Summary of Evidence-based Guideline for **CLINICIANS**

EVALUATION, DIAGNOSIS, AND MANAGEMENT OF CONGENITAL MUSCULAR DYSTROPHY

This is a summary of the American Academy of Neurology (AAN) and American Association of Neuromuscular & Electrodiagnostic Medicine guideline on the evaluation, diagnosis, and management of congenital muscular dystrophy (CMD).

Please refer to the full guideline at *AAN.com/guidelines* for more information, including the complete clinical context and definitions of the classifications of evidence and recommendations.

Given the lack of literature directly relevant to congenital muscular dystrophies (CMDs) for some of the clinical questions, some of the following recommendations are based in part on evidence from other neuromuscular disorders of childhood.

General Recommendations

Clinical Context

Patients with CMD may develop various combinations of cardiovascular, gastrointestinal/nutritional, neurologic, ophthalmologic, orthopedic, and pulmonary manifestations (EVID). Multidisciplinary teams are recommended in the care of patients with complex neuromuscular conditions such as amyotrophic lateral sclerosis (RELA). Neuromuscular specialists, particularly child neurologists and physiatrists with subspecialty training, are key members of such teams, as are physicians from other specialties (e.g., cardiology, gastroenterology, neurology, ophthalmology, orthopedic surgery, pulmonology) and allied health professionals with relevant expertise (e.g., dieticians, genetic counselors, nurses, nurse practitioners, occupational therapists, physical therapists, and speech–language pathologists) (PRIN).

Level B	Physicians caring for children with CMD should consult a pediatric neuromuscular specialist for diagnosis and management.
	Pediatric neuromuscular specialists should coordinate the multidisciplinary care of patients with CMD when such resources are accessible to interested families.
	When genetic counselors are available to help families understand genetic test results and make family-planning decisions, physicians caring for patients with CMD might help families access such resources.

Use of Clinical Features, MRI, and Muscle Biopsy at Diagnosis

Clinical Context

Patients with some of the classic CMD subtypes, including collagenopathies and dystroglycanopathies, have distinct phenotypic features that may help focus the diagnostic process (EVID).

Level B	Physicians should use relevant clinical features such as ethnicity and geographic location, patterns of weakness and contractures, the presence or absence of CNS involvement, the timing and severity of other organ involvement, and serum creatine kinase levels to guide diagnosis in collagenopathies and in dystroglycanopathies.

Clinical Context

Interpretation of muscle biopsy findings, especially in children, is heavily dependent on technique and the experience of the pathologist or neuromuscular specialist who interprets the studies. Proper interpretation of these studies requires knowledge of the clinical context as well as availability of advanced testing capabilities. The knowledge obtained from a muscle biopsy may help families and providers better understand the disease process affecting specific patients (PRIN).

Level C	Physicians might order muscle biopsies that include immunohistochemical staining for relevant proteins in CMD cases for which the subtype-specific diagnosis is not apparent after initial diagnostic studies, if the risk associated with general anesthesia is determined to be acceptable.
Level B	When muscle biopsies are indicated in suspected CMD cases, they should be performed and interpreted at centers experienced in this test modality. In some cases, optimal diagnostic information may be derived when the biopsy is performed at one center and interpreted at another.

Clinical Context

Typical brain MRI findings of white matter abnormalities in merosinopathies can be found consistently above the age of six months, and the structural brain abnormalities that often accompany the dystroglycanopathies are well documented (EVID).

Muscle ultrasound and MRI studies can help distinguish neurogenic from myopathic disorders and show pathognomonic patterns for specific CMD subtypes (EVID). Muscle MRI studies likewise can help identify CMD subtypes, including collagenopathies and *SEPN1*-related myopathies (EVID).

Level B	Physicians should order brain MRI scans to assist with the diagnosis of patients who are clinically suspected of having certain CMD subtypes, such as merosinopathies and dystroglycanopathies, if the potential risk associated with any sedation is determined to be acceptable and if a radiologist or other physician with the appropriate expertise is available to interpret the findings.
Level C	Physicians might order muscle imaging studies of the lower extremities for individuals suspected of having certain CMD subtypes such as collagenopathies (ultrasound or MRI) and *SEPN1*-related myopathy (MRI), if the risk associated with any sedation needed is determined to be acceptable and if a radiologist or other physician with the appropriate expertise is available to interpret the findings.

Genetic Diagnosis

Clinical Context

Targeted genetic testing often identifies causative mutations in the classic CMD subtypes (EVID). However, the cost of traditional Sanger sequencing for some of the larger causative genes presents an obstacle to universal application of such sequencing, even though the testing is readily available (RELA). Genetic diagnoses are beneficial to the patient, as they often enable physicians to provide more accurate prognoses and facilitate genetic counseling and family-planning discussions, and may enable patients to become more aware of future clinical trials for which they may be eligible (PRIN).

Level C	When available and feasible, physicians might order targeted genetic testing for specific CMD subtypes that have well-characterized molecular causes.

Clinical Context

Our systematic review indicates that a large number of patients with CMD do not have mutations in one of the currently known genes (EVID). The cost of next-generation sequencing (whole-exome and whole-genome sequencing) is dropping rapidly, to the point where these technologies are now readily available to many researchers who seek novel causative disease genes (RELA).

Level C	In individuals with CMD who either do not have a mutation identified in one of the commonly associated genes or have a phenotype whose genetic origins have not been well characterized, physicians might order whole-exome or whole-genome sequencing when those technologies become more accessible and affordable for routine clinical use.

Complications and Treatment

Clinical Context

Patients with CMD experience a broad spectrum of respiratory, musculoskeletal, cognitive, and cardiac complications with variable tempo between individuals (EVID). Providers may, in appropriate circumstances, extrapolate from early-onset neuromuscular and neuromotor diseases for which consensus guidelines have been developed on the basis of both established principles of care and limited outcomes and intervention trials (RELA). There are currently no curative CMD subtype-specific interventions (EVID). Thus, all complication screening and interventions are intended to promote growth and potential development, mitigate cumulative morbidities, optimize function, and limit mortality while maximizing quality of life (EVID).

Level B	At the time of diagnosis, the physician should advise families regarding areas of uncertainty with respect to clinical outcomes and the value of interventions as they pertain to both longevity and quality of life. Physicians should explain the multisystem implications of neuromuscular insufficiency and guide families as they make decisions with regard to the monitoring for and treatment of CMD complications.

Respiratory Complications

Clinical Context

Patients with respiratory failure from neuromuscular-related weakness may experience conspicuous respiratory symptoms but often do not have symptoms such as dyspnea that precede the onset of respiratory failure (RELA). Noninvasive and invasive interventions are routinely utilized for children with CMD (PRIN). Pulmonologists, critical care specialists, and respiratory therapists with pediatric training and experience with neuromuscular disorders are most likely to offer treatment options that optimize respiratory outcomes and minimize infection risks and complications (PRIN).

Level B	Physicians should counsel families of patients with CMD that respiratory insufficiency and associated problems may be inconspicuous at the outset.
	Physicians should monitor pulmonary function tests such as spirometry and oxygen saturation in the awake and sleep states of patients with CMD, with monitoring levels individualized on the basis of the child's clinical status.
	Physicians should refer children with CMD to pulmonary or aerodigestive care teams, when available, that are experienced in managing the interface between oropharyngeal function, gastric reflux and dysmotility, and nutrition and respiratory systems, and can provide anticipatory guidance concerning trajectory, assessment modalities, complications, and potential interventions.

Complications from Dysphagia

Clinical Context

Patients with neuromuscular disorders often experience dysphagia (impaired swallowing), with implications for growth and nutrition (RELA). Swallowing dysfunction may manifest as failure to thrive and may also increase the risk of admission to critical care units and mortality (PRIN). Dysphagia may be diagnosed through standard multidisciplinary evaluations and radiologic studies (PRIN). Safe and adequate nutrition is necessary for optimal health, and thus the potential benefits of improved nutrition with a gastrostomy must be weighed against the potential risks associated with an invasive procedure (PRIN).

Level B	Neuromuscular specialists should coordinate with primary care providers to follow nutrition and growth trajectories in patients with CMD.
	For patients with CMD, physicians should order multidisciplinary evaluations with swallow therapists, gastroenterologists, and radiologists if there is evidence of failure to thrive or respiratory symptoms (or both).
	For patients with CMD, a multidisciplinary care team, taking into account medical and family considerations, should recommend gastrostomy placement with or without fundoplication in the appropriate circumstances.

Cardiac Complications

Clinical Context

Patients with CMD experience both functional and structural cardiac complications, but the frequency of these for many of the subtypes is unknown. On the basis of more extensive experience with cardiac complications in Duchenne muscular dystrophy (MD) and Becker MD, cardiac involvement may be subclinical and evident only on echocardiography or electrocardiography (or both) in the earlier stages; such involvement may be amenable to pharmacologic therapy (RELA).

Level B	Physicians should refer children with CMD, regardless of subtype, for a baseline cardiac evaluation. The intervals of further evaluations should depend on the results of the baseline evaluation and the subtype-specific diagnosis.

Periprocedural Complications

Clinical Context

Patients with neuromuscular diseases are at increased risk for periprocedural complications, including airway problems, suboptimal pain control, pulmonary complications, prolonged recovery times, and complications of bed rest and deconditioning (RELA).

Level B	Prior to any surgical interventions and general anesthesia in the setting of CMD, physicians should discuss the potential increased risk of complications with patients' families, as these factors may affect decision making with regard to whether to consent to certain elective procedures.
	When children with CMD undergo procedures involving sedation or general anesthesia, physicians should monitor longer than usual in the immediate postoperative period to diagnose and treat respiratory, nutritional, mobility, and gastrointestinal mobility complications.

Musculoskeletal Complications

Clinical Context

Patients with CMD are at increased risk of musculoskeletal complications, including skeletal deformities and contractures (EVID). Range-of-motion exercises are straightforward interventions that generally do not involve significant risk, but the efficacy of such exercises has not been established (EVID). Data on the efficacy of bracing are also lacking for children with CMD (EVID). It is generally accepted that orthopedic surgical interventions such as heel cord–lengthening procedures relieve tendon contractures at least in the short term; however, the long-term efficacy is unclear (PRIN). Neuromuscular blocking agents (e.g., botulinum toxin) can cause prolonged worsening of weakness in patients with neuromuscular diseases (RELA).

Level B	Physicians should refer to allied health professionals, including physical, occupational, and speech therapists; seating and mobility specialists; rehabilitation specialists; and orthopedic surgeons, to help maximize function and potentially slow the progression of musculoskeletal complications in children with CMD.
	Physicians may recommend range-of-motion exercises, orthotic devices, heel cord–lengthening procedures, or a combination of these interventions for children with CMD in certain circumstances.
Level C	Physicians might avoid using neuromuscular blocking agents (e.g., botulinum toxin) in patients with CMD, unless the contractures are determined to cause significantly greater impairment than would any potential worsening of weakness in the targeted muscle groups.

Educational Adjustments

Clinical Context

Prior to school age, children at risk for developmental delays are eligible for early intervention services as federally mandated. The Individuals with Disabilities Education Improvement Act of 2004[1] guarantees children with disabilities a free and appropriate public education (PRIN).

Level B	Physicians should refer children with CMD to special education advocates, developmental specialists, and education specialists when appropriate for individual circumstances.

[1] Individuals with Disabilities Education Improvement Act of 2004, Pub L No 108-446, 20 USC 1400.

This guideline was endorsed by the American Academy of Pediatrics, the American Occupational Therapy Association, the Child Neurology Society, and the National Association of Neonatal Nurses.

Study Funding

Funding for this publication was made possible (in part) by grant DD10-1012 from the Centers for Disease Control and Prevention. The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention. The remaining funding was provided by the American Academy of Neurology.

Definition of Clinical Context Terms
EVID = Evidence-based conclusions for the systematic review
PRIN = (Stipulated axiomatic) principles of care
RELA = (Strong evidence from) related conditions not systematically reviewed

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Copies of this summary and additional companion tools are available at *AAN.com* or through AAN Member Services at (800) 879-1960.

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