REVIEW OPEN ACCESS

Consensus-based care recommendations for adults with myotonic dystrophy type 1

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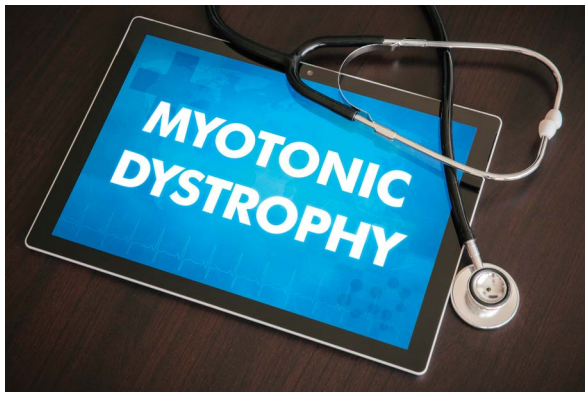
Abstract

Purpose of review

Myotonic dystrophy type 1 (DM1) is a severe, progressive genetic disease that affects between 1 in 3,000 and 8,000 individuals globally. No evidence-based guideline exists to inform the care of these patients, and most do not have access to multidisciplinary care centers staffed by experienced professionals, creating a clinical care deficit.



Recent findings

The Myotonic Dystrophy Foundation (MDF) recruited 66 international clinicians experienced in DM1 patient care to develop consensus-based care recommendations. MDF created a 2-step methodology for the project using elements of the Single Text Procedure and the Nominal Group Technique. The process generated a 4-page Quick Reference Guide and a comprehensive, 55-page document that provides clinical care recommendations for 19 discrete body systems and/or care considerations.

Summary

The resulting recommendations are intended to help standardize and elevate care for this patient population and reduce variability in clinical trial and study environments.

Described as "one of the more variable diseases found in medicine," myotonic dystrophy type 1 (DM1) is an autosomal dominant, triplet-repeat expansion disorder that affects somewhere between 1:3,000 and 1:8,000 individuals worldwide.[1] There is a modest association between

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increased repeat expansion and disease severity, as evidenced by the average age of onset and overall morbidity of the condition. An expansion of over 35 repeats typically indicates an unstable and expanding mutation. An expansion of 50 repeats or higher is consistent with a diagnosis of DM1. DM1 is a multisystem and heterogeneous disease characterized by distal weakness, atrophy, and myotonia, as well as symptoms in the heart, brain, gastrointestinal tract, endocrine, and respiratory systems. Symptoms may occur at any age. The severity of the condition varies widely among affected individuals, even among members of the same family.

Comprehensive evidence-based guidelines do not currently exist to guide the treatment of DM1 patients. As a result, the international patient community reports varied levels of care and care quality, and difficulty accessing care adequate to manage their symptoms, unless they have access to multidisciplinary neuromuscular clinics.

Consensus-based care recommendations can help standardize and improve the quality of care received by DM1 patients and assist clinicians who may not be familiar with the significant variability, range of symptoms, and severity of the disease. Care recommendations can also improve the landscape for clinical trial success by eliminating some of the inconsistencies in patient care to allow more accurate understanding of the benefit of potential therapies.

Methods

The Myotonic Dystrophy Foundation (MDF) recruited clinicians from the United States, United Kingdom, Canada, and Europe who have experience in the treatment of individuals living with DM1 to develop consensus-based care recommendations.

The project included a Steering Committee of 10 and a total Working Group of 66 clinical professionals, with additional support from the US Centers for Disease Control and Prevention and the services of a facilitation firm, Interaction Associates (San Francisco), that provided the meeting facilitation necessary to execute the Nominal Group Technique portion of the methodology. MDF provided project design, development, and management support.

To streamline the project timeline and lower project cost, MDF developed a 2-phased, consensus-building methodology using components of the Single Text Procedure[2] and the Nominal Group Technique.[3–5] These facilitation approaches were selected because they could be effective within the context of the limited clinical care data available for DM1, the clinical content already available, and the complexities of working across a large, multinational group of experts.

The Working Group was divided into 8 Study Area subcommittees, each led by a Steering Committee chair who identified members for his or her Study Area. The Study Areas were each assigned several body systems affected by myotonic dystrophy.

Working Group subcommittee members began the consensus-building project by creating the background reading lists for their Study Areas. These reading lists were refined as the project moved forward, and the Study Area lists serve as the bibliography for the final Consensus-based Recommendations.

The Single Text Procedure, using a single document as a starting point to incorporate the input and contributions of stakeholders, was used to begin the consensus-building effort. In this process, stakeholders add, subtract, and refine a draft text that becomes the foundation for a final ratified document.

Working with MDF, Margaret Wahl, RN, organized the draft document, drawing substantially from care content in the MDF Toolkit developed by the MDF's Scientific and Medical Advisory Committee, as well as several other key references.[6–9] MDF circulated the draft document to Working Group members, along with other materials designed to help coordinate the editing and revision process. Working Group members read the draft content for their Study Areas and provided Study Area-specific recommendations. MDF aggregated all the revisions and suggestions into a single updated document. Recommendations in conflict were circulated to the group for discussion and resolved through serial conference calls.

The Steering Committee reviewed the aggregated document, offered revisions, and then returned it to the full Working Group. This process was repeated until the Steering Committee and Working Group achieved consensus.

Sixty-six Steering Committee and Working Group members then met for a face-to-face summit that involved the second phase of the project, the Nominal Group Technique.

The Nominal Group Technique is a face-to-face, structured group meeting led by an experienced facilitator. Participants engage in a serial discussion of each revised, updated, or newly-generated recommendation led by the facilitator. MDF engaged 7 professional facilitators from Interaction Associates to drive consensus building in Study Area subcommittee meetings at the summit.

MDF then created an updated document aggregating the changes from the facilitated discussions, and the full Working Group went through the same facilitated process again with the new document, which concluded the Nominal Group Technique portion of the process.

MDF then created a postsummit, updated document based on full-group feedback at the meeting. This version was used to conduct a final series of rounds of edit solicitation and updated document review through email and conference call. These efforts led to the final consensus-based care recommendations and Quick Reference Guide for Adults with DM1, which were completed in mid-2017. The Quick Reference Guide is provided as an appendix, and the full document is available online (appendix e-1, links.lww.com/CPJ/A53). Both feature flowcharts and other infographics for ease of use.

Results

See full recommendations at Neurology.org/cp.

Life threatening symptoms—Clinical care recommendations

- Surgery, anesthesia, and pain
  - See MDF's *Practical Suggestions for the Anesthetic Management of a Myotonic Dystrophy Patient* (myotonic.org/clinical-resources) for anesthesia risks and recommendations before any surgeries or procedures requiring anesthesia.
  - DM1 patients have adverse reactions to medications used for anesthesia and analgesia, including opioids; interactions of the cardiac, respiratory, muscle, and CNS manifestations in each DM1 patient can lead to a variety of untoward responses, including mortality, before, during, and after surgery.
  - Serious adverse events to anesthesia and opioids can occur throughout the course of DM1 and have been reported in patients whose DM1 symptoms were mild.
  - Intellectual impairment, cognitive dysfunction, and/or hypersomnolence may adversely affect the patient's ability to re-emerge from anesthesia. Include premorbid cognitive or intellectual dysfunction as part of preoperative assessment preoperatively (if nonemergency intervention) because these manifestations along with preoperative sleep deprivation can complicate the patient's immediate postoperative care and long-term recovery.
  - Most serious complications occur in the postanesthesia period.
  - See full recommendations at myotonic.org/clinical-resources.
- Respiratory symptoms
  - Pulmonary complications are the leading cause of death in DM1 patients. Clinicians must monitor issues such as recurrent pneumonia at baseline and serially (±6 months), with pulmonary function tests, at least forced vital capacity (FVC).
  - Refer DM1 patients with respiratory symptoms including ineffective cough (normal peak expiratory cough flow rate is >270 L/min), respiratory insufficiency, recurrent pulmonary infections, prominent snoring, maximal inspiratory pressure is <60 cm H_2O or FVC values of 50% less than predicted normal values to a pulmonologist knowledgeable in neuromuscular disorders.
  - Vaccinate for pneumonia and flu; treat respiratory infections quickly and use cough assistance and mechanical ventilation as needed along with obtaining consultations from respiratory therapy and pulmonary medicine groups.
  - Some patients will eventually require either nighttime ventilator support or full-time ventilation. Most patients with chronic respiratory insufficiency respond to noninvasive ventilatory support (NIV). Patients experiencing acute respiratory failure require endotracheal intubation with positive pressure ventilation.
  - For chronic respiratory insufficiency, use supplemental oxygen with caution and in conjunction with NIV (see Surgery, anesthesia, and pain).
  - If surgery is planned, reassess clearance capacity if needed, possible adaptation to NIV or cough assistance.
  - See full recommendations at myotonic.org/clinical-resources.
- Cardiovascular symptoms
  - Cardiac complications are the second leading cause of death in DM1.
  - The most common cardiac issues are arrhythmias (sinus bradycardia, heart block, atrial fibrillation and flutter, and ventricular tachycardia).
  - Palpitations, chest pain, dyspnea, orthopnea, lightheadedness, and syncope warrant cardiac investigation.
  - Significant cardiac involvement that subsequently leads to adverse cardiac events is often asymptomatic.
  - Impulse—conduction abnormalities on a standard 12-lead ECG including sinus rate <50 BPM, PR interval >200 ms, QRS duration >100 ms, left anterior or posterior fascicular block, abnormal Q-waves, atrial tachycardia, fibrillation, or flutter, and ventricular arrhythmias are indicative of cardiac involvement.
  - Refer patients with cardiac symptoms, abnormal annual or biennial ECG indicative of cardiac involvement, and patients aged above 40 years without previous cardiac evaluation to a center experienced in DM1 care.
  - Cardiology referral for all DM1 patients is reasonable if part of a multidisciplinary program or if the practitioners providing primary care are uncomfortable assessing cardiac history, examination, or ECG.
  - See full recommendations at myotonic.org/clinical-resources.

- Pregnancy and obstetric management
  - Women with DM1:
    - Have increased risk of miscarriage, preterm delivery, and respiratory insufficiency during pregnancy (especially in the 3rd trimester) and failed labor during delivery; extreme care should be taken with analgesics and sedating anesthetic drugs (see MDF's *Practical Suggestions for the Anesthetic Management of a Myotonic Dystrophy Patient* [myotonic.org/clinical-resources]).
    - Should consult with a high-risk obstetrics and gynecology (OBGYN) care provider before delivery and obtain ongoing antenatal care.
    - Fatigue rapidly during labor and are at risk of postpartum hemorrhage, particularly after prolonged first or second stage or if there has been polyhydramnios.
    - Should be induced only at direction of obstetrician and after all necessary consultants assisting with the delivery are notified.
  - Sexually active patients with DM1:
    - Should be referred to genetic counseling and family planning services if of child-bearing age.
    - Should receive parental counselling for prenatal genetic diagnosis or discussion of preimplantation genetic diagnosis.
  - Include a pediatric or neonatal specialist present at delivery; intensive neonatal care is recommended for neonates that may have DM1; anticipate need for feeding tube and ventilator support.
    - Access to a pediatric or neonatal specialist is recommended even if the fetus is known to be unaffected.
  - See full recommendations at myotonic.org/clinical-resources.

Severe symptoms and conditions—Clinical care recommendations

- Skeletal muscle weakness and rehabilitation
  - Evaluate annually for:
    - Swallowing and speech difficulties
    - Mobility, balance, and falls
    - Activities of daily life—including self-care
    - Activities in home, school, work, and community.
  - Refer to specialists, including physical therapists (PTs), occupational therapists (OTs), speech pathologists, dieticians, social workers, and others.
  - Encourage moderate intensity (aerobic and resistance training) exercise.
  - See *Role of Physical Therapy in the Assessment of Individuals with Myotonic Dystrophy* at myotonic.org/clinical-resources.
  - See full recommendations at myotonic.org/clinical-resources.
- Skeletal muscle myotonia
  - Myotonia can cause muscle stiffness, prolonged hand grip, pain, and speech and swallowing difficulties.
  - Mexiletine or other antimyotonia medications may be considered for myotonia treatment. Mexiletine is contraindicated for DM1 patients with cardiac involvement. See full recommendations regarding mexiletine at myotonic.org/clinical-resources for more information on cardiac implications.
- Ocular symptoms
  - Relevant eye manifestations of DM1 include cataracts (occurring in most patients), strabismus, and other ocular motility problems, myopia, and astigmatism in congenital and juvenile-onset patients.
  - Recommend annual eye examination, including slit-lamp eye examination.
  - Advise patient on safety measures regarding adjusting to changes in light (from dim to bright) while driving, especially at night, related to the effects of cataracts, and on protecting the cornea, especially as weakness of the face (due to m. orbicularis oculi weakness) and eye closure muscles progress.
  - Surgically remove cataracts when they interfere with activities of daily living; see Surgery, anesthesia, and pain control section regarding anesthesia risk.
  - Consider ophthalmic lubricants for dry eye, typically caused by m. orbicular oculi weakness affecting eyelids and cornea.
  - Consider eyelid crutches before surgery for ptosis (due to m. levator palpebrae weakness); see Surgery, anesthesia, and pain control.
  - See full recommendations at myotonic.org/clinical-resources.
- Gastrointestinal symptoms
  - Ask about problems with chewing, swallowing, drooling, reflux, bloating, abdominal pain, bowel movement frequency and characteristics, diarrhea, and incontinence.
  - Physical examination should include abdominal palpation, including around gall bladder, and rectal examination for anal sphincter spasm and dyssynergic defecation for symptomatic patients.
  - DM1 patients are at risk for pseudo-obstruction and experience other problems that may cause actual obstruction of small or large intestine, including endometriosis, acute gallbladder inflammation, ruptured ovarian cysts, sigmoid volvulus. Monitor potential obstructions to determine whether they are pseudo or actual and treat accordingly.
  - Nonmedical interventions:
    - High-fiber diet for diarrhea or constipation; increase water intake
    - Nutritional supplement for weight loss, weight gain, or dysphagia
    - Dysphagia therapy referral for oral pharyngeal dysphagia.
  - Medical interventions:
    - Loperamide for diarrhea control
    - Laxatives for constipation

- First-line therapy: MiraLAX, Senna, Ducusate, or Linaclotide
- Second-line therapy: Bisacodyl, Lubiprostone, Linaclotide

■ Avoid oils—if the above fails, refer out for anal manometry
■ Metoclopramide for gastroparesis, pseudo-obstruction, reflux
■ Antibiotics for bacterial overgrowth-induced diarrhea (based on breath testing)
■ Enteral feeding only for recurring pneumonia or severe dysphagia causing weight loss or causing inability to swallow safely without recurrent aspiration
■ Mexiletine can be considered to treat diarrhea or constipation. Mexiletine is contraindicated for DM1 patients with cardiac involvement. See full recommendations regarding mexiletine at myotonic.org/clinical-resources for more information on cardiac implications.

○ See full recommendations at myotonic.org/clinical-resources.

- Neuropsychiatric symptoms
  - ○ Advise patients that DM1 is also a "brain disorder" that can involve cognitive deficits and changes in cognition over time.
  - ○ Include psychiatric and behavioral examination at baseline, and during regularly scheduled follow-up appointments or when symptoms appear; consider baseline MRI to assess DM1-related abnormalities (e.g., fluid-attenuated inversion recovery hyperintensities, particularly in the temporal poles, and dilated perivascular spaces, often colocalizing) and track over time.
  - ○ Refer patients with psychiatric or behavioral disorders, those with late-onset phenotype, and patients with cognitive complaints to mental health care professional for testing and follow-up; patients may have limited insight into these issues—consider input from partners and family members as appropriate.
  - ○ DM1 patients with a late-onset phenotype can exhibit fast decline in certain cognitive functions.
  - ○ See full recommendations at myotonic.org/clinical-resources.
- Psychosocial symptoms
  - ○ Assess patient's social circumstances in household; consider and be aware of possible child neglect, acute financial need, unsafe driving, unsafe or unsanitary home; refer to social services, support programs, and organizations.
- Excessive daytime sleepiness (EDS) symptoms
  - ○ Assess for EDS with the Epworth Sleepiness Scale or a similar standardized questionnaire instrument; prescribe sleep study if sleep disturbance is suspected.
  - ○ Monitor periodic limb movements (muscle activity during sleep), as well as EEG, and respiratory measures during sleep study to assess possible obstructive sleep apnea and CNS mediated sleep apnea.
  - ○ Refer to a pulmonologist and/or sleep specialist if EDS scores are positive on scales.
  - ○ Question patients re: alcohol or caffeine consumption, medications, and sleep habits for contribution to EDS.
  - ○ Evaluate the effect of possible respiratory muscle weakness (FVC value sitting and supine) on the presence of EDS.
  - ○ If nocturnal or daytime hypoventilation is suspected, consider noninvasive positive pressure ventilation, and refer to a pulmonologist with experience in neuromuscular diseases re: possible need for NIV launching.
  - ○ Consider modafinil for treatment if coexisting CNS alteration is suspected as the cause of EDS.
  - ○ Consider cognitive behavioral therapy or behavioral therapy for apathy; also help treat fatigue; psychostimulant treatment can be considered if apathy is associated with an impairing level of fatigue or EDS.
  - ○ See full recommendations at myotonic.org/clinical-resources.
- Endocrine and metabolic symptoms
  - ○ Follow criteria from the American Diabetes Association re: the type of initial testing to obtain: typically, fasting blood glucose or HbA1c and if symptomatic diabetes is suspected.
  - ○ Consider formal glucose tolerance testing to monitor glucose control in patients; request serial measurement of HbA1c and fasting plasma glucose annually and coordinate care with a diabetes specialist as necessary.
  - ○ Consider treating insulin resistance with lifestyle changes in diet and exercise.
  - ○ Measure liver and bilirubin levels at baseline and annually; chronic liver enzyme elevation is typical and does not necessarily indicate the need for obtaining a liver biopsy.
  - ○ Request thyroid stimulating hormone and circulating thyroid hormone (thyroid-stimulating hormone [TSH] and Free T4) level tests at baseline and at least every 3 years; more frequently if indicated.
  - ○ Test for hyperlipidemia through serum blood lipid levels at baseline and every 3 years; more frequently if indicated. Treat hyperlipidemia per current practice.
  - ○ Sex-specific recommendations:
    - ■ Inquire about painful or irregular menstruation, ovarian cysts, endometriosis, and reproductive history.
    - ■ Inquire about erectile dysfunction; consider further workup and medications to treat erectile dysfunction. Consider possible cardiovascular risks-side effects associated with some erectile dysfunction medications (over the counter and prescribed).
    - ■ Inquire about infertility and family planning.

The 2-step methodology used to drive this consensus-building process enabled a streamlined and relatively low-cost medical guideline development process.

  - See full recommendations at myotonic.org/clinical-resources.
- Tumors
  - Look for pilomatrixomas (skin tumors); refer to surgeons for safe removal.
  - Train patients to detect pilomatrixomas (small, a hard lump under the skin on the head, neck, arms, torso, and legs).
  - Follow general population cancer screening guidelines, particularly for breast, testicular, cervical, and colon cancer.
  - Evaluate suspicious new CNS, abdominopelvic, and thyroid symptoms for possible cancer; consider cancers of the brain, uterus, and ovary.
  - See full recommendations at myotonic.org/clinical-resources.

Conclusions

The recommendations in this study are intended to lead to more informed and prepared clinical professionals and more readily available and high-quality care for affected families. The Consensus-based Care Recommendations support an international clinical trial environment that is better prepared to successfully assess the effectiveness of the potential therapies. The 2-step methodology used to drive this consensus-building process enabled a streamlined and relatively low-cost medical guideline development process, resulting in care recommendations available to clinicians in a timely manner.

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Appendix

Appendix is available after References section.

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Consensus-Based Care Recommendations for Adults with Myotonic Dystrophy Type 1

Quick Reference Version

The studies & rigorous evidence needed to drive the creation of an evidence-based guideline for the clinical care of myotonic dystrophy type 1 (DM1) patients have not yet been executed for all affected body systems & manifestations. In order to improve & standardize care for this disorder now, more than 60 leading myotonic dystrophy (DM) clinicians in western Europe, the United Kingdom, Canada & the United States have created the *Consensus-Based Care Recommendations for Adults with Myotonic Dystrophy Type 1.*

Summary recommendations from the Consensus-Based Care Recommendations are below. The full compendium of recommendations by body system & their disease manifestations is available here **http://www.myotonic.org/clinical-resources**.

LIFE THREATENING SYMPTOMS – CLINICAL CARE RECOMMENDATIONS

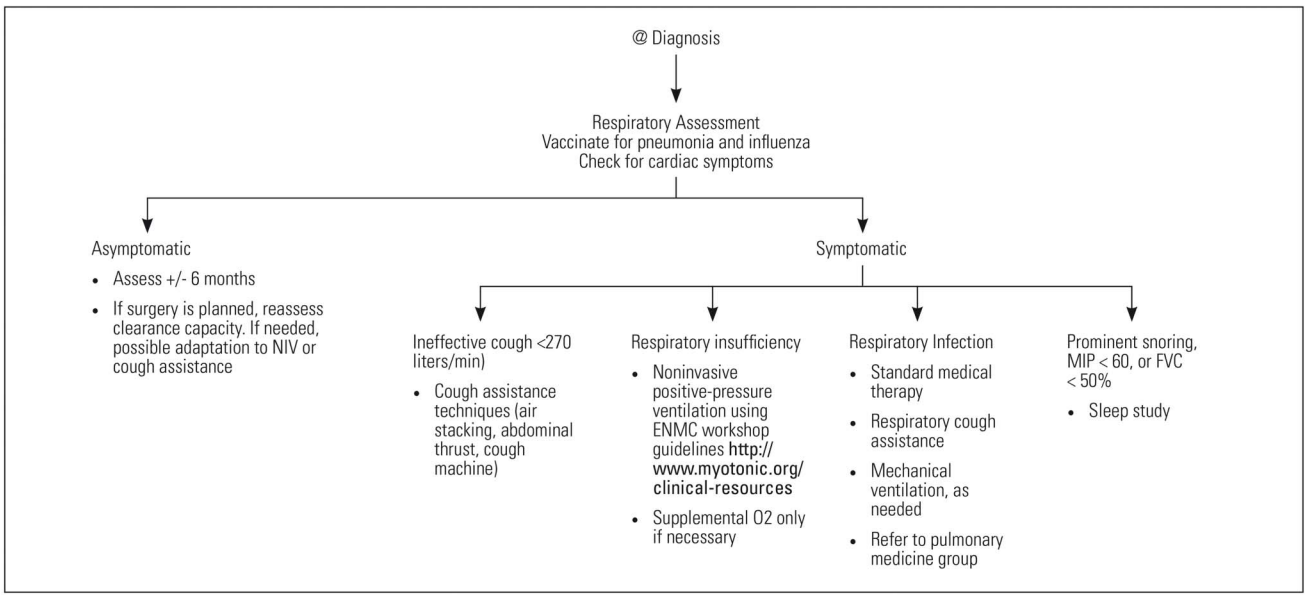
Surgery, anesthesia & pain

- See Myotonic Dystrophy Foundation's *Practical Suggestions for the Anesthetic Management of a Myotonic Dystrophy Patient* for anesthesia risks & recommendations before any surgeries or procedures requiring anesthesia **http://www.myotonic.org/clinical-resources**
- DM1 patients are far more likely to have adverse reactions to medications used for anesthesia & analgesia; interactions of the cardiac, respiratory, muscle & central nervous systems in each DM1 patient can lead to a variety of untoward responses before, during & after surgery
- Serious adverse events can occur throughout the course of DM1 & have been reported in patients whose DM1 symptoms were mild
- Behavioral & cognitive abnormalities need careful assessment & management preoperatively (if time permits & if it is possible) since these manifestations along with hypersomnia & preoperative sleep deprivation can complicate the patient's immediate postoperative care & long term recovery
- Most serious complications occur in the post-anesthesia period
- See full recommendations at http://www.myotonic.org/clinical-resources

Respiratory symptoms

- Pulmonary complications are the leading cause of death in DM1 patients. Clinicians must monitor issues such as recurrent pneumonia at baseline & serially with pulmonary function tests, at least forced vital capacity (FVC)
- See full recommendations at **http://www.myotonic.org/clinical-resources**

Fig. 1 Respiratory Care Recommendations Flowchart



Cardiovascular symptoms

- Cardiac complications are the second leading cause of death in DM1
- The most common cardiac issues are arrhythmias (sinus bradycardia, heart block, atrial fibrillation & flutter, & ventricular tachycardia)
- Palpitations, chest pain, dyspnea, orthopnea, lightheadedness, & syncope warrant cardiac investigation
- Significant cardiac involvement that subsequently leads to adverse cardiac events is often asymptomatic
- Impulse or conduction abnormalities on a standard 12-lead ECG including sinus rate < 50 BPM, PR interval > 200 ms, QRS duration > 100 ms, left anterior or posterior fascicular block, abnormal Q-waves, atrial tachycardia, fibrillation, or flutter, & ventricular arrhythmias are indicative of cardiac involvement
- Refer patients with cardiac symptoms, abnormal annual or biennial ECG indicative of cardiac involvement, and patients over the age of 40 years without previous cardiac evaluation to a center experienced in DM1 care
- Cardiology referral for all DM1 patients is reasonable if part of a multidisciplinary program or if the practitioners providing primary care are uncomfortable assessing cardiac history, exam, or ECG
- See full recommendations at http://www.myotonic.org/clinical-resources

SEVERE SYMPTOMS & CONDITIONS – CLINICAL CARE RECOMMENDATIONS

Skeletal muscle weakness & rehabilitation

- Evaluate annually for:
  - Swallowing & speech difficulties
  - Mobility, balance & falls
  - Activities of daily life – including self-care
  - Activities in home, school, work & community
- Refer to specialists, including PTs, OTs, speech pathologists, dietitians, social workers & others
- Encourage moderate intensity (aerobic & resistance training) exercise
- See *Role of Physical Therapy in the Assessment of Individuals with Myotonic Dystrophy* at www.myotonic.org.
- See full recommendations at **http://www.myotonic.org/clinical-resources**

Skeletal muscle myotonia

- Myotonia can cause muscle stiffness, prolonged hand grip, speech & swallowing difficulties
- Mexiletine may be considered for myotonia treatment. Mexiletine is contraindicated for DM1 patients with cardiac involvement. See full recommendations regarding mexiletine at **http://www.myotonic.org/clinical-resources** for more information on cardiac implications.

Pregnancy & obstetric management

- Women with DM1:
  - Have increased risk of miscarriage, pre-term delivery, & respiratory insufficiency during pregnancy (especially in the 3rd trimester) & failed labor during delivery; extreme care should be taken with analgesics & sedating anesthetic drugs (see MDF Anesthesia Guidelines here **http://www.myotonic.org/clinical-resources)**
  - Should consult with a high-risk OBGYN prior to delivery & obtain ongoing antenatal care
  - Fatigue much more quickly during labor & are at risk of postpartum hemorrhage, particularly after prolonged first or second stage or if there has been polyhydramnios
  - Should be induced only at direction of obstetrician & after all necessary consultants assisting with the delivery are notified
- Sexually active patients with DM1:
  - Should be referred to genetic counseling & family planning services if of child-bearing age
  - Should receive parental counseling for prenatal genetic diagnosis or discussion of preimplantation genetic diagnosis
- Include pediatric or neonatal specialist at delivery; intensive neonatal care is recommended for neonates that may have DM1; anticipate need for feeding tube and ventilator support
  - Access to a pediatric or neonatal specialist is recommended even if fetus is known to be unaffected
- See full recommendations at **http://www.myotonic.org/clinical-resources**

Excessive daytime sleepiness symptoms

- Assess for excessive daytime sleepiness (EDS) with Epworth Sleepiness Scale or similar standardized questionnaire instrument; prescribe sleep study if sleep disturbance is suspected
- Monitor periodic limb movements (muscle activity during sleep), as well as EEG, respiratory measures during sleep study to assess possible obstructive sleep apnea & central nervous system mediated sleep apnea
- Refer to pulmonologist &/or sleep specialist if EDS scores are positive on scales
- Question patients re: alcohol or caffeine consumption, medications & sleep habits for contribution to EDS
- Evaluate impact of possible respiratory muscle weakness (forced vital capacity value sitting & supine) on presence of EDS
- If nocturnal or daytime hypoventilation is suspected, consider non-invasive positive pressure ventilation, and refer to pulmonologist with experience in neuromuscular diseases re: possible need for NIV launching
- Consider modafinil for treatment if coexisting central nervous system alteration is suspected as the cause for EDS
- Consider cognitive behavioral therapy (CBT) or behavioral therapy for apathy; psychostimulant treatment can be considered if apathy is associated with an impairing level of fatigue or EDS
- See full recommendations at **http://www.myotonic.org/clinical-resources**

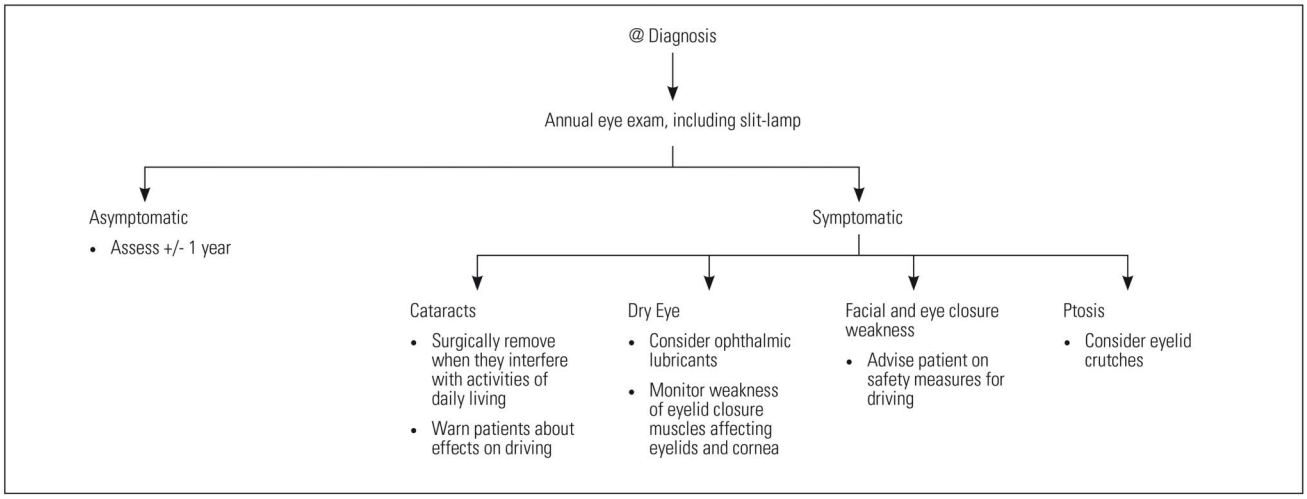
Gastrointestinal symptoms

- Ask about problems with chewing, swallowing, drooling, reflux, bloating, abdominal pain, bowel movement frequency & characteristics, diarrhea & incontinence
- Physical exam should include abdominal palpation, including around gall bladder, & rectal exam for anal sphincter spasm & dyssynergic defecation for symptomatic patients
- DM1 patients are at risk for pseudo-obstruction, & experience other problems that may cause actual obstruction of small or large intestine, including endometriosis, acute gallbladder inflammation, ruptured ovarian cysts, sigmoid volvulus. Monitor potential obstructions to determine whether they are pseudo or actual & treat accordingly
- Non-medical interventions:
  - High-fiber diet for diarrhea or constipation; increase water intake
  - Nutritional supplement for weight loss, weight gain or dysphagia
  - Dysphagia therapy referral for oral pharyngeal dysphagia
- Medical interventions:
  - Loperamide (gentle use) for diarrhea control
  - Laxatives for constipation:
  - First line therapy: Miralax, Senna, Ducosate or Linaclotide
  - Second line therapy: Bisacodyl, Lubiprostone, Linaclotide
  - Avoid oils – if above fails, refer out for anal manometry
  - Metoclopramide for gastroparesis, pseudo-obstruction, reflux
  - Antibiotics for bacterial overgrowth-induced diarrhea (based on breath testing)
  - Enteral feeding only for recurring pneumonia or severe dysphagia causing weight loss or causing inability to swallow safely without recurrent aspiration
  - Mexiletine can be considered to treat diarrhea or constipation. Mexiletine is contraindicated for DM1 patients with cardiac involvement. See full recommendations regarding mexiletine and cardiac involvement.
- See full recommendations at **http://www.myotonic.org/clinical-resources**

Ocular symptoms

- Relevant eye manifestations of DM1 include cataracts, strabismus & other ocular motility problems, myopia, & astigmatism in congenital & juvenile-onset patients
- See full recommendations at **http://www.myotonic.org/clinical-resources**

Fig. 3 Ocular Recommendations Flowchart



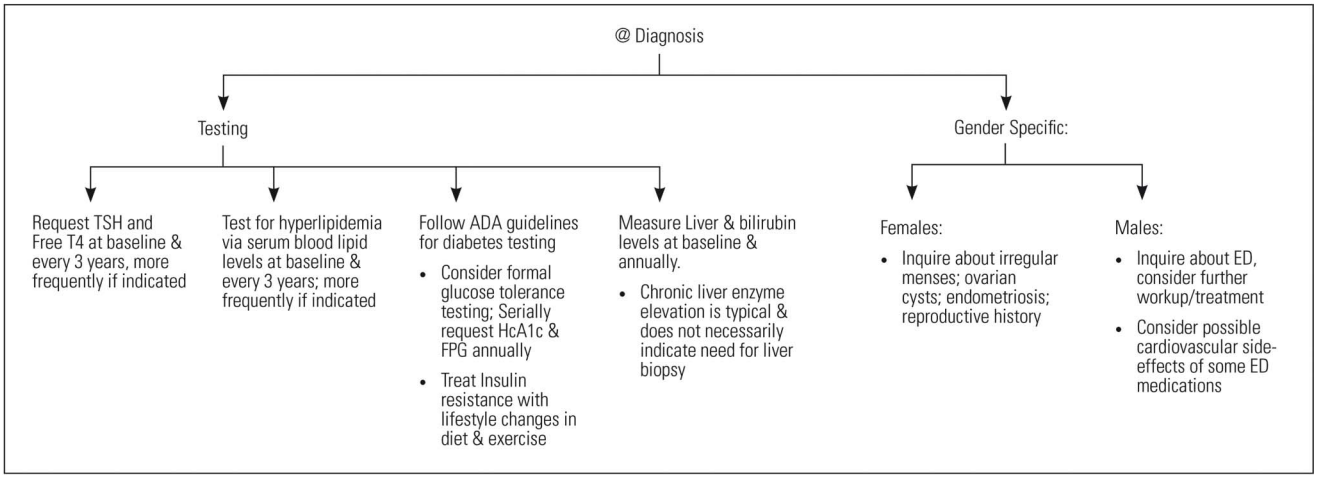
Tumors

- Look for pilomatrixomas (skin tumors); refer to surgeons for safe removal
- Train patients to detect pilomatrixomas (small, hard lump under skin on head, neck, arms, torso, legs)
- Follow general population cancer screening guidelines, particularly for breast, testicular, cervical & colon cancer
- Evaluate suspicious new CNS, abdominopelvic & thyroid symptoms for possible cancer; consider cancers of the brain, uterus & ovary
- See full recommendations at **http://www.myotonic.org/clinical-resources**

Endocrine & metabolic symptoms

- See full recommendations at **http://www.myotonic.org/clinical-resources**

Fig. 4 Endocrine & Metabolic Care Recommendations Flowchart



Neuropsychiatric symptoms

- Advise patients that DM1 is also a 'brain disorder'
- Include psychiatric & behavioral examination at baseline, & during regularly-scheduled follow up appointments or when symptoms appear
- Refer patients with psychiatric or behavioral disorders, those with late-onset phenotype & patients with cognitive complaints to mental health care professional for testing & follow up; patients may have limited insight into these issues – consider input from partners & family members as appropriate
- DM patients with late-onset phenotype can exhibit fast decline in certain cognitive functions
- See full recommendations at **http://www.myotonic.org/clinical-resources**

Psychosocial symptoms

- Assess patient's social circumstances in household; consider & be aware of possible child neglect, acute financial need, unsafe driving, unsafe or unsanitary home; refer to social services, support programs & organizations

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A full list of authors and an overview of the methodology used to develop consensus for these recommendations can be found here: **http://www.myotonic.org/clinical-resources**