FAMILIAL OSTEOARTHROPATHY OF THE FINGERS

A. C. ALLISON,* LONDON, ENGLAND, and B. S. BLUMBERG,† OXFORD, ENGLAND

From the Department of Biochemistry, University of Oxford

This paper is concerned with a genetically determined abnormality of the hands characterised by enlargement and loss of mobility of the proximal and distal interphalangeal joints. The abnormality appears in childhood; in later life the clinical and radiographic signs resemble those of some forms of chronic arthritis, but other features are distinctive. The abnormality appears to be one of a group of conditions in which the epiphyses of the bones undergo avascular necrosis, such as Legg-Calvé-Perthes' disease of the capital epiphysis of the femur and Freiberg's disease of the second metatarsal head.

The name of Thiemann is often associated with a rather diverse group of conditions in which there is avascular necrosis of the phalanges of the hands. Usually only one or two of the fingers have been involved (Thiemann 1909, Fleischner 1923, Kloiber 1926, Weil 1929, Dahs 1930, Dessecker 1930, Esau 1930), but patients have been described in whom nearly all the fingers and some of the toes were affected (Armstrong 1919, Shaw 1954).

The familial incidence of avascular necrosis of the phalanges has been noted by Armstrong (1919), Ryffel (1933), Sylvest (1940), Trippel (1950) and Shaw (1954). The mode of inheritance has been described as dominant, with strong penetrance. In one of our families twenty-three and in the other twenty persons were affected. It is clear that the appearance of the abnormality is controlled by a single autosomal gene which manifests itself in nearly all persons who are heterozygous for it. However, in one of our families there was a consanguineous marriage between affected persons. Two of the offspring of this marriage showed much more severe deformities than the rest, and it is suggested that they may have had a double dose of the abnormal gene. If this is so, the character cannot strictly be regarded as a "dominant," since the effects of the mutant gene in single and double dose are observably different. The general significance of this and similar observations in relation to the problem of dominance and recessivity of abnormal human traits is discussed elsewhere (Allison and Blumberg 1958).

CLINICAL MATERIAL

The material consists of two families showing what appears to be the same deformity. The proposita in the first family lives in a market town in Gloucestershire. Members of the family live in the neighbourhood, in Birmingham, and have emigrated to Australia, Canada and America. More complete information is available for this family and it will be presented in detail. Twelve affected members were seen either by the authors or by other physicians. Information on the remaining close relatives was obtained from several members of the family, cross-checked and confirmed by correspondence. The second family is from Berkshire, with some members resident in Wales. Five affected members of this family were seen, and the history of the others was obtained from relatives. There is no known relationship between the two families.

CASE REPORTS

FAMILY 1

Case 1—A woman aged forty-nine years (P in Fig. 4) was seen at the Radcliffe Infirmary, Oxford, in 1956 with the complaint of increasing thirst, hunger and urinary frequency, and was found to have diabetes mellitus, easily controlled by diet. There was no family history

* Member of the scientific staff of the Medical Research Council.
† Fellow of the Arthritis and Rheumatism Foundation.
FAMILIAL OSTEOARTHRPATHY OF THE FINGERS

FIG. 1
Case 1—Photograph of the hands.

FIG. 2
Case 1. Figure 2—Radiograph of right hand. Figure 3—Radiograph of right foot.

VOL. 40 B, NO. 3, AUGUST 1958
of this disease. Changes in her hands were noticed as an incidental finding. She was said to have had "rheumatic fever" as a child, but remembered only that she had a febrile illness which kept her confined to bed for several weeks at about the age of ten years. She noticed occasional pains in her hands and wrists, usually when working in the cold. She had never been handicapped by the deformity; as a young woman she was able to play the piano, which she had since stopped for lack of interest. No other joints were involved. There was no history of relevant previous illness or occupational hazard.

On examination the general health appeared to be satisfactory, and there was no relevant abnormality in the respiratory, cardiovascular or neurological systems.

In the hands there was a nodular enlargement of the proximal and distal interphalangeal joints of all the digits (Fig. 1). Those of the terminal joints on all fingers (but not the thumbs) resembled Heberden's nodes. Movement at the distal interphalangeal joints of the fingers was limited to 10 degrees, and at the proximal interphalangeal joints to 90 degrees. Movement at the interphalangeal joints of the thumbs was 10 degrees. The terminal phalanges of the fingers were shortened. There was slight restriction of flexion at both wrists, but this was not accompanied by a deformity. There were no juxta-articular nodes. The feet showed hallux valgus. There was no deformity or restriction of movement in any other joint, nor any tenderness of joints or muscles. No tophi were present.

Investigations—The erythrocyte sedimentation rate was 11 millimetres in the first hour (Westergren), blood uric acid was 3·6 milligrams/100 millilitres. Haemoglobin and white cell content of the blood were normal.

Radiographic examination. Hands—The phalanges were small and stubby. The interphalangeal joints showed marked lipping and narrowing of the joint space with some flattening of the surfaces, as in osteoarthritis (Fig. 2). There were slight changes in the carpal bones. Feet—Both feet showed hallux valgus (Fig. 3). Changes like those in the fingers were seen in the joints of the great toe and, to a lesser extent, in the interphalangeal joints of the other toes. The other joints of the lower limb appeared normal, as did the spinal column and chest.

The family—The incidence of the digital abnormality in members of the family is shown in Figure 4, and a comparison of the involved and uninvolved members is shown in Table I. Several members of the family complained of intermittent pains in the hands and in the back, but there was no consistent difference from the clinical picture of the proposita. None had
any other form of arthritis. All affected members of the family seen were functionally normal and many were employed in hard physical labour. The degree of involvement varied somewhat. A few subjects showed only slight abnormality, which might have been overlooked in any other family. All those affected stated that they had first noted the deformity at an early age (five to fifteen years) and that it had increased only slightly with the passage of time.

**FAMILY 2**

**Case 2**—The proposita in the second family was a woman aged sixty-one years (P in Fig. 7). In 1941 she was admitted to the Radcliffe Infirmary for treatment of a scalp wound. While she was being investigated, Dr A. M. Cooke noticed that her hands were deformed. She recalled that the joints of her fingers had been enlarged since she was at school, probably aged about twelve years. She had never had pain in the fingers or been inconvenienced by the joint enlargement, and could play the piano and do embroidery.

*On examination* the general health appeared good. In the hands there was a nodular enlargement of the proximal and interphalangeal joints of all the fingers (Fig. 5). The terminal phalanges were shortened. Movement was limited to about 50 degrees in the proximal joints and 15 degrees in the distal joints. The enlargement of the joints was firm and bony, and covered by normal skin. There were no tophi, and the other joints were clinically normal.

*Investigations*—The erythrocyte sedimentation rate was 8 millimetres in the first hour (Westergren). The blood uric acid was 2·8 milligrams/100 millilitres. Haemoglobin and white cell content of the blood were normal.

*Radiographic examination. Hands*—The changes were like those in Case 1, with involvement of the metacarpophalangeal joints of all the digits (Fig. 6). All the phalanges were shortened. Both wrists were involved.

**Case 3**—A male cousin of the patient in Case 2 (IV, 14 in Fig. 7) was seen in 1954, when he was aged forty-seven years. He had marked deformities of both hands, which had been present since he was a young child. The phalanges were all much shortened, with marked bony thickening at the interphalangeal joints of all fingers and of both thumbs; there was also slight thickening of the metacarpophalangeal joints. The range of movement at the metacarpophalangeal joints was nearly normal, but was restricted to about 20 degrees at the proximal interphalangeal joints and less than 10 degrees at the distal interphalangeal
FIG. 5
Case 2—Photograph of the hands.

FIG. 6
Case 2—Radiographs of hands.
joints. The patient had had no pain in the hands but was conscious of some functional disability. He had been in good health. He failed to keep an appointment for full examination, and returned to Wales. Two years later he was reported to have died, the cause of death being unknown.

As shown in Figure 7 this patient was the offspring of a first cousin marriage between two affected persons. He was much more severely affected than his brother (IV, 13 in Fig. 7) and other members of the family examined by one of the authors. An elder brother (IV, 10 in Fig. 7) was reported to have been severely affected, but he had died at the age of fifty-six from coronary thrombosis before the present investigation began.

**DIFFERENTIAL DIAGNOSIS**

The condition we have observed can be distinguished from osteoarthritis, rheumatoid arthritis and gout by its early age of onset, equal sex incidence, benign course, absence of symptoms, characteristic joint distribution, lack of abnormal laboratory findings, and its well defined genetic control. There is some resemblance to primary generalised osteoarthritis (Kellgren and Moore 1952), but signs of the latter begin later in life, and usually show less symmetrical affection, without shortening of the phalanges. The deformity of the distal interphalangeal joints in our cases resembled that of Heberden's nodes, but the accompanying changes in the proximal interphalangeal joints, the early age of onset and equal sex incidence mark the condition as distinct. The benign course and lack of general skeletal involvement differentiate it from osteoarthritis deformans endemica (Goldstein and Nikiforov 1931) and from Morquio's disease (Ritvo 1955).

**DISCUSSION**

The condition we have observed appears to be one of a group of diseases characterised by avascular necrosis of the epiphyses. The pathological changes shown by similar patients were described by Desseecker (1930) who concluded from histological examination that it was an avascular necrosis, thus confirming the suggestions of radiologists. The epiphyses appear to become damaged by compression and splitting, and defects occur as a result of

---

**FIG. 7**

Pedigree of family 2. ○ = unaffected females; □ = unaffected males; ● = affected females; ■ = affected males; □ = marked involvement; P = proposita. Note the consanguineous marriage of involved cousins and their offspring in generation III, IV, and the greater degree of involvement of two of the offspring.
absorption of bone. The growth of the phalanx is retarded and the epiphysis and metaphysis are widened. Later, there is a regeneration of the epiphysis which joins with the metaphysis at about the time of puberty. The etiology and pathogenesis are unknown, but presumably the initiating stimulus and the localisation of the defect to a particular joint are genetically determined. Occasionally, more than one site may be affected: Ryffel (1933) described a case in which Perthes' disease of the right femoral head was observed in a five-year-old boy; five years later the patient had avascular necrosis of the phalanges of both hands. The average age of onset in our cases was before puberty, which agrees with most of the other reports.

### TABLE 1

**The Offspring of Affected Individuals (Number at Risk) and the Numbers Affected in Each Family**

(The offspring of the cousin marriage in family 2 are excluded. Only the sub-families for which complete information is available are included in family 2)

<table>
<thead>
<tr>
<th>Family</th>
<th>Number at risk</th>
<th>Number affected</th>
<th>Percentage involved</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Males</td>
<td>Females</td>
<td>Total</td>
</tr>
<tr>
<td>Family 1</td>
<td>17</td>
<td>25</td>
<td>42</td>
</tr>
<tr>
<td>Family 2</td>
<td>11</td>
<td>7</td>
<td>18</td>
</tr>
<tr>
<td>Both</td>
<td>28</td>
<td>32</td>
<td>60</td>
</tr>
</tbody>
</table>

The mode of inheritance of the condition in both families resembles that previously described by Armstrong (1919) and others (Ryffel 1933, Sylvester 1940, Trippel 1950, Shaw 1954). From the compiled results in Table I it is clear that the condition has appeared in our families in nearly half the offspring of matings in which one partner had it. Thus it seems that the appearance of the abnormality is controlled by a single gene segregating in these families, which has nearly complete penetrance in the heterozygous phase. If the report is correct one carrier of the gene in the second family showed no defect. The expression of the gene varies somewhat, but in general gives rise to only a relatively slight deformity. The presence of two severely affected persons among the offspring of the consanguineous mating in family 2, however, suggests that they may represent the effects of the abnormal gene in double dose. If this is so, the type of inheritance cannot strictly be regarded as "dominant," because the abnormal homozygote is different from the heterozygote. In a number of other instances, when it has been possible to compare persons homozygous for abnormal genes with those showing heterozygous effects, the two have been found to be different (Allison and Blumberg 1958). It therefore seems that human abnormalities very rarely show the typically dominant type of inheritance.

**Summary**

1. Two unrelated families with a genetically determined arthritis-like syndrome of the joints of the hand and wrist are described.
2. The condition begins before puberty, is relatively painless and is not functionally disabling. The condition resembles that described by Thiemann and appears to fall into the group of avascular necrosis.
3. The appearance of the abnormality is controlled by a single autosomal gene which manifests itself in nearly all persons who are heterozygous for it. Two of the offspring of a marriage between affected persons showed much greater involvement than their siblings.
This suggests that they may represent the effect of the abnormal gene in double dose. If this is so, the type of inheritance cannot strictly be regarded as "dominant," since the abnormal homozygote is different from the heterozygote.

The authors are much indebted to Dr A. M. Cooke and Dr D. Pyke for bringing to their attention cases admitted to the Radcliffe Infirmary, Oxford, under the care of the former. Dr Henry Burger, of the Royal Australian Air Force, kindly examined two of the patients and provided us with photographs and radiographs.

REFERENCES


SYLVEST, O. (1940): Case of Pterygium Colli combined with Thiemann-Fleischner Disease and abnormality of Patella. Ugeskrift for Laeger, 102, 1,270.

