BILATERAL HEREDITARY MICRO-EPIPHYSIAL DYSPLASIA OF THE HIPS

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Examining an eight-year-old boy who for four years had been suffering from pain in his knees, I found restriction of abduction and medial rotation at both hips. He was small for his age (Fig. 2) and intelligent. The other joints and spinal column appeared normal. Radiographs of the hips (Figs. 3 and 4) showed remarkably small epiphyses. The joint space was widened and the joint line intact. There was no fragmentation of the epiphyses, nor was there any abnormality of the acetabula. Radiographs of the shoulder showed delayed fusion of the nuclei of the upper epiphyses of the humerus (Fig. 5), and the same applied to the nuclei of the carpus (Fig. 6). I knew that the sixty-seven-year-old grandmother of the boy suffered from osteoarthritis of both hips. The radiographs (Fig. 8) showed, in addition to the classical features of osteoarthritis, an obvious flattening of the head, and a prominent spur supero-laterally. When the boy's mother—daughter of the woman just mentioned—was questioned, hip complaints came to light and these were confirmed objectively when it was found that abduction and medial rotation were restricted. The radiographs (Fig. 9) again showed the remarkably flattened head with the supero-lateral spur formation. Like her mother, this woman was small but well proportioned. There were no anomalies of the other joints. She had four children, of whom the two daughters had no complaints, but the two sons, eight and five years old, did show changes. The younger brother gave the same radiographic picture as the elder brother described above: a small epiphysis of a homogeneous structure with an intact joint line (Fig. 7).

There was now reason enough to examine the whole family, and the family tree is shown in Figure 1. From this it appears that the disease is transmitted as a dominant; that is to say, approximately 50 per cent of the children of a diseased parent are affected and that a healthy parent has no child with this disease.

The man who brought the disease into his family had two sisters who did not have the disease, as none of their issue was affected. Nothing is known about his parents. In all he
produced thirty-eight descendants of the first degree, all carriers of the autosomal dominant gene, of whom seventeen had the disease (45 per cent). Of these there were six male and eleven female carriers.

### TABLE I

**INCIDENCE OF AFFECTED OFFSPRING IN TEN FAMILIES**

<table>
<thead>
<tr>
<th>Family</th>
<th>With anomalies</th>
<th>Healthy</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>3</td>
<td>2</td>
<td>5</td>
</tr>
<tr>
<td>B</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>C</td>
<td>1</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>D</td>
<td>4</td>
<td>6</td>
<td>10</td>
</tr>
<tr>
<td>E</td>
<td>1</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>F</td>
<td>2</td>
<td>4</td>
<td>6</td>
</tr>
<tr>
<td>G</td>
<td>1</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>H</td>
<td>2</td>
<td>1</td>
<td>3</td>
</tr>
<tr>
<td>J</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>17</strong></td>
<td><strong>20</strong></td>
<td><strong>37</strong></td>
</tr>
</tbody>
</table>

The second generation numbers five descendants, of whom three had certain anomalies (Figs. 8 and 10) and one had osteoarthritis of both hips, but of a different kind (Fig. 11). She was not included in the total of those affected. Her children could not be examined. Inquiry showed that they had no hip or knee complaints. This patient is very important from a viewpoint of heredity.

The third generation has fifteen members, of whom six were certainly affected (Figs. 9 and 12) and one (dead) probably affected. The latter was not included.

The fourth generation consists of seventeen first degree descendants, of whom eight are certainly affected (Figs. 2 to 7, and 13 and 14).

Nearly all the members of the Delft family have only hip anomalies. There are two men who suffer from knee complaints and show dysplasia of the femoral condyles.

There are no anomalies of the spinal column. The children examined show that the epiphysial nuclei of the carpus are late in appearing, and pseudo-epiphyses are visible on the
distal ends of the first phalanges. The adults do not possess the short, plump hands that characterise dysplasia epiphysialis multiplex.

One may thus assume that this hereditary hip disease constitutes a generalised epiphyseal growth disturbance, in which the epiphyses about the hip joints are the most seriously affected.

**CHARACTERISTICS OF EPHYSEAL GROWTH DISTURBANCES OF THE DELFT FAMILY**

The characteristic features of the epiphyseal disturbance in the Delft family may be summarised as follows:
1) Transmitted as a dominant hereditary factor with great penetrance. 2) Symmetrical distribution on the two sides. 3) Affection of the epiphyses, especially of the hips. 4) Onset at the age of four at the latest. 5) Metaphysis, neck and diaphysis and acetabula are not involved. 6) The upper epiphyses of the femur of the children are reduced in depth and show a homogeneous, coarse structure without necrosis or fragmentation. There are no marginal erosions. 7) There is no dwarfism, but the patient is short, especially in the lower limbs. 8) The unaffected members of the family are of normal stature. 9) The shape of the hands is normal. 10) The epiphyseal nuclei at the upper end of the humerus fuse late. 11) The ankles are not affected. 12) Intelligence is normal. 13) There are no endocrine or metabolic disturbances.

**Radiographic changes in the various generations**—The radiographs of affected members of the second generation (three patients) show severe osteoarthritis of the hips, with flattening of the femoral heads and supero-lateral beaks and cyst formation. The femoral neck is shortened but there is no coxa vara. One member of this generation has osteoarthritis of the hips of a different type, and is not included in the series. Radiographs of the third generation show six members with the same flattening of the femoral head and supero-lateral beaks and cysts as in the older patients. The femoral neck is shortened but there is no coxa vara. The joint space is hardly or not at all diminished.

The radiographs of the fourth generation differed according to the age of the subject. In one child of five and in four children of eight a small epiphysis of more or less homogeneous coarse structure was seen, without marginal erosions and without zones of sclerosis, rarefaction or fragmentation. The contours of the epiphysis are regular. The metaphysis does not show rarefaction where it borders the epiphysis. The joint space is wide. There is no anomaly of the acetabulum, and no coxa vara.

The epiphyseal nuclei of the upper end of the humerus and in the hand are delayed in their development (Figs. 5 and 6). Two children of the fourth generation—one aged eleven and the other aged thirteen—present a different radiographic picture that reminds one of that of the parents (third generation), in that the head is slightly flattened, with supero-lateral protuberances, but wide joint space (Fig. 14). There is no anomaly of neck or acetabulum.

**DIFFERENTIAL DIAGNOSIS**

Several hereditary epiphyseal disturbances of the hip have been recorded. Jéquier and Fredenhagen (1948) and Hamsa and Campbell (1953) described familial cases of osteochondritis juvenilis (Perthes' disease). The radiographs from my cases differ from those of Perthes'
disease. Moreover, only exceptionally has Perthes’ disease been located elsewhere than in the hips, and seldom if ever are both hips affected at the same time, so that the symmetrical appearance that I have described does not occur. Despite the longer duration of the complaints.

FIG. 3
Right and left hips of W. R., the first patient seen, aged eight years (61 in Figure 1). Note the small epiphyses

FIG. 4
W. R. Figure 4—Arthrograph of right hip. Figure 5—Right shoulder.

the typical Perthes’ syndrome was not found in any of the five younger children. It is possible that in the bilateral familial case of “Perthes’ disease” the cause may be found in an epiphysial growth disturbance of a rather serious character (serious because there is an evident necrosis) and may thus be comparable with the other familial epiphysial growth disturbances.
FIG. 6
Left carpus of patient W. R.

FIG. 7
Right and left hips of L. R., the brother of W. R. (62 in Figure 1). The epiphyses are small.
Dysplasia epiphysialis multiplex—Fairbank described dysplasia epiphysialis multiplex in 1935. In some cases the disease was familial. Characteristics are stunted growth and short fingers with stumpy ends. Radiographically, the epiphyses are irregular in density and contour. Separate ossification centres often occur, so that there is some stippling on the periphery, but never so much as in dysplasia punctata. Hips, shoulders and ankles are especially affected. As described by Fairbank the disease differs from the picture of the Delft family.

Morquio-Brailsford's disease—In Morquio-Brailsford's disease epiphysial dystrophy is found with typical changes in the spinal column and in most centres of ossification, especially of
FIG. 10
Left hip of another affected member of the second generation—a man aged sixty-two (2 in Figure 1; brother of the patient referred to in Figure 8).

FIG. 11
An unaffected member of the second generation (6 in Figure 1). There is osteoarthritis of a different kind.
the hip. Here too, the acetabula are typically enlarged and irregular. I regard these lesions as an epiphysial reaction to weight bearing, with consequent disturbance of epiphysial growth.

Ribbing's disease—In this disease, which is inherited recessively, the affected members of the family are physically well developed, in contrast with those of the Delft family. Radiographically there is a clear relationship with osseous avascular necrosis, which was lacking in my cases.

Cretinism—Cretinism is characterised by dwarfism and infantilism. In the hips both the early changes and the final deformity may be indistinguishable from those of Perthes' disease.

FIG. 12
Left hip of an affected member of the third generation (cousin of the patient referred to in Figure 9).

COMMENT

It seems that in the cases that I have described the epiphyses are too small and are unable to meet the demands of daily life. In so far as this is to be judged radiologically we only see with advancing age a widening and flattening of the epiphyses, with beak formation. This adaptation proves to be inadequate, as indicated by the occurrence of early osteoarthritic changes in these deformed heads.

In the upper extremities the small size of the epiphyses is of little importance, except perhaps in those who regularly perform hard manual work. In the lower extremities, however, the small epiphyses are clearly not equal to the demands of weight bearing.

The wear and tear of daily life affected the epiphyses in my patients without causing necrosis; and ossification did not occur from multiple centres as in Fairbank's disease and in dysplasia epiphysialis punctata. One may imagine that, when the functional stability of the hips is seriously disordered, the daily burden, which in this case becomes excessive, gives rise to a picture like that of Perthes' disease, with necrosis and its sequelae. In the Delft cases the stability of the hips is still sufficient to prevent necrosis, but not the flattening.
Many examples are known in which the capital epiphyses have been damaged by injury, infection, avascular necrosis or epiphysiolsis, and in consequence have been unable to stand up to the daily wear and tear, and the same may happen in cases of subluxation with incongruity of the femoral head and acetabulum. The congenital hereditary or non-hereditary deformities of the hip epiphyses may act in a similar way. Such a picture is worst in Morquio’s disease. When the deficiency is less severe the appearance may be that of Perthes’ disease.

**FIG. 13**
Another affected member of the fourth generation (second cousin of patients W. R. and L. R. (Figs. 1 to 7)).

**FIG. 14**
Another affected member of the fourth generation.

which, when both hips are affected, I regard as an epiphysial growth disturbance with necrosis, like Fairbank’s disease and Ribbing’s disease.

The Delft cases belong to this type, but the epiphysial affection is less serious: fragmentation of the femoral head does not occur and the joint line is intact. Considered in this way, Perthes’ disease represents a more serious reaction than the changes found in the Delft family. In Morquio’s disease the epiphyses are so severely affected that the hip becomes unstable: thus the picture is again different, and it must be regarded as the most serious reaction. The
epiphysial growth disturbances give radiographic appearances that depend on the seriousness of the affection of the epiphyses and the action of gravity. The ultimate result is the same with all these disorders—namely incongruity of the joint planes with accelerated degeneration of the cartilage.

SUMMARY

1. A family is described of which several members in four generations suffered epiphysial growth disturbances of an unusual kind in the capital epiphyses of the femur, with shortness of stature.
2. This disorder forms one of a group of epiphysial growth disturbances which embraces several recognised disorders, whose effects on the epiphyses vary in severity. They may occur sporadically or they may be inherited as recessive or dominant characters.
3. Differentiation depends on the behaviour of the joint line—in other words, whether the epiphysis starts to show defects through inability to sustain the stress of weight bearing. In the most serious cases the picture is that of Morquio-Brailsford’s disease; when the changes are less severe the appearance may be that of bilateral Perthes’ disease. Differential diagnosis is no longer possible in later life, because the ultimate condition of the defective femoral heads is the same. Only in the hereditary cases is one able, by studying the capital epiphyses of the hip in childhood, to differentiate between the changes like those of Perthes’ disease on the one hand, and micro-epiphysial dysplasia without necrosis on the other.

REFERENCES