Nutrition Considerations in Duchenne Muscular Dystrophy

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Abstract
Duchenne muscular dystrophy (DMD) is a serious degenerative muscular disease affecting males. Diagnosis usually occurs in childhood and is confirmed through genetic testing and/or muscle biopsy. Accompanying the disease are several nutrition-related concerns: growth, body composition, energy and protein requirements, constipation, swallowing difficulties, bone health, and complementary medicine. This review article addresses the nutrition aspects of DMD. (Nutr Clin Pract. XXXX;xx:xx-xx)

Keywords
Duchenne muscular dystrophy; muscular dystrophies; nutrition assessment; nutritional support; nutrition therapy

Duchenne muscular dystrophy (DMD) is a recessive X-linked disease characterized by progressive muscle weakness. In 1991, Emery1 attempted to calculate the frequency of several neurological conditions and concluded that DMD occurs in 1 of every 3500 live births. DMD, which exclusively affects males, results from a mutation of the gene responsible for generation of a protein called dystrophin. This gene is found in all types of muscle. The absence of dystrophin results in progressive muscle degeneration, with a 75% loss of muscle mass by 10 years of age.2 On average, children with DMD experience loss of independent ambulation by 13 years of age.3,4 In addition, patients with DMD will have further complications of the digestive and cardiovascular systems due to deterioration of the smooth and cardiac muscles, respectively.

Initial symptoms of DMD include delayed walking (>16–18 months of age), and DMD may be suspected in children who experience frequent falls, difficulty running, and difficulty climbing stairs.5 Muscle hypertrophy, especially of the calves, is a common feature of DMD.6 A classic sign of proximal muscle weakness that presents in affected boys is the Gowers’ maneuver, which can be observed when a child raises himself from the floor. The child will use his hands to walk himself up into a standing position rather than using leg strength to lift up to a standing position.3,6

Screening for DMD may involve testing creatine kinase levels, which will be increased in patients with DMD.5 Official diagnosis of DMD involves genetic testing of the dystrophin gene and/or a muscle biopsy.5 Most patients are typically diagnosed when they are 5 years of age.5

Current medical treatment consists of steroid therapy with prednisone or deflazacort, an oxaline analogue of prednisone. Glucocorticoid treatment is currently the only medication available to slow the progression of muscle weakness in DMD.5 This treatment, which has changed the natural history of DMD, can cause side effects, including weight gain, poor bone health, behavioral problems, short stature, and reflux.6,7

Steroids are typically started between 4 and 8 years of age once motor skills have plateaued but before motor skills decline.5 Anticipatory guidance should be given to patients with DMD at the introduction of steroid treatment as a strategy to prevent excessive weight gain.5

Although there is no cure for DMD, ample research is being performed to develop therapies that target the pathology of DMD and improve muscle regeneration.3 Areas of research currently in different phases of clinical trials include cell-based therapy, gene therapy, antisense oligonucleotide therapy, stop codon read-through therapy, and growth factor pathway therapy.3

Multidisciplinary management of DMD is becoming increasingly important as advances are made in the management of the disease and patients are living longer. Multidisciplinary clinics with access to a range of medical professionals, including cardiologists, pulmonologists, neurologists, dietitians, nurses, rehabilitation specialists, orthopedists, physical therapists, geneticists, and primary care physicians, are crucial as patients with DMD need expert advice regarding diagnosis, preventing complications, and managing disease progression.3,6

As the patient with DMD ages, nutrition intervention transitions from prevention of weight gain to concern for undernutrition.4,8 Chewing and swallowing difficulties should routinely be

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assessed, and enteral feedings, including gastrostomy tubes, should be considered with severe swallowing difficulties or weight loss resulting from the inability to consume adequate nutrition orally.\textsuperscript{3,10} Gastrointestinal (GI) complications, including constipation, delayed gastric emptying, and reflux, are observed in patients with DMD and require nutrition and/or medication therapy to alleviate symptoms.\textsuperscript{3,11–13} Complementary and alternative medicine is frequently used among the DMD patient population to aid in treatment and alleviate symptoms of the disease.\textsuperscript{14} Although there may be some possible benefit from using complementary and alternative therapies, caution needs to be used, as further research is needed to validate the safety and efficacy of such treatment.

DMD is multisystemic. The impact on the skeletal, cardiac, and smooth muscles leads to respiratory, cardiovascular, orthopedic, and nutrition complications.\textsuperscript{3} The aim of this review is to provide a comprehensive analysis in relation to the nutrition aspects and complications associated with DMD.

**Anthropometrics**

Several retrospective and prospective studies address weight, height, and body composition related to DMD that attempt to measure changes in growth over time, with and without steroid treatment.\textsuperscript{4,15–18} In 1988, Griffiths and Edwards\textsuperscript{15} proposed a growth chart for DMD that accounts for progressive muscle loss at a rate of 4\% decline per year. However, there are no widely accepted growth charts specifically designed for boys with DMD, and the World Health Organization (WHO) and Centers for Disease Control and Prevention (CDC) 2000 growth charts are used to measure growth for ages 0–24 months and 2–20 years, respectively, in clinical settings.\textsuperscript{19} At birth, weight and length in males with DMD are similar to that of standard distribution patterns in males,\textsuperscript{16,17} suggesting that the disease progression is potentially responsible for the differences in height and weight. Currently, there is not enough information to use mid-upper arm circumference and triceps skinfold as anthropometric measurements in DMD beyond standard usage.

**Weight**

The percentage of males with DMD at the 90th percentile weight-for-age increases during childhood up to 12 years of age; however, there is no significant difference in weight trends in ambulatory, steroid-naive males with DMD compared with the CDC 2000 weight-for-age growth chart for boys aged 2–12 years.\textsuperscript{18} Despite the absence of steroid use, the rate of weight gain appears to increase from ages 7–10 years and continues to increase so that the average weight of ambulatory, steroid-naive males with DMD is greater than the averages of the CDC 2000 growth charts, suggesting that weight gain in DMD is more complicated than increased appetite as a side effect of steroid use.\textsuperscript{17} Additional studies also suggest that the greatest risk for overweight/obesity occurs in the preteen to teenage years (9–17.7 years), while undernutrition and weight loss become a greater concern around age 18 years.\textsuperscript{4,8,20}

**Height**

Several studies demonstrate that children with DMD are shorter on average than the typical male child. These differences in height can be seen as early as 2 years of age, as 30\% of children with DMD from ages 2–5 years present with short stature.\textsuperscript{16} There are significant differences in height among ambulatory, steroid-naive males with DMD aged 2–12 years compared with the CDC 2000 growth chart for height/age. However, this same study does suggest a slight increase in height velocity around 10 years of age.\textsuperscript{18} These results suggest that short stature in DMD is independent of steroid use.

It has been suggested that low human growth hormone (hGH) is partially responsible for the short stature of males with DMD.\textsuperscript{21} Reduced muscle tone leading to poor bone turnover is another suggested cause of short stature.\textsuperscript{17} However, one study demonstrated no significant correlation between specific markers of growth and muscular weakness with height, and the exact etiology of short stature in DMD remains unclear.\textsuperscript{17} Genetics may partially predict height outcomes as short stature is more prevalent among children with distal deletions of the DMD gene. Central mutations are also associated with short stature but to a lesser degree than distal deletions.\textsuperscript{16}

It is important to acknowledge the difficulty of obtaining height measurements in a nonambulatory population, which may explain why most studies evaluating height focus on the years prior to loss of ambulation, which typically occurs in the preteen or early teen years. Knee height, tibial length, and/or upper arm length may be used to estimate height in nonambulatory patients with DMD,\textsuperscript{22} although it should be noted that measuring arm span requires the ability to hold out the arms straight, a capability that may diminish over time in patients with DMD. Additional factors affecting accuracy of height measurements include limited range of movement, joint contractures, and scoliosis.\textsuperscript{23}

Scoliosis and other curvatures of the spine are common problems among children and adults with DMD and may affect up to 90\% of patients.\textsuperscript{24,25} Scoliosis is particularly a concern among nonambulatory patients, and prolonging ambulation may reduce the severity of scoliosis.\textsuperscript{26} Curvatures of the spine tend to worsen with puberty;\textsuperscript{24} however, puberty often coincides with the increased wheelchair dependence in patients with DMD. Three main types of spinal deformities have been identified in DMD that may include scoliosis, kyphosis, and/or lordosis.\textsuperscript{27} Spinal surgery is commonly used to treat scoliosis; however, any surgery is not without complications.\textsuperscript{28} Nonsurgical treatment for scoliosis involves wheelchair modifications that provide additional head and neck support.\textsuperscript{25,26} Curvatures of the spine not only affect overall height, but a strong correlation exists between scoliosis and pulmonary
function.29 Several studies advocate for monitoring scoliosis at the loss of ambulation, using nonsurgical methods to prevent the progression of scoliosis, and providing early surgical intervention as deemed medically necessary.24,26,29

**Body Mass Index and Body Composition**

Given the noted increases in weight and short stature, it is no surprise that body mass index (BMI) tends to be higher in children with DMD compared with CDC growth trends.18 Several studies suggest that BMI does not accurately depict body composition in this population.30,31 Research varies in approaches to measuring body composition for DMD. Several methods are used to measure lean muscle mass, but the most commonly used include dual-energy X-ray absorptiometry (DEXA),30,32,33 bioelectrical impedance,34 and magnetic resonance imaging (MRI).35 Elliott et al34 suggest that bioelectrical impedance is a minimally invasive, cost-effective way to measure body composition in a clinical setting.

Body composition is of significant concern in DMD as lean body mass has been shown to correlate with muscle function. Increases in fat mass may be due to adipose infiltrations into the skeletal muscles in patients with DMD.33 For this reason, patients with DMD may present with a body weight and BMI within normal ranges; however, these measurements do not provide information about the percentage of lean body mass. Tarnopolsky et al36 showed that creatine monohydrate supplementation increases lean body mass, increases dominant hand-grip strength, and decreases bone breakdown. While several studies measure body composition in patients with DMD, less is known about preserving lean body mass.

**Comparative Standards for Energy, Protein, and Fluid Requirements**

Estimating energy requirements in patients with DMD is rather challenging, particularly complicated by the use of corticosteroids early on, but also due to the degenerative loss of muscle mass throughout the course of the disease.4 Currently, there are not any predictive equations to assist in estimating energy needs in patients with DMD undergoing steroid treatment.37 In the early years of diagnosis, children with DMD ambulate independently or with assistance of orthotic devices. In later years, respiratory function is significantly affected, requiring the use of mechanical ventilation.38 Predictive equations exist for intubated patients but are not specific to DMD.39

Over- and undernutrition occur in approximately 54% of patients with DMD from 10–13 years of age. Overnutrition, or obesity, has been suggested to be multifactorial in this population and can be associated with decreased physical activity and ambulation, replacement of muscle with fat and connective tissue,8 and use of corticosteroids. Patients should not be overfed in an attempt to increase the body’s production of muscle proteins. This practice not only is ineffective, as it will not increase muscle synthesis, but also may lead to excessive weight gain and obesity.38 Excessive weight gain further worsens skeletal malformations, which may increase the likelihood of patients needing orthopedic surgery. In addition, obesity may complicate the outcomes of such surgeries.8

Malnutrition may worsen muscle wasting38 and affect physical abilities and activities of daily living in patients with muscular dystrophy.35 Weight loss due to muscle wasting occurs over time, which causes weakness, self-feeding difficulties, and dysphagia resulting in suboptimal energy, protein, and micronutrient intake.31 Utilization of CDC BMI-for-age charts may assist practitioners with determining whether patients are in the categories of over- or undernutrition, but as aforementioned, BMI may not be the most accurate predictor of nutrition status in patients with DMD.30,31 Further research in this area is needed.

**Energy Requirements**

Resting energy expenditure (REE) is thought to be affected in DMD. REE is defined as the minimum amount of energy required for maintaining metabolically active components of fat-free mass. Approximately 30% of a human’s REE is consumed by the liver, 20% by muscle, and 20% by the brain.40 Out of total energy expenditure (TEE), REE makes up nearly 60%–70%, the greatest percentage of total energy needs. To determine TEE, the REE is multiplied by activity factors based on the patient’s level of physical activity.41

While data are limited by small sample sizes and also complicated by the wide range of ages and stages of muscular dystrophy,42 some studies have shown that loss of muscle in DMD is associated with a lower REE.38,43–45 while other studies have not.35 Shimizu-Fujiiwara et al43 examined a group of 77 patients with DMD, with ages ranging from 10–37 years, and found that the REE in this population was significantly lower than the norm. Hogan44 observed REE in 4 patients with DMD, with ages ranging from 11–22 years, as well as in 2 patients with Becker muscular dystrophy, all of whom had lower REEs than the standard population. Hankard et al45 found that muscle loss is associated with a lower REE in obese boys with DMD. Gonzalez-Bermejo et al38 found that REE was significantly lower (22%) in a small, intubated DMD population compared with a nonintubated, non-DMD population. These findings are consistent with other findings showing that ventilated patients have lower energy needs.39 In contrast, Zanardi et al15 found that of 9 children with DMD aged 6–12 years, results did not show that a loss in muscle mass was associated with a lower REE.

The Academy of Nutrition and Dietetics recommends using indirect calorimetry when determining REE in obese children and teenagers41; in clinical settings, indirect calorimetry remains the gold standard of estimating energy expenditure.39 The use of indirect calorimetry requires access to a metabolic cart, which can be costly, is large in size, and requires routine
maintenance and calibration, as even the smallest change in calibration can affect patient outcomes. An alternative to a metabolic cart is the handheld indirect calorimeter, which is portable, more cost-effective, and easy to operate. However, it cannot be used for patients who are intubated.

When indirect calorimetry is not an option, predictive equations may be used. Several equations exist to help estimate energy requirements. In the DMD population, the Schofield equation has been suggested to be the most accurate predictive equation. The Harris-Benedict equation has been shown in 2 studies to overestimate energy needs. Due to having a lower REE, boys with DMD do not require the same amount of calories as healthy children without DMD. Some literature suggests estimating caloric needs at approximately 80% of the Dietary Reference Intake (DRI) for ambulatory DMD boys and 70% of the DRI for nonambulatory boys. Energy needs should be individualized based on ambulation and overall physical ability. Caution should be used when estimating energy requirements; a negative energy balance may lead to loss of lean body mass, which, once lost, may not be restored.

Obesity prevention, which involves education in the early years of diagnosis, is more favorable than calorie restriction in those patients who are already obese. However, obese patients with DMD still require nutrition intervention to decrease potential side effects of obesity.

### Protein Requirements

Little research has been done with regard to specific protein requirements within the DMD population. Protein intake should, at a minimum, meet the DRI for age. Acceptable percentages for protein intake are 10%–30% of total calories for boys 4–18 years of age. There is currently not any evidence suggesting that boys with DMD require additional protein. Table 1 summarizes estimated energy and protein needs for males in all age groups.

<table>
<thead>
<tr>
<th>Age, y</th>
<th>Basel Metabolic Rate, kcal/kg/d</th>
<th>Dietary Reference Intake—Energy a</th>
<th>Dietary Reference Intake—Protein b</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>kcal/d</td>
<td>kcal/kg/d</td>
</tr>
<tr>
<td>3</td>
<td>57</td>
<td>1020</td>
<td>85</td>
</tr>
<tr>
<td>4–5</td>
<td>48</td>
<td>1402</td>
<td>70</td>
</tr>
<tr>
<td>6–7</td>
<td>48</td>
<td>1279</td>
<td>64</td>
</tr>
<tr>
<td>8</td>
<td>48</td>
<td>1186</td>
<td>59</td>
</tr>
<tr>
<td>9–11</td>
<td>36</td>
<td>1756</td>
<td>49</td>
</tr>
<tr>
<td>12–13</td>
<td>36</td>
<td>1599</td>
<td>44</td>
</tr>
<tr>
<td>14–16</td>
<td>28</td>
<td>2385</td>
<td>39</td>
</tr>
<tr>
<td>17–18</td>
<td>28</td>
<td>2230</td>
<td>37</td>
</tr>
<tr>
<td>&gt;18</td>
<td>28</td>
<td>2550</td>
<td>36</td>
</tr>
</tbody>
</table>

aEstimates based on Schofield equations for calculating basal metabolic rate in children.
bBased on estimated energy requirement with physical activity level = sedentary.
cBased on Recommended Daily Allowance.

### Fluid requirements

Currently, there are not any fluid guidelines geared specifically to DMD. However, intake of adequate fluid is recommended due to the increased risk of constipation due to low muscle tone. Ability to drink adequate fluid may be complicated by dysphagia, which worsens through the course of the disease. Calculation of fluid requirements begins with an estimate based on the patient’s weight but may be individualized as needed. Fluid calculations based on both height and weight are available but should be used only with an accurate height, but due to the discrepancies in obtaining heights in this population, these equations should be used with caution. Table 2 demonstrates how to estimate fluid needs based on the Holliday-Segar method.

<table>
<thead>
<tr>
<th>Weight, kg</th>
<th>Fluid Needs</th>
</tr>
</thead>
<tbody>
<tr>
<td>1–10</td>
<td>100 mL/kg</td>
</tr>
<tr>
<td>11–20</td>
<td>1000 mL + 50 mL/kg for each kg &gt;10 kg</td>
</tr>
<tr>
<td>&gt;20</td>
<td>1500 mL + 20 mL/kg for each kg &gt;20 kg</td>
</tr>
</tbody>
</table>

### Feeding difficulties and gastrostomy placement

Feeding difficulties may be partially responsible for weight loss in DMD in the late teen and adult years. A variety of chewing and swallowing difficulties are reported in patients with DMD. Most common include facial weakness, reduced mastication, and poor tongue coordination. Macroglossia and malocclusion are also observed in some patients. These problems result in increased mealtimes and increased episodes of choking. The ability to self-feed is another concern for older patients. In a retrospective study of 30 patients with DMD, many of the cohorts experienced pharyngeal residue. However, this did not necessary result in aspiration. This study concludes that oral phase dysphagia is more common in DMD than in oropharyngeal dysphagia and that video fluoroscopic swallow studies
(VFSS) are most helpful in patients who may have had recurrent chest infections and in recommending texture modifications for patients who may be fearful of eating.9

Modifying the textures of foods is one way that patients with DMD can manage chewing difficulties.4,9,51 Textures of foods can be separated into 4 primary categories and is referred to as the dysphagia diet. A level 1 dysphagia diet describes pureed foods, while a level 4 dysphagia diet includes all textures of foods. Table 3 shows the different levels of dysphagia diets with some examples of foods in each category.52 In addition, the viscosity of liquids can be altered to be easier for patients with dysphagia to swallow. Thin liquids (1–50 centi-Poise [cP]) can be thickened to nectar (51–350 cP), honey (351–1750 cP), or spoon-thick (>1750 cP) consistencies.52 Observing feeding may help clinicians recommend texture modifications for patients with DMD presenting with chewing/swallowing difficulties.9

As previously mentioned, undernutrition and weight loss are common in patients with DMD in their late teens and beyond. Enteral feedings provide an alternative to oral feedings; however, reports vary in the incidence of gastrostomies used in patients with DMD.4,10 In a retrospective study of 25 patients with DMD with gastrostomies, the primary reason for placement was poor weight gain with the secondary reason being dysphagia.10 While gastrostomy placement improved weight status in many of the patients, it is unclear if gastrostomy placement increased life span and/or quality of life in patients with DMD.10 The relationship of gastrostomy placement and respiratory status may be a possible area for research.

### GI Complications

Complications of the GI tract are relatively common in DMD. GI symptoms were reported by 47% of patients in a study conducted by Pane et al,4 in which 118 patients with DMD completed a survey assessing the prevalence of GI involvement. Common GI complications associated with DMD include constipation, reflux, and delayed gastric emptying.

#### Constipation

Constipation is the most common GI complication among patients with DMD, and it increases with age. In the Pane et al study previously mentioned, 36% of patients reported having constipation, with 60% of these patients older than 18 years of age experiencing constipation. Consistent with this report of constipation occurring more frequently in older patients with DMD, Boland et al. report that smooth muscle involvement of the GI tract occurs in the second decade of life, whereas skeletal muscle failure is often seen in the first decade of life.53

Constipation can result from a variety of factors including smooth muscle involvement of the colon, immobility, weakness of abdominal wall muscles and inadequate fluid intake.54 Boland et al53 reported 21% of patients in their study (7 of 33 patients) had smooth muscle manifestations related to the digestive tract. Gottrand et al54 observed that 10 of 12 patients experienced constipation, and 7 of 12 had an abnormal colonic transit time.

Altered function of the smooth muscle cells is one possible explanation of constipation in patients with DMD. However, another factor to consider is fiber intake. A double-blind, randomized placebo-controlled study by Weber et al13 determined that daily ingestion of dietary fiber resulted in increased defecation frequency and increased stool softness in a non-DMD pediatric population with controlled chronic constipation when stool softeners and enemas were discontinued. Despite these positive benefits of a high-fiber diet, the study did not observe a reduced colonic transit time among patients receiving dietary fiber or eliminate the need for stool softeners and enemas.53 Table 4 describes fiber requirements based on age in males 4–18 years of age.48

The approach to treating constipation is determined by the type of constipation a patient experiences. Bulk-forming laxatives are used for patients with inadequate oral diet and to soften stools.55 These should be used with caution in the immobilized patient with decreased peristalsis, since bulking agents can lead to impaction, making the issue worse. Stimulants are

### Table 3. Dysphagia Diet.

<table>
<thead>
<tr>
<th>Description of Texture</th>
<th>Some Examples of Foods</th>
</tr>
</thead>
<tbody>
<tr>
<td>Level 1</td>
<td>Stage 1 and 2 baby foods, applesauce, yogurt without pieces of fruit</td>
</tr>
<tr>
<td>Purees, consistent texture throughout, requires no chewing</td>
<td>Oatmeal, mashed potatoes, banana, refried beans, canned fruits and tender-cooked vegetables</td>
</tr>
<tr>
<td>Level 2</td>
<td>Chopped meats and fish, breads, most fruits without skins or seeds</td>
</tr>
<tr>
<td>Mechanical altered, requires some chewing</td>
<td>All foods allowed</td>
</tr>
<tr>
<td>Level 3</td>
<td>Soft foods, requires more chewing</td>
</tr>
<tr>
<td>Chopped meats and fish, breads, most fruits without skins or seeds</td>
<td>All foods allowed</td>
</tr>
<tr>
<td>Regular</td>
<td>Chewing likely required</td>
</tr>
</tbody>
</table>

### Table 4. Fiber Requirements in Males Aged 4–18 Years: 2010 Dietary Guidelines for Americans.

<table>
<thead>
<tr>
<th>Age, y</th>
<th>Fiber/d, g</th>
</tr>
</thead>
<tbody>
<tr>
<td>4–8</td>
<td>25</td>
</tr>
<tr>
<td>9–13</td>
<td>31</td>
</tr>
<tr>
<td>14–18</td>
<td>38</td>
</tr>
</tbody>
</table>
helpful when the cause of constipation is slow transit time, and stool softeners are useful when the patient has difficulty in evacuation. Stool softeners and stimulants are used to treat acute constipation, and osmotic laxatives such as magnesium hydroxide, lactulose, and polyethylene glycol 3350 may need to be taken daily if constipation persists.

Constipation treatment should be individualized to each patient and take into consideration the cause and severity of the issue. Many patients should be on a bowel regimen for chronic constipation such as maintenance therapy, including the use of stool softeners, and appropriate eating habits, including consuming a high-fiber diet and ensuring adequate fluid intake. It is important to recognize and adequately treat constipation as constipation can lead to decreased appetite and thus decreased oral intake, which is particularly problematic for the patient who is already malnourished. Table 5 summarizes medications commonly used in the treatment of constipation ranging from natural supplements to suppositories.

A newly recognized complication associated with chronic constipation and its treatment with laxatives and enemas is severe metabolic acidosis, a potentially preventable life-threatening condition. Symptoms may include reduced fluid and food intake, abdominal pain, and distension. A study by Lo Cascio et al. revealed that 8 of 55 patients with DMD aged 20–36 years experienced metabolic acidosis over a 5-year period. All patients were receiving treatment for chronic constipation with laxatives and enemas and were on positive pressure ventilation. Metabolic acidosis was found to be a result from the intestinal loss of bicarbonate from diarrhea or after forced laxative therapy by enemas. Other contributors to metabolic acidosis include insufficient caloric intake and dehydration.

**Delayed Gastric Emptying/Reflux**

Another complication associated with the altered function of gastric smooth muscle cells is delayed gastric emptying. Borrelli et al. demonstrated that gastric emptying time in patients with muscular dystrophy is significantly more delayed compared with controls and is also worse at follow-up as the disease progresses. This is of significant importance because delayed gastric emptying can contribute to gastroesophageal reflux and to malnutrition due to delayed delivery of nutrients to the intestine.

Reflux is another GI complication associated with DMD; however, in a survey of patients with DMD, only 4% (5 of 118) required the use of medication treatment for gastroesophageal reflux, with the majority of patients reporting occasional heartburn. Although nutrition interventions should be recommended for patients experiencing symptoms of reflux, some patients with DMD may require medication therapy, including proton-pump inhibitors or H2 receptor antagonists. Secondary medications such as prokinetics, sucralfate, and neutralizing antacids may be needed in combination with proton-pump inhibitors or H2 receptor antagonists.

**Corticosteroid Treatment and Nutrition Implications**

Treatment with corticosteroids, such as prednisone or deflazacort, can alter the natural course of disease in DMD. The benefits of steroid treatment include extended ambulation by 2–5 years, decreased requirement of spinal surgery, improved cardiopulmonary function and thus a lower risk of cardiomyopathy, delayed requirement for nasal ventilation, and improved quality of life. One study done in 2007 that followed outcomes of daily, long-term use of corticosteroids found that this treatment extended ambulation by 3.3 years, while a more recent study in 2014 found that daily treatment extended ambulation by 2 years. Daily treatment has been

**Table 5. Medications Used in the Treatment of Constipation.**

<table>
<thead>
<tr>
<th>Category</th>
<th>Examples</th>
<th>Mechanism</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bulking agents</td>
<td>Natural bran</td>
<td>Soluble fiber forms gel in colon; retains water increasing normal contraction of intestinal muscles</td>
</tr>
<tr>
<td></td>
<td>Guar gum</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Psyllium</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Methylcellulose</td>
<td></td>
</tr>
<tr>
<td>Stool softeners</td>
<td>Docusate sodium</td>
<td>Secretion of water in intestine adds moisture to stool</td>
</tr>
<tr>
<td></td>
<td>Mineral oil</td>
<td></td>
</tr>
<tr>
<td>Osmotic</td>
<td>Magnesium hydroxide</td>
<td>Draws water into the colon from surrounding tissues</td>
</tr>
<tr>
<td></td>
<td>Polyethylene glycol 3350</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Lactulose</td>
<td></td>
</tr>
<tr>
<td>Oral stimulants</td>
<td>Senna</td>
<td>Irritates intestinal mucosa</td>
</tr>
<tr>
<td></td>
<td>Bisacodyl</td>
<td></td>
</tr>
<tr>
<td>Other stimulants</td>
<td>Glycerin suppositories</td>
<td>Eliminates stool by inducing a distended colon</td>
</tr>
<tr>
<td></td>
<td>Sodium phosphate enemas</td>
<td></td>
</tr>
</tbody>
</table>
shown to be more effective compared with alternative, intermittent schedules (such as 1 week on, 1 week off).\(^6\) Corticosteroids are typically prescribed at the age that ambulation is first affected, around 6–7 years of age, and may be given for a period ranging from 3–10 years.\(^5\)

**Bone Health**

Corticosteroid treatment is not without side effects. Decreased bone mineral density is a common side effect of corticosteroid therapy that requires special medical attention.\(^6\) Other side effects of steroids include behavioral changes, height stunting, abnormal weight gain, cataracts, delayed puberty,\(^7,6\) and, to a lesser extent, impaired glucose tolerance, hypertension, decreased resistance to infections, and GI irritation.\(^6\)

The effects of corticosteroid treatment, combined with decreased mobility, contribute to the increased risk of poor bone mineral density in the DMD population. However, recent studies have suggested that even prior to commencement of steroid treatment, children with DMD may have low serum 25-hydroxyvitamin D levels and poor bone health at diagnosis.\(^6\) Also, it has been noted that increased bone turnover and low serum 25-hydroxyvitamin D levels exist in patients with DMD with or without steroid treatment.\(^6\) Over time, poor bone health may lead to fragility fractures, which is indicative of osteoporosis.\(^6\) DEXA scans are recommended for assessing bone mineral density.\(^6\) For accuracy, DEXA values must be adjusted for height due to the reduced growth pattern and shorter stature in patients with DMD.\(^6\)

Nutrition intervention to promote adequate bone mineral density includes adequate intake of calcium and vitamin D, especially in patients treated with corticosteroids. Recommended elemental calcium intake for boys 4–8 years of age is 1000 mg/d and increases to 1300 mg/d for boys aged 9–18 years. After 18 years of age, 1000 mg/d calcium is recommended. Dietary sources rich in calcium include dairy products (milk, yogurt, and cheeses), green leafy vegetables (kale, broccoli, Chinese cabbage), canned fish (sardines and salmon), and fortified foods (certain cereals, nondairy milk substitutes, and breads).\(^6\) Calcium intake during adolescence is already a concern, as soft drinks may replace calcium-rich beverages during this crucial age bracket for bone development.\(^6\) Recommended intake of vitamin D for all ages after infancy is 600 IU/d.\(^6\) Dietary sources rich in vitamin D include cod liver oil, dairy products, fortified nondairy milk substitutes, sockeye salmon, and canned tuna.\(^6\) Sun exposure converts vitamin D into an active, usable form\(^6\); patients with decreased physical activity and/or wheelchair users are less likely to have adequate sun exposure.

Supplements may be used to ensure adequate intake of calcium and vitamin D. Two primary forms of calcium supplements widely available are calcium citrate and calcium carbonate.\(^6\) Calcium citrate could be considered the preferred method of supplementation due to better absorptive properties, the option to take with or without food, and decreased GI side effects. For patients prescribed H2 receptor antagonists or proton-pump inhibitors, calcium citrate is recommended over calcium carbonate due to carbonate needing an acidic environment for adequate absorption.\(^6\) However, the drawbacks of calcium citrate include cost and pill size, due to calcium citrate containing a smaller percentage of elemental calcium than calcium carbonate (21% vs 40%, respectively).\(^6\) Calcium carbonate may be given in the form of antacids, which may contain 200–400 mg elemental calcium per chewable tablet.\(^6\) This option may improve compliance due to taste and ease of administration, and it also may aid in treating GI symptoms caused by corticosteroid use. The decision to recommend calcium carbonate or calcium citrate should involve adherence and risk vs benefits. Many calcium supplements also contain vitamin D, ranging from 200–400 IU per tablet, decreasing the need for an additional vitamin D supplement.

**Weight Gain**

In the DMD population, obesity has been documented in as young as 7 years of age. More than half of patients with DMD are classified as obese by 13 years of age.\(^6\) Weight gain is one of the most common side effects of long-term corticosteroid use.\(^6\) However, it has been noted that many patients with DMD experience obesity even without corticosteroid treatment. For patients with DMD who already struggle with ambulation, excessive weight gain further complicates mobility.\(^6\) As aforementioned, it has been shown that deflazacort may reduce the amount of weight gain associated with steroid treatment.\(^6\) Deflazacort is not currently available in the United States.\(^7\)

Risks of obesity include insulin resistance, dyslipidemia, hypertension, obstructive sleep apnea, and psychological impacts.\(^7\) Weight management guidance should be offered prior to the commencement of steroid treatment, with the anticipation that abnormal weight gain may occur.\(^7\) Basic guidelines for weight management can be tailored toward the patient and family’s needs and may involve dietary changes, exercise as tolerated and/or medically feasible, and behavior modification.\(^7\) Dietary intervention and strategies for weight loss involve reducing intake of sugar-containing beverages and calorically dense foods, reducing the number of meals consumed outside the home,\(^7\) and using the MyPlate model to increase consumption of fruits and vegetables.\(^7\) Behavior modification techniques include consumption of meals at the family table and encouraging patients to eat slowly while recognizing satiety cues.\(^7\)

**Complementary and Alternative Medicine**

Complementary and alternative medicine use is common in pediatric patients with DMD. In a study examining the use of complementary and alternative medicine, 80% of 200 caregivers...
of children with DMD and Becker muscular dystrophy reported “ever” using complementary and alternative medicine for their child. Many different types of complementary and alternative medication therapies exist, and their frequency of use varies. Mind-body medicine, including aquatherapy, hippotherapy (a treatment strategy using horse movement), self-hypnosis, prayer, and companion animals, was most frequently reported at 61.5% in a study by Nabukera et al. The next common reported practices were biologically based: herbs, diet modifications, megavitamins, and glycoproteins at 48%. Manipulative and body-based practices, such as massage, chiropractic manipulation, and osteopathic manipulation, were reported by 29% of caregivers, and 8.5% reported using therapies involving whole medical systems: acupuncture and homeopathy. A variety of people use complementary and alternative medicine, although families with caregivers who have a college education were associated with a higher use of therapies. Of the aforementioned therapies, healthcare providers were reported to have recommended aquatherapy and special diets most often.

Chinese herbal medicine is another area of interest in the field of complementary and alternative medicine. One study observed a reduction in exercise-induced damage in normal muscle after ginseng supplementation in patients with DMD. It is crucial to consider risks associated with Chinese medicine as it is not formally regulated, and incorrect dosing and unknown content of medicines may have harmful outcomes. In addition, drug interactions with medications, including steroids, should be considered before using any herbal or dietary supplements.

Several studies have used animal models to learn how different pharmaceuticals and supplements affect the DMD disease process. Dog and mouse models are the most commonly used to evaluate DMD. The mouse model for DMD is the mdx mouse. A single-point mutation in the dystrophin gene stops the expression of the dystrophin protein. Chamberlain et al found that rhabdomyosarcomas developed in mdx mice. However, there are few known cases of rhabdomyosarcomas in humans with DMD. The mdx mouse experiences muscle weakness in the legs and a shorter life span.

Antioxidants, including coenzyme Q10 and green tea extract, are of interest due to their ability to reduce oxidative damage in cells, including muscle tissue, and are currently being studied. There is evidence that green tea extract supplemented in the diets of mdx mice reduces muscle damage and improves muscle function by improving force output and improving muscle resistance to fatigue. The Cooperative International Neuromuscular Research Group performed a pilot trial of coenzyme Q10 in thirteen 5- to 10-year-old patients with DMD who were on a prednisone regimen for at least 6 months. Dosing of coenzyme Q10 was determined by a dose escalation design with a goal of serum coenzyme Q10 levels of 2.5 µg/mL. Coenzyme Q10 treatment was shown to increase muscle strength by 8.5% when taken in addition to prednisone therapy. The authors of the study recommend a starting dose of 400 mg/d, increasing by 100 mg/d according to serum coenzyme Q10 levels. For optimal absorption, coenzyme Q10 should be administered with a small, fatty snack.

Muscle inflammation in DMD is of interest because chronic inflammation is thought to contribute to DMD disease pathology. Muscle fibers are less able to regenerate with chronic inflammation and are eventually replaced with fibrous and fatty tissue. Decreasing inflammation has been shown to improve muscle function in mdx mice models. Resveratrol, a polyphenol thought to have antioxidant properties, can reduce inflammation in skeletal muscle. The study of the mdx mouse model showed that resveratrol reduced the infiltration of macrophages and increased expression of utrophin after 10 days of receiving 100 mg/kg resveratrol. Utrophin has a similar structure to dystrophin and can functionally take the place of dystrophin throughout the muscle membrane. The results of this study are of importance because inflammation in young mdx mice enhances muscle damage, thus decreasing muscle function.

Amino acids, including taurine and glutamine, have all been studied and observed to have some benefits on muscle strength or dystrophopathy. Taurine has been observed to maintain muscle strength in exercised mice by counteracting exercise-induced weakness and ameliorating macroscopic chloride conductance, an index of degeneration-regeneration in mdx muscle. The amino acid glutamine is a precursor for glucose synthesis. It is produced mainly by skeletal muscle and is the most abundant free amino acid in the body. Intramuscular concentrations of glutamine are low in patients with DMD. Given that patients with DMD already have lower intramuscular concentrations of glutamine and glutamine is produced by muscle, the need for glutamine in this population may be increased. Two separate studies reveal that acute (5-hour) oral glutamine administration and oral glutamine administration over a longer period of 10 days both inhibit whole-body protein degradation in DMD. Although this is promising, it is important to note that there was no specific advantage to glutamine supplementation alone vs an amino acid control mixture as they both equally inhibited whole-body protein degradation. Although glutamine supplementation has been shown to slow whole-body protein breakdown, acute oral glutamine supplementation inhibits endogenous production of glutamine and does not stimulate protein synthesis as has been observed in healthy adults. This may be due to a protein-saving mechanism in which branched-chain amino acid (glutamine precursor) stores are saved.

Although there have been reported benefits to the use of glutamine supplementation, negative consequences from supplementation should also be considered. The following have been reported by Holecek as side effects of long-term glutamine supplementation: altered amino acid transport resulting in impaired absorption of amino acids, altered glutamine metabolism, and altered ammonia transport. In addition, further research is needed to determine the effect of chronic...
glutamine supplementation on the immune system and whether the risk of cancer is increased with the use of long-term glutamine supplementation. There can also be withdrawal effects after discontinuation of long-term glutamine supplementation. The body adapts to intake of large amounts of glutamine by enhanced glutamine breakdown and decreased synthesis of endogenous glutamine; thereby, withdrawal of chronic glutamine can lead to a deficiency of glutamine due to the body’s adaptive responses.87

Creatine supplementation has been observed to improve muscle health by decreasing muscle necrosis in mdx mice,80 and creatine monohydrate supplementation for 4 months in patients with DMD resulted in increased handgrip strength and decreased fat mass.30 Creatine monohydrate can be used in the absence or in addition to corticosteroid therapy.36 Further research may explore optimal dosing of creatine monohydrate supplementation on preservation of lean body mass.

Protandim is an over-the-counter dietary herbal supplement manufactured by LifeVantage Corporation (Salt Lake City, UT). Protandim has been shown to reduce oxidative damage in mdx mice. It has been reported that Protandim decreased thio-barbituric acid–reacting substances (TBARS) after 30 days of supplementation in a population of 29 healthy volunteers. TBARS are a reliable indicator of oxidative stress levels in dystrophic muscle and have elevated concentrations in the muscle of patients with DMD. Similarly, plasma and muscle TBARS concentrations were decreased in an mdx mice study after 6 months of Protandim supplementation. Of note, there was no significant difference observed in motor function between mice receiving Protandim or normal diet.80

Conclusions

While there are many ways to manage the symptoms of DMD, either by using steroids to prolong mobility or by using therapies to improve quality of life, there is no cure for DMD. Clinicians have the difficult task of providing treatment options with an ultimately undesirable outcome. Much of the nutrition-related research in DMD is limited by small sample sizes, but some trends are seen across many studies, contributing to their validity. Comparing growth curves and energy requirements of patients with DMD with unaffected individuals may provide some information about the disease course. However, preserving lean body mass is of the greatest priority as it has the potential to improve quality of life and possibly extend the already short life span of patients with DMD.

Statement of Authorship

J. Davis, E. Samuels, and L. Mullins equally contributed to the conception/design of the research; contributed to the acquisition, analysis, and interpretation of the data; drafted the manuscript; critically revised the manuscript; and agree to be fully accountable for ensuring the integrity and accuracy of the work. All authors read and approved the final manuscript.

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