

Appendix: Diagnosis and management of Duchenne muscular dystrophy, an update, part 3: Primary care and emergency medicine, psychosocial care, and transitions of care across the lifespan

Methods

It is important to understand that the guidance in this update is not conventionally evidence-based. As is typical for a rare disease, there is a lack of large-scale and randomized, controlled trials in this field, with the possible exception of studies favoring the use of corticosteroids.¹ Therefore, as we did with the 2010 care considerations,^{2,3} the guidance in this document were developed using a method that queries a group of experts on the appropriateness and necessity of specific interventions, using clinical scenarios. This method is intended to “objectify” expert opinion, and to make the care considerations a true reflection of the views and practices of the expert panel based on their interpretation and application of the existing scientific literature. This methodology is designed to produce an essential “tool kit” for DMD care; only interventions that have been deemed both appropriate *and* necessary are recommended. For a detailed discussion of Methodology, see Part 1 of these care considerations.

Search strategy and selection criteria

Articles for the literature review were identified by searching Medline, Embase, Web of Science, and the Cochrane Library databases for peer-reviewed English-language articles published from 2006 through September 2013 for the eight original topics and from 1990 through September 2013 for the three new topics. The literature was searched using the key search terms of “Duchenne” or “muscular dystrophy,” or both, paired with one of 626 search terms. The detailed search strategy and terms are included in the appendix. The literature search identified 1,215 articles after duplicates were removed. Reviews, meta-analyses, case series, case reports, animal models, and articles on unrelated diseases or Becker muscular dystrophy only were excluded upon further review. Of the 672 remaining articles, the steering committee reviewed 430 articles that were potentially relevant to the update of the care considerations. The steering committee members then classified each one using the following criteria: (1) consistent with the existing care considerations, (2) conflicts with the existing care considerations, (3) requires an update to the care considerations, or (4) presents promising research. Articles that were identified as required for the update were used to create clinical scenarios in accordance with the RAND method. Subject matter experts, with the assistance of RTI, also continually updated the references during the development of the manuscript. Before publication, an updated literature search was conducted for articles published between October 2013 and July 2017, which identified 880 articles. Committee chairs reviewed 115 articles potentially relevant to care and updated the references and text as necessary.

Emergency Management

Emergency Card and Advance Directives

General care considerations for the emergency care of individuals with DMD are available from the organization Parent Project Muscular Dystrophy.⁴ Ideally, individuals with DMD should carry an emergency card provided by their neuromuscular specialist that includes their diagnosis, list of medications, and baseline medical status, including the results of recent pulmonary and heart function studies. Any history of recurring medical problems such as pneumonia, heart failure, nephrolithiasis, or gastric paresis should be identified, with a brief discussion of initial assessment and management. Individuals with DMD should also have a copy of relevant past test results, such as electrocardiograms (ECGs), unless these data are available through an electronic medical record. With this background information, the emergency medicine provider can customize the evaluation and treatment to that particular individual’s most common problems.

When practical, individuals with DMD should arrive at the emergency department with their usual medications and home medical equipment, such as their non-invasive ventilator and cough assistance device. It is important to engage the individual and his caregiver in the diagnostic and therapeutic process to avoid unnecessary complications and to identify therapeutic interventions that are likely to be well tolerated and effective.

The individual's neuromuscular specialist should be contacted after the initial assessment to discuss disease management. Emergency medicine providers should inquire as soon as possible about the presence of advance directives (including Provider Orders for Scope of Treatment or POST documents, relevant in some parts of the United States). Some individuals with DMD will have elected to forego invasive interventions, such as endotracheal intubation and/or cardiac compressions; others have existing directives that permit "partial" resuscitation measures, such as non-invasive ventilation or intravenous cardiac medications. For further discussion, see the Transitions of Care across the Lifespan in part 3.

Respiratory Status (see the Respiratory section in Part 2 of this series for further details)

When an individual with DMD arrives in the emergency department, immediate attention should be given to respiratory status. Early involvement of appropriate specialists, such as pulmonologists and respiratory therapists, is advisable. Severe, acute respiratory complications are common in individuals with DMD, especially among individuals who are non-ambulatory and whose baseline forced vital capacity is < 50% predicted. Those individuals are likely to have weak cough and hypoventilation. Although the individual may not appear distressed, it is critical to recognize the importance of symptoms such as dyspnea, trouble speaking because of breathlessness, weak cough, and chest congestion due to mucus plugs. Unlike individuals with good muscle strength, individuals with advanced DMD do not manifest signs of respiratory distress such as increased work of breathing or chest retractions. Instead, they are more likely to present with shallow breathing and tachypnea, which may remain undetected.⁵

In DMD individuals with impaired cough and ventilation, otherwise mild upper respiratory tract infections can progress to life-threatening mucus plugging and respiratory failure very rapidly. In this setting, even mild hypoxemia (SpO₂ < 95% in room air) is highly concerning. Unless cardiac in etiology, hypoxemia is almost always due to mucus plugging and/or hypoventilation. Treatment with oxygen alone can be catastrophic, if the underlying cause of the hypoxemia is not addressed. Instead, the individual should be treated with continuous non-invasive ventilation, along with frequent application of assisted cough therapy (preferably with a cough assistance device; or, if unavailable, with manual cough assistance followed by suctioning, including "deep" tracheal suctioning, when necessary). Oxygen saturation should be monitored closely using pulse oximetry (and oxygen can be added to the non-invasive ventilator circuit, if needed). If indicated, a blood gas can be obtained to assess for hypercapnia. A chest radiograph should be obtained to assess for atelectasis or pneumonia, preferably as a portable film (i.e., do not send the individual to the radiology department if transporting him will interrupt vital therapies such as assisted ventilation).

Because of their decreased jaw mobility and macroglossia, airway management in individuals with DMD is complex.⁶ In the rare event that endotracheal intubation is necessary (assuming intubation is not prohibited by the individual's advance directive), early involvement of providers with appropriate expertise, such as anesthesiologists, is necessary. If the individual with DMD with respiratory distress had a recent fracture, orthopedic surgery, or significant soft tissue injury, then fat embolism syndrome should be considered (see the Orthopedics section in Part 2 and the Fractures subsection below).

Cardiomyopathy (see the Cardiology section in Part 2 for more details)

With improvements in respiratory management, cardiomyopathy has emerged as a leading cause of death in individuals with DMD.⁷ Individuals with DMD typically show signs of cardiac dysfunction in the second decade of life and may present to the emergency department with cardiac complaints such as arrhythmias, chest pain, and heart failure.⁸ The signs and symptoms of heart failure in individuals with DMD are often subtle, because the individuals are non-ambulatory. Tachycardia, edema, abdominal pain, nausea, decreased appetite, sleep disturbance, and weight loss may have a cardiac origin and should be appropriately evaluated. Early consultation with a cardiologist is essential. Troponin I, B-type natriuretic peptide, ECG, and echocardiogram all may be useful in evaluating an individual with DMD presenting with cardiac concerns. It should be noted that presentation with severe chest pain, even in the younger individual with DMD, should not be discounted until cardiac causes have been excluded. The most likely cause of the pain is musculoskeletal, but troponin elevation and ECG changes have been recognized in individuals with DMD presenting with acute chest pain. The etiology of these changes has not been definitively demonstrated but likely represents the natural history of disease progression.

Arrhythmias

A baseline resting sinus tachycardia is common among individuals with DMD who are older than 7 years of age.⁹ The etiology of the tachycardia has not been definitely established and is likely related to the underlying dystrophin abnormality. In addition, the ECG is typically abnormal, even in young children. For example, the presence of Q waves on the ECG may be expected. The newly acquired study should be compared to a previous ECG if available. Ready availability of the most recent ECG allows for rapid comparison during acute illnesses. Individuals with DMD may also be prone to arrhythmias. During acute illnesses, continuous cardiac monitoring may be indicated. See the Cardiology section in Part 2 of this series for more details.

Impacts of Chronic Steroid Therapy

Chronic, daily glucocorticoid therapy is often begun at an early age in individuals with DMD to prolong ambulation and delay cardiopulmonary dysfunction (see the Neurology section in Part 1). Alternative dosing regimens are widely used (e.g., every other day and weekend-only therapy). Prednisone and deflazacort are the most common preparations in use. As a result, individuals with DMD are at risk of a host of steroid-related side effects, including adrenal suppression, fractures, peptic ulcer disease, hypertension, and infections. Chronic steroid therapy and non-ambulation may also increase the risk of nephrolithiasis and must be considered (in addition to musculoskeletal causes, like vertebral fractures) when an individual presents with back pain.¹⁰

Individuals treated with chronic steroids should not miss their usual doses. Stress steroid dosing should be given early in the course of acute illnesses. In critical emergency situations involving adrenal insufficiency, we endorse treatment with hydrocortisone in a dose of 50 mgs IV/IM for children < 2 years old and 100 mgs IV/IM for children/adults ≥ 2 years old.¹¹ Stress dosing with hydrocortisone should be continued at a dose of 50 to 100 mg/m² of body surface area/day divided every 4 to 6 hours until illness has resolved. The PJ Nicholoff Steroid Protocol provides a general overview for managing adrenal suppression including a list of precipitating factors, stress dose regimens, corticosteroid dose equivalences, and an approach for weaning steroids safely (see the Endocrinology—Growth/Puberty/Adrenal Insufficiency section in Part 1).¹² Early involvement of appropriate specialists, such as endocrinologists, is advisable.

Fractures (see the Orthopedic/Surgical Management and Endocrinology—Bone Health Management and Osteoporosis sections in Part 2 of this series for more details)

Orthopedic issues are commonly encountered in individuals with DMD and include spine and long bone (especially femur) fractures, scoliosis, and musculoskeletal pain. Early consultation with orthopedics is advisable

Individuals with DMD have multiple risk factors for fractures (chronic corticosteroid use, reduced bone mineral density, decreased muscle strength, and limited or no ambulation). Long bone fractures, especially of the femur, are common in ambulatory individuals because of decreasing strength and frequent falls. Vertebral fractures are often asymptomatic and are an early sign of osteoporosis. Individuals with new-onset back pain should have spinal X-rays done to evaluate for vertebral compression fractures.

Fat embolism syndrome, a rare complication of long bone fracture, can occur in individuals with DMD because of increased bone marrow fat (secondary to osteoporosis and chronic steroid use). This potentially life-threatening diagnosis must be considered in individuals with new-onset dyspnea and/or mental status changes who have relevant risk factors: a recent long bone fracture (of note, there have been case reports of fat embolism syndrome after falls resulting in soft tissue injury only),¹³ a history suggestive of fracture, or recent orthopedic surgery. Further information about fat embolism syndrome is available from the organization Parent Project Muscular Dystrophy.¹⁴

Sedation/Anesthesia Care Considerations (see the Orthopedic/Surgical Management section in Part 2 of this series for more details)

Individuals with DMD are at high risk of a variety of severe complications when they undergo anesthesia or sedation. Issues include complex airway problems, potentially fatal reactions to certain anesthetics and muscle relaxants, and the potential for rapid development of apnea and respiratory failure with conventional doses of sedatives. Thus, early involvement of anesthesiologists is advisable when individuals with DMD require sedation or anesthesia.

Because individuals with DMD are at risk for hypoventilation and apnea, care must be taken when considering narcotic analgesia/procedural sedation. Existing guidelines¹⁵ call for using assisted ventilation in selected individuals during induction, maintenance, and recovery from sedation and anesthesia. Succinylcholine is contraindicated because of the potential for rhabdomyolysis and fatal hyperkalemia. Although not generally applicable to care in the emergency department, when anesthesia is necessary, a total intravenous technique should be used, with strict avoidance of inhalational anesthetics that may cause acute rhabdomyolysis and hyperkalemia.¹⁵ When possible, use of local anesthesia is advisable.

Laboratory Values

Individuals with DMD have extremely elevated creatine kinase levels, often 50 to 100 times the normal level. Such levels are typical in this diagnosis and generally need no further evaluation. Alanine transaminase and aspartate transaminase are present in muscle as well as in the liver. As a result, they are typically elevated in individuals with DMD and, therefore, need no further evaluation unless there are specific concerns for liver pathology. Serum creatinine is usually extremely low because of low muscle mass. If renal problems are suspected, a non-muscle-based test, such as cystatin-C, could be used.¹⁶

Transfer/Transport

After initial therapeutic intervention and stabilization, early transfer to a hospital specializing in care of individuals with DMD is advised. Individuals should be transferred via skilled care transport.

Supplementary Table 1. Transition Planning for Housing and Assistance with Activities of Daily Living

Housing
<ul style="list-style-type: none">● Consider the pros/cons and support needed to live in the following settings:<ul style="list-style-type: none">○ The family home○ On a campus during college/university○ In a community setting such as a group home or organized facility○ In a home or apartment with or without a roommate● Home modifications and accommodations for accessibility<ul style="list-style-type: none">○ Consult physical and occupational therapy for recommendations○ Hire architects with accessibility design experience (some vendors offer assessments)○ Learn laws designed to protect the rights of people with disabilities when accessing housing and community resources○ Search for grants, loans, and financial incentives for people with disabilities purchasing or modifying a home for accessibility○ Explore assistive technology to expand access to environmental controls, dwelling entrances, and other areas, using the wheelchair joystick, computer, mobile phone, tablet, or other devices
<hr/> Assistance with Activities of Daily Living
<ul style="list-style-type: none">● PCAs^a can help with activities of daily living (through agencies or hired independently)● Family caregivers need respite and backup● Individual with DMD requires mentoring and training to learn how to direct his own care● Providers^b can assist in standardizing the PCA training process<ul style="list-style-type: none">○ Create daily or weekly routine schedules○ Print images of stretches and equipment used○ Create videos of transfers and stretches being performed in the preferred manner● Explore funding and benefits for care<ul style="list-style-type: none">○ Include the individual with DMD in discussions—mentoring the navigation process○ Enlist social worker or other social services involvement to identify funding sources○ Learn eligibility rules regarding education and employment status○ Explore insurance benefits through employers to pay for a PCA at work● Explore governmental funding for attendant care to support independent living

^a PCA = personal care attendant

^b Providers may include the care coordinator, social worker, physical therapist, occupational therapist, or rehabilitation or neuromuscular specialists.

Supplementary Table 2. Transition Planning for Transportation and Community Connections

Transportation

- Providers should discuss options for safe transportation and make referrals for:
 - Independent driving with vehicle modifications
 - Requires physical therapy/occupational therapy driver evaluation and instruction*
 - Modifications to family-owned vehicle
 - Examples: ramps, lifts, tie-downs to secure wheelchair*
 - Accessible public transportation options
 - Practice using public transportation without caregiver (when appropriate)
-

Community Connections

- Parent, providers, and educators should:
 - Encourage teens/young adults with DMD to seek out opportunities to interact with peers outside of formal school setting
 - Make referrals to psychologists or counselors when instruction/help is needed or to address issues related to anxiety or depression
 - Direct teens/young adults to social groups, events, and clubs
 - Consider leisure activities designed for persons with disabilities, e.g. wheelchair hockey or soccer (football) leagues
 - Assist with troubleshooting logistics (remove barriers to participation)
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* Modifications to drive independently or to add lifts/ramps are often costly and not covered by private insurance in the United States. Enlist social worker to explore funding, grants, regional resources, and used equipment services

Supplementary Table 3. Transition Planning Related to Dating, Intimacy, and Sexuality

- Providers should initiate open discussions on these topics during adolescence:
 - Assess interest, knowledge, and self-esteem
 - Discuss topics of reproduction and relationships
 - Review genetic counseling, inheritance, and family pedigree
 - Identify sibling carriers
 - Review X-linked inheritance (all daughters of a man with DMD will be carriers; no sons will be affected*)
 - Introduce concepts of family planning and prenatal/preimplantation genetic diagnosis
 - Providers should initiate discussion on these topics and refer to resources outside the clinic setting**:
 - Provide guidance (pros and cons) about online social media and dating
 - Make referrals to marriage and relationship counselors
 - Introduce adult social groups, including online social groups (e.g., DMD Pathfinders [<https://dmdpathfinders.org.uk/>], Living with MD group)
 - Address concerns about physical fitness in regard to acts of intimacy or self-pleasure (e.g., cardiopulmonary risks of sex and the risk of bone fracture, if relevant)
 - Identify other resources to help with intimacy (e.g., books about sex with physical disability or sex therapists who have experience counseling people with disabilities)
 - Provide guidance on talking with the PCA about issues related to sexuality and intimacy
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*Assuming the mother is not a carrier.

**When age, developmentally and socially appropriate.

Supplementary Table 4. Example Resources for Transitions in Education

Decision/Stage	Resource
Transition planning	<p>Government-funded rehabilitation agencies (vocational rehabilitation)</p> <p>Parent Project Muscular Dystrophy (PPMD) Education Matters (http://www.parentprojectmd.org/site/PageServer?pagename=Care_educational_edmatters)</p> <p>Got Transitions? (http://www.gottransition.org)</p> <p>MDA Young Adult Programs (education, employment, independent living) (https://www.mda.org/young-adults)</p> <p>Guide to Transition, Muscular Dystrophy Campaign—UK (http://www.muscular dystrophyuk.org/app/uploads/2015/02/transition-guide-factsheets-web.pdf)</p>
Decisions about living away from home for education/work	<p>MDA’s Campus Accessibility Considerations (https://www.mda.org/sites/default/files/College_Campus_Accessibility_Questionnaire.pdf)</p> <p>PPMD 2015 Duchenne Transitions Conference archive (http://community.parentprojectmd.org/profiles/blogs/ppmd-duchenne-becker-transitions-meeting-recap)</p>
Programs serving people with special health care needs or disabilities on campus or while working	<p>Office of Disability Services for Students (college)</p> <p>Human Resources Office (work)—benefits manager</p> <p>Student/Employee Health Office—enlist occupational therapists, personal assistants</p>

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