

## “Advances in CMT Research & Clinical Care”

MDA Public WebEx – December 13, 2011

Guest Presenters: Michael Shy, M.D., Gita Ramdharry, Ph.D. & Frank Lombardi

During the WebEx, participants sent questions to the presenters Michael Shy, M.D., Director of the CMT Clinic at Wayne State University and MDA Medical Advisory committee member; Gita Ramdharry, Ph.D. of St George’s Hospital and Kingston University’s School of Rehabilitation in London; and Frank Lombardi, 2004 [MDA Personal Achievement Award](#) Recipient and [MDA National Task Force on Public Awareness](#) member; provided below are the questions submitted by members of the MDA community, along with answers offered by our esteemed presenters. Please share additional questions with MDA at [healthcareservices@mdausa.org](mailto:healthcareservices@mdausa.org).

### Questions & Answers

*Q: What is/are the practical symptom(s) of a patient with slow NCV?*

**Dr. Shy:** There are not typically symptoms that are caused by slow NCV (nerve conduction velocity). The NCV slowing determines whether the disease process starts in the myelin (slow NCV) or in the axon (normal NCV but small waves). Symptoms are often the same and findings on the neurology exam are also often similar for patients with slow or normal NCV. This is why we need to do the NCV to determine whether the CMT is the result of problems in myelin (as in CMT1) or the axon (as in CMT2).

*Q: I have heard that CMT is a peripheral nerve disease; what does that mean? Does it affect the head and other peripheral components of the body?*

**Dr. Shy:** Peripheral nerves are nerves that start in the spinal cord or from what is called the brainstem that is located just above the spinal cord. These nerves travel to the legs, arms, trunk, and face. The brain, brainstem and spinal cord are called the central nervous system (CNS). Since these nerves I described above have left the CNS towards the periphery of the body they are called the peripheral nervous system or PNS. Most impairment that patients with CMT notice occurs at the far ends (furthest away from the CNS) of the longest nerves in the body, those going to the feet and hands. Therefore the most severe abnormalities in CMT usually occur in the feet and hands.

*Q: Would an accident (i.e.: a car incident, a fall, etc.) exacerbate CMT-1A? I was diagnosed at age 35 and am now 60. I was rear-ended while parked on the side of the road in May. Is there any research or information related to this?*

**Dr. Shy:** To the best of my knowledge there is not good evidence that trauma exacerbates weakness or sensory loss in most forms of CMT.

*Q: Can you comment on the work and the technology that is being done at Sagamo BioSciences on ZFP (Zinc Finger Protein) and any info on the clinical trials?*

**Dr. Shy:** Zinc finger nuclei are an emerging technology that allows scientists to introduce genetic mutations at specific sites in genes so that cellular or abnormalities of different types of CMT (or other genetic diseases) can be created. These are being used in collaborations between the CMTA, the NIH and investigators at the University of Wisconsin to develop genetic models to test candidate treatments that are derived from cellular assays for specific types of CMT. Because the technology is not available to target every Schwann cell (the cells that make myelin) or neuron in the body this technology is not capable of directly being used to treat patients, at least at the present time.

*Q: My wife has CMT. She seems to have more pain and spasms at night. Is this explained by the CMT? Is there anything we could do to help with this?*

**Dr. Shy:** I believe that this depends on what is causing the pain and spasms and what type of pain she is experiencing. For example [during the live webinar presentation] Dr. Ramdharry discussed treatments for muscle cramps, musculoskeletal pain and neuropathic pain in her elegant presentation. How best to treat your wife's pain depends on whether it falls into these groups and whether this is something associated with her CMT or totally distinct which I can't tell without examining or speaking with her.

**Dr. Ramdharry:** Many people find that they suffer cramps more at night and that can be troublesome. From a physical therapy perspective I advise people to gently stretch the leg muscles before going to bed and if it is worse with the cold then heated blankets or hot water bottles to keep the muscles as relaxed as possible.

**Frank Lombardi:** Since childhood, I have experienced very painful calf cramps attributable to CMT. For me, they occur in unpredictable patterns, primarily at night either as I'm trying to fall asleep or at some point during the night. My cramps are excruciatingly pain full; they come in waves and tend to last for significant periods of time. My calf muscles actually con-cave and pulse during these painful episodes.

I have found that the following activities have helped with my calf-ramps:

- Increased overall physically activity: (Includes afternoon and evening walks)
- Eating more fruits and vegetables, especially those that contain significant levels of potassium. (Bananas are my favorite – Low sodium V8 juice)
- Wearing proper fitting footwear,
- Consciously lowering my sodium intake
- Consciously increasing my water intake. I drink between 7-10/8oz glasses of
- water daily
- Doing exercises that safely stretch-out my heel cord and calf muscles

While I still experience calf cramping, I have been able to better control the severity and frequency of occurrence by some 80%, compared to pre-exercise timelines.

I highly recommend discussing with your doctor and or a physical therapist versed in CMT disease prior to embarking on an exercise routine.

*Q: I present symptoms of CMT, yet my Athena Diagnostic results for a Partial CMT - Dominantly only exam came back 100% normal. I am the only person in my family who has been tested and yet three of my siblings have more-severe symptoms. Can you recommend any next steps?*

**Dr. Shy:** The Athena panel does not test all potential causes of CMT. Our initial steps are first to obtain a pedigree (family history). Did your parents have symptoms or was it just your siblings? This would help us determine whether the inheritance pattern was Autosomal Dominant or Autosomal Recessive for example. The next step would be to get nerve conduction velocities done on the arms to determine whether the problem is from demyelination or axonal loss. We would then use these results together to determine which genes to test for to determine the cause. Autosomal dominant and autosomal recessive forms of CMT put different people in the family at risk for developing CMT.

*Q: My son was diagnosed with CMT Type 5. How common is Type 5, and can you share information about it?*

**Dr. Shy:** CMT type 5 means that in addition to evidence of a peripheral neuropathy there is also evidence of abnormalities that originate from the spinal cord or occasionally brain. Typically this means that deep tendon reflexes (where they tap your knee with a reflex hammer) are brisk rather than diminished or that your big toe goes up rather than down when the doctor scratches the bottom of your foot. CMT5 is rarer than other groups of CMT like CMT1 or CMT2. Like these other groups, however, there are subtypes depending on which specific gene is causing the disease. There is also overlap between groups. For example, mutations in a gene called mitofusin 2 (MFN2) cause CMT type 2A. If an affected patient also has brisk reflexes or up-going toes the same patient could be classified as CMT5 as well.

*Q: I had genetic testing done in 2008 but it was inconclusive. Are advances still being made in determining the types of CMT?*

**Dr. Shy:** There are probably close to 20 genetic causes of CMT that were not known in 2008. Also, only a minority of CMT genes are tested in commercial panels or by companies in the U.S. so that negative commercial testing does not mean that the genetic cause of your CMT is in an unknown gene.

*Q: I have CMT1A and I have found that stretching greatly reduces or eliminates painful muscle cramps. Do you also recommend using bands to stretch ankles, in all four directions (up/down/left/right)?*

**Dr. Ramdharry:** The rubber bands that I use tend to be to strengthen muscles. They provide resistance to a movement and strengthen the muscles. With the legs, I find

stretching using your own body weight is best. For example, with the calf muscles a standing stretch will be much more effective than stretching using a band and your hands.

***Q:** Which is best, bike, treadmill or elliptical? I need balance, what do you recommend (Tai Chi, yoga, etc)? I attend a gym daily... Is it better to use higher weight or longer on a machine?*

**Dr. Ramdharry:** It depends on how good your balance is. The bike is great because it eliminates the need to balance on your legs while you do the exercise. The elliptical trainer requires a bit more balance but I like the fact that it is low impact. The treadmill can be difficult if you have a lot of sensory loss, but it can be great and using inclines rather than speed can be a really good way to up the intensity. Tai Chi, yoga, Pilates, etc. are all great for balance. Regarding weights, I tend to advise lighter weights for longer as I am concerned about high loads with joints that are not protected due to weakness. If your hands are fine then there's no reason why you can't for the arms, but I would be cautious with the legs.

**Frank Lombardi:** Quite honestly, in speaking with many other people with CMT, I have come to realize that while collectively we experience many of the same or similar physical and emotional symptoms that are directly attributable to CMT; we are all very different in our abilities. I feel that this is driven in great part by many different but important factors; such as, disease onset, diagnosis type, at what age we are diagnosed and severity of our individual symptoms; not to mention the aging process. All play a significant role in how we should approach developing an exercise or physical activity routine.

I encourage each of you to consider taking the first step towards adopting some level of physical activity and I applaud those of who have already decided to begin an exercise or physical activity routine. Regardless of age or ability, I truly believe that we all have the Ability to facilitate positive change in our lives. It's about choice!