MUSCULAR DYSTROPHY CANADA
DYSTROPHIE MUSCULAIRE CANADA

NMD4C

Webinar Report

RESEARCH Spotlight
#LetsTalkNMD

OPMD: Clinical and Research Updates
April 6th, 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

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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 TOPIC

OPMD: Clinical and Research Updates

Dr. Cynthia Gagnon

-Research perspectives

Claudia Cote

-Dysphagia in OPMD

Dr. Jean-Denis Brisson

-Strength and mobility in OPMD

Dr. Bernard Brais

-New OPMD scientific insights and treatments

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

OPMD RESEARCH PERSPECTIVES

Dr. Cynthia Gagnon, Ph.D
Clinician-Scientist; Professor at the School of Rehabilitation

SHERBROOKE UNIVERSITY
(QUEBEC)

The highest prevalence of OPMD in the French Canadian Population is due to a founder effect (loss of genetic variation that occurs when a new population is established by a very small number of individuals.)

Occulopharyngeal Muscular Dystrophy (OPMD) is a hereditary dominant disease (passed down from your parents.) It is a proximal myopathy (disease that affects the muscles that control voluntary movement in the body) that causes proximal weakness (muscle weakness closest to the body), ptosis (drooping of upper eyelid), and dysphagia (difficulty swallowing.)

A Natural History pilot study on OPMD ran from 2015-2020 in Quebec. The goal was to understand the key motor impairments, age of onset, and progression in OPMD from patients at the Saguenay Neuromuscular Clinic.

Age of onset for symptoms related to OPMD varies, but the pilot study determined that the average age of onset for dysphagia and ptosis was 54 years old. The onset of secondary symptoms generally occurred 3-5 years after the first. The study also found that mean mortality from the disorder is approximately 77 years of age and the most common cause of death is diseases of the respiratory system.

Impact on participation

Activities of daily living can be severely impacted depending on symptoms when living with OPMD. These activities include household chores, difficulty with stairs, community outings and pre-mature retirement. Quality of life for individuals with OPMD is lower than the general population as individuals are affected physically, causing many changes in their lives.

OPMD RESEARCH PERSPECTIVES

Claudia Cote, PhD Candidate

SHERBROOKE UNIVERSITY
(QUEBEC)

The median age of onset for dysphagia is 54 years of age and it is progressive. Over the course of their life, patients begin to develop strategies to manage their symptoms. For difficulties with swallowing, individuals start to take smaller bites. When individuals begin to cough a lot while eating, they modify or avoid certain foods. Finally, if food is starting to get stuck more often, it is advised that they increase the duration of meal time.

Asking the right questions is key to an effective patient examination and assessment.

It is critical to review the questions you are asking clients because some patients fail to report important clinical symptoms when asked general questions. In addition, patients coping strategies can be so effective that patients perceive little change in their life.
When patients in a recent study were asked, "does food get stuck more frequently than before?" versus "does food get stuck more severely in your throat?" responses to these questions changed drastically.

Patient reported outcome measures

There are no patient-reported outcome measures specifically for OPMD, but a pilot study used the following three measures to assess dysphagia severity.

- The Sydney swallow questionnaire
- The Eating assessment tool
- Swallowing quality of life questionnaire

STRENGTH AND MOBILITY IN OPMD

Jean-Denis Brisson, M.D
Neurologist

CIUSSS SAGUENAY-LAC SAINT-JEAN
(QUEBEC)

Prevalence of proximal weakness

The retrospective pilot study determined that 90% of participants reported that their proximal weakness in their lower extremities started between age 45 and 69. In addition, the data showed that typically, the second symptoms started 6-7 years later. Typically proximal weakness is not the first symptom seen in OPMD.

Affected Muscles in OPMD

Muscles primarily affected that have fatty replacement include the tongue, adductors, and hamstrings. A prospective study in Saguenay of 34 individuals showed that there is a decline in strength with age that includes shoulder flexors, pinch, hip flexors, hip extensors, and hamstrings.
A 30-second chair-to-stand test, a 10 stair climb, hand prehension, and pinch tests were also performed. It was found that individuals with OPMD performed under 80% of expected test results compared to individuals without OPMD.

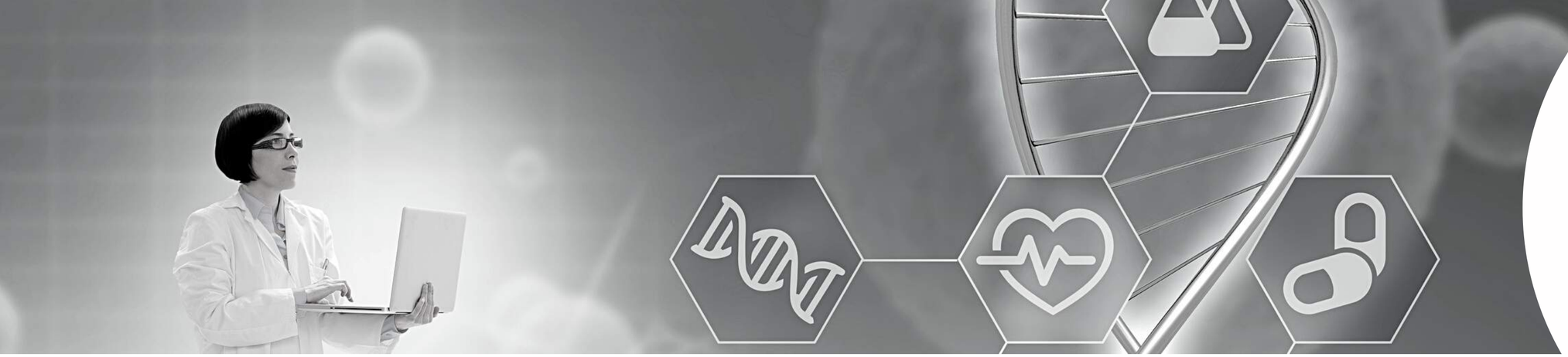
Exercise when living with OPMD is important to replace fatty portions of the muscle.

There are few studies published on exercise in OPMD, but patients are encouraged to exercise in order to replace the fatty portions in the muscles.
When patients indicate they have weakness, the neuromuscular clinic partners with a physical therapist to complete a baseline strength evaluation. Physical well being is also tracked during an evaluation

UPDATE ON THE UNDERSTANDING OF THE PATHOPHYSIOLOGY OF OPMD AND THE DEVELOPMENT OF NEW TREATMENTS

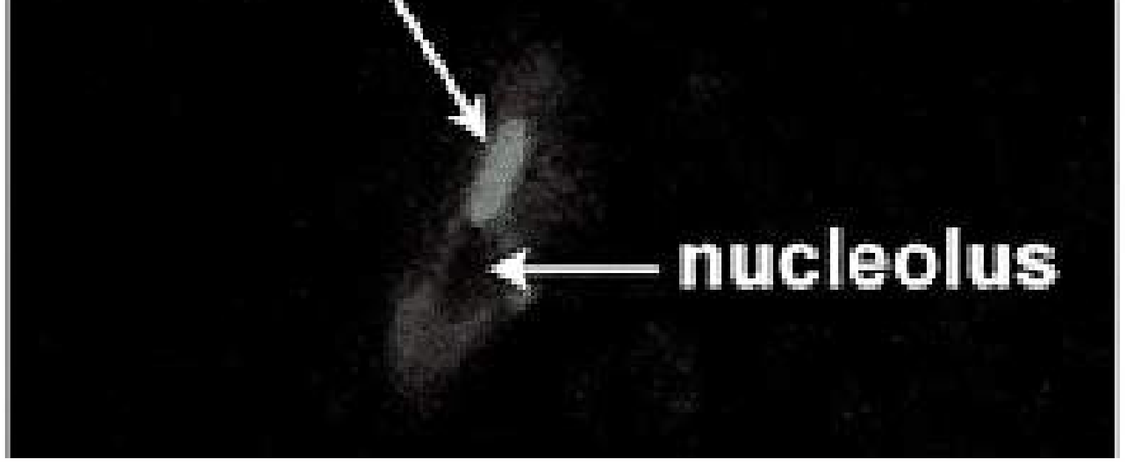
Bernard Brais, M.D.C.M, M.Phil, Ph.D.
Neurologist & Professor of Neurology and Genetics

MONTREAL NEUROLOGICAL INSTITUTE
(QUEBEC)



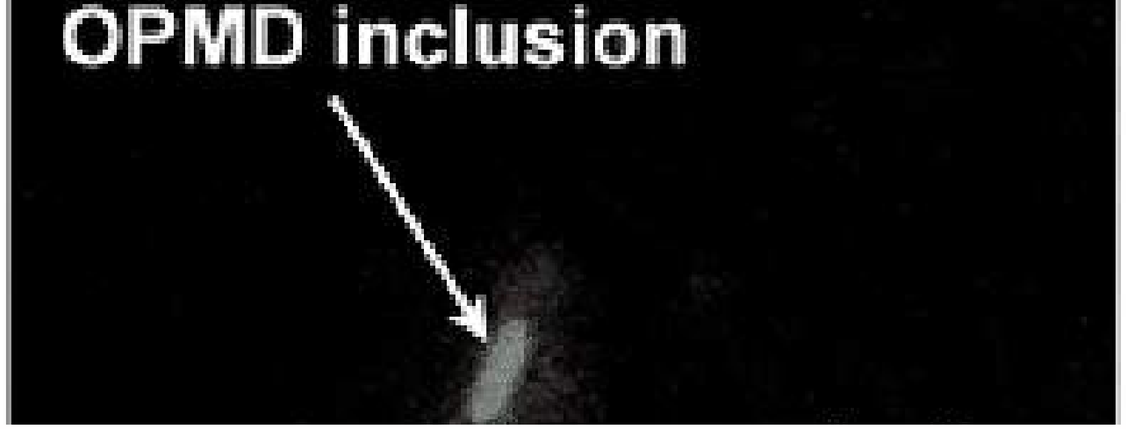
In a study by Brais et al. in 1998, 168 individuals participated from one family living with OPMD.

The cause of OPMD originates from a mutation that lengthens the stretch in a protein. Proteins are like beads and in the case of OPMD instead of 10 beads, you will have 11-18 beads. From 12 beads on, OPMD will present. OPMD will transfer from generation to generation, which is a dominant disease.

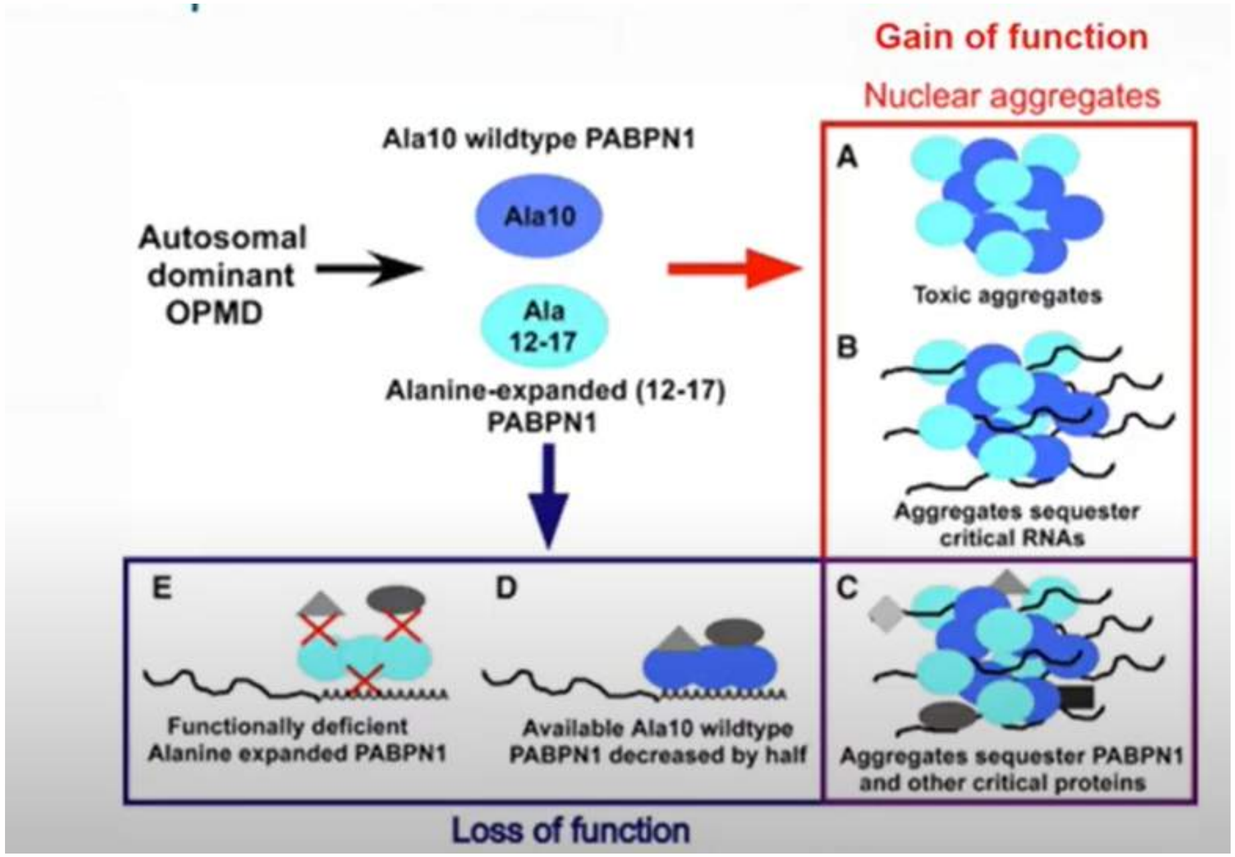


Understanding the pathophysiology of OPMD.

Within the nuclei (contains the cells chromosomes) there is an accumulation of protein in band like structures. PABPN1 is a gene that takes messages that code for protein in our bodies and adds a tail of polyadenine, which helps to control what genes will be expressed. If there is a larger tail the protein tends to accumulate in the foci. The inclusions are mixed (abnormal proteins, etc). It brings a lot of factors into play that can cause many problems in the cell.

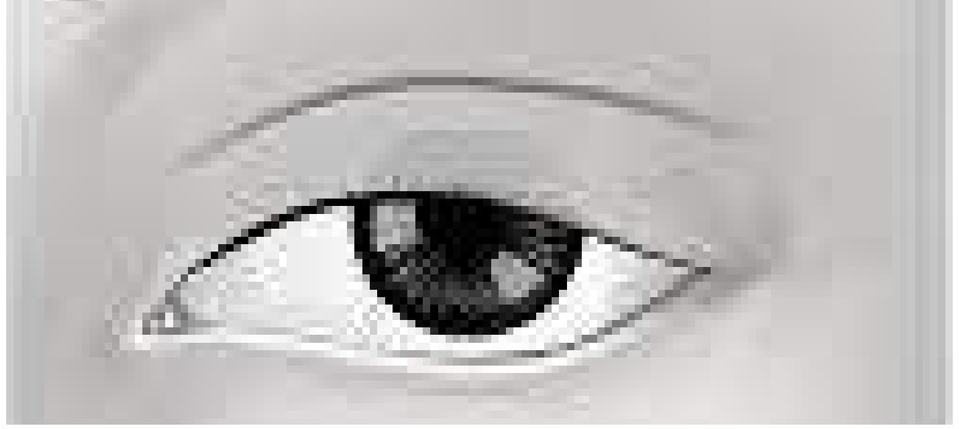


OPMD and Nuclear Inclusion Diagram



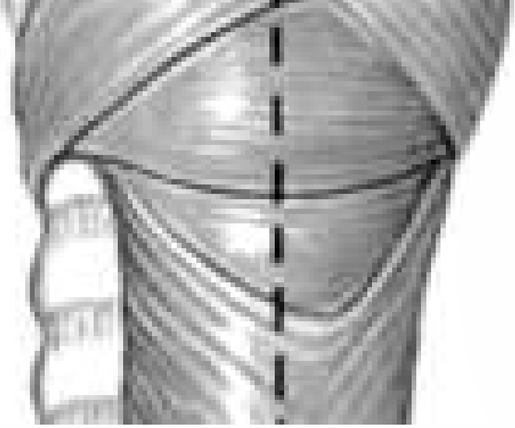
Aging in OPMD

Many researchers say that OPMD is a form of premature aging. One of the weaknesses that comes with OPMD is the proximal weakness and these are muscles we know age quicker than others. The mutation that causes OPMD creates pre-mature aging particularly in muscles that typically age faster.



Treatment of Ptosis

There is treatment available for Ptosis. If you have night vision difficulties, more than 50% coverage of the pupil or cervical pain it is important to get frontal suspension surgery of the eye. The current surgery performed is permanent.



Treatment of Dysphagia

There are different treatments available for Dysphagia.

- Cricopharyngeal dilatation occurs when the surgeon dilates the sphincter and there are symptomatic benefits for the dysphagia symptoms.
- Cricopharyngeal myotomy is where a surgical cut is made to divide the muscle and ease swallowing.
- Cricopharyngeal paralysis with botox can be done, but there is no evidence that it is effective.

Supportive Treatments for OPMD

The recommended treatments for OPMD are as follows:

- Mouth wash
- Pain management
- Head elevation at night
- Lift chairs
- Refrain from statins
- Electric bed
- Adapted vehicle
- Canes, wheelchairs, and scooters

Clinical Trials for OPMD

Please consult with research@muscle.ca for information on clinical trials for individuals with OPMD that are currently recruiting in Canada.

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QUESTIONS?

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