Amyoplasia Involving Only the Upper Limbs or Only Involving the Lower Limbs with Review of the Relevant Differential Diagnoses

Judith G. Hall*

Departments of Medical Genetics and Pediatrics, University of British Columbia, BC Children's Hospital Vancouver, British Columbia, Canada

Manuscript Received: 18 July 2013; Manuscript Accepted: 21 November 2013

Of individuals with Amyoplasia, 16.8% (94/560) involve only the upper limbs (Upper Limb Amyoplasia—ULA) and 15.2% (85/ 560) involve only the lower limbs (Lower Limb Amyoplasia— LLA). The accompanying paper deals with other forms of Amyoplasia [Hall et al., 2013] and discusses etiology. An excess of one of monozygotic (MZ) twins is seen in both groups (ULA 4/94 (4.3%), LLA 5/85 (5.9%)), gastrointestinal (GI) abnormalities thought to be of vascular origin (bowel atresia and gastroschisis) (ULA 16/94 (17%), LLA 4/85 (4.7%)), small or partial absence of digits (ULA 6/94 (6.2%), LLA 8/85 (9.4%)), and umbilical cord wrapping around the limbs at birth (ULA 3/94 (3.2%), LLA 7/85 (8.2%)) (severe enough to leave a permanent groove). Pregnancy complications occurred in 42/60 (70%) of ULA and 36/54 (67%) of LLA. Prenatal diagnosis, after ultrasound usage became routine, occurred in only 7/25 (28%) of ULA and 5/12 (12%) of LLA. This series may represent an over estimate of the complications and associations occurring in ULA and LLA. Differential diagnoses separating LLA from the genetic forms of "lower limb only" arthrogryposis and ULA from "upper limb only" genetic forms of arthrogryposis and Erb's palsy is provided.

© 2014 Wiley Periodicals, Inc.

Key words: Amyoplasia; arthrogryposis; bowel atresia; camptodactyly; club feet; club hands; differential diagnoses; digit loss; dimples; dislocated hips; Erb palsy; extended elbow contractures; gastroschisis; legs only; multiple congenital contractures; twins; vascular malformations

INTRODUCTION

In 1983, upper limb only and lower limb only involvement were distinguished within the group of individuals affected by Amyoplasia [Hall et al., 1983]. Swinyard and Mayer [1963] had earlier noted that 11% of individuals with arthrogryposis had only upper limb involvement and that 43% had only lower limb involvement. Several other types of arthrogryposis with only upper or only lower limb involvement must now be considered, many of them with a genetic basis.

In 1983, other types of upper limb only arthrogryposis had not been recognized. Upper limb contractures with extension of the

How to Cite this Article:

Hall JG. 2014. Amyoplasia involving only the upper limbs or only involving the lower limbs with review of the relevant differential diagnoses.

Am J Med Genet Part A 164A:859-873.

elbow were a helpful distinguishing sign for Amyoplasia. Since 1983, it has been recognized that several other specific entities within the lethal fetal akinesia sequence spectrum and among lethal mitochondrial disorders may also have extended elbows at birth (see differential diagnosis and prenatal diagnosis sections) [Hall, 2009; Wilnai et al., 2012]. In addition to Upper Limb Amyoplasia (ULA), many genetic forms of arthrogryposis with primarily upper limb involvement have been described [Hall, 2013].

Severely shortened and stiff clubfeet in an equinovarus position (known to the orthopedists as "teratogenic" clubfeet because of their severity, not because of known teratogen exposure), markedly decreased muscle mass in the legs, mild to moderate shortness of the long bones of the legs (as seen in severe disuse and/or anterior horn cell loss as in polio), and the presence of dimples over affected joints are the hallmarks of Lower Limb Amyoplasia (LLA). Only two genetic forms of lower limb arthrogryposis were recognized in 1983; now there are at least eight.

The purpose of this paper is to update the data on these two subtypes of Amyoplasia and to provide a differential diagnosis for each.

Conflict of interest: none.

*Correspondence to:

Judith G. Hall, OC., M.D., FRSC, FCAHS, Departments of Medical Genetics and Pediatrics, BC Children's Hospital, 4500 Oak Street, Room C234, Vancouver, BC, Canada, V6H 3N1.

E-mail: jhall@cw.bc.ca

Article first published online in Wiley Online Library

(wileyonlinelibrary.com): 23 January 2014

DOI 10.1002/ajmg.a.36397

METHODS

A comprehensive review of the literature concerning only upper limb and only lower limb involvement in arthrogryposis was undertaken including Medline, London Medical Database's Winter-Baraitser Dysmorphology Database, Possum, and Online Mendelian Inheritance in Man (OMIM). In addition, references collected over 40 years and often not referenced in the above databases were reviewed. Review of 2,500 individuals with arthrogryposis collected by the author over 35 years was also undertaken. Individuals with only upper limb and only lower limb involvement were scrutinized for points of variation. See Hall et al. [2013] for other aspects of Methods. The affected individuals do not represent a specific geographical region or clinic, but rather came from all over North America (and the world); and cannot be considered to represent a population-based sample. It is also important to recognize this information is likely to be biased because of the referral of affected individuals with more complexity and severity. See Hall et al. [2013] for statistical methods.

Fifteen of 109 (13.7%) individuals with arthrogryposis involving only the upper limbs were excluded from the analysis of ULA: four because of insufficient information available; 11 because they appear to represent other conditions (see Table I).

Forty-five of 130 (35%) individuals with only lower limb involvement were excluded from this analysis: three because insufficient information was available, 24 because they appear to have a genetic basis from their family history and reanalysis of clinical features, 16 with unusual additional features and they appear to have an unrecognized/unpublished syndrome rather than Amyoplasia, and one because she had a chromosomal disorder.

Although this collection of affected individuals is likely to represent an overestimate of complications and associations because of the nature of referrals, it affords the opportunity to identify important aspects of both ULA and LLA for future studies.

RESULTS

Among our 560 affected individuals with Amyoplasia, 94 (16.8%) represented ULA, and 85 (15.2%) represent LLA (see also Hall et al.

TABLE I. 15 Individuals with Upper Limb Only Arthrogryposis Removed from Analysis of Upper Limb Amyoplasia

- 4 Insufficient information
- 2 Radioulnar synostosis (possibly AD antecubital pterygium)
- 2 AD Ptyergium syndrome (antecubital webs and scoliosis)
- 2 CNS malformation, scoliosis, ptosis, Duane anomaly seizures
- 2 Vertebral fusion, anomalies, asymmetry, ID (possibly Baraitser London syndrome, or AD pterygium syndrome)
- 1 Probable syndrome: sagittal snyostosis, dislocated radial heads (possibly Rozin-Kilic syndrome)
- 1 Probable syndrome: preaxial polydactyly, ptosis, rotated hands
- 1 Probable neurodysplasia syndrome or a type of camptodactyly: very mild scoliosis with patch of hair on lower spine

Note : AD, autosomal dominant; CNS, central nervous system; ID, intellectual delay.

[2013]). To be included, individuals with ULA had at birth internal rotation of their shoulder, extended and rigid elbow contractures (less than 5° flexion), the forearm held in pronation, and wrists rigidly flexed (Fig. 1). They also had decreased muscle mass throughout the arms, dimples overlying affected joints, decreased flexion creases, and mild shortness of the affected limbs. Their involvement is very similar to the upper limbs in the four-limb Amyoplasia group. All affected individuals were surprisingly symmetrical and most had a glabellar nevus flammeus. Ninety-five percent had internal rotation and limited abduction of the shoulder. All had flexion contractures of the fingers at birth. Most of the time, fingers were cupped and rigidly flexed, but not fisted. Most of the time, they did not have or develop ulnar deviation. Frequently, the thumb was adducted and rigid. To be included in this group, hips, knees, and feet did not have fixed contractures, although occasionally those joints were mildly tight at birth.

As mentioned above, to be included, individuals with LLA had at birth involvement of only the lower limbs, markedly decreased muscle mass, mild shortness of the legs, and the presence of dimples lying over affected joints. Severe foot involvement, almost always in equinovarus position, was present (equinovalgus was occasionally seen) (Fig. 2). Individuals with calcaneal valgus and rocker bottom feet were excluded. Their involvement is very similar to the lower limbs of the four-limb Amyoplasia group. Mild asymmetry of the leg involvement was seen in 15/85 (17.6%) affected individuals. Mild knee involvement was seen in 10/85 (11.8%), where both feet and hips were severe. Hip contractures were present in all, either in flexion or extension. Dislocated hips were present in 44/85 (52%) bilateral in 29/44 (66%) (e.g., 34% of all LLA). Hips held in abduction at birth were slightly less likely to be dislocated. Knees were extended at birth in 43/85 (50.6%) and flexed in 42/85 (49.4%). Hyperextended knees were seen in 8/43 (19%) of the infants with extended knees and half 4/43 (9.3%) of these (e.g., 5% of the total LLA) ended up with unstable knees.

No congenital scoliosis was seen at birth; however, 11/94 (11.1%) of ULA developed mild scoliosis during childhood and 6/85 (7.1%) of individuals with LLA developed mild scoliosis as they began to walk, possibly related to difference in hip and knee responses to therapy. About 15% of both groups had some scoliosis at older ages. Many individuals with LLA position themselves in lumbar lordosis to walk. Four of 94 (4.3%) individuals with ULA and 4/85 (4.7%) of LLA had torticollis at birth. In individuals with LLA, patellae were often small, misplaced, or even missing. Occasionally, mild flexion contractures of the arms were present (particularly the left elbow) at birth in individuals with LLA. These resolved in early infancy with physical therapy.

DEMOGRAPHICS

Among individuals with LLA, there were almost equal numbers of males and females, similar to the sex ratio in a normal population and a little less than the overall Amyoplasia group; however, there is a statistically significant excess of females in the ULA group as compared with the overall sex ratio among all affected individuals with Amyoplasia (see Table II). Fifty-five females (59%) and 39 males (41%) among the 94 individuals with ULA were identified, giving a sex ratio of 0.71 as compared to a sex ratio of 1.12 for the

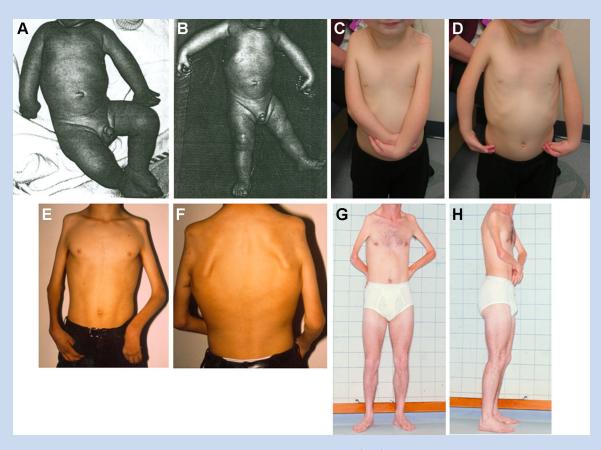


FIG. 1. Upper Limb Amyoplasia. A,B: 2-month-old male with Upper Limb Amyoplasia (ULA). Note normal legs and feet, internal rotation of the shoulders, extended elbows, pronated forearms, flexed wrist, but some shoulder movement. C,D: 5-year-old female with ULA. Note some mild flexion of elbow, limited shoulder and hand movement. E,F: 12-year-old with ULA and moderate elbow flexion, markedly decreased muscle, prominence of shoulder bone, and winging of scapula. G,H: 20-year-old male with ULA, moderate elbow flexion, markedly decreased muscle, mild shortness of involved long bones, normal trunk and lower limbs.

overall group (*P* value of 0.045). This may have implications for pathogenesis as discussed in Hall et al. [2013].

Parental age, month of year born, year born, birth order, and gestational age are all comparable to the total group of Amyoplasia and normal births. Birth dates have statistically significant deficiency in July, August, and December in keeping with the overall Amyoplasia group; see Hall et al. [2013].

There were no deaths in either subgroup. One termination was included in the LLA group.

Birth weight was normal in the ULA group and slightly below normal (between the 10th and 25th centiles) for gestational ages in the LLA group. Head circumference and length (although the latter was difficult to measure in the individuals with LLA) appear normal for gestational age. Height and weight after birth were somewhat low following along the 15th centile for mid-parental height in the LLA group. They were both normal in the ULA group.

FAMILY HISTORY

No recurrence of Amyoplasia has occurred in any of these families. Family histories were not remarkable in the ULA group and included the presence of a relative with: two families with neural

tube defects (NTD), three with thrombophilia, two with malignant hyperthermia, four with clubfeet, and one monozygotic (MZ) twin. In the LLA group, there was a slight increase (when compared to the other groups of Amyoplasia) of clubfoot (eight families) and MZ twinning (three families). Deafness (one), arthritis (one), and cerebral palsy (one) were also seen in relatives.

Six individuals with ULA were adopted (five females and one male). Eleven individuals with LLA were adopted (seven females and four males) and one male was in foster care.

INCIDENCE

If the incidence of Amyoplasia is approximately 1/10,000 births [Hall et al., 2013] and 16.8% of Amyoplasia involves only upper limbs and 15.2% involves only lower limbs, then it can be anticipated that the incidence at birth of ULA and LLA would be in the range of 1/75,000–1/100,000 (we are unaware of any geographically based data).

PREGNANCY COMPLICATIONS

As in other types of Amyoplasia, 70% (42/60) of pregnancies with a fetus with ULA and 67% (36/54) with a fetus with LLA had some

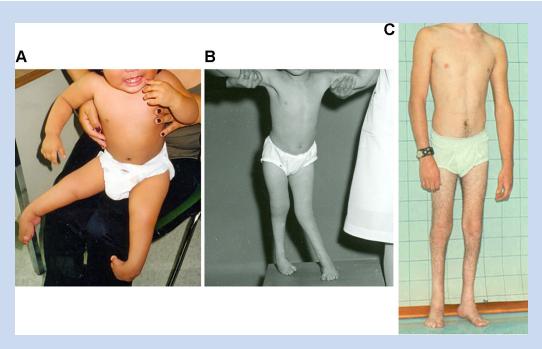


FIG. 2. Lower Limb Amyoplasia. A: 6-month-old female, note normal upper limbs, flexed hips, extended knee, and equinovarus deformity of feet. B: 7-year-old boy with normal arms and hands, extension of knees, decreased lower leg musculature, and residual clubfoot. C. 17-year-old boy with markedly decreased musculature, shortened long bones of legs, and residual foot deformity.

type of first trimester complication (bleeding, infection, fever, etc.) (see Table II).

Among pregnancies with a fetus affected with ULA where information was available, 12/60 (20%) of mothers had serious medical situations during pregnancy (two gestational diabetes, one hypothyroidism, one Crohn disease, and one severe migraines) or drug use (seven took antibiotics, four took recreational drugs) and three experienced severe trauma during pregnancy (one motor vehicle accident and two domestic violence). Large fibroids were present in two pregnancies. None had perinatal long bone fractures. Oligohydramnios was present in 7/60 (11.7%) at birth. Only 7/25 (28%) were recognized prenatally among those born after 1990 when prenatal ultrasound became part of routine care. Thirty-five of 52 (67%) of pregnancies with a fetus with ULA, where information is available, were delivered vaginally (including three breech and two transverse lies), but 17/52 (33%) were cesarean deliveries. The position in utero did not correlate with severity or outcome except for the hyperextended spine in the severely affected group [Hall et al., 2013]. Only one pregnancy (1.6%) utilized ART. Fourteen of 45 (31%) pregnancies occurred shortly after a spontaneous abortion. No structural uterine anomalies were noted. Little information was available about placentas; however, there were three abruptio placentae, one two-vessel cord, and one normal placenta reported.

Among pregnancies with a fetus with LLA, where information was available, 22% (12/54) of mothers had a serious medical situations during pregnancy (three gestational diabetes, six infections treated with antibiotics, and one endometrial sur-

gery), or drug use—two mothers used recreational drugs during pregnancy. Eight of 85 (9.4%) mothers sustained some type of trauma (four attempted termination of pregnancy, two motor vehicle accidents and two domestic trauma) during pregnancy (P value 0.007 when compared to other Amyoplasia groups). Most affected infants with LLA were delivered vaginally (including five breech presentations) but 12/35 (34%) were delivered by cesarean (three of which were transverse lies). Five of 85 (5.8%) infants with LLA sustained fractures at birth. Only 5/42 (12%) were recognized prenatally. The low rate of prenatal diagnosis in Amyoplasia is discussed in Filges and Hall [2012, 2013] and does not appear to relate to severity. Two of 54 (3.7%) pregnancies utilized fertility drugs. Eleven of 52 (21%) pregnancies occurred shortly after a spontaneous abortion (in four pregnancies several spontaneous abortions) and one shortly after a stillbirth (discussed in Hall et al. [2013]). Seven of 85 (8.2%) infants with LLA had umbilical cord wrapping involving the right leg (four) and the left leg (three). Two umbilical cords were described as short. Placentas were reported as normal in four pregnancies.

ADDITIONAL OBSERVATIONS

As with the overall Amyoplasia group [Hall et al., 2013], an increase of discordant MZ twins was observed. Among individuals with ULA, three males and one female were discordant MZ twins (4.3% = 4/94). No dizygotic (DZ) twins were observed, and one other pregnancy was suspected of starting as an MZ pregnancy and

typin 123440313 SSS 241640 GOX 1671127 SSY 915594 418 4104285 SS 518 295640589 rypup 124 124 1.24 1.25 1.45 1.45 0.71 -1 1.17 -111 -111 MyTorial 1.24 1.22 1.41 1.22 1.44 0.71 -1 0.71 -1 0.71 -1 0.71 -1 0.71 -1 0.71 -1 0.71 -1 0.71 -1 0.71 -1 0.71 -1 0.71 -1 0.71 -1 0.71 -1 0.71 -1 0.71 -1 0.71 -1 0.71 -1 0.71 -1 0.71 0.71 0.71 0.71 0.71 0.71 0.71 0.71 0.71 0.71 0.71 0.71 0.71 0.71 0.71 0.71 0.71 0.71 0.72 0.71 0.72 0.72 0.72 0.72 0.72	124 1.02 1.00 16.11 1.01 1.02	upple 1244 1240 150 124 418 414208 511 295504559 prope 124 124 124 124 124 124 418 414208 511 225 2143 225 2143 225 2143 225 2143 2243 2448 644 1266 47 1266 47 1275 448 644 1266 47 1266 1112 1112 1112 1112 1112 222 111 1224 478 544 434 494 434 494 434 494 434 494 434 494 434 448 1112 435 550 5050 2050 1112 1112 222 1112 1244 478 1144 478	NUMBER (% of	Fou 313 [Four-limb 313 (55.9%)	S 41	Severe 41 [7.3%]	Thre (27 (Three-limb 27 (4.8%)	ULA 94 (16.8%)	5.8%]	3) 58	LLA 85 (15.2%)		Total 560
Virtual 1.24 — 1.54 — 0.71 — 1.02 — 1.12 Mirtual 1.24 — 1.24 — 0.71 — 1.28 1.48 0.92 — 1.05 — 1.12 9.95 — 1.12 9.95 — 1.24 0.72 1.48 0.94 6.43 1.44 0.95 — 1.12 1.43 0.95 — 1.26 1.44 0.95 — 1.26 1.44 0.95 — 1.26 1.44 0.95 — 1.12 1.44 0.95 — 0.95 — 1.26 1.44 0.95 — 1.26 0.95 — 1.26 0.95 — 1.26 0.95 — 1.26 0.95 — 1.26 0.95 — 1.26 0.95 — 1.26 0.95 — 1.26 0.95 — 1.26 0.95 — 1.26 0.95 — 0.95 — <t< th=""><th> 124 124 124 125 125 125 145 145 145 146</th><th>Virthorau 1.24 — 1.50 — 1.65 — 1.65 — 1.67 — 1.07 — 1.07 — 1.07 — 1.07 — 1.12 — 1.12 — 1.12 — 1.48 0.0 — — 0.0 — 1.0 — 1.0 — 0.05 — 1.0 — 0.05 0.05 — 0.05 0.05 — 0.05 — 0.05 — 0.05 — 0.05 —</th><th>total group) M/F/Total known</th><th>173/140/313</th><th>25%</th><th>24/16/40</th><th>%09</th><th>16/11/27</th><th>29%</th><th>39/55/94*</th><th>41%</th><th>43/42/85</th><th>51%</th><th>295/264/559</th><th>23%</th></t<>	124 124 124 125 125 125 145 145 145 146	Virthorau 1.24 — 1.50 — 1.65 — 1.65 — 1.67 — 1.07 — 1.07 — 1.07 — 1.07 — 1.12 — 1.12 — 1.12 — 1.48 0.0 — — 0.0 — 1.0 — 1.0 — 0.05 — 1.0 — 0.05 0.05 — 0.05 0.05 — 0.05 — 0.05 — 0.05 — 0.05 —	total group) M/F/Total known	173/140/313	25%	24/16/40	%09	16/11/27	29%	39/55/94*	41%	43/42/85	51%	295/264/559	23%
My Total 1,47/21 2,74 1,24 2,04 3,14 4,14,40 1,14,72 2,14,43 </td <td>My Fund 147/21 6.7/21 6.7/21 1.2.2x 4.4 2.2 5.4 1.2.2x 4.4 2.2 5.4 1.2.2x 4.4 2.2 5.4 1.2.2x 4.4 2.2 1.4 4.0 7.4 4.8 4.4 2.2 5.4 1.2.2x 4.2 1.4 6.44 1.2 2.4 0.0 1.4 6.44 1.2 2.4 0.0 0.0 6.4 1.2 4.6 4.7 5.15.60 2.1 0.0</td> <td>My Carla (1972) (274) (2</td> <td>for subgroup Sex ratio</td> <td>1.24</td> <td>I</td> <td>1.50</td> <td>I</td> <td>1.45</td> <td>I</td> <td>0.71</td> <td>I</td> <td>1.02</td> <td>I</td> <td>1.12</td> <td>I</td>	My Fund 147/21 6.7/21 6.7/21 1.2.2x 4.4 2.2 5.4 1.2.2x 4.4 2.2 5.4 1.2.2x 4.4 2.2 5.4 1.2.2x 4.4 2.2 1.4 4.0 7.4 4.8 4.4 2.2 5.4 1.2.2x 4.2 1.4 6.44 1.2 2.4 0.0 1.4 6.44 1.2 2.4 0.0 0.0 6.4 1.2 4.6 4.7 5.15.60 2.1 0.0	My Carla (1972) (274) (2	for subgroup Sex ratio	1.24	I	1.50	I	1.45	I	0.71	I	1.02	I	1.12	I
12,213 2.34 3.44 14.54 3.27 14.84 6.44 1.694 6.44 1.6169 14.4 9.0560 2,2313 7.3 6.41 14.63 3.27 11.3 16.94 17.4 4.95 4.73 5.1560 4,13 1.124 1.41 1.45 3.27 1.13 1.694 1.74 4.95 4.75 5.1560 4,14 1.213 3.84 1.41 2.45 2.27 3.74 3.94 3.24 3.85 3.44 6.8560 4,13 1.23 3.84 1.41 2.45 2.27 3.74 3.94 3.24 3.94 3.25 3.75 3.94 3.25 3.85 3.45 4,13 1.24 1.24 1.24 1.25 3.75 3.75 3.94 3.25 3.85 3.85 3.45 4,14 1.24 1.24 1.24 1.25 3.75 3.75 3.94 3.25 3.85 3.25 3.25 4,14 1.24 1.24 1.25 1.25 3.75 3.75 3.94 3.25 3.25 3.25 4,15 1.24 1.24 1.25 1.25 3.75 3.75 3.94 3.25 3.25 3.25 4,15 1.24 1.24 1.25 1.25 3.75 3.94 3.25 3.25 3.25 4,15 1.24 1.24 1.25 3.75 3.75 3.94 3.25 3.25 3.25 4,15 1.24 1.24 1.25 1.25 3.75 3.25 3.25 3.25 3.25 4,15 1.24 1.25 1.25 1.25 3.75 3.25 3.25 3.25 3.25 4,15 1.25 1.25 1.25 3.75 3.25 3.25 3.25 3.25 4,15 1.25 1.25 3.45 3.25 3.25 3.25 3.25 3.25 4,15 1.25 1.25 3.45 3.25 3.25 3.25 3.25 3.25 4,15 1.25 1.25 3.45 3.25 3.25 3.25 3.25 3.25 4,15 1.25 1.25 3.45 3.25 3.25 3.25 3.25 3.25 4,15 1.25 3.25 3.25 3.25 3.25 3.25 3.25 4,15 1.25 3.25 3.25 3.25 3.25 3.25 3.25 4,15 1.25 3.25 3.25 3.25 3.25 3.25 3.25 4,15 1.25 1.25 3.25 3.25 3.25 3.25 3.25 4,15 1.25 1.25 3.25 3.25 3.25 3.25 3.25 4,15 1.25 3.25 3.25 3.25 3.25 3.25 3.25 4,15 1.25 3.25 3.25 3.25 3.25 3.25 3.25 4,15 1.25 3.25 3.25 3.25 3.25 3.25 3.25 4,15 1.25 3.25 3.25 3.25 3.25 3.25 3.25 3.25 4,15 1.25 3.25 3.25 3.25 3.25 3.25 3.25 3.25 4,15 1.25 3.25 3.25 3.25 3.25	1,2,2,1,3,3,3,3,4,4,7,3,7,3	1,2,2,13 2,3,4 1,4,4 1,4,5 1	MZ twin M/F/total	14/7/21	6.7% (21/313)	2/3/5	12.2% (5/41)	2/0/2	7.4% [2/27]	3/1/4	4.3% 4/94	2/3/5	5.9% [5/85]	23/14/37	6.6%** (37/560)
tet 1 22713	tert 27.1 2.2 1.1 2.4 1.1 2.4 1.1 1.1 1.1 1.1 1.1 1.1 1.1 1.1 1.1 1	tett 27.13 7.8 1.1 2.4% 0.0 - 0 - 0 - 0 - 0 8.560 sscolar social field	Adopted	23/313	7.3%	5/41	12.2%	4/27	14.8%	6/94	6.4%	12/85	14%	20/260	***%6.8
ptr to the tent 22313	tert 1, 12,313	tett 22013 7% 6/41 146% 3/27 11% 1694* 17% 4/65 4/7% 5/1560 secular secue secular secular secular secular secular secular secular secue secular secula	Died	~	2.2%	1	2.4%	0	1	0	1	0	I	8/260	1.4%
give top secular 17.11 2.4% 0 2.94 2% 0 — 15560 give tope secular 18.1 2.4% 1/41 2.4% 0 2.94 2% 0 — 15560 giv to be top 11.23 11.24 2.4% 2/27 2.6% 6.94 6.2% 8/85 9.4% 689560 giv whour critical magning 2.23.13 7.8 2/41 2.3% 2/27 2.6% 6.94 6.2% 8/85 9.4% 689560 giv whour critical magning 2.23.13 7.8 2/41 2.3% 2/27 3.7% 3.94 3.2% 7/85 9.4% 3.7560 giv whour critical magning 2.24.11 2.4% 1.27 3.7% 3.94 3.2% 7/85 3.7% 3.7560 most secural magning 2.24.11 4.4% 5.27 3.7% 4.94 4.3% 4.7% 4.7560 minester 1.24.11 4.1 4.1 4.1	ggin to pseuding speuding	step th to be step the st	GI defect	22/313	%2	6/41	14.6%	3/27	11%	16/94*	17%	4/85	4.7%	51/560	9.1%**
gin defect 12313 388 1/41 248 0 0 294 2x 0 — 15560 gin defect 12313 388 1/41 248 7/27 288 694 62x 8/85 94x 68/560 derif in origin 35/313 11,23 1241* 298 7/27 288 694 62x 8/85 94x 68/560 gle without 20313 7x 3/41 23x 2227 37x 3/94 32x 7/85 94x 68/560 gle without 20313 7x 3/41 23x 2227 37x 3/94 32x 7/85 94x 68/560 stew whole 1/7313 5x 1/41 4.9x 1/27 37x 1/94 11x 0	gin defect 12313 388 1/41 248 0 0 294 28 0 — 15/560 girt obe defects 15313 3.88 1/41 248 727 268 694 628 865 948 68760 gist obe durin ongs 357313 11.28 12741* 298 727 268 694 628 865 948 68760 gist without migs 227313 78 3741 738 2277 378 378 786 828 37/50 riction migs 207313 6.48 2/41 4.98 1/27 378 1/94 11.8 0 — 24/50 riction migs 207313 6.48 2/41 4.98 1/27 378 378 4750 sis consol vascular 17/313 6.48 1.741 4.185 1/27 378 4750 244 4750 sis consol vascular 17/313 8.8 1.741 4.185	Figure (a) (a) (b) (c) (c) (c) (c) (c) (c) (c) (c) (c) (c	thought to												
ignification 12913 38,8 1/41 24% 0 0 2/94 2% 0 — 15/560 glif to be effect. 35/313 11.2X 1241 29% 7/27 26% 6/94 6.2% 8/85 9.4% 6/850 glis without rings 22/313 7.8 3/41 2.3% 2/27 3.7% 3/94 3.2% 7/85 8/85 9.4% 6/850 6/850 8/85 9.4% 6/850 9.4% 6/850 9.4% 6/850 9.4% 6/850 9.4% 6/85 9.4% 6/850 9.4% 6/850 9.4% 6/850 9.4% 6/850 9.4% 6/850 9.4% 6/850 9.4% 6/850 9.4% 6/850 9.4% 6/850 9.4% 6/850 9.4% 6/850 9.4% 6/850 9.4% 6/850 9.4% 6/850 9.4% 6/850 9.4% 6/850 9.4% 6/850 9.4% 9/850 9.4% 9/850 9.4% <	effect 12313 388 1/41 2.48 0 0 294 28 0 — 15560 alar in origin 135313 11.28 1/41 2.48 7/27 26% 6/94 6.28 8/85 9/85 6/850 alar in origin 135313 11.28 1241* 2.98 7/27 26% 6/94 6.28 8/85 9/85 6/85 gib without 2.2313 7.48 2.247 3.78 3/94 3.27 7/85 8/85 37/86 stronton rice orice vaccular 17.313 5.48 1.441 2.48 5.27* 18.58 1.094 1.18 0 <t< td=""><td>Reference (graph of the part of</td><td>be vascular</td><td></td><td></td><td></td><td></td><td></td><td></td><td></td><td></td><td></td><td></td><td></td><td></td></t<>	Reference (graph of the part of	be vascular												
defect 12213 38% 1/41 2.4% 0 0 2/94 2% 0 - 15/560 last no rigin all an origin all and all and all an origin all and all an origin all and all an origin all and all and all an origin all and all and all an origin all and all and all and all and all and all and all an origin all and all an	defect 12213 38% 1/41 2.4% 0 0 2/94 2% 0 — 15/560 labelin origin l	the better 12313 3.8% 1/41 2.4% 0 294 2% 0 — 15560 glic the better 35.313 11.2% 1241 2.4% 7/27 2.6% 6.94 6.2% 9.6% 9.4% 6.8% 9.6% 9.4% 6.8% 9.6% 9.4% 6.8% 9.6% 9.4% 6.8% 9.4% 6.8% 9.6% 9.4% 6.8% 9.4% 6.8% 9.6% 9.4% 6.8% 9.6% 9.4% 6.8% 9.6% 9.4% 6.8% 9.6% 9.4% 6.8%	in origin												
lation organia special	Figure 1 be large in the part of the part	1,2, 1,2,	Trunk defect	12/313	3.8%	1/41	2.4%	0	0	2/94	2%	0	1	15/560	2.7%
Second column	laber in region and region region without and region region without region region without region region without region region without region region and region and region and region and region region region region region and region and region region region and region and region and region and region region and region a	laber moregan laber more more more accurate	thought to be												
gis without 35,313 11,2% 12,41 29% 722 26% 694 6.2% 8/85 9,4% 68/560 gis without tiction rings 22333 7,4 12,4 12,2 3.7% 194 11,8 0 — 24/560 eous vascular riction rings 20333 6.4% 2/41 4.9% 1.27 3.7% 1/94 1.1% 0 — 24/560 eous vascular riction rings 20333 6.4% 2/41 4.9% 1.27 3.7% 1/94 1.1% 0 — 24/560 submindings 20333 8.6% 1/41 2.4% 5/27* 18.5% 10/94 1.06% 1.1% 34/560 submindings 20333 8.6% 1/341* 41.5% 1.27 3.7% 40/94 4.3% 4/85 1.1% 4/85 4/85 1.1% 4/85 4/86 4/86 4/86 4/86 4/86 4/86 4/86 4/86 4/86 4/86	gls without 35313 11.7% 12.41 29% 7/27 26% 6/94 6.2% 9.4% 68/560 gls without 31.1 1.2.41 2.9% 7/27 2.6% 6/94 6.2% 9.4% 68/560 riction ings 20213 2.4% 2.41 4.9% 1.27 3.7% 1.994 1.1% 0 — 24/560 sous vascular 1.7313 5.4% 1.41 2.4% 5.77 1.8.5% 1.094 1.1% 0 — 24/560 sous vascular 1.7313 5.7% 0 0 0 0 0 0 24/560 1.1% 34/560 sous vascular 1.7313 5.7% 1.74 2.4% 5.77 1.8.5% 1.094 1.1% 0 0 0 0 0 0 0 3/85 2.7560 2.7560 2.7560 3.78 3/860 3.78 3.7560 3.7560 3.7560 3.7560 3.78 3.7560	absolute plane without sign without mines 35/313 11.2% 12/41 29% 7/27 26% 694 6.2% 84% 68/560 pig without mines 20.313 2.4 3.41 2.3% 2/27 26% 694 6.2% 9.4% 68/560 riction mines 20.313 2.4 1.41 2.4% 1/27 3.7% 1.94 1.1% 0 — 24/560 coots vascular riction mines 20.313 5.4% 1.41 2.4% 5/27* 18.5% 1.094 1.06 — — 24/560 coots vascular riction mines 1.7/313 5.4% 1.41 2.4% 5/27* 18.5% 1.094 1.06 0 — — 24/560 silis 2.5/313 8.% 1.7/41 41.5% 1.27 3.7% 3.94 4.3% 4/750 1.1% 4.7% 4/750 1.1% 4.7% 4/750 1.1% 4.7% 4/750 1.1% 4.7% 4/750 1.1% 4.7% </td <td>vascular in origin</td> <td>!</td> <td></td> <td>9</td> <td>į</td> <td>!</td> <td></td> <td></td> <td></td> <td></td> <td></td> <td>!</td> <td>9</td>	vascular in origin	!		9	į	!						!	9
gis without integes 22313	riction rings 22/313 274 374 1 734 2 227 3 74 3 74 3 734 2 227 3 74 3 74 3 734 2 227 3 74 3 74 3 734 3	riction intege cous vascular (1731) 2,4, 1,2	Partial absence	35/313	11.2%	12/41*	%62	7/27	%9Z	6/94	82.9	8/82	9.4%	095/89	12.1%
representation rings 2.2731 7,8 3.41 7.38 2.227 3.7% 3.994 3.2% 7.89 3.7% one social riction rings recons vascular riction rings 2.07313 6.4% 2.41 4.9% 1.127 3.7% 1.994 1.1% 0 — 24/560 neous vascular riction rings 2.07313 6.4% 2.41 4.9% 1.27 3.7% 1.994 1.1% 0 — 24/560 sis 1.07313 5.7% 1.341 1.27 3.7% 4.94 4.3% 4.88 3.5% 4.7560 sis 2.5333 8.6 1.741 41.5% 1.727 3.7% 3.94 3.2% 4.78 4.7560 sis 2.5333 8.6 1.741 41.5% 2.727 3.7% 3.94 3.2% 2.4% 4.7560 sis 3.7 4.3 4.9 3.2 3.7 3.7 4.760 7.7 3.6 2.4 3.7 4.7560 sis <td>triction rings 227313 7,4 3.44 7.3% 2227 3.7% 3.94 3.2% 7.85 8.2% 37/560 riction rings 20.0313 6.4% 2.44 4.9% 1.127 3.7% 1.94 1.18 1.0 — 24/560 sector vescular 17/313 6.4% 2.44 4.9% 1.127 3.7% 1.094 1.05 1.08 — 24/560 sis 2.0313 8.% 13/41* 3.17% 1.22 3.7% 4.94 4.3% 4.05 3.7% 24/560 sis 2.27313 8.% 11/41* 4.15 1.27 3.7% 4.94 4.3% 4.05 1.1% 4.45 4.75 4.75 4.75 sinch sis 2.27313 8.% 11/74 4.15 2.27 3.7% 4.94 4.3% 4.05 1.7% 4.75 sinch sis 1.24 1.24 1.12 3.7% 4.94 4.3% 4.3% 4.75 4.</td> <td>wapping 2223 37% 394 3.2% 78% 37% 366 wapping 20313 6.4% 241 43% 127 37% 194 11% 0 — 24560 onciso vascular 17313 6.4% 241 43% 127 37% 194 11% 0 — 24560 sones vascular 17313 5.4% 1441 248 5727 18-58 1094 1058 185 11% 0 24560 24-560</td> <td>of digits without</td> <td></td>	triction rings 227313 7,4 3.44 7.3% 2227 3.7% 3.94 3.2% 7.85 8.2% 37/560 riction rings 20.0313 6.4% 2.44 4.9% 1.127 3.7% 1.94 1.18 1.0 — 24/560 sector vescular 17/313 6.4% 2.44 4.9% 1.127 3.7% 1.094 1.05 1.08 — 24/560 sis 2.0313 8.% 13/41* 3.17% 1.22 3.7% 4.94 4.3% 4.05 3.7% 24/560 sis 2.27313 8.% 11/41* 4.15 1.27 3.7% 4.94 4.3% 4.05 1.1% 4.45 4.75 4.75 4.75 sinch sis 2.27313 8.% 11/74 4.15 2.27 3.7% 4.94 4.3% 4.05 1.7% 4.75 sinch sis 1.24 1.24 1.12 3.7% 4.94 4.3% 4.3% 4.75 4.	wapping 2223 37% 394 3.2% 78% 37% 366 wapping 20313 6.4% 241 43% 127 37% 194 11% 0 — 24560 onciso vascular 17313 6.4% 241 43% 127 37% 194 11% 0 — 24560 sones vascular 17313 5.4% 1441 248 5727 18-58 1094 1058 185 11% 0 24560 24-560	of digits without												
27313 7% 3.41 2.38 2.27 3.7% 1.94 1.1% 0 — 244560 clicion rings 2.07313 6.4% 2.41 4.9% 1.127 3.7% 1.94 1.1% 0 — 244560 clicion rings 2.07313 6.4% 2.41 4.9% 1.127 3.7% 1.94 1.1% 0 — 244560 nmations 1.0313 6.4% 1.41 2.4% 5.72* 1.65% 1.094 1.06 — 244560 siles 1.0313 6.4% 1.141 4.15 1.127 3.7% 4.04 4.3% 4.85 1.7% 4.7% <td>272313 7% 3.44 2.38 2.27 3.7% 1.94 1.1% 0 — 244/56 cous vascular 17/313 6.4% 2/41 4.9% 1.27 3.7% 1.94 1.1% 0 — 244/56 nomations 17/313 6.4% 1/41 2.4% 5/27* 18.5% 10/94 1.1% 0 — 24/56 summations 18/313 5.4% 1/41 2.4% 5/27* 18.5% 10/94 1.1% 0 — 24/56 allis 2.5/313 6.8% 13/41* 31.7% 1/27 3.7% 4/94 4.3% 4/85 4.7% 4/560 allis 2.5/313 6.8 17/41 41.5% 1/27 3.7% 4/94 4.3% 4/85 3.5% 4/6 sis 17/21 31.27 3.7% 4/94 4.3% 4/85 4.7% 4/5 sis 17/21 3.7% 2.74 11/27</td> <td>viapping 2.273 3.4 2.427 3.7 3.4 1.5 3.4 1.5 3.4 1.5 3.4 1.5 3.4 1.5 3.4 1.5 3.4 1.5 3.4 1.5 3.4 1.5 3.4 1.5 3.4 1.5 3.7 9.9 1.5 1.0 0 0 0 0 2.4 3.5 2.4 4.5 1.5 1.2 3.7 9.9 1.0 0 0 2.4 4.5 1.5 1.2 3.7 9.9 0<!--</td--><td>constriction rings</td><td></td><td></td><td></td><td></td><td></td><td></td><td></td><td></td><td></td><td></td><td></td><td>1</td></td>	272313 7% 3.44 2.38 2.27 3.7% 1.94 1.1% 0 — 244/56 cous vascular 17/313 6.4% 2/41 4.9% 1.27 3.7% 1.94 1.1% 0 — 244/56 nomations 17/313 6.4% 1/41 2.4% 5/27* 18.5% 10/94 1.1% 0 — 24/56 summations 18/313 5.4% 1/41 2.4% 5/27* 18.5% 10/94 1.1% 0 — 24/56 allis 2.5/313 6.8% 13/41* 31.7% 1/27 3.7% 4/94 4.3% 4/85 4.7% 4/560 allis 2.5/313 6.8 17/41 41.5% 1/27 3.7% 4/94 4.3% 4/85 3.5% 4/6 sis 17/21 31.27 3.7% 4/94 4.3% 4/85 4.7% 4/5 sis 17/21 3.7% 2.74 11/27	viapping 2.273 3.4 2.427 3.7 3.4 1.5 3.4 1.5 3.4 1.5 3.4 1.5 3.4 1.5 3.4 1.5 3.4 1.5 3.4 1.5 3.4 1.5 3.4 1.5 3.4 1.5 3.7 9.9 1.5 1.0 0 0 0 0 2.4 3.5 2.4 4.5 1.5 1.2 3.7 9.9 1.0 0 0 2.4 4.5 1.5 1.2 3.7 9.9 0 </td <td>constriction rings</td> <td></td> <td>1</td>	constriction rings												1
riction rings 20313 644 2/41 4.94 1/27 3.7% 1/94 1.18 0 — 24/560 and social soc	inchon miggs 20313 6.4% 2.41 4.9% 1.27 3.7% 1.94 1.1% 0 — 24/560 and one of continuings 20313 6.4% 1.41 2.4% 5.727 18.5% 1.094 1.06% 1.08 1.1% 34/560 and one of continuings 2.5/313 6.4% 1.41 2.4% 5.727 18.5% 1.094 1.06% 1.06% 1.0% 3.85 3.5% 4.6% 34/560 and one of continuings 2.5/313 6.4% 1.7/41 41.5% 1.7/2 3.7% 3.9% 3.9% 3.8% 3.8% 3.8% 4.7/560 and one of continuings 2.5/313 6.4% 1.7/41 41.5% 2.27 7.4% 1.1/94 1.1.1% 6.6% 3.6% 4.7% 2.94/385 and one of continuings 2.5/313 1.3% 2.4% 2.4% 2.4% 3.7% 3.9% 3.9% 3.6% 3.6% 3.6% 3.6% 3.6% 3.6% 3.6% 3.6	integration inggs	Cord wrapping	22/313	%	3/41	7.3%	2/27	3.7%	3/94	3.5%	2/82	8.5%	32/260	£%9.9
cobs vascular 17313 5.4% 1/41 2.4% 5/27* 18.5% 10.94 10.6% 1/85 1.1% 34/560 numations 18831 5.7% 0 0 0 0 0 385 3.5% 21/560 standardis 25/313 8% 13/41* 31.7% 1/27 3.7% 494 4.3% 4/85 4.7% 47/560 stactorisin 25/313 8.6% 17/41* 41.5% 1/27 3.7% 4/94 4.3% 4/85 4.7% 4/7560 sistertesion 27/313 8.6% 17/41* 41.5% 2/27 7.4% 11/94 11.1% 6/85 7.1% 47/560 sistertesion 37/31 8.6% 17/41* 41.5% 1/27 7.4% 11/94 11.1% 6/85 7.1% 47/560 sisting 4/313 13.4% 11/18 61.% 42/60 70% 36/54 67% 34/38 sisting 4/313	books vascular 17/313 5,4% 1/41 2,4% 5/27* 18,5% 10/94 10.6% 1/85 11% 34/560 satisfactors 22/313 8% 13,4% 1/27 3,7% 4/94 4,3% 4/85 3,5% 21/560 sist strunk 22/313 8% 17/41* 41.5% 1/27 3,7% 4/94 4,3% 4/85 3,5% 4/6 sist strunk 22/313 8,6% 17/41* 41.5% 1/27 3,7% 3/94 3,2% 3/85 3,5% 4/6 sist strunk 22/313 8,6% 17/41* 41.5% 1/27 3,7% 3/94 3,2% 3/85 5/1% 63/85 sist strunk 22/313 8,6% 17/41* 41.5% 1/27 3,7% 3/94 3,2% 3/85 5/1% 63/85 sist strunk 22/313 8,6% 17/41* 41.5% 1/27 3,7% 3/94 3,2% 3/65 6/7% 294/385 sist strunk 22/313 8,6% 17/41* 41.5% 1/27 3,7% 3/94 3,2% 3/65 6/7% 294/385 sist strunk 22/313 8,6% 17/41* 41.5% 1/27 3,7% 3/94 3,2% 3/65 6/7% 294/385 sist strunk 22/313 8,6% 17/41* 41.5% 1/27 3,7% 3/94 3,7% 3/65 6/7% 294/385 sist strunk 22/313 8,6% 17/41* 41.5% 1/27 3,7% 3/94 3,7% 3/65 6/7% 294/385 sist strunk 2/182 12% 0 0 0 2/18 11% 1/60 11/7 2/4 3,7% 3/38 1/28 sist strunk 2/182 3,8% 1/26 2,7% 3/6 1/44 3,7% 3/6 3/6 1/27 3/8 1/49/312 sist strunk 2/182 3,8% 1/26 3,8% 0/17 0/% 2/52 3,8% 3/35 6/8 5/8 5/9560 sist strunk 2/182 12,7% 1/48 3,8% 0/17 0/% 2/52 3,8% 3/35 5/8 5/8 5/9560 sist strunk 2/182 12,7% 1/48 3,8% 0/17 0/% 2/52 2,8% 5/9560 sist strunk 2/182 12,7% 1/48 3,8% 0/17 0/% 2/52 3,8% 3/35 5/8 5/9560 sist strunk 2/182 12,7% 1/48 3,8% 0/17 0/% 2/52 3,8% 3/35 5/8 5/9560 sist strunk 2/182 12,7% 1/48 3,8% 0/17 0/% 2/52 2,8% 5/9560 sist strunk 2/182 12,7% 1/48 3,8% 0/17 0/8 2/52 2,8% 5/9560 sist strunk 2/182 12,7% 1/48 3,8% 0/17 0/8 2/52 2,8% 5/9560 sist strunk 2/182 12,7% 1/48 3,8% 0/17 0/8 2/52 2,8% 5/9560 sist strunk 2/182 12,7% 1/48 3,9% 3/95 2,9% 5/9560 sist strunk 2/182 12,7% 1/48 3,9% 3/95 2,9% 5/9560 sist strunk 2/182 12,7% 1/48 3,9% 3/95 2,9% 5/9560 sist strunk 2/182 12,7% 1/48 3,9% 3/95 2,9% 5/9560 sist strunk 2/182 12,7% 1/48 3,9% 3/95 2,9% 5/9560 sist strunk 2/182 12,7% 1/48 3,9% 3/95 2,9% 5/9560 sist strunk 2/182 12,7% 1/48 3,9% 3/95 2,9% 5/9560 sist strunk 2/182 12,7% 1/48 3,9% 3/95 2,9% 5/9560 sist strunk 2/182 12,0% 1/49 3,0% 5/9560 sist strunk 2/182 12,0% 1/49 3,0% 5/9560	rocus vascular 17/313 5.4% 1/41 2.4% 5/27* 18.5% 10/94 10.6% 1/85 11/8 34/560 nametions 1s 18/313 5.7% 0 0 0 0 3/85 1.1% 24/560 sillis 25/313 8% 13/41* 41.5% 1/27 3.7% 4/94 4.3% 4/85 4.7% 4/7560 restriction 22/313 8.6% 17/41* 41.5% 1/27 3.7% 3/94 3.2% 3/85 4.6 sist trunk 22/313 8.6% 17/41* 41.5% 1/27 3.7% 4/94 4.3% 4/85 4.7560 sist trunk 22/313 8.6% 17/41* 41.5% 2/27 7.4% 11.1% 6.8% 3.7% 4/95 4.7% 4.7560 4.7% 4.7% 4.7% 4.7% 4.7% 4.7% 4.7% 4.7% 4.7% 4.7% 4.7% 4.7% 4.7% 4.7% 4.7%	Constriction rings	20/313	6.4%	2/41	4.9%	1/27	3.7%	1/94	1.1%	0	1	24/560	4.3%**
Insignation Insign	Interventions (2.5.3.13) (2.7.4) (3.1.4) (3.1.7.4) (1.2.7) (3.7.4) (3.7.4) (4.9.4) (4.3.4) (4.9.5) (3.8.4) (4.7.4) (4.7.5) (4.7.4) (4.1.5.4) (1.2.7) (3.7.4) (4.9.4) (4.3.4) (4.9.5) (4.7.4) (4.7.5) (4.7.4) (4.1.5.4) (4.1.5.4) (1.2.7) (4.1.4) (4.1.5.4) (4.1.4) (4.1.5.4) (4.1.4) (Infractions (25/313) (27%) (2.60) (2.00) (2.	Sutaneous vascular	17/313	5.4%	1/41	2.4%	5/27*	18.5%	10/94	10.6%	1/85	1.1%	34/560	6.1%**
18313 5,7% 0 0 0 0 0 3,85 3,5% 2,560 184313 5,7% 0 0 0 0 0 0 3,2% 3,5% 2,750 185 13,41 41,5% 12,7 3,7% 40,4 3,2% 3,4% 47,50 rextension 22,313 8,6% 17/41 41,5% 12,2 7,4% 3,2% 3,4% 4,7% 47,50 rinester 182/25 81,8 17/41 41,5% 2,22 7,4% 11,94 11,1% 6,8% 7,1% 47,50 rinester 182/25 81,8 17/41 41,5% 2,22 7,4% 47,60 70% 36,54 67% 294,385 rancy 11/28 3,4% 1,78 5,4% 12/60 70% 36,54 67% 294,385 rancy 11/28 1,24 1,24 1,24 1,24 1,24 1,3% 4,4% 1,46	15.5 15.73 5.74 0 0 0 0 0 3.85 3.5% 21.560 15.5 15.5 13.41* 11.74 1.27 3.7% 4.94 4.3% 3.5% 4.7560 15.5 13.31 7% 17.41* 41.5% 1.27 3.7% 4.94 3.2% 3.85 3.5% 4.7560 sis 22.53.13 8.6% 17.41* 41.5% 1.27 3.7% 4.94 3.2% 3.85 3.5% 4.6 sis 22.53.3 1.74.1 41.5% 1.27 3.7% 4.94 4.3% 4.75 3.5% 4.6 sis 2.273.3 8.6% 1.74.1 41.5% 1.72 3.7% 4.260 70% 36.5 7.1% 6.3750 sis 2.272.5 3.4% 5.18 1.72 3.7% 3.04 3.7% 2.44385 silections 2.722.5 3.4% 5.18 2.18 3.2% 3.04 3.7%	15 15/31 5.7% 0	malformations												
Sist and the statement of the control of sist of the control of sist of the control of t	25/313 8 k 13/41* 31,7% 1/27 3,7% 4/94 4,3% 4/85 4,7% 47/560 rextension 22/313 7 k 17/41* 41,5% 1/27 3,7% 3/94 3,2% 4/85 4,7% 47/560 rextension 27/313 8 ck 17/41 41,5% 2/27 7.4% 11/94 11.1% 6/85 7.1% 46 sis aliends 27/313 8 ck 17/41 41,5% 2/27 7.4% 11/94 11.1% 6/85 7.1% 46 shands 4,313 1,3 2,41 4,8% 1,27 3,7% 3/94 3,7% 3/95 4,7% 47/50 1,1% 6/85 7,1% 6/85 7,1% 6/85 7,1% 6/85 7,1% 6/85 7,1% 6/85 7,1% 6/85 7,1% 6/85 7,1% 6/85 7,1% 6/85 7,1% 6/85 7,1% 6/85 7,1% 6/85 7,1% 6/85	1,14, 1,14, 1,12, 1,12, 1,12, 1,12, 1,12, 1,12, 1,12, 1,12, 1,12, 1,12, 1,12, 1,12, 1,12, 1,12, 1,13, 1,12, 1,13	rismus	18/313	5.7%	0	0	0	0	0	0	3/82	3.5%	21/560	3.8%
returnic 22/313 7% 17/41 41.5% 1/27 3.7% 3/94 3.2% 3/85 3.5% 46 serension 2/313 86% 17/41 41.5% 2/22 7.4% 11/94 11.1% 6/85 7.1% 6/3560 3/3560	2 Ly 313 7% 17/41* 41.5% 1.27 3.7% 3.94 3.2% 3.6% 46 reversion reversion sists 27/313 86% 17/41* 41.5% 2.27 7.4% 11/94 11.1% 6/85 7.1% 63/560 sist rimester 182/225 81% 23/28 82% 11/18 61% 42/60 70% 36/54 67% 294/385 and liness 4/313 13% 2/41 4.8% 1/27 3.7% 3/94 3% 8/85* 94/385 place of signal liness 76/225 3.4% 1/28 2.8% 1/260 20% 12/54 22% 1/60 place of signal liness 76/225 3.4% 5.78 2/8 7/60 20% 12/54 22% 294/385 place of signal liness 76/225 3.4% 5.78 3.78 3.78 3.78 3.78 3.78 3.78 3.78 3.78 3.78 3.78 3.78 3.78 3.78	Frontice S22313 7% 1741* 41.5% 1/27 3.7% 3/94 3.2% 3/85 3.5% 46 sistematical sistem	orticollis	25/313	% &	13/41*	31.7%	1/27	3.7%	4/94	4.3%	4/85	4.7%	42/260	8.4%
extension siss 1741 41.5% 2727 7.4% 11.94 11.1% 6/85 7.1% 63560 siss 182/225 81% 12/41 41.5% 2727 7.4% 11.94 11.1% 6/85 7.1% 63560 analy alications 42/25 81% 23/28 82% 11.1% 42/60 70% 36/45 67% 294/385 anal illness 4713 1.3% 2741 4.8% 1727 3.7% 3/94 3% 8/85 94% 294/385 anal illness 76/25 3.4% 1727 3.7% 276 277 274 3.7% 27385 defore 27/25 3.4% 17.2% 2.8% 7.60 1.1% 2.54 3.7% 1.2 x before 27/187 4.4% 3.7% 1.4% 3.7% 2.54 3.7% 1.2 x before 27/187 4.4% 3.7% 2.54 3.7% 3.2% 3.2% 3.2% <t< td=""><td>extension 27/313 8.6% 17/41 41.5% 2/27 7.4% 11/94 11.1% 6/85 7.1% 65/56 sis 12/25 81% 23/28 82% 11/18 61% 42/60 70% 36/54 67% 294/385 aimester 182/25 81% 23/28 82% 11/18 61% 29/385 294/385 294/385 all litestions 4/313 1.3% 2/41 4.8% 1/27 3.7% 3/94 3.8 8/85 9.4% 18/56 and illness 76/25 3.4% 1/28 2.8% 1/26 2.0% 12/54 3.7% 29/385 and illness 76/25 3.4% 1/28 2.8% 1/26 2.0% 1/27 3.7% 3/28 and illness 76/25 3.4% 14/45 3.4% 14/45 3.7% 3/28 3.7% 3/28 at before 27/182 44/45 3.4% 14/45 3.4% 14/45</td><td>extension 27/313 86% 17/41 41.5% 2/22 7.4% 11/94 11.1% 6/85 7.1% 63/560 sist sist 182/25 81.% 23/28 82.% 11/18 61.% 42/60 70% 36/54 67% 294/385 amountsester 182/25 81.% 23/28 11/18 17/27 3.7% 3/94 3.% 6/85 7.1% 294/385 all lines 76/25 34.% 11/28 2.5% 7/60 20% 12/54 22% 106/385 and lines 76/25 34.% 17/2 28 12/60 20% 22/4 3.7% 37/385 and lines 76/25 34.% 11/8 5.5% 7/60 11.% 2/54 3.7% 37/385 at till 77225 34. 37/20 15. 7/16 44.% 14/45 31.% 11/25 37.8 37/385 at till 37/182 34.% 37/25</td><td>severe trunk</td><td>22/313</td><td>%2</td><td>17/41*</td><td>41.5%</td><td>1/27</td><td>3.7%</td><td>3/94</td><td>3.2%</td><td>3/82</td><td>3.5%</td><td>46</td><td>8.2%</td></t<>	extension 27/313 8.6% 17/41 41.5% 2/27 7.4% 11/94 11.1% 6/85 7.1% 65/56 sis 12/25 81% 23/28 82% 11/18 61% 42/60 70% 36/54 67% 294/385 aimester 182/25 81% 23/28 82% 11/18 61% 29/385 294/385 294/385 all litestions 4/313 1.3% 2/41 4.8% 1/27 3.7% 3/94 3.8 8/85 9.4% 18/56 and illness 76/25 3.4% 1/28 2.8% 1/26 2.0% 12/54 3.7% 29/385 and illness 76/25 3.4% 1/28 2.8% 1/26 2.0% 1/27 3.7% 3/28 and illness 76/25 3.4% 14/45 3.4% 14/45 3.7% 3/28 3.7% 3/28 at before 27/182 44/45 3.4% 14/45 3.4% 14/45	extension 27/313 86% 17/41 41.5% 2/22 7.4% 11/94 11.1% 6/85 7.1% 63/560 sist sist 182/25 81.% 23/28 82.% 11/18 61.% 42/60 70% 36/54 67% 294/385 amountsester 182/25 81.% 23/28 11/18 17/27 3.7% 3/94 3.% 6/85 7.1% 294/385 all lines 76/25 34.% 11/28 2.5% 7/60 20% 12/54 22% 106/385 and lines 76/25 34.% 17/2 28 12/60 20% 22/4 3.7% 37/385 and lines 76/25 34.% 11/8 5.5% 7/60 11.% 2/54 3.7% 37/385 at till 77225 34. 37/20 15. 7/16 44.% 14/45 31.% 11/25 37.8 37/385 at till 37/182 34.% 37/25	severe trunk	22/313	%2	17/41*	41.5%	1/27	3.7%	3/94	3.2%	3/82	3.5%	46	8.2%
sis 27/313 8.6% 17/41 41.5% 2/27 74% 11/94 11.1% 6/85 7.1% 6/350 and illinester 18/225 81% 23/28 82% 11/18 61% 42/60 70% 36/54 67% 294/385 and illiness 76/225 34% 1/28 3.4% 5/18 28% 12/60 20% 12/54 22% 10/6/385 and illiness 7/125 12% 0 0 1/18 5.5% 7/60 11.7% 2/54 3.7% 37/385 and illiness 2/14% 3/20 15/8 2/4 3.7% 3/50 11.7% 2/54 3.7% 3/385 and illines 8/182 49% 7/26 27/25 67% 2/52 33% 1/26 63% 8/17 44% 1/445 3/38 1/26 63% 8/17 47% 1/52 33% 1/29 3/38 1/29 3/38 1/26 3/38 3/38 3/38 3/38 3/38 3/38 and inth 40/313 12.7% 10/41 24% 4/27 14.8% 0/17 0% 2/52 3.8% 3/35 5/80 1/33 3/36 1/38 3/38 1/26 3/38 3/38 3/38 3/38 3/38 3/38 3/38 3/3	sis 27333 8 6% 1741 41.5% 2.27 7.4% 11.1% 6.85 7.1% 6.3560 ninester 182/225 81% 2.3728 82% 11/18 61% 42/60 70% 36/54 67% 2.94/385 ninester 182/225 81% 2.3728 82% 11/18 61% 42/60 70% 36/54 67% 2.94/385 ninester 182/22 81% 2.348 1/28 3.4% 1/28 3.4% 1/28 2.5% 1/28 12% 0 0 0 1/18 2.5% 1/26 2.0% 2/49 3.7% 1/38 1/38 1/4% 1/4% 1/4% 1/4% 1/4% 1/4% 1/4% 1/4%	sist 27/313 8 6% 17/41 41.5% 227 7 4% 11/94 11.1% 6/85 7.1% 63/560 nimester 182/225 81% 12/42 82% 11/18 61% 42/60 70% 36/54 67% 294/385 nal plications 4/313 1.3% 2/41 4.8% 1/27 3.7% 3/94 3% 8/85* 9.4% 18/560 nal illness 7/6/25 3.4% 1/28 3.4% 5/18 2.8% 12/60 20% 12/54 2.2% 106/385 yiramios mild 2/725 3.4% 1/28 3.4% 5/18 2.8% 12/60 20% 12/54 2.2% 106/385 yiramios mild 2/725 3.8 1/28 3/4 4.4% 14/45 3.7% 3.7% 3.7% 3.7% 3.7% 3.7% 3.7% 3.7% 3.7% 3.7% 3.7% 3.7% 3.7% 3.7% 3.7% 3.7% 3.7% 3.7%	hyperextension												
rimester 182/225 81% 23/28 82% 11/18 61% 42/60 70% 36/54 67% 294/385 sand samply shifted to shift at the control of the contro	infractor 18225 81% 23/28 82% 11/18 61% 42/60 70% 36/54 67% 294/385 and but better 27/225 12% 0 0 1/18 5.5% 12/60 11.7% 2/54 5.7% 106/385 and birth 27/125 12% 0 0 2/18 11% 1.60 11.7% 2/54 3.7% 17/30 11/30	inflactor 182/25 81% 23/28 82% 11/18 61% 42/60 70% 36/54 67% 294/385 and allocations and according an according and allocations and according and allocations and according and allocations and allocations and allocations and 27/25 34% 1/28 34% 1/28 27/25 34% 1/28 34% 1/28 27/25 27/25 2	Scoliosis	27/313	8.6%	17/41	41.5%	2/27	7.4%	11/94	11.1%	58/9	7.1%	63/260	11.3%
A 4/313 1.3% 2/41 4.8% 1/27 3.7% 3/94 3% 8/85* 9.4% 18/560 an allihess 76/225 3.4% 1/28 3.4% 5/18 2.8% 12/60 20% 12/54 2.2% 106/385 ydramnios mild 2/725 1.2% 0 0 1/18 5.5% 7/60 11.7% 2/54 3.7% 12/30 platamios mild 2/725 3.4% 3/20 1.4% 2/16* 1.4% 1.6% 2/54 3.7% 1.2% platemios mild 2/725 3.4% 3/20 1.4% 1.4% 1.6% 1.6% 2/54 3.7% 1.2% platemios mild 2/725 3.4% 3/20 1.6% 2/34 3.7% 1.2% platemios mild 2/725 3.4% 3/20 1.6% 2/34 3.7% 1.2% platemios mild 2/725 3.4% 3/20 1.6% 3/35 1.6% platemios mild 2/725 3.4% 3/20 1.6% 3/35 1.6% 1.6% 1.6% 2/182 1.4% 3/20 2.2% 9/17 5.3% 3/52 6.7% 2/35 6.6% 163/312 and birth 93/182 5.1% 1/26 3.8% 0/17 0/% 0/52 0.0 0/35 0/3 3/30 2/182 1.1% 1/26 3.8% 0/17 0/% 0/52 0.0 0/35 0/3 5/36 2/182 1.1% 1/26 3.8% 0/17 0/% 0/52 0.0 0/35 0/3 5/36 all diagnosis 1.8/72 2.5% 5/15 3.3% 3/36 5/35 2.8% 5/42 1.2% 3/310	Adjustment and the subject of the su	and by solutions and solution and so	-irst trimester	182/225	81%	23/28	85%	11/18	61%	42/60	20%	36/54	%29	294/385	76.4%**
lications at 313 2/41 4.8% 1/27 3.7% 3/94 3% 8/85 9.4% 18/560 and lilness 26/25 3.4% 1/28 3.4% 5/18 2.8% 12/60 2.0% 12/54 2.2% 106/385 and lilness 27/25 12% 0 0 1/18 5.5% 7/60 11.7% 2/54 3.7% 37/385 and lilness 27/25 14.4% 3/20 15% 2/16* 44% 14/45 31% 11/52 27/18	lications 4,313 1.3% 2/41 4.8% 1/27 3.7% 3/94 3% 8/85* 9.4% 18/560 and illness 5/6/25 3.4% 5/18 28% 12/60 20% 12/54 22% 106/385 and illness 5/6/25 3.4% 5/18 28% 12/60 20% 12/54 22% 106/385 and illness 5/2/25 3% 0 0 2/18 11% 1/60 1.6% 2/54 3.7% 3.7% 1.2 and illness 5/187 14.4% 3/20 1/18 5.5% 7/16* 44% 14/45 31% 11/52 21% 62/320 and inth 89/182 51% 1/26* 63% 8/17 47% 17/52* 33% 12/35 66% 163/312 and inth 93/182 51% 1/26 63% 8/17 47% 17/52* 33% 3/35 8/7% 13/312 and inth 40/313 12.7% 10/41* 24% 4/27 14.8% 0/94 0/8 5/85 5/85 5/85 6/8 5/9560 and inth 40/313 12.7% 10/41* 24% 4/27 14.8% 0/94 0/8 5/85 5/85 5/9560 and inth and anothing meroutine meroutine.	lications 4/313	pregnancy												
and lithess 4/313 1.3% 2/41 4.8% 1/27 3.7% 3/94 3% 8/85 9.4% 18/56 and lithess 76/25 3.4% 1/28 2.48 1/27 3.7% 3/94 3% 8/85 9.4% 18/56 and lithess 76/25 3.4% 1/18 5.5% 7/60 11.7% 2/54 3.7% 37/385 artifity 2/225 3.% 1/44 1/16 1/60 1.6% 2/54 3.7% 37/385 at before 2/18 1/44 1/46 3.1% 1/45 3.7% 3.7% 37/385 eption 2/18 1/16 4/4 1/44 3.1% 1/52 3.1% 1/52 3.7% 3.7% 3.7% 3.7% 3.7% 3.7% 3.7% 3.7% 3.2% 3.2% 3.2% 3.2% 3.2% 3.2% 3.2% 3.2% 3.2% 3.2% 3.2% 3.2% 3.2% 3.2% 3.2% 3.2% <	and illness 4/313 1.3% 2/41 4.8% 1/27 3.7% 3/94 3% 8/85* 9.4% 18/560 and illness 76/225 3.4% 1/28 2.8% 12/60 20% 12/54 22% 106/385 ydrammios mild 27/225 12% 0 0 1/18 5.5% 7/60 11.7% 2/54 3.7% 37/385 rrility 7/225 3.% 0 0 2/18 11% 1/60 1.6% 2/54 3.7% 37/385 rt before 27/187 14,4% 3/70 15% 7/16* 44% 14/45 31% 11/52 37/38 12/38 12/38 16/3312 all birth 99/182 51% 17/26 63% 8/17 47% 17/52* 33% 12/35 48% 149/312 rese 7/182 3.8% 0.77 0.75 0.75 0.75 0.75 0.75 0.75 0.75 0.75 0.75	a dilliness 7/313 1.3% 2/41 4.8% 1/27 3.7% 3/94 3% 8/85 9.4% 18/560 and illiness 7/6/25 34% 1/28 3.4% 5/18 2.8% 12/60 20% 12/54 2.2% 106/385 104/44minism mild 2/7/25 1.2% 0 0 1/18 5.5% 7/60 11.7% 2/54 3.7% 3/7385 12 12 12 14.4% 3/20 15% 7/16* 44% 14/45 31% 11/52 21% 66% 16/320 eption eption and birth 89/182 49% 7/26 27% 9/17 53% 35/52 67% 2/35 66% 16/3/312 am birth 93/182 1.1% 1/26 3.8% 0/17 0% 2/52 3.8% 3/35 8/7 12/35 3/38 12/35 8/7 13/312 12/38 18/7 12/3 3.8% 0/17 0% 0/52 0 0/3/3 0/3 3/302 and birth 40/313 12.7% 10/41* 24% 4/27 14.8% 0/94 0% 5/85 5/8 5/86 5/8 5/86 0/17 0% 0/35 0% 3/35 0/3 3/302 and birth 40/313 12.7% 10/41* 24% 4/27 14.8% 0/94 0% 5/85 5/8 5/85 5/86 0/17 0/18 0/19 0/19 0/19 0/19 0/19 0/19 0/19 0/19	complications												
nal lilness 76/225 34% 1/28 3.4% 5/18 28% 12/60 20% 12/54 22% 106/385 ydramnios mild 27/225 12% 0 0 1/18 5.5% 7/60 11.7% 2/54 3.7% 37/385 rtility 7/225 3% 0 0 2/18 11% 1/60 1.6% 2/54 3.7% 37/385 rt before 27/187 14,4 3/20 15% 7/16* 44% 14/45 31% 11/52 21% 62/320 eption 27/18 47% 17/52* 31% 11/52 21% 62/320 san birth 93/182 51% 19/26* 63% 8/17 47% 17/52* 33% 12/35 34% 149/312 verse 7/182 3.8% 0/17 0% 2/52 3.8% 0/35 0% 3/302 reat birth 40/313 12/3 3/4 4/27 14.8% <	nal illness 76/225 34% 1/28 5/18 28% 12/60 20% 12/54 22% 106/385 ydramnios mild 27/25 12% 0 0 1/18 5.5% 7/60 11.7% 2/54 3.7% 37/385 rrility 7/225 3% 0 0 2/18 11% 1/60 1.6% 2/54 3.7% 37/385 rt before 27/187 14.4% 3/20 15% 7/16* 44% 14/45 31% 11/52 21% 62/320 eption 27/18 17/6* 44% 14/45 31% 11/52 21% 62/320 eption 27/18 17/6* 44% 14/45 31% 11/52 21% 62/320 san birth 93/182 63% 9/17 47% 17/52* 33% 12/35 8/7 14/3/312 rest 11/8 11/8 0/17 0% 0/52 0 0/35 0% 0/35 </td <td>nal lilness 76/255 34% 1/28 5/18 28% 12/60 20% 12/54 22% 106/385 ydramnios mild 27/255 12% 0 1/18 5.5% 7/60 11.7% 2/54 3.7% 37/385 rrtlity 7/255 3.% 0 0 1/18 5.5% 7/60 11.7% 2/54 3.7% 37/385 rt before 27/187 14.4% 3/20 15% 7/16* 44% 14/45 31% 11/52 2.7% 3.7% 37/385 petion 27/187 3/20 15% 7/16* 44% 14/45 31% 11/52 2.7% <t< td=""><td>frauma</td><td>4/313</td><td>1.3%</td><td>2/41</td><td>4.8%</td><td>1/27</td><td>3.7%</td><td>3/94</td><td>3%</td><td>*58/8</td><td>9.4%</td><td>18/260</td><td>3.2%</td></t<></td>	nal lilness 76/255 34% 1/28 5/18 28% 12/60 20% 12/54 22% 106/385 ydramnios mild 27/255 12% 0 1/18 5.5% 7/60 11.7% 2/54 3.7% 37/385 rrtlity 7/255 3.% 0 0 1/18 5.5% 7/60 11.7% 2/54 3.7% 37/385 rt before 27/187 14.4% 3/20 15% 7/16* 44% 14/45 31% 11/52 2.7% 3.7% 37/385 petion 27/187 3/20 15% 7/16* 44% 14/45 31% 11/52 2.7% <t< td=""><td>frauma</td><td>4/313</td><td>1.3%</td><td>2/41</td><td>4.8%</td><td>1/27</td><td>3.7%</td><td>3/94</td><td>3%</td><td>*58/8</td><td>9.4%</td><td>18/260</td><td>3.2%</td></t<>	frauma	4/313	1.3%	2/41	4.8%	1/27	3.7%	3/94	3%	*58/8	9.4%	18/260	3.2%
ydramnios mild 27/225 12% 0 1/18 5.5% 7/60 11.7% 2/54 3.7% 37/385 rtility 7/225 3% 0 0 2/18 11% 1/60 1.6% 2/54 3.7% 37/385 rtility 7/225 3% 0 0 2/18 11% 1/60 1.6% 2/54 3.7% 12 eption 27/18 14/45 31% 11/52 21% 66/320 eption 49/182 49/2 67/2 33% 12/25 67% 2/35 66% 163/312 asan birth 93/182 51% 63% 9/17 47% 17/52* 33% 12/35 34% 149/312 verse 7/182 3.8% 0/17 0% 2/52 3.8% 0/35 0% 3/30 read birth 40/313 12/2 3.8% 0/17 0% 0/52 0 0/35 0% 5/35 5/36	ydramnios mild 27/225 12% 0 1/18 5.5% 7/60 11.7% 2/54 3.7% 37/385 rtility 7/225 3% 0 0 2/18 11% 1/60 1.6% 2/54 3.7% 37/385 rtility 7/225 3% 0 0 2/18 11% 1/60 1.6% 2/54 3.7% 12 eption 27/18 14,4% 3/20 15% 4/4 14/45 31% 11/52 21% 66/320 all birth 89/182 49/8 7/26 27/8 9/17 47% 17/52* 33% 12/35 66% 163/312 san birth 93/182 51% 63% 8/17 47% 17/52* 33% 12/35 34% 149/312 rese 2/182 11.2% 3.8% 0/17 0% 2/52 3.8% 3/35 8.7% 13/312 rese 2/182 11.2% 10/41* 24%	ydramnios mild 27/225 12% 0 1/18 5.5% 7/60 11.7% 2/54 3.7% 37/385 artility 7/225 3% 0 0 2/18 11% 1/60 1.6% 2/54 3.7% 37/385 artility 7/225 3% 0 0 2/18 11% 1/60 1.6% 2/54 3.7% 12 eption 27/187 14.4% 3/20 15% 7/16* 27/3 31% 1/52 21% 62/320 eption 27/187 3/18 3/75 67 23/35 66% 163/312 an birth 93/182 1/26 3.8% 0/17 0% 2/52 3.8% 3/35 8.7% 149/312 rerse 2/182 11.1% 1/26 3.8% 0/17 0% 0/52 0 0/35 0% 3/302 rerse 1/18 1/27 1/28 3.8% 0/17 0% 0/35 0 <td>Maternal illness</td> <td>76/225</td> <td>34%</td> <td>1/28</td> <td>3.4%</td> <td>5/18</td> <td>28%</td> <td>12/60</td> <td>20%</td> <td>12/54</td> <td>25%</td> <td>106/385</td> <td>27.5%**</td>	Maternal illness	76/225	34%	1/28	3.4%	5/18	28%	12/60	20%	12/54	25%	106/385	27.5%**
trefity 7/225 3% 0 0 2/18 11% 1/60 1.6% 2/54 3.7% 12 12 to before 2/187 14.45 14.45 11.52 21% 62/320 eption 89/182 49% 7/26 2/2 9/17 53% 35/52 6/2 2/3 33% 12/312 and birth 93/182 51% 19/26* 6/3% 8/17 47% 17/52* 33% 12/35 6/3 149/312 erre at birth 40/313 12.7% 10/41* 24% 4/27 14.8% 0/94 0% 5/85 5/8 5/15 33% 18/10 ultrasound utbefore 2/182 3.8% 0/17 0% 0/95 0% 0/95 0% 3/302 erre at birth 40/313 18/72 25% 5/15 33% 3/6 5/8 5/8 5/8 5/8 5/8 5/8 5/8 3/160	treifity 7/225 3% 0 0 2/18 11% 1/60 1.6% 2/54 3.7% 12 12 to before 2/187 14.45 31% 11/52 21% 62/320 eption 89/182 49% 7/26 2/2% 9/17 53% 35/52 6/2% 23/35 66% 163/312 and birth 93/182 51% 19/26* 63% 8/17 47% 17/52* 33% 12/35 66% 149/312 erre at birth 40/313 12.7% 10/41* 24% 4/27 14.8% 0/17 0% 0/95 0 0/35 0% 3/302 ending all diagnosis 18/72 25% 5/15 33% 3/6 5/2 28% 5/25 12% 38% 160 me routine	rtility 7/225 3% 0 0 2/16* 44% 1/60 1.6% 2/54 3.7% 12 rt before 27/18* 14.4% 3/20 15% 7/16* 44% 14/45 31% 11/52 21% 62/320 eption eption 27/18* 49% 7/26 27% 9/17 53% 35/52 67% 23/35 66% 163/312 and birth 93/182 51% 19/26* 63% 9/17 47% 17/52* 33% 12/35 34% 149/312 rerse 7/182 3.8% 0/17 0% 2/52 3.8% 3/35 8.7% 149/312 rerse 2/182 11.% 1/26 3.8% 0/17 0% 0/52 0 0/35 0% 3/302 rerse 11.7% 10/41* 24% 4/27 14.8% 0/94 0% 5/85 5/86 59/560 rerse 5/15 5/15 <	Oligohydramnios mild	22/225	12%	0	0	1/18	2.5%	09/2	11.7%	2/54	3.7%	32/385	89.6
th before 27/187 14.4% 3/20 15% 7/16* 44% 14/45 31% 11/52 21% 62/320 eption eption all birth 89/182 49% 7/26 27% 9/17 53% 35/52 67% 23/35 66% 163/312 and birth 93/182 51% 19/26* 63% 8/17 47% 17/52* 33% 12/35 87% 149/312 are abirth 27/182 3.8% 0/17 0% 2/52 3.8% 3/35 8.7% 13/312 are abirth 40/313 12.7% 10/41* 24% 4/27 14.8% 0/94 0% 5/85 5.8% 59/560 ultrasound the before 27/187 25% 3/20 3/20 0/35 0% 3/302 all diagnosis 18/72 25% 5/15 33% 3/6 5/8 5/8 5/8 5/8 3/160	th before 27/187 14.4% 3/20 15% 7/16* 44% 14/45 31% 11/52 21% 62/320 eption eption 89/182 49% 7/26 27% 9/17 53% 35/52 67% 23/35 66% 163/312 and birth 89/182 51% 19/26* 63% 8/17 47% 17/52* 33% 12/35 34% 149/312 erre at birth 2/182 1.1% 1/26 3.8% 0/17 0% 2/52 3.8% 3/35 8.7% 13/312 2/182 1.1% 1/26 3.8% 0/17 0% 0/52 0 0/35 0% 3/302 ald diagnosis 18/72 25% 5/15 33% 3/6 50% 7/25 28% 5/42 12% 38/160 me routine eption 14.4% 3/20 1/26 3.8% 3/35 66% 163/312 21.8% 3/35 8.7% 3/35 8.7% 3/302 22.8% 3/35 5/35 5/35 3/36 23.8% 3/36 5/35 12% 3/36 24.8% 3/36 5/35 12% 3/36 25.8% 3/36 5/35 12% 3/36 25.8% 3/36 5/35 12% 3/36 25.8% 3/36 5/35 12% 3/36 25.8% 3/36 5/35 12% 3/36 25.8% 3/36 5/36 25.8% 3/36 5/36 12% 3/36 25.8% 3/36 5/36 12% 3/36 25.8% 3/36 5/36 12% 3/36 25.8% 3/36 5/36 12% 3/36 25.8% 3/36 5/36 12% 3/36 25.8% 3/36 5/36 12% 3/36 25.8% 3/36 5/36 12% 3/36 25.8% 3/36 5/36 12% 3/36 25.8% 3/36 5/36 12% 3/36 25.8% 3/36 5/36 12% 3/36 25.8% 3/36 5/36 12% 3/36 25.8% 3/36 5/36 12% 3/36 25.8% 3/36 5/36 12% 3/36 25.8% 3/36 5/36 12% 3/36 25.8% 3/36 5/36 12% 3/36 25.8% 3/36 5/36 12% 3/36 25.8% 3/36 5/36 12% 3/36 25.8	th before 27/187 14.4% 3/20 15% 7/16* 44% 14/45 31% 11/52 21% 62/320 eption eption eption 89/182 49% 7/26 27% 9/17 53% 35/52 67% 23/35 66% 163/312 and birth 93/182 51% 19/26* 63% 8/17 47% 17/52* 33% 12/35 34% 149/312 and birth 93/182 11.4% 1/26 33.8% 0/17 0% 2/52 33.8% 3/35 87% 13/312 and diagnosis 18/72 25% 5/15 33% 3/6 50% 7/25 28% 5/42 12% 38/160 and routine 14.4% 4/27 14.4% 0/94 0% 5/85 5.8% 5/9560 and routine 15.7% 10/41* 24% 4/27 14.8% 0/94 0% 5/85 5.8% 5/9560 and routine 16.7320 26% 163/312 33% 3/16 33% 3/16 3/12 3/12 3/12 3/12 3/12 3/12 3/12 3/12	ART/fertility	2/225	3%	0	0	2/18	11%	1/60	1.6%	2/54	3.7%	12	3.1%
eption 89/182 49% 7/26 27% 9/17 53% 35/52 67% 23/35 66% 163/312 asan birth 93/182 51% 19/26* 63% 8/17 47% 17/52* 33% 12/35 34% 149/312 verse 7/182 3.8% 1/26 3.8% 0/17 0% 2/52 3.8% 13/35 8.7% 13/312 rea at birth 40/313 12.7% 10/41* 24% 4/27 14.8% 0/94 0% 5/85 5.9% 59/560 ald diagnosis 18/72 5/15 38 3/6 5/85 5/85 59/560 ultrasound 40/313 10/41* 24% 4/27 14.8% 0/94 0% 5/85 5.8% 59/560	eption 89/182 49% 7/26 27% 9/17 53% 35/52 67% 23/35 66% 163/312 asan birth 93/182 51% 19/26* 63% 8/17 47% 17/52* 33% 12/35 34% 149/312 verse 7/182 3.8% 0/17 0% 2/52 3.8% 17/35 8.7% 13/312 verse 2/182 1.1% 1/26 3.8% 0/17 0% 0/52 0 0/35 0% 3/302 read birth 40/313 12.7% 10/41* 24% 4/27 14.8% 0/94 0% 5/85 5.9% 59/560 ultrasound 18/72 5/15 33% 3/6 50% 7/25 28% 5/42 12% 38/160	eption 89/182 49% 7/26 27% 9/17 53% 35/52 67% 23/35 66% 163/312 and birth 93/182 51% 19/26* 63% 8/17 47% 17/52* 33% 12/35 34% 149/312 serse 7/182 3.8% 1/26 3.8% 0/17 0% 2/52 3.8% 3/35 8.7% 149/312 reat birth 40/313 12.7% 10/41* 24% 4/27 14.8% 0/94 0% 5/85 5.8% 59/560 ald diagnosis 18/72 5/15 33% 3/6 50% 7/25 28% 5/42 12% 38/160	Ab/just before	27/187	14.4%	3/20	15%	2/16*	44%	14/45	31%	11/52	21%	62/320	19.4%
all birth 89/182 49% 7/26 27% 9/17 53% 35/52 67% 23/35 66% 163/312 ean birth 93/182 51% 19/26* 63% 8/17 47% 17/52* 33% 12/35 34% 149/312 verse 7/182 3.8% 1/26 3.8% 0/17 0% 2/52 3.8% 13/31 rice at birth 40/313 12.7% 10/41* 24% 4/27 14.8% 0/94 0% 5/85 59/560 ald diagnosis 18/72 5/15 33% 3/6 50% 7/25 28% 5/42 12% 38/160	all birth 89/182 49% 7/26 27% 9/17 53% 35/52 67% 23/35 66% 163/312 ean birth 93/182 51% 19/26* 63% 8/17 47% 17/52* 33% 12/35 34% 149/312 verse 7/182 3.8% 1/26 3.8% 0/17 0% 2/52 3.8% 13/35 8.7% 13/312 rea at birth 40/313 12.7% 10/41* 24% 4/27 14.8% 0/94 0% 5/85 5.9% 59/560 all diagnosis 18/72 5/15 33% 3/6 50% 7/25 28% 5/42 12% 38/160 me routine 33% 3/6 50% 7/25 28% 5/42 12% 38/160	all birth 89/182 49% 7/26 27% 9/17 53% 35/52 67% 23/35 66% 163/312 ean birth 93/182 51% 19/26* 63% 8/17 47% 17/55* 33% 12/35 34% 149/312 rerse 7/182 3.8% 1/26 3.8% 0/17 0% 2/52 3.8% 3/35 8.7% 149/312 rereat birth 40/313 12.7% 10/41* 24% 4/27 14.8% 0/94 0% 5/85 5.8% 59/560 ald diagnosis 18/72 25% 5/15 33% 3/6 50% 7/25 28% 5/42 12% 38/160	conception												
ean birth 93/182 51% 19/26* 63% 8/17 47% 17/52* 33% 12/35 34% 149/312 verse 7/182 3.8% 1/26 3.8% 0/17 0% 2/52 3.8% 3/35 8.7% 13/312 reat birth 40/313 1.1% 1/26 3.8% 0/17 0% 0/52 0 0/35 0% 3/302 reat birth 40/313 12.7% 10/41* 24% 4/27 14.8% 0/94 0% 5/85 5.9% 59/560 ald diagnosis 18/72 5/15 33% 3/6 50% 7/25 28% 5/42 12% 38/160	ean birth 93/182 51% 19/26* 63% 8/17 47% 17/52* 33% 12/35 34% 149/312 verse 7/182 3.8% 1/26 3.8% 0/17 0% 2/52 3.8% 3/35 8.7% 13/312 rea at birth 40/313 1.2% 10/41* 24% 4/27 14.8% 0/94 0% 5/85 5.9% 59/560 ald diagnosis 18/72 5/15 33% 3/6 50% 7/25 28% 5/42 12% 38/160 me routine 18/72 16/20 16/20 16/20 16/20 16/20 16/20 17/20 18/20 18/20 18/20 18/20 12% 38/160	ean birth 93/182 51% 19/26* 63% 8/17 47% 17/52* 33% 12/35 34% 149/312 verse 7/182 3.8% 1/26 3.8% 0/17 0% 2/52 3.8% 3/35 8.7% 13/312 re at birth 40/313 1.2% 10/41* 24% 4/27 14.8% 0/94 0% 5/85 5.8% 59/560 tal diagnosis 18/72 25% 5/15 33% 3/6 50% 7/25 28% 5/42 12% 38/160 me routine 10	Vaginal birth	89/182	49%	2/26	25%	9/17	23%	35/52	%29	23/35	%99	163/312	25%
Forse 7/182 3.8% 1/26 3.8% 0/17 0% 2/52 3.8% 3/35 8.7% 13/312 13/312 2/182 1.1% 1/26 3.8% 0/17 0% 0/52 0 0/35 0% 3/302 3/302 1.1% 10/41* 24% 4/27 14.8% 0/94 0% 5/85 5.8% 59/560 ald diagnosis 18/72 25% 5/15 33% 3/6 50% 7/25 28% 5/42 1.2% 38/160 altrasound	Forse 7/182 3.8% 1/26 3.8% 0/17 0% 2/52 3.8% 3/35 8.7% 13/312 2/182 1.1% 1/26 3.8% 0/17 0% 0/52 0 0/35 0% 3/302 Fire at birth 40/313 12.7% 10/41* 24% 4/27 14.8% 0/94 0% 5/85 5.8% 59/560 ald diagnosis 18/72 25% 5/15 33% 3/6 50% 7/25 28% 5/42 12% 38/160 me routine	rerse 7/182 3.8% 1/26 3.8% 0/17 0% 2/52 3.8% 3/35 8.7% 13/312 2/182 1.1% 1/26 3.8% 0/17 0% 0/52 0 0/35 0% 3/302 Ire at birth 40/313 12.7% 10/41* 24% 4/27 14.8% 0/94 0% 5/85 59/560 Ial diagnosis 18/72 25% 5/15 33% 3/6 50% 7/25 28% 5/42 12% 38/160 me routine me routine 18/72 12% 12% 12% 12% 38/160	Cesarean birth	93/182	51%	19/26*	63%	8/17	47%	17/52*	33%	12/35	34%	149/312	48%
2/182 1.1% 1/26 3.8% 0/17 0% 0/52 0 0/35 0% 3/302 rre at birth 40/313 12.7% 10/41* 24% 4/27 14.8% 0/94 0% 5/85 5.8% 59/560 all diagnosis 18/72 25% 5/15 33% 3/6 50% 7/25 28% 5/42 12% 38/160 ultrasound	2/182 1.1% 1/26 3.8% 0/17 0% 0/52 0 0/35 0% 3/302 rre at birth 40/313 12.7% 10/41* 24% 4/27 14.8% 0/94 0% 5/85 5.8% 59/560 all diagnosis 18/72 25% 5/15 33% 3/6 50% 7/25 28% 5/42 12% 38/160 me routine	2/182 1.1% 1/26 3.8% 0/17 0% 0/52 0 0/35 0% 3/302 rre at birth 40/313 12.7% 10/41* 24% 4/27 14.8% 0/94 0% 5/85 5.8% 59/560 altrasound solutions at a second solution of the second solu	Transverse	7/182	3.8%	1/26	3.8%	0/17	%0	2/25	3.8%	3/35	8.7%	13/312	4.2%
40/313 12.7% 10/41* 24% 4/27 14.8% 0/94 0% 5/85 5.8% 59/560 18/72 25% 5/15 33% 3/6 50% 7/25 28% 5/42 12% 38/160	40/313 12.7% 10/41* 24% 4/27 14.8% 0/94 0% 5/85 5.8% 59/560 18/72 25% 5/15 33% 3/6 50% 7/25 28% 5/42 12% 38/160	40/313 12.7% 10/41* 24% 4/27 14.8% 0/94 0% 5/85 5.8% 59/560 18/72 25% 5/15 33% 3/6 50% 7/25 28% 5/42 12% 38/160	Face	2/182	1.1%	1/26	3.8%	0/17	%0	0/52	0	0/35	%0	3/302	1%
18/72 25% 5/15 33% 3/6 50% 7/25 28% 5/42 12% 38/160	18/72 25% 5/15 33% 3/6 50% 7/25 28% 5/42 12% 38/160	18/72 25% 5/15 33% 3/6 50% 7/25 28% 5/42 12% 38/160	Fracture at birth	40/313	12.7%	10/41*	24%	4/27	14.8%	0/94	%0	2/82	2.8%	29/260	10.5%**
after ultrasound	after ultrasound became routine	after ultrasound became routine	Prenatal diagnosis	18/72	25%	5/15	33%	3/6	20%	2/25	28%	5/42	12%	38/160	23.8%
	became routine	became routine	after ultrasound												

Note: Denominator based on the number of affected individuals/pregnancies where reliable information was available, thus it may be an underestimate or overestimate. M, male; F, female; Gl, gastrointestinal; ULA, Upper Limb Amyoplasia; LLA, Lower Limb Amyoplasia; ART, assisted reproductive technologies; Ab, abortion.

*Statistically significant when compared to the other subgroups (P < 0.05).

**Statistically significant when compared to population prevalence (P < 0.05).

was then resorbed. It should be noted that two of these MZ twins (one male, one female) were quite severely affected in their upper limbs, but were born with extended elbows. Birth weights were in a normal range.

Among these individuals with LLA, three females and two males were MZ twins, 5.9% (5/85) (Fig. 2). One DZ pair of twins (where one had LLA) was also observed. In three pregnancies, producing female infants with LLA, a twin abortus was passed during the first trimester.

In the individuals with ULA, gastrointestinal (GI) anomalies thought to be associated with vascular compromise [Hoyme et al., 1983] (see Table II) were markedly increased: 17% (16/94; P value = 0.035) (particularly gastroschisis) compared to other types of Amyoplasia [Verhagen, 1981; Hoyme et al., 1983; Collins et al., 1986; Robertson et al., 1992]. Four males and five females had gastroschisis (9/94), one male and four females had bowel atresia (5/94) and one female and one male had both gastroschisis and bowel atresia (2/94). Only two of the individuals with ULA and GI abnormalities had partial absence of digits and one other had constriction rings with partial absence of digits. In addition to the GI anomalies, 2% (2/94) of individuals with ULA had abdominal wall muscle defects without GI anomalies; these were probably secondary to vascular compromise.

Among the individuals with LLA, GI abnormalities thought to be of vascular origin were also increased (4.7%; 4/85), albeit not to the extent of other subgroups. One male with gastroschisis, two females with bowel atresia (one a MZ twin), and one male with bowel atresia (where apparently a twin was lost early) were observed. No abdominal wall defects were present.

Among individuals with ULA, partial absence or small digits [Biesecker et al., 2009] were present in 8.4% (6/94), four males and two females (see Table II). Five males had involvement of their feet rather than affected fingers or arms. In these individuals, the underdevelopment involved small toes, cutaneous syndactytly, split foot/partial absence of toes, and split foot. Two of the five males with feet involvement also had finger involvement. One female had only finger involvement. One severely affected female MZ twin had partial absence of both fingers and toes associated with constriction rings. Additionally, one male and one female were said to have small hands with mild cutaneous syndactyly of fingers, but not partial absence of the digits. Umbilical cord wrapping, involving both upper and lower limbs, and leaving a groove on the limb was seen in three individuals with ULA.

Among our LLA individuals, partial absence of digits was present in 9.4% (8/85). Six had toe involvement and two had finger involvement. None had constriction rings; however, four individuals with LLA had a scar or groove on the posterior calf (of whom only two had partial absence of toes). Umbilical cord wrapping of legs was seen in 7/85 (8.2%).

Table III is a list of other unusual findings seen among individuals with ULA. Table IV lists unusual findings in individuals with LLA. The high number of cutaneous vascular malformations in ULA is worth mentioning, but it is not necessarily seen together with GI abnormalities or partial absence of digits. Ten of 94 (10.6%) individuals with ULA (three males and seven females) had cutaneous vascular malformations (apparently venous) [Mulliken and Glowacki, 1982]. It is also notable that in individuals with ULA that

TABLE III. Upper Limb Amyoplasia—Additional Anomalies not Reported on Table II among the 94 Affected Individuals

ORTHOPEDIC/LIMB AND TRUNK

Digit loss 7
Mild asymmetry 9
Polydactyly preaxial 1
Mild early leg involvement 11
Hyperextended back (3 severe, 3 mild) 6
Torticollis 4
Scoliosis 1
High riding scapula 8
Elbow subluxation 2
Rapid resolution 2

CRANIOFACIAL

Large ears 8 Upturned nose 8 Trismus 1

Prominent metopic suture 2 Lambdoid stenosis 1

SKIN

Cutaneous vascular malformation 10 Streaky pigment (no other unusual

features) 4 Hirsutism 2

Two hair whorls (one with constriction

rings) 2

Unusual dimples

Sacral 2

Buttocks 1

Inner arm 2

 $\it Note$: PDA, patent ductus arteriosus; VSD, ventricular septal defect; ASD, atrial septal defect; CNS, central nervous system.

EYECongenital glaucoma 1

Esotropia 3
CARDIAC 4

OBESE 2

PDAs treated resolved 2 VSD/ASD closed space 1 Myotoma mitral valve 1

GENITOURINARY 3

Unilateral renal agenesis 1 Distended bladder 1 Hydronephrosis 1

CNS

Staring spells resolved 2 Large head 1 Tethered cord 1 Developmental delay/ Intellectual delay 2

mild asymmetry (in nine) was present at birth. Rapidly resolving positional leg tightness had been present in 11 individuals. Streaky pigment was present in four (without other abnormalities), large ears in eight, and small upturned nose in eight were also observed in this group of Amyoplasia.

Among individuals with LLA, mild asymmetry was present in 15 (see Table IV).

The associated anomalies seen in individuals with ULA and LLA may well be over represented because of the referral pattern of these affected individuals.

NATURAL HISTORY

Individuals with ULA did surprisingly well. At least 60% developed good use of their hands by school age. They were all ambulatory, independent, and aside from two who were apparently mildly intellectually disabled, they were apparently bright, intelligent individuals, although formal cognitive assessments were not performed.

Individuals affected with LLA also did relatively well. Because the upper limbs were spared, braces, and crutches were relatively easily used, and daily living skills and independence was achieved by most. Outcome was often surprisingly good considering the severity of

TABLE IV. Lower Limb Amyoplasia—Additional Anomalies not Reported on Table II among the 85 Affected Individuals

ORTHOPEDIC/LIMB AND TRUNK

Mild asymmetry 15 Mild early arm involvement 6

Trunk hyperextension 3 Scoliosis—late 12 Knee hyperextension 5

Mild cutaneous syndactyly of digits 2

Radial head dislocation 1 Small appearing buttocks 4

CRANIOFACIES
Large ears 8
Trismus 4
Otitis 1

Ptosis 1

OBESE 3

UNUSUAL SENSITIVITY TO PAIN 2

SKIN

Streaky pigment

(no other unusual features) 1

Hirsutism 2

Unusual dimples—sacral 2 Hair whorl—lateral 1 Abdominal diastasis recti 3

CARDIAC VSD 2

ASD 2 Murmur 1 GENITOURINARY

Hydronephrosis 1

CNS

Tethered cord 2 **RESPIRATORY**Needed early 0₂ 1

Note: VSD, ventricular septal defect; ASD, atrial septal defect; CNS, central nervous system.

deformity in the newborn period. This may relate to the author's impression that they have a determined personality and apparently high intelligence [Hall et al., 2013]. The ability to walk without crutches usually depended on hip muscles. A small buttock was a poor prognostic sign; however, because of arm strength, all were ambulatory [Sells et al., 1996]. Those with recurvatum responded best if treated early.

The excess of GI anomalies is striking in both groups, particularly in the ULA group. The excess of females among the ULA group when compared to overall Amyoplasia and the LLA group seems to be important as it may suggest differential gender and timing of effects on cranio-caudal progression and vascular compromise when comparing ULA and LLA to overall Amyoplasia (see Table II) to four limb involvement with Amyoplasia. The excess of MZ twins and the high number of documented complications early in pregnancy in both groups suggest some type of vascular compromise may be occurring early. In addition, timing during fetal development, timing during pregnancy and gender differences in development may be important in understanding the pathogenesis (see Hall et al. [2013] for the pathogenesis discussion).

The finding that partial absence of digits mainly involves the feet in the ULA group suggests a different mechanism may be underlying the compromise of digits than that which leads to the contractures.

DIFFERENTIAL DIAGNOSIS

The greatest emphasis of this paper is the recognition that genetic forms of upper limb only and lower limb only arthrogryposis must be considered in the differential diagnosis of affected individuals.

Table V lists genetic forms of arthrogryposis associated with primarily upper limb involvement. Most of the individuals with these conditions have flexed elbows at birth. Although flexed elbows may be seen in the rare severe form of Amyoplasia, those individuals

with severe Amyoplasia always had all four-limb involvement. However, some individuals with lethal forms of arthrogryposis [Hall, 2009] have had extended elbows in utero, and these can be confused with Amyoplasia prenatally. Unfortunately, less than 30% of the affected individuals in this report (born after 1990) with ULA were recognized prenatally even though prenatal ultrasound was the standard of care, particularly in a pregnancy with complications. Filges and Hall [2012, 2013] discuss ways to improve detection of Amyoplasia and arthrogryposis with prenatal diagnosis.

Lethal Congenital Contracture Syndrome Type 2 [Landau et al., 2003], lethal lower motor neuron deficiency [Vuopala et al., 1995a], skeletal muscle maturation defect [Vuopala et al., 1995b], absent pyramidal cells Biscegli type [Bisceglia et al., 1987], and failure to myelinate peripheral nerves [Seitz et al., 1986] have all been reported with extension contractures of the arms [Hall, 2009]; however, all of these disorders include generalized contractures and the fetal akinesia deformation sequence. They are for practical purposes lethal at or before birth. When extended elbow contractures are seen prenatally, these disorders should be considered. They are all thought to be inherited in an autosomal recessive pattern.

The camptodactylies are a diverse group of disorders characterized by congenital contractures of the fingers. Many have family members with more extensive involvement so they should be considered in the differential diagnosis of ULA (see Table VI).

Among the disorders in Table V, ULA is the only condition with extension of the elbow at birth. There are six autosomal dominant, three autosomal recessive, and two apparently X-linked inherited forms of arthrogryposis with primarily upper limb involvement. As yet, none of the genes have been identified for those disorders. Amyoplasia in general, as well as ULA specifically, is thought to be sporadic. The mechanism is unknown [Hall et al., 2013] at this time.

The finding of an extended elbow at birth and ULA has also been reported in a child with a mutation of a mitochondrial gene (*SURF1*). This appears to be a rare presentation for mitochondrial disorders [Wilnai et al., 2012].

Passing consideration in the differential diagnosis of ULA should be given to brachial plexus palsy of the Erb palsy type (secondary to birth trauma) because the positioning of the arm at birth is similar and a difficult delivery is frequent in Amyoplasia. However, the limb is flaccid in Erb palsy compared to Amyoplasia where significant contractures are present at birth. Of interest, the fifth and sixth cranial nerves are usually injured during birth in individuals with Erb palsy and this area of the cervical spinal cord is also likely to be involved in Amyoplasia involving upper limbs [Dunn and Engle, 1985; Alfonso et al., 2000; Doumouchtsis and Arulkumaran, 2009].

Distinguishing ULA from other disorders is important because of its sporadic nature and known natural history. Upper limb Amyoplasia is a clinical diagnosis, so caution should be exercised in making the diagnosis. See Table II for comparison to other subgroups of Amyoplasia.

Only two genetic forms of lower limb arthrogryposis had been recognized in 1983; however, at least eight genetic forms have now been defined. Most of the non-Amyoplasia forms of lower limb only arthrogryposis have specific indicators that are helpful for recognition. X-ray of the spine, hips, and legs are particularly important in recognizing non-Amyoplasia forms of lower limb involvement.

TABLE V. Genetic Forms of Arthrogryposis with Primarily Upper Limb Involvement

References Shun-Shin	[1954], Wallis et al. [1988], Reichenbach et al. [1995], Liebenberg, 1973, Hall [1990]	Mead and Martin [1963], Camera et al. [1991]	Carnevale et al. [1973], Friss et al. [1973], Kawira and Bender, 1985, Prontera et al.	[2006] Baraitser [1982], Lizcano-Gil et al. [1995]	Figuera et al. [2002]	Hunter and Stevenson [2008], Ardinger [2000], Armstrong et al. [2008]	Mietens and Weber [1966], Canevale and Ruiz-Carcia [1976], Waring and Rodrigues (1980), Nagano et al. [1977], Salmon and Lindenbaum Lindenbaum [1978], Martinez-Glez et al. [2076]	Kilic et al. [1998], Garcia-Ortiz et al. [2006], Rozin et al. [1984]
Lower limb involvement No lower limb	involvement	No lower limb involvement	Minor lower limb involve- ment Crouch- ing position	O N	I	1	Crouching position [increases]	Crouching
Intellect Okay	5	Okay	Окау	0kay	QI Pijw	Окау	Mild- moderate intellectual disability	0kay
Other Web across elbow	joint, R/O Nail Patella syndromes	Short humerus	Short stature Pectus Seizures Pelvic dysplasia	Occasional torticollis	Cortical thickening Long bones Ocular hypertelorism Fusion of lid to	Pectus Deafness Myopia Myopia Meningioma Short stature Short limbs Congenital heart Pulmonary stenosis Hypospadias Epiphysaal	Corneal opacities, Corneal scleroderma Short stature	Craniosynostosis Short stature Small mouth
Facial involvement No		° Z	Possibly, mild	Okay	Okay	Deep set eyes	Pinched nose	↓ Facial movement
Ptosis No		° N	Variable	o N	No ptosis	Myopic	Strabismus Nystagmus	Yes Fibrosis of medial rectus Myopia Prominent eyes
Vertebral fusion No		o N	Multiple vertebral fusions	Cervical vertebral fusion,	No No	^o	2°	Yes
Scoliosis No		ON O	Scaliosis often present	Moderate scoliosis	No scoliosis	Yes	° Z	Yes, mild winging of scapula
Hand Okay	,	Okay	Frequently ulnar flexion contractures, Cutaneous syndactly of fingers	Camptodactyly, Lack of DIP creases	Hands, long thin camptodactyly	Camptodactyly and clinodactyly, Cutaneous syndactyly of fingers, Thumb subluxation	Camptodactylly	Camptodactyly Fusion carpals
Wrist Okay		Okay	Fused carpals and tarsals	Okay	Flexed	1	Okay	Okay
Elbow Held in flexion	Limited extension and rotation Maldeveloped RU joint Posterior subluxation of radius Small olecranon	Humeral ulnar fusion or maldevelopment	Held in flexion Pterggium at elbow	Limited elbow extension	Окау	Cubitus valgus Full extension Limited pronation	Dislocated radial heads Fixed flexion	Mild flexion
Neck & shoulder contracture a) Shoulder okay,	upper arm muscle markedly decreased	b) Shoulder okay, upper arm muscle decreased	Mildly contracted Absent long head of trapezius Mild webbing	±torticollis	Striking neck, pterygia, short neck, muscle sclerotic	Long neck Stiffness in 30 sec	Prominent trapezius	Low hairline
Inheritance AD		ΑD	AD	AD	PD	Φ	RA	AR
Antecubital	pterygium	Antecubital pterygium	AD Pterygium syndrome	Baraitser/ London Camptodactyly	Guadalajara camptodactyly III	Hunter. MacDonald syndrome	Mietens syndrome	Rozin-Kilic camptodactyly

		References Shalev et al., 2005	Lin and Gettig [1990], Hedera and Innis [2002]	Urban and Rogers [1979], Pagnan and Gollop [1988]	Present entry
	Lower limb	involvement No	Sometimes mild	Small feet	By definition no—if involved = other types of Amyoplasia
		Intellect Okay	Severe ID	Mod-severe ID	Normal
		Other Peri-umbilical hypopolasia Short stature	Omphalocoele Agenesis corpus callosum VSD Trigonencephaly Pectus Hypoplasia genitalia Craniosynostosis Craniosynostosis Flattened epihysis	Wormian bone Osteoporosis Obses, Hypognadism, Hypoplastic optic nerves Short	Short limb Marked ↓ muscle mass
	Facial	involvement Long myopathic facies Small jaw		Окау	Round with Glabellar nevus flammeus
		Ptosis	Yes Blepharophi mosis	° Z	Upper limbs Sporadic F>M Marked internal Extended, Flexed Cupped Practically No Practically Amyoplasia roration, sloping pronated shoulders 90% Shoulders 90% Note: AR, autosomal recessive; F, female; M, male; RVO, rule out; RVU, radioulnar; DIP, distal interphalangeal; VSD, ventricular septal defect; BA, bone age; ID, intellectual disability
ontinued)	Vertebral	No fusion	2	Hemivertebrae Lumbar Iordosis	No :t; BA, bone age; IC
TABLE V. [Continued]		Scollosis No	°Z	[©]	Practically never entricular septal defec
		Hand Camptodactyly Brachydactyly Hypermobile joints Cutaneous syndactyly of fingers	Camptodactylly	Camptodactyly	Cupped
		Wrist Okay	1	Okay	Flexed ulnar, DIP, distal ir
		Elbow Web and flexion	Limited supnation	Okay	Extended, pronated rule out; R/U, radio
	Neck & shoulder	contracture Neck webbing Short neck	ı	Short neck	Marked internal rotation, sloping shoulders 90% female; M, male; R/O,
		Inheritance AR	X linked vs. AR all males reported	X.linked vs. AR all males reported	Sporadic F>M omal recessive; F,
		Shalev type	Lin-Gettig syndrome	Urban- Rogers-Myer	Upper limbs Amyoplasia Note: AR, autosc

TABLE VI. Types of Camptodactyly that are Variable Within Families and Often may Involve Lower Limbs as well as Upper Limbs

Autosomal dominant syndromes

Welch and Temtamy (classic, isolated)

Baraitser, Lizcarno (mainly uppers, scoliosis, torticollis, cervical vertebral fusion)

Christian (platyspondyly, vertebral fusions, carpal and tarsal fusions)

Deafness and camptodactyly (tall stature)

Emery Nelson (flat at face, abnormal nose)

Guadalajara III (spinal defects, hypertelorism, brain structural anomaly)

Hunter MacDonald (scoliosis, deafness, congenital heart defects, and meningioma)

Autosomal recessive syndromes

ARC (arthropathy, pericarditis)

Guion arthropathy, Almeida (MR, skin tag, CP, and arachnodactyly) Guadalajara I (facies unusual, thoracic skeletal abnormalities, microcephaly)

Guadalajara II (short neck, hypoplastic patellae, DD, microcephaly) Ichthyosis and Windmill—Vane (Baraitser) (ichthyosis, seizures—possibly two types)

Lin-Gettig syndrome (agenesis corpus callosum, craniosynostosis, MR)

Pagon Gallop (MR, obesity, osteoporosis, large epiphyses)

Pointer syndrome (extended second digit)

Richieri-Costa I (lethal, hypoplastic digits)

Richieri-Costa II (MR, long face, cleft lip)

Rozin and Kilic (scoliosis, lateral rectus fibrosis)

Tel-Hashomer (short stature, normal IQ, prominent forehead, hypertelorism)

van den Ende-Gupta Syndrome (arachnodactyly, blepharophimosis, "surprised" facies)

X-linked Syndromes

Aarskog syndrome

 ${\it Note:} \ \, {\it ARC, arthrogryposis, renal dysfunction, cholestasis syndrome; CP, cleft palate; DD, developmental delay; IQ, intelligence quotient; MR, mental retardation.}$

Adapted from: Hall JG. 2013. Arthrogryposes (Multiple congenital contractures). In: Rimoin DL, Pyeritz RE, Korf BR. editors. Emery and Rimoin's principle and practice of medical genetics. 6th edition. Churchill Livingstone: New York. Chapter 161, pp 1–101.

Table VII lists the recognizable forms of arthrogryposis that usually affect only the lower limbs. Fleury and Hageman [1985] and Frijns et al. [1994] described families with autosomal dominant inheritance which lacked dimples overlying affected joints, but the two families apparently had linkage to different regions of the genome. The family described by Adams et al. [1998] had progressive manifestations. Autosomal dominantly inherited coalitions of the tarsals have been described and would be identified on X-rays [Gregersen and Petersen, 1977].

Several autosomal recessive inherited forms of lower limb only arthrogryposis have been described. Pelvic dysplasia has been reported by Ray et al. [1986] and Sarralde et al. [1998]. Mutations in *FKBP10* (FK506 binding protein 10) have been found in individuals with Kuskokwim syndrome [Barnes et al., in press]. No other genes have been associated with these lower limb phenotypes at this time. Furhmann syndrome should be recognizable because of the angulation of the long bones [Aynaci et al., 2001].

TABLE VII. Genetic Forms of Arthrogryposis with Primarily Lower Limb Involvement

References	12g23-24		Fleury and Hageman	[1985]	Frijns et al.	[+66+					Adams et al.	[1998]			Gregersen	Dotoroon	[1927]			Mississip	Wright [1920]	[0.67]		Barnes et al.	[in press]	Petajan et al. [1969]	Wright and	Aase	[1969]	Allelic to	Raas/ Rothchild	Lipson et al.	[1991]	Huber et al.	[2003]	Aynaci et al.	[2001]	Ray et al. [1986], Oh	[1976]
Other	Sensoru and	bladder intact	Osteopenia		Lax upper	Weak neck	Decreased	reflexes	sensory and bladder	intact	Sensory	okay, slowly progressive	0		Dysplasia of	chibitigacai	tarsals and	fibula and	tibia	4	Southern Inuit 2/	1000!	carriers	Normal	reflexes				i	Dimple at	angulated	2						Osteoporosis	
Intellect	Z				N						۷				¥					2	N N								9	ID, CNS	abnormal							Q/Q PIIW	
Scoliosis	Related to hip	disease	Slight lordosis, kyphosis		Weak lumbar area	alla lieck illuscies					Lumbar lordosis	slowly progression to uppers	<u>.</u>		S S					tid circilor	No scollosis, but	sis in inches		Long overriding	pedicles	Cystic boney	200		=	ON.								Lumbar lordosis leading to	scoliosis
Dimples	No dimples				I						1				+					-	+								-	+At angle								Yes	
Short	+				+						I				+					-	+									+								IUGR	
Uppers	V				NL perhaps	involve-	ment, lax	upper joints			N				¥					N don	NL-web at	*								Normal								٦ ٧	
Muscle					\rightarrow	Particularlu	prominent				\rightarrow		↓ Below	knee	I					-	→									\rightarrow								ightharpoons	
Ankles/Feet	Eauinovarus	or pes planus			Walks on toes						Flexed toes		Overlapping	equinovarus	Talus-	dicelecia	ugspidsid			Rigid flat feet	feet flexed	ankle							:	Flattened flail	feet	Hypoplastic	lateral feet	Poly/syn/	oligo. dactulu	Coalition	tarsals	Pes planus	
Knees	Flexion		Absent patellae		I						Extended				I					or lices of	NO parenae			Flexed	:	Walk on knees	Web		:	Flexed hypoplastic	fibula							Flexion	
Hips/Pelvis	Flexion				Maybe dislocated						Normal				Normal					And to the state of the state o	Abauctea nips			Dislocated hips	:	Boney cystic pelvis			-	Angulated femur,	short broad femurs, hupoplastic pelvis							Limited adduction	
Inheritance	AD		Linked to 12q23–24	Variable expression	, OA	Not linked to 12a					AD				AD feet only					Q	AA			Mutation		FKBP10 17q21.2	2/1000 Southern	Inuit in Alaska	are carriers	AR								AR, Caribbean	
	Fleuru)			Frijns						Adams				Coalitions					Similar Social	NUSKOKWITI									Fuhrman	syndrome							Ray, Sarralde	
	↔				2						m				4					ر	ر								C	0								ш	

		References Sarralde et al. [1998]								Xq23-Xq29		Zori et al.	[1998]				Peoples et al.	[1983],	Shurtleff	et al.	[1986],	210tugura	[1981]	Fullana	et al.	[1986]		
		Other Short lower segment								Thin trunk		Neuroconduc-	tion and	EMG normal	Normal	muscle	Asplenia Loss	bladder,	±sensory,	ostepenia,	cardiac	anomalies						
		Intellect								Ŋ							→Some ↓										Z Z	
		Scoliosis Mild wedged and cuboidal vertebrae								No							Progressive	lordosis									Aquire lordorsis and some mild scollosis	
		Dimples								Unknown							No										+ + +	
	Short	stature Increasing	Short	stature						ı							Related to	level Often	IUGR								Short lower segment	
[Continued]		Uppers Winged scapula	Wide neck							NL							Usually NL	•									J _Z	
TABLE VII. [Continued]		↑ Muscle								\rightarrow		Thin	tendons				→										$\stackrel{ ightarrow}{ ightarrow}$	
		Ankles/Feet Calcaneous valgus	Prominent	heels	Toes flexed	Equinovarus	Clubfeet	toes	Coalitions of tarsals	Vertical tali		Flat feet					Clubbed feet										Usually severe equinovarus	
		Knees								Severe flexed or ex-	tended contrac-	3					Flex or extended										Lots missing patel- lae	
		Hips/Pelvis Narrow dysplastic acetabulum	Notched iliac wing	:	Delayed ossification femoral head	Hypoplastic iliac bone				½ have hip extension	contractures						Hip flexed Hip	dislocated									Usually involved	
		Inheritance ? consanguinity								X-linked							Multifactor	occasionally ?	AR								Sporadic, related to vascular combromise	
										Zori type							Spinal	dysplasias/	Caudal	regression							Lower Limb Amyopiasia	
										Ŀ							9										_	

Note AD, autosomal dominant; AR, autosomal recessive; NL, normal limits; IUGR, intrauterine growth restriction; D/D, developmental delay.

Spinal dysraphism, including caudal regression, is usually sporadic, but can occur with maternal diabetes. Familial recurrence of spinal dysraphism with lateralization defects has been reported in which there is an excess of males [Fullana et al., 1986].

Focal femoral hypoplasia is usually sporadic, but may be seen with maternal diabetes; however, it should readily be recognized on X-ray by the loss of the femoral head.

Zori et al. [1998] described an X-linked inherited form of lower limb only arthrogryposis.

Four individuals with attempted termination of pregnancy were included in the LLA group since their lower leg findings were typical of LLA. Four other affected individuals experienced trauma early in pregnancy (two motor vehicle accidents, two domestic violence). Two mothers of individuals with Amyoplasia had surgery and anesthesia during pregnancy and were also included, again because their lower limb findings were typical of LLA and they may help to define the timing of events in Amyoplasia. Lower limb contractures have been reported with early CVS (chorionic villus sampling) and were indistinguishable clinically from the clinical description of LLA [Boyd et al., 1998; Stoler et al., 1999]. Thus, maternal uterine insults, particularly around 10–11 weeks, may predispose to LLA.

Lower limb Amyoplasia appears to be the most common cause of lower limb only arthrogryposis, but the diagnosis should be made with care since the implications for a sporadic condition and the well defined natural history of LLA come with diagnosis.

THERAPY

Treatment is outside the scope of this paper. However, early mobilization by physical therapy is essential to avoid further muscle atrophy. Many excellent papers exist regarding both upper and lower limb therapy in arthrogryposis and specifically in Amyoplasia (see Hall et al. [2013] for discussion) [Weeks, 1965; Katz et al., 1967; Curtis and Fisher, 1969; Williams, 1973; Doyle et al., 1980; Johnson et al., 1987; Staheli et al., 1987; Szöke et al., 1996; Axt et al., 1997; Niki et al., 1997; Murray and Fixsen, 1997; Lee, 2005; Fucs et al., 2005; Bevan et al., 2007; Sponseller et al., 2009; Gogola et al., 2010; Yang et al., 2010; Burgess and Robbe, 2012; Lampasi et al., 2012; Wada et al., 2012]. The aim of orthopedic procedures is to increase function, achieve a functional position, and minimize hospitalization time. Care must be given to avoid fracturing the long bones with vigorous physical therapy since the long bones are relatively gracile and osteopenic apparently from disuse in utero and after birth.

Improvement in outcome over the last 35 years, during which these affected individuals have been collected has been impressive. It is almost entirely related to early physical therapy rather than immediate casting and/or surgery [Fisher et al., 1970; Carlson et al., 1985; Hahn, 1985; Sells et al., 1996; Dillon et al., 2009]. Early physical therapy seems to allow muscle to stop the process of atrophying because of non-use. There does appear to be a window after birth (about 4 months) where increase in range of motion and preserving of some muscle tissue can be accomplished; (see Hall et al., 2013). In addition, the extra connective tissue around joints seems to be more responsive to stretching during the first 4 months than it is later in childhood [Swinyard and Mayer, 1963].

Many individuals with ULA have little functional muscle in their arms. The amount of muscle present can be assessed by imaging studies. As in all arthrogryposis surgery, release of the thickened joint capsules and avoidance of recurrence of contractures is challenging. Release of severe camptodactyly and the adducted thumb may be helpful. Bringing the wrist to neutral may improve finger function. Severely affected individuals often use their two arms as pincers with one elbow more extended and the other more flexed. Utilizing the shoulder and the scapula, may help to move the arms in this fashion. If mobilization of the elbow is achieved and deltoids are strong, occasionally, deltoid transfer improves elbow function. The development of appliances to move the arm and wrist (such as the WREX exoskeleton system developed by Wilmington Robotics) are promising [Taricco and Aoki, 2009].

In individuals with LLA, the Ponseti method [Morcuende et al., 2004] and Botox injections of the feet may provide some improvement early, but rarely achieve full mobilization in the very rigid and small feet present in Amyoplasia. Thick joint capsules and short ligaments often require surgical attention. The flexed knee in 50% in individuals with LLA often presents a challenge and may require femoral reduction to gain extension of the knee. The frequently dislocated hip usually requires surgery.

POTENTIAL ETIOLOGIES AND MECHANISMS

The potential etiologies and mechanisms leading to Amyoplasia are discussed in the accompanying article on Amyoplasia [Hall et al., 2013], as well as the need for future studies.

SUMMARY

Almost 17% of individuals affected with Amyoplasia among the 560 individuals have ULA and just over 15% of individuals have LLA. The positioning of limbs is typical for Amyoplasia with markedly decreased muscle mass, mild shortness of long bones, dimples overlying affected joints, and rigid joint contractures. Other features of Amyoplasia including an excess of discordant MZ twins, an increase in GI anomalies thought to be of vascular origin, and increased occurrence of small and partially absent digits are associated with ULA and LLA. Intrauterine growth restriction is not associated with ULA. Both ULA and LLA are sporadic. However, the excess of females and particularly females with GI anomalies thought to be vascular origin present in ULA may provide clues to mechanisms or etiology as discussed in Hall et al. [2013]. This article provides the differential diagnoses of genetic forms of arthrogryposis primarily involving either just the upper or just the lower limbs.

ACKNOWLEDGMENTS

The author thanks the many colleagues who have referred and shared affected individuals of arthrogryposis; as well as the families and affected individuals; The University of British Columbia's Departments of Pediatrics and Medical Genetics; The Children and Family Research Institute; Kimi Tanaka and Kimberly Aldinger for technical assistance; and the Walkers and Gales for their support and the superb editorial assistance from the *American Journal of*

Medical Genetics. The comments reviewers were very helpful. Specific thanks to the following people: E. Baptiste, P. Benke, S. Bamforth, C. Blank, M. Bocian, M. Bressler, S. Carter, J. Coldwell, T. DeWeert, N. Gilman, S. Glass, L. Gouldsborough, J. Graham, M. Gruble, D. Hanel, J. Herrmann, W. Horton, E. Hsia, L. Hudgins, S. Jay, M. Jones, T. Kelly, V. Kimonis, G. Kleinman, C. Lafer, D. Lehman, L. Low, G. Lowie, B. Lowry, T. Massagle, E. McArthur, M. Partington, M. Pembrey, D. Pilz, L. Raffel, C. Reilly, H. Schuer, D. Shurtleff, E. Steinweg, M. Stephan, T. Stevens, J. Stewart, J. Sweeney, C. Toutas, C. Verchere, D. Woeste, R. Beauchamp, M. Bell, B. Bundle, M. Burgess, J. Carey, R. Conn, P. Dignan, U. Froster-Iskenius, R. Kendall, C. Lengyel, J. Marlin, D. Moershel, V. Mosca, M. Parkinton, M. Sabrio, S. Schmutz, H. Toriello, and A. Wagner.

REFERENCES

- Adams C, Suchowersky O, Lowry RB. 1998. Congenital autosomal dominant distal spinal muscular atrophy. Neuromuscul Disord 8:405– 408.
- Alfonso I, Alfonso DT, Papazian O. 2000. Focal upper extremity neuropathy in neonates. Semin Pediatr Neurol 7:4–14.
- Ardinger HH. 2000. Delineation of the Hunter-MacDonald syndrome. Proceedings of the Greenwood Genetic Center 19:92.
- Armstrong L, Graham GE, Schimke RN, Collins DL, Kirse DJ, Costello F, Ardinger HH. 2008. The Hunter-MacDonald syndrome with expanded phenotype including risk of meningioma: An update and review. Am J Med Genet A 146A:83–92.
- Axt MW, Niethard FU, Döderlein L, Weber M. 1997. Principles of treatment of the upper extremity in arthrogryposis multiplex congenita type I. J Pediatr Orthop B 6:179–185.
- Aynaci FM, Aynaci O, Ahmetoğlu A, Celep F. 2001. Fuhrmann syndrome associated with cortical dysplasia. Genet Couns 12:49–54.
- Baraitser M. 1982. A new camptodactyly syndrome. J Med Genet 19:40-43.
- Barnes AM, Duncan G, Weis M, Paton W, Cabral WA, Mertz EL, Makareeva E, Gambello MJ, Lacbawan FL, Leikin S, Fertala A, Eyre DR, Bale SJ, Marini JC. in press. Kuskokwim syndrome, a recessive congenital contracture disorder, extends the phenotype of FKBP10 mutations. Hum Mutat 34:1279–1288.
- Bevan WP, Hall JG, Bamshad M, Staheli LT, Jaffe KM, Song K. 2007. Arthrogryposis multiplex congenita (amyoplasia): An orthopaedic perspective. J Pediatr Orthop 27:594–600.
- Biesecker LG, Aase JM, Clericuzio C, Gurrieri F, Temple IK, Toriello H. 2009. Elements of morphology: Standard terminology for the hands and feet. Am J Med Genet A 149A:93–127.
- Bisceglia M, Zelante L, Bosman C, Cera R, Dallapiccola B. 1987. Pathologic features in two siblings with the Pena-Shokeir I syndrome. Eur J Pediatr 146:283–287.
- Boyd PA, Chamberlain P, Hicks NR. 1998. 6-year experience of prenatal diagnosis in an unselected population in Oxford, UK. Lancet 352:1577–1581.
- Burgess RC, Robbe R. 2012. Long-term results of forearm shortening and volar radiocarpal capsulotomy for wrist flexion deformity in children with amyoplasia. J Hand Surg Am 37:322–325.
- Camera G, Piccinini A, Zucchinetti P, Pozzolo S. 1991. Pterygium of the elbow and post-axial polydactyly on the hands as sign of hereditary onyco-osteodysplasia: 4 Familial cases. Pathologica 83:365–372.

- Carlson WO, Speck GJ, Vicari V, Wenger DR. 1985. Arthrogryposis multiplex congenita. A long-term follow-up study. Clin Orthop Relat Res 194:115–123.
- Carnevale A, López Hernández A, De los Cobos L. 1973. Familial pterygium syndrome with probably dominant transmission linked to the X chromosome. Rev Invest Clin 25:237–244.
- Carnevale A, Ruiz García FJ. 1976. Mietens-Weber syndrome. A case report (author's transl). Carnevale and Ruiz-García [1976] Rev Invest Clin 28:347–351.
- Collins DL, Kimura K, Morgan A, Johnson DG, Leonard C, Jones MC. 1986. Multiple intestinal atresia and amyoplasia congenita in four unrelated infants: A new association. J Pediatr Surg 21:331–333
- Curtis BH, Fisher RL. 1969. Congenital hyperextension with anterior subluxation of the knee. Surgical treatment and long-term observations. J Bone Joint Surg Am 51:255–269.
- Dillon ER, Bjornson KF, Jaffe KM, Hall JG, Song K. 2009. Ambulatory activity in youth with arthrogryposis: A cohort study. J Pediatr Orthop 29:214–217.
- Doumouchtsis SK, Arulkumaran S. 2009. Are all brachial plexus injuries caused by shoulder dystocia? Obstet Gynecol Surv 64:615–623.
- Doyle JR, James PM, Larsen LJ, Ashley RK. 1980. Restoration of elbow flexion in arthrogryposis multiplex congenita. J Hand Surg Am 5:149–152.
- Dunn DW, Engle WA. 1985. Brachial plexus palsy: Intrauterine onset. Pediatr Neurol 1:367–369.
- Figuera LE, Ramírez-Dueñas ML, Dávalos IP, Cantú JM. 2002. Guadalajara camptodactyly type III: A new probably autosomal dominant syndrome. Clin Dysmorphol 11:243–247.
- Filges I, Hall JG. 2012. We are failing to identify disorders of fetal movement—Why? Prenat Diagn 32:919–920.
- Fisher RL, Johnstone WT, Fisher WH, Jr. Goldkamp OG. 1970. Arthrogryposis multiplex congenita: A clinical investigation. J Pediatr 76:255–261.
- Fleury P, Hageman G. 1985. A dominantly inherited lower motor neuron disorder presenting at birth with associated arthrogryposis. J Neurol Neurosurg Psychiatry 48:1037–1048.
- Frias JL, Holahan JR, Rosenbloom AL, Felman AH. 1973. An autosomal dominant syndrome of multiple pterygium, ptosis, and skeletal abnormalities. International Conference on Birth Defects, Vienna. Excevpta Medica, 19.
- Frijns CJ, Van Deutekom J, Frants RR, Jennekens FG. 1994. Dominant congenital benign spinal muscular atrophy. Muscle Nerve 17:192–197
- Fucs PM, Svartman C, de Assumpção RM, Lima Verde SR. 2005. Quadricepsplasty in arthrogryposis (amyoplasia): Long-term follow-up. J Pediatr Orthop B 14:219–224.
- Fullana A, Garcia-Frias E, Martinez-Frias ML, Razquin S, Quero J. 1986. Caudal deficiency and asplenia anomalies in sibs. Am J Med Genet Suppl 2:23–29.
- García-Ortiz JE, Castañeda-Cisneros G, López-Cardona MG, Sánchez-Corona J, Patiño-García B, García-González CL, Nazará Z, Dávalos-Rodríguez N, Rodríguez LX, García-Cruz D. 2006. Camptodactyly, joint contractures, facial, and skeletal defects: Further delineation of the Rozin camptodactyly syndrome. Am J Med Genet A 140A: 1245–1249.
- Gogola GR, Ezaki M, Oishi SN, Gharbaoui I, Bennett JB. 2010. Long head of the triceps muscle transfer for active elbow flexion in arthrogryposis. Tech Hand Up Extrem Surg 14:121–124.

- Gregersen HN, Petersen GB. 1977. Congenital malformation of the feet with low body height. A new syndrome, caused by an autosomal dominant gene. Clin Genet 12:255–262.
- Hahn G. 1985. Arthrogryposis. Pediatric review and habilitative aspects. Clin Orthop Relat Res 194:104–114.
- Hall J. 1990. Somatic and germ-line mosaicism in autosomal dominant antecubital pterygium. Clin Genet 37:160.
- Hall JG. 2009. Pena-Shokeir phenotype (fetal akinesia deformation sequence) revisited. Birth Defects Res A Clin Mol Teratol 85:677–694.
- Hall JG. 2013. Arthrogryposes (multiple congenital contractures). In: Rimoin DL, Pyeritz RE, Korf BR, editors. Emery and Rimoin's principle and practice of medical genetics. 6th edition. New York: Churchill Livingstone. Chapter 161 pp 1–101.
- Hall JG, Aldinger KA, Tanaka KI. 2013. Amyoplasia revisited. Am J Med Genet A.
- Hall JG, Reed SD, Driscoll EP. 1983. Part I. Amyoplasia: A common, sporadic condition with congenital contractures. Am J Med Genet 15:571–590.
- Hedera P, Innis JW. 2002. Possible third case of Lin-Gettig syndrome. Am J Med Genet 110:380–383.
- Hoyme HE, Jones MC, Jones KL. 1983. Gastroschisis: Abdominal wall disruption secondary to early gestational interruption of the omphalomesenteric artery. Semin Perinatol 7:294–298.
- Huber J, Volpon JB, Ramos ES. 2003. Fuhrmann syndrome: Two Brazilian cases. Clin Dysmorphol 12:85–88.
- Hunter AG, Stevenson RE. 2008. Gastroschisis: Clinical presentation and associations. Am J Med Genet C Semin Med Genet 148C:219–230.
- Johnson E, Audell R, Oppenheim WL. 1987. Congenital dislocation of the knee. J Pediatr Orthop 7:194–200.
- Katz MP, Grogono BJ, Soper KC. 1967. The etiology and treatment of congenital dislocation of the knee. J Bone Joint Surg Br 49:112–120.
- Kawira EL, Bender HA. 1985. An unusual distal arthrogryposis. Am J Med Genet 20:425–429.
- Kilic I, Kilic BA, Ergin H, Aygün MG, Aksit MA. 1998. Camptodactyly, myopia, and fibrosis of the medial rectus of the eye in two sibs born to consanguineous parents: Autosomal recessive entity? Am J Med Genet 77:28–30.
- Lampasi M, Antonioli D, Donzelli O. 2012. Management of knee deformities in children with arthrogryposis. Musculoskelet Surg 96:161–169.
- Landau D, Mishori-Dery A, Hershkovitz R, Narkis G, Elbedour K, Carmi R. 2003. A new autosomal recessive congenital contractural syndrome in an Israeli Bedouin kindred. Am J Med Genet A 117A:37–40.
- Lee HS. 2005. Amyoplasia congenita of the lower extremity: Report in a premature baby. Yonsei Med J 46:567–570.
- Liebenberg F. 1973. A pedigree with unusual anomalies of the elbows, wrists and hands in five generations. S Afr Med J 47:745–748.
- Lin AE, Gettig E. 1990. Craniosynostosis, agenesis of the corpus callosum, serve mental retardation, distinctive facies, camptodactyly, and hypogonadism. Am J Med Genet 35:582–585.
- Lipson AH, Kozlowski K, Barylak A, Marsden W. 1991. Fuhrmann syndrome of right-angle bowed femora, absence of fibulae and digital anomalies: Two further cases. Am J Med Genet 41:176–179.
- Lizcano-Gil LA, García-Cruz D, Sánchez-Corona J, Cantú JM. 1995. Spondylo-camptodactyly syndrome: A distinct autosomal dominant entity? Clin Genet 48:173–176.

- Martínez-Glez V, Lapunzina P, Delicado A, Tendero A, Mori MA, de Torres ML, Fernández L, Palomares M, Pajares IL. 2006. Mietens-Weber syndrome: Two new patients and a review. Clin Dysmorphol 15:175–177.
- Mead CA, Martin M. 1963. Aplasia of the trochlea—An original mutation. J Bone Joint Surg 45-A:379–383.
- Mietens C, Weber H. 1966. A syndrome characterized by corneal opacity, nystagmus, flexion contracture of the elbows, growth failure, and mental retardation. J Pediatr 69:624–629.
- Morcuende JA, Dolan LA, Dietz FR, Ponseti IV. 2004. Radical reduction in the rate of extensive corrective surgery for clubfoot using the Ponseti method. Pediatr 113:376–380.
- Mulliken JB, Glowacki J. 1982. Hemangiomas and vascular malformations in infants and children: A classification based on endothelial characteristics. Plast Reconstr Surg 69:412–422.
- Murray C, Fixsen JA. 1997. Management of knee deformity in classical arthrogryposis multiplex congenita (amyoplasia congenita). J Pediatr Orthop B 6:186–191.
- Nagano A, Kurokawa T, Tachibana S, Tsuyama N. 1977. Meitens' syndrome. Arch Orthop Unfallchir 89:81–86.
- Niki H, Staheli LT, Mosca VS. 1997. Management of clubfoot deformity in amyoplasia. J Pediatr Orthop 17:803–807.
- Oh WH. 1976. Arthrogryposis multiplex congenita of the lower extremity: Report of two siblings. Orthop Clin North Am 7:511–515.
- Pagnan NA, Gollop TR. 1988. Prader-Willi habitus, osteopenia, and camptodactyly (Urban-Rogers-Meyer syndrome): A probable second report. Am J Med Genet 31:787–792.
- Peoples WM, Moller JH, Edwards JE. 1983. Polysplenia: A review of 146 cases. Pediatr Cardiol 4:129–137.
- Petajan JH, Momberger GL, Aase J, Wright DG. 1969. Arthrogryposis syndrome (Kuskokwim disease) in the Eskimo. JAMA 209:1481–1486.
- Prontera P, Sensi A, Merlo L, Garani G, Cocchi G, Calzolari E. 2006. Familial occurrence of multiple pterygium syndrome: Expression in a heterozygote of the recessive form or variability of the dominant form? Am J Med Genet A 140A:2227–2230.
- Ray S, Peterson PD, Scott CI Jr. 1986. Pelvic dysplasia associated with arthrogrypotic changes in the lower extremities. A new syndrome. Clin Orthop Relat Res 207:99–102.
- Reichenbach H, Hörmann D, Theile H. 1995. Hereditary congenital posterior dislocation of radial heads. Am J Med Genet 55:101–104.
- Robertson WL, Glinski LP, Kirkpatrick SJ, Pauli RM. 1992. Further evidence that arthrogryposis multiplex congenita in the human sometimes is caused by an intrauterine vascular accident. Teratology 45:345–351
- Rozin MM, Hertz M, Goodman RM. 1984. A new syndrome with camptodactyly, joint contractures, facial anomalies, and skeletal defects: A case report and review of syndromes with camptodactyly. Clin Genet 26:342–355.
- Salmon MA, Lindenbaum RH. 1978. Mietens' syndrome. In: Salmon MA, Lindenbaum RH, editors. Developmental defects and syndromes. Aylesbury, England: HM+M Publishers Ltd. 285.
- Sarralde A, Reynoso MC, Nazará Z, Soto F, Hernández A. 1998. Prenatal growth retardation, pelvic hypoplasia, and arthrogrypotic changes of lower limbs: A distinct autosomal-recessive disorder. Am J Med Genet 75:453–460.
- Seitz RJ, Wechsler W, Mosny DS, Lenard HG. 1986. Hypomyelination neuropathy in a female newborn presenting as arthrogryposis multiplex congenita. Neuropediatrics 17:132–136.

Sells JM, Jaffe KM, Hall JG. 1996. Amyoplasia, the most common type of arthrogryposis: The potential for good outcome. Pediatrics 97:225–231.

- Shalev SA, Spiegel R, Hall JG. 2005. A syndrome characterized by contractures and pterygia of upper body associated with umbilical hernia, short stature, and distinctive face in an Arabic family. Am J Med Genet A 138A:236–240.
- Shun-Shin M. 1954. Congenital web formation. J Bone Joint Surg 366:268–271.
- Shurtleff DB, Menelaus MB, Staheli LT, Chew DE, Lamers JY, Stillwell A, Wolf LS. 1986. Natural history of flexion deformity of the hip in myelodysplasia. J Pediatr Orthop 6:666–673.
- Sponseller PD, Yang JS, Thompson GH, McCarthy RE, Emans JB, Skaggs DL, Asher MA, Yazici M, Poe-Kochert C, Kostial P, Akbarnia BA. 2009. Pelvic fixation of growing rods: Comparison of constructs. Spine 34:1706–1710.
- Staheli LT, Chew DE, Elliott JS, Mosca VS. 1987. Management of hip dislocations in children with arthrogryposis. J Pediatr Orthop 7:681–685.
- Stoler JM, McGuirk CK, Lieberman E, Ryan L, Holmes LB. 1999. Malformations reported in chorionic villus sampling exposed children: A review and analytic synthesis of the literature. Genet Med 1:315–322.
- Swinyard CA, Mayer V. 1963. Multiple congenital contractures. Public health considerations of arthrogryposis multiplex congenita. JAMA 183:23–27.
- Szöke G, Staheli LT, Jaffe K, Hall JG. 1996. Medial-approach open reduction of hip dislocation in amyoplasia-type arthrogryposis. J Pediatr Orthop 16:127–130.
- Taricco LD, Aoki SS. 2009. Rehabilitation of an adult patient with arthrogryposis multiplex congenita treated with an external fixator. Am J Phys Med Rehabil 88:431–434.
- Urban MD, Rogers JG, Meyer WJ, III. 1979. Familial syndrome of mental retardation, short stature, contractures of the hands, and genital anomalies. J Pediatr 94:52–55.
- Verhagen AD. 1981. Gastroschisis and congenital contractures: Coincidence or syndrome? J Pediatr Surg 16:605–607.

- Vuopala K, Ignatius J, Herva R. 1995a. Lethal arthrogryposis with anterior horn cell disease. Hum Pathol 26:12–19.
- Vuopala K, Pedrosa-Domellöf F, Herva R, Leisti J, Thornell LE. 1995b. Familial fetal akinesia deformation sequence with a skeletal muscle maturation defect. Acta Neuropathol 90:176–183.
- Wada A, Yamaguchi T, Nakamura T, Yanagida H, Takamura K, Oketani Y, Kubota H, Fujii T. 2012. Surgical treatment of hip dislocation in amyoplasia-type arthrogryposis J Pediatr Orthop B 21:381–385.
- Wallis CE, Shun-Shin M, Beighton PH. 1988. Autosomal dominant antecubital pterygium: Syndromic status substantiated. Clin Genet 34:64–69.
- Waring GO, III Rodrigues MM. 1980. Ultrastructure and successful keratoplasty of sclerocornea in Mietens' syndrome. Am J Ophthalmol 90:469–475.
- Weeks PM. 1965. Surgical correction of upper extremity deformities in arthrogrypotics. Plast Reconstr Surg 36:459–465.
- Williams PF. 1973. The elbow in arthrogryposis. J Bone Joint Surg Br 55:834–840.
- Wilnai Y, Seaver LH, Enns GM. 2012. Atypical amyoplasia congenita in an infant with Leigh syndrome: A mitochondrial cause of severe contractures? Am J Med Genet A 158A:2353–2357.
- Wright DG. 1970. The unusual skeletal findings of the Kuskokwim syndrome. Birth Defects Orig Artic Ser 6:16–24.
- Wright DG, Aase J. 1969. The Kuskokwim syndrome: An inherited form of arthrogryposis in the Alaskan Eskimo. Birth Defects Orig Artic Ser 5: 91–95.
- Yang SS, Dahan-Oliel N, Montpetit K, Hamdy RC. 2010. Ambulation gains after knee surgery in children with arthrogryposis. J Pediatr Orthop 30:863–869.
- Zlotogora J, Elian E. 1981. Asplenia and polysplenia syndromes with abnormalities of lateralisation in a sibship. J Med Genet 18:301–302.
- Zori RT, Gardner JL, Zhang J, Mullan MJ, Shah R, Osborn AR, Houlden H, Wallace MR, Roberts S, Yang TP. 1998. Newly described form of X-linked arthrogryposis maps to the long arm of the human X chromosome. Am J Med Genet 78:450–454.