MUSCULAR DYSTROPHY CANADA
DYSTROPHIE MUSCULAIRE CANADA

NMD4C

Webinar Report

RESEARCH Spotlight
#LetsTalkNMD

Oculopharyngeal muscular dystrophy (OPMD): Clinical & Research Updates
April 6/2021

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

Research perspectives:
Dr. Cynthia Gagnon

Dysphagia in OPMD:
Claudia Côté

Strength and mobility in OPMD:
Dr. Jean-Denis Brisson

New OPMD scientific insights and treatments:
Dr. Bernard Brais

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

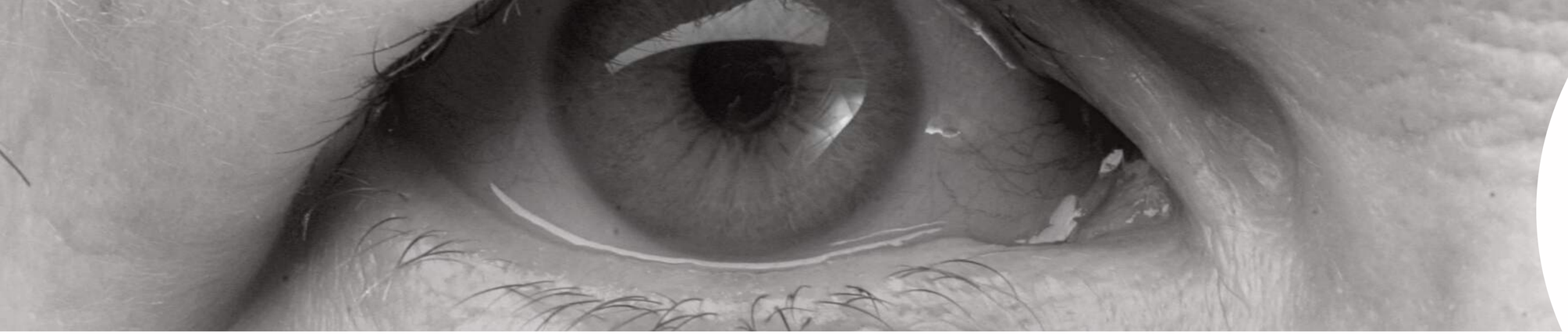
RESEARCH PERSPECTIVES

Cynthia Gagnon, OT, PhD
Clinician-Scientist
Professor

SHERBROOKE UNIVERSITY FACULTY OF MEDICINE AND HEALTH SCIENCES

The highest prevalence of Oculopharyngeal muscular dystrophy is in the French-Canadian population due to a founder effect. Clusters have also been reported in the Bukhara Jews of Isreal and a Hispanic population in New Mexico. OPMD affects both men and women, usually first appearing in people after 40 years of age.

OPMD is a rare, adult-onset, progressive proximal myopathy with eyelid ptosis, ophthalmoplegia, dysphagia, upper and lower proximal weakness.



The second symptom arrives 3-5 years after the first symptom. Proximal weakness (weakness of upper/lower limbs) presents approximately 7 years after initial symptom.

For most patients affected by OPMD, the first symptom can be ptosis (drooping or falling of eyelid), dysphagia (difficulty swallowing) or both at around 50 years of age.

The major causes of death in those with OPMD include aspiration pneumonia, influenza, chronic lower respiratory disease or disease with respiratory involvement. However, co-morbidities were similar to the general population, which highlights no other muscle manifestations.

The median age of death for those affected by OPMD is 77 years of age. Compared to onset of ptosis or dysphagia, a shorter survival time is observed after the onset of proximal weakness.

While OPMD reportedly has a little effect on the life expectancy because repeated aspiration occurs only at the more advanced stage, OPMD impacts the quality of life in patients. In fact, health-related quality of life in those with OPMD is lower than the general population. The physical domain is more affected than the mental domain. Severity of dysphagia was linked to low social functioning.

OPMD can negatively impact participation in activities of daily life including reduced ability to do household chores, premature retirement, difficulty with stairs and community outings.

Older adults affected by OPMD report increased fatigue and pain, which disrupts daily life activities, social participation, and ambulation.

As adults age with OPMD, they are most in terms of mobility, independent personal care and health and participating in recreational activities.

DYSPHAGIA IN OPMD

Claudia Côté, RD MSc, PhD Candidate
Dietician and Doctoral Student

SHERBROOKE UNIVERSITY FACULTY OF MEDICINE AND HEALTH SCIENCES

Coping strategies to address swallowing difficulties include reduce bite sizes/sips, increasing meal duration, careful food selection and avoidance of certain foods (e.g., raw vegetables). Because of this patients may be at nutritional risk.

OPMD affects the pharyngeal muscles resulting in swallowing disorders. Swallowing difficulties can depend on food texture (more difficulty with hard/dry food). Food getting stuck in the throat and coughing/choking are common experiences for those with OPMD.

As body composition may be altered in people with neuromuscular disease (proportional reduced muscle mass and higher fat), future research is needed on body-mass-index in those with OPMD.

Nutritional risk is almost twice as high in people with OPMD compared to a group of people without swallowing issues. This suggests a need for nutritional risk screening and dietary counselling in OPMD patients.

STRENGTH AND MOBILITY IN OPMD

Jean-Denis Brisson, MD
Neurologist

CIUSSS SAGUENAY-LAC-SAINT-JEAN
INTERDISCIPLINARY RESEARCH GROUP ON
NEUROMUSCULAR DISORDERS

An early combination of fat replacement in the tongue, adductor magnus and soleus can be helpful for differential diagnosis.

OPMD mostly affects proximal lower extremities: hip muscle, lower leg (calf) muscle, hamstring muscle, and tongue (fatty replacement on tongue). Severity of hip muscle weakness predicts the need of a mobility aid at a younger age.

Compared to individuals of the same age with a healthy status, people with OPMD experience limitations in walking. In particular, people with OPMD have a reduced walking distance over 6 minutes.

To overcome fatty replacement and atrophy (weakness) of muscles, it is encouraged that people with OPMD to be as active as possible. Gentle home-based exercises that focus on hip muscle function and hamstring muscle are encouraged; consult with physician and physiotherapist.

PATHOPHYSIOLOGY OF OPMD AND DEVELOPMENT OF NEW TREATMENTS

Bernard Brais, MD, M. Phil, PhD
Neuromuscular Specialist
Professor of Neurology and Genetics

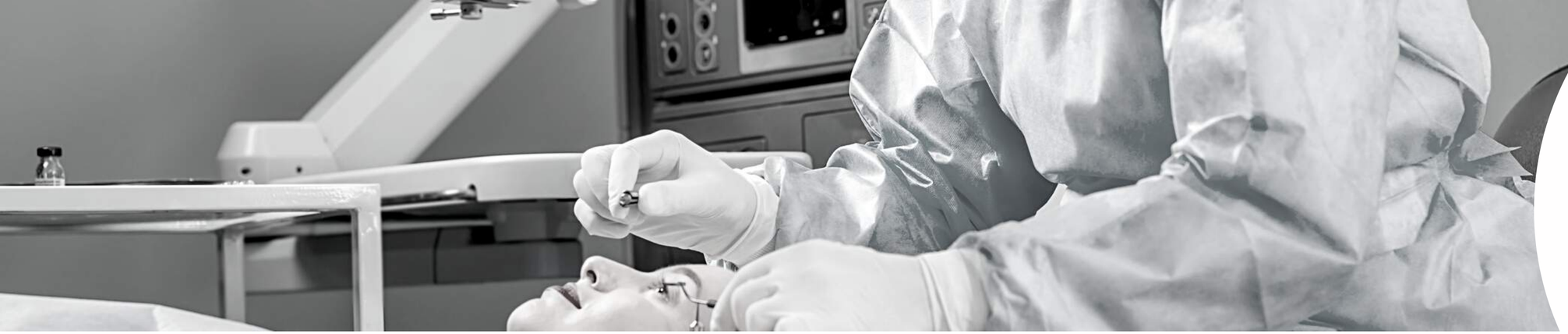
MCGILL UNIVERSITY

98% of French-Canadians share the same historical mutation. More than 12 repeats indicates the condition is dominant in nature.

The underlying cause of OPMD is the abnormal expansion of (GCN)n repeats in the PABPN1 gene, located on the chromosome 14. In OPMD, 11–18 repeats are noted, while 10 repeats are noted in normal condition.

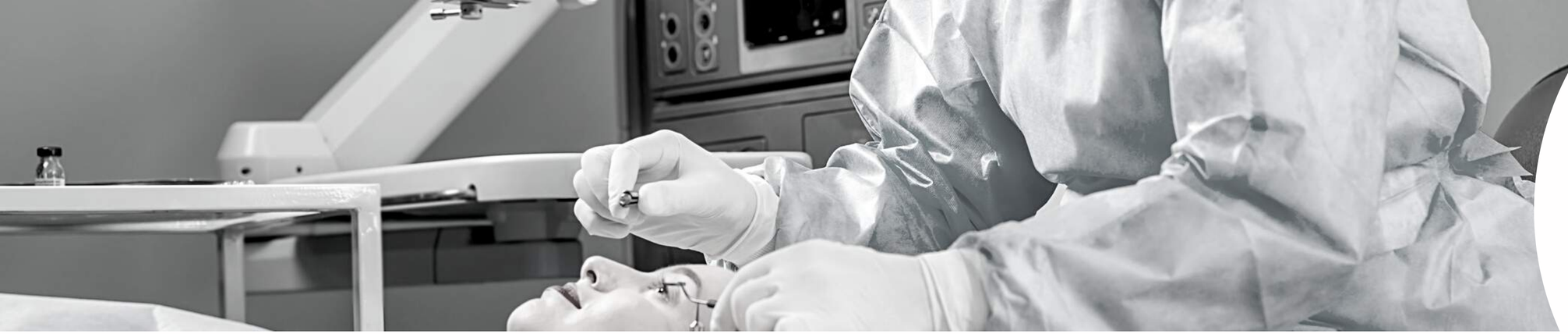
Reduced PABNPN1 expression in muscle cell culture causes myogenic defects, suggesting that PABPN1 loss-of-function causes muscle weakness in OPMD and in the elderly.

OPMD has been linked to premature ageing. PABPN1 expression declines from midlife onward. In OPMD, aggregation of expanded PABPN1 causes an additional decline in the level of the functional protein, which is associated with severe muscle weakness in OPMD (especially for muscles that tend to decline with age).



The treatment of eyelid ptosis may include blepharoplasty by resection of the elevating palpebral fascia or frontal suspension of the eyelids. Frontal suspension is the permanent solution.

Permanent surgeries are recommended for people with OPMD who have major symptoms, such as significant night vision difficulties and neck pain.



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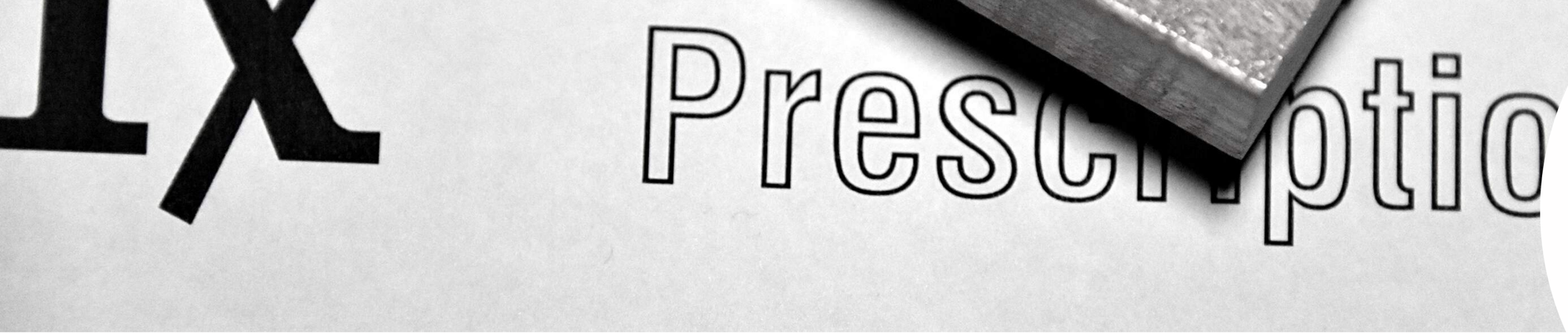
Permanent surgeries are recommended for people with OPMD who have major symptoms, such as significant night vision difficulties and neck pain. There are also surgeries for moderate to severe dysphagia: cricopharyngeal dilatation. Botox has been recommended, but not best option.



At this point, there are treatments in development. Many of the drug development studies are being explored in animal models and new techniques like genetic silencing/CRISPR are being used. Drug wise, beside Trehalose, more work needs to be done. If a drug is found for OPMD, it can likely apply to other ageing-related conditions.

There is still no treatment for progressive limb girdle weakness, but mouth wash, head elevation at night, lift chair and electric bed, pain management are helpful. Statins treatment should be avoided as it can make the condition worse.

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QUESTIONS?

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