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A Radiological Atlas

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Foreword from R. O. Murray

With 55 Figures (124 Separate Illustrations)

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Professor Bryan J. Cremin, F.R.A.C.R., F.R.C.R
Head, Department of Radiology,
Groote Schuur and Red Cross Childrens Hospital,
University of Cape Town,
Rondebosch 7700, South Africa

Professor Peter Beighton, M.D., Ph.D., F.R.C.P., D.C.H.
Department of Human Genetics,
Groote Schuur Hospital,
University of Cape Town,
Observatory 7925, South Africa

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1842

Foreword

The tremendous expansion of medical knowledge during the last few decades, together with the introduction of many new diagnostic techniques, has demanded such a degree of specialisation that no single individual can be conversant with all the information available. More and more emphasis, therefore, has been placed on the importance of teamwork and close collaboration between associated disciplines. The bone dysplasias of infancy represent a classical example of this concept. Only a few years ago these heritable conditions were divided into a relatively small number of entities, for many of which "atypical variants" were accepted. More recent studies have resulted in appreciation and early recognition of a large number of these disorders, thanks to co-operation between paediatricians, radiologists, geneticists and biochemists. Not only may a reasonably accurate prognosis be offered for the affected child in many instances, but, almost of greater value, genetic counselling concerning the chance of subsequent offspring being similarly affected has become available to parents.

Most radiologists have little opportunity of becoming familiar with this rapidly widening field of diagnosis, so that the occasional case which may be encountered is likely to engender diagnostic difficulty. This Atlas should facilitate greatly the solution of the problem. It has been prepared by Professor CREMIN, an outstanding paediatric radiologist whose work has been known and admired by me for many years, in close collaboration with his colleague Professor BEIGHTON, a geneticist of great distinction. The combination of systematic assessment of the radiological evidence and the genetic characteristics of the conditions described provides a comprehensive account of the present state of knowledge. As the authors point out the field, as yet, has not been explored completely and the hope may be expressed that further information, when it become available, will be incorporated in future editions. The authors are to be congratulated on this excellent and up-to-date contribution to the literature of a difficult subject.

London, June, 1978

R. O. MURRAY

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Cape Town, June, 1978

BRYAN J. CREMIN
PETER BEIGHTON

Glossary of Useful Terms

Acromelia	Shortening of distal portion of limb
Acromesomelia	Shortening of the middle and distal portion of the limb
Appendicular	Dependent portions of the skeleton
Axial	Trunk portion of the skeleton
Campomelia	Bent limb
Clinodactyly	Deviation of a finger
Congenital abnormality	An abnormality which is present at birth, but not necessarily genetic
Diaphysis	Middle portion of the shaft of a long bone
Diastrophic	Twisted
Dysostosis	A defect in ossification or modeling
Dysplasia	Intrinsic growth disturbance
Dystrophy	Growth disturbance influenced by external factors
Hexadactyly	Six digits
Hypertelorism	Wide gap between the orbits
Mesomelia	Shortening of the middle portion of limb
Metaphysis	Extremity of the shaft of a long bone
Metatropic	Changeable
Micrognathia	Small jaw
Micromelia	Short limb
Nanism	Small stature or dwarfism
Phenotype	Outward expression of genetic constitution
Platyspondyly	Flattening of vertebrae
Polydactyly	Supernumerary digits
Post-axial	Ulnar or fibular side
Pre-axial	Radial or tibial side
Rhizomelic	Proximal portion of a limb
Siblings	Offspring of the same parent
Symphalagism	End to end fusion of contiguous phalanges
Syndactyly	Soft tissue or bony union between adjacent digits
Thanatophoric	Death bearing

Important terms used in clinical genetics are explained in Chapter Two.

Comments on Terminology

Because of the confusion in terminology concerning the bone dysplasias, a sub-committee of the European Society of Pediatric Radiology met in Paris in 1969 and elaborated a nomenclature that divided the Constitutional (Intrinsic) diseases of bone into those with unknown and known pathogenesis. The unknown group were further divided into osteochondrodysplasias (abnormalities of cartilage and/or bone growth and development), dysostoses (malformation of individual bones, single or in combination), and other groups.
The osteochondrodysplasias were subdivided into three groups, the first of which were defects of growth of tubular bones and/or spine that manifested (A) at birth and (B) in later life.

This portion of the nomenclature is given below:

Constitutional Diseases of Bones with Unknown Pathogenesis.

Osteochondrodysplasias (abnormalities of cartilage and/or bone growth and development)

1. Defects of growth of tubular bones and/or spine.

A) Manifested at birth

1. Achondrogenesis
2. Thanatophoric dwarfism
3. Achondroplasia
4. Chondrodysplasia punctata (formerly stippled epiphyses) (several forms)
5. Metatropic dwarfism
6. Diastrophic dwarfism
7. Chondro-ectodermal dysplasia (ELLIS-VAN CREVELD)
8. Asphyxiating thoracic dysplasia (JEUNE)
9. Spondylo-epiphyseal dysplasia congenita
10. Mesomelic dwarfism: type NIEVERGELT; type LANGER
11. Cleido-cranial dysplasia (formerly cleido-cranial dysostosis).

B) Manifested in later life

1. Hypochondroplasia
2. Dyschondosteosis
3. Metaphyseal chondro-dysplasia type JANSEN

4. Metaphyseal chondro-dysplasia type SCHMID
5. Metaphyseal chondro-dysplasia type MCKUSICK
   (formerly cartilage-hair hypoplasia)
6. Metaphyseal chondro-dysplasia with malabsorption and neutropenia
7. Metaphyseal chondro-dysplasia with thymolymphopenia
8. Spondylo-metaphyseal dysplasia (KOZLOWSKI)
9. Multiple epiphyseal dysplasia (several forms)
10. Hereditary arthro-opthalmopathy
11. Pseudo-achondroplasic dysplasia
    (formerly spondylo-epiphyseal pseudo-achondroplasic dysplasia)
12. Spondylo-epiphyseal dysplasia tarda
13. Acrodysplasia
    a) Rhino-trico-phalangeal syndrome (GIEDION)
    b) Epiphyseal (THIEMANN)
    c) Epiphyso-metaphyseal (BRAILSFORD)

The nomenclature was revised in Paris at a further meeting in 1977 and the proposed first portion is given below:

1. Defects of growth of tubular bones and/or spine.

A) Identifiable at birth

1. Achondrogenesis type I (PARENTI-FRACCARO)
2. Achondrogenesis type II (LANGER-SALDINO)
3. Thanatophoric dysplasia
4. Thanatophoric dysplasia with Clover-leaf Skull
5. Short rib-polydactyly syndrome type I (SALDINO-NOONAN)
   (perhaps several forms)
6. Short rib-polydactyly syndrome type II (MAJEWSKI)
7. Chondrodystrophia punctata
   a) Rhizomelic type
   b) Dominant type
   c) Other types
   d) Exclude symptomatic stippling in other disorders
      (ZELLWEGER syndrome, Warfarin embryopathy and others)
8. Campomelic dysplasia
9. Other dysplasias with congenital bowing of long bones
10. Achondroplasia
11. Diastrophic dysplasia
12. Metatropic dysplasia (several forms)
13. Chondro-ectodermal dysplasia (ELLIS-VAN CREVELD)
14. Asphyxiating thoracic dysplasia (JEUNE)
15. Spondylo-epiphyseal dysplasia congenita (SPRANGER-WIEDEMANN)
16. Other spondylo-epiphyseal dysplasias recognizable at birth
17. KNIEST dysplasia
18. Mesomelic dysplasia
    a) type NIEVERGELT
    b) type LANGER (probable homozygous dyschondrosteosis)

c) type ROBINOW
d) type RHEINARDT
e) Others
19. Acromesomelic dysplasia
20. Cleido-cranial dysplasia
21. LARSEN syndrome
22. Oto-palato-digital syndrome

B) Identifiable in later life

1. Hypochondroplasia
2. Dyschondrosteosis
3. Metaphyseal chondrodysplasia type JANSEN
4. Metaphyseal chondrodysplasia type SCHMID
5. Metaphyseal chondrodysplasia type MCKUSICK
6. Metaphyseal chondrodysplasia with exocrine pancreatic insufficiency and cyclic neutropenia
7. Spondylo-metaphyseal dysplasia
   a) type KOZLOWSKI
   b) Other forms
8. Multiple epiphyseal dysplasia
   a) type FAIRBANK
   b) Others
9. Arthro-ophthalmopathy (STICKLER)
10. Pseudo-achondroplasia
    a) Dominant
    b) Recessive
11. Spondylo-epiphyseal tarda
12. Spondylo-epiphyseal dysplasia (other types)
13. DYGGVE-MELCHIOR-CLAUSEN dysplasia
14. Spondylo-epi-metaphyseal dysplasia (several types)
15. Myotonic chondrodysplasia (CATEL-SCHWARTZ-JAMPEL)
16. Parastremmatic dysplasia
17. Tricho-rhino-phalangeal dysplasia
18. Acrodysplasia with retinitis pigmentosa and nephropathy (SALDINO-MAINZER).

This book concerns itself only with the conditions in Group (A) i. e. those manifested at birth. It follows closely the updated nomenclature but conditions such as the oto-palato-digital syndrome have been omitted as their diagnosis may be largely clinical.

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Introduction

Just over a decade ago at an International Congress of Pediatric Radiology, the doyen of the meeting was overheard to say "these infantile bone dysplasias all look the same to me." Many others, ourselves included, had the same problem! Since then there has been an explosion of interest in the subject and, with the accumulation of clinical and radiographic data, the features of a number of specific disorders have now been clearly defined. These entities differ widely in their complications and prognosis but they are all heritable conditions with a specific recurrence risk. For these reasons diagnostic accuracy is crucial and in most instances this can now be achieved.

Diagnosis usually depends upon the radiological recognition of a pattern of skeletal change. To recognize this pattern and obtain the maximum information a system and sequence for examining the infant's radiographs must be followed. The majority of diagnostic features are present in (I) the limbs, (II) the thorax and pelvis, (III) the spine, and (IV) the skull. For easier reading we have presented the radiographic features in this order in the text. If after noting and comparing these features the reader is unable to reach a decision then the case probably belongs to an undiagnosable or undelineated category.

Diagnosis is not always easy, but there is little doubt that the problem of skeletal dysplasia in infancy will play an increasing role in modern pediatric radiology. Considerable attention is focused on this topic and trainees in this specialty are expected to have knowledge and a balanced perspective for their examinations. Similarly, the genetic background and potential lethality of many of these disorders is of importance to pediatricians and obstetricians.

We have attempted to produce a concise atlas which contains the relevant information rather than a comprehensive monograph. Wherever possible salient points are discussed in the light of our own practical experience in the Radiology and Genetic departments of the University of Cape Town Medical School. With four exceptions the illustrations are also derived from these sources. We have aimed at simplicity and clarity, and the references which have been selected refer to up-to-date reviews or articles. For further reading a list of relevant articles and monographs is given in the appendix.

The general layout of the appropriate sections of the recently updated (1977) Paris Nomenclature for Constitutional Disorders of Bone has been followed, and in accordance with modern trends we have preferred the term "dysplasia" to that of "dwarfism." Similarly, eponyms have been retained only when they are hallowed by time or where they are in everyday usage.

Chapter 1

Clinical and Genetic Evaluation of the Neonate with Skeletal Dysplasia

In the skeletal dysplasias a firm diagnosis is essential for meaningful prognostication and effective genetic counseling. This is usually dependent upon the accumulation and correlation of information from a number of sources and as several of the skeletal dysplasias are potentially lethal the opportunity to obtain objective evidence may be fleeting. In these circumstances, a full clinical, genetic, and radiographic evaluation is imperative.

Clinical Evaluation

Many of the skeletal dysplasia syndromes present as short-limbed dwarfism and can be grouped according to the prognosis in the perinatal period:

1. Lethal
Achondrogenesis
Thanatophoric dysplasia
Asphyxiating thoracic dysplasia (severe neonatal type)
Short rib-polydactyly syndromes
Campomelic dysplasia
Homozygous achondroplasia

2. Sometimes lethal
Chondroectodermal dysplasia
Chondrodysplasia punctata (rhizomelic type)
Diastrophic dysplasia
Metatropic dysplasia
Osteogenesis imperfecta congenita
Hypophosphatasia (infantile type)
Osteopetrosis—precocious form

3. Not usually lethal
Achondroplasia
Spondyloepiphyseal dysplasia congenita
Mesomelic dysplasia

Certain clinical features are of value as diagnostic indicators, although it must be emphasized that these are neither consistent nor specific:

1. Caput membranaceum
Osteogenesis imperfecta congenita
Hypophosphatasia

2. Cleft palate
Diastrophic dysplasia
Campomelic dysplasia
Spondyloepiphyseal dysplasia congenita

3. Contractures (club foot, flexed digits, etc.)
Diastrophic dysplasia
Chondrodysplasia punctata (sometimes)
Metatropic dysplasia
Campomelic dysplasia
Mesomelic dysplasia—Nievergelt form

4. Supernumerary digits
Short rib-polydactyly syndromes
Asphyxiating thoracic dysplasia
Chondro-ectodermal dysplasia

Genetic Evaluation

Genetic investigations are now an integral component of clinical practice. The neonatal skeletal dysplasias all have a genetic basis and a working knowledge of fundamental concepts concerning the major patterns of inheritance is essential for their understanding and investigation.

A detailed family history will often indicate or at least provide a clue to the probable mode of transmission of a particular disorder. In turn, this information can be used to support or refute a clinical or radiographic diagnosis. For practical purposes the only forms of inheritance likely to be encountered in the neonatal skeletal dysplasias are autosomal dominant and autosomal recessive. In the former case, the condition is handed down from generation to generation and an affected individual has an even chance of transmitting the abnormal gene to each of his or her children. In the latter, clinically normal parents each carry a gene for a particular disorder which only becomes manifest in those of their offspring who receive both of these genes. For any further offspring of this particular couple the risk of the recurrence of the disorder is one in four for every subsequent pregnancy.

This brief account is an oversimplification as many other factors enter into the situation, such as new mutation and genetic heterogeneity. Nevertheless, the following facts should be adduced in every case:

a) Any brothers or sisters with the condition? (i.e., affected siblings and normal parents would suggest autosomal recessive inheritance)

b) Any other affected kin? (i.e., an affected parent would suggest autosomal dominant inheritance)

c) Parents' ages? (i.e., in a sporadic case advanced paternal age would be evidence in favor of new dominant mutation)

d) Parental consanguinity? (i.e., if the parents are related to each other, the condition is likely to be autosomal recessive)

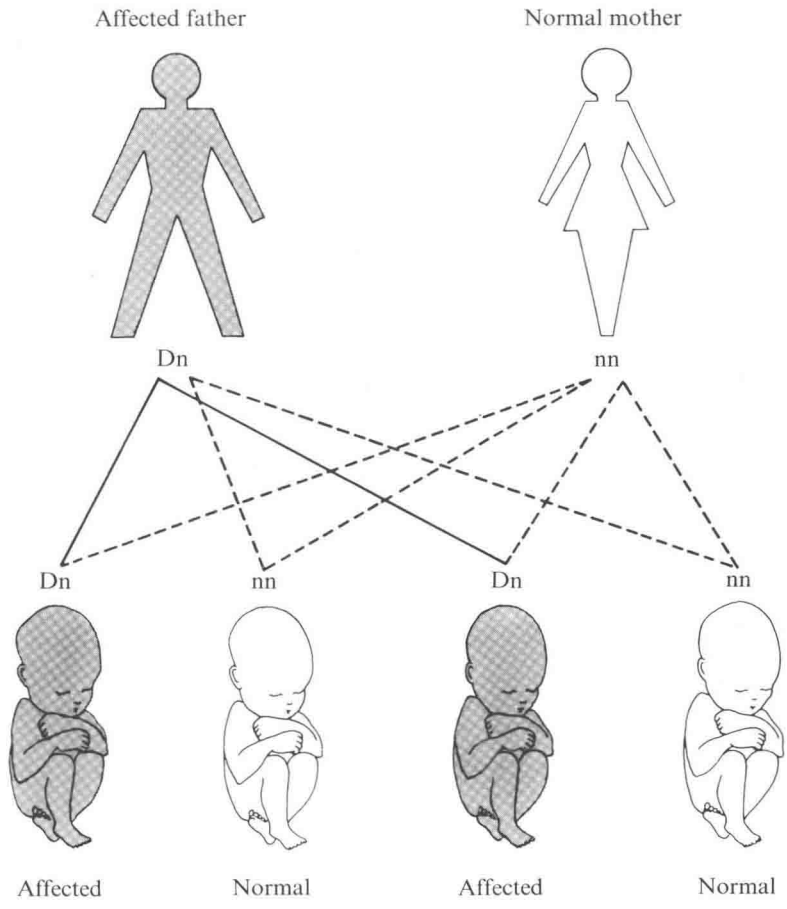
Atypical or undiagnosable neonatal skeletal dysplasias are frequently encountered. With the accumulation of data a number of these have been elevated to syndrome status. Information concerning the probable genetic background provides important clues to their pathogenesis and permits the estimation of recurrence risks.

Genetic Counseling and Antenatal Diagnosis

If a couple has produced a child with a skeletal dysplasia, they will wish to know the prognosis for life and health and the likelihood of recurrence at any future pregnancy. If an accurate diagnosis has been reached this information can be provided. In this situation it is the genetic counselor's duty to ensure that the parents have a clear understanding of the implications of the condition and of the magnitude of the risks of recurrence. He is also obliged to point out the options that are available; these may include avoidance of pregnancy, therapeutic termination, and antenatal diagnosis.

At present amniocentesis is the method of choice in this rapidly expanding field of prenatal diagnosis. In this procedure a needle is passed through the abdominal wall into the uterus and a specimen of amniotic fluid is withdrawn. This is usually undertaken at the 14th to 16th week after conception. Fetal cells can be obtained by centrifugation of this fluid and cultured for the investigation of their cytogenetic status and metabolic activity. By this means certain fetal abnormalities can be recognized sufficiently early to permit selective termination. However, the chromosomes are normal in the skeletal dysplasias and in the majority, the underlying biochemical defects have not been identified. For these reasons, with the exception of hypophosphatasia, they cannot be diagnosed by amniocentesis.

In fetoscopy an optic system attached to a needle is inserted into the gravid uterus. In this way direct visualization of the fetus is possible. Structural defects such as limb-shortening are visible and this technique, therefore, holds considerable promise for the antenatal recognition of the skeletal dysplasias. There are, however, technical problems in fetoscopy and so far it has not found a place in routine practice.



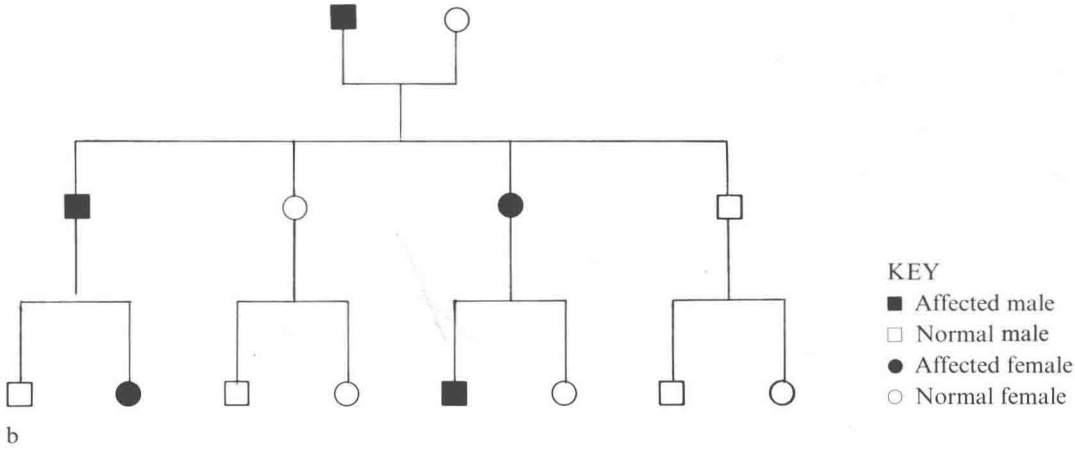


Fig. 1-1. (a) Mechanism of autosomal dominant inheritance. An individual with the abnormal gene, labeled (Dn), will have the clinical features of the disorder. (b) Pedigree of a family with an autosomal dominant disorder such as achondroplasia. Any individual with the abnormality has an even chance of producing an affected child at each episode of procreation, irrespective of the sex of the parent or offspring. The gene is transmitted from generation to generation and approximately equal numbers of males and females are affected