Introduction: Extremities
This SMFM Consult Series focuses on the extremities. Malformations that involve the extremities are seen frequently on ultrasound images and can be isolated or associated with other anomalies. The fetal extremities are an integral part of the fetal anatomic survey, and detection of skeletal anomalies is a key component of prenatal diagnosis. The basic anatomic survey (CPT 76805) requires documentation only of the presence of arms and legs. A detailed anatomic survey (CPT 76811) requires documenting the number, architecture, and position of the arms, legs, hands, feet, and digits. Systematic examination of the extremities should include a review of absence or hypoplasia of individual bones along with an assessment for bowing, fractures, abnormal ossification, or evidence of abnormal symmetry (eg, discrepant femur diaphysis lengths). If abnormalities of the extremities are suspected, these findings should be correlated with other anatomic structures or biometry (eg, spine, skull, thorax) for the possibility of skeletal dysplasia or specific genetic syndromes.

The long bones should be examined in the sagittal view, and images should include bilateral views of the femur, humerus, radius, ulna, tibia, and fibula (Figure 1). The femur and humerus diaphysis lengths are measured optimally with the beam of insonation perpendicular to the shaft, excluding the distal epiphyses. Coronal views of the arms and legs, at the level of the hands and feet, should allow verification of hand/foot positions and their relationship to the long bones (ie, normal positioning of the ankle and wrist; Figure 2). If technically feasible, a plantar view of the feet should also be documented. Hand and foot digits should be counted, typically in a transverse (axial) or coronal view (Figure 3). Suspected abnormalities of joint movement should be documented, although the examiner should be cautious of any transient positions that could mimic a pathologic condition. Three-dimensional ultrasound imaging can sometimes be helpful in demonstrating anomalies of the extremities. Nomograms are available for various biometric measurements.

If a limb abnormality has been detected and a search for other abnormalities has been completed, the patient should be counseled about the clinical significance of the findings, prognosis, and other considerations for pregnancy management. Genetic counseling and options for diagnostic genetic testing should be offered. A multidisciplinary team should be convened to discuss postnatal surgery, genetic evaluation, and physical therapy support, if necessary.

This series reviews the sonographic diagnosis, genetic evaluation, and potential treatment and outcome of the following abnormalities that affect the fetal extremities:

- Amniotic band sequence
- Arthrogryposis

The practice of medicine continues to evolve, and individual circumstances will vary. This opinion reflects information available at the time of its submission for publication and is neither designed nor intended to establish an exclusive standard of perinatal care. This presentation is not expected to reflect the opinions of all members of the Society for Maternal-Fetal Medicine (SMFM). Reprints will not be available.

All authors and Committee members have filed a conflict of interest disclosure delineating personal, professional, and/or business interests that might be perceived as a real or potential conflict of interest in relation to this publication. Any conflicts have been resolved through a process approved by the Executive Board. The Society for Maternal-Fetal Medicine has neither solicited nor accepted any commercial involvement in the development of the content of this publication.

This document has undergone an internal peer review through a multilevel committee process within SMFM. This review involves critique and feedback from the SMFM Publications and Document Review Committees and final approval by the SMFM Executive Committee. SMFM accepts sole responsibility for document content. SMFM publications do not undergo editorial and peer review by the American Journal of Obstetrics & Gynecology. The SMFM Publications Committee reviews publications every 18-24 months and issues updates as needed. Further details regarding SMFM Publications can be found at www.smfm.org/publications. All questions or comments regarding the document should be referred to the SMFM Publications Committee at pubs@smfm.org.
When coding for isolated fetal extremity abnormalities (for example, radial ray malformation, polydactyly, clubfoot) the SMFM Coding Committee recommends using the International Classification of Diseases—10 code series O35.8xx0–O35.8xx9 (non-central nervous system fetal malformation). When coding for fetal extremity abnormalities with higher suspicion for chromosomal or genetic syndromes, the International Classification of Diseases—10 code series O35.1xx0–O35.8xx9 may be used as well.

**ACKNOWLEDGMENTS**

The authors wish to acknowledge Mary E. Norton, MD, Jeffrey A. Kuller, MD, and Angie C. Jelin, MD, for providing a review of the genetics content and Joseph Wax, MD, for providing a general review of the content of this Consult.

**REFERENCES**

FIGURE 2
Hand and foot positions

A, Normal positioning of the wrist; B, normal positioning of the ankle.

FIGURE 3
Digits

A, Normal hand; B, normal foot.
Amniotic Band Sequence

Society for Maternal-Fetal Medicine; Manisha Gandhi, MD; Martha W. F. Rac, MD; Jennifer McKinney, MD

**Introduction**

Amniotic band sequence results from in utero entrapment of fetal parts by fibrous bands, which leads to a collection of malformations that can affect multiple organ systems.\(^1\)\(^-\)\(^3\)

There is typically an asymmetric distribution of these defects; the most common manifestations involve limb deformities.\(^4\) The cause of amniotic band sequence is unclear and has been ascribed to both intrinsic and extrinsic factors.\(^1\),\(^2\),\(^5\) The intrinsic model suggests that formation of amniotic bands and resultant anomalies are due to disruption of the developing embryonic disk; the extrinsic model, which is accepted more widely, suggests a sequence mechanism of disruption of the amnion that leads to the entanglement of fetal structures by mesodermic bands.\(^2\),\(^5\) In most cases, the cause is unknown, and there are no commonly accepted risk factors. The severity of amniotic band sequence varies from relatively minor to being lethal to the fetus. The incidence varies from 1 in 1200 to 1 in 15,000 live births.\(^6\)

**Definition**

Amniotic band sequence is a collection of fetal malformations that are associated with fibrous bands that entangle or entrap various fetal parts in utero.\(^1\)

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**Ultrasound Findings**

A constellation of multiple fetal abnormalities, particularly asymmetric limb and digital amputations and constrictions, should make one suspect amniotic band sequence. Defects can be isolated or multiple and usually do not follow a specific pattern.\(^4\) The following ultrasound findings are characteristic of amniotic band sequence:

- Bands in amniotic fluid appear as thin echogenic strands attached to the defect and usually connect to the uterine wall. It is important to note that visualization of bands is not required to suggest the diagnosis.\(^1\),\(^4\) Random anomalies that do not follow a pattern should lead to suspicion for amniotic band sequence (Figure 1).
- Constriction ring defects of the extremities typically are present.\(^1\),\(^7\),\(^8\) These usually involve fingers or toes with or without edema of a distal extremity.\(^4\) These constriction rings can lead to amputation of limbs or digits and the appearance of syndactyly on ultrasound imaging (pseudosyndactyly) [Figure 2].
- Craniofacial deformities can include single orbital involvement, severe clefts that do not conform to a pattern of developmental clefts, severe nasal deformity, or asymmetric encephaloceles.\(^1\),\(^4\),\(^9\),\(^10\)

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**FIGURE 1**

Amniotic bands attached to fetal torso

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**FIGURE 2**

Amniotic band that involves the upper extremities

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microarray analysis may be considered.

If an unusual distribution of defects raises suspicion for amniotic band sequence, one should look carefully for bands and scan in various maternal positions to see if the fetus stays in a fixed position or if bands restrict certain movements. Occasionally, fetal movement can help reveal amniotic bands.

**Associated Abnormalities**

It is important to evaluate all organ systems because there can be limb, craniofacial, or body wall abnormalities as described earlier. Diagnostic accuracy relies on the ability to connect all sonographically visualized abnormalities to a direct disruption from the amniotic bands.

**Differential Diagnosis**

The differential diagnosis depends on the type of anomalies and the type of amniotic disruption that is seen. The differential includes the following conditions:

- **Body stalk anomaly:** Fetal abdominal wall adherent to placenta, short umbilical cord, no cranial or limb defects, no evidence of fibrous bands
- **Specific craniofacial defects or abdominal wall defects:** Typically isolated and can cause specific functional abnormalities that are associated with embryologic development
- **Amniotic sheets:** Amnion wrapped around synecchiae and a structurally normal, mobile fetus; importantly, amniotic band sequence should not be diagnosed in the absence of fetal abnormalities.
- **Chorion-amnion separation:** No entrapment of fetal parts, no associated bands

**Genetic Evaluation**

Genetic evaluation in the setting of amniotic band sequence is not typically recommended. These cases are generally sporadic with no family history and no increased risk or incidence based on race or sex.

Although a few familial cases have been reported, almost all cases are sporadic with no identified underlying genetic cause. If the diagnosis of amniotic band sequence is uncertain, chromosomal microarray analysis may be considered.

**Pregnancy and Delivery Management**

A detailed ultrasound examination is recommended to identify the extent of the abnormalities. Pregnancy termination is an option that should be discussed with all patients in whom a fetal anomaly is detected. Fetoscopic in utero lysis of bands is an investigational approach that has been reported to have favorable outcomes for extremities at risk because of constriction bands, although this procedure is associated with an increased risk of premature rupture of membranes and preterm birth. Assessment of arterial and venous flow across constriction bands in the extremities detected with Doppler imaging has been reported to be possible and potentially useful, although experience and data are limited. Antenatal surveillance is appropriate in some cases, including if fetal growth restriction is present. Mode of delivery should be based on the usual obstetric indications, and site of delivery should be based on the severity and type of anomalies.

**Prognosis**

The prognosis is widely variable and depends on the severity and extent of the findings.

**Summary**

Amniotic band syndrome can vary in severity, depending on the organ systems that are affected; findings are typically asymmetric in distribution. The limbs are affected most commonly, and investigational fetal interventions have been reported. Patients can be reassured that recurrence is rare.

**REFERENCES**

Arthrogryposis

Society for Maternal-Fetal Medicine; Martha W. F. Rac, MD; Jennifer McKinney, MD; Manisha Gandhi, MD

Introduction
Arthrogryposis or arthrogryposis multiplex congenita describes joint contractures in two or more areas of the body and is present in 1 in 3000 live births. It is usually a feature of abnormal neurologic development or primary muscular disorders of the fetus. More than 400 conditions are associated with this finding, which makes a specific prenatal diagnosis challenging.

Definition
Fetal arthrogryposis detected with prenatal ultrasound imaging is defined as ≥2 joint contractures in >1 body area. Arthrogryposis is not a specific diagnosis but rather is a descriptive term for multiple contractures that can be associated with many different medical conditions.

Ultrasound Findings
Arthrogryposis is a clinical finding caused by a lack of fetal movement (fetal akinesia). The severity of arthrogryposis is related directly to the duration of decreased fetal movement. Characteristic ultrasound findings include flexion abnormalities of both the proximal and distal joints (Figure 1); these are usually seen with decreased or absent movement of the affected extremity. In addition to the extremities, the jaw, spine, and fetal neck can also be involved; attention should be paid to the mobility of these joints as well. Hypomineralization of the long bones has been reported.

Joint contractures usually do not become evident until the second trimester. First-trimester ultrasound findings can include increased nuchal translucency and cystic hygroma. A high index of suspicion is necessary because the diagnosis of arthrogryposis is difficult. In one series, almost 75% of cases were missed on prenatal ultrasound imaging. When arthrogryposis is suspected, a detailed ultrasound examination should be performed to detect other abnormalities that may give insight into the underlying cause and guide patient counseling. Three-dimensional ultrasound imaging sometimes can provide more detailed information about the affected extremity (Figure 2). With multiple abnormalities, especially if central nervous system abnormalities are suspected, magnetic resonance imaging may provide additional information regarding prognosis.

Associated Abnormalities
Abnormalities in every organ system have been reported in association with arthrogryposis. An increased nuchal translucency and cystic hygroma have been reported in the first trimester and may indicate lethal forms of arthrogryposis. Central nervous system abnormalities that have
been reported with arthrogryposis include cerebral and cerebellar hypoplasia, ventriculomegaly, and holoprosencephaly. Gastroschisis and bowel atresia can be seen in primary myopathies. Polyhydramnios is often present and results from decreased fetal swallowing. Micrognathia, cleft palate, hypertelorism, fetal growth restriction, pulmonary hypoplasia, and mildly shortened long bones comprise the phenotype known as fetal akinesia sequence or Pena-Shokeir phenotype. Osteoporosis from lack of fetal movement occurs most frequently in the fetal long bones and can predispose to fractures, usually at the time of delivery.

**Differential Diagnosis**

The differential diagnosis of arthrogryposis is extensive. More than 400 conditions are characterized by this finding, and the features and severity can vary dramatically. Genetic patterns of inheritance vary from single-gene disorders to chromosomal abnormalities, such as trisomy 18. Arthrogryposis may be inherited as an autosomal recessive, autosomal dominant, or X-linked trait, and some cases are thought to have multifactorial inheritance, with both genetic and environmental factors. Maternal infections (e.g., rubella, Zika, and Coxsackievirus) and environmental factors have also been associated with arthrogryposis; therefore, obtaining a history of maternal exposures and a family history is important. Witters et al. reported a specific diagnosis in only 53% of cases using prenatal information and fetopathologic specimens.

**Genetic Evaluation**

Genetic variants, duplications, deletions, and chromosomal abnormalities are found in approximately 30% of cases of arthrogryposis. Diagnostic testing (amniocentesis or chorionic villus sampling) with chromosomal microarray analysis (CMA) should be offered when arthrogryposis is detected. Karyotype analysis or fluorescence in situ hybridization with reflex to CMA may be reasonable if a common aneuploidy is suspected. Gene panel testing or exome sequencing may be useful because CMA does not detect single-gene (Mendelian) disorders; more than 350 gene variants have been reported to cause different types of arthrogryposis. Testing for spinal muscular atrophy and congenital myotonic dystrophy in particular should be considered. If exome sequencing is pursued, appropriate pretest and posttest genetic counseling by a provider experienced in the complexities of genomic sequencing is recommended. If the pregnancy ends in a stillbirth or neonatal death, an autopsy should be offered. After appropriate counseling, cell-free DNA screening is an option for patients who decline diagnostic testing, although it is likely to have a low diagnostic yield because aneuploidy causes only a small number of cases.

**Pregnancy and Delivery Management**

A detailed ultrasound examination should be performed and should include comprehensive imaging of the intracranial structures (e.g., a neurosonogram) and the fetal heart. A fetal echocardiogram and fetal magnetic resonance imaging to assess for intracranial abnormalities should be considered if cardiac or central nervous system abnormalities are suspected or with other clinical indications (e.g., enlarged nuchal translucency). Testing for maternal viral infections should be considered, including rubella, Zika, and Coxsackievirus, if risk factors are present. Referrals to pediatric neurology, orthopedics, and neonatology should be considered.
termination is an option that should be discussed with all patients in whom a fetal anomaly is detected. Shared patient decision-making requires thorough evaluation and multidisciplinary counseling regarding prognosis. The specific finding of arthrogryposis generally does not affect delivery management, although delivery at a tertiary care center with pediatric genetics, neurology, and orthopedic consultation may be considered to be appropriate for the clinical findings. If the jaw or cervical spine is suspected to be involved, a multidisciplinary approach and the involvement of neonatology, anesthesiology, and potentially otolaryngology services to assure airway access at birth may be required.

**Prognosis**
The prognosis of arthrogryposis depends on the underlying cause, the extent of the contractures, and associated abnormalities. In some cases, the contractures can improve with postnatal treatment, and early physiotherapy and orthopedic intervention are recommended to help with joint motility. Some infants who are born with arthrogryposis will have a good outcome, although the prognosis is dependent on the underlying cause.

**Summary**
Arthrogryposis or arthrogryposis multiplex congenita is defined as ≥2 joint contractures in >1 body area and is present in 1 in 3000 live births.1 It is usually a marker for abnormal neurologic development or primary muscular disorders of the fetus. When suspected, a detailed ultrasound examination should be performed to detect other abnormalities that may give insight into the underlying cause and guide patient counseling. Because more than 400 conditions are associated with this finding,2 genetic counseling should be offered. Mode of delivery should be based on usual obstetric indications. The prognosis will depend on the underlying cause; however, with the appropriate physiotherapy and orthopedic intervention, many infants with isolated arthrogryposis have a good outcome. 

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Congenital talipes equinovarus (clubfoot)

Introduction
Congenital talipes equinovarus (clubfoot) is one of the most common congenital malformations; it affects 1–3 in 1000 live births and occurs twice as often in male fetuses.1,2 It can be unilateral (30–40%) or bilateral (60–70%) and can be either an isolated malformation (50–70%) or complex and associated with other structural or genetic anomalies (30–50%).2-7

Definition
Clubfoot is a structural deformity of the foot and ankle with hindfoot equinus (plantar flexion), varus of the heel (inward rotation), supination, and adduction of the forefoot (plantar cavus).8

Ultrasound Findings
A diagnosis of clubfoot can be made as early as 13 weeks of gestation; 85% of diagnoses are made between 13 and 23 weeks of gestation.2,7,9 Before 13 weeks of gestation, a transient clubfoot position can be present as part of normal development.10 To diagnose clubfoot, one must visualize both the tibia and fibula in the same plane as the sole of the foot (Figures 1 and 2). Abnormal positioning persists over the duration of the scan.2,11 It is important to visualize the foot away from the uterine wall to avoid the false appearance of a clubfoot from fetal positioning. In all, 70–75% of isolated cases are confirmed at delivery, with a reported false-positive rate of 10–20%; 5–13% are confirmed as complex postnatally.2,12,13

Associated Abnormalities
Depending on the cause, there are numerous possible associated anomalies. The most frequent anomalies include central nervous system and spinal anomalies (52%), other musculoskeletal anomalies (28%), and thoracic anomalies (12%).7

Differential Diagnosis
The differential diagnosis of clubfoot is extensive. Clubfoot can be caused by both extrinsic and intrinsic causes. Extrinsic factors that can affect fetal foot position in utero include oligohydramnios, breech presentation, Müllerian anomalies, multiple gestation, amniotic band sequence, or amniocentesis at <15 weeks of gestation.1,2,11,13,14

Intrinsic factors (8,13,15-17) include the following causes:
- Chromosome abnormalities (30% complex, 2% isolated), including trisomy 18, 13, 21; 4p, 18q, and 22q11.2 deletion syndromes; sex chromosome abnormalities; microdeletions; or duplications3,13,18,19

FIGURE 1
Clubfoot

Coronal view shows the long axis of foot in the same plane as the tibia/fibula.

Genetic syndromes such as Larsen; Gordon; Pierre-Robin; Pena-Shokeir; Meckel-Gruber; Smith-Lemli-Opitz; Roberts; TARP (talipes equinovarus, atrial septal defect, Robin sequence, persistence of left superior vena cava); and Lambert, among others.

Skeletal dysplasias such as Ellis van Creveld syndrome, diastrophic dysplasia, chondrodysplasia punctata, camptomelic dysplasia, atelosteogenesis, and mesomelic dysplasia.

Neuromuscular conditions that include arthrogryposis multiplex congenita, myotonic dystrophy, and spinal muscular atrophy.

Other neurologic abnormalities such as neural tube defects, holoprosencephaly, and hydranencephaly.

Genetic Evaluation
Diagnostic testing (amniocentesis or chorionic villus sampling) with chromosomal microarray analysis (CMA) should be offered when a club foot is detected. If ultrasound findings or screening test results are suggestive of a common aneuploidy, it is reasonable initially to perform karyotype analysis or fluorescence in situ hybridization, with reflex to CMA if these test results are normal. If there are additional anomalies, consanguinity, or a family history of a specific condition, gene panel testing or exome sequencing may be useful because CMA does not detect single-gene (Mendelian) disorders. If exome sequencing is pursued, appropriate pretest and posttest genetic counseling by a provider who is experienced in the complexities of genomic sequencing is recommended. After appropriate counseling, cell-free DNA screening is an option for patients who decline diagnostic evaluation if a common aneuploidy is suspected.

Pregnancy and Delivery Management
A detailed ultrasound examination should be performed with attention to other joints to assess for arthrogryposis multiplex congenita. Examination should also include comprehensive imaging of the intracranial structures (eg, a neurosonogram) and the fetal heart. A fetal echocardiogram and fetal magnetic resonance imaging should be considered if cardiac or central nervous system abnormalities or a syndromic cause is suspected. Magnetic resonance imaging has been reported to improve the detection of associated anomalies in complex, but not isolated, cases. Pregnancy termination is an option that should be discussed with all patients in whom a fetal anomaly is detected. Shared patient decision-making requires a thorough evaluation and multidisciplinary counseling regarding prognosis. The specific finding of clubfoot does not generally affect delivery management, although delivery at a tertiary care center with pediatric genetic and orthopedic surgery consultation may be appropriate with additional clinical findings. Management of complex cases depends on the constellation of anomalies. Mode of delivery is based on usual obstetric indications.

Prognosis
The prognosis depends on associated conditions but is generally excellent for isolated clubfoot. Perinatal death and neurodevelopmental and musculoskeletal issues are more likely with complex cases. Families should be referred to pediatric orthopedics for evaluation for postnatal treatment. The current usual approach to therapy is the Ponseti method, which involves foot manipulation, serial casting, bracing, and monitoring for and treatment of relapse if it occurs. Estimates for cases that require postnatal surgical intervention...
have been reported to range from 12–50%, although surgical treatment has been decreasing with time.\textsuperscript{2,5,22}

**Summary**

Clubfoot is a common congenital malformation of the foot and ankle. It can involve one or both feet and can be an isolated finding or associated with other anomalies. Diagnosis should include a detailed ultrasound examination to look for associated anomalies and genetic counseling and diagnostic testing. Timing and route for labor and delivery are not altered for isolated cases. Prognosis depends on associated conditions and underlying genetic abnormalities, but the majority of cases can be corrected with manipulation and serial casting postnatally.

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Polydactyly

Introduction
Polydactyly is a condition in which one or more extra digits are present. The extra digit can be located on the ulnar or fibular side of the extremity (postaxial), the radial or tibial side of the extremity (preaxial), or centrally.\textsuperscript{1,2} Polydactyly is more common in black infants than white infants and is more frequent in male infants than female infants.\textsuperscript{3} Although most cases are isolated, polydactyly is associated with more than 100 genetic syndromes.\textsuperscript{1,2,4}

Definition
Polydactyly is defined as \( \geq 1 \) extra digits of the hands or feet that may or may not contain bone.

Ultrasound Findings
Ultrasound findings include the presence of an extra digit on the hand or the foot. When suspected, polydactyly should be confirmed in the coronal and axial plane. Syndactyly may also be present. Polydactyly can be unilateral or bilateral\textsuperscript{1,2,5} (Figure 1). Because the extra digit may or may not contain bone, a diagnosis with two-dimensional ultrasonography can be difficult. When suspected, a three-dimensional ultrasound examination may provide more detailed evaluation of the digits\textsuperscript{6} (Figure 2). If polydactyly is identified, a detailed ultrasound examination is recommended to determine the presence of other abnormalities. Location of the extra digit (preaxial versus postaxial) should be assessed because most nonsyndromic polydactyly is postaxial.

Associated Abnormalities
Polydactyly often is an isolated finding but can be associated with other abnormalities if a genetic syndrome is present.\textsuperscript{1,2} Not all abnormalities that are associated with a specific genetic syndrome can be seen with ultrasound imaging.

Differential Diagnosis
The differential diagnosis of polydactyly includes syndromic and nonsyndromic causes. The list of syndromes that are associated with polydactyly is extensive; the following list represents some of the more common syndromes:

- Trisomy 13\textsuperscript{7}: Central nervous system abnormalities, growth restriction
- Meckel-Gruber syndrome\textsuperscript{8}: Occipital encephalocele, renal cystic dysplasia, autosomal recessive inheritance
- Diabetic embryopathy\textsuperscript{9,10}: Cardiac, renal, skeletal, and central nervous system abnormalities
- Smith-Lemli-Opitz syndrome\textsuperscript{11}: Central nervous system abnormalities, abnormal genitalia, autosomal recessive inheritance
- Carpenter syndrome\textsuperscript{12}: Craniosynostosis, midface hypoplasia, heart defects, autosomal recessive inheritance
- Pallister-Hall syndrome\textsuperscript{13}: Pituitary hamartoma, autosomal dominant inheritance
- Greig cephalopolysyndactyly syndrome\textsuperscript{14}: Polydactyly with syndactyly, macrocephaly, hypertelorism, autosomal dominant inheritance

FIGURE 1
Polydactyly

Two-dimensional image of right upper extremity shows postaxial polydactyly.

Genetic Evaluation

Once polydactyly is diagnosed, it is important to determine whether it is isolated or a part of a genetic syndrome. Because isolated polydactyly often is inherited in an autosomal dominant fashion, the parents should be evaluated, and a family history should be collected. Location of the extra digit can be helpful in the classification of syndromic vs nonsyndromic polydactyly; most syndromic cases are preaxial and inherited in an autosomal recessive fashion with a recurrence risk of 25%. Exceptions include Greig cephalopolysyndactyly syndrome and Pallister-Hall syndrome, which have an autosomal dominant inheritance.

Diagnostic testing (amniocentesis or chorionic villus sampling) with chromosomal microarray analysis (CMA) should be offered when polydactyly is suspected to be part of a genetic syndrome. If screening or other ultrasound features are suggestive of a common aneuploidy, it is reasonable initially to perform karyotype analysis or fluorescence in situ hybridization, with reflex to CMA if these test results are normal. If there are additional anomalies, consanguinity, or a family history of a specific condition, gene panel testing or exome sequencing may be useful because CMA does not detect single-gene (Mendelian) disorders. If exome sequencing is pursued, appropriate pretest and posttest genetic counseling by a provider who is experienced in the complexities of genomic sequencing is recommended. After appropriate counseling, cell-free DNA screening is an option for patients who decline diagnostic evaluation if a common aneuploidy is suspected.

Pregnancy and Delivery Management

A detailed ultrasound examination should be performed once polydactyly is diagnosed. Additional imaging, such as a fetal echocardiogram, should be considered if other anomalies are present or a syndromic cause is suspected. Referrals to pediatric orthopedics or plastic surgery should be considered based on sonographic findings. Pregnancy termination is an option that should be discussed with all patients in whom a fetal anomaly is detected, although isolated polydactyly typically has an excellent prognosis. The specific finding of polydactyly does not generally affect delivery management, although delivery at a tertiary care center may be appropriate based on the presence of other anomalies.

Prognosis

Prognosis is excellent with isolated polydactyly. Resection of the extra digit is possible; complexity and timing vary and depend on the degree of digit development. In the setting of a suspected genetic syndrome, the prognosis depends on the severity of associated abnormalities.

Summary

Polydactyly is a condition in which ≥1 extra digits are present. It can be preaxial (ulnar or fibular side), postaxial (radial or tibial side), or central. Although the majority of cases are isolated, more than 100 genetic syndromes are associated with polydactyly. Ultrasound findings are variable, depending on the presence of bone; three-dimensional imaging can be helpful. The presence of polydactyly should prompt a detailed ultrasound examination to look for associated abnormalities. Genetic counseling should be offered to determine the likelihood of an underlying genetic syndrome and to discuss prenatal diagnostic options. Resection of the extra digit varies in complexity, depending on the degree of digit development.

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Radial Ray Malformation

Society for Maternal-Fetal Medicine (SMFM); Manisha Gandhi, MD; Martha W. F. Rac, MD; Jennifer McKinney, MD

Introduction
Radial ray malformation refers to a spectrum of congenital anomalies that involve the radius, radial carpal bones, or thumb.¹ Radial ray anomalies and associated malformations range from unilateral, sporadic defects to bilateral defects that are associated with multiple malformation syndromes.² This rare malformation occurs in 1 in 30,000 live births.³

Definition
Radial ray malformation is a spectrum of anomalies that involves the absence or hypoplasia of the radius, radial carpal bones, or thumb.¹

Ultrasound Findings
The typical finding on ultrasound imaging is of a single forearm bone and radial deviation of the hand⁴ (Figures 1 and 2). This diagnosis should be suspected in the presence of the following findings⁵:

- Absent or hypoplastic radius
- Abnormal hand position (radial deviation that is fixed on prolonged scanning)
- Thumb may or may not be present
- Other anomalies present, which suggests a syndromic cause

Three-dimensional imaging can improve visualization of subtle anomalies of the limbs and provide clearer imaging of the anomalies that can be helpful when counseling patients and families.⁴,⁶

Associated Abnormalities
Radial ray defects can be isolated or syndromic and associated with multiple anomalies. Abnormalities of any organ system, including musculoskeletal, spinal, cardiothoracic, gastrointestinal, or genitourinary, can be associated with radial ray defects.

Differential Diagnosis
The differential diagnosis depends on the type of anomalies and whether the findings are isolated or associated with other malformations.⁵ Common associations include the following findings:

- VACTERL (Vertebral defects, Anal atresia, Cardiac defects, TracheoEsophageal fistula, Renal anomalies, and Limb abnormalities, specifically of the radial ray) association⁷
- Aneuploidy (trisomies 13 and 18)
- Holt-Oram syndrome⁷,⁸: Cardiac defects with upper extremity anomalies
- Diabetic embryopathy: A range of anomalies that affect multiple organ systems (limb, cardiac, central nervous system)

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- Diabetic embryopathy: A range of anomalies that affect multiple organ systems (limb, cardiac, central nervous system)
• TAR (Thrombocytopenia-Absent Radius) syndrome: Bilateral absence of radii with thumbs present (thrombocytopenia develops in utero or within first few months of life; this syndrome can include other skeletal, cardiac, and genitourinary anomalies).

• Fanconi pancytopenia syndrome: Radial ray defect (49%) and genitourinary, skeletal, gastrointestinal, and central nervous system abnormalities; café-au-lait spots (skin pigmentation abnormalities caused by melanin deposition) are common, and progressive bone marrow depletion leads to transfusion-dependent anemia in the first two decades of life.

• Teratogens: Fetal valproate syndrome is the most common teratogenic syndrome associated with radial ray malformation; this syndrome includes limb and facial anomalies and cognitive delays.

• Ectrodactyly: Absence or deficiency of ≥1 digits; it often is associated with cleft lip with or without cleft palate but rarely is associated with radial ray defects.

• Amniotic band syndrome: Constrictive rings of fibrous tissue that generally appear as amputated limbs.

Genetic Evaluation
Diagnostic testing (amniocentesis or chorionic villus sampling) with chromosomal microarray analysis (CMA) should be offered when a radial ray malformation is detected. If screening or other ultrasound features are suggestive of a common aneuploidy, it is reasonable initially to perform karyotype analysis or fluorescence in situ hybridization, with reflex to CMA if these test results are normal. Many syndromes are associated with radial ray malformations; they can be sporadic, autosomal dominant, autosomal recessive, or X-linked. If there are additional anomalies, consanguinity, or a family history of a specific condition, gene panel testing or exome sequencing may be useful because CMA does not detect single-gene (Mendelian) disorders. If exome sequencing is pursued, appropriate pretest and posttest genetic counseling by a provider who is experienced in the complexities of genomic sequencing is recommended.

Thrombocytopenia-absent radius syndrome is often caused by a deletion, which may be identified by CMA on one allele, and a sequence variant that may be detected by sequencing on the second allele. After appropriate counseling, cell-free DNA screening is an option for patients who decline diagnostic evaluation if a common aneuploidy is suspected.

Pregnancy and Delivery Management
A detailed ultrasound examination should be performed and should include assessment of all of the long bones and the hands. The fetal heart should be evaluated carefully, and a fetal echocardiogram should be considered given the association with syndromic disorders. Referrals to pediatric orthopedics or other subspecialty services should be based on additional sonographic findings. Pregnancy termination is an option that should be discussed with all patients in whom a fetal anomaly is detected. Shared patient decision-making requires a thorough evaluation and multidisciplinary counseling regarding prognosis. The specific finding of a radial ray malformation generally does not affect delivery management, although delivery at a tertiary care center with pediatric genetics and orthopedic surgery consultation should be considered, as appropriate for the clinical findings. After delivery, the infant should be referred to a specialist for potential reconstructive surgery. Radial ray malformations that are associated with other system anomalies or syndromes are managed based on the severity of the findings.

Prognosis
The prognosis in isolated cases includes functional limitations that result from the skeletal deformity. Reconstructive surgery may improve the mobility of the affected limb. Prognosis also depends on the severity of associated abnormalities, underlying causes, and potential association with genetic syndromes. Isolated findings are usually sporadic, with a low recurrence risk. Recurrence of syndromic cases depends on the underlying cause.

Summary
Radial ray malformations are most commonly an isolated finding and can be unilateral or bilateral. Careful examination of the entire fetus will help determine whether there are associated anomalies. A genetic evaluation is recommended to determine the presence of an underlying syndrome. Prognosis depends on the severity of associated abnormalities and the presence of a genetic abnormality. Reconstructive surgery may improve limb mobility.

REFERENCES
