MYOPATHIES AND GASTRO-INTESTINAL INVOLVEMENT

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Disclosure

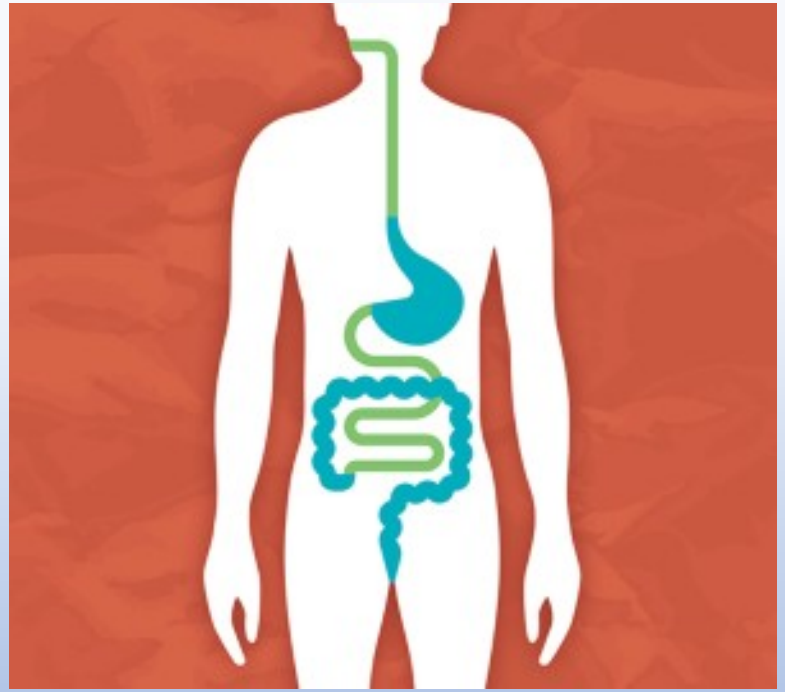
- On-site PI Pharnext (CMT)
- Co-investigator FORCE trial (postpolio syndrome)
- Member Data Monitoring Committee Novartis (SMA)
- Chair Data Monitoring Committee Dynacure

Learning objectives

At the end of this lecture the learner

- Has insight into the gastro-intestinal manifestations of the most common myopathies
- Knows how to approach and examine a patient with a myopathy presenting with gastro-intestinal symptoms

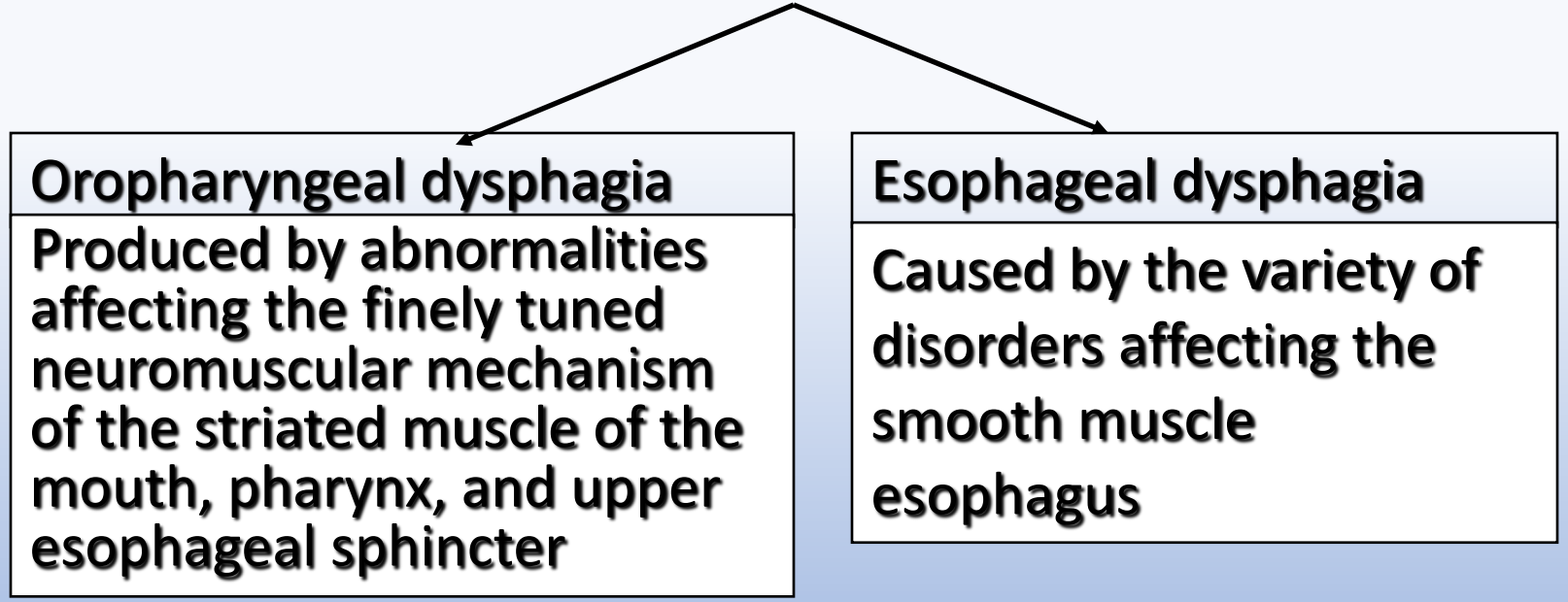
Gastrointestinal problems in patients with myopathies



Lack of appetite
Dysphagia
Early satiety
Vomiting
Abdominal pain
Constipation
Diarrhea
Bowel incontinence
Pseudo-obstruction
Gall bladder problems

Dysphagia

Two distinct syndromes



The oropharyngeal swallow

- Oral stage (bolus chewing and fragmentation)
- Pharyngeal stage (bolus transition from the mouth to the upper opening of the oesophagus)
- Oesophageal stage (bolus progression towards the stomach)

Clinical presentation of swallowing problems:

- food sticking in the throat
- difficulty initiating a swallow
- nasal regurgitation
- coughing during swallowing

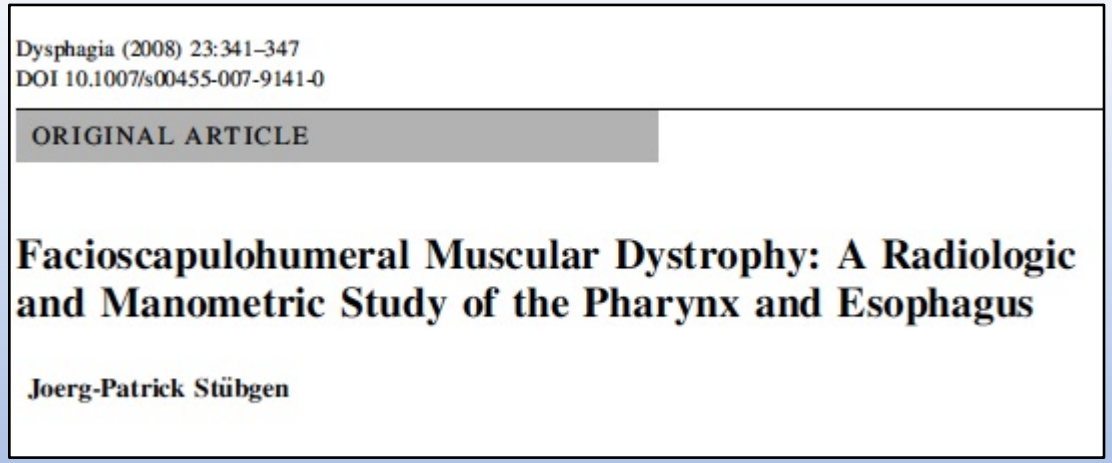
Dysphagia

- Oropharyngeal dysphagia affects
  - respiratory safety (aspiration)
  - swallowing efficacy -> insufficient nutrition and hydration
  - quality of life

Underrecognition of dysphagia in neuromuscular conditions

‘Disorders of deglutition are probably underrecognized in patients with muscle disease. Patients without complaints of deglutition are usually not evaluated for a swallowing disorder.

Therefore, subclinical swallowing problems may be overlooked.’



Dysphagia (2008) 23:341–347
DOI 10.1007/s00455-007-9141-0

ORIGINAL ARTICLE

Facioscapulohumeral Muscular Dystrophy: A Radiologic and Manometric Study of the Pharynx and Esophagus

Joerg-Patrick Stübgen

Assessment of dysphagia

Patient related outcome (PRO)

- Sidney swallow questionnaire (SSQ) – validated visual analogue scale for a symptomatic severity report by the patient. The SSQ is simple to conduct and can be performed in about 10 minutes.
- Swallowing quality of life (SWAL-QOL): more detailed tool based on 44 items that report quality of life concepts.
- EAT10: self-administered questionnaire
- Neuromuscular disease swallowing status scale (NdSSS): generic dysphagia clinical scale based on eight levels of disability

Assessment of dysphagia

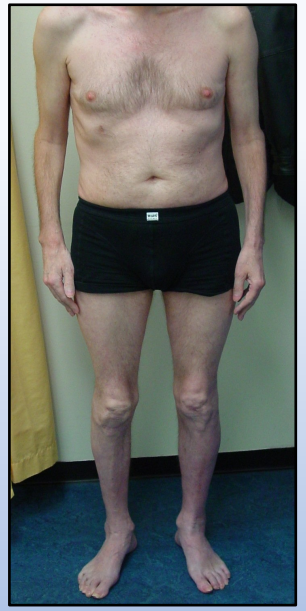
Bedside testing:

- Timed cold water drinking test measures the severity of dysphagia by timing the process of drinking 80 cc of cold water.
- Test of masticating and swallowing solids (TOMASS), validated and reliable quantitative assessment of a solid bolus

Instrumental tests

- Fiber optic endoscopic evaluation of swallowing (FEES) is used to evaluate swallow safety and efficiency
- Maximal tongue pressure (MTP)
- Manometry assessing the upper esophageal sphincter
- Surface EMG
- Imaging: Videofluoroscopic swallowing study (VFSS), scintigraphy, Real time MRI

Myotonic dystrophy type I



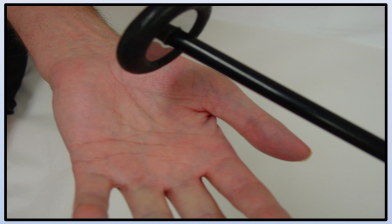
- Early onset dysphagia
- Often unnoticed
- Increased duration of meal time
- Coughing while drinking
- Choking on foods
- Nasal regurgitation
- Piecemeal deglutition
- Weight loss
- Aspiration pneumonia

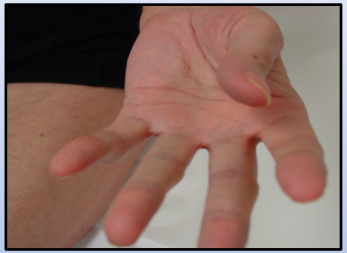
Dysphagia (2014) 29:319–331
DOI 10.1007/s00455-013-9510-9

ORIGINAL ARTICLE

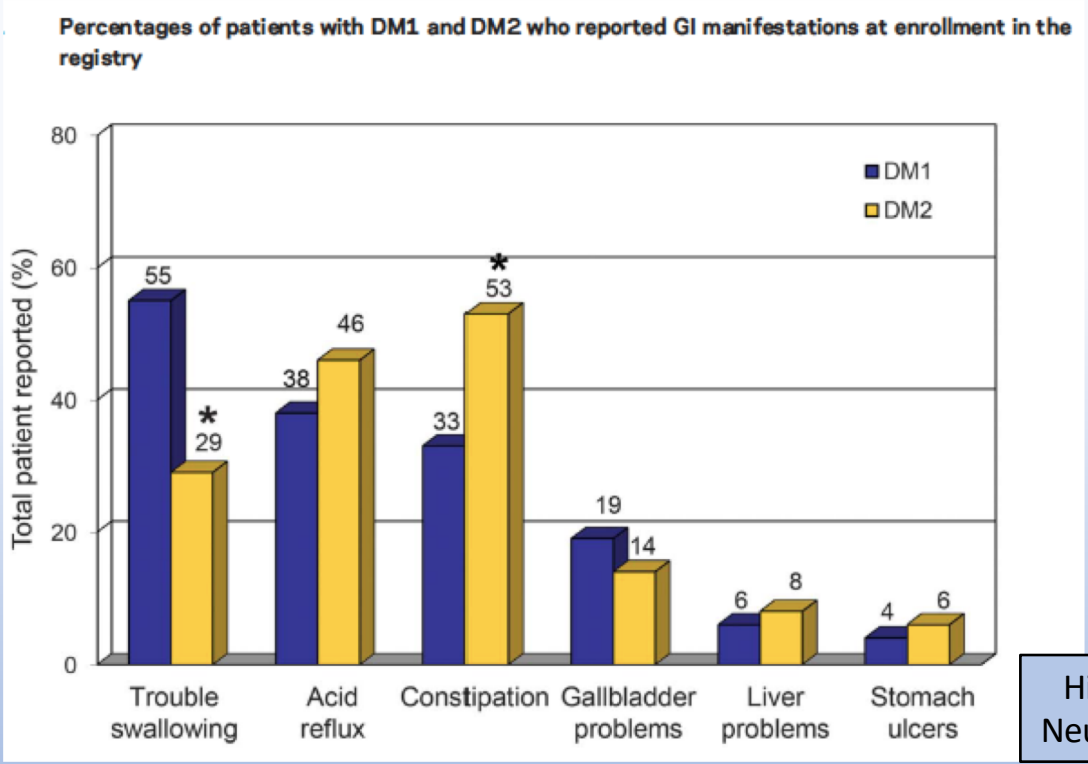
Oropharyngeal Dysphagia in Myotonic Dystrophy Type 1: A Systematic Review

Walmari Pilz · Laura W. J. Baijens · Bernd Kremer





High frequency of gastrointestinal manifestations in DM type 1 and type 2



Registry encompassing
913 DM1 pts (52.5% female) &
180 DM2 pts (61.7% female)

Patient-reported questionnaire

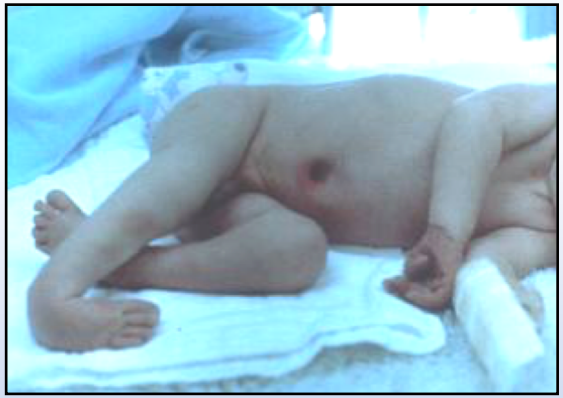
Hilbert et al.
Neurology 2017

Congenital myotonic dystrophy

Exploratory study: Orofacial function in CMD
(Berggren et al. Muscle Nerve 2018)

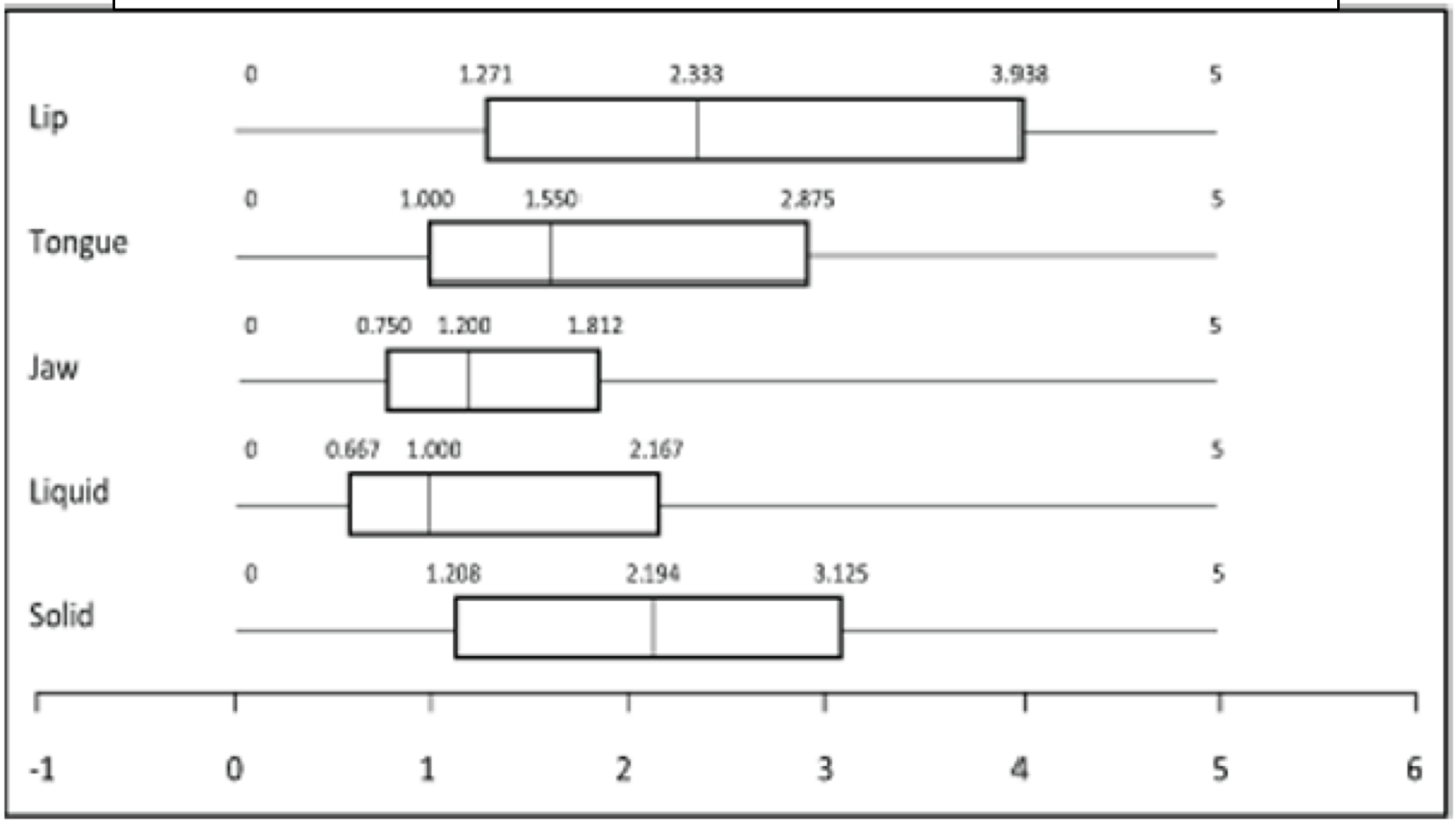
41 CMD pts 0.5 – 13.22 years
and 29 healthy controls

18/24 children with CDM
demonstrated dysarthria;
11 participants non-verbal



Courtesy - Peter Barth

Box plots showing the median interquartile range of the Oral Motor Feeding Rating Scale swallow assessment ratings by orofacial region and food type.



Oculopharyngeal muscular dystrophy

- In 32% (pharyngeal) dysphagia first symptom
- Swallowing difficulty mainly to solid food
- Symptoms: a sense of throat blockade and coughing and choking during eating -> affecting eating habits (e.g. small bites) and prolongation of eating time
- Progressive nature dysphagia -> therapeutic interventions within a mean of eight years from onset.

Côté et al. Muscle & Nerve 2019; Brisson et al. Muscle & Nerve 2020

Male, 75 y/o at referral
dysphagia ignored for a long time

- Developed gait difficulty due to weakness of left leg
- At the same time weakness of trunk muscles and arms
- Hoarse voice and swallowing difficulty (admitted to have progressive speech and swallowing difficulty since ~ 20 years)

Previous hx: cataract surgery at age 74 & 75 yrs

Family hx: Mother may have had a ‘muscle disease’

Ex/ Facial weakness, ptosis. Weak cough
Moderate generalized atrophy/weakness
No sensory disturbances; no myotonia;
no fasciculations
Normal reflexes, left plantar response extensor

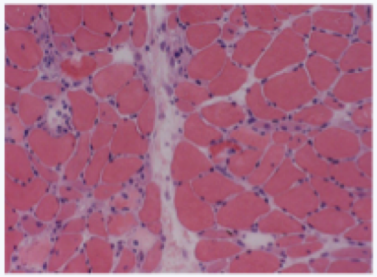
EMG: Neurogenic; repeat EMG: myopathic
CK slightly elevated (205 IU/L (ULN 190))
Muscle bx: some neurogenic features,
no rimmed vacuoles
Videofluoroscopy: silent aspiration

Diagnosis

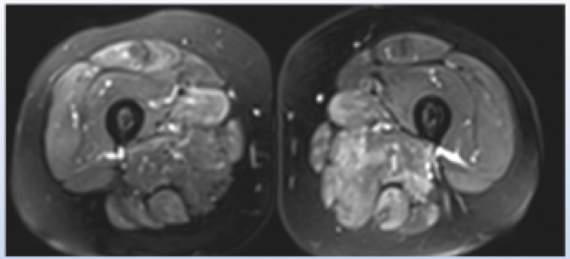
DNA analysis: (GCN)12 repeat expansion exon 1 PAPBN1 gene

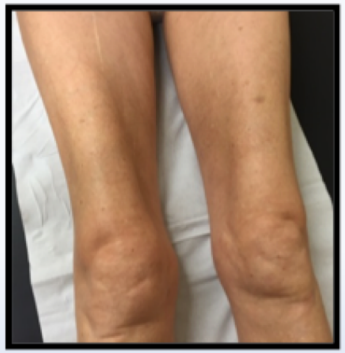
Dx: Oculopharyngeal muscular dystrophy, autosomal dominantly inherited

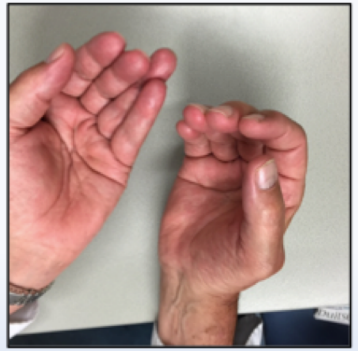
Dysphagia in myositis (IMNM, IBM, ICI)



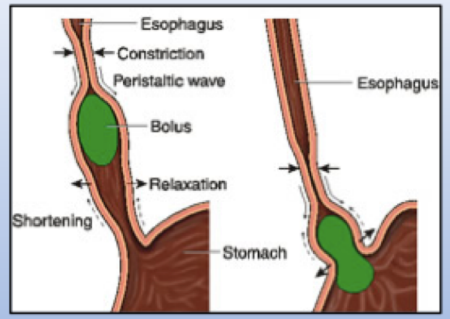
IMNM







IBM



Prevalence of 36% in IIM and in IBM of 56%

Taira et al. J Neurol Sci 2020; Labeit et al. J.Clin Med 2020

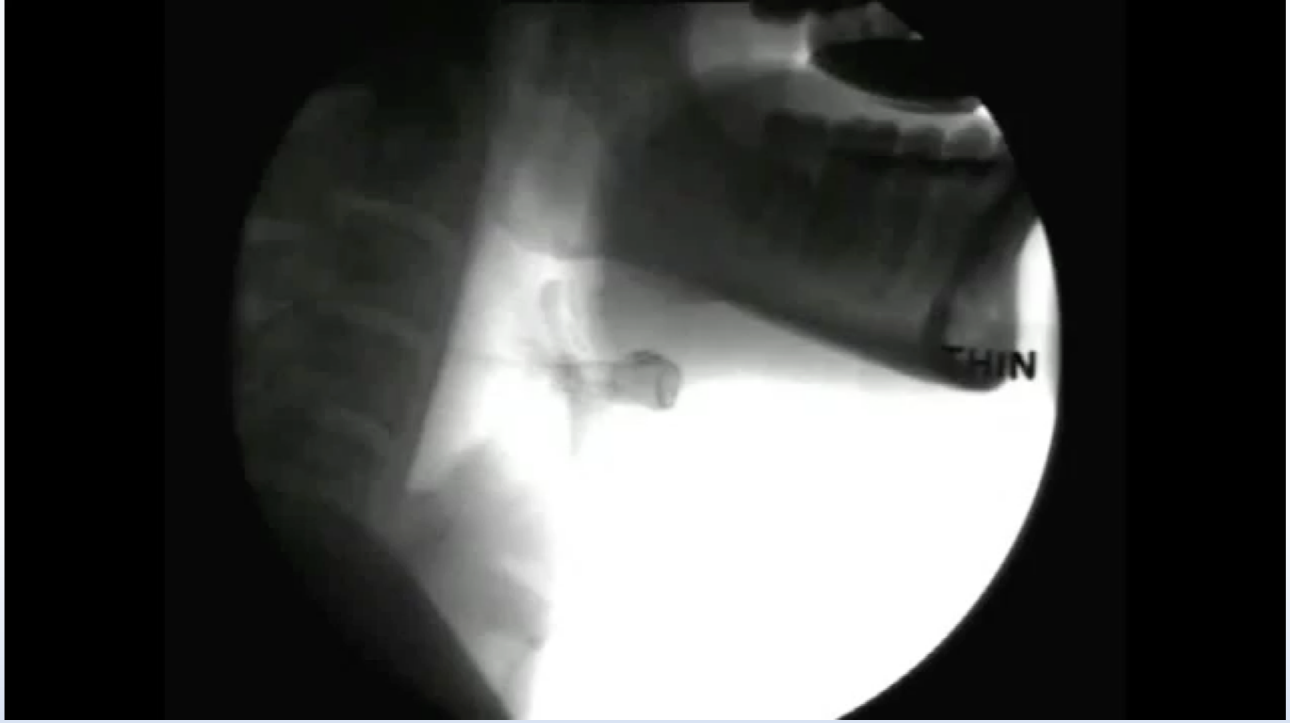
Dysphagia as presenting symptom

Male, referral at age 65 years

History

- Progressive dysphagia since about one year (solid food)
- Coughs while eating, choking occurs
- Sometimes food comes through the nose
- Lost 7 kg over the past year

- Referral to ENT and gastro-enterologist

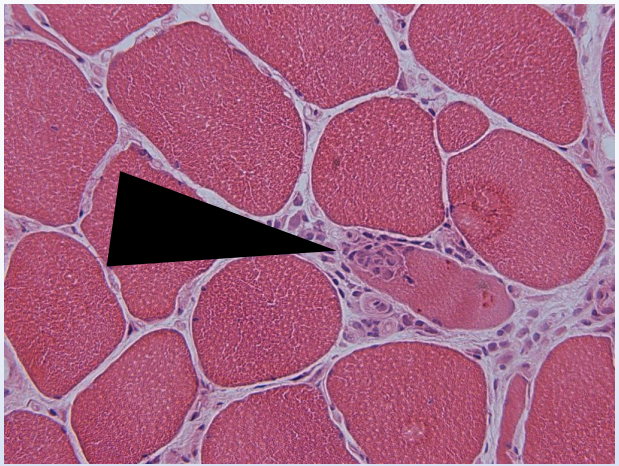


Videofluoroscopy

- Hypertrophy of m. cricopharyngeus
- Stasis of contrast
- Overflow of contrast to trachea

Referral to neurology and follow-up

- Botox effective for about one year
- Complains about fatigue in the legs
- ‘Feels like I have run the marathon’
- MRI: not contributory
- Anti-cN1A autoantibodies: negative
- Muscle biopsy consistent with IBM



Dx IBM - Follow up: Progressive weakness of the deep finger flexors; dysphagia slowly progressive

Congenital myopathies

Natural history of a large pediatric cohort

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Mariacristina Scoto, PhD
Adnan Y. Manzur, MD
Stephanie A. Robb, MD
Lorenzo Maggi, MD
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ABSTRACT

Objective: To assess the natural history of congenital myopathies (CMs) due to different genotypes.

Methods: Retrospective cross-sectional study based on case-note review of 125 patients affected by CM, followed at a single pediatric neuromuscular center, between 1984 and 2012.

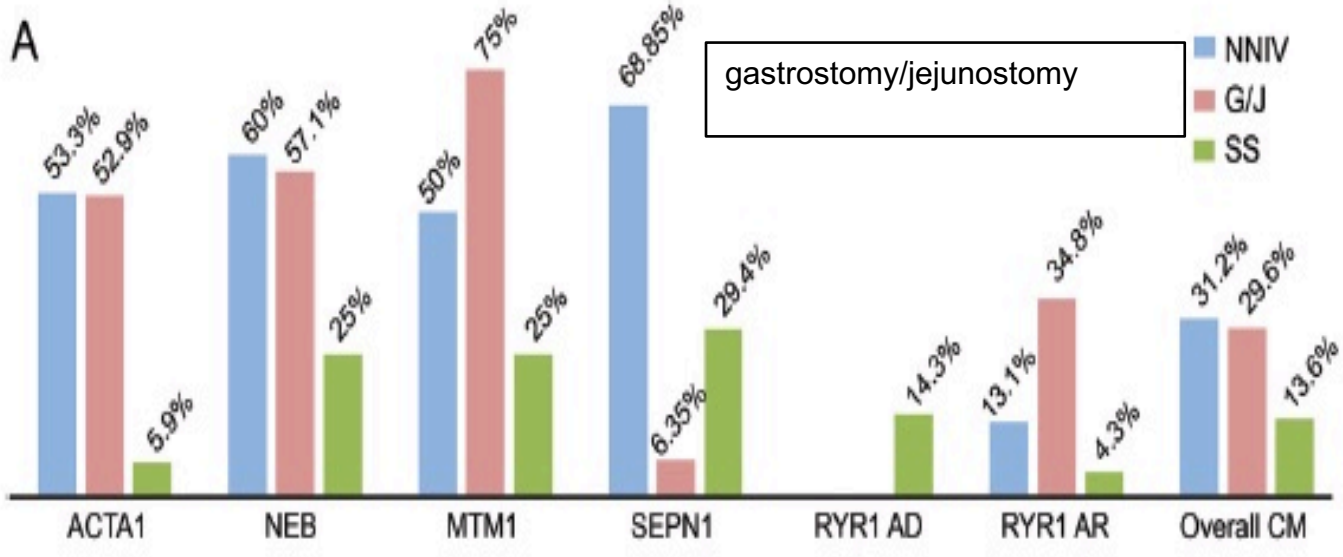
Results: Genetic characterization was achieved in 99 of 125 cases (79.2%), with *RYR1* most frequently implicated (44/125). Neonatal/infantile onset was observed in 76%. At birth, 30.4% required respiratory support, and 25.2% nasogastric feeding. Twelve percent died, mainly within the first year, associated with mutations in *ACTA1*, *MTM1*, or *KLHL40*. All *RYR1*-mutated cases survived and did not require long-term ventilator support including those with severe neonatal onset; however, recessive cases were more likely to require gastrostomy insertion ($p = 0.0028$) compared with dominant cases. Independent ambulation was achieved in 74.1% of all patients; 62.9% were late walkers. Among ambulant patients, 9% eventually became wheelchair-dependent. Scoliosis of variable severity was reported in 43%, with 1/3 of (both ambulant and nonambulant) patients requiring surgery. Bulbar involvement was present in 46.4% and required gastrostomy placement in 28.8% (at a mean age of 2.7 years). Respiratory impairment of variable severity was a feature in 64.1%, approximately half of these patients required nocturnal noninvasive ventilation due to respiratory failure (at a mean age of 8.5 years).

Conclusions: We describe the long-term outcome of a large cohort of patients with CMs. While overall course is stable, we demonstrate a wide clinical spectrum with motor deterioration in a subset of cases. Severity in the neonatal/infantile period is critical for survival, with clear genotype-phenotype correlations that may inform future counseling. *Neurology*® 2015;84:28–35

Colombo et al.
Neurology 2014

Congenital myopathies

Figure 4 Respiratory, feeding, and orthopedic procedures



Mitochondrial myopathies

Therapeutic Advances in Gastroenterology *Review*

Gastrointestinal manifestations of mitochondrial disorders: a systematic review

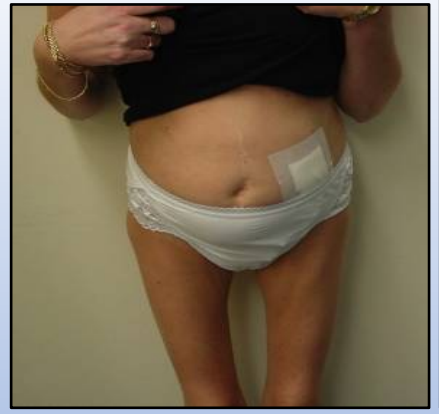
Josef Finsterer and Marlies Frank

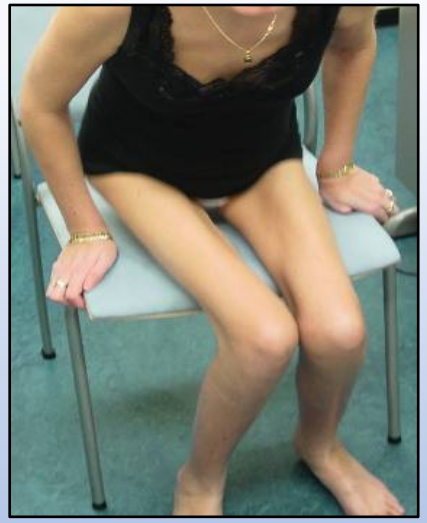
Ther Adv Gastroenterol
2017, Vol. 10(1) 142–154
DOI: 10.1177/1756283X16666806

Frequent gastrointestinal manifestations:

- poor appetite
- gastroesophageal sphincter dysfunction
- constipation
- dysphagia, vomiting
- gastroparesis
- GI pseudo-obstruction
- diarrhea
- pancreatitis and hepatopathy

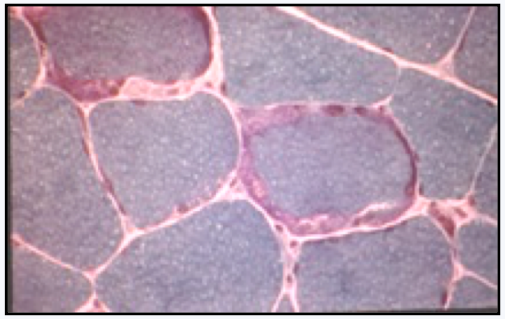
Mitochondrial myopathies and dysphagia





Female 39 years
Previous hx: congenital deafness, infantile encephalopathy, pseudo-obstruction syndrome
Ex/
- Facies myopathica
- Vertical gaze paresis, strabismus
- Limb-girdle weakness, neck flexor weakness, flexion contractures knees

Muscle bx: RRF



Diagnosis based on clinical picture: MNGIE-likepicture
Myopathy and external ophthalmoplegia
Neuropathy
Gastro-**I**ntestinal
Encephalopathy

No mutation in thymidine phosphorylase gene but
MELAS mutation: m.3243A>G (tRNAleu)

Duchenne muscular dystrophy and dysphagia

Swallowing difficulty due to increaed tongue thickness (oral phase) in early non-ambulatory patients

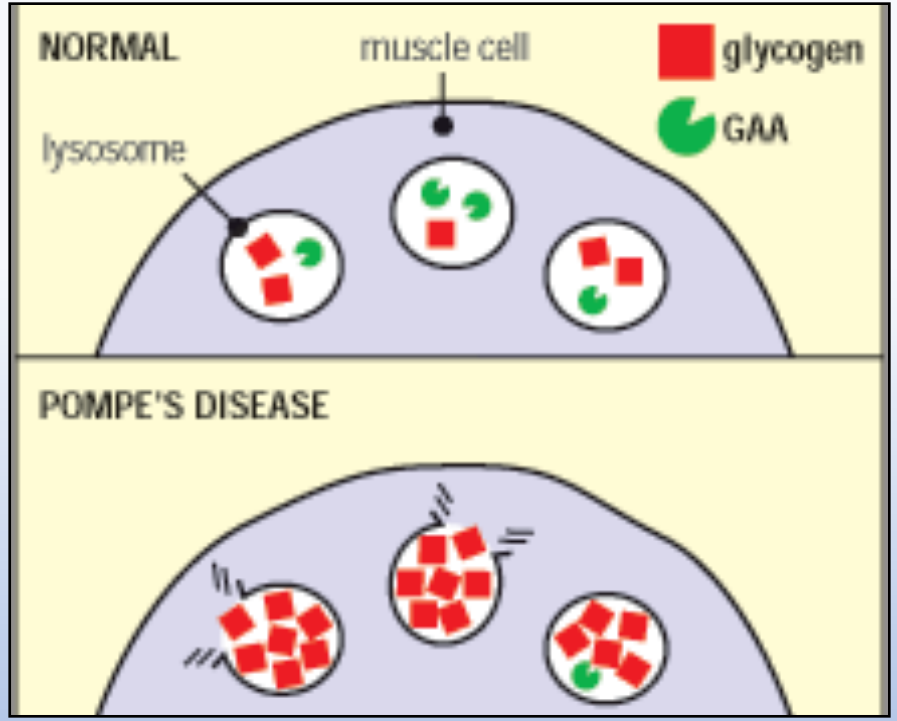
More problems with swallowing of semisolid and solid food than thin liquid, especially in advanced stages.
(Toussaint et al. 2016; Van den Engel-Hoek et al. 2013)

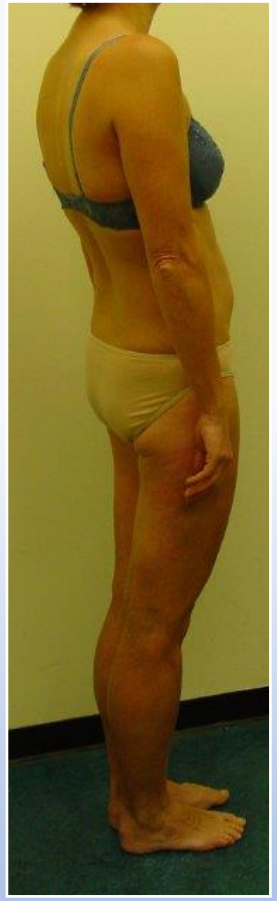
Also paucisymptomatic chronic obstipation
(Lo Cascio et al. Plos One 2016)

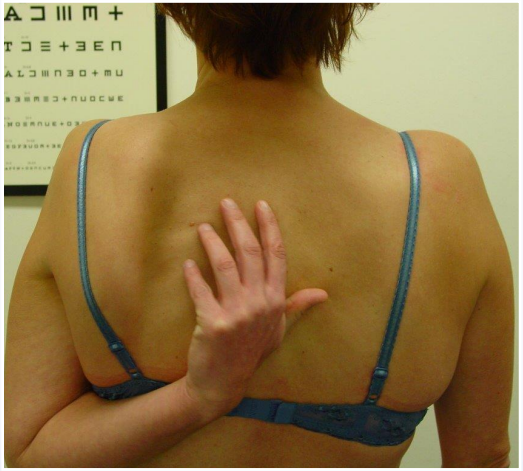
Pompe disease and dysphagia

Pompe disease (glycogen storage disease type II),

Two broad subtypes: infantile-onset and late-onset Pompe disease







Female, 38 yo.

Late walker and walking difficulty since ~10 years

Dysphagia in Pompe disease

IOPD: Study on 13 patients

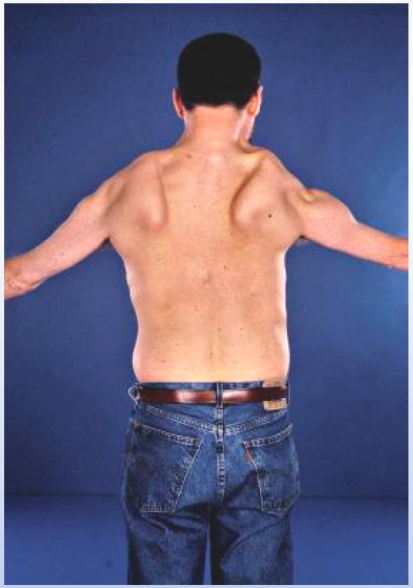
- Dysphagia in all 13 subjects
  - Weak suck in 69%
  - Pharyngeal stage signs in 100%, including a pharyngeal swallow delay (92%) and pharyngeal residue (77%)
  - Airway invasion in 76.9% of subjects, including penetration in five (38.46%) and silent aspiration in an additional five (38.46%)
- ERT in infantile Pompe disease can be beneficial in a fair proportion of patients leading to autonomous feeding.

LOPD: - Lingual weakness (80%), tongue weakness (80%)

-1/3 dysphagia

Jones et al. Dysphagia 2010

Facioscapulohumeral dystrophy and dysphagia



Most FSHD patients do not complain about dysphagia SWAL-QOL ->25% have symptoms

- increased eating duration
- fear of choking
- eating fatigue

Wohlgemut et al. Neurology 20006; Mul et al. Neurology 2019;

Take home messages

- Dysphagia or other manifestations of GI involvement frequent in almost all myopathies
- Dysphagia often goes unnoticed
- Dysphagia may lead to undernutrition, aspiration pneumonia and reduced quality of life
- Various assessment tools: PROs, bedside tests (fluids and solids) and instrumental tools (e.g. fiberoptic endoscopic evaluation of swallowing, maximal tongue pressure, manometry of the upper esophageal sphincter, surface EMG and imaging

I hope that you have achieved your learning objectives!