

# Consensus-based Care Recommendations for Congenital & Childhood-onset Myotonic Dystrophy Type I

## Quick Reference Version

Myotonic recruited clinicians from the United States, Canada, & Europe who have experience in the treatment of children with myotonic dystrophy type I (DM1) to develop consensus-based recommendations. See full recommendations at [www.myotonic.org](http://www.myotonic.org)

## RECOMMENDATIONS

### Diagnosis & classification

- The diagnosis of DM1 should be suspected in any child with a family history of DM1 &/or presenting with one or more of the following features:
  - Eyelid ptosis &/or oral motor weakness
  - Distal weakness, primarily of the finger & wrist flexors, without contractures, or weakness of the neck flexors
  - Myotonia or “stiffness” of muscles
  - Autistic features or social communication difficulties
  - Attention deficit disorder, anxiety & other behavioral problems
  - Developmental delay &/or Intellectual disability
  - Learning disabilities (e.g. dyslexia, dyscalculia)
  - Excessive daytime sleepiness
  - Gastrointestinal issues: constipation or diarrhea
  - Scoliosis
  - Arrhythmia
  - Prolonged recovery or respiratory arrest following anesthesia
  - Neonatal features of hypotonia, weakness, club foot, respiratory distress or feeding problems
- The classification of congenital & childhood-onset DM1 is provided in **Table 1**. Note that diagnosis may be made retrospectively after reviewing symptom onset. Fetal tissue with long CTG repeats should not be called CDM as this diagnosis is reserved for newborns. In these cases, we would suggest use of fetal DM1 as more appropriate

### Genetic counseling

- Genetic counseling in affected families should convey information about:
  - The inheritance pattern of disease (autosomal dominant inheritance)
  - The wide variability in the scope & severity of DM1 symptoms, even within the same family
  - The possibility of changes in symptom scope & severity over time
  - The likelihood that the mutation will expand & the disease will become more severe as it is passed from generation to generation (anticipation)
  - Particular attention to the possibility of a minimally-affected mother giving birth to a severely affected child
  - Options for family planning
- Do not use CTG repeat numbers, if available, for genetic advice or prognostication; these need to be discussed with a genetic counselor. Specifically, repeat size may be an indicator of severity, but it does not provide any information about the prognosis

**Table 1. Classification of Congenital & Childhood-onset Myotonic Dystrophy**

#### Congenital myotonic dystrophy

- Physical signs or symptoms attributable to DM1 in the pre- &/or perinatal period:
  - Reduced fetal movement
  - Polyhydramnios
  - Respiratory failure
  - Feeding problems
  - Weakness & hypotonia
  - Talipes &/or other contractures
- Need for medical intervention or hospitalization
- Generic confirmation of expanded CTG repeat size

#### Childhood myotonic dystrophy

- Symptoms attributed to myotonic dystrophy prior to age 18 years
- Genetic confirmation of expanded CTG repeat size
- Some classification systems further divide this group into a childhood form with symptoms <10 years & a juvenile form with symptoms between 10 & 18 years

### Focus on CDM

- Once a family has had a child with CDM, there is an increased risk that the next affected child with DM1 is likely to have congenital form as well

### Neonatal care

- A high-risk obstetrician should provide prenatal obstetric care for mothers known or suspected to carry a child with DM1
- Pediatric or neonatal specialist should be present at delivery if a mother is known to have DM1, or if the child is known or suspected to have DM1

### Focus on CDM

- Children with CDM will often need management in a NICU with the capability to deal with breathing & feeding support, & that has a range of neonatal & consulting specialists who can manage genetic, respiratory, GI, orthopedic, neuromuscular, neurosurgical, & cardiac issues. See **Figure 1** for neonatal care

### End of life counseling & management

- Recommend the introduction of palliative care at the time of diagnosis & at regular intervals thereafter. When a formal pediatric palliative care team is available they should be consulted

## Focus on CDM

- Introduce the concept that the natural history of the disease is one of progressive muscle strength improvement, however the complications of CDM can be critical & have a high risk of mortality, particularly in the first year of life
- Advise families or caregivers that invasive & noninvasive ventilation, & nutrition via gastrostomy tube are acceptable parts of care for patients with CDM

## Surgery & anesthesia

- Educate all caregivers that anyone administering an anesthetic should be aware of the DM1 diagnosis
- When possible combine procedures under a single sedation
- Arrange for a pre-anesthetic visit for all children planning to have deep sedation for a diagnostic test, procedure or surgery. If possible, include a pulmonologist with expertise in neuromuscular diseases during this visit

For procedures requiring anesthesia, see *Myotonic's Practical Suggestions for the Anesthetic Management of a Myotonic Dystrophy Patient and Anesthesia Quick Reference Guide* at <https://www.myotonic.org/toolkits-publications>

## Focus on CDM

- It is worth noting that children with CDM are at a higher risk of anesthetic complications given the underlying respiratory involvement as opposed to those with childhood onset

## SYSTEMS-BASED CARE RECOMMENDATIONS

### Respiratory

- Signs of respiratory problems in children with myotonic dystrophy include ineffective cough, recurrent pulmonary infections, orthopnea, dyspnea, poor sleep, morning headaches, apnea, fatigue & snoring

### Focus on CDM

- For CDM children who remain on longer term trach ventilation there is often improvement in respiratory strength over time & consideration to decannulate a tracheostomy should be made after careful consideration with the multidisciplinary team including neurology, respiratory, ENT, & the family. Consideration of airway control, respiratory infection frequency, ability to tolerate a facial or nasal mask for NIV & compliance & cooperation with maintenance pulmonary therapy such as cough assist, breath stacking etc. Testing for hypoventilation in sleep should be done prior to decannulation
- Cardiovascular
- Inform families of the risks of arrhythmias & cardiac dysfunction & the importance of prompt medical attention if symptoms are observed (i.e. palpitations, pre-syncope, syncope, dyspnea, chest pain, unexplained fatigue)
  - A 12-lead ECG should be performed at DM1 diagnosis, if normal & the patient remains asymptomatic, ECG should be performed annually & warrants more investigation if the patient is symptomatic
  - As specific medications such as mexiletine & psychostimulants are antiarrhythmic, an electrocardiogram (ECG) prior to use, again within three months of starting therapy, & then at serial intervals is recommended

- Consider in-hospital cardiac monitoring to detect arrhythmias if admitted for longer duration than typical following surgical procedures or if admitted due to severe illness or infection
- Evaluate & treat using American Heart Association AHA *Management of Cardiac Involvement Associated With Neuromuscular Diseases: A Scientific Statement From the American Heart Association 2017* <http://circ.ahajournals.org/content/136/13/e200.long> & ACC [American College of Cardiology]/AHA [American Heart Association]/ESC [European Society of Cardiology] *Guidelines for Management of Patients with Ventricular Arrhythmias & the Prevention of Sudden Cardiac Death* (see <https://www.ncbi.nlm.nih.gov/pubmed/16949478>) -section on pediatric issues 13.4

## Skeletal muscle weakness, orthopedic complications, & rehabilitation

- Children should be evaluated early & often for physical, occupational, & speech therapy needs with specific attention to:
  - Feeding concerns & dysphagia
  - Gross motor delay
  - Gross & fine motor weakness
  - Dysarthria & potential augmentative & alternative communication (AAC) needs
  - Language acquisition delays
- The spine should be assessed for scoliosis &, if necessary, consider bracing or referral to orthopedic surgeon
- Children should be encouraged to participate in speech therapy targeting speech, language, & communication from a very early age

### Focus on CDM

- Newborns with CDM often having difficulty feeding & alternative nutrition should be considered. After about a year of actively working with a speech therapist or occupational therapist, most children can generally start on oral feeding
- Children with CDM experience progressive improvement in their proximal strength until adolescence, at a minimum. Therefore, children should be encouraged to participate in physical activity
- Prevention of joint contractures are key to management & should be closely monitored with early initiation of stretching. Treatment of talipes equinovarus & other joint contractures should include initial stretching regiment & appropriate ankle bracing (for talipes equinovarus). Serial casting may be considered

## Skeletal muscle myotonia

- Mexiletine (Mexitil) is an option for myotonia, if it is demonstrated & is distressing to the patient
  - As mexiletine is an antiarrhythmic, an electrocardiogram (ECG) prior to use, again within three months of starting therapy, & then at serial intervals is recommended

## Ocular & hearing management

- Baseline audiometry should be performed, especially at school age
- Ophthalmological assessment at diagnosis & on a regularly, at least yearly, basis regarding hyperopia, astigmatism, strabismus & visual acuity to prevent involvement of visual impairment
- Eyelid ptosis; if ptosis becomes severe & interferes with vision, intervention such as eyelid "crutches" that can be inserted into glasses may be warranted. Try crutches as a remedy for ptosis before eyelid surgery is considered, due to anesthesia risks. Ophthalmic lubricants for dry eye may be considered

## Gastrointestinal & genitourinary management

- Presence of gastrointestinal symptoms such as abdominal pain, constipation, fecal incontinence or diarrhea may be a frequent problem. The symptoms may mimic irritable bowel syndrome – IBS. Fiber supplementation (more than 8 grams daily) is the first line treatment
- Gentle laxatives (see below) for constipation. Oils should be avoided. If a patient does not respond to the first- or second-line recommendations below, a referral to a gastrointestinal specialist for anal manometry should be considered:
  - First-line therapy recommendations: polyethylene glycol (Miralax), senna (Ex-Lax, Senokot), docusate (Colace) or lactulose (Cholac)
  - Second-line therapy recommendations: bisacodyl (Dulcolax, Correctol), lubiprostone (Amitiza) or linaclotide (Linzess)
  - Metoclopramide (Reglan) may be used to reduce the symptoms of gastroparesis, pseudo-obstruction & gastric reflux. Long-term use is not recommended because this drug can cause tardive dyskinesia
- Cholestyramine & loperamide are other options in presence of mainly diarrhea & anticholinergic drug such as hyoscyamine sulfate in presence of IBS. As anticholinergic drugs may be antiarrhythmic, see **Cardiac section on management**
  - Mexiletine may be considered for refractory diarrhea or constipation, as the drug may be antiarrhythmic, see Cardiac section on management
- If bacterial overgrowth is found on breath testing, treating with antibiotics may reduce diarrhea

### Focus on CDM

- As mentioned in the neonatal care section, children with CDM may require a temporary feeding tube. If dysphagia persists, consider enteral nutrition. Refer to speech therapy. Children should be periodically re-assessed for improving dysphagia
- Children with CDM often benefit from dysphagia therapy. With aggressive dysphagia therapy, children with CDM often are able to feed orally within the first year of life

## Endocrine & metabolic

- DM1 male patients should undergo a detailed physical examination in search of gonadal atrophy or cryptorchidism
  - Patients should have a HbA1c & thyroid stimulating hormone (TSH) & FreeT4 level measured at baseline & every 3 years, or if there is a clinical suspicion

## NEURODEVELOPMENTAL CARE RECOMMENDATIONS

### Recommendations (See Table 2)

- Neuropsychological testing should be performed in every child with DM1 to delineate cognitive strengths & weaknesses. This may include:
  - Psychometric assessment of global intellectual ability & adaptive functioning
  - Assessment of executive functions
  - Assessment of social cognition
  - Assessment of visuomotor integration & visuospatial ability
  - Assessment of receptive & expressive language abilities
  - Assessment of excessive daytime sleepiness

**Table 2. Neurodevelopmental Management in DM**

Cognitive & psychometric tests should be performed at diagnosis, preschool, & 2-3 more times before adulthood	
Domain/symptom assessed	Potential treatment
Global intellectual ability & adaptive function	Serotonin-enhancing antidepressants if excessive anxiety or other treatable psychiatric symptoms present
Social cognition	Remediation programs to enhance social emotional abilities (visual contact, joint attention, emotional regulation)
Executive function	Cognitive remediation programs to enhance executive efficiency (impulsivity, attention, working memory, & mental flexibility) using dedicated software (e.g., Cogmed®)
Visuomotor integration & visual spatial ability	Specific remediation programs
Learning disabilities (specific tests for dyscalculia, dyslexia, & dyspraxia)	Language remediation & reading therapy
Excessive daytime sleepiness	Psychostimulants if attention deficits are associated with an impairing level of fatigue or excessive daytime sleepiness
Autism spectrum disorder, attention deficit disorder	Refer to mental health professional

- Assessment of learning disabilities (specific tests for dyscalculia, dyslexia & dyspraxia)
- The assessments should be performed in the congenital form in preschool age & should be repeated, depending on the level of functioning, 2-3 times before adulthood. In childhood DM1, neuropsychological testing is recommended at diagnosis & repeated in preschool or school age & college period
- Patients with psychiatric or behavioral issues should be referred to a mental health care professional for assessment of autism spectrum disorders, attention deficit disorders with or without hyperactivity, alexythimia & other behavioral problems
- Psychostimulants if attention deficits are associated with an impairing level of fatigue or excessive daytime sleepiness (see **Excessive daytime sleepiness**). As psychostimulants may be antiarrhythmic, see Cardiac section on stimulant management
  - Serotonin-enhancing antidepressants if excessive anxiety or other treatable psychiatric symptoms are present
  - Specific cognitive remediation programs to enhance social emotional abilities (visual contact, joint attention, emotional regulation) or executive functions efficiency (inhibitory control, attention, working memory, & cognitive flexibility) using dedicated software (e.g., Cogmed®)

- Language remediation & reading therapy should be considered due to the presence of cognitive deficits, even in children with normal intelligence. Attention deficit, fatigability, & visual-spatial construction dysfunction, can result in specific learning disorders with impairment in reading & spelling as well as in mathematics

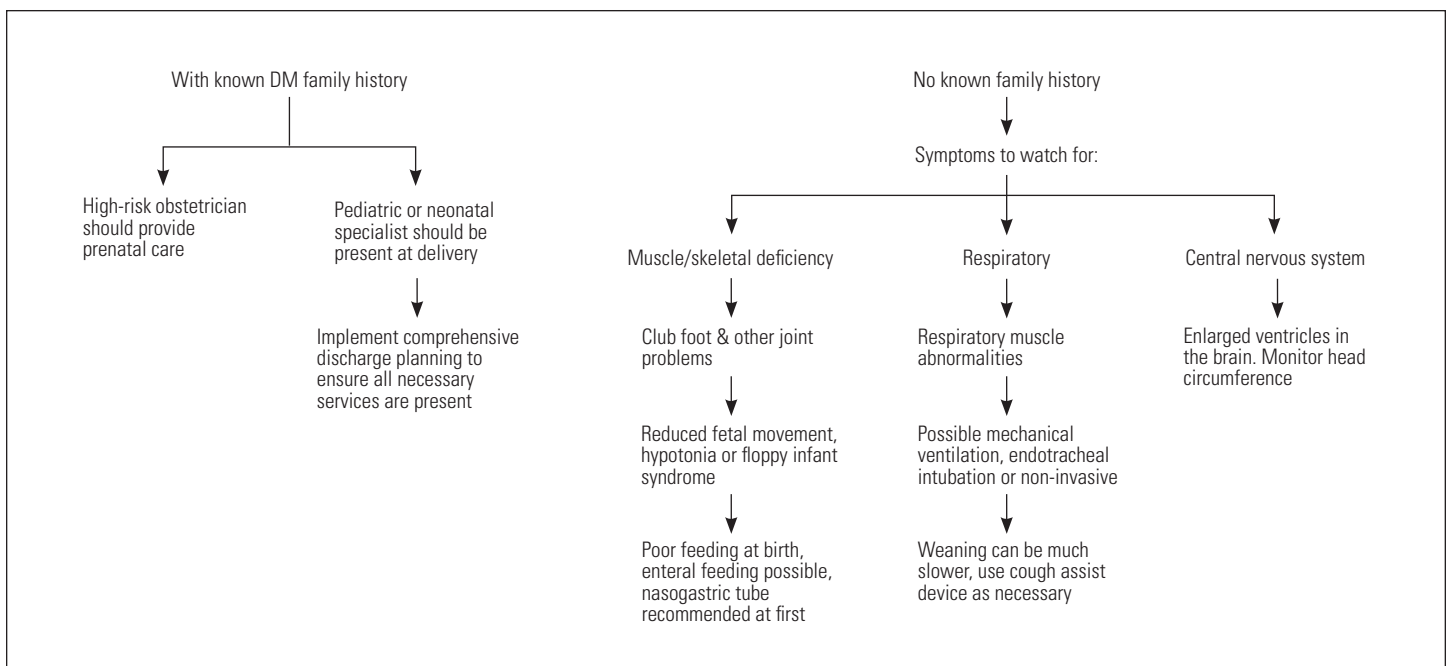
## Psychosocial management

- Children with DM1 should have access to appropriate psychological & therapy services at an early age to ensure they are fulfilling their maximum potential & learning coping strategies for later life. The modification of activities including social engagement strategies would provide a foundation for each child to grow in confidence & esteem

## Excessive daytime sleepiness

- Children should be screened for signs of EDS, including prolonged naps, or falling asleep in school
- Possible sleep apnea should be evaluated with overnight oximetry or polysomnogram
- Positive-pressure ventilation can be considered if a DM1 patient's sleepiness is thought to be related to nocturnal or daytime hypoventilation or sleep apnea. Patients should be referred to pulmonologists who have experience in neuromuscular diseases for consideration of assisted ventilation
- Stimulant therapy with a psychostimulant such as modafinil (Provigil), methylphenidate, or other stimulant can be considered if central hypersomnia is suspected. Often difficulty staying awake in school is a triggering factor. Special care should be taken in children with previously detected cardiac arrhythmia. (See **Cardiac section on stimulant management**)

Fig. 1 DM Neonatal Care Flowchart



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A full list of authors & an overview of the methodology used to develop consensus for these recommendations can be found here: <https://www.myotonic.org/toolkits-publications>