Arthrogryposis

The term arthrogryposis, otherwise known as arthrogryposis multiplex congenital or AMC, refers to a diverse number of non-progressive conditions at birth that are characterized by multiple joint contractures and muscle weakness throughout the body. Arthrogryposis is not generally considered to be a specific disease, but rather it is considered more of a symptom complex or description of clinical findings that is characterized by multiple contractures involving more than one area of the body. 1,2 The name for this condition, arthrogryposis, is derived from the Greek words “arthro” – which means “joint” or pertaining to the joints and connecting bone structures – and “gryp-, gryps,” which means “crooked, hooked, curved, or rounded,” and it is described as “congenita” because it is present in individuals from birth. Its name thereby provides a fairly accurate description of the appearance of individuals born with arthrogryposis, as their joints are characterized by evident malformation or dislocation (See Figure 1). When left untreated, arthrogryposis can be an extremely debilitating condition that may limit individuals for their entire lives, but with proper management from a multidisciplinary team of doctors, physical therapists, and counselors, individuals can often live independent and successful lives1.

In the United States, arthrogryposis is a condition that affects one in every three thousand live births.1 This number in and of itself is difficult to quantify, but to put it in more meaningful terms, there are nearly four babies born each day with arthrogryposis in the United States3. The life span of individuals with arthrogryposis depends upon the severity of the syndrome along with any associated conditions, but often it is normal1. There does not appear to be any racial or ethnic tendency towards arthrogryposis, and females and males are generally equally affected except when as a result of an X-linked recessive condition1. However, the etiology of arthrogryposis is multifactorial in that there is not a single known cause of the disorder. Instead, it can be caused by any number of conditions, including genetic disorders, or environmental causes that may affect the central or peripheral nervous system, the connective tissue, or vascular supply4. There are two very general types or categories of arthrogryposis: distal arthrogryposis – sometimes known as Type 1 arthrogryposis, – and amyoplasia. Distal arthrogryposis makes up more than half of the known cases of arthrogryposis in the United States, and it is thought to almost always be an autosomal dominantly inherited mutation. 1,4,5 So named because it typically affects the peripheral joints, particularly the feet and hands, distal arthrogryposis and its specific etiology is not yet fully understood. One of the theorized mechanisms for this condition suggests that when the mutated gene is expressed, it affects the sarcomeric protein genes and causes the muscles to form incorrectly6. Because bones and joints rely on normal muscle forces and connective tissue forces in order to develop and form appropriately, the affected fetuses ultimately have malformation and contractures of their joints6. However, this is still just a theory, as clinical findings tend to be highly variable with fluctuating penetrance and expression in the cases that have been studied6. In addition, different mutations on X-linked recessive genes as well as autosomal recessive genes have been found in cases that present with the same clinical syndrome, indicating that although there is likely a large genetic component to the presentation of distal arthrogryposis, it has a great deal of genetic heterogeneity. 1,6

The second general type or category of arthrogryposis is known as amyoplasia. From the Greek words “amyo” meaning “no muscle” and “plasis” meaning “molding, formation”, amyoplasia is typically associated with motor neuron dysfunction, and it is believed to comprise about 43% of reported cases of arthrogryposis. 1,4 The Greek meaning of the name “amyoplasia” as “no muscle formation” is appropriate given that children born with the condition have extremely diminished muscle bulk in their extremities4. However, like the distal arthrogryposis type, there is not a great deal known about the specific etiology of amyoplasia, although some researchers believe that most of these cases are sporadic without a genetic link1. However, one known factor that is a major contributor to the presentation of either type of arthrogryposis (but particularly amyoplasia given the lack of muscle bulk present) is “fetal akinesia,” or decreased fetal motion in utero. 1,4 Early in development, movement is crucial for the correct development of the joint and surround soft tissue structures. Any lack or significant decrease in fetal movement may lead to malformation of the bony joint structures along with development of extra connective tissue, leading to a stiff, immobile joint1. As in most musculoskeletal conditions, the longer the immobility, the worse the contracture of the joint and surrounding tissue, and since fetuses are more or less trapped for an average of nine months, infants who have fetal akinesia are typically on the more severe end of the spectrum for arthrogryposis4.

Although fetal akinesia may certainly contribute to arthrogryposis, it alone is not a sufficient etiology, especially in light of the fact that amyoplasia is not believed to have a clear genetic link1. Rather, researchers believe that in many cases arthrogryposis may be a result of any number of intrinsic or extrinsic causes1. The intrinsic causes are generally fairly straightforward. Along with genetics, they include conditions of the fetus itself that lead to arthrogryposis, such as neurological malformation of the spinal cord or areas within the brain that lead to abnormal development, connective tissue disorders that affect joint formation, etc1. The extrinsic causes are a bit more complicated, and a great deal of research has gone into investigating these potential causes. Some of the suggested extrinsic causes of arthrogryposis from the late twentieth century included insufficient room or abnormal shape of the maternal uterus, low amniotic fluid, maternal infection or drug use, and trauma1. It was thought that arthrogryposis could potentially be attributed to the mother, whether it was her own body’s shape and health or her decisions during pregnancy. However, a study that was conducted from 1978 to 2012 found that over the course of 35 years, only 1.3% of the identified cases of arthrogryposis even presented with maternal uterine structural anomalies, leading researchers to conclude that, if anything, it is a very rare primary cause of arthrogryposis7. Likewise, another study found that there was “no evidence to support the suggestion that arthrogryposis is frequently a result of environmental or structural causes including uterine structural anomaly, intra-uterine infection, etc.” 5(p.10) These authors found that among over eight hundred cases of arthrogryposis, there were “normal frequencies of bleeding, hormone treatment during gestation, amniotic fluid leakage, uterine anomaly, maternal illness, and maternal and paternal age”, suggesting that these factors were not responsible – at least not solely – for the presentation of arthrogryposis5. However, the researchers did find that the frequency of polyhydramnios – or too much amniotic fluid surrounding a fetus – was dramatically increased among the cases of arthrogryposis where infants did not survive, leading them to conclude that polyhydramnios appeared to be an indicator of a poor prognosis when associated with fetal akinesia5. Other studies investigating possible extrinsic causes of arthrogryposis include a review of three case studies from 1996 in which there were failed terminations of pregnancy and the children were subsequently born with arthrogryposis. The researcher posited that the presentation of arthrogryposis was “due to vascular compromise during the attempted termination with secondary loss of functional neurons leading to fetal akinesia and subsequent contractures.”8(p.297) It was also thought that the contractures might have additionally been compounded by an limitation of movement from the rupture of the fetal membranes8. The same author conducted a follow-up study that supported this correlation between failed termination of pregnancy and infants born with arthrogryposis in 2012, finding that infants who survived the attempted termination – whether surgical or pharmaceutical – were at increased risk to be born with arthrogryposis along with a greater than fifty percent change of having intellectual disability9. This appears to be specific to the correlation with termination of pregnancy given that the majority of individuals with arthrogryposis tend to flourish with an average or above average intellect1.

Although these theorized intrinsic and extrinsic etiologies and genetic mutations are often used to label which of the types of arthrogryposis an individual may have, there are no significant differences among the clinical characteristics, and there is “substantial overlap” between them10. The resultant arthrogryposis usually looks the same due to overlapping conditions between sporadic, neurogenic, myopathic, and genetic etiologies, and so the signs and symptoms of arthrogryposis remain objectively universal4. In general, arthrogryposis affects all four extremities and major peripheral joints, including hands, wrists, elbows, shoulders, hips, feet, and knees1. Distal arthrogryposis may have more hand and foot involvement, and very severe cases of arthrogryposis may affect additional joints such as the spine and jaw1. Joint involvement is most clearly noted by the presence of certain postures, some of which may be somewhat typical in infants – like holding thumbs tucked into the palms of hands in a fist, and some are clearly abnormal – like knee extension with dislocation1. Some of the most frequently seen postures in the lower extremities of infants with arthrogryposis include hips that are flexed, abducted, and external rotation, often with dislocation and knees that are either flexed or extended, usually with foot deformities such as clubfoot or vertical talus1. Postures of the upper extremity tend to be more variable but include internal shoulder rotation, elbows extended, though they may be sometimes flexed, with forearm pronation, wrist flexion, ulnar deviation, finger flexion, and thumbs tucked into palms1 (See Figures 1 and 2). In addition, infants born with arthrogryposis often have very thin and atrophied arms and legs and the skin around their joints do not have the flexion creases one would typically see on babies1. Although there may be additional problems associated with arthrogryposis such as scoliosis, respiratory issues, facial conditions, and abdominal hernias, these are not very common1. Babies who have arthrogryposis are often in breech position due to the fact that they are unable to kick and rotate into the proper position prior to delivery, so oftentimes these babies are scheduled to be delivered by cesarean section if a diagnosis of arthrogryposis has already been made1.

The actual diagnostic assessment for arthrogryposis may happen either at birth based upon the appearance of the baby’s limbs and joints or it may be found while the baby is still in utero via ultrasound. Arthrogryposis may be detected if any sort of abnormal limb appearance or significant lack or change of fetal movement is noted during a routine ultrasound1. However, a definitive diagnosis may not be possible until further tests are run. Oftentimes doctors will take blood in order to examine it for abnormalities or genetic mutations, and frequently muscle biopsies are performed in order to determine a cause or rule out certain conditions1. Whether an infant has been diagnosed in utero or if arthrogryposis is suspected after birth, postnatal evaluations by pediatric specialists are crucial in order to get an accurate diagnosis.2 These doctors will usually complete a thorough investigation of the pregnancy history along with examination of clinical findings in utero and following birth, and they can provide information, counseling, and education to parents and caregivers2.

Once a diagnosis is made for an infant with arthrogryposis, it is important that the baby have routine doctors appointments in order to ensure adequate nutrition and growth, particularly if there were any complications over the course of the pregnancy or during delivery. However, after the baby is medically stable, treatment for arthrogryposis is primarily based in physical therapy1. Although there is no outright cure for arthrogryposis, functionality, independence, and quality of life can be greatly improved through physical therapy along with comprehensive multi-disciplinary treatment that includes psychosocial support for confidence and motivation, nutrition, and possibly surgery1. Physical therapy may initially treat very severe cases of arthrogryposis with stretching, casting, strengthening, and mobility training in order to improve range of motion and help a child become more independent, but sometimes it is not enough and surgery is required1. Surgery may range from something as simple as an Achilles tendon release to complex procedures like limb lengthening and spinal surgery1. However, it is usually treated as a type of last resort following extensive physical therapy.

Physical therapy treatment for arthrogryposis may look different for different individuals given the severity of the case and the age of the patient. In infants and very young children, interventions and rehabilitation are started early – as soon as the infant is medically stable – and are intensive in order to address problems and prevent future deficits10. Usually, a multidisciplinary team comprised of a pediatrician, orthopedist, and physical therapist treats infants and young children with arthrogryposis. 1,10 Imaging may be done via radiography or ultrasound in order to minimize diagnostic errors and in order to get an idea of what corrective treatments may be most appropriate for positioning joints whether casting or surgery10. In most infants with arthrogryposis, physical therapy will have two major aims: to improve range of motion and functionalityin the joints and to help stimulate movement and neurological development10. Techniques to increase the mobility of the joints may include massage and passive stretching, mobilization of articular joints, kinesiotaping of wrist/hand, and mobilization and treatment for clubfeet10. Physical therapy interventions in order to help stimulate cognitive development may include positional therapy, stimulation of sensory and proprioceptive systems, and reflexes stimulation10. Casting or bracing may be used to correct joints, and intensive physical therapy with daily exercises continued by parents provides an opportunity to improve range of motion and reduce the need for “radical invasive corrections”10,11,12. Usually, isolated hip contractures can be managed conservatively, and an extensive program of bracing and physical therapy may allow for future functional ambulation in children12. Nevertheless, about 76% of patients with arthrogryposis affecting the feet, 39% with knees affected, and 18% with hips affected require surgical correction10. These surgical procedures may include soft tissue release, tendon release, femoral shortening-extension osteotomy, gradual correction with Ilizarov or other equipment, etc.11 Despite the high rate of surgeries required to correct joint and limb contractures, the fact that children with arthrogryposis tend to have normal speech and learning capabilities improves their prognosis because they are able to learn self-care and become independent with at least some aspects of their treatment1. One of the major goals for small children with arthrogryposis is that of functional ambulation, although certain individuals may have improved ambulatory potential than others. 11,12 In general, hyperextension deformities such as anterior subluxation and dislocation or recurvatum tend to have a better prognosis for walking ability than individuals with knee flexion contractures.11,16 Likewise, extreme muscular weakness in the lower extremity and involvement of the upper extremities makes the prognosis for ambulation less likely12. Nevertheless, with proper medical care and vigorous therapy, the potential for leading productive, rewarding, and independent lives is very good. And although specific physical therapy interventions for infants and young children with arthrogryposis may vary, the overarching theme stresses the earliest possible initiation of corrective action for improving mobility and functionality and having a positive prognosis.

In older children, adolescents, and adults, treatment for arthrogryposis is slightly different. Although there remains a focus on joint mobility and overall functional independence, there are fewer options once individuals get larger and are no longer growing13. Casting, bracing, and surgical interventions are most often successful in younger children10, and so school-aged kids most often are learning compensation for any remaining deficits. Physical therapy is still extremely important in order to aid in learning ambulation and other functional mobility skills, maintaining joint mobility and reducing contractures in children who are unable to be as active, and providing equipment and positioning for non-ambulators.10,11 However, despite the fact that arthrogryposis is not a progressive disorder, by adolescence physical therapy and functional interventions are geared more towards management and maintaining a healthy, active lifestyle, and information about rehabilitation programs for adolescents and adults with arthrogryposis are extremely rare1,13. Nevertheless, one case study looked into the results of a thirty five year old woman with arthrogryposis who had never received treatment and ended up receiving surgery along with an Ilizarov eternal fixator for her hip13. She underwent one physical therapy session a week for 15 weeks following removal of the Ilizarov in order to correct contractures and allow her to stand upright and walk with assistive device13. The researchers indicated that the treatment was successful and the patient was able to walk average distances with an adapted reciprocating walker and Canadian crutches, although they did not indicate what interventions were included13. Given this case, adults who have not been treated for their arthrogryposis may be able to show significant improvements in function and mobility, but the most consistently positive prognoses come from early and intensive interventions with young children. 10,13

While arthrogryposis is overall a fairly manageable disorder with good outcomes, there are some complications that may accompany it. Very recent studies have shown that some children with arthrogryposis experience dysfunctional voiding including urinary incontinence, a history of urinary tract infections, and altered renal function due to changes in the neurogenic bladder. However, researchers have not yet been able to pinpoint what causes these changes, and further study is necessary14. In addition, rapidly progressive scoliosis is common in children with arthrogryposis, with the most common curvature of the spine from T5 to L28. However, rib distraction with a Vertical Expandable Prosthetic Titanium Rib, or VEPTR, has been shown to be a fairly successful treatment for controlling scoliosis and kyphosis (beyond the standard scoliosis surgical treatment) while maintaining the child’s thoracic growth15.

Arthrogryposis multiplex congenital (along with being a bit of mouthful to say) is surprisingly common given how rarely it’s addressed in physical therapy education. However, although arthrogryposis can cause severe motor dysfunction and impose limitations on many different life experiences, early planning and correcting of deformities with a multi-disciplinary medical team along with physical therapy to enable improved joint mobility and function allows the greatest opportunity for individuals to live rewarding, independent lives.

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Figure 1. Three-day old infant with severe arthrogryposis.

Image credit: Binkiewicz-Glinska et al. (2013). Accessed December 1, 2014 from <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3833971/>.

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Figure 2. Images A and B show show extended elbows, pronated forearms, and flexed wrists and fingers in an infant with arthrogryposis. Image C of another baby with arthrogryposis shows bilateral hip dislocations and clubfeet.

Image credit: *Indian J Radiol Imaging.* Aug 2010; 20(3): 174–181. doi:10.4103/0971-3026.69349. Accessed December 1, 2014 from <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2963757/figure/F0015/>.

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