0:04

Good afternoon, everyone, and welcome to today's program on hereditary neuropathy and genetic testing.

0:11

I'm thrilled to have two special guests today talk about hereditary neuropathy and the benefits of genetic testing.

0:18

During this webinar, we will address the problem of misdiagnoses and the benefits of getting genetic testing early on to lead patients down the right path for treatment.

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This program will also address the value of genetic counseling for families that are impacted by hereditary diseases.

0:36

My name is Lindsay Culbert, I'm the executive director at the Foundation for Peripheral Neuropathy.

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And again, I'm so very pleased that each of you have joined us today to learn more about this topic.

0:49

Before we get started, just a few housekeeping issues.

0:53

I wanted to let everyone know that this presentation is being recorded, and the recording link will be e-mailed to you, so you can view it again later and also uploaded to our website.

1:04

Please submit any questions you have via the questions box, and we will try our best to answer them during the end of our webinar.

1:13

And at any point, if you're having trouble with the audio, please feel free to dial in by phone.

1:19

The e-mail that you received to dial in for this presentation is also the same e-mail that includes the phone dial in instructions.

1:30

At this time, I'm pleased to introduce both of our special guests, today.

1:35

Doctor Sammy Kayla is joining with us, with more than 20 years of experience in diagnosing and treating patients with a variety of neurologic diseases and he's an attendee neurologist's at Penn Presbyterian Medical Center.

1:49

He co-founded the pen Amalea Dosa Center, one of the largest multi-disciplinary programs in the United States, treating patients with hereditary and acquired amyloidosis.

2:00

They are a group that is active in clinical trials and cutting-edge therapies for this group of diseases.

2:06

Doctor Kellis, other interests include treating patients with acquired inflammatory neuropathy, such as chronic inflammatory ..., poly neuropathy, also known as ..., and other myopathy is.

2:19

Also joining us today is Shauna Failing.

2:23

Shauna ... is a certified genetic counselor specializing in neurology.

2:28

She works with people who have a family history of neurological disorders, especially Hunton Huntington's disease, a progressive and incurable brain disorder.

2:39

She sees as many as 15 patients a day at the University of Iowa hospitals and clinics, guiding them through all phases of genetic testing.

2:48

Thank you, again, both of you, for joining us today.

2:51

And at this time, I'm pleased to welcome doctor Keller, onto the screen so he can begin his presentation.

3:00

Thank you again.

3:02

Thank you so much, Lindsey and your team for inviting me to this really special program, it's always a delight to talk and educate people about amyloidosis, disease that I've treated for a very long time, and I'm excited to see patients with amyloid because we have a lot to offer.

3:28

So I'm going to talk for about 15 minutes or so and go through exactly what is amyloid, what is amyloid neuropathy?

3:39

And and some of the therapies that are currently available?

3:44

It's always difficult.

3:45

I'd just say right now to answer a specific patient questions about their own particular problem and the IAEA not to be rude.

3:55

But I always like to, defer to the health care provider that is seeing you, in particular.

4:04

Um, so so amyloid, the word amyloid, uh, means you have a protein in the body that is ms. folding. And when it Ms. Folds, it doesn't work properly.

4:20

And it becomes what we call a toxic protein or a protein that is now damaging to dish to different tissues or Oregon systems.

4:31

And so there are many things that the many diseases that in which amyloid proteins are involved, Alzheimer's disease, for example, the diseases that we're talking about today do not typically affect the brain so they don't cause an Alzheimer like picture. But rather they cause nerve problems.

4:54

And so what is a nerve and what are nerve problems?

4:58

Nerves are the wires of the body, if you will.

5:02

And the air, they are the wires that connect, the impulses, that are coming from the brain and the spinal cord, to the muscles, to make the muscles move to the skin to help feel so they bring information from the skin, from the feet from the hands back up to the brain.

5:24

And the brain then interprets what the nerves, the electrical signals that the nerves have passed onto edge.

5:35

So when people have a peripheral neuropathy from whatever cause, not just amyloid, I mean, the most common ones in the United States today are nerve problems cause, or neuropathy as we call them from diabetes.

5:51

For example, um, other, there are many other causes of neuropathy if you drink too much alcohol for a very long time, you can get an neuropathy if you have take some medications like chemotherapy, drugs or other drugs you can get an neuropathy.

6:11

So neuropathy fees by and large cause a combination of numbness, tangling, and weakness, some combination like that Now You have to remember that even though I said amyloid doesn't cause brain problems, there are many other problems in the brain from other diseases like MS or strokes that cause numbness or tingling and weakness.

6:44

So, it's up to your doctor, primarily, the neurologist, or the nurse practitioner to figure out if the numbness or tingling that a person is has is due to a brain problem, or a nerve problem, or what what we call, localizing the problem.

7:03

localizing the origin of the nominative, tingling or pain.

7:09

Um, neuropathy is and especially neuropathy is that cause are caused by amyloidosis cause both numbness, tingling and weakness.

7:23

This is in contrast to diabetic neuropathy, which you know, some people in the audience may also have. And Diabetic neuropathy typically doesn't cause a lot of weakness unlike amyloid neuropathy.

7:36

So people who have diabetes and have amyloidosis, sometimes it's hard to sort out which is causing the problem. Is it the diabetes, or is it the amyloid or is in both?

7:47

And why it becomes important to figure out what the cause of the neuropathy is, is because there are special treatments that are they can be given, Um, it's that the neuropathy from, from amyloid, And let me just talk about that for a second.

8:07

Is a process that is typically right, rather slow going, but not very slow. So slow going meaning. it takes it precedes over months to years, rather than minutes to days or weeks. So some neuropathy is that move very quickly, like that. I like guillain barre syndrome, for example, or chronic, inflammatory demyelinating poly neuropathy. That's a mouthful. But so see, IDP, so-called.

8:42

So those are all these, um, for progress, fairly quickly, over over weeks to months, rather than months to years, the way you see an amyloid.

8:56

But, and amyloid can be tricky to, to diagnose.

9:02

The reason is that the neuropathy, when it starts in amyloidosis, it looks like any other neuropathy.

9:09

So it looks like the very common ones, like, like I said, neuropathy from diabetes neuropathy from alcohol use, you know, people over the age of 60.

9:21

About 10% of them will develop a neuropathy just by virtue of aging alone, so, um, it's and all of those neuropathy they looked the same in the beginning, and so there's a little bit of nominates a little bit of thinking and typically begins in the in the feet.

9:41

There may be Carpal Tunnel Syndrome associated with it, and so nominate ...

9:46

in the feet and then if you have that numbness or tingling in the first three fingers of either hand, um, which way can you up from sleep at night? That's typical of Carpal Tunnel and and people with amyloid can also get the carpal tunnel.

10:04

But people with diabetes can also get carpal tunnel and a peripheral neuropathy end the distinction and the difference is that over time so over months or even a year or a couple of years, people with amyloid will typically get weaker.

10:20

In that they have trouble with the muscles up here, the what we call, the proximal muscles, the muscles closest to the body as opposed to the hands which are the distal muscles.

10:32

So people who have proximal muscle weakness and amyloid people with diabetes typically don't get that.

10:40

And also, people with amyloid will have trouble getting up from a chair because the thighs are weak the thigh muscles.

10:49

The Buttock muscles are weak, and so they have trouble getting up out of a chair getting up off the toilet seat, getting up and down steps.

11:00

So approximate what we call proximal weakness or weakness in the muscles closest to the body, as opposed to the feet or the hands, are typical features of amyloid, but they're not typical features of diabetes.

11:14

But but, like I said, these may take a while to develop and show up.

11:20

So if you have a peripheral neuropathy and that is not really changing over many, many years, it's very unlikely that it's from diabetes.

11:29

On the other hand, if you have a neuropathy that is changing over months, or even a couple of years, and becoming worse than you know, that that's not typical of diabetes, then you have to look for other things, and among them is amyloid.

11:47

People with amyloid also have other organs because this is, like, I said, a protein that becomes abnormal.

11:55

And that protein may get into the heart tissue, and so they may may get a, what we call a heart failure oral cardiomyopathy.

12:06

Again, very important to figure that out because that is treated in a particular way by certain specialists, and, and it can be an emergency.

12:16

Because even though I told you that amyloidosis and amyloid neuropathy typically develops over a long time, there are some forms of amyloid and that I'll get to in a minute that are more or less a medical emergency.

12:35

But just to continue with the different organs that are affected, the amyloid protein, the abnormal protein, can developing many organs of the body. Heart failure is one of them, the stomach and the and the, the bowel is another and that can cause diarrhea. And constipation or alternating diabetic diarrhea and constipation.

13:04

People with amyloid also have what's called lightheadedness or ortho static hypotension, meaning they stand up rapidly and the blood vessels don't, um, work properly. And so, patients become lightheaded need to sit down or chains stand up for a very long time.

13:27

Um, other organs that are affected are rare.

13:35

The eyes can become affected. The lumbar spine can give symptoms that are akin to spinal stenosis.

13:47

Can become effected.

13:51

Anyway, the, um, the different kinds of amyloid that cause the symptoms that that I just described, ARR, either inherited or what we call acquired.

14:09

So, when, when amyloid is inherited, and Sean is going to tell you a lot more about that, you can do what's called genetic testing.

14:21

And figure out what gene is abnormal.

14:25

Um, you need to be sure that the amyloid, that is found in body part, is not due to what we call light chain disease.

14:46

So, amyloid light chain is different from hereditary amyloidosis, hereditary amyloidosis, If when you do the genetic testing, you will find a genetic abnormality or variant that the channel will describe. When you see your neurologist or cardiologist, they will do a chain a test for what's called light chain disease.

15:12

So amyloid light chain is made by a group of cells that is, that are behaving like a malignancy, and need to be treated by an oncologist or hematologists, So light chain disease like hereditary disease, like what we call wild type disease.

15:34

We're and wild type is the third type of amyloid, so we have hereditary, we have light chain disease, we have wild type disease, and wild type. There are no genetic abnormalities. And there is no cancer underlying it.

15:50

and it typically causes just the heart to become failing Oregon nerve develop heart failure.

15:58

Um, I've said a lot now so far, so this is sort of a whirlwind tour of amyloid.

16:09

Let me just briefly touch on the therapies.

16:13

So, the therapies that the neurologist and the cardiologist primarily treat are hereditary amyloidosis.

16:23

And, like I said, hereditary amyloidosis. There may or may not be a family history. So, it doesn't always have a family history.

16:34

As part of the, the patient's background.

16:38

But you can do the genetic testing and you find the, the one protein, called TTR, or trans Thai written.

16:49

Now that protein, that's what it becomes the amyloid as Janneke is a malformed protein and it becomes the protein that sits in the nerves or sits in the heart, and causes of the failure of those organs.

17:05

We have learned that by lowering the amount of that protein that gets secreted into the bloodstream, so that the protein is made in the liver and then it's secreted or pushed into the circulation and it circulates around the bloodstream and goes to different parts. and it does carries some hormones and stuff.

17:32

But the point is that if you lower the amount the liver is making, you're lowering the amount of toxic protein in the heart and in the nerves.

17:43

And so, you lessen the damage. That's happening to those organs.

17:49

And that's how we're treating this disease now, so it's very important to get a timely diagnosis.

17:54

Because the sooner you make the diagnosis, the less organ damage there is and you can prevent, we have shown now, many studies have shown that you, the, the sooner you get treatment for this disease, the less Oregon injury there is, and the better off you're likely to be.

18:19

So, this is sort of a word, not only to a patient who has amyloid hereditary amyloidosis, but it's also a word of advice to the family members because, um, when you get tested in a timely way and that doesn't know, Hereditary amyloidosis doesn't show up until people are typically in their late forties, early fifties or sixties or seventies. So you don't want to be testing people who are in their teens or twenties, as I'm sure Shah will touch on.

18:54

But later on, in life, in middle age, or later, it's a good idea to get tested because then you can get connected to an amyloid expert in the area where you live and they can keep an eye on things and hopefully prevent serious injury and improve a patient's life.

19:19

And so, Lyndsey, this is all I'm going to say right now and we'll be happy to carry on and answer questions later.

19:29

Sounds great, doctor Kalla, thank you so much.

19:32

and as he just suggested, we will be taking questions later on.

19:37

But before we do, I'd like to invite Shauna to come back onto the screen so she can present her presentation as well. Shauna. Thank you so much again.

19:50

Sure. Thank you for inviting me. So I just wanted to go do a brief overview. In general of hereditary neuropathy is we have a big multi-disciplinary or hereditary neuropathy clinic here where we specialize

in a variety of different types of genetic diseases that cause problem with the peripheral nerve. So we heard about a lot of different types of peripheral neuropathy which is a problem with those long nerves that go out from the spinal cord to the hands and feet. And this is specifically about hereditary forms of peripheral neuropathy.

20:29

So these are some of the questions I'll just be reviewing. What is a hereditary peripheral neuropathy? What are different forms? Genetic testing? What is it, and why do people get it and genetic counseling?

20:44

So, as I mentioned, peripheral neuropathy is a problem with a long nerves that leave the spinal cord and go out to the hands and feet. And we heard a lot of different types of peripheral neuropathy. But what sets different types of hereditary forms apart is there is a gene change that's leading to those symptoms. And we can test and determine what type of genetic problem is leading to the damage to the peripheral nerves. It is a mouthful, but they refer to these as peripheral nervous, because they are in the periphery of the body. And so, and affecting the nerve cells as opposed to things like directly muscle cells or those types of things which are myopathy.

21:32

So, we try in neurology we tried to sort of localize where the problem is coming from originally.

21:40

And in the peripheral nerves that can localize to what we call the myelin, which is the outside part of the peripheral nerve or it can localize to the axon which is the center part of that nerve. And you can kind of think of it as an electrical wire where the myelin would be sort of a rubber part of that nerve. And the metal part would be like the X on the center part of .... So there's kinda two components and you may do things like an EMG or nerve conduction studies to measure different parts of the peripheral nerve and in order to localize where the problem is coming from.

22:21

But in general, there can be a variety of different symptoms such as sensory symptoms, loss of sensation or pain symptoms that can come from peripheral neuropathy, these.

22:33

They can also cause a hereditary neuropathy is can cause things like muscle weakness or loss of the ability to detect your, where your body isn't space appropriate assumption. If people can have kind of changes to their gait, or they may have problems with hand function or changes in foot structure, that sort of thing.

22:57

When we look at general subtypes of neuropathy is there's kind of huge groups that we look at, Amyloidosis is one of those. There's also conditions such housed under their sharp Marie tooth disease umbrella. Even in these subsets, like for CMT or Charcot Marie Tooth Disease, there's over 100 different genetic forms of CMT.

23:21

So you can see that this is quite a diverse group of conditions, and it's not always simple to be able to determine what the genetic cause is or how it's being passed on in the family, and that's where genetic counselors can help.

23:41

So genetic testing, medical genetic testing is a little bit different than some of the tests that are available, what we call direct to consumer testing, which you can order a kit and send a way to look at Ancestry or these types of things. Medical genetic testing, typically it involves a blood test, or we might do a saliva test and it's usually ordered by a provider or a genetic counselor or someone in a medical, no institution or a place. And, it's linked to a specific medical condition that either is that individual has, or if they have a family history. And we're trying to identify the genetic cause for that condition.

24:27

This is a type of specialty testing that, again, goes through a ordering provider, and usually to a specialty lab that is approved to do that type of testing, and it can be complex to know which lab to use. Like I said, there's many different genes associated with these conditions, and there might be varying costs associated with it. So, genetic counselors help people to navigate those.

24:56

This is an old map, but it's just a map of even some of the genes that have had been identified. This is in 20 15 for genetic neuropathy and there's even more now.

25:09

Our group does a lot of gene discovery as part of this process because there's types of of inherited neuropathy is that people we haven't identified the genetic cause yet, so even in the last year we've helped identify five new genetic causes of hereditary neuropathy. So you can see that this list of genes is ever expanding.

25:32

So, hereditary neuropathy is not one disease even though it the symptoms can be fairly similar one to another. It is actually really a lot of different diseases housed under this umbrella, there's over 100, there's hundreds of genetic causes for neuropathy. And the symptoms can be highly variable in terms of age of onset, in terms of severity of disease, and how it's passed on in a family or what we call the pattern of inheritance.

25:59

Even, just today and being in clinic, I, you know, had a gentleman that was, you know, asking all, Is this really genetic? You know, my symptoms didn't start till I was in my sixties. And, you know, the answer is, yes, it can still be genetic, even if it didn't start in childhood. So, it really just depends on the genetic cause and what it takes to get to the point where someone might experience symptoms. So because of that, genetic testing can be complicated, and, you know, working with your local provider can help, or working with a genetic counselor can help you navigate that process.

26:39

These are just a smattering of some of them. Genetic testing labs that offer neuropathy panels at this time. they're not all the same in terms of what's offered on those panels, Like in terms of the number of genes or which genes, they vary in cost, and they change all the time. So again, it's a complicated process, too.

27:00

Get to that diagnosis.

27:02

And I just want to touch on what we're what we mean when we say genetic testing and what that process looks like in a medical context. So when we are looking at genetic testing oftentimes now genetic testing is offered in a panel type of process where you're looking at a collection of genes that have all been linked to a certain disease like hereditary neuropathy. And so, you might order a panel with, for example, 100 genes on it, what they're looking for is there.

27:32

The genetic testing process means that you're looking at specific genes that are localized on a variety of different chromosomes. So, a gene is sort of the instruction manual or like the recipe for a particular protein that functions in our body. So, we have many different genes on each chromosome. The chromosome is sort of like the housing structure or the bookshelf, where these instruction manuals are kept.

28:00

And when you look at a gene up close, it's represented by a string of letters.

28:07

A very simple sort of genetic alphabet that uses four letters, A, C, T, and G, And those are strung together on three letters with three letter genetic words.

28:18

That's spell out to the cell, what it needs to make, and how it needs to meet that.

28:22

So these three letter genetic words, each code for a specific amino acid and those amino acids are strung together like beads on a string that make the proteins that function in our body. So that's kind of a basic bio 101, going back to, you know, school of our genetic information.

28:42

So when we are doing genetic testing, we are looking at sort of the spelling to see, is there a spelling change that may lead to a different amino acid being created, and that could cause an abnormal protein, something that's not functioning like it should be? So, we're actually looking at the spelling and the

number of the letters. And if they're the correct letters, but it's the correct spelling in order to see if if this is functioning or not.

29:09

There's other things that you can also look for in terms of if there are problems where there are missing letters, deletions, like deleted part of the gene, then you might have a non functional protein because, you know, something is missing as part of that protein or, you know, there can be insertions and different things like that.

29:33

But that's the premise of genetic testing is sort of looking at that code and seeing are, is this instruction manual, correct? Are there changes that are there that should not be there?

29:45

So a lot of times people haven't encountered a genetic counselor and I just want to touch on what our role is in the healthcare system.

29:56

We are genetic counselors help people understand and adapt to the medical and psychological and familial implications of genetic disease and my specialty in neurology means that I work with folks with hereditary. Neuropathy is or even also central nervous system conditions that are genetic that affect the nervous system and you can find your local genetic counselor on the National Society of Genetic Counselors website, which I indicated there. So, we help patients or families, we help guide them through the testing process, to pick an appropriate lab, to be able to get an appropriate test, which may allow them to have answers about what's going on in their medical health.

30:44

We help to facilitate the most cost effective approach to testing, because genetic testing has really dramatically come down in cost, but it can be challenging to know what the appropriate test is and how much it's going to be. So we navigate that for patients.

31:00

We tried to allow patients to get the test that will yield the most likely positive test result, giving them answers.

31:10

If, as I mentioned, not everyone who has genetic testing can find the genetic cause to theirs symptoms, and that's because we don't know all the genetic causes of disease yet. In any can, and, you know, I know many specialties but in particular for hereditary neuropathy.

31:28

And we also go through the pros and cons of testing for patients in terms of making an informed choice and whether testing is appropriate for them.

31:37

So, some of the reasons people do genetic testing is to determine if other family members are at risk for family planning options. So, it may not just be for treatment, but if you identify a genetic cause of a disease in the family, then you know who's at risk, and in some cases, you can then use that information to prevent passing that genetic disease onto future generations.

32:06

These are some of the family planning options that, excuse me, genetic counselors might discuss, including testing during or before pregnancy or other options for people to build families if they want to prevent passing a genetic disease on.

32:24

Other reasons is just having a definitive diagnosis.

32:28

People live for years with, you know, these conditions that can progress over time.

32:33

And people a lot of times just want a name for what's going on and that gives them an understanding of what they have a name to describe it and maybe resources in a community where they can reach out to and then of course, possible access to treatments or clinical trials. So there are this is a rapidly changing environment in terms of hereditary neuropathy and there's clinical trials coming around the bend. We've heard just recently with related to ... treatments for that particular gene that causes neuropathy associated with amyloidosis.

33:09

So these treatments are, you know, coming available, or in clinical trials, And currently it's really important to have a genetic known genetic cause, so you're eligible for those types of treatment.

33:23

So we were talking earlier about gene gene silencing. And that's an approach for, potentially, for, you know, some of the treatments for these types of conditions, particularly for ... related amyloidosis, where we're going back to that analogy when you are looking at our genetic coder.

33:44

Or, it's kind of like a recipe or a blueprint, and you, the cells, use that information to then create the protein. Or, in this case, just using this analogy, the cake, and you need to, you know, have the correct recipe in order to produce the protein, that functions in the body. And if there's changes in that recipe, there will be changes in the way that that protein potentially functions in the body.

34:11

But you need entities to help with this process, to create that cake you have in the recipe, and you need sort of a chef in some ways to create the the protein or the cake and gene silencing, sort of takes the chef out of the picture.

34:27

so that even though people say it's still have the same genetic code, it's not being created into any sort of protein.

34:34

And therefore, it can block whatever that abnormal or toxic protein was doing, because it's no longer being created in the body anymore. So that's just kind of an example of one of the types of gene therapies that we use to potentially treat more and more of these diseases.

34:54

Some people they decide that genetic testing is is not for them. For example, there may be a risk of inconclusive results are not really giving an answer for them and and what? what do they do Then? They still, kinda, at the end of the day, are in the same situation where they don't really know what's causing their symptoms.

35:13

There can be an emotional impact on the family system: positive or negative, from positive or negative results, and, you know, a lot of these diseases, because they're a genetic effect, other people in, they make people feel people might feel guilt about passing on a genetic disease, things like that. So, this goes into some of that decision making. Genetic testing is not available for everyone. We don't know all the genetic causes, and then there's complicated additional tests that might be done, such as research based genetic testing. Sometimes people have concerns about genetic discrimination, So genetic counselors talk about what, what genetic discrimination is, and ways to protect yourselves, things like that.

35:58

Then, like I mentioned before, there's varying degrees of cost associated with this. And that often is a big question that people have is, What's this going to cost me? And so, genetic counselors how to navigate that? And there's other issues that we discuss, for example, a lot of local phone here.

36:18

A lot of these end up, know, being genetic diseases that people could potentially pass on their to their children. And so, at what age do you offer a genetic test?

36:29

And, and how is that offered? Usually we're not testing minor children for adult onset conditions. So we would talk about genetic testing options when people are over the age of 18.

36:45

So in summary, there's many, many different types of hereditary neuropathy and genetic testing can be informative for family members and for individuals.

36:57

So that's why a lot of times people decide to work with a genetic counselor or their physician to do testing. In general, genetic testing can be complex. So we encourage people to seek out genetic counseling to help make that decision decision. And in many cases, or in some cases right now, it can lead to treatments or clinical trials.

37:18

But we expect that to be increasing in the future, and I'm just going to end there, and then we can go back to the group for questions.

37:29

Thank you so much, Shawna. I'm gonna pop on as well. Just to say thank you again to both of our presenters, we've had quite a slew of questions that have come in over the course of this presentation, so I'm gonna go ahead and turn it over to both of you for some of these questions. If you're comfortable coming back on-screen, feel free to. Otherwise, I'll just stay on screen and ask them accordingly.

37:54

So, one question is, how are new variants discovered?

37:59

So obviously, some people have had extensive genetic tests done, and none of the known variants have shown up.

38:06

So how, how our new variants discovered and how are those unknowns soon to become known variants?

38:17

So Shawna, you want to take that?

38:20

Sure.

38:21

So we so kind of thinking of a variance is our changes within a gene.

38:29

So we can identify new variants or new changes within a gene. But there's also gene discovery that occurs as well. And that's looking at genes in general and what is associated with a particular disease.

38:46

And so there's kind of two processes we're talking about here, two levels, I guess. So, we are actively doing gene discovery and that is where you say there's, you know, there's over 100 different types of hereditary neuropathy. However, when we know someone has a form of hereditary neuropathy, we cannot always find their genetic cause. And so we enroll people in research studies where they're the identified genetic data is housed in a platform where we can look at that data and compare it to other families with unknown hereditary neuropathy is. And if we identify a change in a gene that is consistent across that group of people, then that is potentially a new gene that's identified is causing the new form of hereditary neuropathy.

39:41

So we've recently, like I said, just in the last year, discovered five new genes. two years ago, we discovered a new gene called sword, and that's now in clinical trials.

39:54

So gene discovery, then, can feed into clinical trials where people can have access to treatment. So gene discovery is a really important process to be able to kind of figure out what's broke apart. So you can try to figure out a way to know how to fix it.

40:11

Variant changes occur all the time in medicine. We're constantly offering genetic testing to people. And you can find of what a change, which we call a variant that may or may not be linked to a particular disease, even in genes that we know. Cause hereditary neuropathy variants. New variants are found all the time. And so we encourage providers working with patients to report variance, because it's really important, for the future of our knowledge, of these genes. You know, so even in genes, like TTR, which we've talked about, or, or CMT genes, there can be changes, and we don't know if they actually cause disease. Or if they're just a benign change, that can be found in the population. And so, reporting those variants are really important for the future, on patients and these diseases, So we can interpret what they mean.

41:06

And there, there may be people in the audience who've had genetic testing, and they get reports back. That's a variant of uncertain significance. And that's exactly what that is. It's a change, and we don't know, we can't interpret it, we don't know if it's connected to a person's disease or not. And so that's where putting those reports out there in the public can help us understand.

41:29

And is there any one genetics test that covers the most common inherited types of neuropathy, specifically that you know, I'm Shauna.

41:40

There are many panels for hereditary neuropathy.

41:45

I kind of showed a slide of a smattering of labs across the United States that are all due hereditary neuropathy testing. And so, they can be, you know, they can be anywhere from, you know, 20 to 40 genes upwards of hundreds of genes.

42:05

And so really, it's getting an evaluation, localizing maybe, where the problem might be starting in the nerve and letting that guide your providers to what test would be appropriate for you to be able to get the most likely answer.

42:23

OK, doctor Carla.

42:26

So if a person is tested and found to have amalea doses and they are successfully treated to stop further damage, is the previous damage?

42:38

Are those tissues ever able to heal or is it kind of non reversible?

42:46

Right.

42:46

So it really depends on how damage those tissues are. Tissues typically can heal. It also depends on what other medical conditions a patient has.

42:58

So if a patient has diabetes, for example, and already has an Arab athey from Diabetes and has, then developed a second problem, like, amyloidosis, it may not Peale, as well.

43:11

So both depends on how advanced they are, and and what there, what we call comorbidities or other illnesses.

43:23

Sure.

43:25

And are there specific blood tests, that people should do, to learn more about either the likelihood, or getting, namely a dosa, or having amalea doses?

43:39

Is there are specific tasks or specific blood tests that you guys know about?

43:46

Well, so, like, like many things in medicine, it's not one test that makes a diagnosis.

43:55

You need to have, I mean, even if you have an abnormal gene, or let me put it this way, a gene that's connected to a known amyloid condition like the V 30 M gene, or the V 122 ... gene, or any of those other genes, that doesn't necessarily mean you have amyloidosis. You can just be a genetic carrier. So you have the gene, but you don't have the disease itself.

44:23

And so there is no one test that we do to make the diagnosis and a diagnosis of amyloid is really made by tissue biopsy rather than a blood test per se.

44:39

So, really, I think if there's a concern about amyloid, you really need to talk to us and amyloids specialist.

44:51

And, you know, Shawna and you just referenced this, doctor Calla, but is what's the risk of passing inherited? Neuropathy is onto children, should patients be concerned about that, and to what extent?

45:09

Because there's many different types of inherited neuropathy, there's many different ways that it can be passed on in a family, so gene identification, or identifying the genetic cause helps us to know who else might be at risk in the family, and that's one reason people do genetic testing.

45:28

So one way, for example, if a particular gene is associated with autosomal dominant inheritance, in that case, the gender of the parent, or the child, doesn't matter. There is a 50% or one in two chance of passing that genetic disease on to each child.

45:49

But if it's recessive, meaning that, again, gender doesn't matter in that case.

45:54

But in recessive inheritance, both parents have to be carriers of a genetic disease in order for a child to be affected.

46:02

So, in that case, the child, it's a close to 0% chance that a child would be affected.

46:08

So those are pretty big differences, you know, 50% to 0%.

46:13

And so, knowing the genetic cause would allow us to give more accurate risk or assessments for children of someone who's affected. And that's another reason why people might want to do testing.

46:31

Are there any recent advancements in testing or other just treatment modalities. Generally, with inherited neuropathy, such as CMT, or ....

46:46

Is there anything kind of that you, either of you would want to highlight for things that are coming out soon or just recently came out?

46:58

So first of all, just a small clarification see, IDP is not an inherited neuropathy.

47:08

That is, it's what we call an autoimmune neuropathy. So your immune system gets confused and starts that attack, your own nerves.

47:18

There are always new therapies and new modalities of treating people with peripheral neuropathy.

47:30

And and this is a plug for people to get involved in clinical trials.

47:37

And this is how we figure out new treatment modality's and ones that are not even available.

47:47

On a commercial basis so that you can't get it because your insurance company won't cover this kind of thing.

47:53

And it's just, I just want to be clear that this is not being in a clinical trial, doesn't mean you're a guinea pig.

48:03

And that's really important, because you're not, it's not something that we're just testing on You. I think these are, these trials are done in a very thoughtful way. They, they are the ethics of a trial are considered, if there are available therapies, you're not denied those therapies. So, I just want people to understand that and being involved in the clinical trial is really a way to advance science and to advance the treatment for everybody and hopefully to advanced treatment for the patient themselves.

48:38

And our organization has a list of various clinical trials that we highlight that are focused on peripheral neuropathy, So I just want to highlight that for those that are watching today.

48:49

But do either of you have any other suggestions on identifying a clinical trial that is appropriate and, and something that would be helpful for the advancement of, of finding more answers.

49:04

There are trials that are listed on clinical trials dot gov is a great website to look up.

49:12

You can just put in your kind of disease of interest, or condition of interest. And it'll pull up different clinical trials that are being offered. Some of those are what we call natural history studies. So those are understanding how a particular condition progresses over time.

49:32

So you're not really it's not those are not interventional trials where you are getting a medication or intervention.

49:39

But they are still very important, because that's how we design interventional trials, is knowing how the disease typically progresses, and developing outcome measures, to be able to measure, disease over time, and then being able to use that knowledge in an interventional trial, to see if you're slowing a particular condition down or Stopping the disease.

50:02

Based on your knowledge of that condition.

50:04

There are as we Identify more and more genetic causes of neuropathy, those are going to be progressing Into the clinical trials space right now. one of the most common forms of CMT CMT one A is going to be entering into human trials space soon. It's already gone through many levels of, like, animal studies and things like that. So these are very exciting.

50:29

and we hope that as these become more and more available, that these as if they work, that these treatments are then going to be models for treating other types of inherited neuropathy is, so that you can kind of use the same techniques to bring more human rare forms of inherited neuropathy into the clinical trial space, and into treatments.

50:55

And a lot of these inherited neuropathy is like CMT too, and it's so rare that patients are actually Not even able to find a clinical trial or their clinical trials for every form.

51:09

I know that's kind of an impossible question to answer because it depends on when and where people are searching but For the rare for the rare neuropathy is that people are wanting to participate with clinical trial on what do you what's what's done the next step if they can't find something and they still want to get involved a different way?

51:29

Are kind of broadening your search? So instead of saying CMT to and look for trials related to CMT because then that you're gonna find their researchers that are interested in CMT in a broad sense, including Those more rare forms of inherited neuropathy.

51:48

So looking at organizations, you know, support organizations that include all forms of neuropathy just not, you know, not specific types Or Looking for clinical trials? like on clinical trials dot gov website that specifically deal with the broader sense of that disease? We here? We do a lot with CMT in general, and we enroll people with any form of CMT, including unknown forms of CMT.

52:15

So even if someone has not been genetically defined, you know, so those are, you know, there are researchers that are, you know, you don't have to be so specific, I guess.

52:29

And is pain a common symptom of amyloidosis, specifically, doctor Carla, do you know if that's a common symptom? or is that something that might be associated with a different form of neuropathy? Instead?

52:42

Pain is a common symptom, but it's not a necessary symptom. So, not everybody who, as amyloid neuropathy has pain, they may just have nominates and tingling. Like, everybody, not everybody with diabetic neuropathy has pain.

52:58

And then other forms of neuropathy, or even inherited neuropathy can be painful or painless, you know? So, it's, it's really very variable.

53:09

And, the last question that I kind of want to throw at both of you before we close out today's session is, you know, a lot of our patients are frustrated. We know a lot about the causes, but we don't know enough about the solutions.

53:21

And I'm curious if either of you could just speak to that with respect to Y, As I said, you might know, it would be coming or thoughts of hope for our patients, so that they know that we are here trying to figure stuff out.

53:39

So, it is, you know, medicine is always advancing, and there are always new things on the horizon.

53:46

Um, I think the best approach is to establish a good relationship with somebody who's an expert in the area of your disease and, And be in touch with that person.

54:00

Once a year, once every couple of years, once every six months, depends, because, you know, there are always new things that pop up, and they may pop up from time to time, and, you know, unfortunately, that, you may, you may not be right on that part on your doctor's radar.

54:16

So that's why it's always good to just check in, even if you don't have anything that's immediately treatable. It is frustrating and I, I get that, I get that.

54:26

Thank you.

54:28

I think, from my perspective, as a genetic counselor, my style of counseling has really dramatically changed.

54:35

Because, you know, it, if there was a time, when we would say, and this is what you have, this is the genetic disease.

54:43

And right now, there's, there's nothing right now, we can do about it, but, now, there are, you know, we, there are treatments that are becoming available or going into the clinical trial space.

54:55

And, so, counseling and talking with patients, we say, This is what the disease is, and these are the ways that there are either ways to potentially treat this disease, or, you know, So, you're You're kind of changing the way you provide information to patients, because things have changed.

55:15

So, dramatically, I would say, even in the last 10 years, and we have a real, You know, optimism about the future, of treating these diseases.

55:26

You know, TTR related neuropathy is one of those success stories, I think that there's going to be many more on the horizon.

55:34

So, I would also say that this, this research happens, not in a silo, but as a partnership with people. So people who are living with these diseases, partnering with researchers and research teams to be able to help move things forward, and allow us to help develop outcome measures or develop ways of measuring things that are important to the patient.

55:59

And not just something that a physician can measure. Like, we use things like a tuning fork to measure sensation but does not really matter whether someone can feel a tuning fork on a day-to-day basis. No. So we need measurements of of symptoms that really profoundly impacts a day-to-day life for people. And, so, it's only with partnering, partnering with patient advocacy groups, and patients living with the disease that, we can move these forward. And I've just been really, you know, part of my job, 50% of my job is an involved in research and helping with these trials. And it's just been amazing to partner with families and individuals affected by these diseases through my career, because they're very dedicated people out there of wanting to help us all move this forward to cares.

56:50

I agree, and I second that.

56:51

I think that's also a great way to kind of conclude this session, because, as a patient advocacy group, we also rely so much on anew and fellow experts on advancing more more answers. And so thank you both again.

57:09

I also want to thank Al Nylon for sponsoring this extremely fascinating and informative webinar. As I mentioned, this will be housed on the foundation for peripheral neuropathy, website for the for the foreseeable future.

57:22

So we hope that a lot and many more people will be able to learn about this and, you know, do more follow ups in the future. So thank you again everyone for joining the session. There will be a survey at the end. We hope that you take it, This is our opportunity to continually know what our, what our patient population is looking forward, looking for more answers. We hope you'll continue to support us so that we can continue to do these kinds of programs. And again, doctor Kalish, Shauna, thank you both so very much for your expertise today.

57:57

We're so very thankful and have a good rest of your day everyone and keep in touch. Thank you again. Thank you. Thank you very much.