THE INHERITANCE OF SLIPPED UPPER FEMORAL EPIPHYSIS

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Two hundred and fourteen cases of slipped upper femoral epiphysis were reviewed. Fourteen families provided more than one case, and in 23 other families the index case had one or more close relatives with osteoarthritis of the hip, six of whom had probably suffered from a slipped epiphysis. The mode of inheritance is discussed and is thought to be an autosomal dominant with variable penetrance in the majority. There was a significantly higher proportion of girls in the familial group of cases.

The Grampian Region of Scotland has until recently had a stable population, and it has been easier to carry out familial surveys than in most other parts of Britain. Slipped femoral epiphysis has a greater familial incidence than is commonly supposed (Kirmisson 1918; Irwin 1946; Burrows 1957; Wilson, Jacobs and Shechter 1965). A familial tendency has, indeed, been denied (Scott 1956). In 1967, however, I reported eight families in which more than one case had occurred (Rennie 1967), and by 1972 had collected 11 such families and a further eight families in which a patient with slipped femoral epiphysis had a close relative with osteoarthritis of the hip (Rennie 1972). A survey is now reported of 214 patients comprising all those recorded in the Grampian Region since an orthopaedic service started in 1937, and 11 traced through hospital records of an earlier date. Since 1948, the Orkney and Shetland Isles have been included, with an increase in the number of cases and total population of nearly half a million. Information was obtained from hospital records and from a questionnaire asking for details of first, second and if possible, third-degree relatives. A number of families were interviewed, and it was possible to obtain a family history in 140 or approximately 65 per cent of the 214 cases.

RESULTS

The average annual number of slipped epiphyses from 1941 to 1980 is 4.7 and the variation over this period has been small (Table 1). Before 1940, a girl with slipped epiphysis appeared to be a rarity. The increased proportion of patients with bilateral involvement in the last two decades probably reflects an increased awareness by both surgeon and patient of the possible involvement of the contralateral hip.

Fourteen families contributed 31 cases of slipped epiphysis—an incidence of 14.5 per cent of the total number of patients or 22 per cent of those for whom a family history was obtained. In two families, father and daughter were affected. Four families provided a total of 10 affected siblings. In four other families an index patient had an affected aunt or uncle and, in four further families, there were affected cousins.

These cases of familial slipped epiphysis were then considered as a group in order to determine any difference between them and the series as a whole, and those in whom the family history was negative or unobtainable. The main finding was a difference in the sex incidence. In the whole series there were 164 boys and 50 girls, a male to female ratio of 3.3 to 1. In those in whom the family history was negative or unobtainable, the ratio was 147 to 36, approximately 4 to 1, and in the familial group there were 17 boys and 14 girls, a ratio of 1.2 to 1. This is statistically significant ($\chi^2=8.39; P>0.01$). This increased incidence in the less affected sex in the familial group is typical of conditions showing a genetic effect. Bilateral cases were slightly more frequent in the familial group but the difference was not statistically significant.

There was nothing remarkable in the physical build of the patients in the familial group, except that four of them were reported to be notably overweight, and one

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Table 1. The number of cases recorded and the proportion of bilateral and of female patients

<table>
<thead>
<tr>
<th>Date</th>
<th>Number of cases</th>
<th>Annual number</th>
<th>Ratio of unilateral to bilateral cases</th>
<th>Ratio of male to female patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Before 1940</td>
<td>26</td>
<td>—</td>
<td>12</td>
<td>25</td>
</tr>
<tr>
<td>1941–50</td>
<td>50</td>
<td>5.0</td>
<td>4</td>
<td>4.5</td>
</tr>
<tr>
<td>1951–60</td>
<td>50</td>
<td>5.0</td>
<td>16</td>
<td>3.2</td>
</tr>
<tr>
<td>1961–70</td>
<td>42</td>
<td>4.2</td>
<td>2.5</td>
<td>1.6</td>
</tr>
<tr>
<td>1971–80</td>
<td>46</td>
<td>4.6</td>
<td>2.5</td>
<td>3.3</td>
</tr>
</tbody>
</table>

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was undoubtedly undersized. Weights had not, however, been recorded. In the majority of familial cases the onset was gradual, following an injury of greater or lesser degree some weeks or months previously, but there are some examples of slipping without previous injury and of acute traumatic slip. In the familial group the children were almost equally from an agricultural or an urban background, whereas in the non-familial group twice as many lived in a town. It might be thought that farmers' sons had more heavy work to do in their adolescence than their urban counterparts, and this might constitute an added factor of trauma.
epiphysis, ascribed to a fall six months previously, although radiologically this appeared to be a gradual slip.

A maternal uncle was later treated for osteoarthritis of the hip which did not have the radiological characteristics of an old slipped epiphysis. One grandmother was reported to have had stiff hips, and two of her cousins had undergone operations for osteoarthritis of the hips.

Family 5. Four siblings were affected (Fig. 8). The eldest boy developed a slip on the right side in 1941 at the age of 16. His brother had bilateral slipped epiphyses one year later also at the age of 16. Both related the onset of symptoms to being kicked by cows. The third brother developed a slip on the left side at the age of 15 after carrying a sack of potatoes and during the following year his right hip showed typical radiographic changes of lesser degree. Two years later the eldest daughter, aged 13, was admitted to hospital with a three-week history of symptoms of spontaneous onset in the left hip. The fourth son died in infancy and the two younger siblings remained unaffected.

As shown in Figure 8, there has as yet been no disease in the next generation. The mother of this family had normal hips on clinical and radiographical examination, and there was no history of hip problems in the father of the family, in any of his nine brothers, or in any grandparents.

Family 6. One member of each of three generations was affected; a grandparent had an osteotomy in 1927, his nephew had an acute displacement in 1947 and his great-niece had a slip of gradual onset in 1969.

There was one family with two unilaterally affected brothers whose grandmother was reported to have had a stiff hip, and one family with a unilaterally affected uncle and nephew. In another family an aunt and her niece were affected. The aunt had ovarian agenesis, a left slipped epiphysis, and bilateral Madelung's deformity.

The niece was much overweight and had bilateral slipped epiphyses.

In a further family, the aunt had unilateral involvement and her nephew bilateral slipped epiphyses, and in four other families there were affected cousins each with a single slipped epiphysis. There were no identical twins in the series but two binovular twins, each of whom was the only involved member of the family.

In the 12 families in which family trees were adequate to make the calculation, 9 of 55 first-degree relatives of the index case and 4 of 93 second-degree relatives were undoubtedly affected. It was not possible to calculate the proportion of affected third-degree relatives. From the 1950 census of the region with its total population of 450,000, and the known annual rate of slipped epiphysis in patients from 11 to 16 years of age, an annual rate of incidence of 1 in 12,000 can be calculated for this age group. Each individual will incur this risk in each of the six years, giving a 1 in 2000 chance that an individual will develop a slipped epiphysis before skeletal maturity. This provides evidence for a genetic effect in the families which have been described.

This review also shows a high incidence of osteoarthritis of the hip in the families of children with slipped epiphysis. Family 4, reported above, included two patients with slipped epiphysis, and also showed osteoarthritis of the hip in two previous generations. Other families had an association of a single case of slipped epiphysis with an ancestry of osteoarthritis.
Family 7 (Fig. 9). A girl aged 13 was admitted with a left slipped femoral epiphysis (Fig. 10). Her father aged 43 was already attending the clinic for osteoarthritis of the hip (Fig. 11). Although he had no history of hip trouble in adolescence, his radiographs showed the characteristics of old slipped epiphysis. An aunt and an uncle subsequently required hip arthroplasties (Fig. 12), while the girl’s grandfather and two of his brothers were known to have had stiff hips, one reported radiologically as “advanced osteoarthritis of both hips”. Furthermore, one of her father’s cousins had osteoarthritis of the hip, and in another, “hip trouble” had started when he was 14. In this family there is a dominant pattern of inheritance of hip disability and it seems likely that in some cases there had been a slipped femoral epiphysis.

Family 8 (Fig. 13). A boy aged 17 developed bilateral slipped epiphyses. He also had knock knees requiring supracondylar osteotomy, and adolescent kyphosis. His sister came to an osteotomy for osteoarthritis of the hip at the age of 45. Their deceased father had “stiff hips”, and an aunt also had an osteotomy for osteoarthritis. One grandfather was “crippled with rheumatism in his legs only” in his thirties, while his wife was also reported to have been “crippled with rheumatism”.

Family 9. A 14-year-old boy was seen with a slipped epiphysis in the left hip. He also had osteochondritis with wedging of the eighth dorsal vertebra. His father had marked lumbar scoliosis and three of his paternal uncles were known to have had osteoarthritis and his mother had rheumatoid arthritis.

There were 17 families in which patients with slipped epiphysis had a total of 24 first or second-degree relatives with radiologically proven osteoarthritis of the hip. These comprised four fathers, two mothers, one sister, eight uncles, seven aunts, and two grandfathers of index patients. There were also eight first or second-degree relatives reputed to have osteoarthritis including two fathers, four grandfathers, and two grandmothers of the index patients. Several of these cases of osteoarthritis of the hip probably originated in slipped epiphysis.

Radiographs of the hips of an index patient (Fig. 14) and of her mother (Fig. 15). The aunt of a 13-year-old patient with slipped epiphysis had undergone total hip arthroplasty and stated that “her hip had never been free of trouble since she was 12”. The deceased father of an 11-year-old girl with a slipped epiphysis had suffered from advanced osteoarthritis of the hip and radiological reports stated that “changes may be secondary to slipped epiphysis”. There were four families in which a parent had osteoarthritis of the hip radiologically typical of a slipped epiphysis (Figs 14 and 15) but without a previous history of this.

In six additional families, reputed cases of osteoarthritis of the hip were reported in two fathers, two grandfathers, two grandmothers, and an aunt and an uncle. The symptoms in the fathers of both index patients had started in adolescence.

**DISCUSSION**

It seems likely that the incidence of slipped epiphysis in first-degree relatives of index cases should be materially higher than the ratio of nine cases in 55 reported above. The numbers of cases of slipped epiphysis and of osteoarthritis of the hip related to index cases of slipped femoral epiphysis are reported in Table II.

<table>
<thead>
<tr>
<th>Table II. The number of cases of slipped epiphysis and of osteoarthritis of the hip related to index cases</th>
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</thead>
<tbody>
<tr>
<td>Patients with slipped epiphysis</td>
</tr>
<tr>
<td>Families</td>
</tr>
<tr>
<td>All slipped epiphyses</td>
</tr>
<tr>
<td>Multiple cases in families</td>
</tr>
<tr>
<td>Definite OA hip</td>
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<tr>
<td>Reputed OA hip</td>
</tr>
</tbody>
</table>
From these figures it is possible to calculate, for this series, the incidence figures for slipped epiphysis and osteoarthritis. Thus the number of patients with slipped epiphysis who were related to another patient with slipped epiphysis was 31 in a total of 214 which is a 14.5 per cent incidence. The number of patients with slipped epiphysis closely related to patients with slipped epiphysis or osteoarthritis was 54 in a total of 214, or 25 per cent. Fourteen families included more than one patient with slipped epiphysis from a total of 197 families, an incidence of 7.1 per cent, while 37 of the 197 families included a patient with osteoarthritis of the hip, an incidence of 18.8 per cent.

The mode of inheritance is uncertain and has mixed features. In two families, a father with slipped epiphysis had a daughter similarly affected. In three other families a father with osteoarthritis of the hip which was probably due to slipped epiphysis had a daughter with slipped epiphysis. The frequency of this finding suggests the possibility of an X-linked dominant inheritance. On the other hand, two fathers whose wives were reputedly unaffected had a history compatible with slipped epiphysis and sons with slipped epiphyses. This possible inheritance could not be by an X-linked factor. While there is the possibility of multifactorial inheritance, the degree of dominance seen in many families makes it more likely that the pattern is one of an autosomal dominant with variable penetrance. This pattern also fits best the mode of inheritance in the nine families in whom a parent with osteoarthritis had a child with slipped epiphysis.

Family 5 (Fig. 8) does not, however, show the pattern of dominant inheritance. This family shows four affected siblings with two normal siblings past the age of puberty, a radiologically normal mother, and a reputedly normal father with nine normal brothers. This could be the pattern of autosomal recessive inheritance. It is not unusual for apparently similar conditions to be inherited in two different ways.

This series of 214 patients suffering slipped upper femoral epiphysis, includes a small group in whom there is an increased familial incidence and a larger group of patients who have a close relative with osteoarthritis of the hip. The most usual form of inheritance appears to be as an autosomal dominant with variable penetrance. There is a materially increased chance of a second case in the family of a girl suffering from slipped upper femoral epiphysis.

I acknowledge my debt to the Consultant Orthopaedic Surgeons of the Grampian Region who have all referred their cases. I am also indebted to Major Alec Grieve RAMC and to Dr Geoffrey Douglas who during a period of elective study did much work in tracing and questioning patients.

REFERENCES