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Inherited Retinal Diseases, Genetic Testing, and What Eye Care Professionals Can Do Today

Announcer:

Welcome to ReachMD. This medical industry feature, titled “Inherited Retinal Diseases, Genetic Testing, and What Eye Care Professionals Can Do Today” is sponsored by Janssen Pharmaceuticals, Incorporated. Here’s your host, Dr. Charles Turck, who will be joined by Dr. Mark Pennesi, who has received compensation from Janssen for his participation in this program. This podcast was approved under cp-367502v1.

Dr. Turck:

Approximately 165,700 people in the United States are affected by inherited retinal diseases, also referred to as IRDs. Because treatment options for these conditions are limited, genetic testing plays an important role in the patient journey of people living with IRDs.

Today, we'll dive deeper into the potential of genetic testing for IRDs including identifying treatment and matching patients to investigational clinical trials specific to the mutations they carry.

This is ReachMD, and I'm Dr. Charles Turck. Joining me to discuss treatment access is Dr. Mark Pennesi. Dr. Pennesi is a Professor of Ophthalmology, and an Inherited Retinal Disease Specialist affiliated with the Casey Eye Institute at the Oregon Health and Science University School of Medicine. Dr. Pennesi, thanks for being here today.

Dr. Pennesi:

Thank you for having me.

Dr. Turck:

Let's jump right into some background on IRDs. Dr. Pennesi, would you give us a brief summary of what IRDs are? And what are some of the most common IRDs you see?

Dr. Pennesi:

Sure. So inherited retinal diseases are a collection of diseases caused by mutations in genes that are important for the structure and function of the retina. And mutations in these genes lead to retinal degeneration, and ultimately, vision loss. And there are over 270 different genes that have been associated with inherited retinal degeneration. And this explains the wide variation of pathophysiology and outcomes in this class of diseases. For example, you can imagine that a gene that affects the rod photoreceptors, which are the cells that we use for nighttime vision, would first present as a problem with impaired nighttime vision. Whereas, if you had a gene that affected the cone photoreceptors, which we use for daytime vision, the patient might present with central vision loss or problems with color vision.

And most IRDs affect the photoreceptors, but some are associated with the retinal pigment epithelium, which is a thin layer of tissue that supports the retina, and other genes can affect inner retinal function as well. Now, the inheritance pattern can vary quite a bit, and we can see autosomal dominant inheritance, autosomal recessive inheritance, X-linked inheritance, and even mitochondrial inheritance rarely. When we think about some of the common inherited retinal degenerations, the most common IRD is retinitis pigmentosa, or RP for short, and that has a estimated prevalence of about 1 in 4,000 individuals in the U.S. and Europe. Another common IRD is Usher syndrome, which is a syndromic form of RP where patients have congenital hearing loss and RP and that affects about 17 in 100,000

patients. The final common IRD is Stargardt's Disease, which affects about 1 in 10,000 patients, and this tends to present a little bit differently because it affects the cone, so it often presents as a macular dystrophy or a cone rod dystrophy.

Dr. Turck:

Now to get us a little more familiar with retinitis pigmentosa, would you tell us more about this common IRD?

Dr. Pennesi:

Right. So, RP is the most common IRD, and as I mentioned, there are 270 different genes that can cause inherited retinal degenerations but, there are about 90 of these that are associated with retinitis pigmentosa. So, RP can present at any age, but most commonly presents in young adulthood. And the features that most commonly are reported are nyctalopia, or night blindness. Patients also reported problems with their dark adaptation if they go into a movie theater, they may have to wait, before they can find their seat. And as the disease progresses, it starts to impact peripheral vision. And as this becomes severe, patients can even develop tunnel vision, and ultimately, patients can lose central vision over time.

Now, RP can also show several different forms of inheritance. Autosomal recessive is most common. There's autosomal dominant. But probably the most severe is X-linked retinitis pigmentosa. And with X-linked retinitis pigmentosa, there are three different genes, that are causative. And X-linked RP makes up about 6% to 16% of RP patients in the United States. And they present with symptoms that are similar to typical RP, but they tend to come on much earlier. So, a common story would be a young boy who's 7 or 8, who has a loss of night vision. There also tends to be a more rapid progression of loss of the peripheral vision and even the central vision. And in fact, many of these patients can go legally blind by age 45.

Now, since the disease is X-linked, it primarily affects males, since men have only one X chromosome, so there's no backup chromosome. But interestingly, female carriers have the mutation can also be affected, but they're much more variable. And females can range from being completely asymptomatic, to having disease that is just as severe as men. And this has to do with X chromosome inactivation. Since females have two X chromosomes, they do have a backup, and the cells randomly choose which chromosome they use. So, depending on the pattern of X inactivation, we can get different severity.

Now, in terms of treatments for retinitis pigmentosa, unfortunately, there’s really not a whole lot we can do with the exception of gene therapy for RPE65 mutations, which is one rare disease, we really don't have anything that is effective. We do recommend patients have a diet high in antioxidants and omega-3 acids and avoid things that might cause oxidative damage, such as smoking. We also try to refer our patients to a low-vision specialists, as many of them will benefit from those services, including orientation and mobility training, and ultimately, some patients need a white cane or guide dog. However, in spite of the past, there are potential therapies in development, using gene therapy for patients with X-linked retinitis pigmentosa.

Dr. Turck:

For those just joining us, you're listening to ReachMD. I'm Dr. Charles Turck, and today I'm speaking with Dr. Mark Pennesi about inherited retinal diseases, or IRDs for short. This medical industry feature titled, Inherited Retinal Diseases and Genetic Testing: What Eye Care Professionals Can Do Today, is sponsored by Janssen Pharmaceuticals, Incorporated, and Dr. Pennesi has received compensation from Janssen for his participation in this program.

Now, let's switch gears to genetic testing for patients with IRDs, Dr. Pennesi. Are there any benefits to genetic testing of these individuals?

Dr. Pennesi:

Absolutely. I think that's a great question. I think genetic testing is very important. And at least in the past, I found that eye care professionals may not initially see the value of genetic testing if they've already made a clinical diagnosis. But I think it's important that we change that mindset.

There are very important reasons to get testing. The American Academy of Ophthalmology recommends genetic testing for most patients with a suspected inherited retinal dystrophy. And the reason for this is that we really want to find the underlying gene so that we can start to use potential new therapies.

And I think it's important maybe to dispel some misconceptions about genetic testing. First, genetic testing is difficult to get. There are now a number of programs that can help patients get genetic testing.

The other is that genetic testing is expensive and not covered by insurance. I think it's important that patients visit a inherited retinal degeneration specialist because, many times we do have ways of getting genetic testing.

So, it's really important to get genetic testing, but we know that there are still some barriers to it. At one large healthcare system in the U.S., only 1.5% of people with a suspected IRD received genetic testing. Whereas, at a specialty practice like my own, we test over 95% of our patients for genetic testing, and that's how important this is.

Now, why would we want to get genetic testing? Well, first off, it confirms the patient's diagnosis. And even though you may have a diagnosis of RP, and the symptoms may look similar, we really do need to know the underlying genetic mutation for many of the treatments that are going to come in the future.

Second, genetic testing can reveal more than just eye health. As I mentioned earlier, some of these genes are syndromic genes and are associated with other systemic issues. For example, a number of IRD genes, that are syndromic, have been associated with problems of the kidney. And so, by identifying that we can often get patients screened earlier for those kinds of systemic conditions.

Dr. Turck:

And what are your thoughts on the importance of genetic retesting?

Dr. Pennesi:

Yeah, I think that's a really important question as well. The technology for genetic testing is changing rapidly. So even if a patient had a negative test 5 years ago, we should retest them, because the ability to find these genes has improved vastly. So, with the current technology, we can solve up to 76% of the cases of patients with IRDs. So, if you haven't had testing in a long time, or you had testing, that was negative, it's important to regularly get retesting.

The other reason is that every lab has a little bit different makeup of their panels. So, if you have a rare gene, it may not have been on that particular panel. So, we do encourage our patients to get routine testing. And that can best be done at a specialty center.

Dr. Turck:

Where could patients go if they'd like to learn more?

Dr. Pennesi:

Yeah, there's some great resources online, for patients who are interested in learning about genetic testing. And one can be found at the website, www.eyesongenes.com.

Dr. Turck:

Now, looking at what may be on the horizon, do you anticipate any upcoming IRD-specific treatment options?

Dr. Pennesi:

Yeah, there are many coming. We have dozens of clinical trials, for potential therapies for different types of inherited retinal degenerations. So we already have one FDA approved treatment for RPE65. But there are multiple gene replacement therapies underway, specifically for X-linked retinitis pigmentosa, as well as many other genes. So I think the next 10 years is going to be a really exciting time in the field, because we're going to see more and more therapies that are gene specific. And beyond that, maybe even some therapies that are gene independent.

Dr. Turck:

Before we close, Dr. Pennesi, are there any closing remarks about IRDs you would like to leave for our listeners?

Dr. Pennesi:

Yeah, I think it's really important that patients have hope. Although we haven't had therapies in the past for these diseases, the technology is advancing rapidly. But it's also important that, patients take a little bit of ownership and try to do what they can, in particular, making sure that they get genetic testing, so that the doctors can understand what exactly is the origin of their disease, and we can match them up with potential future therapies.

Dr. Turck:

Those are great comments for us to think about as we come to the end of today's program. I want to thank my guest, Dr. Mark Pennesi, for helping us better understand genetic testing for inherited retinal diseases. Dr. Pennesi, it was great speaking with you today.

Dr. Pennesi:

Thank you very much.

Dr. Turck:

I'm Dr. Charles Turck. Thanks for listening.

Announcer:

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And to learn more about genetic testing for inherited retinal diseases, visit eyes on genes dot com, that’s eyes on genes G E N E S dot com.