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The Cryptid Sloth Show Episode 2: What's in A Name?

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Transcript

What's in a name? Well, when it comes to CMT you might want to hold on tight because you're in for one hell of a ride.

[Theme Music]

Stop standing there! Attention, everyone!

The Cryptid Sloth Show: Where CMT and Life Meet.

With your host...

Kenneth Raymond

[Theme Music Ends]

Hi, everybody! Thanks for tuning in to The Cryptid Sloth Show

Podcast: Where CMT and Life Meet. I'm your host, Kenneth Raymond, and I have CMT.

Charcot Marie Tooth disease, or CMT for short, just one name in a sea of many. It's the most common inherited peripheral nervous system disease. CMT is also known by several other names, some of which are Hereditary Motor Sensory Neuropathy, Hereditary Sensory Autonomic Neuropathy, distal Hereditary Motor and Sensory Neuropathy, Peroneal Muscular Atrophy, and the list goes on, and on, and on, and on. They all essentially refer to the same set of diseases though. Why do I say this? We'll get to that answer in a moment, and that answer might surprise you.

With CMT being inheritable, there are four ways that CMT can be inherited. These four ways are called the inheritance patterns. The inheritance patterns are confusing. The genetic mutations that

cause CMT are confusing. There's so many types, each confusingly caused by a different confusing gene mutation. CMT is as confusing as it gets. For all the confusing variability of CMT, there's only a couple of things that don't change—there's always an exception to the rule and CMT is inherently confusing. Amid all this confusion, there is an easy-to-follow method for keeping track of all the confusion.

CMT with all its many types and subtypes has a categorized naming classification system. You may have heard of these. You may have heard CMT 1A. You may have heard CMT 4C. You may have heard CMT X1, or some refer to it as 1X. Well, there's a method and a madness to how these got their names.

The current classification system and that's what I'm going to call it for ease of discussion, a classification system, categorizes the types according to the inheritance patterns, that is, how the type is inherited. The inheritance patterns are Autosomal Dominant, Autosomal Recessive, and then X-Linked Dominant and X-Linked Recessive, together as a single X-Linked category. I explained these inheritance patterns in detail in detail in episode one, if you'd like to learn more about these. These categories organize further according to the component of the peripheral nerve that the disease primarily targets, that is, the myelin or the axon.

These categories represent the types. The types then subdivide into subtypes that receive the sequential letter designation that correlates with the order of the underlying gene mutation discovery for that type.

Hopefully, I haven't lost you yet. This does get easier though, I promise you.

Using this classification system naming convention, types receive a number: 1, 2, 4, etc., and subtypes receive a letter: A, B, C, D, and so on. With all things CMT, there are exceptions to these rules. However, the basic structure of this classification system is a [type][subtype] format.

Currently, there are six basic naming categories for CMT. The categories are 1, 2, 4, X-Linked, Dominant Intermediate, and Recessive Intermediate. The Type 1's, or, CMT 1, are demyelinating and autosomal dominant in inheritance. The Type 2's, or, CMT 2, are axonal, and are either autosomal dominant, or autosomal recessive in inheritance. The Type 4's, or, CMT 4, are demyelinating and autosomal recessive in inheritance.

You may have heard CMT Type 3, 5, 6, or 7. However, these are now archaic, as subtypes under these categories were reshuffled into the current type categories as causative gene mutations were identified and as researchers developed new understandings of CMT.

The X-Linked types, or CMT X, are caused by a mutation in a gene that lives on the X chromosome. The X link subtypes can be either dominant or recessive, and they are termed X-Linked dominant or X-Linked recessive. Both modes of X-Linked Inheritance categorized together as a single category, simply X-Linked CMT.

Now, with X-Linked CMT, unlike CMT 1, 2, and 4, the letter comes before the number, but the letter is always "X," to signify X-Linked CMT. I know, state the obvious, right? Just called me Mr. Obvious today. The last two remaining groups don't have a number or a single letter to represent them though. These two groups, together, are known as Intermediate CMT.

Intermediate CMT gets its name from the nerve conduction characteristics that are associated with each of the Intermediate types, but this does not refer to disease severity as the name, "Intermediate," might imply. What does that mean? Well, I'm glad you asked. It's not as confusing as it sounds once we break it down.

The nerve conduction characteristics of demyelinating CMT and those of axonal CMT can be distinctly different from one another. These characteristics are usually discernible with a nerve conduction study. In general, as a general rule-of-thumb, normal nerve conduction velocities, the speed at which a peripheral nerve transmits a signal, are around 50 to 60 meters per second. In general, usually, typically, the nerve conduction characteristics of demyelinating CMT exhibit conduction velocities that are below 38 meters per second. In general, usually, typically, nerve conduction, characteristics of axonal CMT exhibit conduction velocities that are around 38 meters per second, to as fast as only slightly slower than normal.

This is CMT important, Mmm k? In general, as a general rule-of-thumb, demyelinating CMT has nerve conduction characteristics that are slower than 38 meters per second, and axonal CMT has nerve conduction velocities that are faster than 38 meter per second.

We're solid, right? Yeah? Well, good, because then along comes Intermediate CMT throwing a giant monkey wrench into that well-oiled demyelinating-axonal rule-of-thumb.

The nerve conduction characteristics of intermediate CMT exhibit nerve conduction characteristics that overlap that which is characteristic of demyelinating CMT and that which is characteristic of axonal CMT Intermediate CMT is the name given because the nerve conduction characteristics are neither demyelinating nor axonal they are somewhere in between, they are Intermediate. I mentioned nerve conduction velocity here, but it's not the only parameter that's measured when evaluating nerve conduction characteristics. There are several others, just to be clear.

Compound Muscle Action Potential, or "CMAP," Sensory Nerve Action Potential, or "SNAP," F-Wave Latency, and a few others are all measured, and the data those parameters provide illustrate a nerve conduction characteristic. Again, it's a lot of fancy talk, I know, but we'll go into depth on what those parameters represent in a future episode, but for today, with what we're talking about, nerve conduction velocity is the only one we need to focus on.

Nerve conduction velocity is fairly straightforward compared to the other measured parameters. The other parameters have a lot of variability. Nerve conduction velocity, however, while it does have some variability, essentially has a set of numbers that is understood to represent either demyelinating CMT, or a set is numbers that is known to represent axonal CMT. When a doctor takes into consideration the nerve conduction velocities, together with the other measured parameters, they can then have enough diagnostic information to determine if the CMTer's CMT is demyelinating or if it's axonal. Intermediate CMT, however kind of crosses those barriers, just to make diagnosing CMT that much more difficult for the doctor.

But now that we have all the tech stuff out of the way, let's get back to talking about the naming classification categories, 'cause this is what this episode's about, the name.

The classification of Intermediate CMT is determined according to the respective inheritance patterns associated with each of the Intermediate CMT named categories. Intermediate CMT can be either autosomal dominant in inheritance or autosomal recessive in inheritance. As such, Intermediate CMT that is autosomal dominant carries the designation "CMT-DI," and this designation represents Dominant Intermediate CMT. I know, the "D-I" comes after, not before but we say it, "Dominant Intermediate CMT." Likewise, Intermediate CMT that is autosomal recessive in inheritance carries the designation, "CMT-RI," and this is referred to as Recessive Intermediate CMT. Again, I know, the "R-I" comes after "CMT," but we say it before "CMT." I don't make the rules, I just follow them. Sometimes. Anywho...

Each of these two Intermediate CMT categories have several subtypes. Each subtype is represented by a letter: A, B, C, etc. What do all these letters represent though? That's actually the easy part.

Will all these different categories, the letter that appears after the number, as in: 1A, 2A, 4J, and in the case of Intermediate CMT: D-I-A, R-I-B, etc., correlates with the order in which the underlying gene mutation identification occurred. "A" would be the first gene mutation, "B" would be the second, and so on, except that the exact mutation responsible for CMT-DIA has not been fully nailed down. What? An exception? Say it isn't so! I know, right? One common thread with CMT: there is always an exception.

[♪ Bruh! ♪]

Getting back, in CMT 1A, it's an autosomal dominant demyelinating type, and it was the first one of the Type 1's to have its underlying gene mutation identified. In CMT 2A it's an autosomal dominant axonal type and it was the first one of the Type 2's to have its underlying gene mutation identified. In CMT 4J it's a subtype that has an autosomal recessive inheritance pattern, and it was the 11th… ish... one of the type 4's to have its underlying gene mutation identified. 11th... ish... because "J," is, like, the 11th… letter in the alphabet, but… there's a 4B1, B2, and B3 before we move on to 4C, but you get the point.

You see? Easy peasy. There's not much to it once we break it down. Let's do a quick recap though, so I don't lose you

The number used in the classification of CMT describe whether it is demyelinating and autosomal dominant: CMT 1, axonal: CMT 2, demyelinating and autosomal recessive: CMT 4. The letter then describes the order: first, second, third, etc., that the responsible gene mutation identification occurred for that number. Piece of cake.

But then X-Linked League showed up and threw in a giant wrench of their own. Like Intermediate CMT, the X-Linked CMT naming classification category is a little different than the others. Are you seeing the common thread, here? For every rule of CMT, there's an exception.

In this classification naming convention for X-Linked CMT, the "X" is first. State the obvious right? Bear with me. I briefly touched on this in the first episode. X-Linked used to be

considered, named, categorized, classified, included with the Type 1's. This was when there was only one X-Linked subtype. This is changed as there are now six X-Linked subtypes. X-Linked CMT is demyelinating. When there was only one X-Linked subtype, because the subtype is also dominant in inheritance, albeit X-Linked dominant, it made sense to categorize it with the Type 1's, remembering that the Type 1's are demyelinating and dominant in inheritance, albeit autosomal dominant. However, as scientists made additional discoveries of X-Linked CMT gene mutations, it made better sense to create a new category specifically for X-Linked CMT.

Coming full circle now, with the X linked category, the "X" is first to indicate that it's an X-Linked CMT. I know, state the obvious. The "X" is then followed by a number: 1, 2, 3, etc. The number denotes the order in which the underlying gene mutation was identified. Currently, there are six subtypes of X-Linked CMT: X1, 2, 3, 4, 5, and 6. X1 and X6 are dominant in inheritance, and the other four are recessive in inheritance. And, again, I fully explain these inheritance patterns in the first episode if you'd like to learn more.

The intermediate CMT classification convention is a little different in the same regard as X-Linked CMT. However, unlike X-Linked CMT starting with the letter followed by a number, Intermediate CMT does not use numbers to denote subtype. Instead, and even though Intermediate CMT names are all letters, Intermediate CMT subtype classification uses the same chronological sequential letter format beginning with the letter "A," such as CMT-D-I-A, CMT-D-I-B, etc. And, now that I've confused you with these exceptions to the naming rules there are some additional exceptions to Type 1 and Type 2 CMT.

[♪ Bruh! ♪]

The current naming convention for CMT tells us that CMT 1 is demyelinating and autosomal dominant in inheritance, right? If your doctor diagnoses you with CMT 1 you know that it represents that you have a demyelinating CMT and it's autosomal dominant in inheritance. These are the rules. Since rules are made to be broken though, there's a little bit of controversy around 1F.

Sometimes, you'll see CMT 1F expressed as CMT 1F/2E, or 2E/1F, depending on author. This happens because both subtypes are caused by mutations in the same gene: the NEFL gene. For some, mutations in this gene cause a demyelinating CMT; for others, an axonal CMT. Hence, 1F/2E. Mutations in the same gene are also associated with causing Intermediate CMT-G, and some argue that the 1F designation should be scrapped in favor of Dominant Intermediate-G because of the nerve conduction characteristics exhibited by 1F.

Another exception to the CMT 1 classification is the subtype of the acronym all its own: HNPP. The exception here is the acronym. Make no mistake though, HNPP is a type of CMT, and it is the only type of CMT that is considered to be episodic in nature. I'll include a link about this in the show notes for you.

HNPP is an acronym that stands for Hereditary Neuropathy with liability to Pressure Palsy. HNPP is categorized as a CMT 1 because HNPP is autosomal dominant in inheritance, and because the primary disease process is demyelinating. Coincidentally, HNPP is the genetic opposite of CMT 1A. What do I mean by that?

CMT 1A is caused by a duplication of the PMP-22 gene. HNPP, being the genetic opposite is caused by a deletion of that very same gene. “Normally,” yes, I'm using finger quotes in the air here, “normally,” there are two copies of a gene. A CMTer with 1A has three copies of the PMP-22 gene, and the vast majority of CMTers with HNPP have only one copy. Although in the majority of cases HNPP is caused by a deletion of the PMP-22gene, it can also be caused by point mutations within the PMP-22 gene. What's a point mutation? A point mutation is a mutation that occurs within the gene as opposed to the gene being duplicated or deleted. Moving on to CMT 2.

Classification naming category rules for CMT tells us that CMT 2 is axonal and autosomal dominant in inheritance. However, there's exceptions to this rule. Why? Because, apparently, rules are made to be broken and the autosomal dominant criteria literally do not apply to CMT 2 even though nobody has directly said so.

The underlying gene mutations that cause 2A2B, 2B1, 2B2, 2B3, 2B4, 2B5, 2DD, 2R, and 2S are autosomal recessive in inheritance. 2K, 2P, as in Pam, and 2T, as in Tom can be autosomal dominant or autosomal recessive in inheritance. There are even some autosomalrecessive subtypes that are known only by their associated genes: SORD CMT and DST CMT, no number, no letter. What's with the double letters though, Mr. Dudely von Dudeness? Well, there's a thing about those double letters.

CMT2CC, 2DD, and 2EE are a thing because researchers got to the letter, "Z," with naming the Type 2 CMT subtypes. The letter that follows the number, 2O, for example, represents the sequential order that the underlying mutation was discovered, right? For CMT 2 researchers ran out of letters once they hit, "Z," so they rounded the bend and started doubling up, starting with 2CC. There isn't a 2AA, and there is no 2BB; and the reasons are truly fascinating.

Back in the day, the first underlying causative gene mutation identified for CMT 2 was a mutation in the KINESIN Family Member 1B gene, or the KIF1B, for short. This discovery was designated CMT 2A in accordance with the classification naming conventions. A few years later, researchers found that the data associating KIF1B to autosomal dominant axonal CMT, or CMT 2A for short, I know, that's a mouthful, was flawed and inaccurate. Scientists further determined that the actual underlying responsible gene mutation for 2 was a dominant mutation in the good ole MITOFUSIN2 gene. The confusion with the actual gene involved, and I'm just spitballing here, could very well have come from the two genes being remarkably close neighbors. I mean close-close. How close? The same biological mailing address.

The MFN2 and the KIF1B genes both have their chromosomal location at chromosome 1p36.22. This location is the genetic address that scientists use for describing the genes home address within our DNA. The address is simply known as the gene's cytogenic location. This address, like a mailing address, is fairly easy to decipher.

The first character in 1p36,22 represents the chromosome, in this case, chromosome 1. The next is either a lower case "p" as in Pam, or lower case "q." Chromosomes are each divided into a short arm and a long arm, just for keeping track. The short arm is designated "p," and the long arm is designated "q." The next set of characters represent the position and subposition band, respectively, within the chromosome arm that the gene calls home. The address for MFN2 and KIF1B: 1p36,22, transaltes to chromosome 1, short arm, position 36, subposition 22. It is the two genes' House number, Street, City, Zip Code.

Given this tad little bit of information, it's easy to see how the two genes could have been confused for causing 2A. Once researchers identified that MITOFUSIN2 mutations were really the cause of 2A, a naming shuffle took place. Go figure. This is where some of that confusion though really takes off. I'm going to try to simplify it though.

Now that the underlying gene mutation responsible for 2A had been sorted out, the mutations in KIF1B originally associated with 2A moved to the esignation of 2A1 and the newly identified mutations in MFN2 received a 2A2 name. That's easy enough, right? But this gets better though.

Although the data associating KIF1B mutations with causing 2A was determined to be inaccurate, the publication establishing the association hasn't yet been retracted. Sometimes things get retracted, sometimes they don't. This one hasn't. It's still bouncing around out there in Internetshirestonvilleland. You can still find it.

Rewinding though, for sake of clarity at that time, KIF1B remained 2A1 to designate that it preceded the identification of the MFN2 mutation. In kind, the MFN2 mutation received the 2A2 designation to indicate that its identification follows the KIF1B discovery. So, 2A1 is KIF1B; 2A2 is MFN2. Things were fine like this for a while until researchers identified a recessive mutation in MITOFUSIN2 causing a CMT Type 2. This, of course, caused things to get shuffled, yet again. This recessive mutation discovery happened around 2010-ish. This discovery received a 2A2B designation.

With the dominant MITOFUSIN2 mutation being named 2A2, it made sense to call this new recessive mutation 2A2B. In an attempt to not totally confuse us CMTers, some researchers started calling dominant MITOFUSIN2 CMT 2A2A and recessive MITOFUSIN2 CMT 2A2B. Because keeping track of these was difficult at best, and because CMTers were becoming uber-confused, the 2A names got shuffled, again, to where we are now. Totally not confusing, right?

So, currently, the KIF1B mutation associated with causing CMT isn't included in any of the named subtype listings for CMT2 or even in CMT. And, I'll have more on this, here, before we're done. But currently, the dominant MITOFUSIN2 causative mutation for CMT is designated 2A; and the recessive MITOFUSIN2 mutation still remains 2A2B, because totally not confusing. 2A1 is now, simply, 2A.

These named subtype changes reflect that CMT really is about mutations in genes and not about the genes themselves. If you've been diagnosed with CMT2A1, 2A2, or 2A2A and you can't seem to find any info on your diagnosis, all of this name reshuffling is why. The now former 2A1, 2A2, and 2A2A are, now, collectively known as, just simply, 2A. There isn't any publication or notice given to CMTers that says, "hey, by the way, we made some changes over here." Instead, things just happen. Again, because totally not confusing. What's up with B1, B5 though?

Scientists have broken away from continuing with double-letter subtype names for CMT 2. Instead, they now favor adding a number after the letter, "B." The name CMT 2B refers to an axonal CMT that is autosomal dominant in inheritance. Specifically, autosomal dominant mutations in the RAB7 gene are associated with causing CMT2B. But, CMT 2B plus an additional number after the, "B," as in 2B1, 2B2, 2B3, 2B4, and 2B5 are autosomal recessive in inheritance. Yeah, totally not confusing at all.

[♪ Bruh! ♪]

Why though, has KIF1B disappeared from the CMT rolls? That answer comes from Dr. Stephan Züchner, a world-renowned molecular neurologist and CMT expert, who is also credited with with many CMT causing mutation discoveries. In the CMT Association's 2020 Patient and Family Conference, held virtually this past November 7th, Dr. Züchner was answering questions in a Q & A chat session. Several people asked questions about their KIF1B caused CMT. Dr. Züchner explained that KIF1B is not only not causative for CMT, but that researchers believe that KF1B isn't associated with any inheritable neuropathy. He explained that the types of CMT that were associated with KIF1B mutations are actually caused by mutations in the MFN2 gene.

Now, a couple of minutes ago, I mentioned that there are some subtypes of CMT that don't have a [number]-[letter] name designation, that they are simply called by their associated gene name. In the same conference, and I'll put a link to this in the show notes, Dr. Züchner gave a presentation on research progress regarding Type 2 CMT. Dr. Züchner, with many others, identified 2 new responsible mutations in 2020, and both cause a Type 2 CMT: the DST gene and the SORD1 gene. The SORD1 gene mutation is thought to be the most common cause of autosomal recessive axonal CMT, too. Kind of cool.

There's an unwritten rule that the person who discovers the CMT causing mutation gets to the subtype that is associated with that mutation. When asked about the subtype associated with the DST and the SORD mutations, Dr. Züchner explained that they probably won't get a [number][letter] name, that they'll just be referred to by the associated gene: SORD CMT and DST CMT. So, it looks like we might be going through yet another CMT naming format shift. Totally legit not confusing.

Remember at the beginning when I said that CMT and a bunch of other acronyms all referred to the same thing? Everything we've talked about up this point had to be covered before getting to this next part.

CMT is an acronym for three doctors, right? Doctors Charcot, Marie, and Tooth. HMSN stands for Hereditary Motor and Sensory Neuropathy. dHMSN stands for distal Hereditary Motor and Sensory Neuropathy. HSAN stands for Hereditary Sensory and Autonomic Neuropathy. Where the "CMT" acronym represents the fathers of modern-day neurology, these other acronyms are used by many doctors as definitions for what CMT is and for what CMT anatomically involves. What do I mean by this?

Well, CMT is hereditary: "H." Sometimes, it's a motor neuropathy: "M." Sometimes, it's a sensory neuropathy: "S." Sometimes, it's a distal neuropathy, that is, affects only the farthest points from the spinal cord: "d." Sometimes, it's an autonomic neuropathy: "A." Sometimes, it's a combination of these, and sometimes, it's all of these. Regardless of which, it is always a peripheral neuropathy: "N." If all of these are CMT, and CMT is all of these, why all the acronyms and disease names if they're all the same name? This is the begging question.

Washington University at Saint Louis has one hell of a comprehensive website catalog of all of these acronyms, diseases, and etc. I'll put a link in the show notes for you. But cruising their website, there is an interesting correlation between CMT and HMSN: CMT 1 and HMSN 1 are mirrored. CMT 2 and HMSN 2, are mirrored. OMIM, O-M-I-M, verifies this. What do I mean by this though?

CMT 1A and HMSN 1A have the same genetic cause. CMT 1B and HMSN 1B have the same genetic cause. CMT 2A and HMSN 2A have the same genetic cause. HMSN 1 subtypes are the exact same as the CMT 1 subtypes in every way shape and form. The same is true for HMSN 2 and CMT 2. The only difference is the acronym—the name. These two are mirrored. The mirroring ends here, though. Along these lines, some doctors draw their distinction for using the HMSN acronym over the CMT acronym, explaining that HMSN describes the disease, and CMT is a name for three guys.

[♪ Bruh! ♪]

CMT 3, which is the category for Dejerine-Sottas disease, is archaic, as CMT 3 subtypes were reclassified into the other current Type categories. HMSN 3, however, is still in use, and, represents the various types of Dejerine-Sottas.

CMT 4 and HMSN 4 do not translate with each other. CMT 4 has 12 named subtypes. HMSN 4 has no subtypes, but, has the same genetic cause as CMT 4G, according to the Washington University website.

CMT 5, 6, and 7 are also archaic, as they were reclassified when CMT 3 was. However, there are a few HMSN 5 subtypes, and there are several HMSN 6 subtypes. CMT 5 and CMT 6 reclassification predates the HMSN 6 being created. HMSN 6A is caused by dominant mutations in the MFN2 gene, just as is CMT 2A, and, it includes optic atrophy just as does CMT 2A.

HSAN is another inheritable neuropathy that is considered to be CMT by many, CMT like, by others, and it is treated in some CMT clinics, but the gene mutations that cause HSAN do not have CMT named subtype counterparts and are therefore not interchangeable like CMT 1 and HMSN 1 are.

dHMSN and dHMN are considered CMT by many, but their gene mutations do not have corresponding CMT named subtype counterparts either.

The Inherited Neuropathies Consortium, who is the world leader and authority on CMT naming conventions, amongst many other things CMT, lists 2B1 through 2B5 as autosomal recessive axonal neuropathy, or, AR-CMT, for short, and this category of CMT also includes Giant Axon Neuropathy, or GAN, for short, on their website.

The OMIM website, which, OMIM stands for Online Mendelian Inheritance In Man, O-M-I-M, is a website maintained by Johns Hopkins University, includes all of the acronyms I mentioned, except for GAN, in their phenotype series listing for CMT, and I'll include a link in the show notes for this one.

As I discussed earlier with CMT 1 named subtypes, HNPP, which doesn't even have the CMT name acronym is accepted, literally, by everybody in the CMT sphere, as a type of CMT. CMT is as confusing of a disease as it can get. With all of this confusion regarding the diagnosis name, it's my hope, as a CMTer, that somehow, someway, we can land on one, single, unifying name, whatever that name might be.

[♪ Bruh! ♪]

To recap, because we covered a lot of ground today, Type 1 CMT is autosomal dominant in inheritance and demyelinating. Type 2 CMT is autosomal dominant or autosomal recessive, and axonal. Type 4 CMT is autosomal recessive, and demyelinating. X-Linked incorporates X-Linked dominant and X-Linked recessive. Everything called, "X-Linked," is caused by a mutation in a gene that lives on the X chromosome. Intermediate CMT is categorized according to its inheritance pattern: Dominant intermediate CMT and Recessive Intermediate CMT.

In CMT 1, 2, and 4 the number represents the type, and the letter represents

the sequential order in which the underlying gene mutation was discovered. In X-Linked CMT, “X” represents the type, and a number represents the sequential order in which the underlying gene mutation was discovered. For intermediate CMT, D-I represents Dominant Intermediate, and then a letter represents the sequential order in which the underlying gene mutation was discovered, and the same applies for Recessive Intermediate CMT.

For all of the confusion that surrounds the naming of the CMT 2A, 2A2, and 2AB1 subtypes, researchers now no longer consider the KIF1B mutation to be associated with any type of CMT, and nor is it considered any longer to be associated with any inheritable neuropathy.

Things in the CMT world move and change rapidly. New gene mutation discoveries occur constantly. I do mean constantly. The person who identifies new causative gene mutation gets the honor of naming the subtype that is associated with that new discovery. Recent discoveries are being called by their gene name instead of getting a [number][letter] designation, Or, they're being called by their inheritance pattern and primary disease process as in autosomal recessive axonal.

It's impossible for any one person or organization to keep up with the speed at which CMT moves. Because of these rapid changes, the categorized names we covered today are subject to change at any moment, and without notice. CMT by any name is still CMT. For me, If the CMT experts say it's CMT, then it's CMT, regardless of acronym.

In all of this, how many types of CMT are there? By my count, using all the reputable public sources of information, such as the CMT Association, the Inherited Neuropathies Consortium, the Hereditary Neuropathies Foundation, the MDA, OMIM, Washington University at St. Louis, and others, I've cataloged on my website, thecryptidsloth.com, all 72 subtypes that bear the CMT name. Type 1 has 8 subtypes. Type 2 has 35 subtypes. Type 4 has 12 subtypes. X-Linked has 6 subtypes. Dominant Intermediate has 7, and Recessive Intermediate has 4 subtypes.

It is widely accepted that there are over 100 types of CMT. Where there are only 72 types that carry the CMT acronym, the remainder of the named types are comprised of the other acronyms we discussed today. And, this, is how I arrived at all these various acronyms referring to the same disease: CMT. I just wish that we could settle on just one name, whatever that name might be. Just... one.

[♪ Bruh! ♪]

That's going to do it for today, everybody. Thanks for stopping by, and I'll catch you again next time.

As we close, no matter who you are, no matter where you're listening from, although so very few people have ever heard of CMT, I want you to know that you are not alone, and that we're in this fight together. Thanks for tuning in. Make sure to visit the website at thecryptidsloth.com, a website dedicated to all things CMT, where you'll find our show notes, the episode library and The Cryptid Sloth Blog. Follow us on your favorite social media, and you can find me, your host, Kenneth Raymond, in many of the Facebook CMT groups. Thanks again, and I look forward to talking to you really soon.

This has been The Cryptid Sloth Show Podcast: Where CMT and Life Meet.