MUSCULAR DYSTROPHY CANADA
DYSTROPHIE MUSCULAIRE CANADA

NMD4C

Webinar Report

RESEARCH Spotlight
#LetsTalkNMD

All You Need to Know About CMT: Clinical Updates
01-05/2021

NMD4C (Neuromuscular Disease Network For Canada)

NMD4C launched in January 2020, is a Canadian network that is funded by Muscular Dystrophy Canada and the Canadian Institutes for Health Research.

NMD4C **brings together the country's leading clinical, scientific, technical, and patient expertise on neuromuscular disease.** The rarity and diversity of neuromuscular diseases make interdisciplinary collaboration and networking essential to future progress.

NMD4C strives to train and educate neuromuscular disease stakeholders

Muscular Dystrophy Canada (MDC) and the Neuromuscular Disease Network For Canada (NMD4C) have been working on a monthly webinar series to provide clinical and research updates by highlighting cutting-edge research, current state of clinical care and providing up-to-date information on interdisciplinary guidelines for a variety of neuromuscular disorders to clinicians, researchers, academics and medical/graduate trainees.

The Royal College of Physicians and Surgeons of Canada have accredited our webinars for Continuing Medical Education (CME) credits as part of the Maintenance of Certification Program (MOC).

In line with this new accreditation (CMA Policy; Guidelines for Physicians in Interactions with Industry; standard 22), the primary purpose of the “Neuromuscular Disease Rounds & Educational Webinars” is to address the educational needs of the clinical and research community in order to improve the health care of patients affected by neuromuscular disorders and improve health and quality of life. MDC shares a common interest with NMD4C in improving patient care, improving health outcomes and building clinical and research neuromuscular expertise.

WEBINAR DISCUSSION TOPICS

An update on genetics and diagnosis of CMT:
Dr. Gerald Pfeffer

Rehabilitation Strategies in CMT Disease:
Dr. Stephanie Plamondon

CMT and respiratory concerns:
Dr. Karen Rimmer

Surgical management CMT: One Step Back, Two Steps Forward:
Dr. Ian Le

Disclaimer: Please note the speakers in this webinar might have involvement in the subject matter with real or perceived relationships

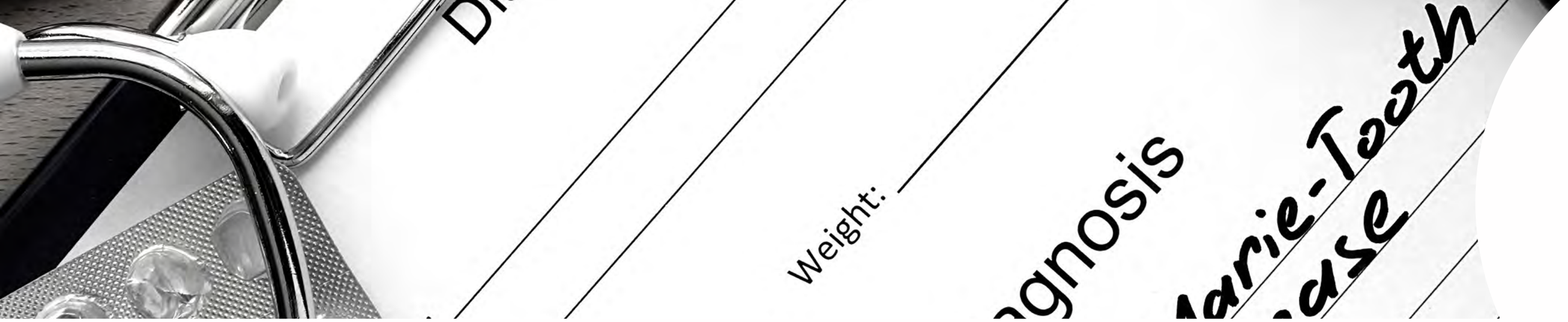
AN UPDATE ON GENETICS AND DIAGNOSIS OF CMT

Gerald Pfeffer, MD PhD
Clinician-Scientist
Assistant Professor

UNIVERSITY OF CALGARY
(CALGARY, ALBERTA)

Charcot-Marie-Tooth disease affects nerves that control muscle movement and those that carry sensory information to the brain. This is why Charcot-Marie-Tooth disease is considered a sensory and motor neuropathy. That is, it affects motor nerves (which control muscle movement) and sensory nerves (which carry sensory information to the brain).

Charcot-Marie-Tooth disease (CMT), also called Hereditary Motor Sensory Neuropathy (HMSN), is a group of inherited disorders that cause damage to the peripheral nerves.



In general, the different group of classifications of CMT includes: CMT1 (dominant demyelinating, CMT2 (dominant axonal), CMT3 (severe demyelinating - DSS), CMT 4 (recessive demyelinating) and CMT5 (neuropathy + pyramidal features). Depending on the different genetic sub-type, there will be a different letter added next to the number to indicate the different genes.

CMT is classified by: (1) phenotype (clinical presentation); (2) neurophysiology (findings on nerve conduction studies, evoked potentials and electronystagmography); (3) inheritance pattern; (4) gene defect.

As CMT progresses, weakness and atrophy occur in the lower legs and feet. This contributes to foot deformities, such as high arches and hammertoes (a condition in which the middle joint of a toe bends upwards). The lower legs may also take on an "inverted champagne bottle" shape due to the loss of muscle bulk.

Typical early/classic features include weakness of the foot and lower leg muscles, which can cause difficulty lifting the foot (foot drop) and a high-stepped gait with frequent tripping or falling, and ankle sprains.

Symptoms of CMT can include speech and swallowing difficulties, breathing difficulties, especially when lying flat (sleep apnea), Kyphosis (abnormal front-to-back spine curvature), constipation, sensory-neural hearing loss, vocal cord paralysis/voice abnormality, loss of ability and tolerance to feel heat, cold and touch, fatigue, neuropathic pain and impaired fine motor skills.

The severity of symptoms can vary greatly among individuals and even among family members with the same gene mutation. Progression of symptoms is usually slow and gradual.

CMT is one of the most common inherited neurological disorders and tools exist to diagnose CMT: next-generation sequencing in the form of specific CMT-associated gene panels, whole-exome sequencing, whole-genome sequencing, mitochondrial sequencing and high-throughput transcriptome sequencing. Genetic testing is important for future therapy.

Over 100 genes have been associated with CMT. Most diagnosed cases (approx. 90%) are associated with 4 genes: PMP22, GJB1, MFN2 and MPZ. These are most common except in certain regions with founder populations/effect.

REHABILITATION STRATEGIES IN CMT DISEASE

Stephanie Plamondon, MD FRCPC
Clinical Associate Professor
Physical Medicine, Rehabilitation Specialist

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Although there is no cure for CMT, supportive therapies improve health-related quality of life. The goal of treatment in CMT is to help individuals cope with the troubling and disturbing symptoms to ultimately improve quality of life.

Mobility, balance and distal motor and sensory limitations (e.g. foot and ankle weakness, and hand-finger weakness), fatigue, pain, and body image negatively impact how people with CMT perceive their quality of life.

When deviations in gait occur, selective fatigue of the hip flexors, hip flexor velocity decreases walking and walking duration. In other words, there is increased energy consumption, decreased postural stability, decreased daily activity levels, decreased steps taken:

Gait abnormalities reported in people with CMT include foot-drop, reduced ankle power at push-off and increased knee and hip flexion for swing clearance (high 'steppage-gait').

Medical treatments for pain may include topical, oral or injection treatments. Some medications are potentially toxic to people with CMT. Before taking any medication or changing medications, individuals with CMT should always check with your physician.

For mobility, activity limitations and pain it is important to consider physical treatments: therapeutic exercise, pacing, footwear, orthotics, bracing, gait or mobility aids and adaptive equipment.

Balance training and pacing strategies have not been studied well in people with CMT, but these are feasible and safe, and have the potential to improve balance and gait, consequently, reducing the risk of falls and fall-related injuries.

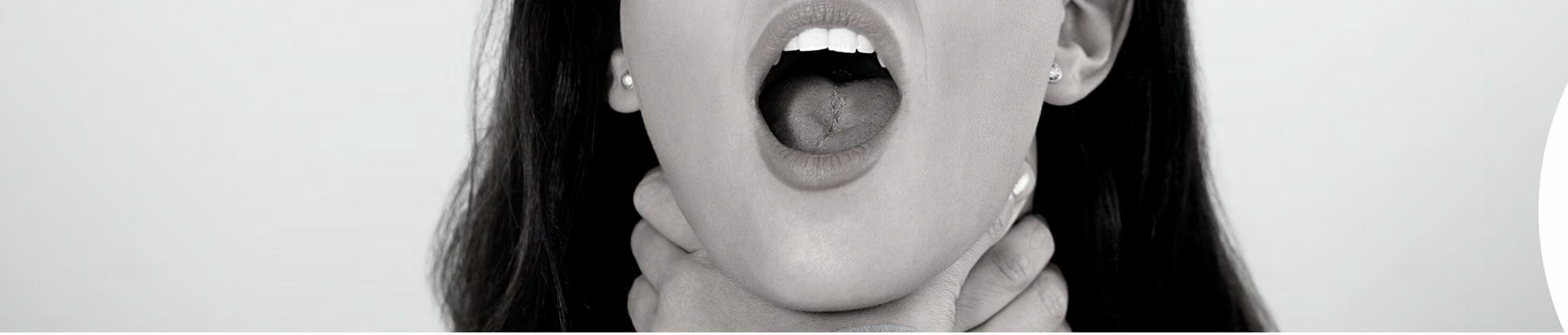
Community-based aerobic cycling exercise and home exercise programs that include stretching, endurance and resistance training of upper and lower proximal muscles are shown to be helpful.

Appropriate footwear is important for people with CMT. In terms of bracing, it is important to consider personal goals as it relates to function, cosmetics and coverage/price. When prescribing braces, it is important to consider contracture/deformity, fluctuating edema (swelling), cognition motivation, weight limits/obesity and whether they are gait training.

Foot orthotics, metatarsal pads, crest pad, correct toes, supportive shoes, custom shoes and high top shoes are important for people with CMT when managing foot deformity and pain.

Wrist weights can help with CMT-related tremors. Upper extremity orthoses and adaptive aids may be prescribed by occupational therapists to help with hand function (e.g., holding utensils).

Keep engaging hands in daily activities. Exercises that focus on increasing fine-motor coordination and strength (use of therapy putty, play dough) are helpful.



Although not a common symptom associated with CMT, there have been reports of people with CMT having issues swallowing called dysphagia. It is important to see a speech language pathologist if CMT is affecting swallowing.

As part of fall prevention and risk for osteoporosis, it is important to take Vitamin D and Calcium as well as protein intake for muscle building. Maintaining a healthy weight is important for mobility.

Neurologists, physiatrists, occupational therapists, physical therapists, orthopaedic specialists, orthotists, mental health professionals, genetic counsellors, social workers, nutritionists, speech language pathologists, audiologists and respirologists are important healthcare professionals when providing collaborative holistic care of people with CMT.

A multidisciplinary supportive care team is critical for long-term management and to improve the quality of life in people with CMT.

CMT AND RESPIRATORY CONCERNS/CONSEQUENCES

Karen Rimmer, MD
Respiratory Neuromuscular Specialist

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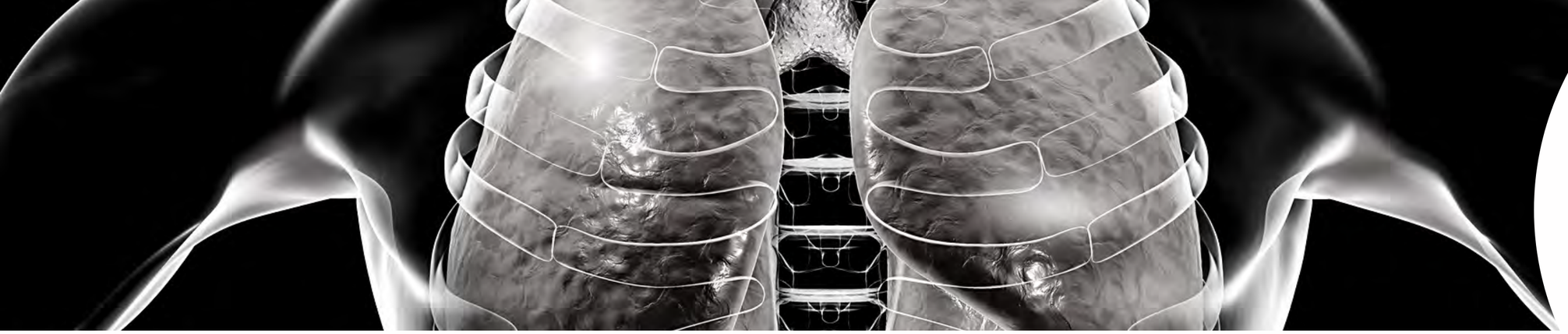
CMT may predispose to sleep-disordered breathing. Restless leg syndrome (unpleasant sensation in the legs accompanied by an irresistible urge to move) is also more common in individuals with CMT, especially at night which can contribute to sleep disturbances (falling asleep or returning to sleep).

People with CMT1 may be at higher risk for sleep disturbances such as sleep apnea — long pauses in breathing during sleep. Many with CMT report poor sleep quality due to fragmentation (interruption), leading to reduction of REM sleep and daytime sleepiness.



CMT can impair respiratory muscles but respiratory problems/issues are usually not reported, or can be missed. For example, if there is asthma, it is important to consider vocal cord involvement.

CMT can contribute to respiratory muscle weakness associated with phrenic nerve damage. Inspiratory and expiratory muscle strength is reduced in some individuals with CMT1A, even if no or only mild symptoms of diaphragm weakness are present.

SURGICAL MANAGEMENT CMT: ONE STEP BACK, TWO STEPS FORWARD

Ian Le, MD
Orthopedic Surgeon

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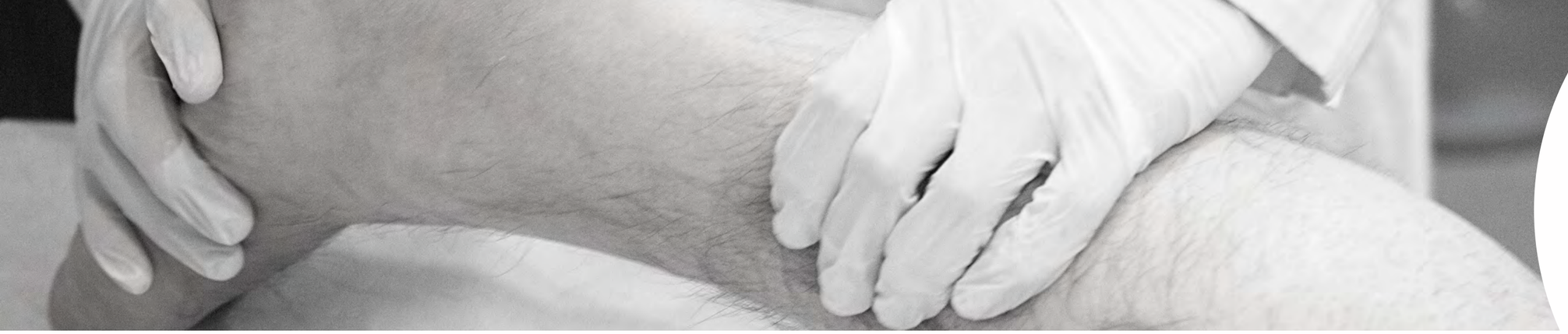
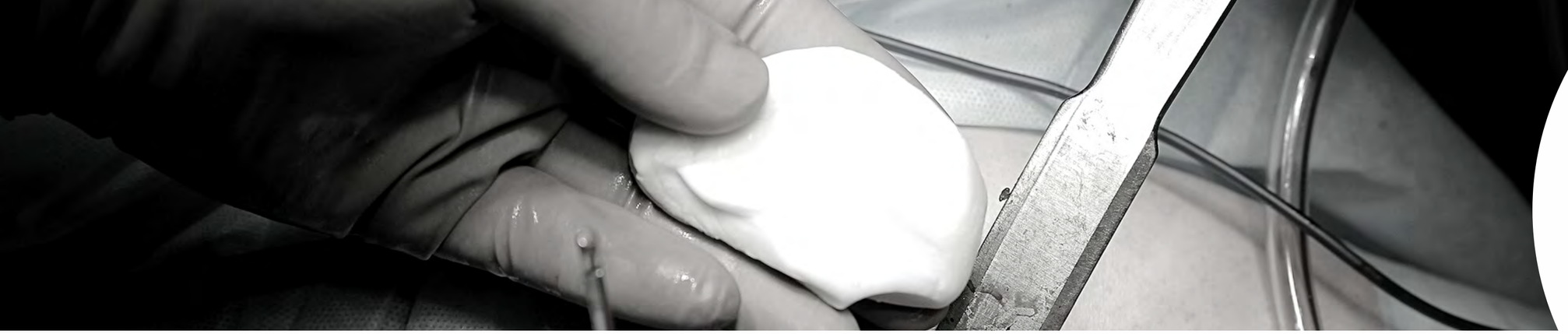


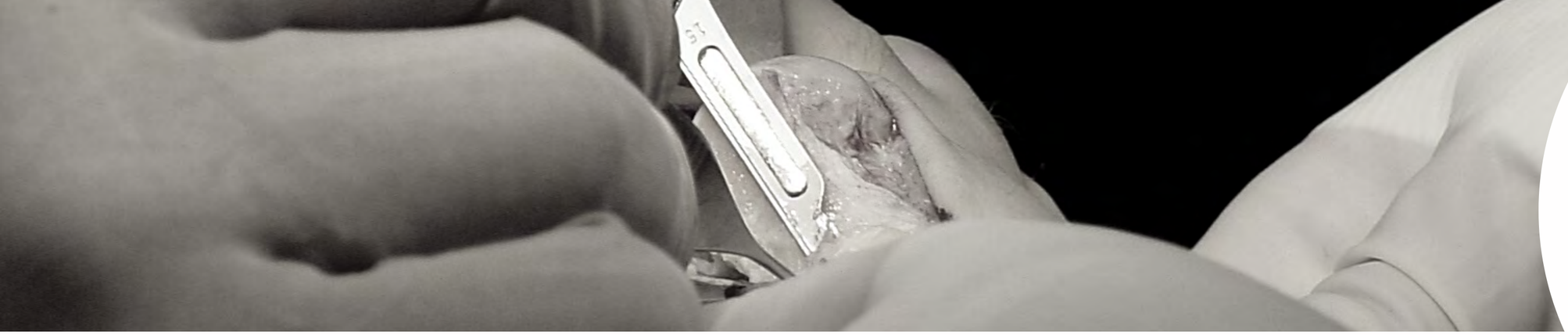
Early orthopaedic involvement minimizes risk for needing surgeries in the future/higher potential for joint preserving options (non-arthrodesis), increased flexibility and minimizes potential for ankle involvement.

Early in the course of CMT, an orthopaedic foot and ankle surgeon should be part of the care team. Orthopaedic involvement, not necessarily surgical intervention, but foot and ankle surgeon assessment is important.



While foot and ankle surgeries are most common, some people with CMT require surgical interventions for hip dysplasia (where the "ball and socket" joint of the hip does not properly form) and scoliosi (a sideways curvature of the spine).

The majority of surgeries performed on individuals with CMT involve the foot. As the peroneal muscles and tibialis anterior, as well as the intrinsic muscles of the foot become weak, contractures can develop, resulting in equinus (the foot stuck pointed down), cavus (a high arch), and varus of the heel (heel that is turned inward).



Goals of surgical interventions are to achieve a plantigrade foot position (foot hits ground and is level) and to try to minimize the progression of foot deformity will reoccur in the future. Surgical procedures can be divided into soft tissue (e.g., tendon transfer, tendon lengthening) and bony procedures (e.g., realignment).

CMT is associated with progressive deformity of feet and risk for re-occurance, but advances in orthopaedic surgical interventions (which focus on forefoot deformity, cavus foot, ankle laxity, and tendon imbalance) can improve functional capacity and improve quality of life.

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