DYSMELIA

A Classification and a Pattern of Malformation in a Group of Congenital Defects of the Limbs

LOTHAR HENKEL,* TÜBINGEN, GERMANY, and HANS-GEORG WILLET†, ZÜRICH, SWITZERLAND

The marked increase—attributed to the use of thalidomide—in the number of congenital malformations of the extremities between 1958 and 1962 gave new stimulus to an investigation into the nature and etiology of these limb defects.

The malformations observed during this period were named “dysmelia” by Wiedemann (1962). This widely accepted term is used to define a group of malformations in which there

![Fig. 1](image1)

**Fig. 1**
Teratological sequence of dysmelia of the upper extremities.

![Fig. 2](image2)

**Fig. 2**
Teratological sequence of dysmelia of the lower extremities.

is hypoplasia, and partial and total aplasia of the tubular bones of the extremities, ranging from isolated peripheral hypoplasia to complete loss of the extremity. Arranged according to their degree of severity they form a teratological sequence, linked by a common morphological pattern to be described in this paper (Figs. 1 and 2). They have occurred as hereditary cases

* Lord Nuffield Scholar, Nuffield Department of Orthopaedic Surgery, University of Oxford; Assistant in the Department of Orthopaedic Surgery, University of Tübingen, Germany.
† Assistant in the Department of Orthopaedic Surgery, Orthopädische Klinik "Balgrist," Zürich, Switzerland.
through several generations in a number of families, and they occur as sporadic cases. When
the effects of thalidomide became apparent the number of these malformations showed a
marked increase and the teratogenic action of an exogenic factor was clearly demonstrated.

In this paper the term "ectromelia" will be used to include those degrees of dysmelia
in which the radius and the tibia with their peripheral rays and the humerus or the femur are
involved. The term "phocomelia" will be reserved for those degrees of dysmelia in which no
remnants of long bones are seen between the limb girdle and the peripheral part (hand or foot).
"Amelia" will be used to indicate the most severe degree of dysmelia, in which there is total
loss of an extremity.

Attempts have been made to name and classify all congenital limb defects in one system,
based on the site, level and extent of the skeletal defects. A topographical classification of
this kind was proposed by Frantz and O'Rahilly (1961) and a revised version with improved
practical usefulness was published by Burch in 1966. In such classifications no allowance can
be made for teratological sequences and specific morphological patterns. Therefore the
malformations of dysmelia cannot be fitted into one of the already existing classifications
without fragmentation of the entity and masking of the common underlying pattern. There
is no room to express the close relationship of the malformations of the hand and the foot
and the distal and proximal parts of the extremity to each other which is so characteristic of
dysmelia.

A classification covering this group is yet important for communication, diagnosis,
development of therapeutic principles, and for better understanding of the anatomy of the
defomed limbs. When classification is based upon morphological patterns which are
characteristic of this particular group, greater understanding is possible without distortion of
the underlying teratological sequence.

MATERIAL

One hundred and forty-two children with dysmelia of the upper limb and thirty-six with
dysmelia of the upper and lower limbs were available for study in the orthopaedic department
of the University of Heidelberg. Fifty-eight cases of limb defect of the upper limb and twenty-
one of the upper and lower limbs were reviewed at the University of Tübingen, and another
nineteen cases of dysmelia of the arm and eleven of the arms and legs at Mary Marlborough
Lodge, Nuffield Orthopaedic Centre, Oxford. A total of 287 patients with 557 malformed
upper limbs and 136 malformed lower limbs were thus the basis of this study.

Limb defects of different character such as congenital amputation, cleft hand or foot
and ulnar and fibular aplasia did not increase in number during the period between 1958 and
1962. Because they differ fundamentally from dysmelia they were not included in this survey
except for comparison.

CLASSIFICATION

The following classification does not attempt to cover the whole range of congenital
malformations of the limbs. It applies to dysmelia only.

Three criteria were used to group the material into different types: 1) Which region of the
limb and which skeletal elements are affected? 2) In which manner are they affected: by
hypoplasia, partial aplasia or total aplasia? 3) Have the affected skeletal elements also
undergone fusion by synostosis?

On these criteria, the teratological sequence of dysmelia was divided into five main
types: 1) distal form of ectromelia; 2) axial form of ectromelia; 3) proximal form of
ectromelia; 4) phocomelia; 5) amelia. In the distal, axial and proximal forms of ectromelia
differences in manifestation appear because there is wide variation in the severity of the
skeletal abnormality and because in some of the cases synostosis occurs as well as reduction.
This necessitates a further subdivision.
**Distal form of ectromelia**—The malformation is confined to the distal part of the extremity and involves the radial ray of the hand and the radius or the tibial ray of the foot and the tibia only. The following are the different types.

*Figure 3—Triphalangism of the thumb. Figure 4—Hypoplasia of the thumb. Figure 5—Triphalangism of the big toe.*

*Figure 6—Hypoplasia of the radius. Figure 7—Hypoplasia of the radius with radio-ulnar synostosis. Figure 8—Partial aplasia of the radius. Figure 9—Partial aplasia of the radius with radio-ulnar synostosis. Figure 10—Total aplasia of the radius.*

*Figure 11—Hypoplasia of the tibia. Figure 12—Partial aplasia of the tibia. Figure 13—Total aplasia of the tibia.*

**Thumb type**—This is the mildest degree of dysmelia. Only the first ray of the hand is affected. The two different manifestations are: first, triphalangism of the thumb, and second, hypoplasia of the thumb (Figs. 3 and 4).
**Big toe types**—Hypoplasia and aplasia of the big toe does not occur as an isolated malformation in our material but only together with more severe defects of the lower limb. Isolated triphalangism and duplication of the big toe occur in dysmelia (Fig. 5).

**Radial type**—The radius and the radial ray of the hand are involved. The ulna is spared. The different degrees of severity are manifested by 1) hypoplasia of the radius; 2) hypoplasia of the radius with radio-ulnar synostosis; 3) partial aplasia of the radius; 4) partial aplasia of the radius with radio-ulnar synostosis; and 5) total aplasia of the radius (Figs. 6 to 10).

**Tibial type**—The tibia and the tibial ray of the foot are involved. The fibula is spared. The different degrees of severity are: 1) hypoplasia of the tibia; 2) partial aplasia of the tibia; and 3) total aplasia of the tibia (Figs. 11 to 13). Tibio-fibular synostosis does not occur in dysmelia.

**Axial form of ectromelia**—The distal as well as the proximal part of the limb is affected. The disturbance of development involves the radius, the radial ray of the hand and the humerus, or the tibia, the tibial ray of the foot and the femur. The ulna and the fibula are spared. The malformed radius or tibia is hypoplastic, partly aplastic or totally aplastic. Partial aplasia in the axial form is unique in that the remnants of the radius are regularly fused with the ulna; it therefore always presents as radio-ulnar synostosis. The remnant of the tibia does not show this tendency towards synostosis.

The different degrees of reduction of the humerus or the femur lead to the following types.

**Upper limb**—1) Long axial type of the arm showing hypoplasia or partial aplasia of the humerus with partial aplasia of the radius and radio-ulnar synostosis (Fig. 14) or with total aplasia of the radius (Fig. 15). 2) Intermediate axial type of the arm showing subtotal aplasia of the humerus with partial aplasia of the radius and radio-ulnar synostosis (Fig. 16) or with total aplasia of the radius (Fig. 17). 3) Short axial type of the arm showing total aplasia of the humerus with partial aplasia of the radius and radio-ulnar synostosis (Fig. 18) or with total aplasia of the radius (Fig. 19).

**Lower limb**—1) Long axial type of the leg showing hypoplasia or partial aplasia of the femur with partial aplasia of the tibia (Fig. 20) or with total aplasia of the tibia (Fig. 21).
Figure 20—Long axial type of the leg showing hypoplasia or partial aplasia of the femur with partial aplasia of the tibia. Figure 21—Long axial type with total aplasia of the femur. Figure 22—Intermediate axial type of the leg showing subtotal aplasia of the femur with partial aplasia of the tibia. Figure 23—Intermediate axial type with total aplasia of the femur. Figure 24—Short axial type of the leg showing total aplasia of the femur with partial aplasia of the tibia. Figure 25—Short axial type with total aplasia of the tibia.

Figure 26—Long proximal type showing hypoplasia of the femur, coxa vara or partial aplasia of the femur without impairment of the distal part of the limb. Figure 27—Intermediate proximal type showing subtotal aplasia of the femur without impairment of the distal part of the limb. Figure 28—Short proximal type showing total aplasia of the femur without impairment of the distal part of the limb.

Figure 29—Phocomelia of the arm. Figure 30—Phocomelia of the leg. Figure 31—Amelia of the arm. Figure 32—Amelia of the leg.
2) Intermediate axial type of the leg showing subtotal aplasia of the femur with partial aplasia of the tibia (Fig. 22) or with total aplasia of the tibia (Fig. 23). 3) Short axial type of the leg showing total aplasia of the femur with partial aplasia of the tibia (Fig. 24) or with total aplasia of the tibia (Fig. 25).

**Proximal form of ectromelia**—This form of ectromelia can be found in the lower limb only. It has no parallel in the upper limb. Only the proximal part of the limb, the femur, is involved. The femur can display all different degrees of reduction, leading to a subdivision into the following types: 1) Long proximal type showing hypoplasia of the femur, coxa vara or partial aplasia of the femur without impairment of the distal part of the limb (Fig. 26). 2) Intermediate proximal type showing subtotal aplasia of the femur without impairment of the distal part of the limb (Fig. 27). 3) Short proximal type showing total aplasia of the femur without impairment of the distal part of the limb (Fig. 28).

**Phocomelia**—The limb deficiency is so severe that humerus, radius and ulna or femur, tibia and fibula are absent. The remainder of the extremity consists of a malformed hand formed by one, two or three ulnar finger rays and ulnar parts of the carpus or of a similarly more or less defective foot. Both are directly attached to a hypoplastic shoulder girdle or to a misshapen pelvis (Figs. 29 and 30).

**Amelia**—Amelia is the most severe form of dysmelia. The arm or the leg is totally missing. The shoulder girdle is hypoplastic and the pelvis is deformed in a box-like shape (Figs. 31 and 32).

### THE PATTERN OF MALFORMATION IN DYSMELIA

On consideration of this classification it becomes evident that the limb deficiencies of dysmelia follow a specific pattern. The extremities are not mutilated in an irregular manner, but the process obeys a number of principles. Their understanding can be achieved only by the systematic analysis of a large number of individual malformations of all different degrees of severity.

The following main principles are the framework of the pattern of dysmelia. 1) A diminution of skeletal material is common to all malformations of this group. 2) The remaining skeletal elements show a disturbance of development and maturation.

### DIMINUTION OF SKELETAL MATERIAL

This obeys certain rules, as follows.

**Reduction tendencies of individual bones**—The individual bones show a variation in the degree of reduction ranging from hypoplasia and minor defects to total aplasia. If cases of the same

![Fig. 33](image)

Reduction tendency of the thumb (as shown by a series of cases of distal ectromelia).

type are arranged according to the size of the defect zone a “reduction tendency” can be shown. The reduction of the skeletal material of the individual bone follows a certain direction and sequence.

**Thumb**—In the mildest cases all tubular bones of the thumb and the first metacarpal are hypoplastic—that is, diminished in length and width—but their characteristic appearance is preserved. The reduction of skeletal material begins at the base of the first metacarpal in
FIG. 34
Reduction tendency of the radius (as shown by a series of cases of distal ectromelia).

FIG. 35
Reduction tendency of the tibia (as shown by a series of cases of distal ectromelia).

FIG. 36
Reduction tendency of the humerus (as shown by a series of cases of axial ectromelia).
the more severe cases. With increasing severity the shaft becomes aplastic. The last remnant of the first metacarpal is its head; then the proximal phalanx becomes defective. The terminal phalanx is preserved until in total aplasia all bones of the thumb have disappeared. This sequence and the reduction tendency of the thumb directed from proximal to distal is shown in Figure 33.

Big toe and first metatarsal—This follows the same trend.

Radius and tibia—The least degree of malformation of the radius or the tibia is represented by hypoplasia. With increasing severity a defect is seen in the distal part of the metaphysis. With more severe deformities this extends in a proximal direction. The head disappears last, before the radius or tibia becomes totally aplastic. The reduction tendency of these two bones is therefore the same and is directed from distal to proximal, as shown in Figures 34 and 35.

Humerus and femur—In the mildest cases of the axial form of ectromelia the humerus and the femur are hypoplastic. More pronounced cases show a defect of bone at the proximal end.
In the humerus this defect is situated just distal to the head and in the femur it is found in the region of the neck and the trochanter. In more severe cases increasingly larger portions of the shaft are aplastic. Relatively small defects affect the proximal third. Larger ones involve the proximal and the middle third of the shaft. In cases of subtotal aplasia the distal epiphysis is the last part to represent the humerus or the femur until it also disappears in total aplasia. This sequence of different degrees shows the reduction tendency of the humerus and the femur to be the same and directed from proximal to distal (Figs. 36 to 38).

Reduction of the limb as a whole—A certain tendency of reduction is not only observed in the individual bones but also in the extremity as a whole. This tendency is illustrated by the teratological sequence (Figs. 1 and 2). With increasing severity more parts of the limb become involved following a distinct sequence.

In the upper limb mild manifestations of the deformity are restricted to the radial ray of the hand. Then follows, with increasing severity, involvement of the radius and only after the radius is either completely absent or its remnants have fused with the ulna is the humerus affected.

In the lower extremity there is more variation. In mild cases only the tibia and the tibial ray are impaired, but in contrast to the sequence in the upper extremity, at each stage of reduction of the tibia the femur can be involved. The tibia need not be totally absent and its remnants need not be fused before the femur shows signs of reduction. Furthermore a sequence of isolated malformations of the femur is observed, in which the distal part of the limb is unimpaired. Corresponding isolated defects of the humerus have neither been found in our material nor described in the literature with any degree of certainty.

With the reduction of the limb mass there is coincidental impairment of the shoulder and pelvic girdles. Its degree depends on the severity of the humeral or femoral defect and it is most pronounced in phocomelia and amelia.

The reduction of the hand and fingers is also strictly dependent on the severity of the defect of the skeleton of the arm. The number of remaining fingers decreases as the defect of the skeleton of the arm increases. Whereas in radial hypoplasia all fingers may be present, their number is reduced to four or even three in the axial types and very often to one in phocomelia (Fig. 39). The reduction of the hand starts at the thumb and progresses from the radial to the ulnar side, so that with increasing severity of the arm deficiency the index, middle and ring fingers are absent.

In principle the same sequence is followed in the reduction of the foot in dysmelia of the lower extremity, but the interdependence between the leg deformity and the defects in the foot is much less defined and a nearly normal foot may be found in severe malformations of the lower extremity (Fig. 40).

If the foot is involved, reduction progresses from the tibial to the fibular rays. Isolated malformations of the tibial ray corresponding to hypoplasia and triphalangism of the radial ray seem to be extremely rare in dysmelia.

The axis of malformation in dysmelia—In the forearm and hand the deformity always affects the radial part of the limb, namely the radius and the radial fingers. Involvement of the humerus as seen in the axial types is never an isolated defect, but is always combined with defects of the radius and the radial rays of the hand. This is another characteristic feature of the pattern of dysmelia: the humerus, radius and radial ray of the hand are combined in an axis of malformation within the skeleton of the upper extremity.

The same combination can also be seen in the lower extremity, where the axis is formed by the femur, the tibia and the tibial ray of the foot. The ulna and the fibula are, however, spared until the deformity reaches a certain degree of severity. In the short axial types the ulna or the fibula is the only long bone of the extremity still existing. They are not both subjected to a reduction tendency, but they are either present as a whole or completely absent when the reduction reaches the stage of phocomelia. The ulna and fibula may, however, show secondary changes due to the absence or deformity of their parallel bone.
Interdependence between the severity of the malformation of the arm and the reduction of the hand and the number of fingers. (Big numbers in the blocks giving the average number of fingers in our cases, small numbers showing the range.)

The number of toes does not reflect the severity of the reduction of the lower limb. Duplication of the tibial ray is almost as frequent as hypoplasia and aplasia. (Big numbers in the blocks giving the average number of toes in our cases, small numbers showing the range. There were not enough cases of phocomelia of the lower extremities in our material to allow inclusion in this Figure.)
**Fusion of adjacent bones**—Another main feature of dysmelia is the fusion of neighbouring bones. Bony fusion in this context does not imply excess bone formation because the skeletal elements undergoing fusion are always hypoplastic or partially aplastic.

By fusion these remnants lose their independence as skeletal elements. Fusion occurs in parallel bones (carpals, tarsals, metacarpals, metatarsals, radius and ulna) (Fig. 41) or in bones arranged longitudinally (phalanges, humerus and ulna) (Fig. 42). In the lower extremity the tendency towards synostosis seems to be limited to the bones of the foot.
DISTURBANCE OF MATURATION OF REMAINING SKELETAL ELEMENTS

The disturbance of skeletal maturation of bones not directly involved in the defect is shown in a retardation of cartilage ossification. This is most obvious in parts of the skeleton in close proximity to the defect. Occasionally in these areas bony structures appear, which were not present in early childhood. This indicates that there have been cartilaginous areas close to the defect which have undergone a very delayed ossification. This process is most marked at the very end of the bone where the adjacent metaphysis is affected by the defect: in the humerus and in the femur delayed ossification can often be expected in the region of the head and neck, whereas in the radius and the tibia it can occur at the very distal end of the defect zone. Furthermore, whole skeletal elements, very often of an irregular and uncharacteristic shape, can appear during childhood, which in the very early years or months have been totally invisible on radiographs. Histological investigations (Willert and Blauth 1966) have demonstrated that these cartilage bodies capable of late ossification represent persistent epiphyses or parts of these.

Skeletal maturation is not only impaired and delayed in the neighbourhood of the defect zone but also in quite distant regions of the affected limbs. Ossification centres far away from the part directly involved tend to ossify in a delayed manner (Fig. 43).

RELATIONSHIP OF THE MALFORMED EXTREMITIES TO EACH OTHER

All our cases of dysmelia of the lower extremities are bilateral. All dysmelias of the upper extremities except fourteen radial types mainly of mild degree are also bilateral. Most cases of dysmelia are not only bilateral, but also symmetrical in manifestation. If one side is more severely affected than the other, the difference remains within certain limits. For instance, a combination of a radial hypoplasia on one side and a short axial type on the other side does not occur in our material (Figs. 44 and 45).

Most patients with dysmelia of the upper extremity (219 of 287 cases) have normal lower limbs, even if the arms are phocomelic or amelic. None of the patients with dysmelia of the

THE JOURNAL OF BONE AND JOINT SURGERY
lower extremity (sixty-eight cases), however, had normal upper extremities. Practically all possible combinations of types of the upper and lower extremities have been observed (Fig. 46).

These relationships between the extremities of either side and the upper and lower extremities apply only to our material, which was collected during the period when the effects of thalidomide were being seen. We gained the impression that they are also found in the hereditary cases. Gross exceptions may, however, be noted in the sporadic cases of dysmelia,

where there may be isolated malformation of the lower limbs and where unilateral cases of phocomelia and amelia have been reported.

**SUMMARY**

A classification of a group of malformations of the extremities is given and an underlying common pattern is developed from a survey of 693 deformed limbs. It is characterised by a certain reduction tendency of the affected bones and the malformed extremity, an axis of malformation and an interdependence between the proximal and peripheral parts of the
<table>
<thead>
<tr>
<th>Normal</th>
<th>Normal</th>
</tr>
</thead>
<tbody>
<tr>
<td>Big Toe Type</td>
<td>Big Toe Type</td>
</tr>
<tr>
<td>Hypoplasia of the Tibia</td>
<td>Hypoplasia of the Tibia</td>
</tr>
<tr>
<td>Partial Aplasia of the Tibia</td>
<td>Partial Aplasia of the Tibia</td>
</tr>
<tr>
<td>Total Aplasia of the Tibia</td>
<td>Total Aplasia of the Tibia</td>
</tr>
<tr>
<td>Long Axial Type</td>
<td>Long Axial Type</td>
</tr>
<tr>
<td>Long Proximal Type</td>
<td>Long Proximal Type</td>
</tr>
<tr>
<td>Intermediate Axial Type</td>
<td>Intermediate Axial Type</td>
</tr>
<tr>
<td>Intermediate Proximal Type</td>
<td>Intermediate Proximal Type</td>
</tr>
<tr>
<td>Short Axial Type</td>
<td>Short Axial Type</td>
</tr>
<tr>
<td>Short Proximal Type</td>
<td>Short Proximal Type</td>
</tr>
<tr>
<td>Phocomelia</td>
<td>Phocomelia</td>
</tr>
<tr>
<td>Amelia</td>
<td>Amelia</td>
</tr>
</tbody>
</table>

**FIG. 45**
Combinations of different types of dysmelia of the right and left legs of nineteen patients which had asymmetrical involvement of the lower extremities. Most (forty-nine cases), not represented in this Figure, have symmetrical involvement of the lower extremities.
DYSMELIA

Combinations of different types of dysmelia in 136 pairs of upper and lower limbs from sixty-eight cases with dysmelia of the upper and lower extremities. The degree of severity of the deficiency of the arms and legs is not related to each other and practically all possible combinations occur. (On some of the bars the number of cases they represent is given to indicate the scale.)
deformed limbs. The group, called dysmelia, has a common morphology, but morphologically identical types have been seen caused by thalidomide and as hereditary or sporadic cases. An attempt has been made not only to name and classify these deformities but also to clarify the underlying principles of their morphology. This will enable the teratologist to see the pattern of these malformations in comparison with that of normal development of the limbs and of experimentally induced limb defects.

We wish to thank Professor R. B. Duthie, Mr B. T. O'Connor and Mr W. S. Steel who gave us much helpful advice in the preparation of this paper. Dr P. J. R. Nichols has kindly allowed us to include his patients from Mary Marlborough Lodge. We are very grateful to Mr R. Emanuel and the staff of the Photographic Department of the Nuffield Orthopaedic Centre for reproducing the illustrations and tables.

REFERENCES


