

THE CARTILAGE SKELETON OF THE FOETUS AS MATRIX FOR SKELETAL ANOMALIES¹

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The aim of this paper is to point out certain normal anatomical properties of the foetal cartilage skeleton which appear to me to lead to an easy understanding of the manifestations of certain skeletal anomalies and of the pathologico-anatomical pictures of certain skeletal diseases.

In my thesis "Cartilage bones and epiphysis problem" there is a description of the development of the cartilaginous skeleton in the foetus, and of the particular characteristics which are significant in this connection. Here only certain main points of the investigation will be discussed.

The cartilaginous skeleton of the foetus appears to have 2 types of surface; one is characterised by a relatively loose connection with the periskeletal tissue, the other by a very firm connection. The distribution of the 2 types of surface is characteristic for each skeletal part, and can be demonstrated in reconstructed specimens as soon as a part is sufficiently differentiated for the surface to be everywhere distinguished.

Figures 1-5 show examples of such reconstructed specimens, magnified 33 times. The sections are 10 microns thick, the cardboard mounts are 0.9 mms. thick, and the layer of glue between the single cardboard sheets is estimated as 0.1 mm. thick. It has thus been necessary to draw the outline of every third sec-

¹ Read at the Scandinavian Orthopedic Associations meeting Stockholm 27. June 1947.

tion. The dots show the extent of the surface-type with firm connection with the periskeletal tissue, and the hatching the extent of the surface-type with loose connection. The $\begin{smallmatrix} 0000 \\ 0000 \end{smallmatrix}$ indicate the area with perichondral ossification. The boundaries between the surfaces of loose and firm connection are drawn with thick lines, and in Fig. 1 the boundaries between ossifica-

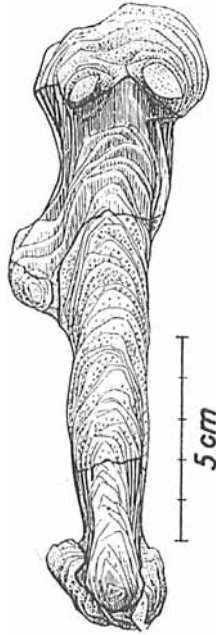


Fig. 1.

Reconstruction of the left femur from an $18\frac{1}{2}$ -day rat foetus, seen from the radial side. Dotted areas indicate cartilage surface with firm connection with the periskeletal tissue. Hatched areas indicate surface with loose connection with the periskeletal tissue $\begin{smallmatrix} 000 \\ 000 \end{smallmatrix}$ indicate the extent of perichondral ossification.

The boundaries for the different areas are drawn in.

tions and cartilage are similarly drawn. Fig. 1 shows a reconstruction of the Right humerus of a rat foetus of $18\frac{1}{2}$ days. Figs. 2-5 are all from reconstructions of a 25 mm. human foetus: fig. 2 shows the Right radius and ulna, fig. 3 the scapular and the acromial end of the clavicle, fig. 4 the femur, and fig. 5 the

Right hip bone with the 5th lumbar vertebra, 5 sacral vertebrae, and 4 coccygeal vertebrae.

It can be seen easily from the reconstructions that there is a tendency for the division between the 2 types of surface to correspond with the final epi-diaphyseal boundary. Therefore I have introduced new definitions for the terms diaphysis and epiphysis since any area of the skeleton whose surface has a

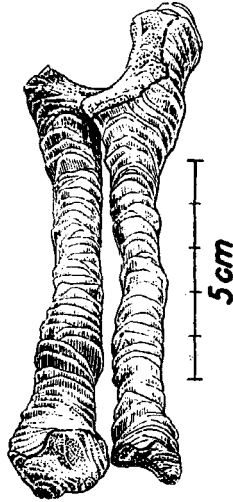


Fig. 2.

Reconstruction of the right radius and ulna from a human foetus of ca. 25 mm., seen from the ventral side. The dotted areas indicate cartilage surface with firm connection with the periskeletal tissue. Hatched areas indicate surface with loose connection with the periskeletal tissue.

The boundaries between the 2 surface areas are drawn in.

loose connection with the periskeletal tissue is a diaphysis, and any area whose surface has a firm connection is an epiphysis. The logical terms for the types of surface are therefore diaphyseal and epiphyseal.

The diaphyseal surface has 2 further characteristics: its muscle insertions, when present, are indirect via the periskeletal tissue; and perichondral ossification may occur when ossification takes place.

The epiphyseal surface on the other hand has the following characteristics, in addition to its firm connection with the periskeletal tissue: it is either a joint surface, or it gives direct attachment to muscles, tendons, ligaments or joint capsule; and when ossification takes place perichondral ossification never occurs.

However, the most interesting point is that these 2 types of

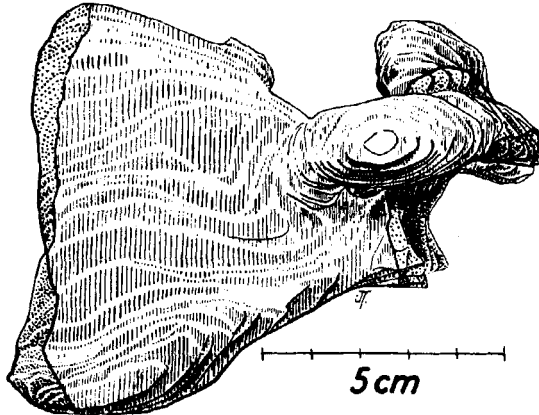


Fig. 3.

Reconstruction of the right scapula and the acromial end of the clavicle from a human foetus of ca. 25 mm., seen from the dorsal side.

Markings as in Fig. 2.

surface are found in vertebrates with permanent cartilage skeletons, and on the permanent cartilage of mammals.

The surface-types are in fact well-defined anatomical conceptions which are unrelated to ossification.

Since the conceptions, diaphysis and epiphysis, are defined according to the fixed arrangement of the surface-types in individual parts of the skeleton, they are independent of ossification and are definite morphogenetic distinctions at all stages of ontogenesis, and in all kinds of vertebrates.

The conceptions of epiphysis and diaphysis as hitherto accepted are purely descriptive distinctions which can only be applied to ossifying skeletal parts, and of which the boundaries change in the course of ontogenesis.

The histological pictures of the 2 types of surface are seen in figures 6-9. Fig. 6 shows a cross-section of the humerus at the shoulder-joint in an 18-day rat foetus. Above can be seen the sharp division between the cartilage and the periskeletal tissue which is here very thick, and correspondingly the connection

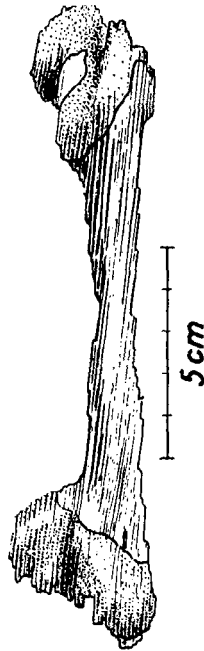


Fig. 4.

Reconstruction of the right femur from a human foetus of ca. 25 mm., seen from the flexor side. Markings as in Fig. 2.

between cartilage and tissue is relatively loose; the muscle is attached indirectly via the periskeletal tissue: here, therefore the surface is of the diaphyseal type. On the left the periskeletal tissue continues into the outermost layer of the joint surface. On the right is seen an intimate relation between cartilage and periskeletal tissue: here, therefore the surface is epiphyseal. Deep to the biceps tendon there is again diaphyseal surface, and on the left of it is seen a projection which is part of the lesser tubercle, and here there is firm connection between cartilage and

periskeletal tissue, and direct muscle attachment. Then comes the joint surface.

Fig. 7 shows clearly that the joint surface can be described as epiphyseal. Part of the femoral head of an 18½-day rat foetus is shown in high magnification. Below on the right can be seen the sharp demarcation between cartilage and pariskeletal tissue,

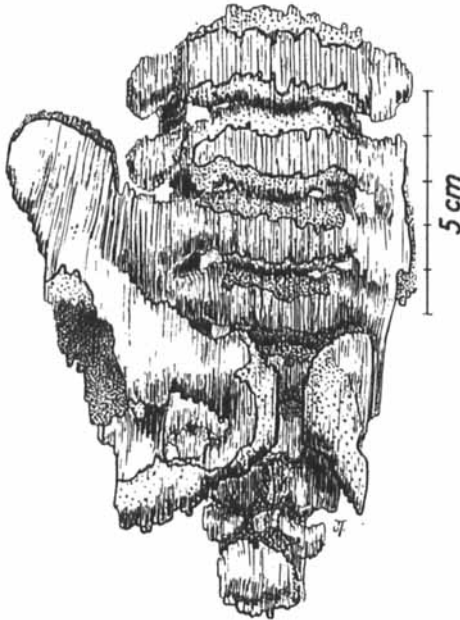


Fig. 5.

Reconstruction of the right hip bone, sacrum, coccyx and 5th lumbar vertebrae from a human foetus of ca. 25 mm. seen from the ventral side. Markings as in Fig. 2

and also how this passes into a cartilage tissue of a slightly different structure from that further inside the head, though with a quite smooth transition. I interpret this in the following way: the perichondrium on the joint surfaces is transformed into cartilage and forms the substratum for the permanent joint-cartilage. Here, therefore, the connection is particularly firm, and the surface can be termed epiphyseal. Fig. 8 shows a longitudinal section of the femur from an 18½-day rat foetus.

The ossification zone is seen below; medially there is diaphyseal surface right up to the joint surface and again in the fossa between the head and the greater trochanter; then there is epiphyseal surface on the outer half of the trochanter, and again diaphyseal surface along the lateral side of the femur.

Fig. 9 shows the same femur as in fig. 8 but 100 microns

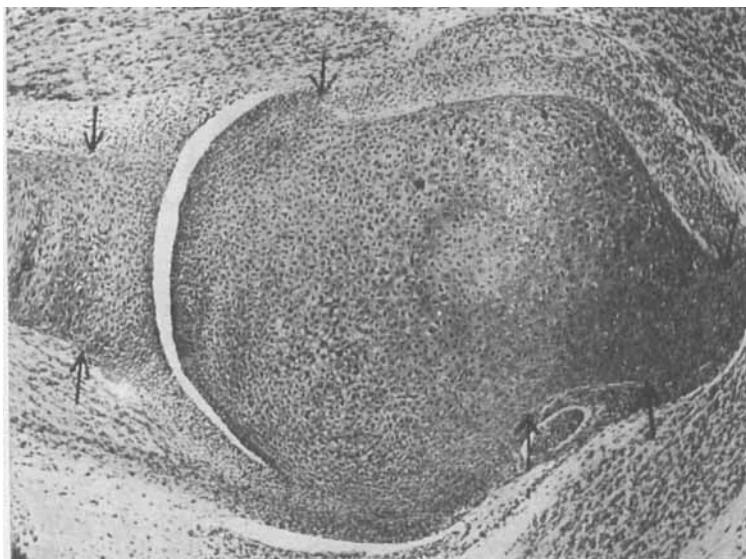


Fig. 6.

Section through the left humerus, shoulder joint and a small part of the scapula, from an 18-day rat foetus. Section No. 45-12 of the series of transverse sections. Magnified 73 times; stained with Haemotoxylin-Eosin. The section is 10 μ thick. The arrows point to the zones of transition between the cartilage surfaces having respectively loose and firm connection with the periskeletal tissues. Concerning the surface of the joint see Fig. 7 and the text of the paper.

away from the section shown there. There is the same arrangement and in addition the lesser trochanter with its epiphyseal surface is seen.

The opiphyses can be divided into 2 groups; those which form part of a joint, and those which serve only as muscle inser-

tions. The first group I term arthrophyse, the second apophyses.

A skeletal part consists therefore normally of a diaphysis and epiphyses. The epiphyses may be simple arthrophyse, or simple apophyses, or a combination of both.

Everything which is connected with a diaphysis or with an epiphysis, or with both, keeps that connection unchanged

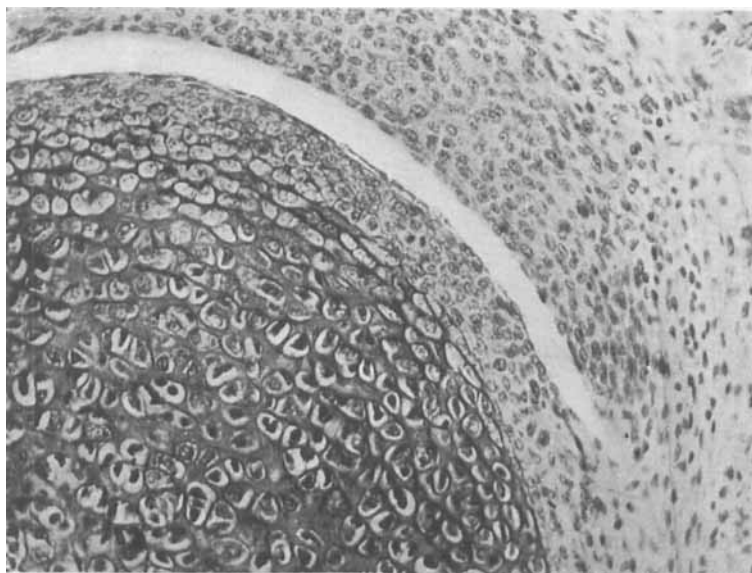


Fig. 7.

Detail of the left femoral head and hip joint from an 18½ day rat foetus. Section No. 67-4 of the series of sagittal sections. Magnified 290 times: stained with Haematoxylin-Eosin. The section is 10 μ thick. One sees how the periskeletal tissue passes into the cartilage, which gradually becomes indistinguishable from the skeletal cartilage. The periskeletal tissue is converted into cartilage on the joint surface and forms the substratum for the future joint cartilage.

throughout the course of ontogenesis. Transition from epiphysis to diaphysis never occurs. The epi-diaphyseal boundaries are fixed. The epiphyses and diaphyses are relatively independent of one another, in so far as they have different growth energies; they change their relative sizes, but their relation to their sur-

roundings remains unchanged throughout ontogenesis. This description alters a number of established assumptions, but the new conception is based on anatomical facts. Further arguments are found in my thesis.

The chief difference between the hitherto accepted definitions of epiphysis and diaphysis, and those which are set out here, is well illustrated by Fig. 1.



Fig. 8.

Section through the left femur and hip joint from an 18½ day rat foetus. Section No. 115-1 of the series of frontal sections. Magnified 43 times: stained with Haemotoxylin-Eosin. The section is 10 μ thick. The arrows point to the zones of transition between the cartilage surfaces having loose and firm connection respectively with the periskeletal tissue. The distance between the sections shown in Figs. 8 and 9 is 100 μ .

This figure represents—as the option states—the reconstruction of a humerus from an 18½-day rat foetus. According to the older definition of epiphysis and diaphysis, the ossified area (marked $\begin{smallmatrix} 0000 \\ 0000 \end{smallmatrix}$) is diaphysis, while all the cartilaginous area belongs to the epiphyses. But a distinction based on the type of surface shows a boundary which corresponds with the final epi-diaphyseal junction. In the figure this boundary is represented by the line drawn between the hatched and dotted areas.

The figure shows, therefore, that, according to the new definitions of epiphysis and diaphysis, part of the diaphysis is ossified and the rest of it is still cartilage, just as the epiphyses are cartilage.

It follows, at any rate indirectly, from what has been said, that ossification of the skeleton which is preformed in cartilage is a relatively subordinate process, since it must follow the

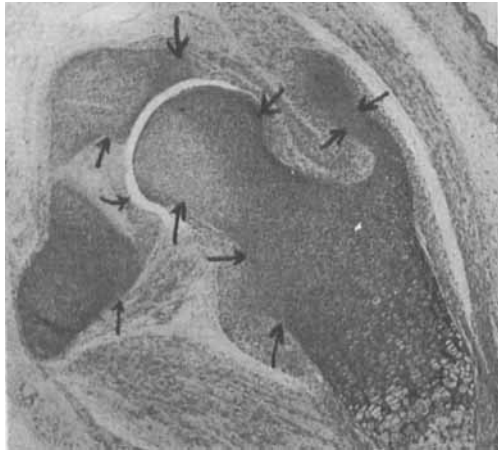


Fig. 9.

Section through the left femur and hip joint from an 18½ day rat foetus. Section No. 117-3. Magnified 43 times: stained with Haematoxylin-Eosin. The section is 10 μ thick. Marking as in Fig. 8; here the lesser trochanter is also seen, as well as the defect at the bottom of the acetabulum.

The distance between the sections shown in Figs. 8 and 9 is 100 μ .

lines determined by the anatomical arrangement and growth of the cartilage skeleton.

The normal growth of a skeleton preformed in cartilage depends on the growth of the cartilage skeleton. This is obvious for the epiphysis, where a layer of cartilage persists over the surface until the end of the growth period. In the diaphysis longitudinal growth also depends on the growth of the cartilage, but growth in thickness is only indirectly dependent since it

depends on the normal circumferential growth of the epiphyses and of the epiphyseal cartilage plates.

Thus the cartilaginous skeleton is the primary factor in the normal development of any part which is preformed in cartilage.

With the exception of the true diseases of ossification, e.g. osteogenesis imperfecta, rickets, and osteomalacia, it is the cartilaginous skeleton which forms the matrix for a large number of skeletal anomalies and diseases—in the sense only that it is the site of the abnormal development; nothing is said here about the cause. I quote here only a few examples, as I omit altogether the enormous variety of skeletal changes which are found in severe deformities.

An example of the milder skeletal anomalies is shown in Fig. 5, which shows, amongst other things, the os sacrum from a 25 mm. foetus. On the right side there is lumbarisation of the first sacral vertebra, and sacralisation of the first coccygeal vertebra.

A particularly interesting example of congenital defects is congenital defect of the femur, because it has not hitherto been explained why the femur disintegrates in just those parts which later get separate ossification centres. Already in the 1890's *Hlawáček* considered the femoral deficiency to result from disintegration of the foetal epiphyses, but this view won no support because it was argued that the defect affected the cartilaginous femur at a stage when one could not at all speak of epiphyses.

However, in the light of my investigations on the cartilage skeleton it can be claimed that the cartilaginous femur already consists of a diaphysis and epiphyses, of which the proximal is made up of the capital arthrophysis, and the greater and lesser trochanteric apophyses. It is, therefore, not particularly puzzling that a defect can exclusively affect the diaphysis in such a way that its connection with these areas is lost, and that they in their turn lose their mutual connections. However, we have still no explanation why such defects occur. *Nilssonne* thinks that the defects result from a nutritional disturbance in connection with the vascular channels in the cartilage. Personal-

ly, I believe that anyway in those cases in which there is total absence of the hip-joint—that is to say, absence of the acetabulum and of the capital arthrophysis—one must consider that the defect arises in the 5th-7th weeks, at a time, in fact, considerably before the vascular channels are formed in the cartilage.

In polydactyly *Danforth* has shown, in his recently published work on polydactyly in cats, that the primary deformity is laid down in supernumerary finger or toe buds so that the cartilage *anlage* determines the degree and type of polydactyly.

Foetal chondrodystrophy is a system disease whose most marked characteristic is an abnormal cartilaginous skeleton. It is here quite clear that the connection between the epiphyses and diaphyses is abnormal. The epiphyses project over the edge of the diaphyses in a manner reminiscent of the epiphyseal development of frogs and other anure amphibians. I do not, however, possess any personal material from this disease, though, I believe, in opposition to *Ake Wilton*, that it is a primary disease of cartilage, and has no connection with rickets.

In multiple cartilaginous exostoses the characteristic picture is seen in the cartilage skeleton: where the exostoses develop the normal diaphyseal surface is missing and the exostoses, which occur at the end of the diaphyses, have direct connection with the epiphyses in such a way that they maintain their positions there during growth.

Coxa vara congenita must also be attributed to a defect in the normal diaphyseal surface, as I have already described in a paper delivered before the Dansk Kirurgisk Selskab in February, 1946, indicating that the defect appears in the 2nd month of foetal life.

These fragmentary remarks are intended to stress that the study of the cartilage skeleton's normal and pathological development is of considerable interest for the understanding of the clinical picture of some orthopedic diseases, although it cannot at present contribute much to an improvement in their treatment.

SUMMARY

On the basis of his findings published in his treatise, *Cartilage Bones and Epiphysis Problem*, the author seeks an explanation of the pathologico-anatomical origins of skeletal anomalies, such as congenital defect of femur and polydactyly, and of skeletal diseases, such as foetal chondrodystrophy and multiple cartilaginous exostoses.

ZUSAMMENFASSUNG

Auf Grund seiner Funde, die in seiner Abhandlung *Cartilage Bones and Epiphysis Problem* veröffentlicht sind, sucht der Verfasser eine Erklärung des pathologisch-anatomischen Ursprunges der Unregelmässigkeiten des Skelettes, so wie angeborene Mängel im Schenkelbein und Polydactylie, und des Ursprunges der Krankheiten des Skelettes, so wie Chondrodystrophia fetalis und multiple cartilaginäre Exostose.

RÉSUMÉ

Se basant sur les résultats de ses recherches publiés dans son article sur le problème cartilagino-osseux épiphysain, l'auteur cherche une explication anatomo-pathologique des anomalies du squelette. Comme par exemple l'absence congénitale du femur et les polydactylies ainsi que des maladies ossenses. — Chondrodystrophie foetale et exostoses Cartilagineuses multiples.

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