Arthrogryposis and Amyoplasia

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Abstract

Arthrogryposis (multiple congenital joint contractures) is an uncommon problem. Because there are many causes, correct diagnosis is important to predict the natural history and determine appropriate treatment. Inconsistent terminology has caused confusion about both diagnosis and treatment. Amyoplasia, the most common type of arthrogryposis, is characterized by quadrimelic involvement and replacement of skeletal muscle by dense fibrous tissue and fat. Early physical therapy and splinting may improve contractures, but surgical intervention is often necessary. Aggressive soft-tissue releases in addition to casting may improve joint position. In more severe contractures, osseous surgery also may be needed. Deformity recurrence is common, particularly in skeletally immature patients.

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Arthrogryposis is a group of unrelated diseases with the common phenotypic characteristic of multiple congenital joint contractures. The various causes of arthrogryposis have led to confusion about diagnosis and treatment. Only recently has an effort been made to separate the entities that result in the phenotypic manifestation. The goal of treatment is to optimize independence in performing activities of daily living. Understanding the terminology of arthrogryposis as well as the etiology of the disease process is necessary to assess a child with joint contractures and arrive at a differential diagnosis. Review of the treatment options for amyoplasia, the most common type of arthrogryposis, provides a basis for making treatment decisions.

Terminology

In 1923, Stern[1] coined the term arthrogryposis multiplex congenita to describe three children with symmetrical limited joint motion, internal rotation of the shoulders, involvement of the hands and fingers, and external rotation of the hips. The term often has been loosely applied to patients with other types of multiple congenital contractures. Currently, arthrogryposis encompasses a broad spectrum of diseases, all with the common phenotype of multiple congenital contractures. Amyoplasia increasingly is used to refer to patients with the syndrome originally described by Stern.[2]

With more than 150 distinct entities included under the phenotype arthrogryposis,[3] it is difficult to determine which disease subtypes of patients have been included in published studies. An increasing number of authors have tried to classify their patient populations to provide disease-specific treatment results and recommendations.[4,5] Further complicating the matter is the term distal arthrogryposis, introduced by Hall et al[6] in 1982 to describe a hereditary disease of primarily distal involvement of the hands or feet. Initially divided into two groups (type I with clenched hands and ulnar deviation of the fingers, type II with similar findings but additional deformities), at least nine types of distal arthrogryposis have now been described.[7] In addition, use of the term distal arthrogryposis has been promulgated by others. When evaluating the literature on arthrogryposis, therefore, it is essential to determine whether the patients described are those with the classic disease entity now termed amyoplasia,[2,8] are those with the inherited distal form of arthrogryposis, or are in fact a heterogeneous group of patients with a variety of diseases.

Even the term amyoplasia can be confusing. Described by Hall et al[2] as a specific arthrogrypotic disorder, amyoplasia implies a defect primarily in muscle development. Histologically, the muscle fibers of these patients are hypoplastic with fibroadipose replacement. Other diseases, however, also can result

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in a lack of muscle development and cause multiple congenital joint contractures with similar histologic findings. For example, sacral agenesis is a form of primary segmental amyoplasia in which there is an absence or greatly reduced number of muscle fibers in an otherwise normal extremity.[9] In addition, a decrease in anterior horn cells and white matter, indicating a primary neurogenic cause, has been documented in the autopsy results of a patient with amyoplasia.[10] Others[2] have reported that muscle biopsy results may indicate either a neurogenic cause, a myogenic cause, or both in the same patient. Amyoplasia, therefore, may not specifically describe one single group of patients and may be an intermediate common pathway rather than the primary cause of contractures.

The terminology identifying these conditions likely will continue to evolve as knowledge of the genetic and developmental aspects of these diseases increases. Arthrogryposis here refers to the general phenotype of multiple congenital joint contractures. The terms arthrogryposis multiplex congenita and classic arthrogryposis are not used, and the syndrome described by Stern[1] is referred to as amyoplasia. Distal arthrogryposis identifies the group of inherited diseases that primarily involve the hands, feet, or both.

Epidemiology and Etiology

Mild hip and knee flexion contractures are normal in newborn infants and generally resolve within a few months of birth.[11,12] Multiple congenital pathologic contractures (arthrogryposis), however, occur in about 1 of every 3,000 live births; amyoplasia occurs in 1 of every 10,000 live births.[3] Because arthrogryposis is a phenotype common in a wide variety of diseases, the etiology clearly is multifactorial.

Fetal akinesia (limited fetal movement) seems to be a common element in the development of most types of arthrogryposis. Multiple congenital contractures can be produced experimentally by arresting fetal movement with paralyzing agents such as curare.[13,14] Viral infections and ingestion of alkaloid-containing plants such as hemlock during gestation also have produced arthrogrypotic-like diseases in animals.[15] In humans, numerous environmental factors are associated with fetal akinesia and the development of arthrogryposis, including hyperthermia, oligohydramnios, neural tube defects, anterior horn cell dysfunction, myopathic disorders, and various teratogens. Because amyoplasia is sporadic, genetic factors also must be considered since diseases such as Larsen's syndrome and the distal arthrogryposes (types I and II) are genetically transmitted. No single factor is consistently found in the prenatal histories of patients with amyoplasia; thus, the actual etiology of amyoplasia remains elusive.

Differential Diagnosis

After a thorough history and physical examination are completed, radiographs of all involved limbs should be obtained. A radiograph of the spine can help rule out spinal dysraphism. Amyoplasia in its quadrimelic form is the most common type of arthrogryposis and is relatively easy to recognize, requiring little more than plain radiographs to document deformities. Most other diseases, however, are relatively obscure, requiring further diagnostic testing and consultation with an experienced geneticist. In patients not easily classified as having amyoplasia, additional studies such as serum creatine phosphokinase levels may help identify those with congenital muscular dystrophy. Computed tomography scans of the brain can identify structural brain anomalies. Chromosomal studies are necessary in children with multisystem involvement. Muscle biopsy and electromyography may help distinguish neuropathic from myopathic diseases, but these tests are often inconclusive and their routine use is questionable. Table 1 lists some of the relatively common diseases that cause arthrogryposis.

Amyoplasia

Children with amyoplasia often have severe, deforming joint contractures that can be difficult to treat. The patients often seem to overcome their physical disabilities by successfully manipulating the environment. Treatment is tailored to improve function in performing activities of daily living. Function should never be compromised to improve cosmetic appearance.

All four limbs usually are involved in these patients (84%), although only lower limbs (11%) or, rarely, only upper limbs (5%) may be affected.[16] Generally, the shoulders are internally rotated and adducted, and elbow extension contractures are often present (Fig. 1). If passive motion of the elbow is possible, the biceps and brachialis muscles usually are unable to flex the elbow. The wrists are flexed and ulnarly deviated, and the fingers are partially but rigidly flexed with the thumbs adducted. In the lower extremity, hip flexion and abduction contractures are frequent, and hip dislocation is present in up to 30% of patients.[8] Knee flexion or extension contractures are common, and congenital dislocation of the knee may be seen. Foot deformities such as rigid equinovarus or congenital vertical talus also are frequent.

The involved joints have limited range of motion, with a firm, inelas-

Table 1
Common Causes of Arthrogryposis

Disease	Genetic Influence	Additional Factors/Findings
Amyoplasia	Sporadic	Usually quadrimelic involvement
Myelomeningocele	Multifactorial	Folic acid deficiency
Larsen's syndrome	AD	Joint dislocations, spatulate thumbs, flattened nasal bridge
Distal arthrogryposis type I	AD	Hand, foot involvement
Multiple pterygium syndrome (Escobar's syndrome)	AR	Pterygium of upper and lower extremities, neck
Freeman-Sheldon syndrome (whistling face syndrome)	AD	Whistling appearance to face, ulnar deviation of hands, clubfoot, and congenital vertical talus
Beal's contractural arachnodactyly	AD	Slender limbs with knee, elbow, and hand contractures
Sacral agenesis	Sporadic	Maternal diabetes, exposure to organic solvents, retinoic acid
Diastrophic dysplasia	AR	Clubfeet, hitchhiker's thumb, short stature, scoliosis, hypertrophic pinnae
Metatropic dysplasia	AD, AR	Platyspondylia, kyphosis, scoliosis
Thrombocytopenia with absent radii (TAR) syndrome	AR	Absent radii with thumbs present, knee involvement, thrombocytopenia
Steinert's myotonic dystrophy	AD	Myotonia, typical facies
Spinal muscular atrophy	AR	Anterior horn cell degeneration
Congenital muscular dystrophy	AR	Heterogeneous group of diseases, some with CNS involvement
Moebius's syndrome	Sporadic, AD	VI, VII cranial nerve palsy, micrognathia, clubfoot

AD = autosomal dominant, AR = autosomal recessive, CNS = central nervous system

tic end point to the motion arc. The trunk generally is spared, although scoliosis may develop in about 30% of patients.[8] Overall muscle mass is diminished, and the limbs have a fusiform appearance with a lack of normal skin creases over the joints. Webbing across the elbows or knees may occur, and skin dimpling is often present over the extensor muscle surfaces of subcutaneous joints. Sensation is normal, but deep tendon reflexes often are diminished or absent. There also may be a midline facial hemangioma (nevus flammeus) and micrognathia. Other abnormalities occasionally may be present, including hypoplasia of the labial folds in females, inguinal hernia and cryptorchidism in males, abdominal wall defects, gastroschisis, and bowel atresia.

General Management

Developing guidelines for the management of children with amyoplasia requires a thorough understanding of the natural history of this disease. The only published study[17] to date that has evaluated the long-term outcomes of children with arthrogryposis reported that overall function was related to family support, patient personality, education, and early efforts to foster independence. There was little correlation between physical deformities and function. The primary concern of most parents of children with amyoplasia is whether the child will be able to walk. Because walking is an important normal developmental milestone to parents, their attention to the lower extremity often diverts awareness from the upper extremity, use of which in fact may be the most important factor in the child's ability to achieve independence. Lack of active or passive elbow flexion and inability to grasp may be more disabling than the inability to walk. Thus, the treating physician should help parents focus on factors that will substantially improve the child's function.

The initial treatment of any contracture at birth involves gentle stretching and range-of-motion exercises. Once the position of a joint is acceptable, lightweight splinting may slow recurrence of the contractures. If the joint position is not acceptable, casting or soft-tissue release followed by casting may improve the limb position. Muscle transfers may be considered, but

Figure 1 Clinical appearance of a child with amyoplasia.

many muscles are nonfunctioning, and those that do function often have very limited excursion. Osteotomy ultimately may be necessary but is best left until the child has reached skeletal maturity because recurrence of deformity in immature individuals is commonplace.

Upper Extremity

Little has been published regarding treatment of the upper extremity in children with amyoplasia, and unfortunately complications are extremely complex. Although osteotomy of the humerus to correct the internal rotation of the shoulder is a simple procedure, it is rarely necessary because internal rotation of the shoulder itself usually does not cause a problem. The lack of elbow motors is much more troublesome. Even without contracture, the lack of a functioning biceps muscle makes getting the hand to the mouth difficult. In addition, the wrist position usually is rigidly flexed and the fingers often are stiff, with a relatively small first web space secondary to an adducted thumb. These contractures make holding utensils and writing instruments difficult.

In young children, gentle manipulation may improve the range of motion of stiff elbows and wrists. When passive elbow flexion is present, most children learn to use a table edge to get the hand to the mouth, similar to using a balanced arm feeder. If the child is older and has modified his or her functional activities to the limb positions, various adaptive appliances serve to assist with eating, writing, and dressing. For instance, a simple hook attached to a wall at an appropriate height may help a child in getting his or her trousers up. Use of a modified balanced arm feeder may improve a patient's writing ability.

Some improvement in elbow range of motion may be achieved by triceps muscle lengthening and posterior release.[18] A triceps transfer anteriorly may improve active flexion, but it also can create an elbow flexion contracture. This may cause the patient difficulty in reaching the perineum or using crutches. Thus, one side should be treated at a time. In addition, the surgeon may choose to leave one elbow flexed and the other extended. Other options include a Steindler flexorplasty[19] or transfer of the pectoralis major muscle with a tendon graft. A careful examination of the muscle to be used for the planned transfer is necessary preoperatively to be certain it is functioning with enough power and excursion to be useful after transfer.

Many children learn to write with the wrist and fingers flexed, often holding a pen in a reverse or hyperpronated position (Fig. 2). They also may weave a utensil or pen through their digits. Wrist flexion contractures may be treated with early release and casting. Wrist extensors often are absent, thus leaving the flexor carpi ulnaris as the only functioning muscle. Transfer of this muscle to the dorsum of the wrist may help with hand dorsiflexion if passive extension of the wrist above neutral is possible. If the passive motion is not available, serial casts or a Quengel (extension/desubluxation) cast hinge may be used to achieve extension before transfer. Early one-stage proximal row carpectomy with tendon transfers also has been suggested.[20] In older patients, wrist stabilization (fusion) in slight palmar flexion may improve both appearance and function. Finally, widening the first web space may be attempted, but the lack of web space generally is not the cause of difficulty in grasping, and widening the first web space may make it more difficult for the child to weave an object through the digits.

Lower Extremity

When developing treatment plans for the lower extremity, intervention

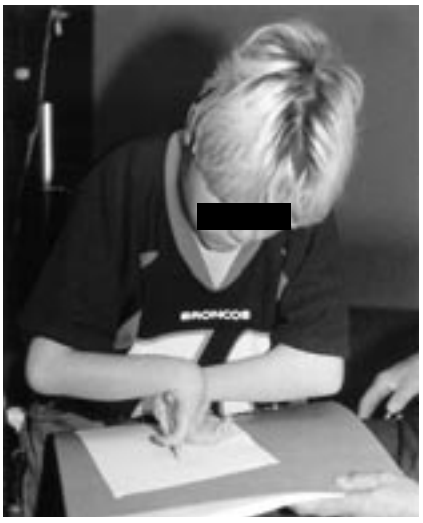

Figure 2 A child with amyoplasia demonstrating his unique writing position.

usually begins at the feet and progresses proximally.

Feet

Clubfoot is the most common foot deformity associated with amyoplasia. Clubfeet usually are quite rigid and tend to be resistant to casting, although some correction of midfoot adduction may be achieved if initiated early. An aggressive soft-tissue release in which all tendons are released (not lengthened) should be done before walking age. Complete correction of the foot must be achieved intraoperatively to provide the best chance for maintenance of a permanent correction. Postoperatively, long-term bracing and night bracing with a well-molded ankle-foot orthosis should be instituted. Some recurrence of the deformity occurs in up to 73% of children.[5]

For a relapsed clubfoot, either a talectomy, a Verebelyi-Ogston procedure (decancellation of the talus), or the use of a circular-frame external fixator to obtain gradual correction is generally required for salvage. Although primary talectomy may occasionally be necessary in very severe cases of untreated clubfoot,[21] it produces both tibiocalcaneal incongruity and loss of the medial column, so in general should be reserved for the relapsed foot. With a talectomy, soft-tissue tension is diminished, allowing the foot to be dorsiflexed. However, failure to fuse the calcaneocuboid joint at the time of talectomy may result in progressive midfoot adduction. The Verebelyi-Ogston procedure potentially avoids progressive midfoot adduction by maintaining the medial column and may allow an easier triple arthrodesis later.[22] The use of a circular-frame external fixator with gradual correction of the deformity is increasing in popularity and acceptance but is technically demanding and cumbersome.[23] It is important to place a wire transversely through the distal tibial epiphysis and lock it to the tibial frame to avoid separation of the distal tibial epiphysis during distraction. In addition, the surgical incisions for any releases done at the time of frame application should be made parallel to the direction of distraction.

Congenital vertical talus is less common but is also resistant to cast treatment. Single- or two-stage release usually results in a plantigrade foot.[24] The anterior tibialis muscle should be transferred to the neck of the talus at the time of soft-tissue release. Permanent support of the arch should be considered because recurrence is common. In older patients, a subtalar fusion may be necessary to correct and stabilize excessive hindfoot valgus. For both clubfoot and congenital vertical talus, a triple arthrodesis may be necessary in older children to obtain a plantigrade foot. This procedure can be difficult and usually requires removing trapezoidal wedges of bone to achieve correction. The limited mobility of the soft tissues makes correction without shortening the bones difficult, and postoperative swelling can be significant.

Finally, some patients report heel pain. Inspection of the heel will reveal a consistent lack of a heel pad, with little more than jelly-like adipose tissue between the tuberosity of the calcaneus and the ground. Providing soft heel cups or padding to an orthosis may help alleviate discomfort.

Knees

The knees are the most difficult problem for these patients. Although both flexion or extension contractures may be present, flexion contractures are more common and disabling. In one study,[25] only 50% of patients with knee flexion contractures became community walkers, whereas all children with knee extension contractures were community walkers. In newborns and infants, a stretching program initiated by physical therapists and continued by the parents can markedly improve the contracture. Because of the high recurrence rate of knee flexion contractures, bracing children who are able to walk and delaying further surgery may decrease the number of surgical interventions. Casting may improve flexion contractures in young children, but care must be taken not to create a posterior dislocation of the tibia on the femur. The Quengel hinge can be used to avoid this problem (Fig. 3). Initially described by Mommsen[26] and later by Jordan[27] for the treatment of knee flexion contractures in juvenile rheumatoid arthritis, Quengel hinges are useful adjuncts to posterior release. Separate thigh and leg portions of the Quengel cast are applied over soft cotton padding, with felt also applied to the posterior thigh above the patella and behind the heel. The hinges are placed so that the point of rotation of the hinge corresponds to the point of rotation of the knee (the center of the femoral condyles). Gradual extension of the knee is obtained at the same time as the tibia moves forward on the distal femur. The bolts are turned a half turn two to four times a day until full extension is achieved. Intermittent lateral radiographs should be made to monitor the position of the tibia in relation to the femur.

Soft-tissue release (usually including the hamstrings, posterior capsule, and posterior cruciate ligament) may facilitate extension in younger patients. This is not an easy procedure because the usual muscle planes are absent and replaced by dense fibrous cords. Identification of the popliteal artery can be difficult. The tourniquet should be deflated during exposure of the back of the knee joint to facilitate the vascular dissection. The S-shaped posterior incision should be avoided because subsequent casting will pull the inci-

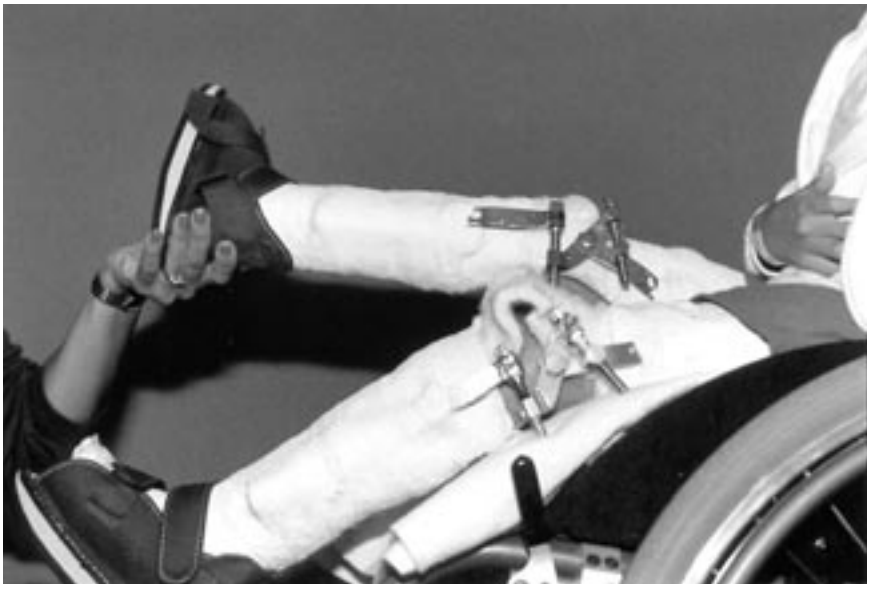

Figure 3 Quengel hinge applied to a lower extremity cast for knee extension.

sion apart. A two-incision method (one posteromedial and the other posterolateral) is preferred and provides additional access to the collateral ligaments, which also may require release. If the knee still cannot be extended after posterior release, there also may be adhesions in the anterior compartment between the patella and the femur. A third incision can then be made medial to the patella to release these adhesions, which may act like a "rug under the door." Full correction at the time of surgery is avoided because the popliteal artery and nerve are usually tight, and a stretch injury may result. Soft-tissue releases and gradual extension by either cast hinges or external fixator may result in improved knee extension, but permanent improvement of the motion arc is rare. Because hypertension has been reported after gradual knee extension, careful blood pressure monitoring is recommended; if it becomes elevated, decreasing the extension usually will result in the pressure returning to normal, and gradual extension then can be initiated. An additional adjunct to posterior release can be a shortening osteotomy of the distal femur to decrease tension on the neurovascular bundle.

In recurrent contractures, extension supracondylar osteotomy with shortening of the femur allows immediate correction of the flexion deformity. By performing a posterior release at the same time, a smaller trapezoidal wedge osteotomy may be done. The osteotomy itself does not change the position of the joint and results in a dogleg-type deformity that may be cosmetically unacceptable (Fig. 4). Recurrence of the deformity occurs at a rate of about 1° per month in skeletally immature individuals.[28] The extension osteotomy may be a reasonable alternative in a skeletally mature individual with knee flexion deformities that prevent walking. However, the extended knee with limited flexion may reduce other abilities, such as sitting and getting in and out of a car. These limitations make a thorough discussion with and understanding by the patient and parents an essential part of preoperative planning.

Patients with knee extension contractures walk well but may have difficulty sitting and rising from a chair. Casting in young children can sometimes improve knee flexion. If the knee is fixed in hyperextension or anteriorly dislocated, a percutaneous release of the quadriceps tendon and casting may be attempted.[29] In general, however, formal quadricepsplasty or an open reduction of the knee is usually necessary. In older children, quadriceps tendon lengthening may improve the ability to flex the knee, but overzealous lengthening can result in later development of a knee flexion contracture.

Hips

External rotation contractures of the hips result in a rather prominent externally rotated gait. These contractures may increase the child's stability by widening the base of stance and generally should not be corrected. Hip flexion contractures are common, and dislocation occurs in 15% to 30% of patients.[8] Early stretching may provide limited improvement to mild contractures, but more severe contractures make walking difficult. Patients compensate for these hip flexion contractures with excessive lumbar lordosis. Those with contractures >45° should undergo surgical release, although patients with lesser degrees of contracture also may benefit.

The hip dislocations in these patients are generally teratologic (not reducible by gentle manipulation at birth). The results of closed reduction have been uniformly poor, often resulting in increased stiffness and redislocation. Because of these poor results, the physician may choose acceptance of the dislocation or open reduction from either an anterior or medial approach. Even with a well-performed open reduction, however, redislocation, stiff-

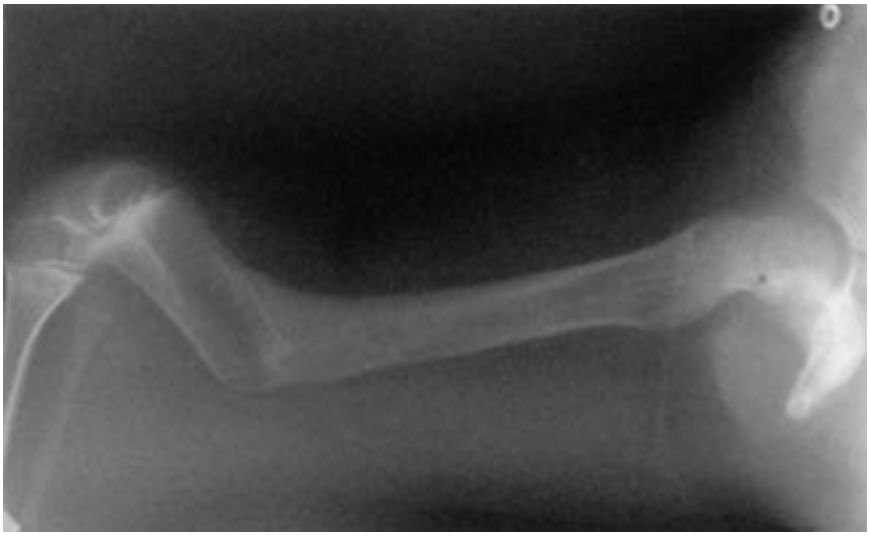

Figure 4 Lateral radiograph of a dogleg-type deformity after distal femoral extension osteotomy.

ness, and osteonecrosis are not unusual.[4,30] In unilateral dislocations, an open reduction should be performed with the patient between 6 months and 1 year of age. There should be a reasonable range of flexion and extension (at least 60°), and the child should have sufficient muscle power to actively move the lower extremities. The surgical approach often depends on surgeon preference. Although most surgeons are more familiar with the anterior approach, the best results have been reported with the medial approach.[4,30,31]

Treatment is more controversial in bilateral dislocations because the chance of obtaining two hips that remain reduced and supple is less likely. If the surgeon and family decide to proceed, bilateral dislocations can be treated by medial open reductions during the same procedure. A spica cast with the hips preferably in extension (although always in the most stable position) should be applied for 8 to 12 weeks. Because there is no evidence that dislocated hips prevent children from walking, a supple hip that is dislocated is preferable to a reduced but stiff hip.

Spine

Although spinal deformity at birth is uncommon, between 30% and 67% of patients will develop a scoliosis during childhood.[32] Therefore, inspection of the spine for the presence of deformity should be done regularly. The curves are usually quite stiff. A variety of patterns may be seen, and pelvic obliquity in the nonambulatory population is common. Curves are often progressive, with increases of up to 6.5° per year.[33] Early curve onset, paralytic curve pattern, and pelvic obliquity are considered signs of poor prognosis for progression. Most curves are resistant to bracing, although it may be attempted to delay surgery in very young children.

Surgical treatment should be considered based on curve progression, age of the patient, and imbalance. An anterior and posterior approach is often necessary for large or particularly stiff curves. Even with this combined approach, correction can be less satisfying than that obtained in an idiopathic patient. Generally, only about 35% correction can be expected from posterior fusion alone.[34] The addition of an anterior release, however, does not guarantee more correction. In a recent study,[32] the mean correction for patients undergoing a combined anterior and posterior procedure was only 44%. In addition, pseudarthrosis may occur in 15% to 30% of patients after posterior spinal fusion, so careful postoperative monitoring also is required.

Summary

Arthrogryposis is a group of unrelated disorders with the common phenotype of multiple congenital contractures. The terminology is confusing and continues to evolve, requiring critical evaluation when assessing published studies. Making a correct diagnosis to determine the natural history or evaluate results of intervention is very important. The etiology of arthrogryposis is multifactorial, and fetal akinesia appears to be a common element. Patients with amyoplasia, the most common type of arthrogryposis, are difficult to treat because of the frequency of contracture recurrence. The physician should inquire about the activities of daily living and pay particular attention to upper extremity function. When treating the lower extremity, an approach dealing with the most distal deformities first, then moving in a proximal direction, is recommended. Children with these disorders usually are bright and motivated, and small improvements in their physical condition may lead to substantial functional improvements.

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