyone, we also really appreciate your engagement asking such thoughtful questions. Thank you so much. I'm

Dr. Cunningham-Rundles: I'm very appreciative, you know. It's just exactly what people want to know.

Emma Mertens: Definitely. Definitely. Alright. Well, doctor Cunningham Rundles, I know you wanna get on with your evening, so I I know you were copying down a few questions. I'm gonna keep going through our slides so we can get everybody wrapped up and on their way

this evening, but we just wanna share.
We're so appreciative. Thank you so much.

Dr. Cunningham-Rundles: You are very welcome. Bye bye, everybody. Have a good evening.

Emma Mertens: Take care. Thank you.

Dr. Cunningham-Rundles: Bye bye.

Emma Mertens: Alright. So with that, we're gonna wrap up our Q and A, and I have just a couple more IDF resources and upcoming events to share with everybody, and then we will kind of be on our way and close out the webinar. So in case you don't know, primary immune dot org is your go to website for additional resources, upcoming events, and more. All IDF materials are free to access, print, or have mailed directly to you. If we didn't get to your question during the program, you can contact our board certified patient navigator through our Ask IDF program.
She will personally connect with you to tackle your question and to direct you to appropriate resources. You can even take IDF on the road with our engaging podcast series. You can find programs like bold conversations, undiagnosed and chronic twenties by searching for the IDF podcast. We also have a YouTube channel where you can find recordings from all of our digital education events and tonight's program will be uploaded and available in the coming weeks. Find a safe and supportive environment to link up with others impacted by PI through our get connected groups.
These groups are free, virtual, and volunteer led opportunities to connect with others with PI all over the US. We offer location based groups, diagnosis specific groups and nationwide groups, and because the groups meet virtually, you can join any group that works for you and your schedule. Check out the IDF calendar of events to find a group that might interest you. In addition to our get connected groups, we also offer facilitated support groups We have ones for young adults aged eighteen to thirty, ones aimed at caregivers and parents, and also ones for spouses and partners. And we also offer peer support if you're looking for something more one on one.
Woc for PI continues through the end of the year with events coming up in Tampa and San Antonio and coast to coast. It's not too late to start a walk team and become a part of the movement. Visit woc for PI dot org to get started. Here at IDF, we're so proud to offer educational programming each month and various in person events throughout the year. Here's a look at what we have coming up later this fall.
And speaking of upcoming events, we are so excited to share dates for our twenty twenty six National Conference, which will be taking place next June in San Antonio, Texas. Visit primary amine dot orgconference to be notified when registration becomes available, and

that will be available very soon. So definitely visit that link and get on our list for conference. We want to also say thank you to our sponsors as well as our wonderful volunteers and supporters who really make programs like this possible. We deeply appreciate your commitment to the PI community.
Thank you so much for your support.

Dr. Cunningham-Rundles: Thank you, Emma.

Emma Mertens: Thank you so much.

Dr. Cunningham-Rundles: Pulling it all together. You and Megan together. Mhmm.

Emma Mertens: Oh, thank you so

Dr. Cunningham-Rundles: much. Yeah.

Emma Mertens: Alright, everybody. Well, that is gonna close us out for this evening. We hope you all learned a lot and took away a lot from this wonderful presentation. Dr. Cunningham Rundle, thank you so much again for your time this evening.
Yeah. And thank you to everyone in our audience for joining us. I'm going to leave the platform up for just a few minutes in case anyone would like to revisit the links that we shared in the chat. Otherwise, take care and have a wonderful rest of your evening. Thank you so much.