FROM THE ROENTGEN DEPARTMENT OF LINKÖPING HOSPITAL, SWEDEN

THE HEREDITARY MULTIPLE EPIPHYSEAL DISTURBANCE AND ITS CONSEQUENCES FOR THE AETIOGENESIS OF LOCAL MALACIAS-PARTICULARLY THE OSTEOCHONDROSIS DISSECANS

By

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For 20 years I have been interested in a constitutional skeletal disease, which I named hereditary, multiple epiphyseal disturbance (H.M.E.). The condition was at that time not unknown in the radiological and orthopaedic literature. In 1929 Kreuz[1], and in 1930 Freund[2], had noticed peculiar alterations of the hip joint, probably of the same nature, and in 1933 Müller and Hetzar[3] had described a "generalized Osteochondritis dissecans of many joints and the spine" in 4 out of 6 members of a family. In the Scandinavian literature Stören[4] had recorded a similar observation, and in his text-book Brailsford[5] described cases of the same type under the designation, chondro-osteodystrophy. It is highly probable that the type of atypical chondrodystrophy described in 1925 by Silfverskiöld[6] and later called Morquio's disease, is a more grave and profound form of the same condition. In the nineteen-forties many cases of the disease were recorded, and I am under the impression that it is not an extremely rare condition. Every radiologist and orthopaedic surgeon may meet it once or twice in his life.

Among recent contributions those by Marquardt[7] and Widemann[8] should be mentioned. In the latter an attempt is made at co-ordinating

1 Fortschr. a. d. Ged. d. Rtg-strahlen *40*, 1929.
2 Ibid. *41*, 1930.
3 D. Zschr. f. Chir. *241*, 1933.
4 Acta chir. scand. *74*, 1934.
5 The radiology of bones and joints, London 1935.
6 Acta radiol. *4*, 1925 and *5*, 1926.
7 Fortschr. a. d. Geb. d. Rtg-strahlen *71*, 1949.
8 Zschr. menschl. Vererb. u. Konstitutionslehre *31*, 1952.

different conditions under the comprehensive heading, dysostosis enchondralis. From my own experience of cases described in 1937[9] and on the basis of a new case found in 1950[10], I shall sum up the description of the condition in the following.

History.—Discomfort begins at the age of 7–13 years, first in the hips and knees, presently also in the ankle joints and fingers. The involvement is generally, but not always, symmetric. Backache sometimes supervenes. In most cases the discomfort is described as a painful stiffness and is felt especially after heavy work. After a few days' rest it is hardly perceptible. With increasing age the pain is harder for patients who do physical labour but milder for persons in sedentary occupations. This fact has suggested to me a way towards the therapy.

Symptoms.—On general examination of my cases of H.M.E. I found no signs of endocrine or metabolic diseases, nor of nervous or mental disorders. The symptoms were strictly topical but multiple, and hardly characteristic at the physical examination. A moderate kyphosis in the thoracal part of the spine, reduced movements of the hip joints, especially of their rotation, are not found in the first years of the disease but occur later in the course. Crepitation may be observed in diseased articulations. Swelling of the joints, particularly in the fingers, is common.

In contrast to the history and general examination, the roentgen picture discloses characteristic, marked and ample findings, which can be divided into two main groups, viz. (I) anatomical variations and anomalies in the shape of secondary ossification centres and—even in early, asymptomatic stages of the disease—signs of multilocular epiphyseal ossification; (II) destructive changes suggestive of (but not identical with) osseous aseptic necrosis (local malacias) such as coxa plana, Scheuermann's disease of the spine, Thiemann's disease of the phalanges, Osteochondrosis dissecans, etc.

Some figures will show the roentgen symptoms better than any description.

Prognosis and therapy.—The prognosis *quoad vitam* is good; *quoad sanationem* it depends on the treatment. My patients from 1937 were members of a timber-cutter's family, and I have observed that the hard work in the woods causes disability of the patients. However, if those suffering from H.M.E. in youth are given light work, e.g. in tailor, shopkeeper or constructor establishments, which I have provided for my patients with the aid of the Swedish Pension Board, I

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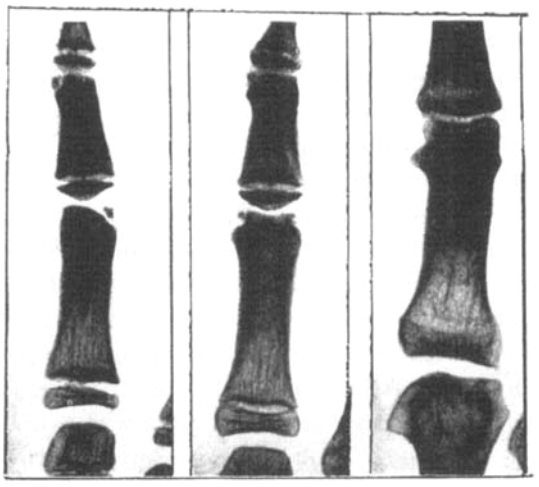
9 Acta radiol. Suppl. 34, 1937.

10 Ibid. *36*, 1951.



a b c

Fig. 1.
Disturbances of the ossification of the phalanges.
a. ♂ 14 yrs. b. ♂ 15 yrs. c. ♂ 22 yrs.

have so far found that they are not at all invalids. The public outlay for the change of occupation has brought in very good returns.

Aetiology.—The question of aetiology of the H.M.E. is divided in two parts, the formal genesis and the aetiology in a restricted sense. As to the formal genesis, I consider the development of multipolar ossification of epiphyseal nuclei in necrosis-like destruction to furnish a

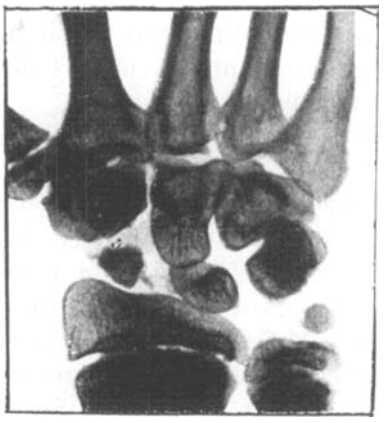
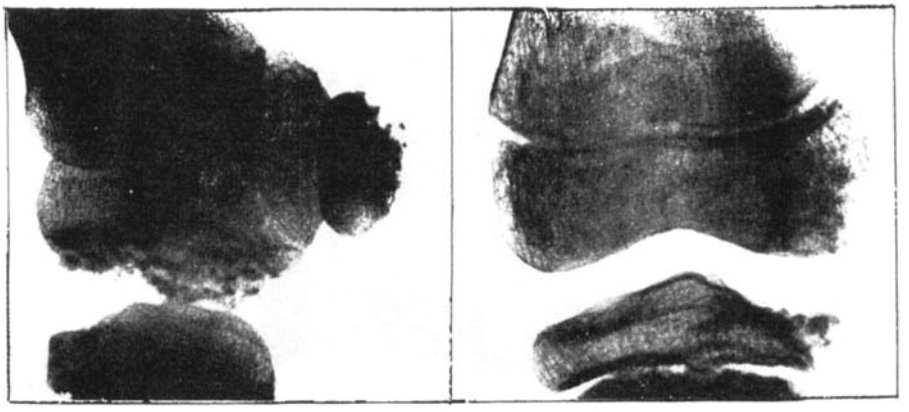


Fig. 2.
Disturbance of ossification of the scaphoid bone and free nucleus of proc. styl. ulnae in a boy aged 15.



a b

Fig. 3 a–b.
Multipolar ossification of the epiphysis of the lower end of femur, ♂ 11 yrs.

good illustration for the doctrine of Lehmann[11] of the constitutionally weak epiphysis. Normal cancellous bone is known to be an ideal structure to support the body weight, and it stands to reason that the gross disturbance of the spongy structure as seen in early stages of H.M.E. must reduce the supporting power of the bone. As to the aetiology in a restricted sense, the disease is a hereditary one; in my cases heredity

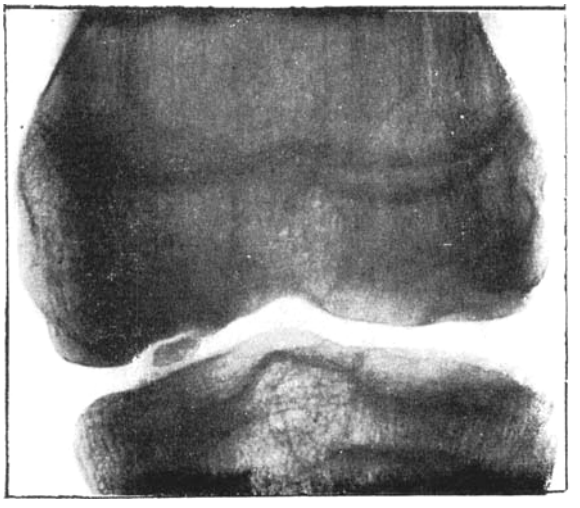


Fig. 3 c.
Osteochondrosis dissecans, ♂ 19 yrs.

[11] D. Zschr. f. Chir. 178. 1922.

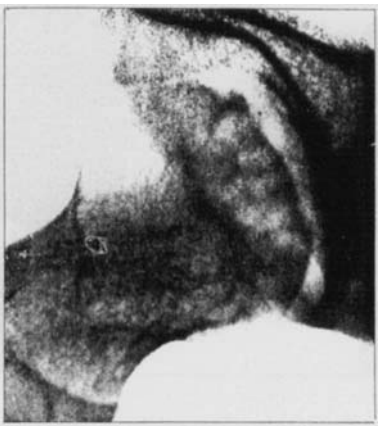
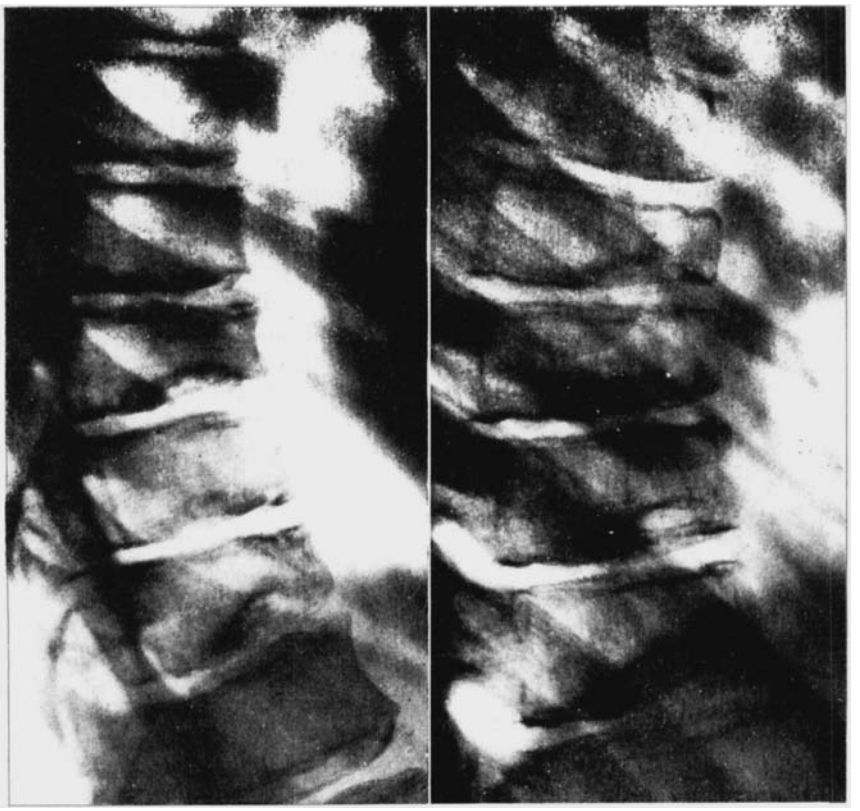


Fig. 4 a.
Destructive changes in the upper femur end, ♀ 19 yrs.

is recessive and parental consanguinity established. At the same time as I brought about a change of occupation I arranged for the patients to be transferred from the isolated residence of their family, and they have married persons from other parts of the country. This must be a fair prophylaxis for their descendants.

While studying the constitutional skeletal disease discussed here, I found during the early phases of the condition definite evidence of multilocular epiphyseal ossification and, in certain instances, pictures of full-grown epiphyses which roentgenologically and pathoanatomic-

Fig. 4 b.
Deformation of the outlines of the upper femur end and arthrosis deformans, ♂ yrs.



a b

Fig. 5.
Destructive changes and deformation of thoracic vertebrae.
a. ♀ 16 yrs. b. ♂ 23 yrs.

ally resembled the picture of Osteochondrosis dissecans (O. diss; cp. Fig. 3).

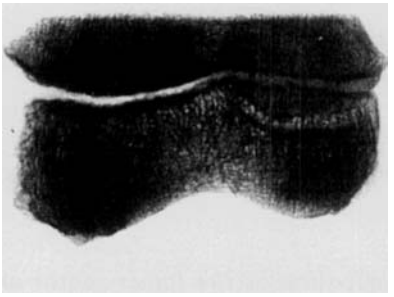
Even during normal epiphyseal ossification of the lower femur end multilocular ossification may be noted, viz. small osseous islets within the articular cartilage, outside the epiphyseal nucleus proper, and, frequently, a small, pit-like depression in the latter. These osseous islets are particularly apt to occur at typical sites, which are the areas of predilection of O. diss. The microscopical picture of these osseous islets is that of normal cancellous bone. They are probably supplied with blood by a terminal artery (Fig. 6).

Proceeding from the hypothesis that the constitutional factor in the

aetiology of the articular loose-body disease might be provided by these accessory centres of ossification, I studied the incidence of the osseous islets in a normal series of young subjects[12]. In 291 children, up to the age of 10, radiograms were taken of both knee-joints. In this series I studied the picture of detached osseous islets within the articular cartilage outside the epiphyseal nucleus proper, compared below with known facts about O. diss.

O. diss.	*Osseous islets.*
Much more common in men than women.	3–4 times more common in boys than girls.
Marked tendency towards bilateral involvement.	As a rule identical on both sides.
Typically located in the medial condyle of the femur.	Much more frequently found in the medial than in the lateral condyle of the femur.
Capitulum humeri 2:d typical localisation.	To be found also in capitulum humeri.
Primary bone necrosis.	Blood supply very likely through terminal artery.
Age at onset of symptoms generally 14–15 years.	Can be observed up to 10 years of age (later not visible but probably persisting for a few years).

In a schematic drawing the site of a large number of accessory ossification centres was indicated within the contours of an adult



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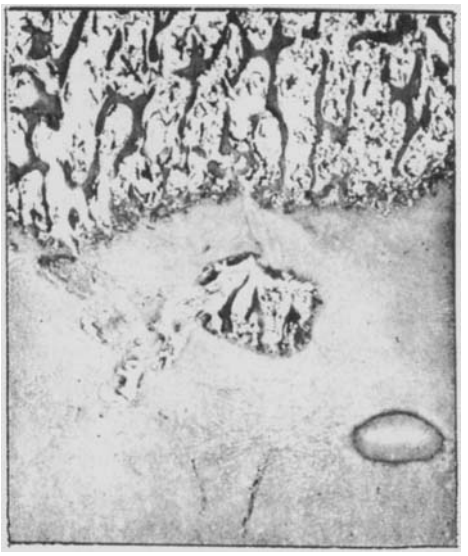

b

Fig. 6.

Accessory bone nucleus of the medial femur condyle in a specimen from a boy aged 5 without any signs of skeletal disturbance. a. radiogram of the specimen, b. photomicrograph of the nucleus.

[12] Acta radiol. 25, 1944.

subject's knee-joint (Fig. 7 a). As will be seen from this figure, in the first place the osseous islets situated most superficially should be suspected to give rise to O. diss. or, in other words, *those that occur comparatively late* in adolescence.

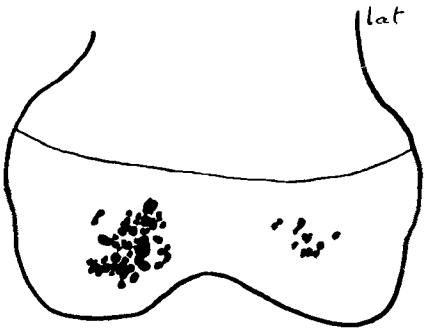

Fig. 7 a.
In the borderlines of an adult lower femur end the places of accessory nuclei in 291 children are indicated (with attention drawn to the accordance of the epiphyseal scar in the adult with the lower end of the femur metaphysis in children).

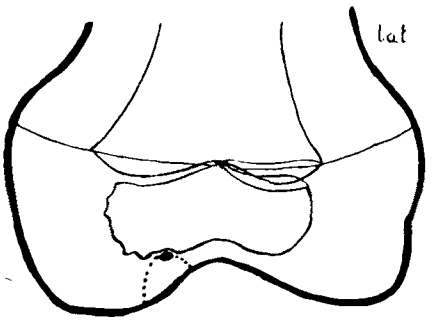

Fig. 7 b.
Borderlines of the lower femur end in a child and an adult respectivly, showing an accessory nucleus in the former. The dotted line indicates presumed growth of the nucleus.

Another schematic figure discloses that the matrix for the piece of bone which in the adult corresponds to the site affected by O. diss., actually is the place where detached osseous islets are common in childhood (Fig. 7 b).

I suppose that during a limited period of growth such osseous islets would remain more or less completely separated from the adjacent cancellous bone by strands and islands of persisting hyaline cartilage, and that this would be the case even at the age when O. diss. develops in most instances, viz. 14 to 15 years. Such an ossification centre would then constitute a *locus minoris resistentiae* to every kind of injury. In this age the epiphysis has come up to a size nearing its borders to the cartilaginous articular surface. Accordingly every injury produces a more localized effect on the osseous tissue than in the early stages of development when the whole bony nucleus is embedded in a thick layer of cartilage softening and dispersing the effect of a trauma. If the position of the demarcated piece of bone is but slightly changed its blood supply might be impaired and necrosis of the bone might ensue.

This theory was strongly supported when I demonstrated that islands and strands of hyaline cartilage are present on the deep side,

i.e. the side adjacent to the spongy bone of the epiphysis, of loose bodies surgically removed from the knee-joint[13].

Further support of my theory was derived from a case of O. diss. with a cartilaginous loose body in the joint, where *in addition to* the loose body a well-defined but not detached, *completely viable* cartilage-bone piece was at operation removed from the matrix, viz. obviously an early precursor of a loose body[14]. This case shows that *primarily there exists the viable, well-defined osseous nucleus, and that necrosis and demarcation will supervene at a later stage.*

Novotny[15] has pointed out that viable accessory bone nuclei in the femoral epiphysis may produce symptoms suggesting O. diss. In cases of this type he has observed roentgenological restitution and subsidence of clinical symptoms after treatment with a plaster cast continued for some time. Probably necrosis and demarcation have been prevented in these instances. In Novotny's opinion my theory as to the origination of O. diss. is supported by his experience. Green and Banks[16] have made similar observations.

Lacroix[17] has stated that the histologic structure of loose bodies indicates a disturbance of ossification; his interpretation, entirely independent of mine, tallies very closely with my theory.

Previously there was a gap in the argument for this theory, inasmuch as I had not *experienced a case of a viable, growing accessory bone nucleus until formation of a loose body took place.* Now I am able to close this gap:

A schoolgirl born in December, 1938, when first seen in June, 1948 at the age of 9½ complained of mild discomfort in the right knee, which had commenced three weeks ago. Save for slight pain at full flexion, physical examination failed to disclose any abnormalities.

The roentgenogram showed a subchondral depression in the cancellous bone at the typical site of O. diss. (Fig. 8). In the original roentgenogram a small osseous nucleus can be seen at this site. Four months later this nucleus had increased in size (Fig. 9).—I observed the development of the nucleus.

1½ years after the first examination it had still further increased.

After slightly more than 2 years it was found to occupy most of the condylar depression. Its structure was still that of viable spongy bone (Fig. 10).

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13 Acta radiol. *25*, 1944.

14 Ibid. *36*, 1951.

15 Acta orthop. scand. *21*, *1951* and Acta radiol. 37, 1952.

16 J. Bone a Joint Surg. *35 A*, 1953.

17 Rev. belge des Sci. med. *13*, 1941.

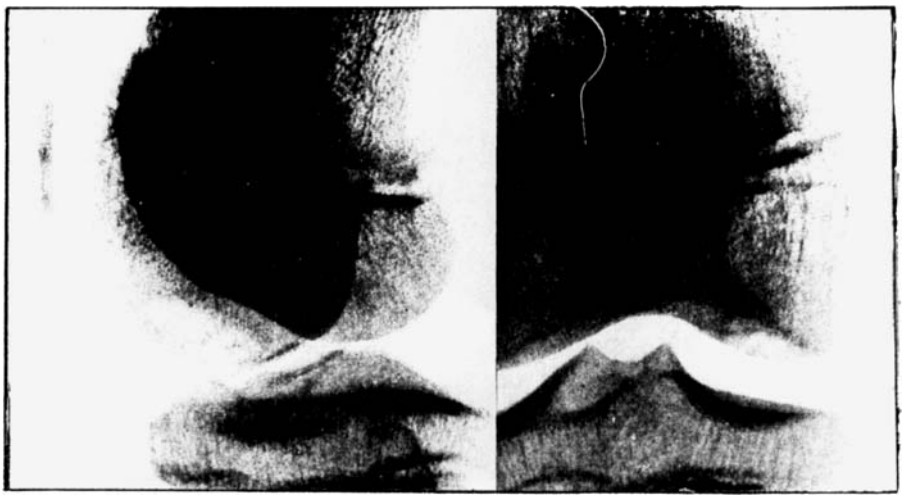

Fig. 8.
Development of Osteochondrosis dissecans (see the text).

3½ years after the first examination the bone nucleus had become compressed, fragmented, exactly like necrotic bone (Fig. 11).

During the whole period the patient attended school, participated in various games and gymnastics, and only occasionally experienced mild discomfort in the affected joint.

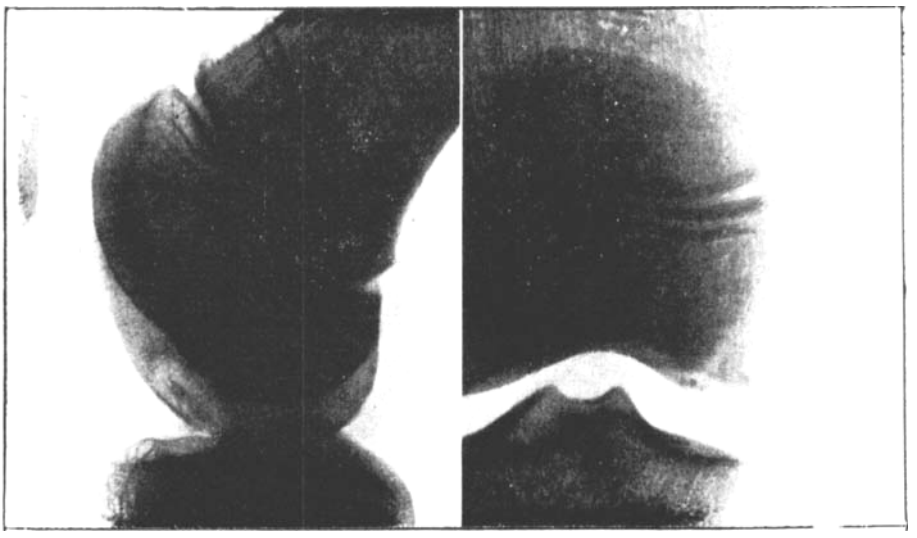

Fig. 9.
Development of Osteochondrosis dissecans (see the text).

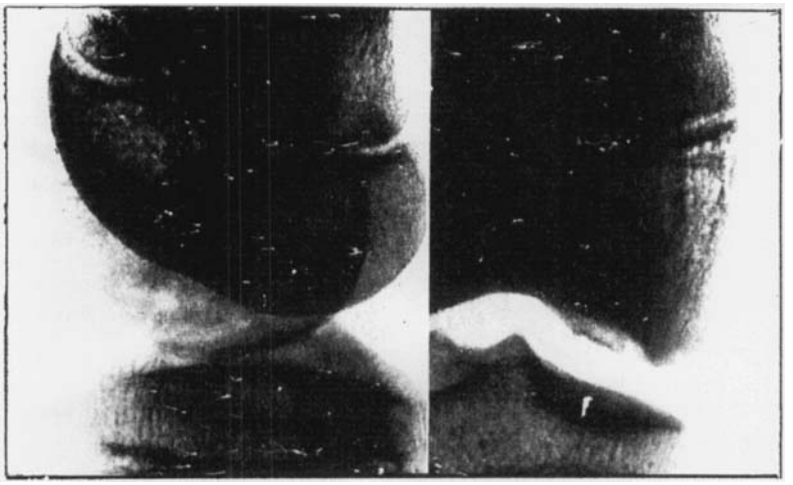

Fig. 10.
Development of Osteochondrosis dissecans (see the text).

In the spring of 1952, when I had observed the patient for 4 years, on a forced walking-tour her right knee became suddenly painful, and its motion was checked at semiflexion. Cautious attempts at moving the knee restored the use of the joint, though full extension was impossible for a couple of days. Subsequently the patient when sitting

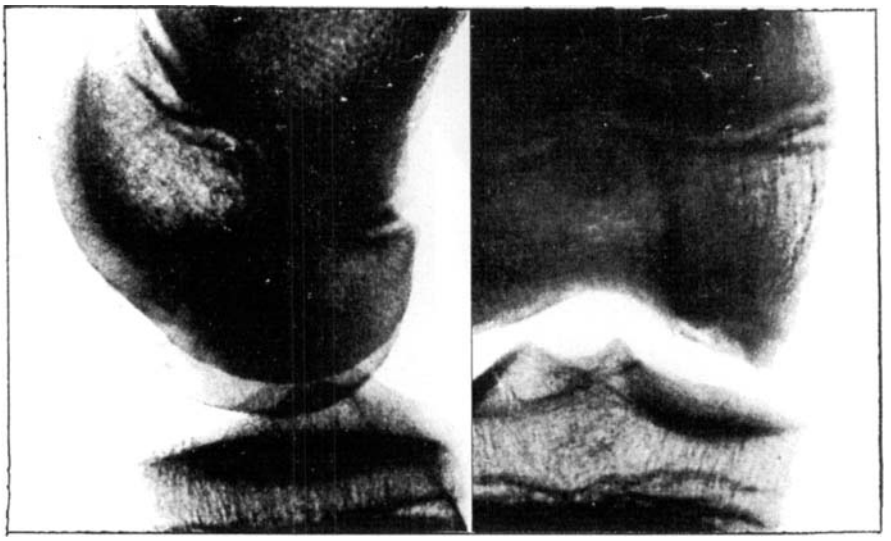

Fig. 11.
Development of Osteochondrosis dissecans (see the text).

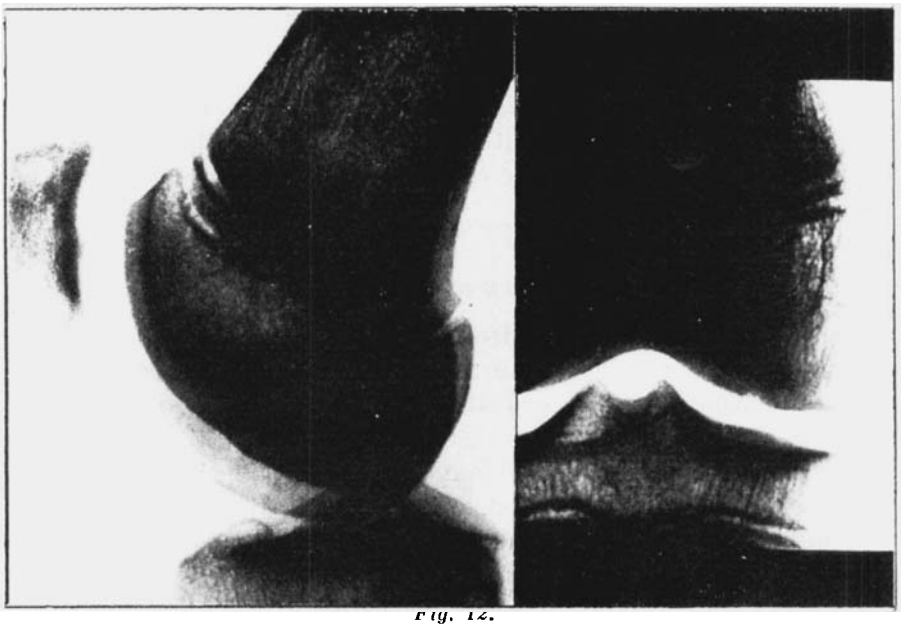

Fig. 12.
Development of Osteochondrosis dissecans (see the text).

with flexed knees sometimes felt that a node emerged on the lateral aspect of the knee. This node disappeared on extension of the leg. I examined the patient six months after the incident. At that time the outline and structure of the femoral condyle had commenced to regain their normal appearance, and the suprapatellar bursa contained a loose body. After some time this body was removed and showed microscopically the typical picture of O. diss. At re-examination in August 1954 the knee-joint was quite normal, and the girl took part in sports and gymnastics. In another radiogram no pathological alterations were visible.

In my opinion this case furnished additional evidence in favour of the theory advanced by me in 1937 and thus summarized:

The aetiology of Osteochondrosis dissecans is complex; it is both constitutional and traumatic. An accessory bone nucleus, detached in childhood, during adolescence partly fuses into the adjacent cancellous bone and partly remains separated from the latter by islands and strands of persisting cartilage. There is an incomplete collateral connexion between the vascular system of the bone nucleus and that of the vicinity. This bone nucleus constitutes the locus minoris resistentiae which enables mild injury or strain—perhaps even within the range of

normal function to produce a slight dislocation with deleterious action upon the blood supply of the bone nucleus.

The advantage of this theory versus all others that deal with the actiogenesis of O. diss. is, that it provides a logical explanation of the collected evidence relating to the clinical and patho-anatomical aspects of this condition.

SUMMARY

The actiology of Osteochondrosis dissecans is complex; it is both constitutional and traumatic. An accessory bone nucleus, detached in childhood, during adolescence partly fuses into the adjacent cancellous bone and partly remains separated from the latter by islands and strands of persisting cartilage. There is an incomplete collateral connexion between the vascular system of the bone nucleus and that of the vicinity. This bone nucleus constitutes *the locus minoris resistentiae* which enables mild injury or strain—perhaps even within the range of normal function—to produce a slight dislocation with deleterious action upon the blood supply of the bone nucleus.

RESUME

L'étiologie de l'ostéochondrose disséquante est complexe; elle est à la fois constitutionnelle et traumatique. Un noyau osseux accessoire, délivré durant l'enfance qui s'est au cours de l'adolescence en partie réuni dans l'os adjacent reste en partie isolé de celui-ci par des îlots et des cordons de cartilage persistant. Il y a une connexion collatérale incomplète entre le système vasculaire du noyau osseux et celui de l'entourage. Le noyau osseux constitue le locus minoris resistentiae qui fait qu'une légère lésion ou surmenage – peut-être même dans le cadre d'une fonction normale – produit une légère dislocation avec action délétère sur l'apport sanguin du noyau osseux.

ZUSAMMENFASSUNG

Die Ätiologie der Osteochondrosis dissecans ist eine zusammengesetzte. Die Ursachen sind konstitutioneller und traumatischer Natur. Ein akzessorischer, im Kindesalter abgegrenzter Knochenkern verschmiltzt im jugendlichen Alter teilweise mit dem benachbarten spongiösen Knochen, teilweise jedoch verbleibt er abgetrennt von demselben durch Inseln und Züge von zurück-bleibendem Knorpel.

Es besteht eine unvollständige kollaterale Verbindung zwischen dem Gefässsystem des Knochenkerns und dem seiner Umgebung. Dieser Knochenkern stellt den *locus minoris resistentiæ* dar, durch den selbst geringe Schäden oder Überanspruchungen-möglicherweise sogar innerhalb des normalen Funktionsbereiches-eine leichte Verschiebung mit nachteiligen Folgen für die Blutversorgung des Knochenkernes hervorrufen können.