0:03
Hi, everyone, welcome to today's program about anti mag peripheral neuropathy.

0:09
We're really excited to welcome doctor Rich Louis' with us as our guest speaker about this very interesting and extremely complex topic.

0:17
My name is Lindsay Culvert. I'm the Executive Director at the Foundation for Peripheral neuropathy. And I just want to thank all of you for attending today's session, and also everyone who might be joining later.

0:30
Before we get started, I just wanted to do a bit of housekeeping. We are recording this presentation. And it will get shared with you, likely by tomorrow, and also uploaded to our website for future viewing.

0:43
If you have any questions at any time during this session, we will try our best to answer them at the end during our Q&A session. Feel free to type them into the questions box on your dashboard, and we will try to answer as many as possible.

0:57
Noting that we prefer to only answer those that are general in nature and not anything that's specifically targeted for any personal medical advice.

1:06
And lastly, if you are having trouble with the audio, please use your phone to dial in. Those instructions can be seen through the e-mail that you received, in order to gain access to the session.

1:20
And now I am pleased to introduce doctor Richard Lewis, who is joining us today. He is the director of the electromyography Lab in the Department of Neurology and co-director of the Neuromuscular Clinic at Cedars sinai in California.

1:34
Before joining cedars sinai, doctor Lewis served as Vice Chief of Neurology, and Director of Clinical Neurophysiology at Harper University Hospital in Detroit.

1:43
He was Professor and Associate Chair of Neurology at Wayne State University School of Medicine, where he directed the hiller amyotrophic Lateral Sclerosis Center.

1:54
He was also co-director of the Muscular Dystrophy Association Clinic at Detroit Medical Center and Director of the Inflammatory Neuropathy Center of Excellence.

2:03
Doctor Lewis is widely known as a leading physician and scientist specializing in inflammatory and inherited disorders that attack nerves.

2:12

He studies ways to improve diagnostic testing and patient evaluation standards, and has been active throughout his career in educational, scientific, and advocacy groups for patients suffering from many different complex diseases, including ALS and guillain barre syndrome.

2:30
And he actually is best known for the discovery and exploration of an autoimmune disorder that bears his name Louis Sumner Syndrome, which is a rare disease that attacks the insulation around nerves and causes progressive weakness, tingling and pain, that usually begin on the hands and arms. So without further ado, I'm pleased to officially welcome doctor Lewis. He is going to be talking today, as I mentioned, about anti meg peripheral neuropathy.

2:58
And we're so lucky to have him today, so, again, doctor Lewis, thank you so much, and, and, it's all yours.

3:06
Thank you, Lindsey. I'm delighted to be here.

3:11
This is a topic that is near and dear to my heart, but it is a complicated one.

3:17
And so, I apologize to those of you who are quite sophisticated about this because I'm going to start with relative basics, just to put it in the framework of understanding, um, what these power proteins are in relationship to other things in our blood, um, so let me see. Hold on me, see if I can.

3:43
They're up tools.

3:47
So what we're going to discuss is what are power proteins?

3:51
What are some neuropathy is there related to them?

3:54
What is mad, which is mile an associate glycoproteins?

3:59
How do the antibodies against Meg cause disease and what treatments are available for anti mac neuropathy and potentially what's available in the future?

4:11
So to get started, the plasma proteins are the power proteins or abnormalities of proteins that come in your blood, but there's lots of protein in your blood, and I thought we should at least get a feel for where these lie.

4:32
So the the major port protein in your blood is albumin, which are basically what we call egg whites when we eat eggs.

4:40
Um, and you can see that that covers about 50% of the plasma proteins.

4:46
An albumin is really a crucial aspect of our blood plasma because it carries hormone's vitamines lipids as relationship to medications.

4:56
We we take, and we'll also kind of controls, to some extent, the ability to keep our fluids within our bloodstream and not have them seep out into a tissue.

5:09
So when someone gets a dema, sometimes it can be because they have very low albumin in the blood.

5:16
And so the fluid or water content of the blood seeps into the skin tissue in subcutaneous tissue globulins, which we're going to talk more about the next largest component, and they cover the about 40% of the plasma proteins.

5:33
They also carry lifts and hormones, but crucially, they are very important in the immune system.

5:38
Then there are some other ones which account for about 10%, including some enzymes, hormones and clotting factors that are not part of the globulin or albumin.

5:50
And so when you donate blood, they we'll take your blood cells and give blood red blood cells.

5:58
If two people who are anemic they'll give platelets to people who have low on platelets and are not clotting well.

6:04
And they'll use the albumen for some people.

6:07
Then they'll also use portions of the Globulins.

6:11
And if you've ever done IVIG, it's from this globulin component of 10000 blood donors that const contrive the IVIG that you're getting.

6:26
So within the gamma globulin component and this is on the square here, I don't know if you can see my tracer.

6:32
But in this rectangle is what we do Is basically cartoon of a serum protein electrophoresis and you can see this gamma globulin. Portioning is at the very end.

6:45
And you can see it is kind of a round kind of hill.

6:49
As opposed to the peak of the albumen here.

6:53
But within this gamma globulin component, there are multiple components which we call immunoglobulin.

7:00
So there's IGG, this IGA, this IGM which is an important one for you.

7:05
If you have anti magnet rapidly this IJ K in IG E then these immunoglobulin, ... are the things that make the antibodies that control infections and disrupt your immune system.

7:27
So oh.

7:31
So you can see that the major immunoglobulin is IGG, which is the fourth one down on the list and that one has different components, um, and they act differently.

7:49
It crosses the Placenta which mean people who have mothers who have IGG disorders, sometimes pass and transient disorder to their infant.

8:02
So one of the classic ones is Bias ...

8:05
Gravis, which is an IGG related disorder.

8:10
Some infants will have a transient 3 to 4 week Maya Steamiest symptom from their mother's antibodies but it doesn't turn into a disease because the end up making their own of antibodies which are not necessarily disease related.

8:26
The other ones you can see here.

8:29
Each of them have their own importance but the one we're going to talk a lot about is IGM.

8:39
So this is a cartoon of an immunoglobulin.

8:43
There's a heavy chain, which is this.

8:47
If you look at the Y, it's the no, this arm of the Y, and then there's the two arms here, which are the light chains within the light chains.

8:59
There's A variable region, and these light chains are the ones that are the ones that identify the connect to the antigen Causey Antibiotics.

9:16
So there's a variable region here and you can see this is where the antigen binding site is.

9:23
So when they see something that they want to attach to, this is what's looking at it.

9:28
So there has to be some.

9:31
Yes, Stoichiometric kind of structural thing, that looks like they can connect.

9:39
So if the antigen has like a, these are cartoons, but you need something that's going to fit with this, triangular part here.

9:48
This one would be more around, This one would be more, you know, Pegg related.

9:54
So these variable regions are the keys to it, and these are the light shapes.

9:59
Some of the light chains are Kappa.

10:02
And some of them a Lambo, Lambda, so and they each have different importance, for instance an anti mag neuropathy.

10:13
The power protein is usually 99% of the time and IGM capper power protein.

10:22
So the cap it identifies the light chain, the IGM tells us which immunoglobulin class.

10:30
The problem is we'll talk a little bit more about Kappa Lambda light chains in a second.

10:37
So the immune system is very complicated and I'm not going to try to explain it all, but the best way to think about it just simplistically, is there cell mediated immunity with T cells?

10:51
And this humor or antibody mediated disease, which is from the B cells, and the plasma cells, And they can they talk to each other, and they relate.

11:04
And there are antigen presenting cells in the T cells that will send present the antigen to the B cell, who will connect to it.

11:17
There are B cells, and there's a whole evolution of cell changes that occur.

11:23
And we're going to talk a lot about B cells because you've probably heard about the treatment with ... map.

11:30

They work on B cells, but memory B cells, which also turn it into plasma cells, they don't get affected because they've already memorized their antigen and knocking out the B cells before it doesn't do any good.

11:51
So here it is, the evolution of the ...

12:00
to go from the stem cells in the bone marrow.

12:05
To the B cells devolution.

12:09
And here's these memory B cells, and you can see they sometimes they can get targeted by the.

12:15
We've talked some AB, which is a CD 20, um, antibody.

12:21
But the plasma cells which are the ones that present these that attack the antigens or not impacted by the B cells B cell inhibition.

12:36
So you need different treatments for plasma cells than you do for things that are come from the B cells and you can see that some B cells we'll have antibodies that will work on antigens but a lot of them, particularly the IGG ones, come from the plasma cell.

12:59
And if you can I'm sorry, let me go back a little bit down at the bottom of this slide, you can see. Oh.

13:07
You can see some of these other medications that have an effect.

13:11
So ... is a ...

13:14
Proteasome inhibitor and it works on a larger range of these evolving B cells in plasma cells.

13:26
So IGM primarily B cells are circulating and are made in the lymph tissue where the IGG mediated immunoglobulin made primarily by the plasma cells in the bone marrow.

13:44
And so you can see the different treatments have to attack different areas, not just different cells.

13:58
So what are power proteins?

14:01
Power proteins are monoclonal and I'll explain that in a second.

14:06
Immunoglobulin, fragments or intact immunoglobulin produce buy a certain clone.

14:13
That's not cone but a malignant clone of plasma cells of these cells.

14:19
So if you remember this nice, smooth, gamma globulin region here, Power Pro Team will be like, a spike within that gamma globulin.

14:30
And if you take this gamma globulin and divide it into IGG IGA IGM, that spike, in the serum protein electrophoresis, will be one of whether it's if it's an IGM Power protein, it will be in the IGM sector of the gamma globulin.

14:48
If it's an IGG will be in the IGG a mono, clonal ...

14:54
of uncertain significance or what they call, you know, abbreviate to M gus, is a small amount of power approaching a large amount of power protein.

15:07
Such as this spike here would be seen in a malignant situation.

15:16
So Martin, the M gus is basically a benign condition.

15:21
The levels of the Power protein tend to be low.

15:25
And depending on the if it's an IGG, there's a low level of abnormal plasma cells or low-level of abnormal B cells for the IGM.

15:41
Then when you the hematologists look at it, they do bone marrow biopsies and there are no indicators of active or malignant disease.

15:51
All patients who develop multiple myeloma once had an IGG or an IGA, usually power approaching, or M gus.

16:03
But only a fifth of patients with M gus will eventually develop myeloma.

16:09
And the usual risk of progression is considered to be about 1% per year.

16:14
So I sinned almost all, if not all my patients with them, Gus, to a hematologist to one, determine whether they have actually have active myeloma at the time and two, to follow them.

16:30
And they determine where they need to be seen yearly, or every two years, I tend to recommend people be seen yearly by a hematologist.

16:41

The hematologists can an oncologist, can monitor the patients for the M gus.

16:48
Having seen many of these patients over many years, if you follow the amount of their Power protein, there's two ways to do that.

16:58
It tends to grow overtime.

17:01
So if someone has an IGM M gus, with a level of 200 IGM in, say, 1975, in 19 80, it could be 300, 985.

17:16
It could be 400 and it gradually increases until the patient develops a malignant transformation where it's very hot.

17:27
So we just follow the quantitative immunoglobulin.

17:32
Or, in this serum protein, we can actually look at the mini monoclonal spike which is the abnormal combe within that population of immunoglobulin.

17:43
So ... patients may not need to be treated.

17:47
And in general, an anti mac neuropathy, there are two different drivers for treatment.

17:55
one driver could be that their neuropathy is severe enough, bothersome enough, that the patient and the neuropathy doctor feels they should be treated, and the alternative approach is the neuropathy doesn't necessarily need to be treated.

18:12
But the patient in the hematologists an oncologist feel that the hematologic situation is significant enough that are required for you.

18:23
So that's why I always work with the hematology oncologist when I'm trying to thinking about treating a patient with anti mag neuropathy or other pair approaching the rub.

18:41
So I've hinted at least that there are differences between IGG and IGM Power proteins and their significance versus an IGM Power Protein, IGG an IGA power proteins are the ones that would be associated with multiple myeloma a disease of the plasma cells in the bone marrow.

19:06
IGM malignancy is usually something in the lymphatic tissue and it's called walden's Drums, Mackall, Globule, anemia.

19:16
There are also some other milder malignant forms, lymph flow plasma side Thomas which can be seen with the IGM Power proteins.

19:29
And this what we used to consider completely benign, actually, can be kind of a low grade, um, malignancy.

19:41
So IGG monoclonal ...

19:44
If we take 100 people over the age of 60 and just check, their immuno fixation, electrophoresis, or their serum protein electrophoresis.

19:57
5% of those patients, five out of one hundred will have an abnormal IGG power protein or M gus.

20:06
If you follow them long enough, 20% of them may become malignant over 20 years.

20:14
We're 10 years.

20:15
Um, so it's important.

20:19
It's nice to know that but many of those patients will have no will malignancy a medical problem from that for their entire lifetime.

20:31
Um, so the IGG is the most common, um, M gus or Power Protein.

20:41
But if you look at that group, if you take 100 patients with an IGG power protein, M gus, only a few of them have a neuropathy that are considered associated with.

20:55
Some of them could have diabetic neuropathy.

20:57
Some of them can have neuropathy is about the cause, but when you look at it, the IGG is not related to neuropathy very frequently, someone who has an IGG power protein.

21:09
The flip side of that is that patients with an IG M power protein which is relatively uncommon compared to IGG.

21:18
You take 100 of those patients with IGM.

21:22
Over half of them will have an associative in the room.

21:25
So it's not as common, much, much stronger li, much stronger association with neuropathy.

21:32

So when I see someone with neuropathy, I tend to get an immuno, fixation electrophoresis, and I'll explain that in a second.

21:44
To see whether that might, they may have something related to their neuropathy, my ears, or my eyes, or something perks up in me when they have an IGM Power approaching IGG tap of power protein.

21:58
I'm less concerned about that. That's a relationship.

22:06
So, as I said, the light chains have some significance as well.

22:14
When I see an IGM kapur Power protein, then I am, it's much more related to anti imagine the ROP athey and neuropathy in general, An IGM Lambda, Power Protein, has less of a direct association with neuropathy.

22:38
When I see lambda light chains however, in any certain circumstance, I get concerned for other disorders, one of them is what we call AL amyloid.

22:49
Now there's a genetic amyloid tooth transfer I written, which is a different type of amyloid disorder, both of them cause neuropathy.

23:01
Both of them can be very serious: the genetic form of amyloid neuropathy.

23:06
Patients were dying within 10 years because of severe neuropathy and also deposition into the heart.

23:14
Needed heart transplants, but we now have treatments for that.

23:18
And excitingly, we're saving lives because of these treatments.

23:23
So these amyloid neuropathy, these that are genetic, we now have some very, very strong treatments for.

23:30
It's been one of the most exciting things in my world in the last 10 years.

23:36
The amyloid is more associated with myeloma.

23:40
So when we see Lambda light chains were very clearly get them to the hematologists And we look for myeloma.

23:49

The other thing we look for is a disorder called poems, which is an abbreviation for Paoli neuropathy.

23:58
Getting big organic ..., either the liver, the spleen, the pancreas, sometimes Endocrine ..., like thyroid disease with diabetes.

24:10
This mono called gamma Kathy, which is almost is always a lambda light chain.

24:16
They can have skin lesions.

24:19
And this is associated with changes in their bone.

24:25
So they actually have some tumors in the bone or blood disease called Casselman Syndrome, and you can test for a blood test called the vascular endothelial growth factor.

24:38
And these patients with poems have extraordinarily high ved Jeff levels.

24:45
And you can see some other criteria that can see this was a deadly disease 20 years ago, now, with some Martin Oncological treatments including bone bone marrow transplant.

24:58
These patients are surviving, living longer and longer, and some times being cured, but it can be a very severe neuropathy.

25:07
so when I see Lambda light chains, the lightbulb goes off and I said, they can have a bad disease, and I get them to hematologist.

25:20
So getting closer to talking about Magna Repatha. Yeah, apologize for the long introduction.

25:26
But as I said, the IGM cap is the one that's most associated and the IGM capping neuropathy is are usually what we are associated with slow nerve conduction velocities on that nerve conduction tests that you've had.

25:43
And about half these IGM Kappa will have anti magna Robert.

25:48
So the screening process is to look for the IGM capra first, then to see if those patients of those patients do they have anti mag antibodies.

25:59
Now there are other antibodies that we know happen, There are ganglia side ammeter bodies to something called G D one A and G D one B, which can have a similar neuropathy to anti-matter.

26:11

But the one we're going to special talk about mostly is the anti-matter.

26:15
And here's a little diagram of what I've already talked about in terms of when they haven't a Lambda Light chain.

26:25
IGM Lambda noora neuropathy may not be tomorrow on anything will have slow nerve conduction and can behave differently than the anti magro the IGM taboos.

26:39
So you can see that this gets very complicated.

26:43
And we in the neuropathy field and the hematology field are trying to get a handle on this.

26:51
And so there is a study going on, primarily in the Netherlands, but yes, Somewhat in the United States called the Imagined Study, which has been a little slow to get moving.

27:04
But is being reactivated and there was just a meeting of people on the imagine study at the Peripheral Nerve Society meetings in Miami in May.

27:15
So there is movement, what trying to understand of the people who have power proteins.

27:22
What is the IGM Power Protein neuropathy relationship?

27:26
And how is anti mag different than some of the other ones?

27:30
And it is a very confusing and complicated topic we need to enroll as many patients as possible to understand this.

27:39
So, what does mile and associated glycoproteins?

27:43
Well, it's a glycol protein, which means a protein that also has a glycol lipids component to it and it's found within the myelin sheath and in the schwann cell.

27:53
So, this is the mylan in this kind of salmon color.

27:59
Um, and up above it would be the Schwann cell, that makes the modeling.

28:06
And so mowing comes from the schwann cell, which is the cell that connects to these axons.

28:13
And as you know, peripheral nerves are basically like electric wires.

28:17
There's wires which you call the axons, this installation, which we call the Mylan.

28:23
Mylan is more than just rubber installation is a very active metabolic component, my own.

28:32
So it's not just insolation, but simplistically from a conduction standpoint. That's what it does.

28:39
And it keeps the electrical signal from seeping out of the axons.

28:45
So you can have very fast conduction going from one node of Ron V eight to another.

28:52
But there are things that connect the mile into the axon.

28:56
And one of them that's part of this system is Mac.

29:01
There's also these other components, which we now know have antibodies associated with them.

29:06
which are what we call nodal, imperil nodal neuropathy.

29:13
But if you mess up this interaction between the Mylan and the axon, you can get very severe, slow conduction slowing and sometimes the conduction will blow up.

29:25
I should have put a video in here about conduction, but sake of time I didn't have this so, do it another time.

29:34
So, airtime Mad neuropathy has very specific blood tests, nerve conduction changes and pathology and the pathology that's associated with anti mag antibodies.

29:52
Is that the mile in which normally is tightly wound around the axon.

29:59
It's now there's an opening a widening of the spaces between the mile.

30:05
So what we call widening of the ..., there aren't many other disorders that do that and with if you look into an immune hemis just a chemical stain for the IGM, you can actually see little IGM deposits on these mile in segments where the antibodies are being deposited on the bow and loops.

30:30
And this widening of the Mile Limit Law, meli changes the conduction uh properties of the microloan and the axon causing conduction changes and will also damage the axon underneath it so, the axon gets destroyed.

30:55
So, that's the pathology of it.

31:01
What happens to people?

31:04
So anti mac neuropathy actually has quite a variation in terms of manifestation, those of you who are on the call, and have anti ..., if I asked 20 of you how it affects you.

31:19
The majority going to say one thing, but there's going to be a minority that's going to have a slightly different, um, way the disorder seems to have presented to them.

31:30
Most patients will have a very slow insidious, sensory disorder.

31:38
So the first thing you'll notice is some numbness or tingling of their toes and feet.

31:43
And it can take years, sometimes 10 or 20 years before it actually effects balance and walking.

31:53
It can affect the toes first but sometimes the fingers and toes can be impact at the same time.

32:00
And it tends to creep up the legs and hands, what we call length dependent fashion.

32:06
The longest nerve fibers in your body are the ones that come from your lumbar spine down to your toes.

32:14
So they can be two feet in length.

32:18
Or if you're NBA basketball player, it could be three feet left.

32:24
They're the longest nerve fibers. We have.

32:27
They are also the ones who can have more places for antibodies to attach to, which may be why the length is a significant aspect of why you manifest the disease.

32:41
While most of the patients have predominantly, if not completely, sensory disorder, some people will have weakness of the hands and feet and we will lose some of their muscle, bone.

32:53
What we call atrophies why some people have more weakness than others is not known.

33:03
So, what does the neurologist's find when we examine you?

33:09
Well, the first thing is, depending on how severe it is, we look to see how drunk you are.

33:15
So, if you're walking with wide base, when we walk, one foot kinda goes almost directly in front of the other.

33:25
But if I can see a space between your legs when you walk, then you're wide based and you may not be able to walk a straight line easily.

33:36
There are many causes of a taxiway.

33:40
In the brain, the cerebellum is R Balance Area.

33:45
If someone had a cerebellum stroke or a genetic disorder of the cerebellum, they can equally look drunk.

33:56
But, in this instance, your ataxia is not from the cerebellum.

34:00
It's from the fact that you're not getting good signals from your feet to keep your balance.

34:06
The way we know that, is that if we asked you to put your feet together and keep your eyes open, most people are able to do that because our vision helps us, with balance, as does our inner ear, and our ...

34:23
system, the inner ear, to that, to the brainstem.

34:27
And as long as you have two of the three components working, the third component being what your signals from your feet are, things do, OK.

34:37
So if I take someone without neuropathy and ask them to close their eyes, they still have their feet working, and their inner ear working, so they don't lose their balance.

34:49
But if you have neuropathy and you can't feel your feet, you only have your vestibular system working, that's not enough to hold your balance, and you'll tend to fall.

35:01
The term we use in Neurology is called a an Abnormal Romberg test, but it's a very good test to tell us whether you are a toxic gait is from sensory disturbance.

35:14
Then we test sensation.

35:16

And the major component of the sensory exam that relates to these ataxia is vibration sense when they put the tuning fork on your toes and ankles position sense, particularly Position Sense.

35:30
These are all from large diameter, sensory fibers, feeling pain in any burning pin, since it burning pain, now normal feeling like you don't feel a hot.

35:43
The hot sand on your feet, those are small diameter fibers.

35:47
They can be affected in this, but they don't affect your balance.

35:52
Associated with this is that you lose your ankle reflexes.

35:56
And sometimes everywhere, your strength may or may not be reduced at your ankles.

36:06
So part of the evaluation of someone with neuropathy.

36:15
Excuse me.

36:17
It's the nerve conduction test.

36:19
I'm sure the favorite thing that you get done to you when you have these are opportunities, but there's a very characteristic pattern of conduction changes, which was identified.

36:31
Bye a group that included my colleague, Austin Sumner.

36:37
Um, which is that what you get is what we call distill accentuated slowey.

36:43
So when they do the moda conduction studies, they stimulate the nerve say at the wrist, record the muscle in your hand, then they'll stimulate the nerve at your elbow and recorded at the same place in your head.

36:59
And if you, the time it takes from the stimulus, two when the muscle responds, it's called the latency and if it's on the stimulation of the wrist is called the distal latency and if you and the one that's from your elbow is called the proximal latency.

37:20
The nerve conduction velocity is the distance from your wrist to the elbow, divided by the latency difference between the just the latency and the proximal weights.

37:33
So normally nerve conduction velocities in the upper extremity in your forearm, run around 50 meters per second to 70 meters per second.

37:46
The distal latency tends to run between 3 and 4 milliseconds, a thousandth of a second.

37:55
The reason we don't talk about a velocity here is because the velocity to the muscle, as many other components than just the nerve, it has delays.

38:06
At the nerve muscle junction.

38:08
It has muscle fiber differences, and temperature is an issue, so we don't usually talk about a distal velocity.

38:17
Actually, if we compute the distal velocity, it tends to run only about 40% of the nerve conduction velocity in the form, so 20 meters per second would be the digital velocity.

38:31
But an anti mag, this just latency, can be twice as slow as the conduction velocity and we have ways to compute this to kind of show this.

38:44
So, this distill, accentuated slowing, it's very characteristic of anti magno rapidly, and it's one of the few neuropathy. Is that actually happens.

38:57
Saying that if you just had it in the medium nerve, which is the nerve, the sensory, which is to the thumb, the muscles of the fun pad of your thumb, and you wake up in the middle of night with your hands asleep.

39:14
The slowing of this desta latency with normal conduction velocity in the form is what we see in the common Carpal Tunnel Syndrome.

39:23
But in anti magna rapidly, we don't just see the median nerve.

39:26
We see it, and the only nerve we see in the nerves in the leg, we see an in virtually every nerve we test.

39:33
So this does still accentuate a slowing is a very key marker of an anti-matter.

39:41
In addition to sensory responses we can find them, or they're very reduced in amplitude.

39:50
So what we do in the testing is we look for the IGM cap of Power Protein.

39:57
If we do this, serum protein electrophoresis, which shows us the albumin in the alpha globulins and some of these other globulins besides that.

40:08
And it's it's not as specific and we miss some of the power proteins and those.

40:15
And so, most of us will do a serum immune fixation which just looks at the gamma globulin fraction. And it's much more sensitive and finding these power proteins.

40:27
If we find this, we then do the anti mag testing, which there's a screening test, then if the screening test shows it up, then we do a specific Western blot to prove that it's anti mac.

40:42
Then what I do is I look for how much IGM there is.

40:47
So if the IGM levels are less than 200 that's pretty normal they may still have this M gus but it still says there's not a lot of IGM being made.

41:00
If it's less than 500, well, I'm not as concerned.

41:04
But, when it gets over 800, that's thought. That's really concerning that there's a malignancy.

41:12
You can also do look for what we call a mini monoclonal spike on this serum protein.

41:18
And if we see it, that will tell us what, how much of the abnormal engulfs there is, the more, the higher the mini monoclonal spike, the more serious it is.

41:31
And I, as I said, I tend to refer these patients to hematologist, oncologist, and I use specific ones who are ones that concentrate in lymphomas or milo.

41:49
So, if once we've identified that they have the power protein, that they have antibiotic antibody, that they have an neuropathy, then. And they have nerve conduction studies that look like anti-matter in the rock.

42:08
They become potentially patients who we can treat free anti-matter up.

42:13
And as I said, sometimes we treat because the blood disorder is such that drives the treatment and sometimes it's the neuropathy.

42:21
And what treatments we use depends on various aspects. If the neuropathy is severe, we're going to be more aggressive.

42:29
If the hematologic problem is malignant, we're going to be more aggressive.

42:33

Because all treatments are basically determined by a balance of the risks that we take by that you take by taking the medicine versus the potential that it's going to do some good.

42:46
So what you're seeing here is basically, then I'm not treating the neuropathy.

42:53
I'm really treating the hematologic disorder because if I can reduce this M gus, then I'm going to reduce the amount of bad stuff, the antibodies and basically impact the neuropathy.

43:11
So I think I've kind of gone over a lot of this.

43:15
Just to know that, if you have pain, burning stinging, pain in your feet, buzzing, that's really painful, There are neuropathic pain medicines.

43:25
They're not going to treat the neuropathy. They just treat that painful symptoms.

43:29
So the neuron TINs and gabapentin or lyrica is pre goblins, and ..., and symbolic ..., and ..., and Pamela lore.

43:39
Those are symptom treatments for pain, but they don't treat your disease, the usual treatments for inflammatory neuropathy.

43:50
The ones that are called C I D P, or chronic inflammatory demolished eating Pauline neuropathy tend not to be effective in anti-matter.

44:01
It's not 100% And there are reports of people responding, two IVIG, usually not to steroids, but in general, that effect is not very strong or very long lasting.

44:16
So unfortunately we don't have any proven treatments for antibiotics but we do have treatments that many of us believe work, and certainly if you can, the hematologists know that it works for their diseases. And so by inference worked for the neuropathy.

44:35
So there is no specific treatment for the anti mad neuropathy Unrelated to the human talk hologic.

44:45
one of the leading scientists in the power proteins neuropathy, had developed a potential treatment for the specific anti mag antibody.

44:59
Developed a company, worked on it, the the approach was very encouraging in differing cell models, but um, had to be stopped because of, as I recall, toxicity issues.

45:13
And so we're still don't have a treatment that just targets the anti-matter.

45:19
Obviously, the more specific the target for your treatment, the less likely that it's going to be toxic in other ways.

45:27
So a specific target for anti mag antibody would be potentially the safest treat.

45:35
But we don't have that yet.

45:41
So, most of you have probably been, at least discussed about the use of Rituximab in B cell depletion, since IGM power proteins are made by B cells, or the pre plasma cells.

45:58
before the memory B cells or before plasma cells, for sure, um, B cell depletion was thought to be a very important treatment.

46:13
And actually, I may have been one of the first people to use this medicine back in 19 95, I believe, the story is, is that I had a patient in Detroit, who was a member at Oakland Hills Golf Course.

46:28
And he said, if I can cure as neuropathy, he would take me to Oakland Hills Golf Course. A very famous golf course. Anytime I wanted.

46:36
well, after some consultation with some of my colleagues, Hopkins, we tried this treatment, I barely knew about it at the time, and sure enough, his neuropathy was basically couldn't remission for 10 or 12 years.

46:50
He did take me to Oakland Hills Golf Course, which was lovely.

46:54
I didn't go as often as he suggested, but, um, so it worked for this patient.

47:02
So we've tried using this in a number of patients as have many peep groups around the world.

47:09
And in these small uncontrolled circumstances many of us have found significant number of patients, not everyone that seemed to respond.

47:22
When you treat with ...

47:23
talks about the circulating B cells as identified by CD 19 an antigen on the B cells, CD 20 is the target for talks about CD 19 is what we use to monitor how many B cells are circulating.

47:41

The B cells go down very quickly within a week or so, less than 1% of what they should be, But they're not gone because they're still sequestered in the lymph nodes bone marrow or another places spleen.

47:55
And so you're not getting rid of all the B cells.

47:58
So it's not the strongest treatments in the world, the reason that the fact that it's not as strong as some also makes it less toxic themselves.

48:10
So when you look at the IGM Levels in these patients they go down.

48:15
So if it was 500, before the treatment, they can go to 400, and the 300, and then 200.

48:22
And if you keep repeating the treatment, the B cells can see at the end, the IGM levels continue to go down and with it the mini monocles but and at some level, when you get the IGM levels down enough, the neuropathy will usually stabilize and can improve.

48:46
So, we tend to treat every six months and some patients every after awhile, every nine months or 12 months, and we can monitor the B cell levels to determine, um, so that's kind of an approach to write talks about.

49:04
There are more aggressive tucks them out treatments.

49:09
Um, so for me, the IGM levels have been very helpful.

49:16
Some of the studies suggest that anti mag levels are more helpful.

49:21
I find them less sensitive for a variety of reasons so I do look at both and we see which one works.

49:30
And that tells me that there's a biologic effect of the treatment on the IGM power protein but it doesn't tell me whether the neuropathy has improved.

49:40
So that is dependent on what you tell me.

49:44
What my exam tells me.

49:46
And at some point I've done studies that show that the nerve conduction changes actually can improve as well.

49:52

They don't get completely normal that they move in the right direction.

49:57
So for it to determine whether the treatment's working, I need your help because it doesn't matter if so much.

50:08
From a neuropathy standpoint, if I say, Oh, yes, your vibration sensors improved.

50:13
What you want is to see improvement in function, your quality of life, to improve, and maybe your discomfort and other things to get better, which is impacting your quality of life.

50:24
So we use formal outcome measures to determine this.

50:30
Um, We use some things that we ask you about. Quality of life skills, or functional rating scales. And then, we use some tests that may be able to help tell us whether you're improving or not.

50:44
And sometimes, you may say, No, I don't think it's helping me very much, but I'll say, you know, it's very early in the game, and I'm seeing that you're walking much better, or a little bit better, or that you're doing a few things better than you thought you were doing before.

51:03
So let's give this more time.

51:08
So, why don't we have an FDA approved treatment for this?

51:16
Well, there have been some clinical trials, um, anti-matter in the rocket the, and unfortunately, they never showed a benefit, and there's a lot of reason why small uncontrolled trials shows seem to show benefit, including things that I've done in others, particularly in Italy and other places.

51:37
And the formal randomized, double blind controlled studies did.

51:43
Some of it has to do with the fact it's a slow insidious disease, and it may take us time to show improvement.

51:51
The studies may not have looked long enough.

51:54
It gets very expensive to keep looking for a year or two years later.

51:59
Sensory disorders are very difficult to show affect.

52:03
It's easy if you have a weak muscle, they get stronger.

52:08
Motor stud motor problems, or simple, they're kind of dumb. They either move where you, either hulin moves, or it doesn't move.

52:17
But sensory stuff is very complicated.

52:20
It's a co-ordinated action of different diameter nerve fibers.

52:25
And so it can be very difficult to ascertain improvement in disorders that are primarily sensor.

52:31
sensor.

52:32
The outcome measures use may not have been sensitive to change they may need to do a longer treatment with more lowering of IGM levels, my own experiences I need to get those IGM levels down well below 400 to be effective.

52:51
And so sometimes you need multiple treatments, but those studies did not do that.

52:57
And some deficits may not be fixable.

53:00
If you've had the disease for 20 years, there are aspects of your disease that are just not going to be fixable, even if we have the cure.

53:10
And you can't always take that into account when you're recruiting patients.

53:15
And it may be that it just was too slow and insidious, and we may not have had enough patients in the trials to see this statistical significance.

53:29
So I've kind of gone a little, maybe a little over.

53:32
I'm going to go a little quick on this, but I'm going to ask you, too, think about this when you talk to your doctors, you need to recognize that you and I don't always talk the same language, what you are concerned about may not be what I think is the real big issue.

53:54
So you need to be very explicit about your worries, concerns, fears, what is really troubling?

54:04
Well, I have to be in a wheelchair, is the unexpressed fear of every patient I see with neuropathy.

54:12
None of them asked me that question.

54:14

Amendment Minority.

54:16
And, so, I've learned to just tell patients, No, you'll, you'll never know. You're going to walk the rest of your life.

54:23
Same thing with shortening, well life.

54:26
Then, there were issues about, what's the long term plan?

54:30
Sometimes the doctors more interested in the short-term.

54:33
Let's think about what we're gonna do now, necessarily worrying about the long term, because until we know how we do in the short-term, it may not be paid to worry about the long term, but I understand why you would want to notice.

54:49
We need to give you realistic prognoses, and we need to, you, and I need to be on the same page about what the treatments are going, what you should expect from the treatments, in the early stages, in the long run.

55:05
And lastly, we need to go over what risks and benefits are.

55:09
Many patients equate side effects and risks.

55:15
A side effect is, I give you a medicine, you get a headache or You get nauseated or you get sleepy.

55:23
And you say, I don't like this and you stop it.

55:26
And within a day, usually, you're back to your soul itself and you say, I don't like that medicine, you don't take anymore.

55:33
No big deal, because it's only a minority of patients who have these side effects.

55:38
Otherwise, they wouldn't be had, it wouldn't be on the market, A risk is, I give you a medicine. You get a severe disease, and you either die, or you're in the hospital, in your damage.

55:50
For a long time, risks are concerning, side effects are not that concerning, because you can stop the medicine, and get rid of them.

56:01

So, we need to understand the variability in the problems in these neuropathy, is, and that's where imagine study comes in. We need better outcome measures, and that's also part of the imagined study.

56:14
And once we do that, we hope we need to develop more treatments, more specific grant imad, and we need to develop new treatments for the Power Point a little less risky.

56:23
The hematologists and oncologists have all kinds of treatments that can treat these power proteins, but they all carry significant risks, and we have to decide when is the right time to treat.

56:35
So, on that note, Oh, I went the wrong way. Sorry. I think.

56:43
I stop. I can stop. Thanks for listening. I hope that was helpful.

56:47
I'm sorry I didn't leave ton of time for questions, but hopefully a lot of them were answered in the talk.

56:52
Yeah, no, thank you so much, doctor Lewis said it was extremely helpful. We are getting in a lot of questions, and I know we only have a few more minutes, so I'll try to see what we can cover and anything else we'll follow up at a later time with specific individuals. You didn't really talk much about physical therapy or exercise. Do you have any thoughts specific to those that have anti mag?

57:19
Um, physical therapy and exercise are good?

57:24
They don't treat the disease.

57:26
They are not, you're not going to overcome the disease with physical therapy or exercise, but you can maximize your function by physical therapy and exercise.

57:37
It has a lot of benefits.

57:39
Physical therapist can help you with your balance.

57:41
They can talk to you about making sure you you don't want to be falling, and I know people don't like using chains.

57:51
I recommend walking sticks for many people because they're socially a bit more acceptable than teens.

57:57

Um, but you need to be able to keep yourself from falling. Physical therapists can help you with that.

58:05
They can help you with your strength, so I think it's very good, but I think you need to have realistic expectations of what they're going to accomplish.

58:15
And do you have any thoughts about diet specific to those that are affected by anti mag?

58:22
There are all kinds of.

58:25
And if my, I'm not, I don't mean to be cynical.

58:31
But there are people take what they call immune diets and things that they think affect their immune system. And maybe they do.

58:41
But to some extent in this, it's not that you have And you're not immune deficient.

58:48
You're you have a segment of your immune system that is overactive.

58:55
So I'm not aware of any diet that is going to be particularly, um, have a major impact on this specific disease you have healthy diet is good.

59:09
I have no objections to one day vitamins.

59:13
If you want to take supplements, it's fine.

59:17
Too much vitamin B six can cause painful neuropathy.

59:21
So I wouldn't do more than A If you're going to do a one day vitamin I wouldn't do a big complex on top of it.

59:29
It's just too much of particularly a B six.

59:32
So I think there are supplements, like ... acid that hope, pain, neuropathy, pay.

59:40
So, my personal preference is to eat a healthy balanced diet.

59:46
And if you want to take multivitamins with it, that's fine. Calcium and vitamin D is generally health helpful, but not specifically for this.

59:56
And it does show up in blood tests. Yes.

1:00:02
So the blood tests that show it is either a serum protein electrophoresis, but more sensitively, a serum immuno, fixation electrophoresis, and whether it's an M gus, which means it's monoclonal come up with the unclear significance.

1:00:19
Usually, meaning it's mild or something that's showing up.

1:00:24
Either myeloma, or amyloid was or waldon comes. That's more dangerous.

1:00:30
Is dependent on the company, keeps in house, how much of that power protein.

1:00:36
But the blood tests show up, the way you screen, for an M gus Or Power Protein is a serum immune, to fixation electrophoresis, or a serum protein electricity.

1:00:47
And you talked a lot about .... Have you, any additional information to share about IVIG when it comes to effective treatments for anti mag?

1:00:59
Yeah, as I said, in general IVIG, it's only minimally effective but, there are patients who seemed to have a response to it.

1:01:14
Um, it doesn't affect the power proteins, so the IGM levels don't go down.

1:01:21
The anti mag levels may or may not go down. It can work on the antibody itself, so at times it works. But in general, most patients have a modest or no effect of IPS.

1:01:34
So, do I sometimes? try it? Yes, sure.

1:01:38
But, but I don't have I'm hopeful, but not necessarily optimistic that it's going to work.

1:01:49
And are there any specific signs that someone's symptoms, or just the condition itself of anti mag is getting better or worse than a person?

1:02:02
Well, the worst usually, the thing the patients will recognize is that the numbness that may have began in the toes over a certain period of time hopefully, its years will go up to their ankles and then above the ankles, then the hands may get maybe the fingertips and then it goes to the wrist.

1:02:23
That's the most clear-cut way.

1:02:25

People notice that my sensory symptoms are getting worse.

1:02:30
Their balance may get worse. That would be another clue, as to getting worse.

1:02:35
And I've had patients hoofs a mind, tingling and numbness was to the wrist, and now with ..., it's too.

1:02:45
It's only in the fingers or went from the mid calf to the ankle.

1:02:50
Now, functionally that may or may not have a major significant, but it helps me know that the Treatment's is on the right track.

1:03:01
Now, that's really interesting. And then I guess the last question is ultimately, is there anything else that you think a patient with anti mags should know? You had mentioned, obviously, the Imagine Study, which is a great program right now, for research.

1:03:20
Is there anything either affiliated with that study or anything else that we should try to highlight before we close the session?

1:03:29
Um, I think the highlight is to work with your clinicians.

1:03:35
I do think if you have a power protein, by the way, there are occasional patients who have an anti mac antibody and not a Power protein.

1:03:45
So there are times that we'll do the anti mag blood testing, even though we don't find the power protein.

1:03:54
It's pretty unusual, but it does happen.

1:03:56
But, basically, you want to make sure that you're working with a hematologist And a neurologist was comfortable or knowledgeable about anti-matter in the rock.

1:04:08
You know, within the scope of all neurology.

1:04:11
Neuropathy is a relatively small component, even though neuropathy is the foundation, I will tell you.

1:04:18
It's probably one of the most common neurologic disorders, but neurologist's tend to deal with strokes and seizures and other things, in some ways, more of an neuropathy.

1:04:31

An anti mac neuropathy is a small percentage of neuropathy, so it's sometimes useful to get to a center of excellence.

1:04:39
And basically, the ...

1:04:42
Foundation, um, has centers of excellence and the foundation for peripheral neuropathy.

1:04:48
It can also hope you find a center that is knowledgeable in this, and it's worth having, at least at some point in your disease.

1:04:59
Someone who's, quote, unquote, an expert, see you to give you some advice who can work with your neurologist, even if it's a thousand miles away.

1:05:12
Now, I think, I think you hit the nail right on the head, doctor Lewis.

1:05:17
And to your point, for those that need to find a center of excellence or a neurologist that specializes in this type of, of research, or this condition, with respect to treatments, and finding better ways to manage your symptoms, feel free to let us know, That's what we're here for.

1:05:35
And, again, I know there were a lot of questions that we didn't have time to answer. And for those, I'm very sorry. I encourage you to follow up with us through e-mail, through phone, and check our website. We will be sure to share as much information as possible as we can, as it becomes known, or help spur with specific questions.

1:05:55
So, again, we'll look at the questions and responses, and you can send them to that would be great, doctor Lewis. So we we might just do that and we can follow up accordingly. So, again, thank you for that offer, doctor Lewis, thank you again for your time today, for those that are joining us live.

1:06:14
Thank you for doing so, for those that are watching this recording later on. As I said, feel free to reach out to us.

1:06:21
At any point, if you have any questions, we're happy to help, whether it's regarding anti mag or any other cause of peripheral neuropathy, that is what our organization is here for to help improve the lives of those living with this condition, bud.

1:06:35
Again, we ran out of time for that, I apologize, but it was a very enlightening conversation, very scientific, which was really exciting and intriguing for me personally. I know I learned a lot, and, again, thank you so much, guys, for that, but, no end.

1:06:52
It's a, it's a tricky no, where your problem lies within the normal functioning.

1:06:59
Oh, yeah, Bought it, so, yeah.

1:07:02
Yeah, no, it is. And Having those answers might, might, might actually get more questions to come later on. But, it's a, it's a good thing for, for patients and for caregivers that are trying their best to understand this condition, and how, and how to treat it and live their best life. So, again, thank you everyone, for joining, and we really appreciate it.

1:07:23
And have a good rest of your day, Everyone, again, thank you so much by air. Thank you.

1:07:31
Thank you.

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