# Scoliosis in Patients with Duchenne Muscular Dystrophy

By Lori A. Karol, MD

Despite recent research developments, Duchenne muscular dystrophy remains a fatal neuromuscular disease, affecting two to three boys in 10,000. It is an inherited X-linked recessive condition caused by a frameshift mutation in the dystrophin gene at the Xp21.2 locus of the X chromosome[1]. Dystrophin is a large cell-membrane protein involved in calcium transport in the muscle cell. Boys with Duchenne muscular dystrophy have an absolute absence of dystrophin, leading to deterioration of the muscle cells and replacement with fibrofatty tissue[2]. This is in contrast to Becker muscular dystrophy, in which less disruptive mutations that do not result in a frame shift lead to production of variable amounts of a smaller, genetically abnormal dystrophin protein[3,4].

Duchenne muscular dystrophy is highly suspected in boys who have a markedly elevated serum creatine phosphokinase level; in two-thirds of such patients, the diagnosis can be confirmed by genetic testing. Approximately two-thirds of affected patients have large deletions or duplications that can be detected with use of the multiplex polymerase chain reaction and Southern blot techniques[5]. Detection of point mutations in the remaining one-third of patients is more difficult. In patients without detectable mutations, muscle biopsy with dystrophin analysis is necessary for diagnosis[6,7]. Staining of muscle biopsy specimens with antidystrophin antibodies in patients with Duchenne muscular dystrophy reveals a complete lack of staining of sarcolemma, whereas specimens from patients with Becker muscular dystrophy do have enough dystrophin present so that partial staining of the sarcolemma is seen[2].

The clinical course of weakness in patients with Duchenne muscular dystrophy is one of relentless progression. Death from pulmonary or cardiac compromise occurs in the second or third decade of life[8].

## Natural History of Spinal Deformity in Duchenne Muscular Dystrophy

The age of onset of scoliosis in boys with Duchenne muscular dystrophy is generally closely linked to the age at which they lose the ability to walk, which generally occurs between the ages of ten and fourteen years. Screening for scoliosis before the child becomes wheelchair-dependent is usually unnecessary. Once the child is unable to walk, anteroposterior sitting radiographs of the spine should be obtained every six months. Many boys with Duchenne muscular dystrophy are quite obese, so clinical screening may not be accurate.

Once the presence of scoliosis is confirmed radiographically, the risk for curve progression is very high. In a group of thirty-three untreated boys for whom radiographs were made serially until within eighteen months of death, the rate of progression averaged 2.1° per month[9]. Oda et al. found that only 15% of forty-six patients with documented scoliosis had had no progression at the four-year follow-up[10].

## Description of Deformity

The scoliotic deformity in boys with Duchenne muscular dystrophy differs in appearance from that seen in patients with idiopathic scoliosis[11]. The scoliosis begins as a gentle, sweeping curve, the apex of which is at the thoracolumbar junction. Over time, the curve progresses and involves the entire thoracic and lumbar spine and results in pelvic obliquity. Whereas idiopathic scoliosis in individuals without Duchenne muscular dystrophy typically is associated with lordosis in the sagittal plane, most boys with Duchenne muscular dystrophy have thoracolumbar and lumbar kyphosis[11]. Lordotic curves are seen less often and have been linked with a decreased risk of progression by some, but not all, studies[9,10]. In their series of forty-six patients, Oda et al. found that the seven patients who did not have progressive spinal deformity had normal sagittal plane alignment (i.e., they had neither kyphosis nor hyperlordosis), had a scoliosis of <30°, and had minimal pelvic obliquity[10].

## Nonoperative Treatment

The results of published studies on the use of spinal orthoses in boys with scoliosis due to Duchenne muscular dystrophy have universally been unfavorable[12-14]. Progression is nearly inevitable, and bracing does not prevent progression. In a study of thirty-two boys managed with spinal orthoses, progression occurred in 94% despite bracing[12]. Rates of curve progression in braced patients with Duchenne muscular dystrophy range from 1° per month[13] to 8° per year[14]. Also, because pulmonary function slowly deteriorates with age and with progression of the curve, if the brace succeeds in delaying progression of the deformity but does not prevent it, surgery becomes necessary at an older age when the cardiopulmonary health of the patient has declined and anesthetic risks have in-

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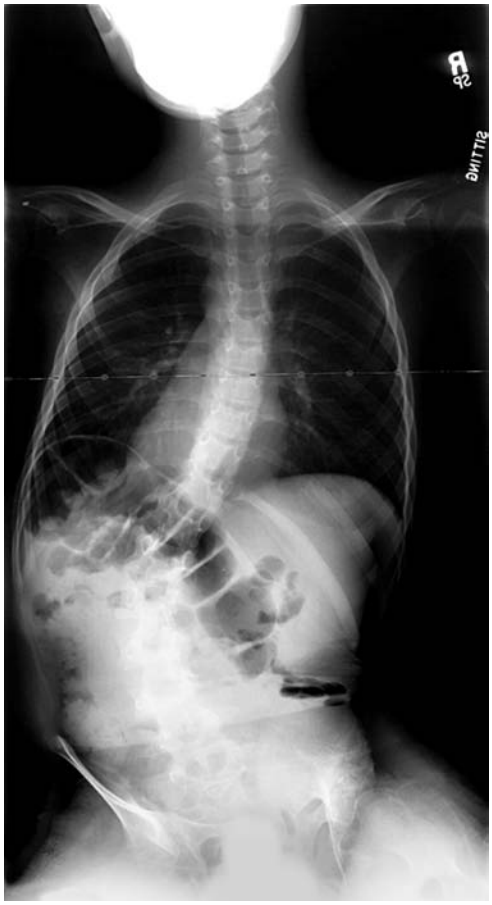

Fig. 1-A

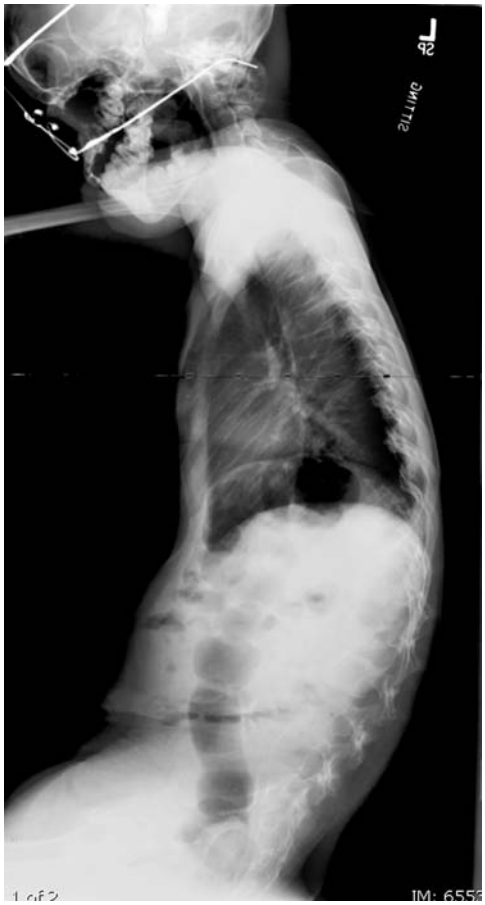

Fig. 1-B

**Fig. 1-A** Anteroposterior radiograph of the spine of a fifteen-year-old boy with Duchenne muscular dystrophy, showing a long, sweeping 41° thoracolumbar scoliosis. The pelvic obliquity measured 17°. **Fig. 1-B** Lateral radiograph of the same patient, showing the typical thoracolumbar kyphosis associated with this disorder.

creased. For this reason, bracing is usually contraindicated in favor of early surgery in patients with Duchenne muscular dystrophy[13,15].

Modification of the wheelchair to accommodate a scoliotic curve is also not effective[13]. Providing supportive seating for patients with scoliosis similarly delays the surgical stabilization of the curve until a time when medical risks may interfere with the safety of the procedure.

## Medical Implications of Spinal Deformity

As previously mentioned, pulmonary function declines during the second decade in boys with Duchenne muscular dystrophy, ultimately leading to death as a result of pulmonary failure[8]. Beginning when the patient loses the ability to walk, pulmonary function, measured as forced vital capacity, decreases annually at a rate of 4% per year[16]. Spinal deformity further diminishes pulmonary function, with each 10° of scoliosis resulting in an additional 4% diminution in forced vital capacity[16]. Therefore, as the spinal deformity worsens and the age of the patient increases, the pulmonary status steadily declines, leading to operative concerns regarding anesthesia and the possible need for permanent mechanical ventilation postoperatively. Similarly, cardiac compromise increases as the patient gets older, with left ventricular dysfunction and arrhythmias documented with advancing age[17].

## Preoperative Concerns

When planning surgical instrumentation and fusion of scoliosis in patients with Duchenne muscular dystrophy, a thorough preoperative evaluation is advised. Even though these children may appear obese, malnutrition is a serious concern. Wound-healing problems and increased infection rates in this group of patients have been reported[18,19]. Maximization of preoperative nutritional status is important to decrease the likelihood of these serious complications.

Pulmonary function testing should be performed to assess the severity of preoperative respiratory compromise. Increased anesthetic risks and the possibility of prolonged or permanent ventilator dependence have been correlated with preoperative pulmonary compromise. A forced vital capacity of <35% has been shown to increase complications[20], although more recent studies have described successful spinal surgery in

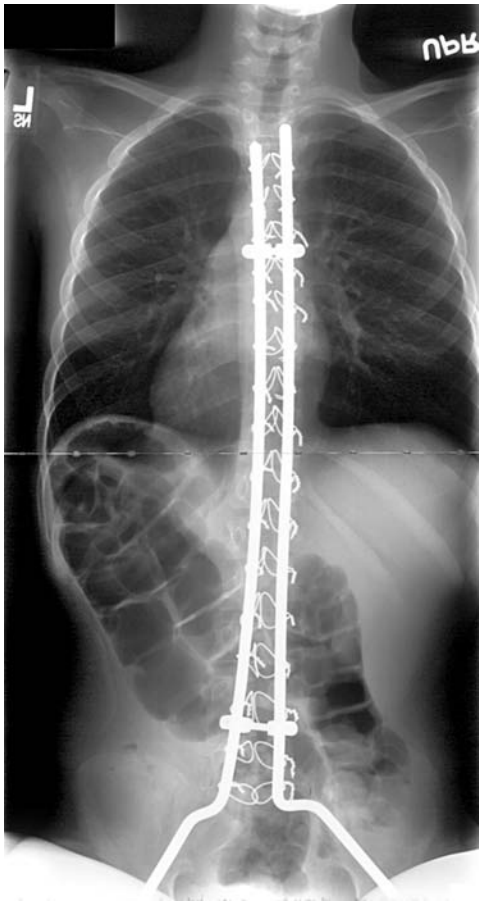

Fig. 1-C

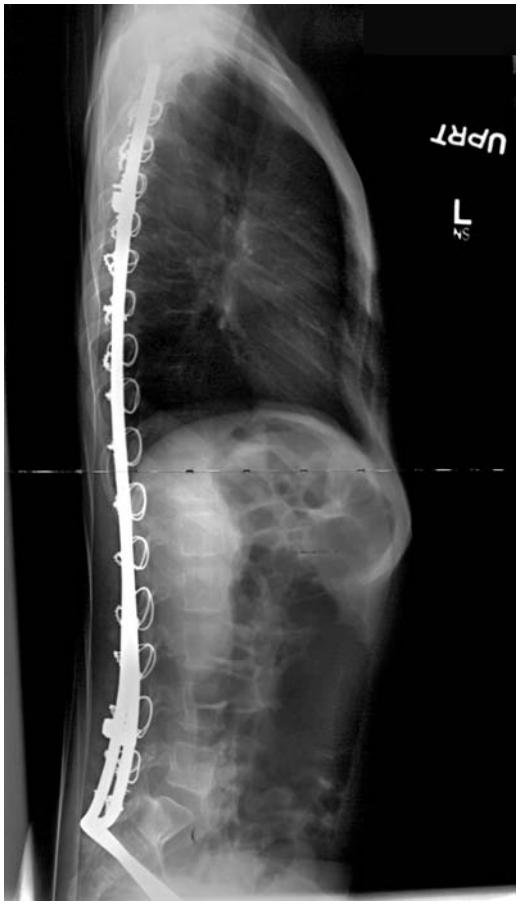


Fig. 1-D

**Fig. 1-C** Anteroposterior sitting radiograph, made following posterior fusion with use of the Luque rod instrumentation with the Galveston technique, showing that the scoliosis and pelvic obliquity are well corrected.

**Fig. 1-D** Lateral sitting radiograph shows that the sagittal plane kyphosis has been improved.

patients with Duchenne muscular dystrophy who had preoperative forced vital capacity of <30% of predicted normal values, particularly with the addition of noninvasive ventilation in the postoperative period[21].

A preoperative sleep study can be helpful in establishing the possible need for postoperative bi-level positive airway pressure support following surgery. Preoperative mask-fitting and the introduction of noninvasive ventilation at night can assist postoperative respiratory recovery in these patients[22,23].

Cardiac evaluation by a pediatric cardiologist should be obtained preoperatively. Reduced cardiac function can substantially alter the anesthetic management of the patient during fusion surgery[24]. Sinus tachycardia is nearly always present, and echocardiograms have shown mitral valve prolapse and abnormal cardiac contractility in some patients[24].

Duchenne muscular dystrophy, along with other dystrophic myopathies, may be associated with an increased risk of malignant hyperthermia[25-28]. Pediatric anesthesiologists are aware of this association and manage these patients by using trigger-free agents[24]. Intraoperative death due to cardiac arrest has occurred[24,26]. While most pediatric spinal surgery is performed under hypotensive anesthesia, reduced cardiac function in this patient population may prohibit the use of hypotensive techniques to minimize blood loss. Recently, a study was published using controlled hypotension in a small group of nineteen patients with scoliosis due to Duchenne muscular dystrophy[29].

Increased intraoperative blood loss is commonly seen in patients with Duchenne muscular dystrophy who undergo spinal fusion surgery[30]. The paraspinal muscles are dystrophic and therefore are difficult to strip subperiosteally due to their fibrous consistency. In addition, the blood vessels, which are muscular by definition, are more friable than normal, leading to increased bleeding. Dystrophin is normally expressed in vascular smooth muscle, so the absence of dystrophin in patients with Duchenne muscular dystrophy may directly contribute to increased blood loss due to lack of vasoconstriction[31]. It should also be remembered that platelet function has been shown to be abnormal in boys with Duchenne muscular dystrophy[32]. The fragile cardiac status of these patients usually is a contraindication to the use of hypotensive anesthesia and necessitates aggressive fluid management; thus,

intraoperative transfusion should be expected and blood products should be readily available.

## Surgical Indications

The goal of spinal fusion surgery in patients with Duchenne muscular dystrophy is to obtain and maintain sitting balance and correction of pelvic obliquity to preserve the ability of the patient to be mobile in a wheelchair for the remainder of his life. The goal of surgery should also be to eliminate the effect of progressive spinal deformity on restrictive lung disease. Most authors agree that pulmonary function does not improve following surgical fusion of the scoliosis in these patients and that respiratory status continues to decline throughout adolescence, but it is hoped that the contribution of progressive spinal deformity on worsening pulmonary function will be eliminated by stabilization of the curve[20,33,34]. Kennedy et al. found that forced vital capacity declined by an average of 3% to 5% per year over a seven-year period both in patients with Duchenne muscular dystrophy who had posterior spinal fusions and in patients who declined surgery for similar spinal deformities[33].

The indication for surgical stabilization of scoliosis in boys with Duchenne muscular dystrophy is different from that in patients with adolescent idiopathic scoliosis. Smith et al. reported that surgical fusion should be performed at the time of loss of ambulation, based on the fact that the vast majority of boys will develop a progressive curve following the cessation of walking[9]. Since pulmonary function is inversely related to the age of the patient, surgery that is performed earlier is safer. Most authors, however, prefer to perform surgery when a scoliotic deformity is documented radiographically, and they recommend surgery when the curve measures 20° to 30°[8,19,35]. A delay in surgery in younger patients allows the curve to progress further, which only compromises the intraoperative status of the patient as the pulmonary function and the cardiac function worsen.

## Surgical Techniques

Segmental spinal instrumentation is recommended in patients with Duchenne muscular dystrophy because the curves are neuromuscular in etiology rather than idiopathic and the bone is relatively osteopenic due to the nonambulatory status of the patient. The most commonly used fixation technique is sublaminar wire fixation, which provides segmental fixation, thereby distributing the forces of correction along the entire area to be fused. Hybrid constructs that make use of a combination of sublaminar wires, hooks, and pedicle screws have been used recently.

Long fusions are recommended, with the proximal extent of the fusion to T2. If instrumentation and fusion are not

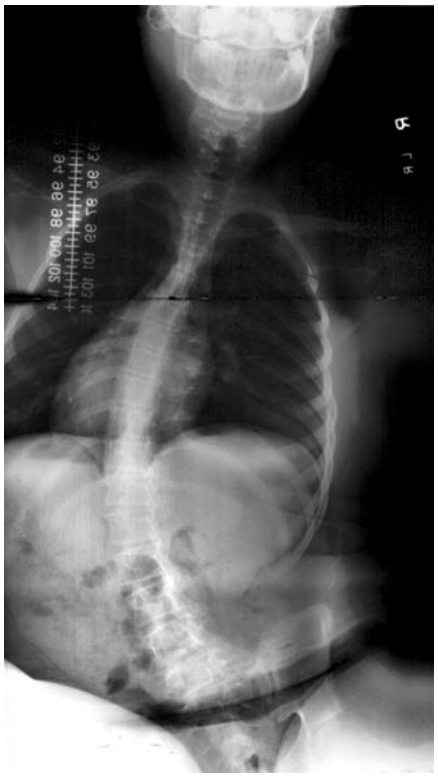

Fig. 2-A

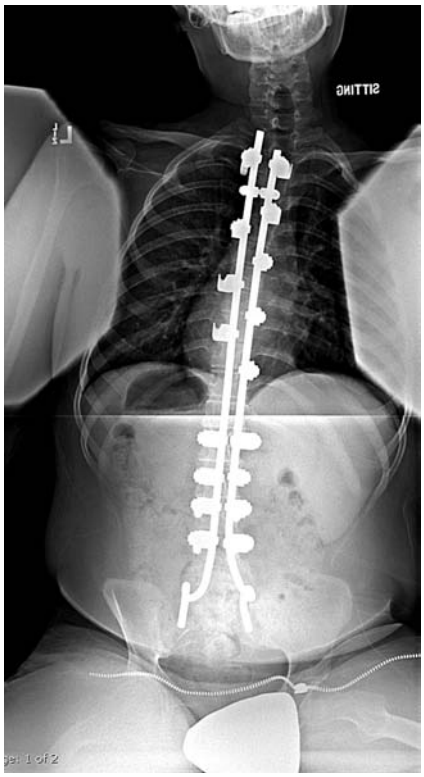


Fig. 2-B

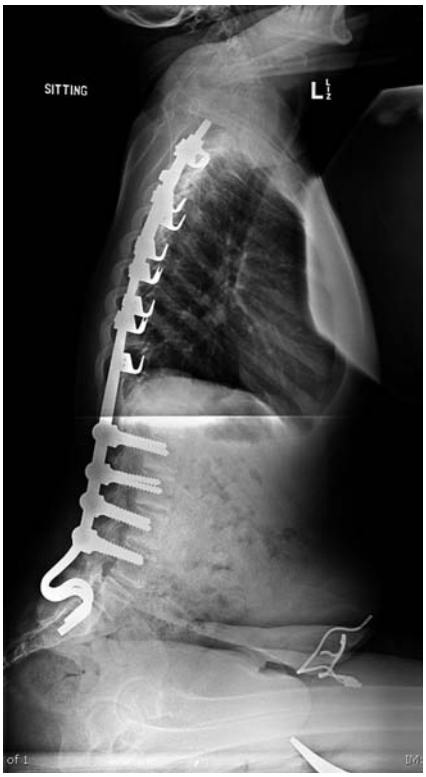


Fig. 2-C

**Fig. 2-A** Anteroposterior sitting radiograph of the spine of a fourteen-year-old boy with Duchenne muscular dystrophy. The scoliosis measured 46°. **Fig. 2-B** Anteroposterior sitting radiograph, made one year following surgery, shows excellent correction of the deformity after a posterior spinal fusion with use of Dunn-McCarthy instrumentation with a combination of hooks and lumbar pedicle screws. **Fig. 2-C** Lateral sitting radiograph of the same patient, made one year following surgery.

carried into the proximal thoracic spine, proximal or junctional kyphosis may be encountered and the patient may lose control of the head[8].

More controversy exists regarding the distal extent of fusion. Fixation to the pelvis or sacrum has been the focus of recent reports[35-39]. Mubarak et al. found that, in small curves with minimal preoperative pelvic obliquity (15° or less), instrumentation and fusion to L5 was adequate at the time of a thirty-four-month follow-up[35]. Likewise, Sengupta et al. reported their results after using newer constructs with lumbar pedicle screws[36]. They studied two groups of patients. The first group consisted of thirty-one patients with an average age of fourteen years. This group underwent a spinal fusion that extended to the pelvis. The average preoperative Cobb angle was 48°, and the average preoperative pelvic obliquity was 20°. The second group consisted of nineteen patients with an average age at surgery of 11.7 years. The patients in this group were treated with thoracic sublaminar wires and lumbar pedicle screws. The average preoperative Cobb angle was 19.8°, and the average preoperative pelvic obliquity was 9°. The authors documented improved correction and maintenance of correction in the group that underwent fusion with pedicle screw fixation to L5. They acknowledged that the preoperative deformity was greater in the patients who had fusion to the pelvis, and concluded that lumbar pedicle screw fixation that stops short of the pelvis is adequate in patients who have minimal deformity and pelvic obliquity.

Other studies have recommended extending instrumentation and fusion to the pelvis, stating that the risk of progressive pelvic obliquity and the potential need for subsequent surgery when the health of the patient has deteriorated merit the additional surgical time and complexity at the time of the initial surgery[37-39]. Alman and Kim studied forty-eight patients with Duchenne muscular dystrophy following spinal fusion[37]. Preoperative indications for fusion to L5 in this study were a Cobb angle of <40° and a pelvic obliquity of <10°. Of thirty-eight children whose fusions did not include the pelvis, thirty-two had an increase in pelvic obliquity at the time of the two-year follow-up visit. The average increase in pelvic obliquity was 8°. Alman and Kim found that curves with an apex distal to L1 were at greatest risk for an increasing pelvic obliquity following fusion to L5[37]. Gaine et al. studied eighty-five patients who had spinal fusions to L4, L5, the sacrum, or the pelvis for scoliosis associated with Duchenne muscular dystrophy and found statistically better maintenance of correction of pelvic obliquity in the eleven patients whose fusion extended to the pelvis than in those whose fusion ended more proximally[39]. Brook et al. found better maintenance of correction of pelvic obliquity in patients in whom the fusion extended to the pelvis than in patients in whom the distal extent of fusion

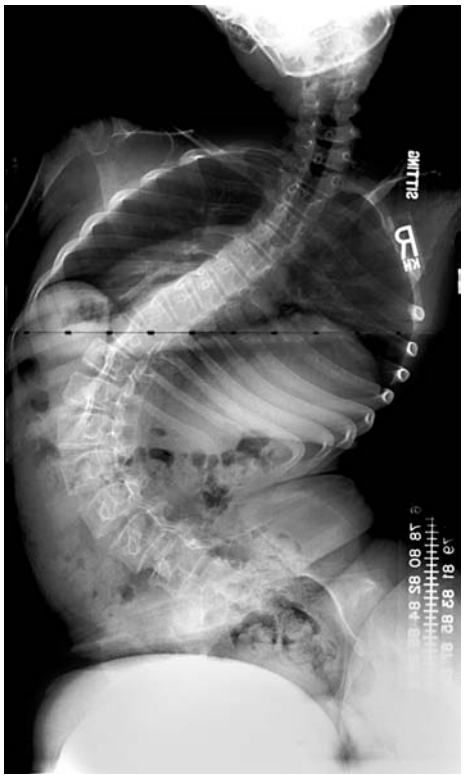

Fig. 3-A

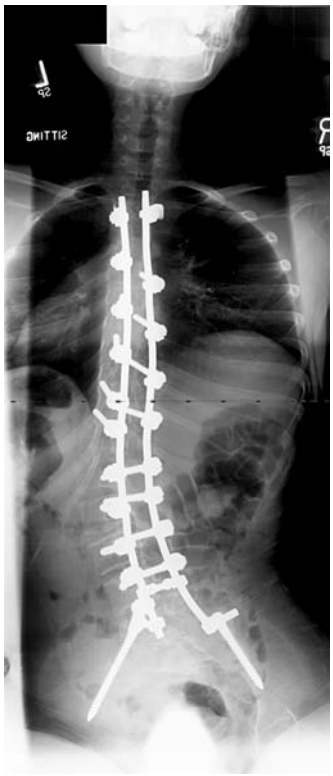

Fig. 3-B

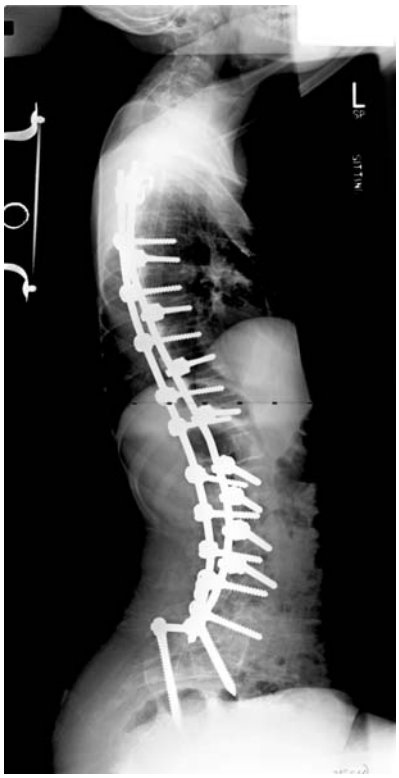

Fig. 3-C

**Fig. 3-A** Anteroposterior sitting radiograph reveals a severe scoliosis, measuring 115°, in a thirteen-year-old boy with Duchenne muscular dystrophy. Pulmonary function testing showed a forced vital capacity of 34%. **Fig. 3-B** Postoperative anteroposterior sitting radiograph after posterior spinal fusion with use of a pedicle screw construct with iliac screws for pelvic fixation. **Fig. 3-C** Postoperative lateral sitting radiograph of the same patient.

was the lumbar spine[40]. Of ten patients in whom the fusion did not extend to the pelvis, six experienced progression of the pelvic obliquity postoperatively, three of whom had >20° of progression in pelvic obliquity. Four of the patients had difficulty with sitting. Ramirez et al. advocated fusion to the pelvis, stating that the added surgical time and morbidity were not sufficient to deter sacral/pelvic fixation in their group of thirty boys who were treated surgically for scoliosis[18].

Techniques for pelvic or sacral fixation vary among studies[40-42]. The most commonly described method for fusion to the pelvis is Luque rod instrumentation with use of the Galveston technique (Figs. 1-A through 1-D). Placement of the pelvic portion of the rods between the tables of the ilia above the sciatic notch allows for correction of pelvic obliquity. Even though this method is commonly used, there is still a need to monitor the patient postoperatively for potential problems with rod loosening or distal migration of the rods.

Unit rods have also been used in the treatment of Duchenne muscular dystrophy[34]. Biomechanically, these rods allow for improved correction of pelvic obliquity. Also, because the rods are precontoured, time is saved intraoperatively. Many surgeons find simultaneous placement of the rods into the iliac wings technically challenging, however, and prefer to use individual Luque rods with proximal and distal crosslinks[40].

A technique commonly used in the neuromuscular population is the Dunn-McCarthy technique, in which precontoured s-shaped rods are looped over the sacral alae (Fig. 2)[41]. By distracting against the ala, correction of pelvic obliquity can be obtained. Sacral fixation is therefore more dependable for patients with osteopenia, since the rods are placed over rather than within the iliac crests. Placement of the rods is decidedly easier when dealing with kyphotic deformities of the lumbar spine, as is commonly seen in patients with Duchenne muscular dystrophy.

Sacral screws[42] have recently been used in combination with pelvic fixation in a small series of twenty-five boys with Duchenne muscular dystrophy. The reported results have been favorable when this technique was used for pelvic and sacral fixation, with excellent correction of pelvic obliquity, no failure of spinal instrumentation at the time of follow-up, and minimal loss of correction postoperatively[42]. Alternatively, techniques of pelvic fixation that make use of screws have been used in some patients (Figs. 3-A, 3-B, and 3-C).

## Postoperative Management

Postoperative care following surgery in patients with Duchenne muscular dystrophy requires aggressive pulmonary management. At our institution, patients are taken off mechanical ventilation as soon as respiratory status permits. Because the preoperative status of these patients has included longstanding severe restrictive lung disease, it is logical that "normal" postoperative lung function will not be achieved before extubation; therefore, extubation should be attempted when there is "adequate" function sufficient to allow the removal of mechanical ventilation. We find post-extubation bilateral positive airway pressure can be helpful in such instances. The immediate involvement of respiratory therapists will help to prevent atelectasis and pneumonia. Patients should be moved frequently, and getting the patient out of bed and into the wheelchair as soon as possible offers great respiratory benefit. When segmental spinal instrumentation is used, postoperative bracing, which can interfere with the ability of the patient to breathe as deeply as possible, should be unnecessary.

Despite aggressive postoperative management, complications in this patient population are commonly encountered. In a study of thirty patients, Ramirez et al. found that eight patients had major complications and five patients had minor complications following surgical treatment of scoliosis[18]. An increased rate of complications has been seen in patients who are more medically fragile. Miller et al. found that pulmonary complications developed in twelve of sixty-eight patients postoperatively[20]. Preoperative forced vital capacity of <35% of normal was an indicator of a greater risk for complications. Another study found similar complications in patients with a forced vital capacity of <30% in comparison with patients with better preoperative pulmonary status[43].

Wound infections are more frequently seen in neuromuscular patients, and boys with Duchenne muscular dystrophy are no exception[18,19]. Careful preoperative assessment of nutritional status may play a role in decreasing the occurrence of this complication. Malnutrition has also been shown to develop postoperatively in patients with Duchenne muscular dystrophy who undergo spinal fusion. The upright and inflexible posture that is achieved due to instrumentation and fusion prevents the boys from slouching forward to the wheelchair tray to feed themselves, resulting in weight loss and malnutrition[44]. A postoperative feeding evaluation performed by an occupational therapist can be helpful in educating the family.

Finally, cardiac failure has been described in boys with Duchenne muscular dystrophy and can be fatal. Many studies have reported sudden death following spine surgery in these patients[25,45,46].

## Influence on Survival

There is controversy regarding the effect of spinal surgery on progressive respiratory failure in patients with Duchenne muscular dystrophy. Although most authors find no proof that pulmonary function tests improve following surgery[20,24,34,47], results of the study by Galasko et al. provided data to the contrary[48]. Galasko et al. measured pulmonary function preoperatively and at six-month intervals following spinal fusion in a group of thirty-two patients with Duchenne muscular dystrophy who underwent spinal fusion and a matched group of twenty-three patients who did not[48]. The patients who underwent fusion had stabilization of forced vital capacity at three years postoperatively and an improved peak expiratory flow rate at five years postoperatively, whereas the patients who did not undergo fusion had a mean annual decrease in forced vital capacity of 8%. To the contrary, however, Kennedy et al. found no difference in seven-year survival curves for seventeen patients who underwent surgery for scoliosis compared with twenty-one patients who did not un-

dergo fusion for similar curves and found that both groups experienced an equal rate of decline in forced vital capacity of 3% to 5% annually[33]. Miller et al. established that the age at which pulmonary function declined to a forced vital capacity of 35% did not differ between twenty-one patients with scoliosis who had spinal fusion and forty-six patients with scoliosis who did not have surgery[34].

While preexisting restrictive lung disease and muscle weakness place a patient with Duchenne muscular dystrophy at risk for perioperative pulmonary complications that may result in the need for a tracheostomy and prolonged ventilator use, the postoperative course is expected to result in continued deterioration throughout the life of the patient. Until recently, the maximum life span of boys with Duchenne muscular dystrophy was approximately twenty years[8]. With an increasing use of bilateral positive airway pressure and nighttime ventilation, the life expectancy of patients is now increasing; in a recent study from Great Britain, Eagle et al. reported up to 53% survival (on Kaplan-Meier survival curves) at age twenty-five for patients who underwent management with ventilation in the 1990s[49]. The prospect of a more prolonged survival further supports the need for surgical stabilization of the spine to maintain seating comfort.

Recently, outcome studies have been performed to assess the experience of the family with regard to scoliosis surgery. High parental satisfaction (approximately 90% would choose surgery again) with improvements in cosmesis and in the ability of patients to sit comfortably have been documented[38,45,46].

## Future Directions

Research is actively underway in the medical treatment of boys with Duchenne muscular dystrophy[8,50-52]. Corticosteroids have been utilized, and Canadian researchers have documented that the use of deflazacort (a derivative of prednisone) prolongs the time that patients are able to walk[50,51]. The use of steroids also appears to have a positive effect on the prevention of spinal deformity[51,53,54]. In a recently published study, the prevalence of scoliosis in boys taking deflazacort was markedly diminished, and only five of the thirty boys treated required surgery for stabilization of spinal deformity, compared with fifteen of twenty-four age-matched boys who were not taking steroids[51]. It is not yet known whether or not the treated cohort of boys will develop scoliosis or if there will simply be a delay in the onset of scoliosis. If scoliosis does not occur in younger boys who receive corticosteroids, and if deformity is absent during the adolescent growth spurt, it is possible that appreciable deformity may be definitively prevented. There are known adverse effects to corticosteroid treatment, however, including obesity and osteopenia. Concerns regarding osteopenia have led to the addition of calcium and vitamin-D supplementation to steroid treatment regimens[55]. The results of comparative studies to assess various corticosteroid treatment regimens have shown that the rate of scoliosis tends to increase when the steroid dosage is decreased[55].

Other medical treatments being investigated for use in patients with Duchenne muscular dystrophy include gentamicin therapy[56]. A small subset of children with Duchenne muscular dystrophy is genetically distinct in that the molecular basis of the disease involves a stop codon rather than a deletion in the dystrophin gene. Gentamicin has been found to inhibit stop codons and allow the production of dystrophin and is thus useful in this subset of affected boys.

While corticosteroids and gentamicin may delay death in patients with Duchenne muscular dystrophy, these medications are not curative. Great attention has been given to gene therapy as the answer to the definitive cure for this fatal disease[57,58]. The dystrophin gene is unfortunately a large and very complex gene and is therefore difficult to transfer successfully into an affected subject. The dystrophin gene (either full-sized or miniaturized) has been grafted via adenoviral vectors in the dystrophin-deficient mouse, but has not yet been grafted in affected boys. Myoblast transfer has also been investigated but has not been found to preserve muscle strength in these patients[59]. Upregulation of dystrophin-related proteins, which can partially compensate for the lack of dystrophin in the cell membrane, is being investigated[57]. ■

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