8. DYSPLASIA EPIPHYSIALIS PUNCTATA

Synonyms—Stippled epiphyses, Chondrodystrophia calcificans congenita (Hünermann)

The chief characteristic of this rare disorder of infancy is the presence of a number of discrete centres of unusual density in many cartilaginous epiphyses and apophyses. Attention was first called to the condition by this author in 1927, two cases being reported briefly. In 1935 he classified it under the title "epiphyseal dysplasia punctularis," this being one of two which, at his request, were suggested by the late Sir Frederick Still. The alternative adjective—punctata, which is no less descriptive and was also suggested independently by Dr Parkes Weber (see Bateman 1936), seems to be preferred in this country and it has therefore been adopted. Details of eight further British cases are now available, all but one of which have been published by various authors. Other cases have been reported under the title of "stippled epiphyses" but the published radiographs do not seem to justify their inclusion in this group. Further search has disclosed an undoubtedly case reported by Conradi in 1914 under the title of "chondrodystrophia foetalis hypoplastica." A few other cases have been reported in the literature of other countries, the title favoured being "chondrodystrophia calcificans congenita" (Hünermann 1931). In all, we have some sixteen cases for study.

Hereditary and familial influences—There is no evidence of hereditary influence and seldom of familial influence in the incidence of this condition. Sex—Females are affected more frequently than males in the proportion of more than two to one.

Age—Fourteen cases were discovered within the first nine months, and some within the first few days of post-natal life. Only two cases were over two years of age: one of these was alive at nine years. The dysplasia undoubtedly begins in foetal life.

Etiology—The cause of the condition is unknown.

Clinical signs—Dwarfing of the short limb type is usually, if not invariably, present. The proximal segments of the limbs are particularly short. Of two cases in which the changes were apparently confined to one lower limb, in one at the age of four weeks the affected limb was short; while in the other, though the legs were equal in length at sixteen months, there was one and a half inches of shortening at the age of nine years. Unfortunately full details are not available in either of these cases. The affected epiphyses are definitely enlarged. Contractures—Flexion of certain joints, with a varying degree of limitation of movement, was present in several cases; the hips, knees, and elbows being the joints particularly affected. In one knee the head of the tibia was subluxated. The wrists were held in a flexed position in one case; and there was ulnar deviation of both hands and rigidity of the wrists in another. In yet another case there was contracture of the fingers. In two cases the hands were described as being long as compared with the forearm; but in another the fingers were blunt, and inclined to the accoucheur position. The feet in one case were rigid although the tarsal bones were not stippled. In one case with involvement of a single leg the foot was valgoid and stiff. In two cases the limbs were said to be "spastic" but without further details, while in a third the reflexes were much exaggerated. Thickening of the skin is mentioned by some German authors. In Bateman's first case, the skin of the palms was deeply furrowed and adherent to the deeper tissues, particularly in the right hand which could not be opened completely. The head has shown no characteristic features, being variously described as normal, rather large, globular, suggestive of oxycephaly, bossed, and even microcephalic. The fontanelle is large. The nose in some was broad and the nostrils large. Bilateral congenital
cataract has been a conspicuous feature of the British cases, being found in six of the ten. Only in one of the cases reported in the literature of other countries is cataract mentioned. Intellect appears to be distinctly dulled, sometimes to the extent of mental deficiency. General weakness, failure to thrive, and in one case, cyanosis, were responsible for the patients being taken to hospital. Blood examinations have revealed nothing of interest.

Radiographic appearances—In radiographs the epiphyses generally are stippled, as if ossifying from many separate centres, the appearance being suggestive of that produced by flicking paint from a brush on to a clean surface. The spots vary in size, but most of them are minute and usually discrete. They also vary considerably in number, and are not always more numerous in older than in younger children. There is evidence that in some cases the spots may become gradually smaller and fewer in number (Hünermann 1931, Hassler and Schalloch 1940, and Jorup 1944). On the other hand they may show a tendency towards fusion, with the formation of a single, more normal, centre of ossification. Often they appear at an earlier date than that at which ossification normally begins in the epiphysis concerned; and they may appear too early by several years. For instance, multiple centres were seen at the upper end of the ulna in a number of cases, and in all these the olecranon epiphysis should not have been visible for some years. Abnormally early ossification, stippled in character, was also seen in the lower humeral epiphysis, the radial head, the floor of the acetabulum, the ischial tuberosity and the neck of the scapula. Occasionally the carpus, tarsus and patella also showed signs of premature ossification. Even though ossification in some epiphyses or in the carpus may proceed normally, without stippling, these centres may have appeared unusually early.

The epiphyses most frequently showing the typical stippled appearance are those of the upper and lower ends of the femur, upper end of the tibia, and upper end of the humerus. The lower end of the tibia, both ends of the fibula, the lower ends of the radius and ulna, and the bones of the hand, are much less frequently affected. This affection differs strikingly from bone dysplasias generally in so far as characteristic changes are often shown in the region of the elbow joint, multiple centres being found at the lower end of the humerus and in the radial head, as well as in the olecranon. In at least four cases the femoral condyles showed a curious appearance, the spots of ossification being arranged around the periphery in a curved line: in two of these the outer condyle only was outlined in this way, the inner showing just a few central spots. In a case with involvement of one lower limb, there was at sixteen months an irregular mottled centre for the lower femoral epiphysis with, in addition, a separate group of small discrete centres for the medial condyle: at nine years, this epiphysis and that for the adjacent tibial head, though both somewhat larger than the corresponding centres of the opposite leg, were approximately normal in outline and density.

In Lightwood's case (1930), more or less normal centres were present in the lower femoral epiphyses close to the metaphyses, with additional stippled centres nearer the articular surfaces of the condyles. The stippling at the ends of the long bones is inclined to be erratic, spots being sometimes seen where no part of an epiphysis should be found, and perhaps absent where ossification should have begun. It is often difficult to decide the correct allocation of the bony spots, particularly if there is contracture of the knee or elbow joints and the shadow of the proximal bone is foreshortened.

In at least two patients the proximal ends of the ribs were stippled, and this in spite of both being infants. In the same two patients the thyroid cartilage showed signs of ossification, and in one the hyoid was stippled. Apart from stippling in the acetabulum and ischium, already referred to, the pelvis, with one exception, was fairly normal in shape and appearance. Stippling has not been seen in the iliac crests. In two patients, aged four months and three weeks respectively, the symphysis showed a median dense vertical line of calcification, and in both wrists there was a single dense centre well to the inner side of the carpus. A similar curiously placed centre near the carpus was also seen in the first case reported by Bateman.
(1936), but in this case two unstippled carpal bones were visible—the capitate and hamate. Stippling of the vertebrae was apparent in several cases, and of the sacrum in four. In at least two cases, each vertebral body was ossifying by two separate centres, one in front of the other: one of these (Lightwood 1930) was examined histologically by Professor H. A. Harris (1933). In a case published by Hassler and Schallock (1940) only a single centre was present for each vertebral body, but stippling was seen in some of the intervertebral discs. These authors also reported calcification in the tracheal rings, in the skin, and even in synovial membrane.

The shafts of the femora and humeri, and occasionally of the tibiae, are decidedly short and thick, the ends being splayed to a marked degree with an irregular surface at the epiphyseal line. At the upper ends of the femur and humerus the enlarged metaphysis often terminates in an oblique surface of considerable extent, being bevelled off on the inner side. In such cases it is difficult to visualise the cartilaginous epiphysis, and to identify the anatomical site of the dense spots correctly. At the upper end of the femur, for instance, the position of the spots sometimes suggests that the greater trochanter is ossifying before the head of the bone. The position of the femur in relation to the pelvis may suggest dislocation of the hip, this being recorded in at least three cases (Lightwood 1930, Hassler and Schallock 1940). In several, the upper end of the ulna seems to be unduly prominent, as if it were subluxated inwards: in others, the lower end of this bone may be bevelled off on the outer side.

The condition of the tarsus varies: ossification may be entirely by stippled centres; or the talus and calcaneus may be normal and only the heel apophysis show marked stippling long before ossification begins normally. In two cases this apophysis appeared in a lateral radiograph as a vertical line, a considerable distance behind the calcaneus. In one case, with changes confined to one leg, the front and back parts of the talus, and the medial cuneiform, were stippled; while the calcaneus, navicular, cuboid, and the greater part of the talus, were of normal density. Irregularity of the outline of the tarsal bones may be the only abnormality seen in the foot.

In one typical case at the age of three weeks (Hilliard 1943), the base of the skull was abnormally dense, and the shafts of some of the long bones, notably the tibiae and the metacarpals, showed triangular dense areas towards each extremity, while the talus and calcaneus, the only two tarsal bones ossified, showed a circular line, slightly more dense than the remainder of the bone, similar to that sometimes seen in osteopetrosis and in chronic poisoning by certain chemicals.

Progress—At present it is impossible to say what the ultimate condition of the epiphyses may be, because no late reports of a case showing generalised changes are available. In the monomelic case already referred to, which was re-examined at the age of nine years, there was clear evidence of fusion of the discrete centres of ossification which had been present at an earlier age, and of general improvement in the appearance of the epiphyses. However, the ankle joint showed gross abnormality in the contour of the bones, and a narrowed and irregular joint space suggestive of arthritis. The femoral head was enlarged and less convex than normal, and the femoral neck was short and wide.

Early death—Half the patients are known to have died, all but one before reaching the age of twelve months. The causes of death were infections involving the lungs or kidneys, and miliary tuberculosis; while in one case death occurred suddenly for no reason which was discovered.

Pathology—Harris (1933) reported patchy mucoid degeneration and cystic spaces in the cartilaginous epiphyses, particularly near the articular surfaces. In some places the areas of degeneration were invaded by blood vessels, and a core of fibrous tissue had formed. In the vertebral bodies which ossified from two centres, there was failure of the usual orientation of cartilage cells, and of normal calcification and ossification. Harris insists that the fundamental error is similar to that which he found in achondroplasia.
Dysplasia Epiphysialis Punctata

Hassler and Schallock (1940) made an exhaustive study of a child with this disorder who died a few days after birth. They found curious circumscribed, polymorphous deposits of chalk in the cartilage; and, near these, larger confluent areas of calcification. In other parts, new bone formation was replacing the chalky areas. They also found diminution of the zone of ossification between bone and cartilage at the epiphysial lines. In places this zone had disappeared completely.

Conradi (1914) illustrates star-like foci of calcification in the cartilage. In the child reported by Lund (1942) who died at the age of four months, the muscles were found to be replaced largely by tough fibrous tissue which apparently accounted for stiffness of the joints. In this case also, histological changes in the bones were said to resemble those of achondroplasia.

Diagnosis—This must depend on radiographic examination. Discrete stippling, as opposed to the mottling and epiphysial irregularity seen in dysplasia epiphysialis multiplex, and also sometimes in cretins, is quite distinctive. If a case could be followed for a few years, and the spots of ossification were given time to fuse, the distinction would probably become more difficult. In a doubtful case, the diagnosis is made easier if there is bilateral cataract.

I wish to express my thanks to friends and colleagues who have supplied me with details of their cases. Figs. 12 and 15 are reproduced by courtesy of the British Journal of Surgery.

References

Conradi, E. (1914): Jahrbuch für Kinderheilkunde und physische Erziehung, 80, 86.
Lightwood, R. C. (1930): Proceedings of the Royal Society of Medicine (Section for the study of Disease in Children, 22), 24, 564.
CASE 6—DYSPLASIA EPIPHYSIALIS PUNCTATA
(Fig. 12.) Child, aged one month, with congenital shortening of the right leg. The child died at age of nine months.

Fig. 12
Case 6. Right lower limb, showing typical stippling of most of the epiphyses and of the tarsal bones. Note that there are two separate groups of ossific centres for the femoral condyles. The tibial head is subluxated.
CASE 7—DYSPLASIA EPIPHYSIALIS PUNCTATA
(Figs. 13–16.) Female child, aged two and a half years. Parents normal. Failed to develop normally from birth. Mentally dull. Double congenital cataract. Marked bossing of skull. Fontanelle closed. Enlargement of epiphyses. Beading of ribs. Fingers have blunt, square extremities. Limitation of movement of knees and elbows. Wassermann negative. Thyroid administration gave no improvement. Gradually wasted, and died of pneumonia when aged three and a half years. (Under Dr Eric Pritchard.)

Fig. 13
Case 7. Right leg showing typical appearances: femoral shaft short, thick, and strong, with metaphyses splayed and the epiphyses stippled. Note the stippling in the ischial tuberosity as well as in the acetabular cup.

Fig. 14
Case 7. Pelvis and hips showing curious shape of the ilia, and, on each side, stippling of the acetabulum and upper extremity of the femur.
Case 7. Left upper limb showing stippled epiphyses, thick shafts of the long bones, premature ossification of the olecranon from many centres, and marked beveling on the inner side of the upper end of the humerus.

Case 7. Feet showing irregular shape of the tarsal bones, a little stippling in the heel, and premature ossification of the calcaneal apophyses.
CASE 8—DYSPLASIA EPIPHYSIALIS PUNCTATA
(Figs. 17–19.) Girl, aged four months. Very feeble. Large head; distended veins; fontanelles widely open; nose depressed. Limbs short, particularly the proximal segments. Hips, knees, and elbows flexed and cannot be extended fully. Feet "solid." Ulnar deviation of hands. Wrists stiff. Reflexes accentuated. Blood chemistry normal. Bilateral congenital cataract. Died during a feed, for no discoverable reason. (Under Dr W. G. Wylie. Case reported by Dr E. Lund, 1942, under another title.)

Case 8. Pelvis and femora, showing central linear ossification in the symphysis, premature stippled ossification of the ischial tuberosities and of the acetabular floor, short thick femora (partly due to fore-shortening) and general stippling of the shapeless upper extremities.

Case 8. Forearms showing the curious densely ossified spot to the inner side of each wrist joint. Stippling in the region of the elbow, including premature ossification in the radial head, can just be seen.
CASE 9—DYSPLASIA EPIPHYSIALIS PUNCTATA
(Figs. 20 and 21.) Male child, aged eleven months—only child of normal parents. Limbs short, particularly the proximal segments. Limitation of movement of hips. Double congenital cataract. Died within a few weeks of acute miliary tuberculosis. (Under Dr R. C. Lightwood who published the case in 1930.)

Fig. 20
Case 9. Left upper limb showing short, thick humerus with splayed metaphyses and bevelling on the inner side of the upper metaphysis, and subluxation inwards of the ulna at the elbow, in addition to stippling at the shoulder and elbow.

Fig. 21
Case 9. Pelvis and femora showing typically short, thick femora with bevelled upper extremities and stippling of epiphyses at both ends. Note the apparent dislocation of the hip joints and the premature ossification of the greater trochanters. The lower femoral epiphyses show centres close to the metaphyses, in addition to stippling confined to the outer condyles.