A REPORT OF SEVEN CASES OF
CHONDRO-OSTEO-DYSTROPHY (MORQUIO'S DISEASE)

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Since its first description by Morquio (1929) this disease has been observed in most European races and in coloured people but has not been reported, so far as I am aware, from the Sudan. To 71 cases reported in the world literature (Whiteside and Cholmeley, 1952) are added seven in three northern Sudanese families. It would not be surprising if abnormalities transmitted as Mendelian recessives were found to be relatively common in a community where consanguineous marriage is the rule rather than the exception.

General Description of the Affected Children

The families of these children were in good circumstances and they had been well fed and well cared for. All six parents appeared healthy and had negative blood Kahn reactions. The affected children were said to have been healthy at birth and to have remained so until the seventh or eighth month when deformity became manifest by gradually increasing kyphosis except in Case 1 in which chest signs were first noticed. The children were being or had been breast fed for the first two years and they had all received cod liver oil in the belief that they were rickety. They had had frequent 'colds', 'bronchitis', 'cough with fever' or 'pneumonia', of which the patient in Case 2 had died.

All the patients showed dwarfing and deformity which were more marked the older the child. The normal development of the head made it appear large by comparison with the stunted trunk and limbs, and the excessive shortening of the trunk gave the arms a false appearance of length. The deformities included shortness of the neck, antero-posterior enlargement of the chest, eversion of the costal margin, pointing of the sternum and dorsi-lumbar kyphosis. The limb bones were short but enlarged at the ends giving the joints a swollen appearance. The large olecranon processes prevented full extension of the elbows and there was ulnar deviation of the hands at the wrist joints. Genu valgum and partial flexion of the knee joints were present and the feet were short, wide, flat, and everted at the ankle. Marked laxity of the muscles and ligaments allowed the joints undue mobility. The milk teeth were well formed but in the two oldest living children the permanent teeth were poor in quality. Dyspnœa at rest was also noted in these two older and more deformed patients. In all the intelligence was normal.

Radiologically the skull and pituitary fossa were normal. The vertebrae were flat, irregular in shape and texture, poorly calcified and drawn out in front to a point which was most marked in the dorsi-lumbar region. The intervertebral spaces were deep (Fig. 3). The antero-posterior diameter of the pelvic brim exceeded the transverse (ape pelvis) and the acetabular roofs were irregular (Fig. 13). The ends of the ribs were abnormally wide. The long bones were short, thick, and poorly calcified. The cortices were thin and the cancellous tissue showed coarse and irregular retication. The metaphyses were irregular, expanded, and in some cases cup shaped. Large irregular epiphyses contained fragmented or multiple ossific centres. The joint spaces were wide. Coxa valga and thickness of the femoral necks were associated with flattened femoral heads (Fig. 13). The proximal ends of the metacarpals and metatarsals were characteristically conical (Fig. 8 and 17).

The First Family

Of the reputedly unaffected children of this family it has been possible to examine only the youngest
who was healthy. In a 10-year-old photograph of the whole family the rest appeared normal.

Case 1.—A girl of the first family (Fig. 2), aged 21 years (height 34\(\frac{1}{2}\) in., weight 41 lb., head circumference 21\(\frac{1}{2}\) in.), was said to have had ‘asthma’ at 3 months and to have shown deformity first in the chest at 7 months of age. She crawled at 18 months and walked between the second and fourth years. Thereafter she gradually stopped walking with increasing deformity. Catamenia started at 18 years and had been regular since.

At the age of 21 this girl was a severely crippled and deformed dwarf who could neither stand nor walk and was unable to raise herself from lying to sitting. She was breathless at rest and the laxity of the muscles and ligaments was very marked. The liver could be felt three fingerbreadths below the costal margin in a protuberant abdomen. The breasts were well developed, and pubic but no axillary hair was present. She had all but three wisdom teeth of her permanent dentition but they were poorly formed and pyorrhoea was severe. Although the radiograph (Fig. 3) shows the characteristic malformation of the vertebral bodies, there was no kyphosis but merely absence of the normal lumbar lordosis.

She was said to have been very miserable since the death of her brother because she now felt she was the only deformed dwarf in the world.

Case 2.—This was a boy aged 14 years at the time of death in February, 1953, from pneumonia. He was not seen but was described as a deformed dwarf. A photograph taken at the age of 4 (Fig. 4) reveals well-marked deformity. Radiographs taken shortly before death show characteristic changes in the vertebral bodies.

X-ray pictures of the long limb bones of Cases 1 and 2 presented characteristic metaphyseal and epiphyseal abnormalities but the shafts, unlike those of the patients from the other two families, were slender rather than thick. Cases 1 and 2 were older and more severely crippled than the others, and it seems probable that the thinness of the long bone shafts (Fig. 5) was due to atrophy from disuse.

The Second Family

The first and second children of this family had died at 45 days and a few minutes after birth respectively and there was no other information.
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about them. The third and fifth were examined and found healthy.

Case 3.—A girl (Fig. 7) aged 6 years (height 32 in., weight 27 lb., head circumference 20 in.) had a full milk dentition and all four sixth-year molars. The clinical and radiological signs of the disease were advanced (Fig. 8) and Harrison's sulcus was well marked on both sides of the chest. The liver extended two fingerbreadths below the costal margin.

Case 4.—A girl (Fig. 9) aged 14 months (height 27 in., weight 18 lb., head circumference 17 1/2 in.) was still on the breast and had a fontanelle which was almost closed. There was right congenital talipes equino-varus. A marked dorsi-lumbar kypho-scoliosis had its convexity to the left and in the radiograph (Fig. 10) the lumbar vertebrae were seen to be asymmetrical and irregular. Because of the youth of this child the radiological changes in the bones, although definite, were not gross.

The Third Family

The father of this family was a half brother to the father of the second family, the two having the same father but different mothers. Similarly the mother was half sister to the mother of family 2, sharing with her the same father. The eldest child of this family was a healthy boy of 10 years and the youngest was a baby girl of 3 months who manifested neither clinical nor radiological evidence of the disease. The father of family 3 had another family of seven healthy children, four boys and three girls, ranging
in age from 2 months to 13 years, by a second wife to whom he was not a blood relation.

Case 5.—A boy (Fig. 12), aged 8½ years (height 52½ in., weight 30½ lb., head circumference 20½ in.), was dyspnoeic at rest but could stand and walk unaided. All the left lower teeth were missing except the two incisors. Of the permanent teeth he had erupted three first molars and the two lower central incisors. The permanent incisors were poor in quality being small, yellow, and having serrated free margins. Both testicles were in the scrotum. This boy was markedly deformed and dwarfed by the disease and the radiographs showed advanced bone changes (Fig. 13).

Case 6.—A girl (Fig. 14), aged 4 years (height 28 in., weight 23½ lb., head circumference 19½ in.), had conjunctivitis and a liver which extended three fingerbreadths below the costal margin. The only marked deformity was the kyphosis in the dorsi-lumbar region. Pointing of the sternum, eversion of the lower ribs, enlargement of the wrists, ulnar deviation of the hand, genu valgum, knee flexion and pes planus were present but not gross. The radiograph of the hand and wrist (Fig. 17) was highly characteristic as it was in all the other cases.

In the skeletal deformities this girl strongly resembled her brother but the changes were of lesser degree (Fig. 15).

Case 7.—A girl (Fig. 16), aged 2 years (height 28 in., weight 19½ lb., head circumference 19½ in.), had conjunctivitis and a liver which extended three fingerbreadths below the costal margin. The only marked deformity was the kyphosis in the dorsi-lumbar region. Pointing of the sternum, eversion of the lower ribs, enlargement of the wrists, ulnar deviation of the hand, genu valgum, knee flexion and pes planus were present but not gross. The radiograph of the hand and wrist (Fig. 17) was highly characteristic as it was in all the other cases.
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Discussion

Morquio's disease is usually regarded as being transmitted as a Mendelian recessive and the patients described here, being of both sexes and the offspring of nearly related parents, conform to this view. Occurrence of the disease in previous generations was denied but there was no opportunity to confirm this statement, which is the usual Sudanese reply to an enquiry into the family history. Of special interest is the attempt of the father of the third family to control his experiment in human genetics by simultaneously marrying a second wife to whom he was not a blood relation and producing by her seven healthy children of both sexes. Jacobsen (1939) described a family in which the transmission was as a sex-linked recessive. All 20 cases were males and had inherited the condition through their mothers. These cases fit into Brailsford's (1948) generalized and progressive type of the disease. Most of the radiological characteristics described by him have been found in the radiographs of these children. The earliest and most easily recognized features are found in the radiographs of the spine and the hand, the anterior projection of the vertebral bodies and the conical proximal extremities of the metacarpals being highly characteristic.

Palpability of the liver was found in a number of these patients but no spleens were felt. It seemed that the liver was displaced downwards by the chest deformity and was not pathologically enlarged.

The permanent teeth when present were poorly formed and the oldest patient had severe pyorrhoea. This was in contrast to the milk teeth which were uniformly good.

Summary

Seven cases of chondro-osteodystrophy occurring in three sets of siblings in northern Sudanese families are described. In each set the parents were close blood relatives. One father had simultaneously produced a large family of healthy children by a second wife to whom he was not a blood relation.

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