CHONDRO-OSTEO-DYSTROPHY

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Chondro-osteo-dystrophy is the name given by the author in 1928 to a disorder of the skeleton which manifested itself during the first three years of life. The child originally described had appeared to be normal at birth but at the age of five months the mother noticed that he had developed a kyphosis in the thoraco-lumbar area. At the age of eighteen months he was able to walk, but always appeared to take up a characteristic position at rest, the body being supported by the hands against the thighs, or, more frequently, by the hands on the flexed knees. In this position the thoraco-lumbar kyphosis was obvious and so was an apparent shortening of the neck. All the joints of the extremities were swollen and he developed knock-knees—appearances which led to the condition being diagnosed and treated as rickets. He looked and was bright and intelligent at three and a half years, when I took his first radiographs (Fig. 1).

Anti-rachitic treatment and thyroid medication were given over a long period but they met with no response. (So far no success has been achieved in any of the patients with any form of treatment.) A back support was fitted because of the kyphosis, which was thought to be due to tuberculous caries. Until the age of ten years he was able to run about even without this support, but it was noticed that he readily tired and took up his hand-knee attitude. This attitude he assumed also during sleep. From the age of ten years he steadily and progressively declined; the musculature became flaccid and atrophied as if in association with the general dystrophic condition of the skeleton. He did not grow, though his limbs appeared long in comparison with his trunk; his neck appeared to get shorter. Towards the end of his twelfth year of life his facial characters became grotesque and when he died at the age of fourteen, after being bedridden for nearly a year, he was but two feet ten inches tall and in weight just over two stone (28 lb., 13 kg.).

RADIOGRAPHIC EXAMINATION

The radiographic appearances of his skeleton at the time were unique. I had seen but two cases which bore any resemblance—a "forme fruste" chondrodysplasia observed by Silfverskiöld (1925) and a somewhat similar condition noted by Grudzinski (1928). Because the radiographs indicated defective and irregular ossification of the epiphyses and growing ends of the diaphyses, which appeared to have become manifest since birth, the term chondro-osteo-dystrophy was applied (after consultation with Sir Arthur Keith) and it was under this term that I demonstrated the radiographs at the Royal Society of Medicine in 1928. The distinctive radiographic features of the skeleton were illustrated and described (Brailsford 1929). At that time we had little serial radiographic evidence of the course of the condition and the purpose of this paper is to present such evidence gleaned from radiographs taken during sixteen or
more years of life in a number of similar cases (Figs. 2 to 21). Morquio described the clinical features of patients with this condition in 1929.

**Early radiographic features**—The chief radiographic features of chondro-osteodystrophy in the early stages are as follows. *Skull*—No appreciable change from the normal. *Spine*—The outlines of the bodies and processes are very irregular and ill-defined (Fig. 17). The bodies are flattened, some showing an anterior tongue with no ossification in the upper and lower epiphysial sites, some being slipper-shaped and of irregular size. The spinal curvature is altered; in the antero-posterior radiograph there is often a lateral displacement at the thoraco-lumbar junction. In the lateral, alteration in curvature may be seen in the cervico-thoracic and in the thoraco-lumbar areas (no epiphyses for the upper and lower plates have been seen even up to twenty-two years of age). In the cervico-thoracic area the compression is associated with shortening of the neck; in the thoraco-lumbar area a kyphosis has been seen associated with vertebral bodies irregular in size and shape; the disc spaces may be as deep as the flattened vertebral bodies. With increasing flattening of the vertebral bodies the sternum is pushed forwards progressively (Fig. 3). *Extremities*—The long bones have been of normal density and have not shown any unusual fragility. The epiphyses have multiple ossific areas and diaphysial extremities are irregular in ossification. The joint spaces, more particularly of the shoulder, wrist, hip, knee and ankle joint, are considerably widened, suggesting overgrowth of cartilage. The nuclei for the carpal and tarsal bones show delay in development and marked irregularity of outline (Fig. 12).

**Later radiographic features**—By a study of the serial radiographic appearances of the skeleton of a number of cases through life it was noted that while the skull remained relatively normal the epiphyses of the larger joints—notably the hip joints—deteriorated (Figs. 6 to 9). The ossific nuclei, which had originally been well formed, disappeared and no further ossification in them occurred. The musculature became progressively weaker, with the result that the joints became unstable and dislocation at the hip joints occurred. The acetabula expanded to the anterior spine and the upper end of the femora (which tend towards valgus deformity) came into cartilaginous apposition with the lateral aspect of the ilia; but later this connection was lost and the joints became somewhat flail—the opposing bony surfaces were irregular in outline being separated probably by dystrophic cartilage (Figs. 6 and 9). In one case subtrochanteric osteotomies were performed to counteract the dislocations, but these were unsuccessful in checking the displacement—indeed the operation appeared to accelerate the dystrophic disintegration (Figs. 14 and 15). At the knee joint, because the epiphyses are ossified from multiple nuclei which have not the stability of the normal entire homogenous nuclei, and because the ossification of the diaphysial extremities is irregular and mechanically unsound, knock-knee deformity develops without any bowing of the shafts of the diaphyses as in rickets (Fig. 13). In the forearm, however, the dystrophic changes at the wrist are associated with bowing due to irregular growth (Fig. 12). Osteotomy, which throws strain on dystrophic cartilage that is undergoing irregular ossification, appears to aggravate the process, but union occurs regularly through surgical fractures of consolidated bones (Fig. 13).

**ETIOLOGY**

It seems probable, from examination of the cases which have come to me since the original presentation, that the condition occurs in both sexes and is associated with some lethal factor in the parents introducing a state of incompatibility. The gravity of the lethal factor appears to be accentuated by consanguinity of parentage; this is illustrated in the case I published of a dystrophic child, the offspring of a brother and sister aged sixteen and fourteen years respectively. But we cannot entirely rule out immaturity of parents or the employment of abortifacients in this case. Disparity in the ages of parents has not been present where all of the children have shown these dystrophic changes in a grave form and no defect has been found in the parents. In one family which had three children so affected,
Case 2. Figure 2—Photographed with a normal youth of the same age, eighteen and a half years. Figure 3—Detail photographs showing dwarfing, deformity of the sternum, enlargement of the joints of the extremities, and displaced hip joints. (See also Figures 6 to 12.)

Figure 4—Cases 4 and 5. The mother with two affected children. The boy (right, Case 4) is aged ten years, and his sister (Case 5) is aged twenty-two years. The girl is mentally advanced for her years. Figure 5—Case 6. Girl aged thirteen and a half years photographed with her brother aged ten years. The girl is now aged twenty-two years. She has not grown since the photograph was taken but is mentally advanced for her years.
one died at two years of age; the others are ten and twenty-two respectively. The eldest child, a youth of twenty-three years, has a further complication associated with fits. The father did not walk until seven years of age, though of normal stature; he died two years ago of aplastic anaemia.

In such cases the lethal factor responsible (which might possibly be the employment of some abortifacient; more widely used perhaps than generally known) operates with each pregnancy but the gravity of the condition has shown some variation. Though syphilis is a common cause of developmental defects, in these patients its presence has not been detected. It has been shown experimentally that irregularities in development can be produced by agents which result in checking growth, interfering with oxygenation, or in the production of toxic products. The effect of these is dependent upon the age of the embryo, the rate of growth of the respective tissues at the time the agents are active, and the duration of time

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Case 2. Figure 8—Condition at age of fourteen years ten months. Note further degeneration of epiphyses and acetabular walls, increased joint space and dislocation. Figure 9—Condition at eighteen and a half years. Note complete dislocation and marked irregularity of all "articular" surfaces.

during which the agents are applied. Similar deformities are produced by different agents acting at the same stage of development. It has not been possible experimentally, even with the earliest implantations, to determine with accuracy the relative contribution of heredity and environment, and though the familiar distribution tends to support the possibility of hereditary lethal factors in the parents we cannot exclude the presence of deleterious agents, toxins—infected or metabolic—or abortifacients, in environment.

In all cases there appears to be induced an associated constitutional weakness, so great in some as to be incompatible with separate life; in others, less severe, the infant survives a few years and then dies from pneumonia or, as in the case of my original patient who died at fourteen years, from a progressive degeneration of all the skeletal tissues. In others—as in the cases which I have now watched for nearly sixteen years and whose radiographs are presented in this paper—the dystrophy shows progressive development and results in dwarfing
Case 2—Spine showing, in the antero-posterior view (Fig. 10) irregular disposition of the vertebrae and, in the lateral view (Fig. 11), "slipper" form of the vertebral bodies, absence of vertebral epiphyses, and disc spaces as wide as the vertebral bodies.

Case 2. Figure 12—Elbow, forearm and wrist at the age of nineteen and a half years. Note irregularity of growth at the elbow, bowing of radius and ulna with delayed ossification, irregular and delayed growth of carpal bones and irregularity of base of metacarpals. Figure 13—Tibia and fibula at the age of eighteen years. Note irregularity and obliquity of joint surfaces and site of osteotomy performed five years previously.
of the skeleton and weakness of the musculature; nevertheless the patient survives to adult life, is of normal or perhaps supernormal intelligence and highly sensitive of the dwarfin, resenting with very reasonable argument any unnecessary investigation or demonstration.

FIG. 14

Case 3. Figure 14—Hip joints at the age of three and a half years. Note failure of ossification of femoral necks and epiphyses. Figure 15—Condition at the age of twenty-four years. Bilateral subtrochanteric osteotomies were performed at the age of seventeen years. Compare position with that shown in Figure 14.

FIG. 15

I have watched by periodic radiographic and clinical examinations for over sixteen years the sequence of changes in the members of several families with this dystrophy. They are so alike in all their clinical and radiographic features as to be indistinguishable from one
Case 4—Spine and pelvis at the age of ten years. In the antero-posterior view (Fig. 16) note the irregular disposition of the vertebrae and dislocation of both hip joints. The lateral view (Fig. 17) shows "tongue" shaped thoracic vertebral bodies and irregularly sized "slipper" shaped upper lumbar bodies. The disc spaces are wide.

Figure 18—Case 4. Hands at the age of ten years showing irregularity and delay in ossification of carpal bones and growing extremities of long bones.

Figure 19—Case 5. Left hand at the age of twenty-two years showing that the epiphyses have fused but the joint surfaces are irregular and some of the bones stunted in growth.
another at certain stages. They constitute a distinct entity. Their ability to get employment is dependent upon the extent of their physical endurance—muscular weakness, headache and eyestrain may seriously curtail activities. Examples of mild forms of the dystrophy have been encountered in the examination of adult dwarfs, who have had no other handicap than the dwarfing, in an otherwise normal life (Engel 1938). They have sometimes been mistaken for achondroplasians but they have the distinctive features of a relatively short trunk compared

Fig. 20
Case 5—Pelvis and hip joints at the age of twenty-two years showing dislocation of both hip joints, marked expansion of the acetabula, and wide and irregular symphysis.

Fig. 21
Hip joints of a patient, otherwise normal, showing disturbed ossification of the head and neck of the right femur caused by injury.
with the limbs. Cases show not only variation in gravity of the generalised condition but variation in the degree of disturbance in different joints—for instance, the changes may be extensive in the hip joints or spine with little irregularity in the other joints.

**DIFFERENTIAL DIAGNOSIS**

*Rickets*—Florid rickets in infancy is characterised by generalised osteoporosis in which the outlines of all the diaphysial extremities and of the early ossific nuclei for the epiphyses are blurred (Brailsford 1948). The epiphyses are ossified from one central nucleus. The bones show absence of compact tissue, exhibit plasticity, and bend with weight-bearing; the deformities of the skeleton, being due to this, are symmetrical and generalised. Since the bones are deficient in calcium they fracture more readily than normal; some show multiple so-called pseudofractures. Consolidation of the bones promptly follows administration of adequate doses of vitamin D and no further deformity develops—indeed considerable correction may occur with growth. More rarely there are cases which show resistance to vitamin D and other medication or are associated with renal disease or hyperparathyroidism, the characteristic features of which are described elsewhere.

*Hypothyroidism*—In this condition there is generalised delay in ossification and the epiphyses are late in showing ossific nuclei; when these do appear they are multiple, and, because the patient is fit enough to subject the epiphyses to weight-bearing and normal function, they later become deformed, for they have not the stability of the epiphysis formed from homogeneous central ossification. The large epiphyses, such as the femoral capital epiphyses, show these defective features best. Good response, with acceleration in growth, consolidation and fusion of the multiple ossific nuclei, follows adequate thyroid medication (Brailsford 1948).

*Osteochondritis*—Although several epiphyses may simultaneously exhibit the characteristic series of changes which follow avascular necrosis, it is more common to find only isolated epiphyses affected. Sometimes both femoral capital epiphyses are affected, but even in these it may be possible to recognise that the change was initiated in each at a different time. Deformities are due to pressure during the plastic stage. Injury to a young epiphysis may delay the appearance of the ossific nucleus, or may cause its decalcification and deformity and result in a delayed ossification from multiple nuclei and permanent deformity (Fig. 21). Such deformity associated with stunted growth may result from the trauma inflicted during reduction of a congenital dislocation.

*Achondroplasia*—This condition is distinguished as a fault in the architect’s plan—the long bones and the bones at the base of the skull are prematurely fused, shortened and thickened, and the bones of the pelvis are squat. The vertebral bodies tend to be square in shape and at birth there is an unusual localised regular thoraco-lumbar kyphosis without any change in the form of the bodies; the epiphysial growth is from single nuclei which progress regularly to maturity (Brailsford 1948). The tuberosities show unusual development. The constitution is good and the musculature well developed, whereas in chondro-osteo-dystrophy the skeletal plan as seen in the newly born may be normal, the defects being due to faulty building material. Occasionally the achondroplasic (even as the normal) may show the additional features of chondro-osteo-dystrophy. In other words hereditary developmental irregularities do not render the skeleton immune from dystrophies, any more than from deficiency disease. Some irregularities of the skeleton appear to be due to their mixing. The features of achondroplasia and chondro-osteo-dystrophy have been well illustrated by Fairbank (1949).

*Gargoylism*—There is a miscellaneous group of dwarfs who are grotesque in appearance. They may or may not exhibit generalised irregularities in the growth of the skeleton which produce dwarfism; there may also be defective development of other systems such as the nervous, circulatory, respiratory, alimentary, genito-urinary or endocrine systems in various combinations. The possible combinations indicate the difficulty in any attempt at their classification. Gargoylism should be regarded as a general term, it cannot be said to include.
any particular character other than a grotesque appearance; even the skeletal lesions may be widely dissimilar. The grotesque dwarf whose features I illustrated and described (Brailsford 1943) had skeletal characters entirely different from those of chondro osteo-dystrophy or any other case described under the term gargoylism, but the grotesque appearances were similar.

SUMMARY
1. The evolution of the skeletal changes in chondro-osteo-dystrophy is described, and typical radiographs of patients observed into late adolescence are shown.
2. The etiology of the condition is discussed.

REFERENCES

Silfverskiöld, N. (1925): A “Forme Fruste” of Chondrodystrophia with Changes simulating several of the known “Local Malacias.” Acta Radiologica, 4, 44.