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Obesity and Endocrine Management of the Patient With Duchenne Muscular Dystrophy

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Abstract

Duchenne muscular dystrophy (DMD) is associated with an increased risk of endocrine complications due to the effects of prolonged glucocorticoid therapy as well as progressive muscle weakness. Categories of complications include obesity and its comorbidities, short stature, pubertal delay, and adrenal insufficiency. Obesity prevention is important for long-term management of patients with DMD. Preventing glucocorticoid-induced weight gain fosters patient mobility, ease of transfer, and reduces sleep-disordered breathing. Metabolic complications from obesity (glucose intolerance, dyslipidemia) also can be avoided. Short stature and pubertal delay may negatively affect self-esteem and peer relationships, and careful monitoring of growth and pubertal development can allow anticipatory counseling, Adrenal insufficiency, a potentially life-threatening complication associated with prolonged glucocorticoid use, must be recognized so as to allow prompt treatment. In this article, we provide a summary of current guidance to ensure comprehensive endocrine management is followed in patients with DMD.

The effect of glucocorticoid therapy on the clinical phenotype in patients with Duchenne muscular dystrophy (DMD) has led to the need for clear recommendations about weight

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management and the monitoring and treatment of endocrine complications. The appetite-promoting and fat deposition effects of GC therapy are prominent in this condition and perpetuate serious obesity-related comorbidities such as diabetes, dyslipidemia, and sleep apnea. Glucocorticoid therapy also suppresses the hypothalamic and pituitary axes, causing an often profound linear growth failure and marked delay in pubertal development. The linear growth failure of DMD is further affected by a direct adverse effect of glucocorticoid therapy on growth plate function. Glucocorticoid dependence due to adrenal insufficiency is another serious consequence of the high-dose glucocorticoid therapy that is typically prescribed in DMD.

All of these issues (obesity, growth failure, delayed puberty, and adrenal insufficiency) can adversely affect quality of life, and adequate treatment of adrenal insufficiency in patients with glucocorticoid dependence is a potential life-saving measure.[1] In this review, we target pediatricians, neurologists, endocrinologists, and weight management clinicians involved in the care of patients with DMD by providing specific guidance on clinical practice in these areas. With appropriate prevention and treatment of glucocorticoid-related comorbidities, it is anticipated that the need to withdraw glucocorticoid therapy to treat the underlying disease will be largely or wholly obviated.

OVERWEIGHT, OBESITY, AND RELATED COMORBIDITIES

Vulnerability to obesity is largely driven by genetic, prenatal, developmental, and psychosocial risk factors. In individuals with DMD, this risk is increased further because of glucocorticoid use, decreased mobility, and reduced energy expenditure due to limited options for physical activity. Increased time and financial pressures for families with children who have special health care needs such as DMD also can contribute to risk of obesity and create barriers to successful weight management.[2] Once weight is gained, biologic adaptations make it extremely difficult to lose weight and therefore prevention strategies are critical.[3] In individuals with DMD, obesity can negatively affect mobility and physical functioning, resulting in falls and fractures; obesity can also exacerbate the metabolic complications associated with glucocorticoid use. Therefore, it is imperative that both obesity prevention strategies and management are incorporated into the care of individuals with DMD.

Little research has been conducted in the area of obesity prevention or management strategies in DMD and in children with physical and developmental disabilities in general.[4] Family-based behavioral interventions have shown modest reduction in BMI in the short-term for children and youth with obesity in the absence of developmental and physical disabilities.[5,6] One small study ($n = 3$) on the treatment of obesity in children with DMD that targeted parents revealed inconsistent changes in body weight, increases in children's perceived quality of life, and increases in healthy foods available at home. However, a larger randomized controlled trial (RCT) is needed to more effectively examine the efficacy of such an approach.[7] Two small pharmacotherapeutic trials have been conducted, one with metformin[8] and the other with topimarate,[9] but there remains insufficient evidence regarding the benefit and safety of these medications in this clinical context. Given the paucity of evidence and research in this area, the unique determinants of obesity in individuals with

DMD should be used to guide effective obesity prevention and management strategies that can feasibly be implemented in their care.

Obesity Prevention

Obesity prevention strategies should be introduced at 3 key time points: (1) diagnosis, (2) time of glucocorticoid initiation, and (3) time of loss of mobility. Particular attention should be given to patients who have a family history of obesity, given the highly hereditary nature of obesity.[10] An increase in weight or BMI z score of ≥0.5 also should trigger intervention.[11]

Obesity prevention strategies should aim to facilitate a healthy home food environment of mostly whole foods, regular and predictable times for meals and snacks that are mostly home prepared, family meals, limits on sugar-sweetened beverage consumption and restaurant meals, and encouragement of screen-free meals and snacks at the table. This should be done in consultation with a dietitian. Obesity prevention strategies also should include counseling around appropriate sleep hygiene and duration, limitations on screen time, and psychosocial assessments and support for both the patients and their caregivers.[12,13]

Although physical activity is a mainstay of obesity prevention strategies, the approach to physical activity recommendations in patients with DMD is more measured, and the role of physical activity in DMD remains controversial.[14] To avoid disuse atrophy and other secondary complications of inactivity, it is necessary that those who are ambulatory or in the early nonambulatory stage participate in gentle functional strengthening activity, including a combination of swimming pool exercises and recreation-based exercises in the community. Swimming is highly recommended from the early ambulatory to early nonambulatory phase and could be continued in the nonambulatory phase as long as it is medically safe. Additional benefits might be provided by low-resistance strength training and optimization of upper body function. Significant muscle pain or myoglobulinuria in the 24-hour period after a specific activity is a sign of overexertion and that the activity should be modified.[15]

Monitoring of Weight Status

Monitoring weight status should include measuring body weight and linear height in ambulatory patients or arm span and segmental length in nonambulatory patients at least every 6 months. Both BMI and weight should be plotted on the appropriate curve to determine the percentile for age. Optimal weight status is defined as BMI between the 10th and 85th percentiles. If height is unavailable or there are significant concerns about its accuracy, weight for age can be used, and an appropriate weight gain trajectory as per the growth curve can be another indicator of optimal weight gain. An increase in weight for age or BMI *z* scores by >0.5 between visits should raise concern and prompt intervention.[11]

Although body composition is altered in individuals with DMD (lower lean body mass and higher fat mass), the role of direct measurement of body composition remains unclear and is not routinely recommended. Direct measures of adiposity have limited accessibility in most clinical settings and are not sufficiently accurate.[16] Although reference data for a number of pediatric dual-energy x-ray absorptiometry body composition measures have been published,[17–19] it remains unclear what their clinical applicability will be both within and

outside of the population with DMD. Longitudinal data on the relation of adiposity in children to future disease risk in adults also is lacking; therefore, no agreement exists about cut-points for excess adiposity that would constitute obesity.[20]

Weight Management

More intensive weight management strategies should be introduced if weight for age or BMI *z* score is increased by >0.5 between visits and/or if BMI is >85th percentile. A referral to an intensive interdisciplinary weight management program or to a clinician with expertise in pediatric weight management should be made if BMI is >85th percentile with associated weight-related health complications and/or if BMI is >95th percentile.

Evidence-based guidelines for managing obesity in individuals with DMD or children with physical and developmental disabilities do not currently exist[4]; therefore, an adaptation of current clinical practice guidelines for managing pediatric obesity, with the exception of physical activity recommendations, should be applied. The principles of weight management are in essence a more intensive application of obesity prevention strategies (as above). Family participation in lifestyle change is essential, and interventions must include nutritional and psychosocial reassessment and support, with frequent follow-up.[6] High-intensity programs (>25 hours of contact with the child and/or family over a 6-month period) were able to demonstrate improvement in weight status 12 months after beginning the intervention.[6] These interventions were focused on counseling and behavioral management techniques to assist with implementation of lifestyle change. Interventions may incorporate a structured daily eating plan with the addition of some self-monitoring (through the use of logs) under the supervision of a dietitian who has training in weight management, with careful attention paid to avoid overly restrictive dieting practices. Personnel should include a registered dietitian, physical activity expert, and mental health professional (social worker, counselor, and/or psychologist) who have training in motivational interviewing, goal setting, monitoring, and positive reinforcement techniques. Interventions must be mindful of, and adapted to, the unique needs of the patient and family. More specific recommendations can be found within the “Recommendations for Treatment of Child and Adolescent Overweight and Obesity.”[21] Practical clinical resources include The 5As of Pediatric Obesity Management[22] and the Healthy Active Living for Families Program.[22]

Monitoring Weight-Related Health Complications

Metabolic complications of obesity include glucose dysregulation, type 2 diabetes, dyslipidemia, and hypertension. The metabolic complications of obesity are often silent and need to be screened to identify and manage them. Table 1 lists comorbidities for which regular monitoring and possible intervention are recommended. Metabolic complications also are highly heritable, and a family history should result in increased vigilance around screening.[23] Glucocorticoid use increases the risk of both obesity and its metabolic complications.

Signs and symptoms of obesity-induced biomechanical complications can typically be elicited on routine history and physical examination. Effective management of

biomechanical complications, especially sleep apnea and sleep-disordered breathing, may help improve success with weight management.[24]

Children and youth with obesity are at increased risk of social isolation and stigmatization.[25] Childhood psychiatric disorders (depression, anxiety), school difficulties, body dissatisfaction, dysregulated eating behaviors, teasing, and bullying have all been linked with pediatric obesity.[26,27] Mental health disorders, as well as some of the pharmacotherapeutic agents that are used to manage them, can complicate weight management, promote weight gain, and affect prognosis and therefore should be routinely monitored through history at clinic visits.[28]

ENDOCRINE DISORDERS: SHORT STATURE, PUBERTAL DELAY, AND ADRENAL INSUFFICIENCY

Growth Failure Causing Short Stature

Short stature is common in individuals with DMD. Observational studies of glucocorticoid-naïve, ambulatory patients with DMD have described a growth pattern marked by (1) normal length at birth, (2) below-average growth velocity in early life, and (3) age-appropriate growth velocity at a below-average height percentile for the remainder of childhood.[28,29] A study of ambulatory patients with DMD revealed that participants were shorter than expected for age by an average of 4.3 cm compared with reference data.[30,31] The authors of a natural history study reported that the median height of participants at age 18 years was below the fifth percentile.[32] The etiology of the impaired growth in individuals with DMD remains unclear because growth hormone secretion in response to provocative testing,[33] circulating growth factors,[28] and skeletal maturation[29] were normal in patients with DMD.

Growth impairment in DMD is exacerbated by glucocorticoid treatment.[34–36] Current recommendations support the initiation of glucocorticoid therapy before functional decline; therefore, patients are exposed to the deleterious effects of glucocorticoid for the majority of their growth.[37] Glucocorticoid treatment regimens vary and may affect growth differently. Growth impairment was observed irrespective of agent (prednisone, prednisolone, deflazacort) in a natural history study.[38] However, an RCT revealed that a weekend-only prednisone regimen resulted in greater growth compared with daily dosing.[39] The mechanisms underlying the growth inhibitory effects of glucocorticoids are complex. Glucocorticoid exposure appears to inhibit growth hormone release,[40] antagonize the peripheral action of growth hormone and IGF-1,[41–43] and induce chondrocyte apoptosis at the growth plate.[44]

Growth should be verified every 6 months in all patients with DMD until puberty has finished and final adult height has been reached.[37] Standing height is acceptable for patients who are still walking, with the results compared with a standardized growth curve. A DMD-specific growth curve derived from glucocorticoid-naïve patients is available for patients ages 2 to 12 years, although its clinical usefulness is untested.[30] Growth is evaluated differently in nonambulatory patients, ideally starting before loss of ambulation to permit tracking of the growth rate during transition from walking to nonambulatory. Arm span,

ulnar and tibia lengths, knee height, and segmental measurements of recumbent length have been proposed.[45] However, these methods have not been specifically validated in DMD. A finding of impaired growth (downward crossing of percentile for height, height velocity <4 cm/year, or height below the third percentile) should prompt consultation with an endocrinologist. A standard clinical evaluation should be performed in all patients with DMD with growth failure to identify treatable hormonal or other causes (Fig 1, Table 2).

The treatment of DMD-related short stature is controversial. Recombinant human growth hormone (rhGH) is commonly used to treat hypothalamic and/or pituitary growth hormone deficiency and a handful of other childhood conditions.[46] To date, no RCTs have been conducted to evaluate the efficacy and safety of rhGH to improve growth in individuals with DMD. The only RCT of rhGH conducted in this population was designed to investigate cardiac outcomes. The researchers found that rhGH was well tolerated and that left ventricular mass increased with treatment. However, no height outcomes were reported.[40] The largest report of clinical rhGH use in individuals with DMD included 39 boys and revealed that growth velocity increased from 1.3 to 5.2 cm/year over 12 months.[47] No detrimental musculoskeletal or pulmonary effects were observed, although 3 boys developed known rhGH-related adverse events (impaired fasting glucose, worsening of scoliosis, and benign intracranial hypertension). Adding to the controversy are theoretical concerns that increased growth may worsen muscle function in this context.[48,49] The relevance of this evidence to humans remains uncertain, however, and clinical trials investigating the use of mazindol, a postulated inhibitor of growth hormone release, yielded inconsistent effects on growth suppression and no benefits on muscle strength.[33, 50–53] In light of limited data and the ongoing controversy, regular use of rhGH in the population with DMD is not recommended. The decision to use rhGH should be made on a case-by-case basis with biochemical evidence of growth hormone deficiency, and after a discussion of the benefits and known plus unknown risks. For example, it is unknown whether rhGH adversely affects muscle strength.

Delayed Pubertal Development

Delayed or absent pubertal development in glucocorticoid-treated patients with DMD is due to hypogonadotropic hypogonadism[54] and may negatively affect physical health, psychosocial development, and self-esteem. Studies have revealed that pubertal delay in individuals with DMD is common, with a prevalence of 50% to 100% in glucocorticoid-treated boys.[55,56] No published RCTs have contained assessments of the safety and efficacy of testosterone to induce puberty in individuals with DMD. However, the authors of a retrospective study of 14 boys treated with testosterone reported patient satisfaction with treatment and increased growth velocity in the first year of therapy.[57] Testosterone is widely used in pediatrics to induce puberty and is specifically advised in treatment of adult men with glucocorticoid- induced hypogonadism.[58]

All patients with DMD should undergo monitoring of pubertal development by physical examination every 6 months starting at age 9 years (Fig 1).[37] A finding of delayed puberty (absence of testicular enlargement ≥4 cm^3 by age 14 years) should prompt referral to an endocrinologist. Testosterone is recommended starting by age 14 years (or by 12 years in

those on glucocorticoids) at a low dose and should be increased gradually over 2 to 3 years until adult testosterone levels are achieved. Examples of commonly used testosterone regimens are provided in Table 3. Patients and families should be counseled about expected effects, including body odor, facial hair, acne, growth spurt, growth plate closure, and increased libido. Testosterone levels should be monitored to adjust dose. Annual monitoring of hemoglobin and/or hematocrit, lipids, and serum glucose should be considered.[58] An unexpected adverse effect on muscle or cardiac health may warrant discontinuation or dose reduction.

Currently, the expected benefit of restoring testosterone to normal physiologic levels is felt to outweigh potential risks of treatment. However, future studies are needed to identify the optimal timing and regimen for testosterone replacement in individuals with DMD.

Glucocorticoid Dependence and Adrenal Insufficiency

Chronic glucocorticoid therapy at the doses used on individuals with DMD leads to a suppressed hypothalamic-pituitary-adrenal (HPA) axis. Patients are therefore at risk for life-threatening adrenal crisis should glucocorticoid therapy be stopped suddenly and also during times of severe injury or illness.[59] All patients on glucocorticoids should be taught the symptoms, signs, and appropriate management of adrenal crisis at the time of initial glucocorticoid prescription, including intramuscular hydrocortisone administrative for home use in the event the patient cannot take his usual glucocorticoid therapy because of vomiting. Patient education should also include emergency administration of intramuscular hydrocortisone and instructions for stress dosing during times of illness, trauma, or surgical intervention (Table 4). The need for education around intramuscular hydrocortisone is testament to the potentially life-threatening nature of adrenal suppression in the face of illness and surgery. Glucocorticoid therapy is never discontinued abruptly, but rather tapered slowly to allow HPA recovery. A steroid taper should adhere to the following guidance: (1) gradual dose reduction; (2) monitoring for signs and/or symptoms of adrenal insufficiency (fatigue, headache, nausea and/or vomiting, hypoglycemia, hypotension); (3) dose increase and slowing of taper in response to signs or symptoms; and (4) continuation of stress steroid coverage until the taper is complete and the HPA axis has been proven normal by an adequate cortisol response to corticorelin or corticotropin stimulation (peak cortisol >20 μg/dL [550 nmol/L]).[60] HPA axis recovery can take months to years.[61,62] Periodic monitoring of 8:00 AM cortisol levels for a return to a normal value (eg, >6 μg/dL [165 nmol/L])[63] can guide the decision around when to discontinue daily steroid therapy and to perform stimulation testing, recognizing that the precise threshold that is used to define a normal 8:00 AM cortisol may vary depending on institution-specific practice standards. Irrespective of the specific threshold that is used to signal discontinuation of daily physiologic steroid therapy, an expert in adrenal suppression management should interpret the 8:00 AM cortisol results in light of the child's clinical status and in accordance with local practice standards. These decisions are typically made in collaboration with an endocrinologist. A protocol for the management of adrenal suppression has been developed previously[64] and endorsed by the DMD Care Considerations Working Group.

CONCLUSIONS

Because of the positive effects of glucocorticoid therapy on ambulation, mitigation of scoliosis, and cardiorespiratory function in individuals with DMD, glucocorticoid therapy has been widely adopted as the standard of care for pediatric and adult patients with DMD. At the same time, the adverse effects of glucocorticoid therapy on weight management and the hormonal milieu are often troubling for patients and in some cases are potentially life-threatening (in the case of glucocorticoid-dependence and adrenal insufficiency). To maintain a positive benefit-to-toxicity ratio, glucocorticoid therapy to treat the underlying disease should be integrated with clinical programs that effectively address the resulting side effects. In most cases, this will require a multidisciplinary effort, with input from neuromuscular specialists, endocrinologists, primary health care providers, and clinicians with expertise in obesity management. A comprehensive approach to monitoring and managing these important side effects should not be viewed as optional but rather a mandatory component of the approach to glucocorticoid therapy in this setting.

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ABBREVIATIONS

DMD:	Duchenne muscular dystrophy
HPA:	hypothalamic-pituitary-adrenal
RCT:	randomized controlled trial
rhGH:	recombinant human growth hormone

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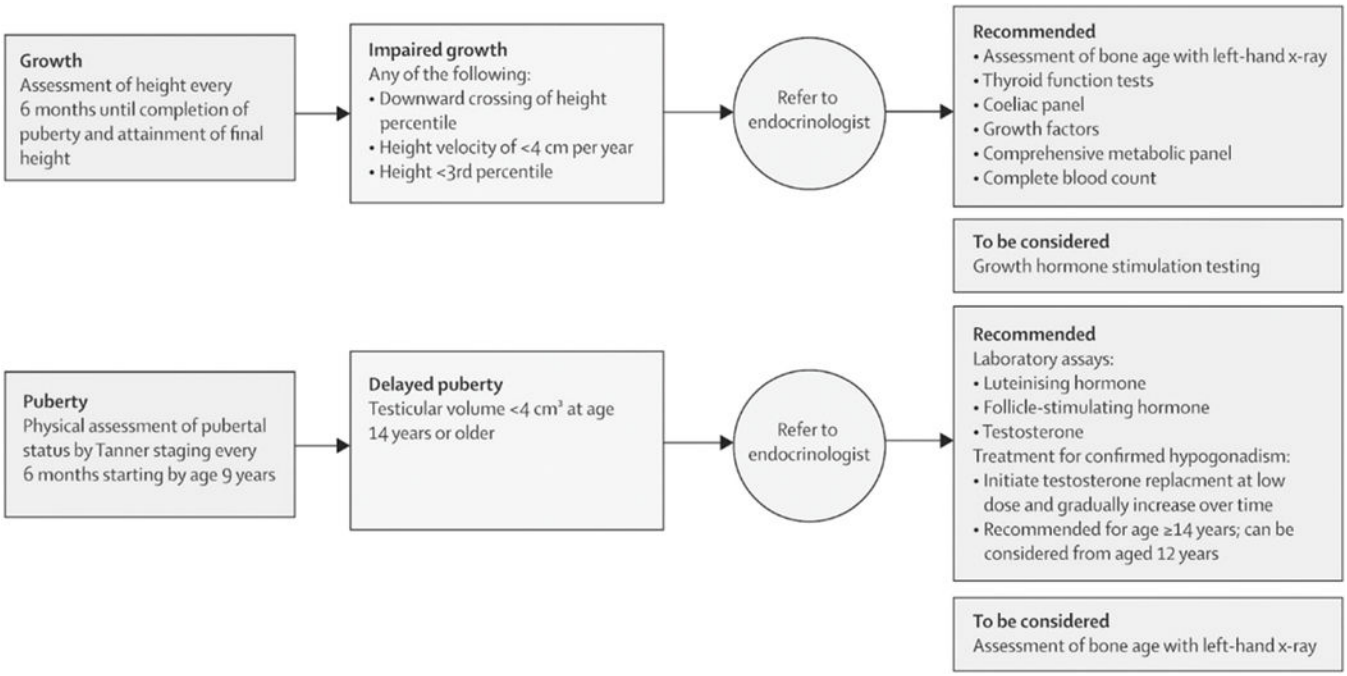

FIGURE 1.

Assessments and interventions for impaired growth and delayed puberty in patients with DMD. (Reproduced with permission from Birnkrant DJ, Bushby K, Bann CM, et al; DMD Care Considerations Working Group. Diagnosis and management of Duchenne muscular dystrophy, an update, part 1: diagnosis, and neuromuscular, rehabilitation, endocrine, and gastrointestinal and nutritional management. *Lancet Neurol.* 2018;17[3]:258.)

TABLE 1

Recommended Monitoring for Obesity-Related Comorbidities

	Recommended Monitoring	Intervention
Hyperglycemia	History: polyuria, polydipsia Annual random blood glucose and A1C If asymptomatic with random blood glucose ≥11.1 mmol/L, repeat random blood glucose within 1 wk	Dietary assessment Endocrine consultation if: symptomatic with random blood glucose ≥200 mg/dL (11.1 mmol/L) or 2 random blood glucose readings ≥200 mg/dL (11.1 mmol/L) in the absence of symptoms and/or A1C ≥6.5 (American Diabetes Association Clinical Practice Guidelines 2015)
Hypertension	Blood pressure should be monitored at each clinic visit (minimum annually, ideally every 6 mo)	Dietary assessment Referral to hypertension clinic if blood pressure >95th% for height and sex on ≥3 occasions taken over wk to mo (Fourth Report on the Diagnosis, Evaluation, and Treatment of High Blood Pressure in Children and Adolescents, NIH)
Dyslipidemia	Random lipid profile annually. If abnormal, arrange for fasting lipid profile	Dietary assessment Refer to lipid clinic if LDL-C ≥160 mg/dL (4.2 mmol/L) and/or non- HDL-C ≥190 mg/dL (4.9 mmol/L) on ≥2 fasting lipid profiles done months apart[23]
Gastroesophageal reflux disease	Inquire about GERD symptoms (heartburn); minimum annually, ideally every 6 mo	H2 blocker or proton pump inhibitors if symptomatic (2010 guidelines)
Obstructive sleep apnea and/or sleep disordered breathing	Inquire about symptoms: morning headaches, daytime somnolence, change in mood, decreased ability to concentrate and/or focus (minimum annually, ideally every 6 mo)	Sleep study and referral to sleep clinic if abnormal
Mental health assessment	Inquire about mood and anxiety symptoms, disordered eating patterns, body image, and school functioning	Referral to mental health professional (social worker, psychologist, counselor) for further assessment and support

GERD, gastroesophageal reflux disease; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; NIH, National Institutes of Health.

TABLE 2

Recommended Biochemical and Radiographic Tests for the Evaluation of Impaired Growth and Delayed Puberty in Individuals With DMD

Impaired growth at any age as defined by any of the following	
Downward crossing of height percentile	
Height velocity of <4 cm/y	
Height less than third percentile	
Recommended	To be considered
Bone age radiograph of left hand	Growth hormone stimulation testing[a]
Thyroid function tests[b]	
Celiac panel	
Growth factors[c]	
Comprehensive metabolic panel[d]	
Complete blood count	
Delayed puberty as defined by	
Testicular volume <4 cm^3 at age 14 y or older	
Recommended	To be considered
Luteinizing hormone[e]	Bone age radiograph of left hand
Follicular stimulating hormone	

[a] Routine use of growth hormone in the treatment of impaired growth is not recommended. Stimulation testing should be performed on an individual basis only in patients in whom a compelling clinical case for the use of growth hormones exists.

[b] Thyrotropin and total or free thyroxine.

[c] Insulin-like growth factor 1 and/or insulin-like growth factor binding protein 3.

[d] Sodium, potassium, chloride, bicarbonate, serum urea nitrogen, creatinine, calcium, albumin, alkaline phosphatase, and alanine- and aspartate-aminotransferase.

[e] Luteinizing hormone, follicular stimulating hormone, and testosterone should be checked at 8:00 AM and assessed by using appropriate pediatric or ultrasensitive assay.

TABLE 3

Example Testosterone Replacement Regimens in DMD Patients With Confirmed Hypogonadism

Formulation[a]	Dose Titration[b]
Intramuscular	
Testosterone enanthate or cypionate	Initiate at 50 mg once monthly Increase dose by 50 mg every 3–6 mo over a period of 2–3 y Typical adult regimens include 150–200 mg every 2 wk or 75–150 mg every wk Serum testosterone levels should be monitored every 3–6 mo Target testosterone levels (drawn 1 wk after injection) in the midnormal range (350–750 ng/dL [12–26 nmol/L])
Transdermal	
Gels (pumps or packets)	Initiate at lowest possible daily dose given formulation
1% gel (12.5–50 mg per application)	Increase dose gradually every 3–6 mo over a period of 2–3 y
1.62% gel (20.25–40.5 mg per application)	Typical adult regimens range from 20.25 to 100 mg daily based on formulation
2% gel (10 mg per application)	Serum testosterone levels should be monitored every 3–6 mo Target testosterone levels (drawn any time) in the midnormal range (350–750 ng/dL [12–26 nmol/L])
Patch	Not commonly used to initiate puberty
2–4 mg per patch applied daily	May be a convenient option for some patients once typical adult replacement levels have been achieved Typical adult regimens range from 2 to 4 mg daily Serum testosterone levels should be monitored every 3 to 6 mo Target testosterone levels (drawn 3–12 h after patch placed) in the midnormal range (350–750 ng/dL [12–26 nmol/L])

[a] Other testosterone formulations may be available depending on country. Consult prescribing information provided by manufacturer for recommended dosing.

[b] Adult dosing and monitoring recommendations adapted from the Endocrine Society Clinical Practice Guideline for testosterone therapy in adult men with androgen deficiency syndromes.[58]

TABLE 4

Management of Adrenal Suppression in Patients on Chronic Glucocorticoid Therapy

Stress Situation	Stress Dosing Recommendations
Mild	25 mg/m^2 per d[a] hydrocortisone or equivalent[b] divided every 6–8 h PO
Mild febrile illness	Continue for 24 h after return to baseline health
Minor surgical procedure requiring anesthesia	
Moderate	50 mg/m^2 per d hydrocortisone or Eq divided every 6–8 h PO, IM, or IV
Moderate illness requiring hospital admission	Consider taper as clinical condition improves
Major elective surgery requiring anesthesia	
Severe	100 mg/m^2 hydrocortisone IM or IV followed by
Severe vomiting, loss of consciousness	100 mg/m^2 per d hydrocortisone divided every 4–6 h IV
Septic shock	Consider taper as clinical condition improves
Severe trauma or illness requiring emergent surgery	
Example steroid taper[c]	
Decrease prednisone and/or deflazacort dose by 20%–25% every 2 wk	
Once physiologic dose is achieved (3 mg/m^2 per d of prednisone and/or deflazacort) switch to hydrocortisone 12 mg/m^2 per d divided in 3 equal doses	
Continue to wean dose by 20%–25% every 2 wk until a dose of 2.5 mg hydrocortisone every other d is achieved	
After 2 wk of every other d dosing, discontinue hydrocortisone	
Periodically check am cortisol or CRH and/or corticotropin stimulated cortisol level until HPA axis is determined to be normal[d]	
Continue stress dose coverage until HPA axis has recovered. This may take up to 12 mo or longer	

AM, morning; CRH, corticorelin; IM, intramuscular; IV, intravenous; PO, per os (oral).

[a]Doses expressed in terms of milligram per body surface area (in meters^2).

[b]Or equivalent. Multiply prednisone dose (milligram) by 4 to convert to hydrocortisone equivalents (milligram). Many patients on standard prednisone regimens will not require supplemental hydrocortisone for mild or moderate stress if able to continue usual home doses.

[c]Adapted from Parent Project Muscular Dystrophy.[1]

[d]Adequate cortisol response to CRH or ACTH stimulation (peak cortisol >20 μg/dL [550 nmol/L]).