Eurocat

European Surveillance of Congenital Anomalies

EUROCAT Guide 3 (2nd Ed)

For the Description and Classification of Congenital Limb Defects

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The Guide was written by Claude Stoll, Pierpaolo Mastroiacovo, Philippe de Wals and Josephine Weatherall in 1986 and revised by Ester Garne and Claude Stoll in 2003-2004.

Approved by members of the EUROCAT Coding Committee:
Marie-Claude Addor, Annukka Ritvanen, Diana Wellesley

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EUROCAT Central Registry
Room 15E12
University of Ulster
Newtownabbey
Co Antrim
Northern Ireland
BT37 0QB

Email: eurocat@ulster.ac.uk
Website: www.eurocat.ulster.ac.uk

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INTRODUCTION

Malformations of the limbs are among the most frequent of congenital disorders[1].
The aim of this book is to provide the clinicians concerned with the care of newborns, and who are not specialist in dysmorphology, a ready reference for describing congenital limb defects that is essential for a correct diagnosis and classification and for monitoring the frequency and distribution of congenital anomalies in the population.

In a baby with congenital limb defects it is important to identify the cause of the anomaly and to estimate the risk of recurrence for the siblings and the progeny of the affected individual. Accurate diagnosis is needed for the prevention of limb defects through genetic counselling and prenatal diagnosis. A good classification of limb malformations is also essential for the epidemiologic surveillance of environmental teratogens and mutagens.

There is an increasing awareness of the aetiologic heterogeneity of congenital limb anomalies[2]. Some are due to an abnormal gene inherited from one or both parents or arising sporadically through a new mutation. Such genes may be dominant as in achondroplasia, or recessive as in the Roberts syndrome. Other anomalies are associated with a chromosomal abnormality such as Trisomy 13 or Trisomy 18. The Thalidomide tragedy focused the interest on exogenous factors. However, the major part of limb defects is probably of multifactorial origin.

The analysis of congenital limb defects recorded in EUROCAT Registries led to the identification of two main methodological problems. The first problem was the poor level of documentation available on the malformations. General terms such as dwarfism, deformity of hand or absence of limb were frequently reported. More details and accurate information are needed for a specific diagnosis and the classification to be made, and for investigating possible aetiologic factors. The second problem was the inadequacy of the classification and coding system used which is the "British Paediatric Association Classification of Disease" based on ICD9[3]. With the introduction of ICD10 there has been some improvement in the coding of limb defects.

GUIDELINES FOR REPORTING LIMB DEFECTS

Recognition of congenital limb defects is usually easy. Examination should be carried out as soon as possible after the birth. In the recognition of congenital malformations there are some general points, which may be helpful as a check list for anyone reading this guide.

Examination of the Baby

General appearance	Observe whether or not the limbs move in the appropriate manner
Weight of the baby	
Length of the baby	
Size of the head	
Shape of the head	
Skin and hair	
Face	
Eyes	
Nose	
Mouth	
Ears	
Back of the body	
Front of the body	
Genitals	
Limbs	The upper and lower limbs should be examined with special attention to the length between joints, joint shape and joint mobility. The tone of the limbs should be noted, particularly if they cannot be straightened or if they are flaccid. The number of fingers and toes, their length, extra digits or fusion of digits should be noted and any digital abnormality illustrated in a drawing. The presence of abnormal palmar creases should be looked for. Examination for hip dislocation or instability should be undertaken by a trained person.

Description of Congenital Anomalies

Any anomaly of limb should be carefully described.

Photographs and radiographs of the abnormal limbs should be made. An X-ray examination of the total skeleton (anterioposterior and lateral projections) should be asked for when a skeletal dysplasia is suspected.
Ultrasound investigations and MRI-scan may be useful in specific situations

Associated anomalies should also be described and photographs taken.

DEFINITIONS AND METHODS OF DESCRIPTION

A definition of the different types of congenital limb defects is given in this section. For each type, a classification of the main sub-types is proposed. There are many systems for classifying limb defects according to the aetiology, the pathological mechanism or the anatomical manifestation. It is not the purpose of these guidelines to recommend a new classification system but to improve the documentation on each case registered which is needed for grouping limb malformations in statistical work, for identifying nosological entities and for conducting researchers on aetiological factors.

As discussed before, malpositions of limbs, mainly clubfoot and dislocation of hip are not included in this section. Osteochondrodysplasia, polydactyly, syndactyly, brachydactyly and reduction defect constitute the main types of limb defects considered. Various malformations of limbs can be associated with amniotic bands. Micromelia and campomelia are descriptive terms meaning respectively shortening and bending of limb. Multiple congenital contractures and joint laxity are alterations in the mobility of joints.

Osteochondrodysplasia

Definition:
Abnormality of cartilage and/or bone growth and development

Classification:
See complete classification in American Journal of Medical Genetics[4] and in references books[5-7] .

a) *Defects of Growth of Long Bones and/or Spine*

1. Identifiable at Birth
   - Usually lethal before or shortly after birth
     - Achondrogenesis type IA and IB
     - Achondrogenesis type II (Langer-Saldino)
     - Hypochondrogenesis
     - Fibrochondrogenesis
     - Thanatophoric dysplasia
     - Thanatophoric dysplasia with clover-leaf skull
     - Atelosteogenesis
     - Short rib syndrome (with or without polydactyly)

I Type I (Saldino-Noonan)
II Type II (Majewski)
III Type III (Verma-Naumoff)
IV Type IV (Beemer-Langer)

- Sometimes lethal
  - Chondrodysplasia punctata
    I Rhizomelic type
    II Zellweger type
    III Conradi Hunermann type
    IV X-linked recessive type
    V Brachytelephalangic type
    VI Tibial-metacarpal type
    VII Vitamin K-dependent coagulation defect
    VIII Other acquired and genetic disorders including Warfarin embryopathy
  - Campomelic dysplasia
  - Kyphomelic dysplasia
  - Achondroplasia
  - Diastrophic dysplasia
  - Metatropic dysplasia (several forms)
  - Chondro-ecto-dermal dysplasia (Ellis Van Creveld)
  - Asphyxiating thoracic dysplasia (Jeune)
  - Spondylo-epiphyseal dysplasia congenital
    Type II collagenopathy
  - Acromesomelic dysplasia
  - Cleido-cranial dysplasia
  - Oto-palato-digital syndrome
    I Type I (Langer)
    II Type II (André)
  - Larsen syndrome
  - Other multiple dislocation syndromes

2. Identifiable in Later Life
   eg. Hypochondroplasia
   Metaphyseal chondrodysplasia (type McKusick)
   Pseudo-achondroplasia
   I Dominant
   II Recessive

b) *Disorganised Development of Cartilage and Fibrous Components of Skeleton*

c) *Abnormalities of Density of Cortical Diaphyseal Structure and/or Metaphyseal Modelling*

eg. Osteogenesis imperfecta (several forms)

Methods of Description:
A complete X-ray is imperative both in fetal deaths and livebirths for a confirmation of the clinical diagnosis and for a type-specific diagnosis to be made.

Give the length of the baby: crown-heel length and crown-rump length.

Describe any other defects found: heart disease, visceral abnormalities, eye defect etc.

Polydactyly

Definition:
Occurrence of complete or partial supernumerary digit(s).

Classification:

a) Pre-axial Polydactyly
The supernumerary digit articulates with the radial (thumb) or tibial) hallux) side. There are two main subtypes:
1. Polydactyly of biphalangeal thumb
2. Polydactyly of triphalangeal thumb

b) Post-axial Polydactyly
The supernumerary digit articulates with the ulnar or fibular side. There are two main subtypes:
1. Type A – the extra digit is fully developed
2. Type B – the extra digit is pedunculated or rudimentary (also called post minimi)

c) Axial
The supernumerary digit is located either between the 2nd and 3rd or between the 3rd and 4th digits.

d) Multiple
   More that one digit is duplicated

e) High Degrees
   This category includes a group of rare types of polydactyly associated with duplication or structures of the limb (eg. tibia) other than the digits.

Syndactyly

Definition:
Fusion of two or more digits (fingers or toes).

Classification:

a) Zygodactyly
   Syndactyly or the 3rd and 4th fingers and/or of the 2nd and 3rd toes. The fusion may be either complete, reaching to the level of the nails, or partial, affecting only the proximal segments of the digits. Zygodactyly 2nd-3rd digits of foot is a minor and common anomaly that should not be reported to the EUROCAT Central Registry if isolated malformation (list of minor malformations for exclusion)

b) Synpolydactyly
   1. Syndactyly of the 3rd and 4th fingers associated with a partial or complete duplication of the 3rd or 4th finger.
   2. Syndactyly or the 4th and 5th toes with partial or complete polydactyly of the 5th toe, which is included in the web.

c) 4-5 Finger Syndactyly
   Syndactyly of the 4th and 5th fingers. Usually toes are unaffected.

d) Complete Syndactyly
   Syndactyly of all fingers or toes; thumb and hallux may be excluded.

e) Syndactyly plus Metacarpal or Metatarsal Synostosis
   Syndactyly may affect every finger or toe and there may be an associated synostosis or metacarpals or metatarsals.

f) Miscellaneous and Other Types
   Eg. metacarpal or metatarsal fusion; total syndactyly with synostosis (Cenani Lenz type).

Brachydactyly

Definition:
Shortening of the digits due to anomalous development of the phalanx or metacarpals/metatarsals.

Classification:

a) Type A
   Shortening is confined to middle phalanx of one or more digits.

b) Type B
   Shortening or absence of terminal phalanx in addition to shortening or middle phalanx.

c) Type C
   Deformity of the middle and proximal phalanx of the 2^{nd} and 3^{rd} fingers. The 2^{nd} finger has a characteristic ulnar deviation. The 4^{th} finger is more or less normal and projects considerably beyond all other digits.

d) Type D
   Shortening and broadening of terminal phalanx of thumbs or great toes.

e) Type E
   Shortening or one or more of the metacarpals, with or without shortening of the metatarsals.

Limb Reduction Defects

Definition:
Absence or severe hypoplasia (meaning hypoplasia and abnormal shape) of skeletal structure of the limb. Include absence of digit or phalange only, associated or not with fibrotic bands.

Classification:

a) Terminal Transverse Defects
   Absence of distal structure of the limb with proximal structures more or less normal. There are many subtypes:

1. Amelia – total absence of the extremities
2. Hemimelia – total absence of forearm and hand or of foreleg and foot.
3. Acheiria – absence of hand
4. Apodia – absence of foot
5. Adactyly – absence of digits
6. Ectrodactyly – total or partial absence of phalanx

b) Proximal-intercalary Defect

Absence or severe hypoplasia of proximal-intercalary part of the limb when the distal structures (ie. the digits), whether normal or malformed, are present:

1. Absence of humerus and/or radius and ulna (with hand normal of near normal)
2. Absence of femur and/or tibia and fibula (with foot normal or near normal)

c) Longitudinal Defects

Absence or severe hypoplasia of lateral part of the limb. There are two main types:

1. Preaxial (Radial-tibial) – absence or severe hypoplasia of preaxial structures of the limb (thumb, first metacarpal, radius: hallux, first metacarpal, tibia).
2. Postaxial (Ulna-fibula) – absence or severe hypoplasia of postaxial structures of the limb (little finger, 5^{th} metacarpal, ulna; 5^{th} toe, 5^{th} metatarsal, fibula).

d) Split Hand-foot

Absence of central digits with or without absence of central metacarpal/ metatarsal bones usually associated with syndactyly of other digits. There are two main subtypes:

1. Typical split hand/foot is characterised by a cone-shaped cleft tapering proximally and dividing the hand into 2 parts, which can be opposed like lobster-claws. In the mildest forms the 3^{rd} digit (middle finger or 3^{rd} tow) is absent but the corresponding metacarpal/ metatarsal bone is almost normal.
2. Monodactyly of the hand is characterised by deficiency of the central and radial digits, such that there is no cleft formation and only one digit is present (usually the 5^{th}).

e) Multiple Types of Reduction Defects
   Infants with more than one type of reduction according to the classification given above. (It is most important that each limb is described separately in such infants).

Sirenomelia

Definition:
Sirenomelia is a sequence characterised by:

a) Fusion of lower limbs of various degrees of severity resulting in only one lower "structure"
b) Sacral defect
c) Anal atresia
d) Abnormal external genitalias
e) Absence of kidneys.

It results from the fusion of the early limb buds at their fibular margins with absence or incomplete development of the intervening caudal structures. There is usually an absence of allantoic vessels and a single umbilical artery arising directly from the aorta.

All degrees of severity are observed, presumably dependent on the relative length and width of the early caudal deficit. The variable consequences are often called the caudal regression syndrome[6].

Amniotic Band Associated Defect

Definition:
Limb reduction defects associated with the presence of necrotic band tissues attached to one or more limbs or other part of the body.

Note:
It is becoming popular to interpret a wide spectrum of defects as a consequence of amniotic bands constricting the limb or other part of the body, or as a consequence of an early amnion rupture.

Although these mechanisms may be causal in some cases, it has not been demonstrated that these mechanisms are responsible in all cases. We do not know if amniotic band and/or rupture of the amnion when present are the

primary pathogenetic mechanism or simply an associated finding resulting from a common cause.

At the present stage of our ignorance it is preferable not to use a term such as Amniotic Band Syndrome, ADAM Complex, Early Amnion Rupture Spectrum to label infants who show a combination of Craniofacial and/or limb defects and/or defects such as[6]:

Craniofacial	*Limbs*	*Other*
Anencephaly, Facial distortion, proboscis Unusual facial clefting Eye defects, encephalocele, meningocele		Placenta attached to head and/or abdomen
Or as:		
Usual cleft lip Choanal atresia	Limb reduction Polydactyly Syndactyly	Abdominal wall defects Thoracic wall defects Scoliosis
Or as:		
Cleft palate (Robin deformation sequence) Ear deformation Craniostenosis	Amniotic bands Amputation Hypoplasia Pseudosyndactyly Distal lymphoedema Foot deformation Dislocation of hip Constriction bands	Short umbilical cord Omphalocele

It is really important to describe the infant's defects in detail and to take a photograph of all cases where a necrotic band or ring constriction is present.

Micromelia

Definition:
This term designates a short limb. Micromelia is usually present in most of the osteochondrodysplasias as part of the disease.

Campomelia

Definition:
Campomelia means bent limb. The limbs are shortened to a mild degree with marked anterolateral bowing. Congenital campomelia can involve all the limbs (as in the campomelic dysplasia) or only one bone, usually the tibia.

Tibia Torsion – bent tibia is present when the fibula is absent. Tibial torsion without absence of fibula occurs in the lower half of the tibia with more often anterior bowing and less often posterior incurvation of this bone.

Multiple Congenital Contractures and Joint Laxity

Definition:
This term does not indicate a diagnosis of any specific disease. It means only altered mobility of two or more different joints or one or more limbs. A description of these disorders and references are available in the paper by J Hall et al[9].

Limb References

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8. Jones KL (1997), "Smith's Recognizable Patterns of Human Malformations: Genetic, Embryologic and Clinical Aspects" 5th Ed, WA Saunders, Philadelphia.

9. Hall JG, Reed SD, Greene G (1982), "The Distal Arthrogryposes: Delineation of New Entities. Review and Nosologic Discussion", Am J Med Genet, Vol 11, pp185-239.

SELECTED EXAMPLES OF CONGENITAL LIMB DEFECTS

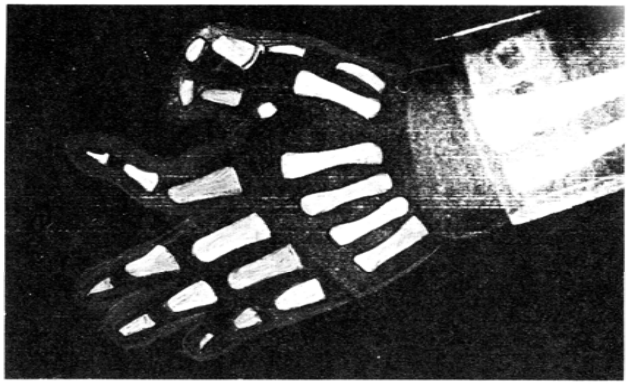
Seventeen examples of congenital limb defects are given in order to illustrate the way these anomalies should be coded and reported to the EUROCAT Central Registry. The given codes are ICD10/BPA extension. The examples selected are:

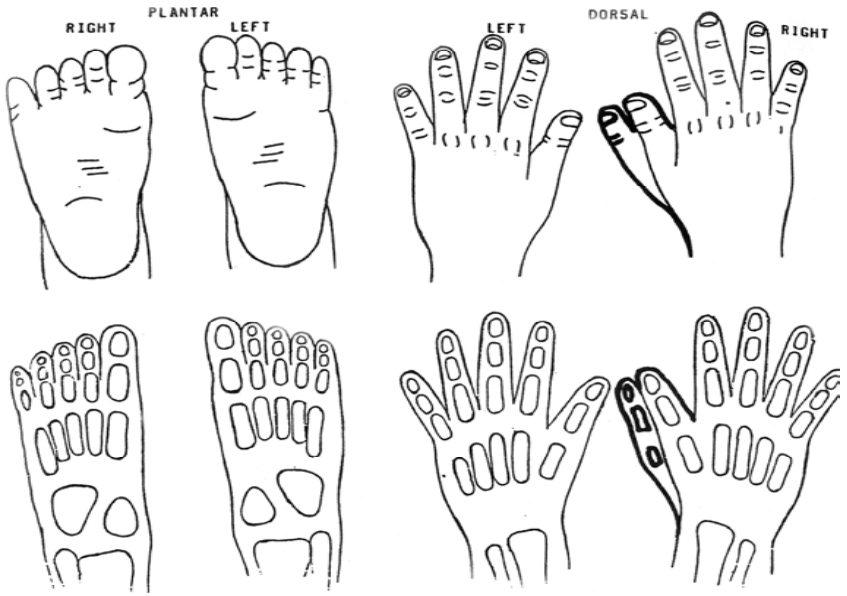
- 2 polydactylies: one preaxial, one postaxial
- 4 syndactylies: zygodactyly of hand, zygodactyly of foot, postaxial synpolydactyly, complete syndactyly
- 8 reduction defects:
  - 2 terminal transverse defects at the arm and at the hand level
  - 2 intercalary defects, one distal and one proximal
  - 2 longitudinal preaxial defects
- 2 split hands: one typical, one monodactyly
- 1 sirenomelia
- 1 amniotic band associated defect
- 1 campomelia: tibial torsion

Brachydactyly is not illustrated, as the diagnosis is usually not recognised at birth. Examples of skeletal dysplasias and multiple congenital contractures are not given and they can be found in reference books [5-7].

Q 691

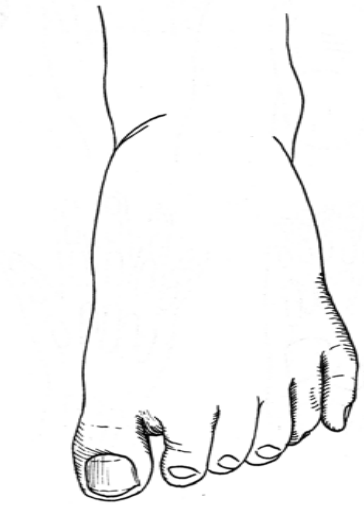
EXAMPLE 1 : Preaxial polydactyly : duplication right thumb.

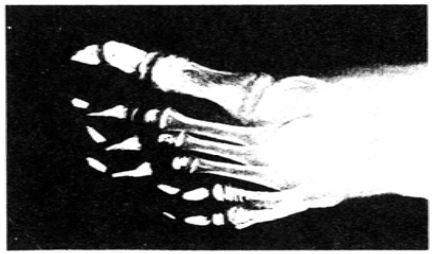


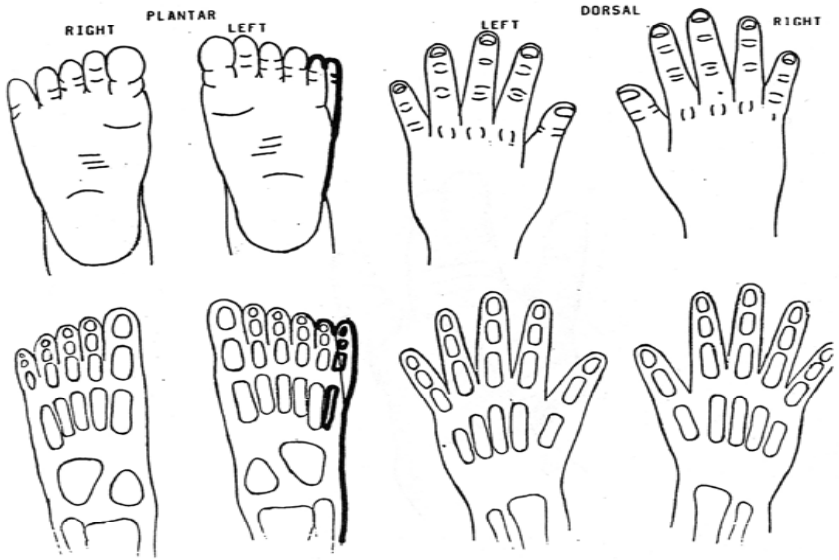


Q 692

EXAMPLE 2 : Postaxial polydactyly type A : duplication 5th toe.

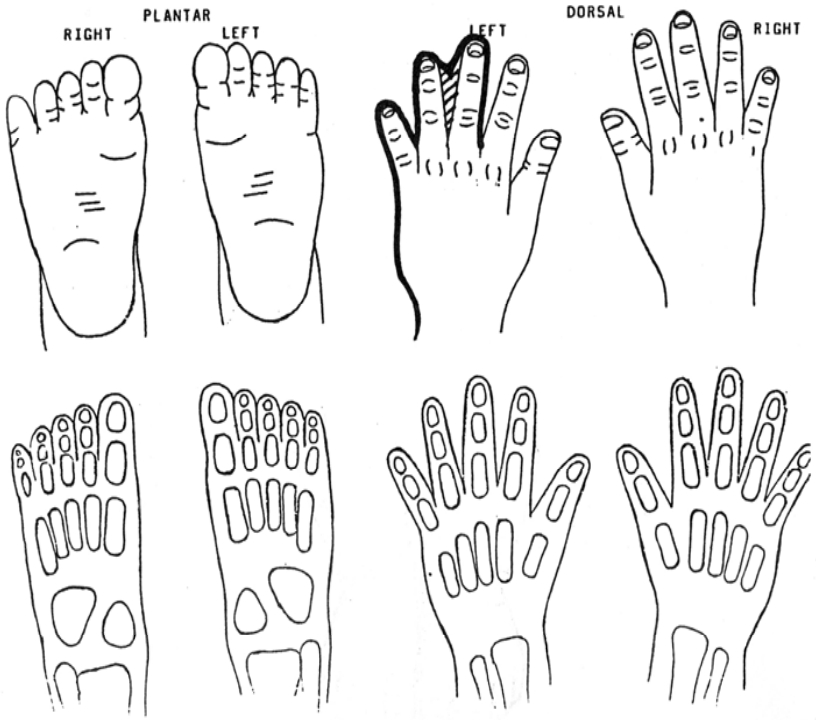






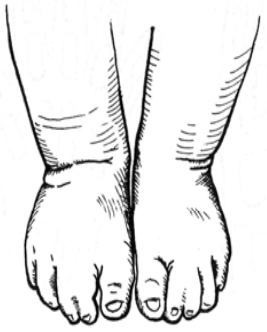
Q 701

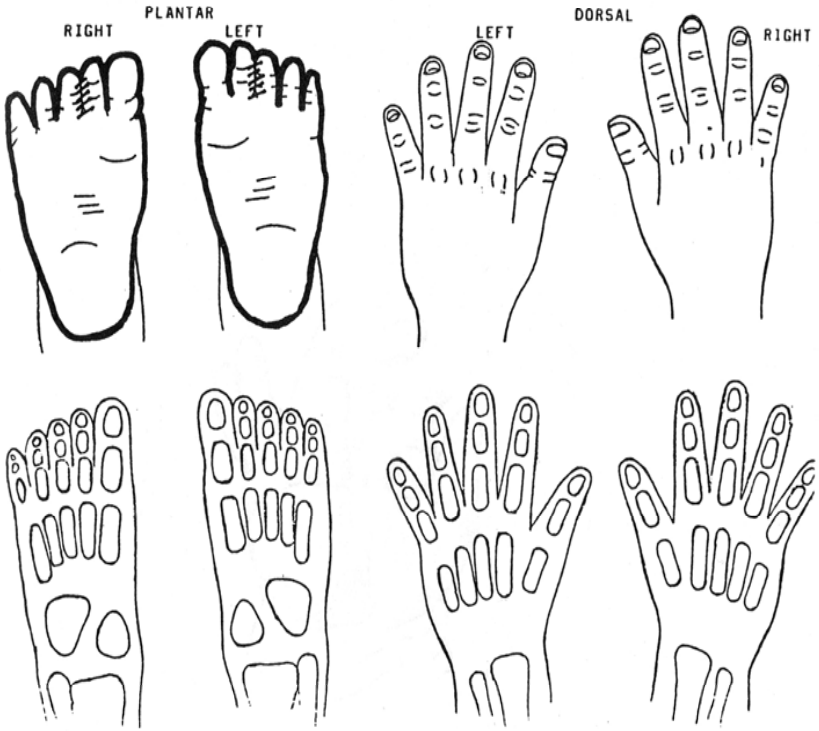
EXAMPLE 3 : Syndactyly type zygodactyly 3rd-4th fingers left hand.



Q 703

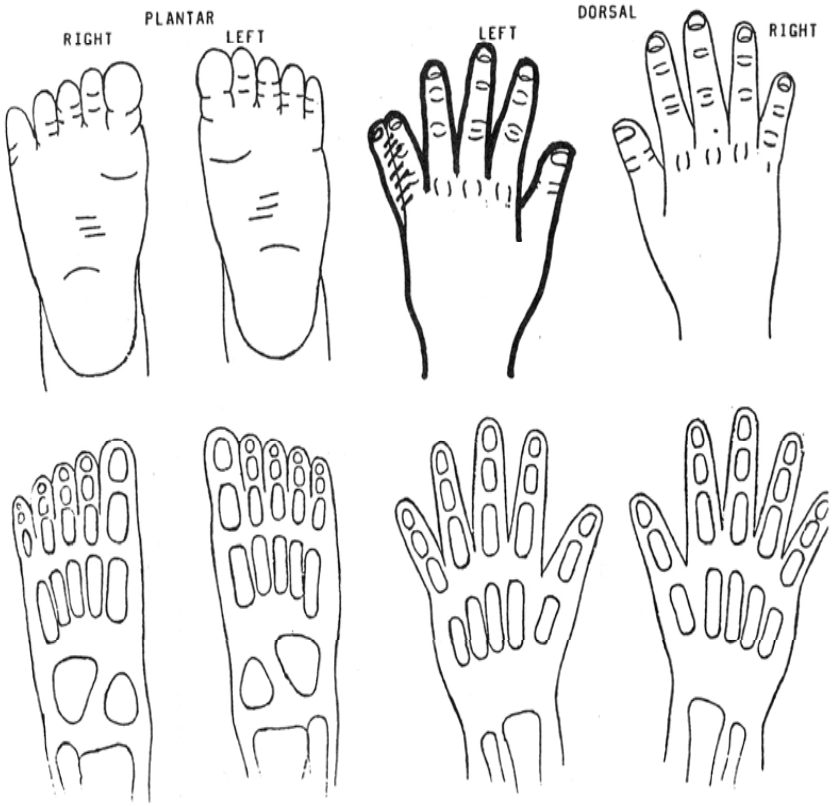
EXAMPLE 4 : Syndactyly type zygodactyly 2nd-3rd digits both feet (this is a minor and common anomaly that should not be reported to the EUROCAT Central Registry).



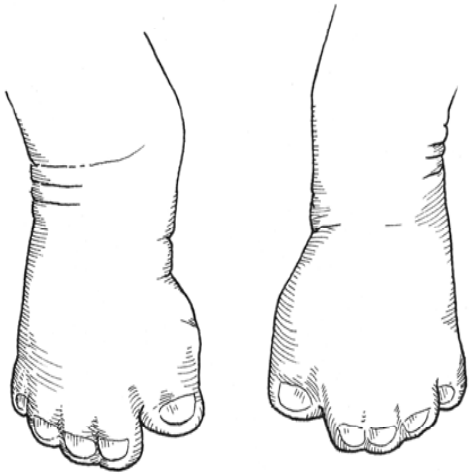


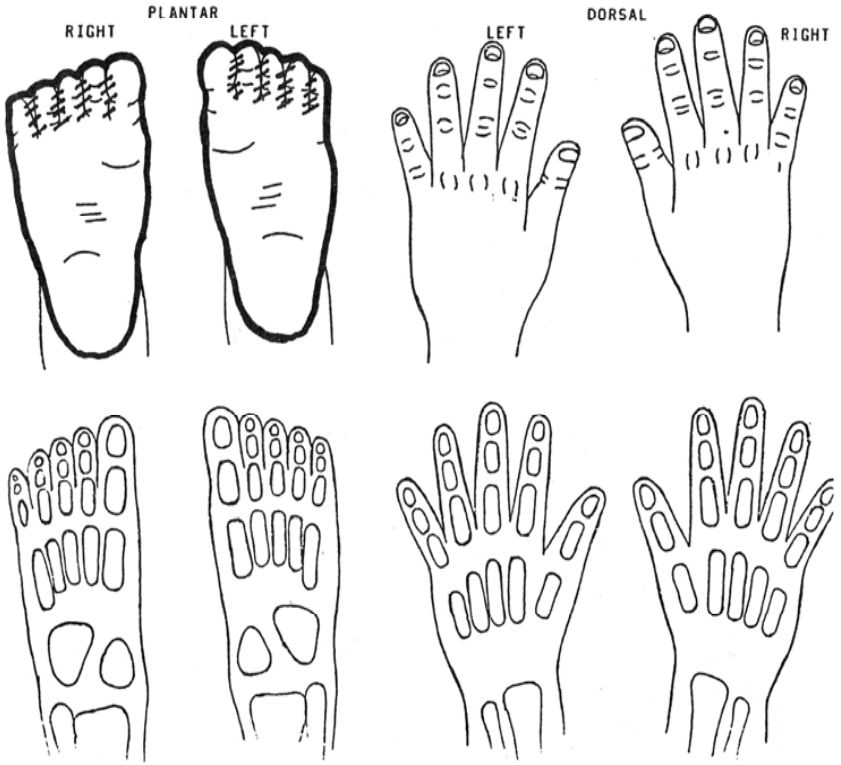
Q 690 and Q 701

EXAMPLE 5 : Postaxial synpolydactyly 5th-6th fingers left hand.



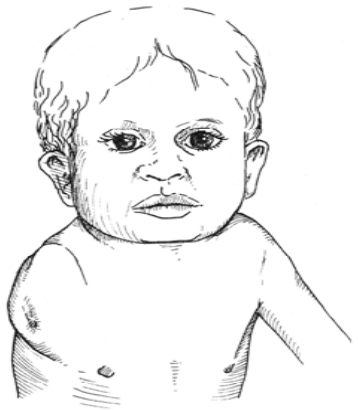
EXAMPLE 6 : Complete syndactyly both feet.

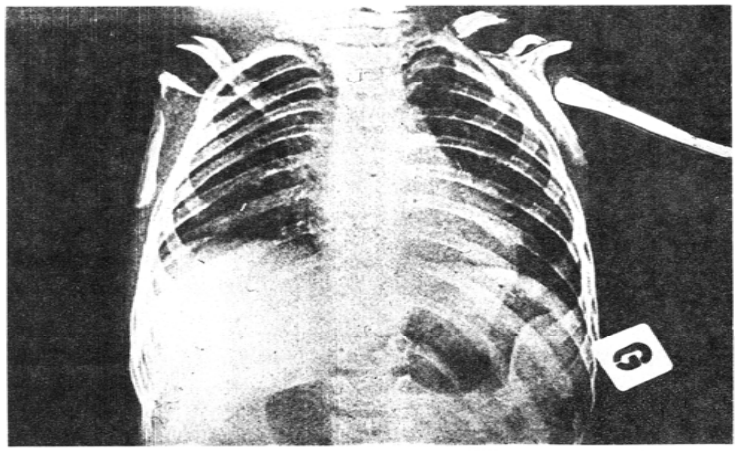


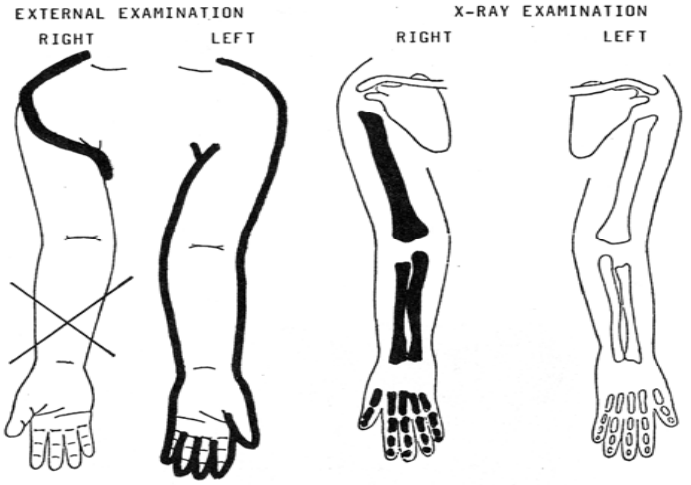


Q 710

EXAMPLE 7 : Terminal transverse reduction defect at the level of right arm (amelia).

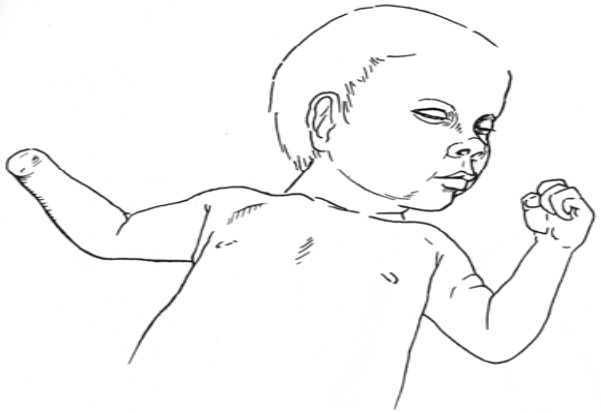


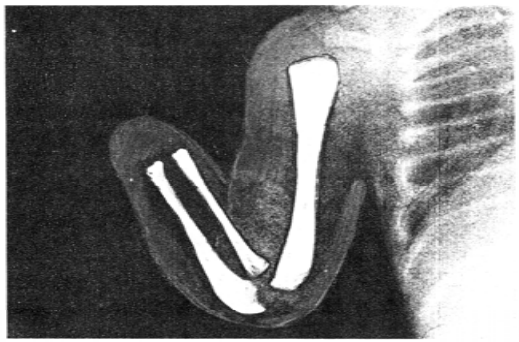


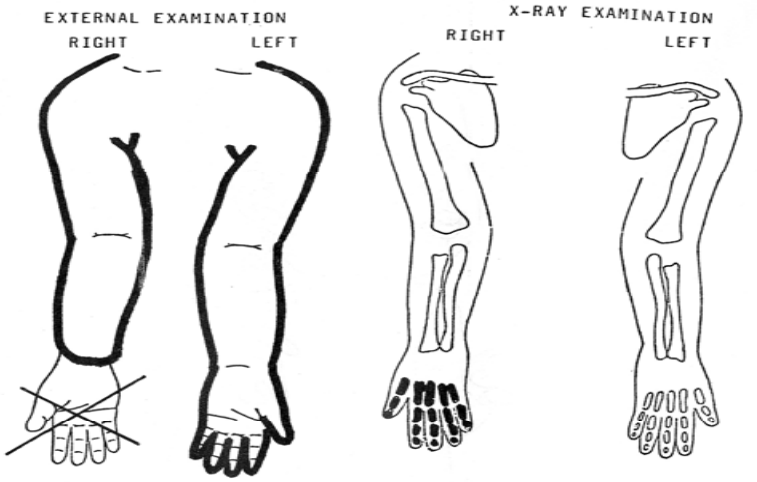


Q 713

EXAMPLE 8 : Terminal tranverse reduction defect at the level of right hand (acheiria).

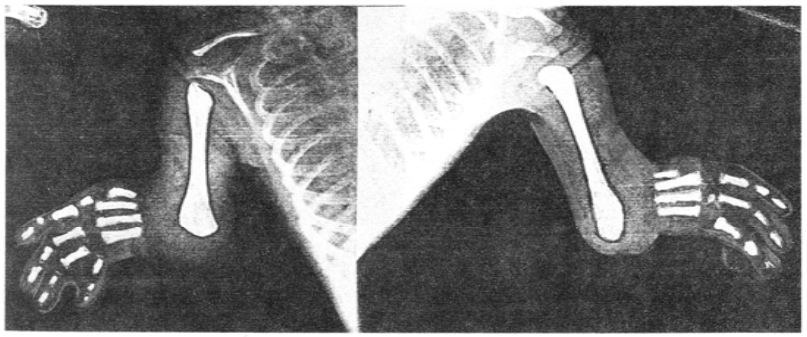


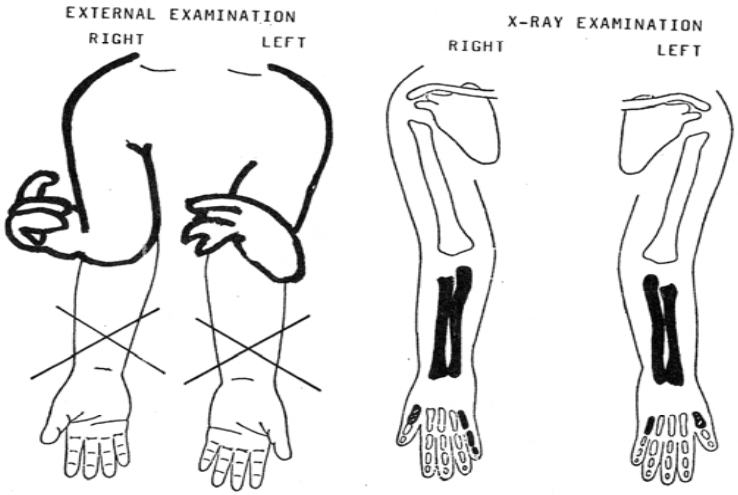




Q 714 and Q 715

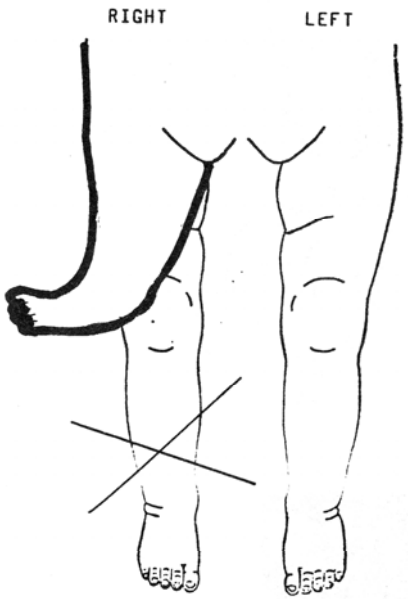
EXAMPLE 9 : Intercalary reduction defect : agenesis of radius and ulna both arms.

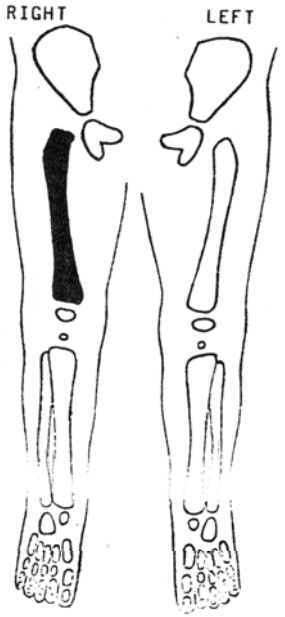




Q 724

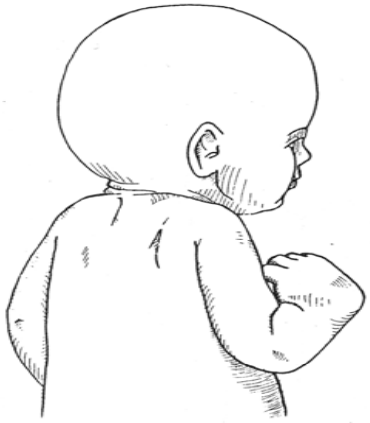
EXAMPLE 10 : Intercalary reduction defect : femoral agenesis right leg.

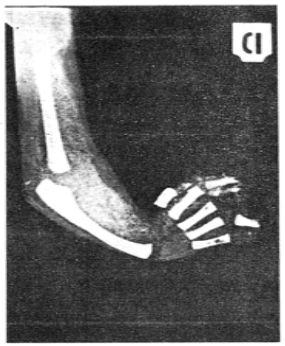


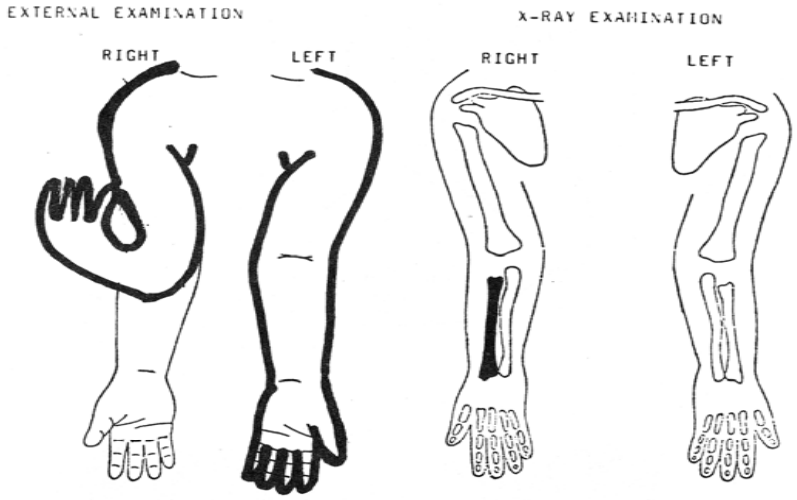


Q 714

EXAMPLE 11 : Longitudinal reduction defect preaxial : radial agenesis right arm.

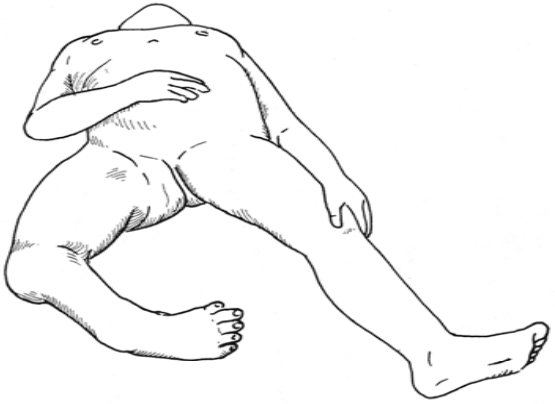


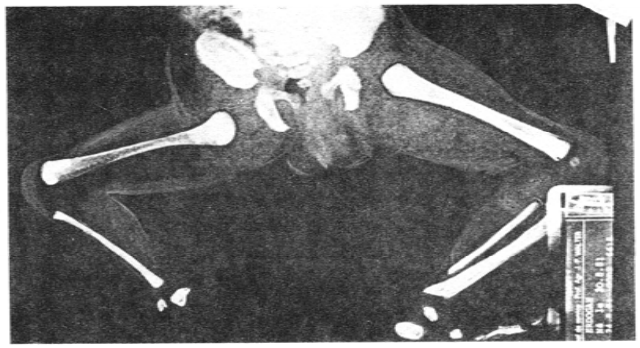


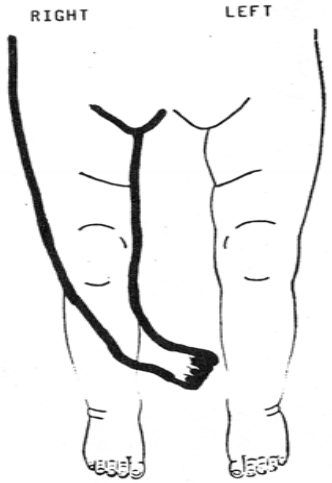


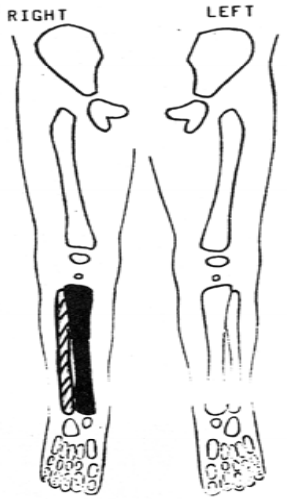
Q 725

EXAMPLE 12 : Longitudinal reduction defect preaxial : tibial agenesis right leg.



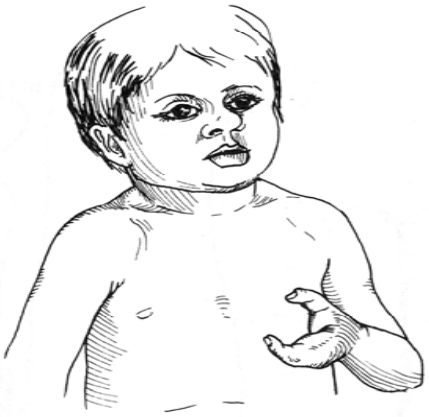


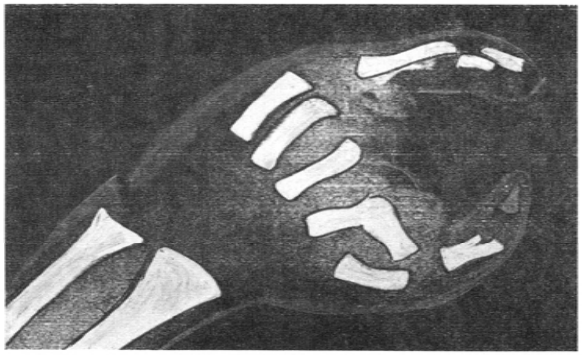


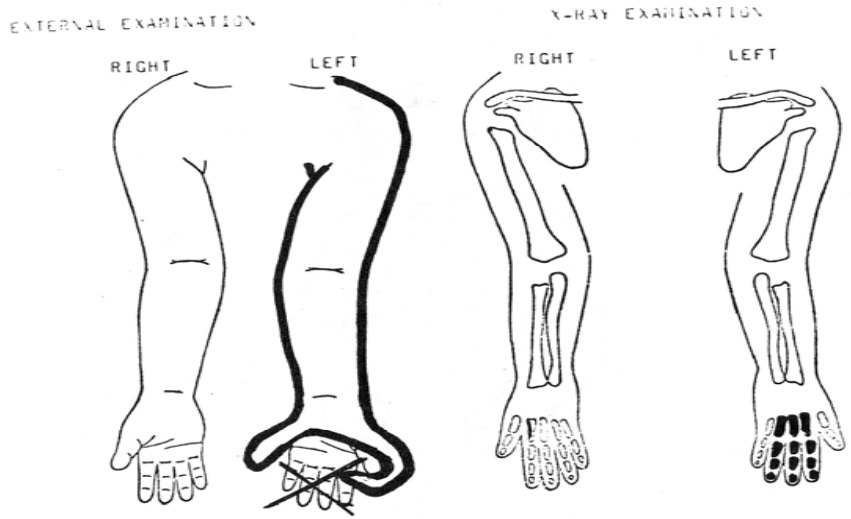


Q 716

EXAMPLE 13 : Reduction defect : typical split left hand.

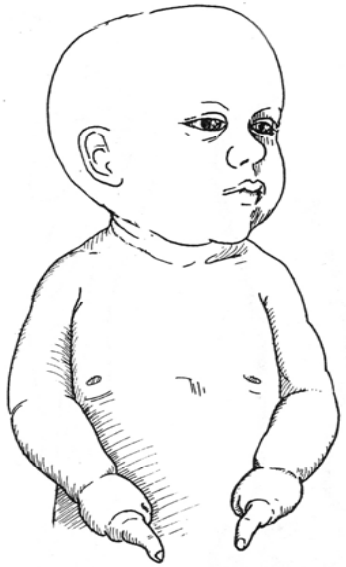


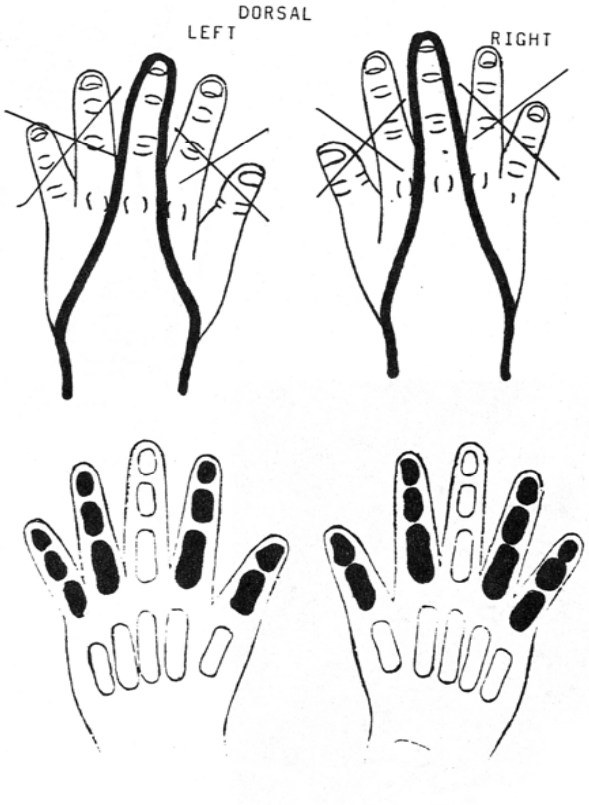




Q 7130

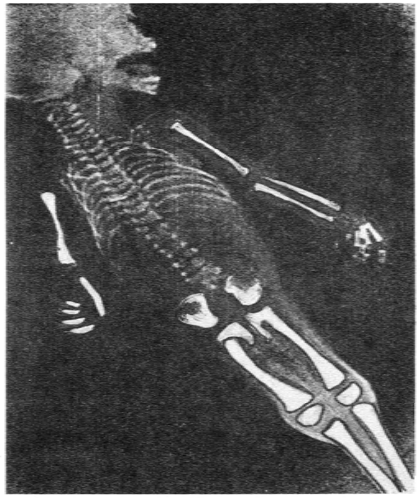
EXAMPLE 14 : Reduction defect : split hand monodactyly type both sides.

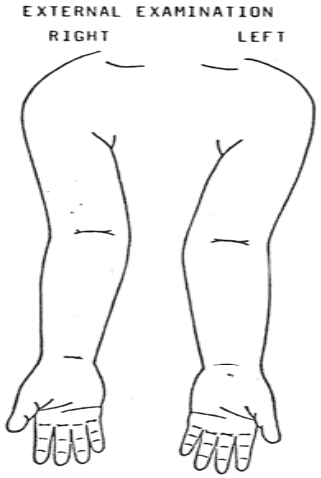


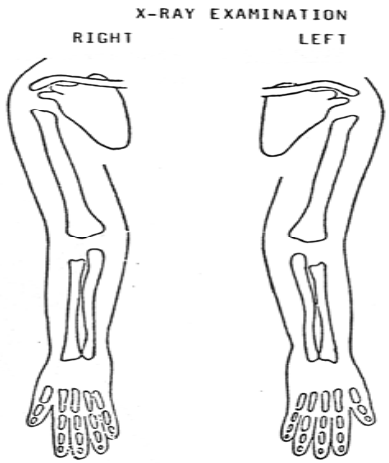


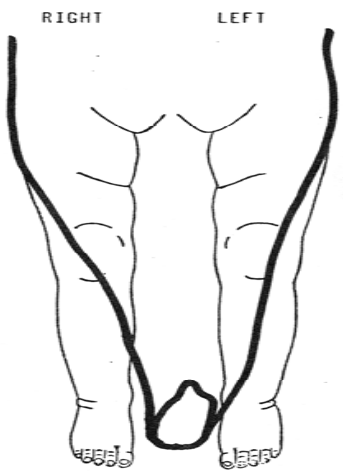
Q 8724

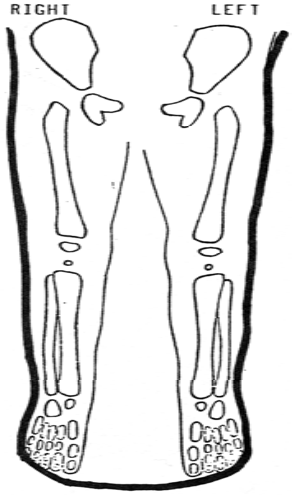
EXAMPLE 15 : Sirenomelia sequence.





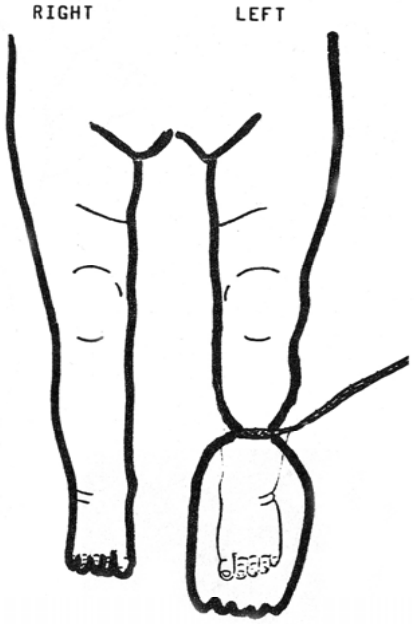






Q 728

EXAMPLE 16 : Defect associated with constriction or fibrotic band left leg.



Q 725

EXAMPLE 17 : Tibial torsion left foot (campomelia).