ORTHOPAEDIC ASPECTS OF THE EHLERS-DANLOS SYNDROME

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The Ehlers-Danlos syndrome is an uncommon familial disorder of connective tissue. The joints are hypermobile and the skin unduly extensible (Fig. 1). The skin tends to split with slight injury leaving wide thin scars on bony prominences (Fig. 2). There is often a bleeding diathesis of variable severity, with ocular, cardiovascular and gastro-intestinal concomitants. Other common stigmata are fleshy swellings known as molluscoid pseudo-tumours, usually in the scarred areas, and calcified spheroids, which may be palpated in the subcutaneous tissues of the forearms and shins (Fig. 3).

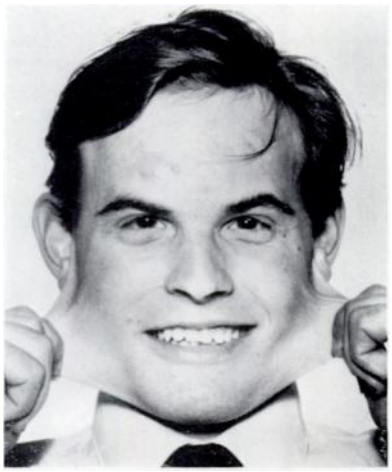

FIG. 1

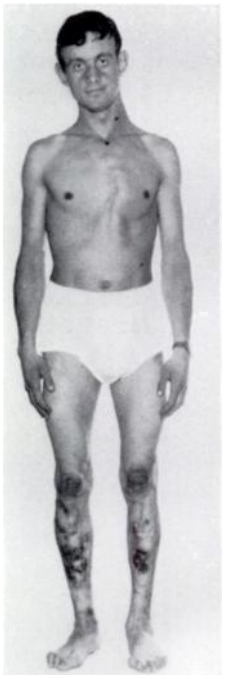

FIG. 2

FIGS. 1 AND 2

Figure 1—The hyperextensible skin in the Ehlers-Danlos syndrome. Figure 2—Scarring of the knees, shins and face and the thoracic deformity are shown.

During an investigation in southern England 100 affected patients were examined; many had diverse orthopaedic features, and the purpose of this paper is to describe and to discuss them on a basis of previous reports.

ASSESSMENT OF PATIENTS

The 100 patients were fully examined, and haematological, biochemical, histological and radiological investigations were done on many of them. Joint hypermobility was assessed by a modification of the method described by Carter and Wilkinson (1964). The patients were given a score of 0 to 5, one point being scored for the ability to perform each of the following tests: 1) passive dorsiflexion of the little finger beyond 90 degrees with the forearm flat on a

table (Fig. 4); 2) passive opposition of the thumb to the flexor aspect of the forearm (Fig. 5); 3) hyperextension of the elbow beyond 10 degrees (Fig. 6); 4) hyperextension of the knee beyond 10 degrees (Fig. 7); 5) forward flexion of the trunk so that the palms of the hands rested easily on the floor (Fig. 8). These tests were all easy to perform and they were quantitative measurements. In tests 1 to 4 an average was taken for the paired joints.

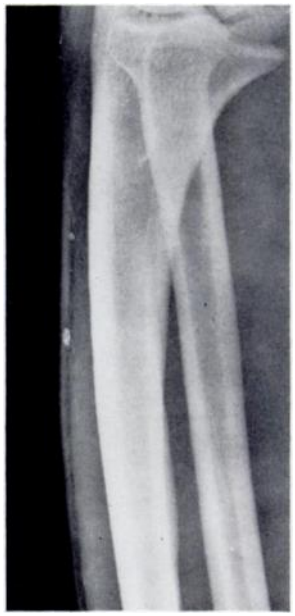

FIG. 3
Calcified subcutaneous spheroids.

CLINICAL FINDINGS

Hypermobility—Most of the patients in the series scored at least 3 on the hypermobility test but in some individuals hypermobility was slight. Laxity involved all mobile joints, particularly the digits (Fig. 9). The fingers could sometimes be pulled out for a considerable distance with widening of the joint spaces (Fig. 10).

Because of extreme hypermobility and hypotonicity, two affected infants were initially misdiagnosed as having Oppenheim's disease, and a third had been thought to have "idiopathic hypermobility."

Dislocation—The degree of hypermobility and the incidence of joint dislocations were closely related. Sixty-three patients had a hypermobility score of 3 or more, and nineteen of these had suffered dislocation of one or more joints. Seven others with a lower score had also had dislocations. Seven patients had suffered dislocations of the finger or thumb, which were multiple in three. Two patients with persistent dislocation of the interphalangeal joints of the thumbs found great difficulty in using a pinch grip.

Three patients had dislocated elbows on single occasions and one had dislocated both elbows on separate occasions. In one of these patients severe fracture-dislocation was caused in a road traffic accident, but the remaining dislocations occurred after minor falls.

Six patients reported single dislocation of one shoulder. A further four patients had recurrent dislocation of the shoulder, and this was bilateral in three. Spontaneous reduction always occurred.

Recurrent dislocation of the temporo-mandibular joint occurred in two patients. These dislocations were always easily reducible, and the tendency to recurrence disappeared as the joints grew stiffer in middle age.

Dislocation of the patellae occurred in eight patients. In seven dislocation was recurrent and in three it was bilateral. All the recurrent dislocations were spontaneously reducible and the patients were not much inconvenienced. One woman underwent patellectomy at the age of twenty-three without any functional improvement.

Seven patients showed prominence of the medial end of one or both clavicles, and radiographs revealed upward dislocation of the sterno-clavicular joint. This was irreducible in all. One patient was a girl of two years, in whom subluxation may have occurred during birth, remaining unnoticed and unreduced.

Enough patients of middle age and beyond were seen to suggest that joint hypermobility and dislocations usually decreased with age, although in those most severely affected improvement did not always occur.

One severely affected girl had congenital dislocation of both hips. No other patient reported hip trouble during childhood, but radiographs of a woman of thirty-one, who had no symptoms referable to the hip, revealed dysplastic subluxed femoral heads with early osteoarthritic changes. The only hip dislocation in an adult took place when a middle-aged woman slipped and fell, dislocating the left hip.

Joint effusion—Twenty patients complained of persistent joint effusions. Of these, fifteen had a hypermobility index of three or more. Fifteen had recurrent effusions in the knees, four in the ankles, three in the elbows and two in the digits. The effusions, which seldom caused symptoms, were associated with activity and usually appeared at the end of the day.

Joint instability—Twenty patients described their joints as " not reliable," " tending to give way," or " weak." Eleven had ankle instability and six had troublesome knees.

FIG. 4

FIG. 5

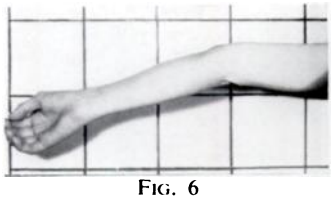

FIG. 6

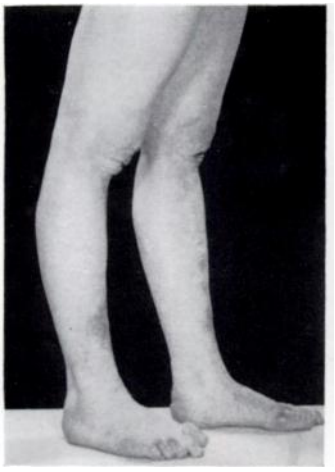

FIG. 7

FIG. 8

Criteria for assessing hypermobility. Figure 4—Hyperextension of the little finger beyond 90 degrees. Figure 5—Passive apposition of the thumb to the flexor aspect of the forearm. Figure 6—Hyperextension of the elbow beyond 10 degrees. Figure 7—Hyperextension of the knee beyond 10 degrees. Figure 8—Forward flexion of the trunk so that the palms of the hands rest easily upon the floor.

In some patients instability of the thumb and finger joints from hypermobility was seen. In extreme cases there was difficulty in picking up large objects with one hand, unscrewing bottle tops and pressing switches. One patient was unable to abduct his right upper arm beyond 90 degrees when carrying a weight, though he had an excessive range of active shoulder movements when he was not bearing a load.

Children who had extreme generalised hypermobility characteristically walked late and fell frequently, and the control of abnormally mobile limbs presented a considerable problem to these infants. Facial scars were often acquired from falls in early childhood.

Severely affected patients often had a characteristic gait. The feet were placed firmly and flatly upon the ground and the hips were hyperextended during weight-bearing to counteract the genu recurvatum, thus enabling the pelvis to remain balanced with respect to the feet. This gait resembled that of tabes dorsalis, and it was accentuated by the concomitant pes planus.

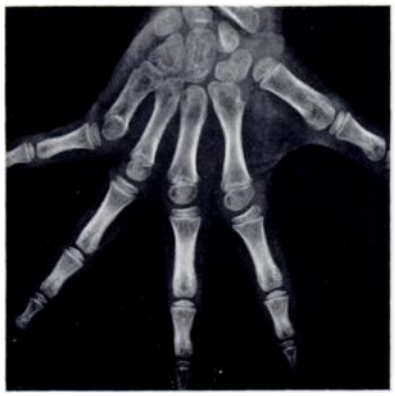

FIG. 9

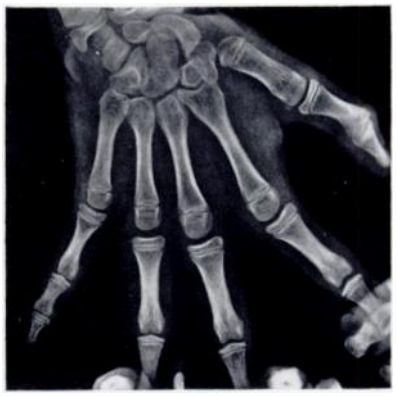

FIG. 10

Figure 9—Active hyperabduction of the fingers. Figure 10—Passive distraction of the finger joints.

Spinal abnormalities—Spinal abnormalities were observed in twenty-three patients. Eighteen had some degree of scoliosis and this was marked in six (Fig. 11). Of the twenty-seven children under the age of fifteen, two had scoliosis of mild degree.

Anterior wedging of the vertebral bodies was seen in several patients when a kyphotic element was present in the spinal curve (Fig. 12). Three patients had marked kyphosis at the thoraco-lumbar junction and their lateral radiographs showed wedging and a slight posterior slip of the first lumbar vertebra relative to the twelfth thoracic and second lumbar vertebrae.

Two patients had a remarkably straight thoracic spine with absence of the normal curve (Fig. 13).

Thoracic cage abnormality—A depressed sternum was found in eight patients and was marked in one. Five other patients, all kindred, had a mild bilateral prominence of the second costochondral junction, and unilateral abnormality of several costochondral junctions was noted in three patients. Minor degrees of thoracic asymmetry were present in a further fourteen patients, several of whom also had thoracic scoliosis.

Two patients had an abnormally long neck, and chest radiographs showed that they had a pronounced sloping of the upper ribs. This deformity disappeared when the shoulders were braced backwards and was probably due to laxity of the ligaments of the shoulder girdle.

Osteoarthritis—Clinical evidence of osteoarthritis was elicited by direct questioning, the criteria used being complaints of pain and increasing joint stiffness. Twenty patients had such symptoms.

Of twenty-two patients over the age of forty, sixteen had symptoms of arthritic changes in one or more joints and six were without symptoms. These six patients were all mildly affected by the Ehlers-Danlos syndrome, three having a hypermobility index of 3, one of 2 and two of 0.

Ten patients complained of knee disabilities but none was bilaterally affected. Five patients had osteoarthritis in both hands, particularly in the thumbs, and one patient had

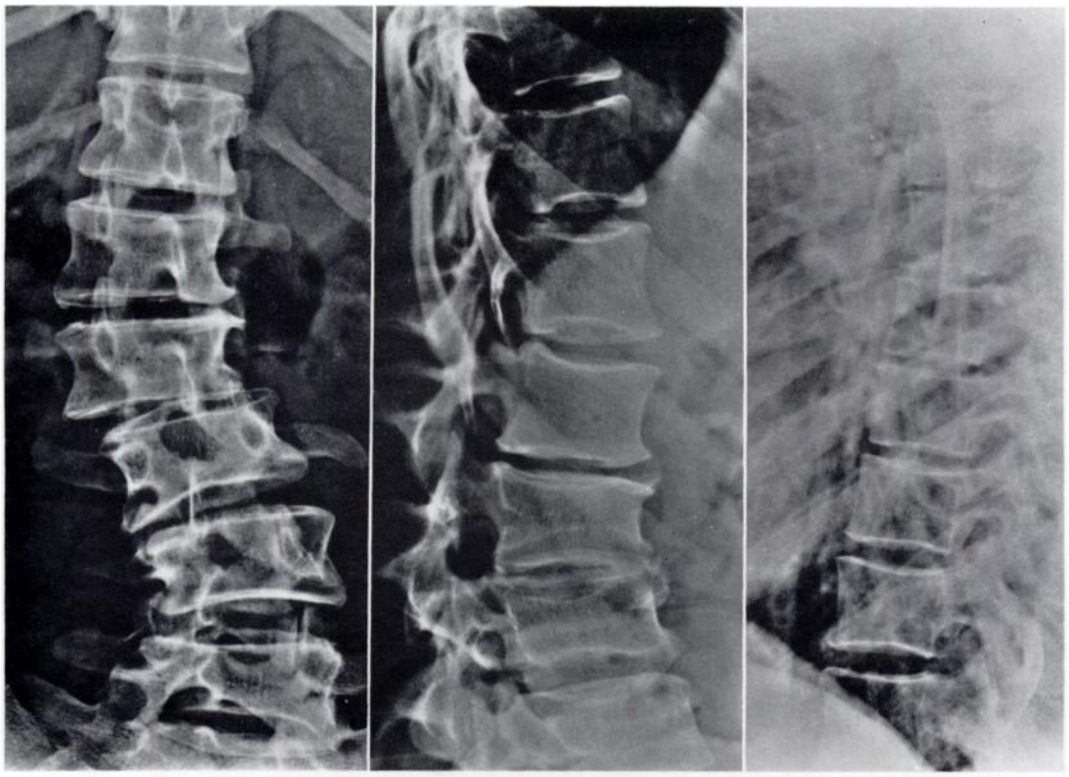

FIG. 11 FIG. 12 FIG. 13

Some ways in which the spine may be affected in the Ehlers-Danlos syndrome. Figure 11—Thoraco-lumbar scoliosis. Figure 12—Anterior wedging of the vertebral bodies. Figure 13—Straight thoracic spine.

fixed flexion deformity of both thumbs (Fig. 14). Two patients had painful ankles and one had bilateral osteoarthritis of the shoulders.

Only two patients were severely incapacitated. One was a man of eighty-two who was chairbound by osteoarthritis of the spine, knees, elbows and hands. The other was a woman of sixty-three who had arthritis of both shoulders and mild changes in the lumbar spine and hips.

Pain in the back was relatively infrequent. Because twenty-three patients had clinically detectable spinal deformity and eighteen had scoliosis which appeared to be from ligament laxity, a high incidence of pain from back strain and osteoarthritis might have been expected. But only six patients complained directly of troublesome backache. All had a hypermobility index of 4 or more and they ranged in age from twenty-four to eighty-two years.

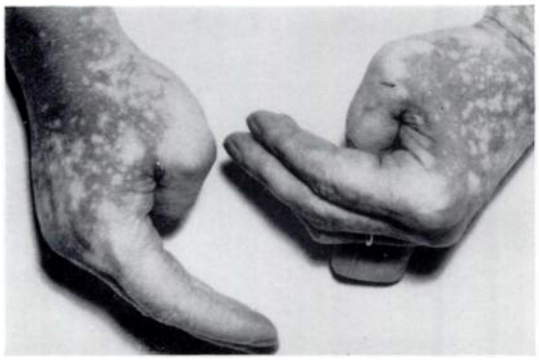

FIG. 14

Fixed flexion deformity of metacarpo-phalangeal joints of both thumbs (the patchy pigmentation is not a feature of the Ehlers-Danlos syndrome).

Foot deformities—Seven patients had talipes equinovarus, in both feet in four. Two of the latter had had surgical correction of both feet.

Pes planus was by far the most common foot deformity that was encountered, with fifty-two patients affected. In some of the younger patients the longitudinal arch was normal when no weight was being borne, but by the age of thirty all patients with affected feet showed both

static and dynamic planus deformity. Most patients with pes planus had hypermobility indices of 3 or more, and the most severe cases occurred in those with an index of 5. The most severe flat feet gave no pain, and difficulty in fitting shoes was the main problem.

Many patients developed hallux valgus with associated bunions and ten had had corrective operations. Claw toes were seen in seven patients.

Patients showing increased stretch of the skin often had " mocassin feet " in which the skin over the flat feet was so loose that they appeared to be wearing an oversize pair of ankle socks.

Bursae—Olecranon and prepatellar bursae were often encountered. These had to be distinguished from haematomata or molluscoid pseudo-tumours which occurred at the same sites. Many patients had undergone operation for excision of these bursae, usually with satisfactory results. Similar bursae were encountered over the calcaneal tendon and in association with hallux valgus.

Ulceration—Two patients had recurrent episodes of spontaneous ulceration involving the elbows and in another the shins were similarly affected. In a further patient bed-sores developed after a spinal operation. In each case healing occurred only after repeated skin grafting.

Haematomata—Patients who bruised readily and had associated haemorrhagic phenomena developed haematomata beneath the dermis and within the deeper tissue planes.

The pressure points were common sites for subdermal haematomata, which appeared as enormous swellings on the knuckles, elbows or prepatellar surface of the knees. Spontaneous bleeding in the thighs or calves was occasionally seen; this complication necessitated blood transfusion in three patients, and several others had been admitted to hospital for exploration and drainage of large haematomata.

Muscle cramps—Forty-three patients reported episodes of severe muscle cramp in the limbs, usually occurring at night and involving the calves. This symptom was most frequent in childhood and often resolved by adult life. Cramps were most frequent and severe in the more hypermobile patients.

Influence of pregnancy—One patient developed pain and paraesthesiae in both shoulders, arms and hands during the third month of pregnancy. Radiographs of the cervical spine showed spondylotic changes. Her symptoms lessened in severity after delivery. Another patient, now aged sixty-three, and her daughter, now aged forty-three, had noticed shoulder instability during pregnancy. They had been unable to abduct their arms beyond 80 degrees because spontaneous subluxation of the shoulder had occurred at this point. The mother had suffered recurrent dislocation of both shoulders until her early fifties, but the daughter was normally symptom-free. The daughter also had a distracted pubic symphysis during labour: after delivery she was unable to walk for six weeks and she suffered symphysial pain for six months.

Peripheral circulatory phenomena—Seven patients had Raynaud's phenomenon and twenty others had acrocyanosis. One patient with severe Raynaud's symptoms had marked acro-osteolysis of the terminal phalanges of both hands. Her fingernails were dystrophic and there was considerable bony resorption.

Chilblains had occurred during childhood in twenty-four patients, but these had persisted into adult life in only eleven.

Bony abnormality—An abnormally large ulnar styloid process was demonstrated in four of the seven patients who had radiological examinations of the wrists. No primary bony abnormality was detected in any of the other patients.

There was no increased incidence of bone fracture in the series, and in the few patients who had fractures there had been no undue delay in bony union.

No case of musculo-skeletal neoplasm was encountered and none of the patients who were examined radiologically had any evidence of ectopic bone formation or any other bony abnormality.

Somotype—Twelve of the patients were of short stature but only three adults were below five feet in height. Two males were unusually tall and thin, but although they appeared to be

" marfanoid " the measurements of their body segments were normal. All the other patients in the series were of normal physique.

DISCUSSION

Many affected patients have orthopaedic complications which are often multiple and vary greatly in severity. Ligamentous and capsular laxity is the basic cause of the dislocations and unstable joints that are frequently encountered.

Such complications were mentioned by Tschernogobow (1892), who reported an affected boy with a dislocated elbow and hip even before Ehlers (1901) and Danlos (1908) had delineated the syndrome. Since then there have been many reports of recurrent dislocation of various joints (Pelbois and Rollier 1952, Pascher and Kanof 1953, Carter and Sweetnam 1960). In particular, congenital dislocation of the hip was present in the patients described by Biering and Iversen (1955), Svane (1966), Aldridge (1967) and Barabas and Barabas (1967). This abnormality should be carefully excluded in every affected baby.

Babies with the Ehlers-Danlos syndrome may be extremely hypermobile, and in the absence of a positive family history the diagnosis of a " floppy infant " of this kind may be very difficult. Two patients in the series were at first thought to have Oppenheim's disease, and a similar misdiagnosis was reported by Schubert (1925), Smith (1939) and McKusick (1966). In the same way a misdiagnosis of Werdnig-Hoffman disease was reported by Dewart (1965), and Geerts (1966) mentioned an affected infant with an " atrophie musculaire de type neurogène."

Spinal abnormalities, which were seen in twenty-three of our patients, have previously been described by many authors, including Rollhauser (1950) and Shapiro (1952). Only two of the patients were under the age of fifteen, suggesting that the development of spinal deformity is caused by the inability of lax ligaments to cope with the stresses of the upright posture. Abnormalities of the vertebral bodies have also been observed by Macfarlane (1959), Coventry (1961) and Svane (1966). The spinal changes are secondary to the postural realignment.

Asymmetry of the thoracic cage is a common feature. Slight degrees of asymmetry were primary and, in some patients, familial. The more severe forms were associated with thoracic spinal abnormality and appeared to be secondary to these changes. When severe, the thoracic deformity might cause displacement of the heart, leading to a cardiac murmur and an unusual electrocardiograph. This situation has led to the misdiagnosis of a structural cardiac defect in a number of patients. Genuine heart lesions are an uncommon concomitant of the syndrome (Beighton 1969).

The incidence of osteoarthritis was directly related to the hypermobility index. Patients with an index of 4 or 5 all developed symptoms of osteoarthritis by the age of forty. A combination of extreme hypermobility and repeated injury could be implicated in all affected joints. The fixed flexion deformities of one patient's thumbs were probably the result of a combination of osteoarthritis and old haemarthroses. Haemarthroses are not common in the Ehlers-Danlos syndrome, but they have previously been described by Murray and Tyars (1940) and Liss and Lynch (1967).

Talipes equinovarus was present in seven patients, all of whom were very hypermobile. It is possible that this deformity was the result of a combination of lax joints and malposition *in utero*.

The bursae, ulcers and haematomata that afflicted many patients were probably the consequence of the tissue fragility and the bleeding diathesis that is inherent in the Ehlers-Danlos syndrome. The tissues are thought to be fragile because of a defect in the cross-linking of the collagen fibrils (Jansen 1955), while the bleeding tendency has been variously ascribed to a coagulation defect (Kashiwagi, Riddle, Abraham and Frame 1965), an abnormality of the vessel walls (Frick and Krafchuk 1956) or a looseness of the perivascular connective tissues

(Fantl, Morris and Sawers 1961). A combination of all these factors may be involved (Day and Zarafonetis 1961).

Many patients, particularly children, complained of cramps in the leg muscles, which occurred mainly at night. A similar feature was reported by McKusick (1966). These cramps occurred in the most hypermobile patients and tended to resolve when adult life was reached. Kirk, Ansell and Bywaters (1967) made a comparable observation in their patients with simple joint hypermobility. It is possible that the cramps are the result of overstretching of the muscles from the hypermobility of the joints.

The exacerbation of the symptoms of cervical spondylosis and the occurrence of shoulder joint subluxation and pubic symphysial distraction during pregnancy have not previously been noticed in the Ehlers-Danlos syndrome. These events were probably influenced by relaxin, a hormone which is a physiological product during pregnancy, and which normally causes an increase in connective-tissue laxity to facilitate parturition (Adamson, Roberts and Wilson 1934).

The peripheral circulatory abnormalities which were observed in several patients have been reported on many occasions (Ross and Dooneief 1957, Turkington and Grode 1964). The only previous report of acro-osteolysis in a patient with the Ehlers Danlos syndrome was that of Newton and Carpenter (1959), who described the same patient in an earlier stage of her illness.

None of the patients in the series had any evidence of primary bony abnormality, and there was nothing to suggest any increase in bone fragility. Katz and Steiner (1955) described the radiological appearances of bone deposits which had formed adjacent to the greater trochanters of their patient. These changes could have been due to the ossification of a pre-existing haematoma.

A liability to musculo-skeletal neoplasm does not seem to be a feature of the Ehlers-Danlos syndrome, and the sarcomata which were described by Johnson and Falls (1949) and by Sestak (1962) probably represented chance associations.

Slight histological changes of bone structure have been described by Julkunen, Rokkanen and Jounela (1967), and these workers demonstrated abnormalities on microradiology and on tetracycline fluorescence studies. The significance of these changes is not yet apparent.

The Ehlers-Danlos syndrome is usually inherited as an autosomal dominant trait, and for this reason there is a 50 per cent chance that any child of an affected patient will have the condition. An X-linked recessive form of the syndrome has recently been described (Beighton 1968*a*). These patients do not have a great degree of joint laxity, but dislocations and effusions are not infrequent. Four other clinically distinct forms of the syndrome may be recognised (Beighton 1968*b*), and there is a consistent incidence of orthopaedic complications within each of these entities. For this reason, the recognition of these types of the Ehlers-Danlos syndrome has a bearing on the prognosis and the treatment of any complications which might arise (Beighton and Horan 1969).

SUMMARY

1. The orthopaedic features of 100 patients with the Ehlers-Danlos syndrome are described.
2. The significance of these findings is discussed and comment is made of their relationship to the other stigmata of the syndrome.

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This paper forms part of a thesis submitted by P. Beighton to the University of London for the M.D. degree.

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