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THE REACTION TO MECHANICAL TRAUMA IN GROWING ARTICULAR CARTILAGE

An experimental study on rabbits and a comparison of the results with the pathological anatomy of osteochondritis dissecans

BY

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To my Wife

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Helsingfors, November 1961.

Gustav Tallqvist

INTRODUCTION

In 1955, A. LANGENSKIÖLD published a paper called »Can Osteochondritis Dissecans Arise as a Sequel of Cartilage Fracture in Early Childhood?». It was an experimental study based on a series of 12 rabbits. By surgical intervention at an early age a mechanical lesion of the cartilage of the medial femoral condyle was induced, and some 100 days later the radiological and histological findings resembled to such a degree those of osteochondritis dissecans that the hypothesis cited above seemed to be justified.

The experimental lesion of the knee joint was described as follows: »With a small sharp scoop a fragment of cartilage 1 by 2 by 2 mm in size was gouged from the medial condyle so that it remained attached to the femur only by a narrow bridge of synovial tissue near the edge of the intercondyloid fossa. This fragment consisted of pure cartilage and the concavity produced in the joint cartilage did not reach the epiphyseal bony nucleus». The results were described in the following way: »Ten animals were killed after a period varying between 33 and 116 days after operation. In eight of these, a typical joint-mouse containing a bony nucleus surrounded by cartilaginous tissue was found. — — — The diameter of the joint-mice was about twice that of the original cartilage fragments separated at operation. — — — Seven joint-mice produced experimentally and containing bone were examined histologically. — — — the bony nucleus in each of them was entirely surrounded by a cartilaginous layer. The layer facing the joint cavity was considerably thicker than that facing the concavity. The structure of the former layer was fairly regular and similar to normal joint cartilage, the latter being irregular and consisting in part of fibrocartilage. The concavity was lined with a layer of irregular connective tissue or fibrocartilage. The bone tissue and the marrow of two of the joint-mice seemed necrotic, while the others contained living bone and marrow. There were abundant rests of cartilaginous tissue in the bony nuclei.» Furthermore, LANGENSKIÖLD found that »the fragment grows at about the same rate as the condyle and it maintains its shape and function as a part of the condyle».

The relevant literature is of little help in attempting to account for the phenomenon described above. DANIS & LABARRE (1957) took a piece of fibrous cartilage from fracture callus and implanted it into the anterior chamber of the eye of rat, where the fragment ossified. SEGGEL (1904) and LACROIX (1959) reported similar results with articular cartilage implanted into the eye, under the renal capsule or into the peritoneal cavity.

On the other hand, LANDELLS (1957) stated that »cartilage may live, grow and calcify (but not ossify) when completely detached from the bone, provided it has free access to the synovial fluid».

There is no evidence of cartilage ossifying without preceding vascularization. TRUETA (1958) suggested that the osteoblasts are developmental forms of the endothelial cells of the capillaries.

An attempt, therefore, at elucidating the mechanism of the phenomenon described by LANGENSKIÖLD necessitated a study of the vascularization of the piece of cartilage. The fragment had been detached except for a narrow bridge of synovial tissue. Did vascularization of the loose body take place via this piece of tissue? Were there any other routes by which the invasion of capillaries was possible? To what extent was the reference to osteochondritis dissecans made by LANGENSKIÖLD justified? Did he only demonstrate a close resemblance between two phenomena which were independent of each other? Or is it possible to contribute to the clarification of the genesis of osteochondritis dissecans by studying in detail the phenomenon described by LANGENSKIÖLD?

The purpose of the present study was to throw further light on the mechanism and conditions of the phenomenon described by LANGENSKIÖLD and, if possible, to answer the questions posed above.

SURVEY OF THE LITERATURE

The embryology of cartilage

When cartilage develops from mesenchymal tissue, the star-shaped anastomosing cells of the latter grow and the connecting cellular processes become shorter. The intercellular substance diminishes and finally disappears, so that the cells form a syncytium. In this, the cytoplasm adjacent to the nuclei changes into cartilage cells, while the remaining mass of the syncytium develops into the matrix or ground substance of the cartilage. By growth of the ground substance the cartilage cells are pushed farther and farther apart, and between the cells collagen fibrils are formed in the matrix. The latter is saturated with chondrin and thus assumes a uniform structureless appearance. The cartilage cells divide and form small groups of cells. Between the cells in the groups, too, ground substance develops so that the cells are pushed apart. This mode of growth is called intussusception. When the cartilage is surrounded by connective tissue, it also grows by addition of new layers of tissue, which is called appositional growth (BROMAN & HÄGGQVIST 1945).

Vascularization and ossification of the epiphyses

With regard to the vascularization and ossification of the foetal epihyses there is no essential developmental difference in the rabbit, rat, guinea-pig and man (STUMP 1924). Initially, the foetal epihyses consist solely of cartilage. During the second third of foetal life they are invaded by primitive connective tissue (STUMP 1924), which together with blood vessels penetrates into the cartilage through canals before ossification begins (WATT 1928, HAINES 1933, HURRELL 1934, RING 1955). »During the first 2 days after birth the cartilage canals are still vascular, but sections on the 3rd day show that the canals are occupied by proliferating connective tissue and no erythrocytes can be seen» (RING 1955). RING believed that the ossification of the cartilage is due to the invasion of new vessels from the perichondrium,

when the vascularity of the old cartilage canals has decreased and the nutrition of the surrounding cartilage has been disturbed.

Enchondral ossification is similarly described by most writers, and the course is the same in the diaphyses and epiphyses of the long bones as in the short bones. »The ossification of the epiphyses of the long bones develops in all respects as though it were an independent bone, and the process is exactly similar to that found in the short, irregular bones such as the tarsals and carpals» (WATT 1928). Ossification is preceded by typical structural changes in the centre of the cartilaginous epiphysis. The cartilage cells increase in size, and vacuoles develop in their peripheral cytoplasm. The nuclei swell and lose some of their chromatin. The matrix surrounding these cells decreases in volume. According to many authors, blood capillaries now penetrate from the periphery of the epiphysis (BROMAN & HÄGGQVIST 1945, BENNINGHOFF 1949, RING 1955, HAM 1957, MAXIMOW & BLOOM 1958, TRUETA 1958). The matrix surrounding the hypertrophic cartilage cells calcifies and the cells die. The resulting cavities are invaded by capillaries, primitive bone is deposited at the walls of the cavities, and by the course of development, spongy bone is formed. Thus, a bony nucleus develops which grows concentrically.

In the new-born child the cartilage of the distal femoral epiphysis is supplied by vessels, some of which penetrate along the margins of the condyles and anastomose with each other in the cartilage of the condyles. The centre of the epiphysis is supplied by vessels running near the site of the future epiphyseal plate. This vascular pattern is maintained in adult life (CROCK 1960). In the adult rabbit the corresponding vessels are similarly arranged (BROOKES & HARRISON 1957). It may be assumed that the pattern is the same in the new-born rabbit (MORGAN 1960).

The skeletal development of the rabbit as compared with that of man

HEIKEL (1960) stated that »both man and the rabbit have at birth or shortly after, a radiologically demonstrable nucleus in the distal femoral epiphysis and the proximal tibial epiphysis, but in no other epiphysis. It may therefore be concluded that they are both born at almost the same skeletal age». Hence, the rabbit seems to be a suitable laboratory animal for experiments involving the distal femoral epiphysis. The whole growth period of the rabbit, to the time of final ossification of the epiphyseal plates, covers

some 225 days. After the age of 150 days, however, growth is slight (HEIKEL 1960). For practical purposes, therefore, the first 150 days of life may be regarded as covering the growth period of the rabbit.

Anatomy of the articular cartilage

In the adult, articular cartilage has a typical structure, the collagen strands in the matrix forming arches placed at right angles to the joint surface. The cartilage cells, too, arrange themselves in incomplete rows following the same pattern. The system of collagen fibrils in articular cartilage is a direct continuation of the collagen fibrils in the periosteum. Nerves and blood vessels are lacking in adult articular cartilage (BENNINGHOFF 1949, HAM 1957, MAXIMOW & BLOOM 1957).

Nutrition of the articular cartilage

The articular cartilage is believed to be supplied in part by the subchondral blood vessels, in part by the synovial fluid (STRANGEWAYS 1920, MOORE 1948, INGELMARK & SÄÄF 1948, HIRSCH 1951, BAILEY & SELLE 1959). Direct contact between the subchondral marrow cavities and the basal parts of the articular cartilage was demonstrated by HOLMDAHL & INGELMARK (1951). Since the points of contact were more numerous where the articular cartilage is not normally exposed to great pressure and less numerous where greater pressure is exerted, the writers concluded that compression may be a factor of significance in the transportation of fluid to and from the articular cartilage. Similar views were expressed by GIBSON (1955).

Regressive changes in cartilage

The following four phenomena are generally accepted as signs of decreased vitality in cartilage: a) vacuolization and accompanying hypertrophy of the cytoplasm in the cell, b) decreased or suspended stainability of the nuclei of the cells, which initially may be of normal size and shape, but later become pyknotic, c) calcium deposits in the matrix, d) formation of parallel fibres in the ground substance, which have nothing in common with the collagenous fibres of the cartilage (asbestos transformation). Simultaneously

with the last-mentioned phenomenon, the development of cavities in the cartilage, and formation of cartilage in these, have been observed (MAXIMOW & BLOOM 1958).

The regenerating capacity of cartilage

It is generally believed that after a section or the creation of an excision defect in hyaline cartilage in adult mammals, regeneration originating in the cartilage itself does not occur (BENNINGHOFF 1949, MAXIMOW & BLOOM 1958). If the cartilage is surrounded by perichondrium, the latter produces connective tissue, which is converted into more or less imperfect hyaline cartilage (BENNINGHOFF 1949, RAO 1954, GIBSON 1955, BRIZZI 1959). Regeneration of cartilage originating in the perichondrium was observed by HESS (1955), who induced an experimental fracture of the spinal column of guinea-pig foetuses *in utero*.

According to some writers, however, a section or excision defect in cartilage lacking a perichondrium heals, though slowly and incompletely. SHANDS (1931) stated that the healing of such lesions passes through the following stages: a) fibrin, b) granulation tissue, c) connective tissue, d) cartilage cells in connective tissue, e) fibrous cartilage and f) hyaline cartilage. Similar observations have been reported by other writers, *e. g.* GIES (1883), FISHER (1922), SCHMIDT (1924), BENNET, BAUER & MADDOCK (1932), BENNET & BAUER (1935), BENNINGHOFF (1949) and BUCHER (1955). Regarding the question as to whether the healing results in fibrous or hyaline cartilage, opinions differ. FISHER (1922) found that healing was more pronounced when the lesion was situated near the margin of the joint surface than when the centre of the joint surface was affected.

A section or excision defect in articular cartilage involving the subchondral bone has been shown to run through a similar, but more rapid, process of healing (GIES 1883, FISHER 1922, SCHMIDT 1924, SHANDS 1931, BENNET, BAUER & MADDOCK 1932, NAGURA 1937). In this case an invasion of connective tissue from the marrow cavities of the subchondral spongy bone takes place. The connective tissue in the deeper parts of the defect is converted to bone, while the connective tissue nearer the surface remains at the stage of fibrous cartilage. After making an incision in articular cartilage and subchondral bone in growing rabbits NAGURA (1937) observed complete healing of the cartilage and the development of cartilage callus (Knorpelkeimgewebe) subchondrally. Later, the callus underwent slow enchondral ossifica-

tion. A similar course was observed when an infraction of the subchondral bone was created and the articular cartilage was left intact (NAGURA & KOSUGE 1938, BURCKHARDT 1948).

The reaction of cartilage to transplantation

It is a common observation that cartilage, when transplanted, maintains its vitality longer than other tissues (SEGGEL 1904, AXHAUSEN 1912, RAO 1954, HAM 1957, BALLANTYNE & CONVERSE 1958, BAXTER, GOLDSTEIN & MCMILLAN 1958, CRAIGMYLE 1958, DE PALMA 1960). It has been reported that mitoses do not occur, but that the cells nevertheless remain alive (HAM 1957, BALLANTYNE & CONVERSE 1958). The criteria generally accepted for vitality of cartilage are normal stainability, shape and size of the cartilage cells and their nuclei, and normal stainability and structure of the matrix. The capacity of cartilage for surviving transplantation has been attributed to its slow metabolism (BYWATERS 1937, HAM 1957). It has been observed that cartilage which normally does not ossify in its original site, does not ossify after transplantation, either. By contrast, foetal joint cartilage, or cartilage taken from fracture callus, ossifies when implanted into the eye or under the renal capsule in laboratory animals (DANIS & LA BARRE 1957, LACROIX 1959). GIES (1882) implanted embryonic cartilage into the knee joint of dogs and observed in one case that the fragment was surrounded by connective tissue peripherally and degenerated centrally, in another case that the fragment was completely resorbed. SEGGEL (1904) excised a piece of articular cartilage from the femoral condyle of young rabbits (weighing under 2 kg) and implanted it into the peritoneal cavity. He observed that the graft was converted into bone tissue. RAO (1954) took a piece of cartilage from the xiphisternum of 6-month-old rats and implanted it into the peritoneal cavity. In one case out of 48 the graft was in part converted into osteoid tissue.

Experimentally created joint-mice

A large number of studies have been reported involving the experimental production of joint-mice. The results have been largely similar.

When a piece of cartilage is mechanically detached from the joint surface without injuring the subchondral bone, the fragment is either resorbed, or reunites with the joint capsule, or it is later found as a loose body in the joint cavity (GIES 1882, HILDEBRAND 1896, STRANGEWAYS 1920,

BENNET, BAUER & MADDOCK 1932). Initially, the piece of cartilage seems to maintain its vitality, but later it shows degenerative changes. Although the fragment, when it unites with the joint capsule, is surrounded by vascular connective tissue, it is not invaded by blood vessels, nor does it ossify (BENNET, BAUER & MADDOCK 1932).

When a piece of cartilage together with a piece of underlying bone tissue is mechanically separated from the joint surface, the fragment unites with the site from which it has been detached, or it unites with the joint capsule or with that part of the joint which is not lined with cartilage (BARTH 1898, CORNIL & COUDRAY 1905, RIMANN 1905, AXHAUSEN 1923, SCHMIDT 1924). In certain cases the fragment is completely resorbed. The investigations cited above were all performed on adult or nearly adult animals.

Certain other experiments performed on articular cartilage

According to NAGURA (1937) and BURCKHARDT (1948), a growing individual differs from an adult with regard to the reaction of the articular cartilage and the subchondral bone to incision. These writers used 15- to 49-day-old rabbits. Their experimental techniques and results were broadly speaking similar. After incision of the articular cartilage and the underlying bone NAGURA reported complete healing of the cartilage. The cleavage in the subchondral spongy bone was filled with a cartilage-like tissue, which showed a tendency towards enchondral ossification. This process was strikingly slow, and several months after operation, changes in the surroundings of the lesion were still going on.

REHBEIN (1950) subjected the distal femoral epiphysis in adult dogs to repeated blunt trauma. During an observation time of 48 days the injured site exhibited an area of necrotic bone and cartilage limited by a streak of vascular, loose tissue. Proximal to this streak, osteoblasts were seen in large numbers, and distally there was extensive resorption of the bone tissue. Radiologically, the findings resembled osteochondritis dissecans.

Certain features of the pathological anatomy of osteochondritis dissecans

The macroscopic finding. On gross inspection of the joint surface the findings may be completely negative (KROH 1928), or there may be an area of the joint surface differing from the surrounding tissue in that it exhibits

a paler, yellow-white colour or may yield elastically to pressure (COLVIN 1920, LEHMANN 1923); or it may be relatively raised (KROH 1928, KING 1932). The affected area may be bounded by a shallow score in the joint surface or by a cleavage, which more or less completely surrounds and separates it from the surroundings and from the underlying tissues (COLVIN 1920, LEHMANN 1925, KROH 1928). In the latter case a fragment of cartilage or of cartilage and bone is found in a concavity of corresponding size. The fragment may adhere to the concavity by a bridge or a hinge of intact articular cartilage, connective tissue or bone tissue (LEHMANN 1925, KING 1932, DE PALMA 1955). The fragment may, alternatively, be found as a loose body in the joint, in which case fragment and concavity seldom correspond to each other with regard to shape. Growth of the separate fragment *in situ* has been observed radiologically by certain writers (FREIBERG 1923, SCHELLER 1960, LACROIX, FIEVEZ & CAMBIER 1961, LANGENSKIÖLD unpublished observations), while others have found that the fragment grew when it was a loose body (PHEMISTER 1924, DE PALMA 1955).

Microscopic findings. A concavity in the subchondral zone of the bone is typical of osteochondritis dissecans. As a rule, a piece of bone is found in the concavity, separated from the epiphyseal bone by connective tissue or by cartilage. The latter may be fibrous (RIBBING 1951) or hyaline (LEHMANN 1923), and it may be completely or partially divided by a cleavage into a layer lining the concavity and another lining the corresponding surface of the fragment. In certain cases the cleavage reaches a point just under the joint surface (LEHMANN 1925), in others it includes the joint surface. As a rule, fibrous cartilage is found on both sides of the cleavage (FAIRBANK 1933), but hyaline cartilage (NEUMAN & SUTER 1918, LEHMANN 1923, BIANCHI, GOIDANACH & ZANASI 1955), vascular connective tissue (KIRSCHNER 1909, COLVIN 1920, KAPPIS 1920, STÖREN 1934), young cartilage (LACROIX 1941) and islands of hyaline cartilage in fibrous cartilage (LEHMANN 1925) have also been observed. According to the majority of writers the bone tissue in the separate fragment is necrotic, particularly when the fragment is a loose body in the joint (MARTENS 1899, BOERNER 1903, KIRSCHNER 1909, LEB 1924, LEHMANN 1925, ROMBOLD 1936, BIANCHI, GOIDANACH & ZANASI 1955, SMITH 1960). In a fragment retained in its concavity, many investigators have observed living bone, or living bone together with necrotic bone (BARTH 1898, MARTENS 1899, BOERNER 1903, KAPPIS 1917, FISCHER 1921, LEHMANN 1925, KING 1932, FAIRBANK 1933, LINDEMANN 1957, LACROIX, FIEVEZ & CAMBIER 1961). Furthermore, the centre of the fragment has been reported to exhibit osteoid tissue (KROH

1928, FAIRBANK 1933), living bone marrow and erythrocytes (LEHMANN 1925). In cases showing a direct connection between the fragment and the bone tissue of the concavity, osteoblasts and osteoid tissue have been observed in the proximity of this bridge, while the bony nucleus has otherwise been necrotic. In addition, islands of hyaline cartilage in the bony nucleus of the fragment have been observed (LEHMANN 1925). Many writers have observed that the bone trabeculae in the fragment are thicker and the marrow cavities narrower than in the surrounding subchondral bone (LEHMANN 1925, BIANCHI, GOIDANACH & ZANASI 1955, and others). The part of the fragment facing the joint usually consists of hyaline cartilage with a normal structure and living cells (KIRSCHNER 1909, WEIL 1921, LEHMANN 1925, ROMBOLD 1936). Only occasionally does it exhibit regressive changes (PHEMISTER 1924). A common observation is that this hyaline layer of cartilage is not equally thick throughout, but increases in thickness at the periphery of the fragment, thus forming a frame around the underlying bony nucleus (LEB 1924, LEHMANN 1925, LACROIX 1941, BIANCHI, GOIDANACH & ZANASI 1955). LACROIX (1941) showed that the cartilage cells in this marginal area are arranged in parallel with the cleavage surrounding the fragment.

In cases where the fragment is completely detached from the concavity, the margins of the latter are rounded, and in later stages the concavity itself is filled with fibrous cartilage, which is ossified deeper down (KROH 1928, FAIRBANK 1933).

MATERIAL AND METHODS

The material consisted of a total of 114 rabbits aged one to 12 days, divided into five series including 16—40 animals each. In each series the animals were operated upon in a way which was typical of the series. The animals were sacrificed, one at a time, at various intervals up to an age of 102 to 200 days.

General operative technique. Under aseptic conditions arthrotomy of the right knee joint was performed under local anaesthesia (0.25 per cent Xylocain), while the left knee was left intact as control. A longitudinal, ventral skin incision was made and the joint was opened by parapatellar approach. The patella and the quadriceps tendon were dislocated in the lateral direction, and the joint surface of the medial condyle was exposed by flexion of the joint.The operation was performed on the articular cartilage of the medial condyle, and the resulting lesion was carefully measured. Operation and measurement were performed using a binocular preparation microscope and magnification 4—25 xx, which enabled measurement to the nearest 0.1 mm. Then the joint was closed in layers with catgut. No dressing was applied. Infection developed in two cases, which were omitted from the report.

Method of investigation. Post-mortem, the knee joints were cautiously opened. All noticeable deviations from the normal control side were *measured* and *photographed* using the above-mentioned preparation microscope. In addition, both femora were freed from all soft parts and *roentgenograms* were taken in at least two planes at right angles to each other. After fixation in neutral formalin and decalcination in EDTA (ethylenediaminetetraacetic acid) the preparations were embedded in paraffin and sectioned at 5 μ in either the frontal or the sagittal plane. The sections were stained with haematoxylin and van Gieson. Sectioning was performed in an incomplete series throughout the preparation, which rendered *histological examination* of all parts of the specimen possible.

The following operations were performed in the different series:

Series A »large fragment». With a small sharp scoop a fragment of cartilage

was partially detached from the medial femoral condyle so that the border of the condyle facing the intercondyloid fossa was left intact. Thus, a small »hinge» of cartilage and ligament tissue was left between the fragment and the femur (Fig. 1, page 25). Fig. 2, page 25, is a roentgenogram and a corresponding contour drawing of the femur of the animal in the antero-posterior projection. The dotted line in the drawing indicates the outline of the cartilage and shows how the fragment was detached (arrow). In this series the fragment was 1.4—1.8 mm thick and included the whole breadth of the condyle in the plane of the joint surface.

The series consisted of 20 animals operated upon at an age of 5 to 11 days and sacrificed at different intervals up to an age of 102 days.

Series B »small fragment». The same operation was performed as in series A, but in this series the thickness of the fragment was only 0.7—1.2 mm (Fig. 38, page 49). A similar bridge of tissue was left as in series A.

A total of 40 animals were operated upon at an age of one to 12 days and sacrificed at different intervals up to an age of 200 days.

Series C »hinge of ligament tissue». The technique was otherwise the same as in series A, but the cartilage was completely split so that the hinge consisted solely of ligament tissue attached to the margin of the cartilage (Figs. 62 and 63, page 65). The fragment was 0.5—1.0 mm thick and included only a part of the breadth of the condyle in the plane of the joint surface. After detachment the fragment was replaced in its concavity.

The series included 18 animals operated upon at an age of 7 to 8 days and sacrificed at different intervals up to an age of 200 days.

Series D »loose fragment». Using the same technique as in series A the fragment was completely detached from the joint cartilage of the medial condyle and replaced in its concavity. The fragment was made 0.3—1.1 mm thick and included only a part of the breadth of the condyle in the plane of the joint surface.

A total of 16 animals were operated upon at an age of 7 to 11 days and sacrificed at different intervals up to an age of 120 days.

Series E »intracartilaginous cleavage». A double-edged tiny knife-blade bent to the shape of a semicircle was inserted into the joint cartilage at the medial margin of the medial femoral condyle in the transverse direction towards the intercondyloid fossa. Thus a crescent-shaped canal was formed, which was concave to the surface and extended to near the joint surface in the portion of the cartilage facing the intercondyloid fossa. By rotating the instrument round its long axis the canal was then widened in the ventral and dorsal directions towards the joint surface. In this way a piece of joint carti-

lage with the shape of a crescent was separated from its surroundings, the most superficial layer of the joint cartilage excepted (Figs. 93 and 94, page 85). The piece was made about 1.0 mm thick and included the whole breadth of the condyle in the plane of the joint surface.

A total of 18 animals were operated upon at an age of 6 to 8 days and sacrificed at different intervals up to an age of 150 days.

RESULTS

In the following account of the results, cases are described which were typical of the postoperative development in the series in question.

Series A «large fragment«

Stage 1 (series A)

This is the situation immediately after operation. For details see page 21, and the opposite page, Figs. 1 and 2.

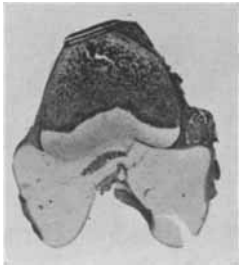


Fig. 1

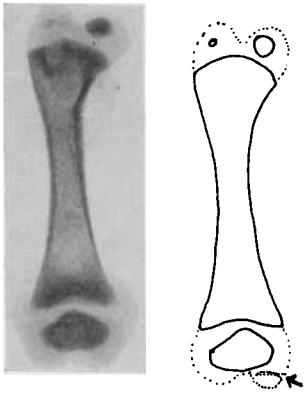


Fig. 2

Stage 2 (series A)

This stage is represented by an animal sacrificed 7 days after operation.

Microscopic findings. The fragment lies in a corresponding concavity, and the ossification of the epiphysis has proceeded almost to the bottom of this (Fig. 3). Fig. 5 shows that the cleavage between fragment and concavity is filled with loose, young granulation tissue with fibrin in the meshes and newly-formed capillaries. At the bottom of the concavity, a communication with the vessels of the ossified zone is seen (Fig. 4). At the medial margin of the fragment the cleavage is bridged by proliferating vascular connective tissue, originating in the perichondrium and penetrating between the fragment and the concavity (Fig. 6).



Fig. 3

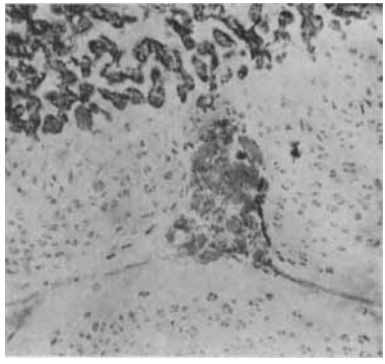


Fig. 4

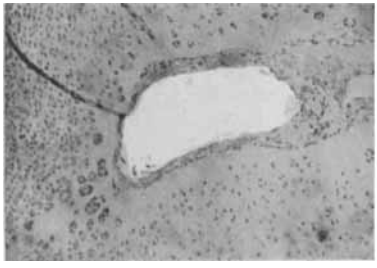


Fig. 5

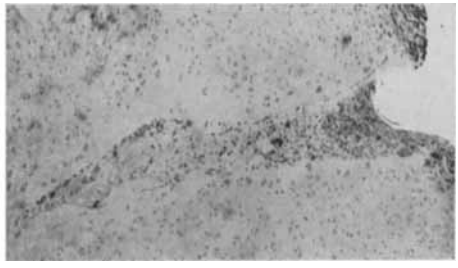


Fig. 6

Stage 3 (series A)

This stage is represented by an animal sacrificed 13 days after operation.

Microscopic findings. The fragment lies in a corresponding concavity. The ossification of the epiphysis has proceeded so far that in the zone of ossification, at the site of the lesion, a shallow concavity has developed, in contrast to the convexity seen in the intact lateral condyle (Fig. 7). The cleavage between fragment and concavity contains granulation tissue rich in cells, which particularly in the lateral part of the cleavage resembles primitive cartilage (Fig. 8). The granulation tissue is highly vascular, and the vessels anastomose with the vessels in the perichondrium of the medial side, the vessels in the intercondyloid fossa (Fig. 8) and the vessels in the marrow cavities of the ossified zone. From the granulation tissue in the lateral part of the cleavage a small protrusion surrounded by osteoid tissue penetrates into the cartilaginous mass of the fragment (Fig. 8). Another section shows a transverse vessel penetrating from the intercondyloid fossa into the lateral portion of the fragment. Apparently this vessel is not surrounded by osteoid tissue (Fig. 9). The medial portion of the cleavage is bridged by vascular connective tissue originating in the perichodrium.

The *roentgenogram* shows a shallow concavity in the outline of the subchondral bone of the operated medial condyle (Fig. 10).



Fig. 7

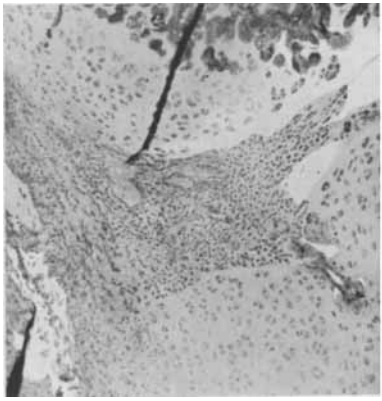


Fig. 8

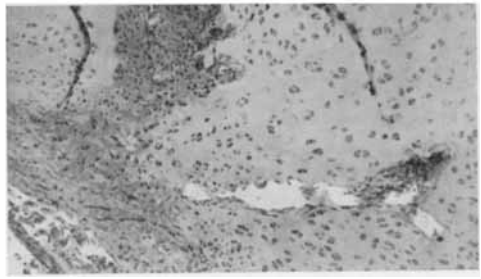


Fig. 9



Fig. 10

Stage 4 (series A)

This stage is represented by an animal sacrificed 16 days after operation.

Microscopic findings. The fragment lies in its concavity (Fig. 11). The concavity is separated from the subchondral zone of ossification by a thin layer of cartilage (Fig. 12). The cleavage between fragment and concavity is visible, and the innermost part of it is filled with vascular granulation tissue, rich in cells. The medial part of the cleavage is bridged by vascular connective tissue originating in the perichondrium. Within the cartilaginous mass of the fragment there is a small centre of ossification near the bottom of the concavity (Fig. 12). This ossific centre shows osteoid tissue and blood vessels which communicate with the vessels of the epiphyseal spongy bone via the vascular granulation tissue in the lateral portion of the concavity. Where the vessels penetrate the cartilage, minute osteoid trabeculae are seen.

The *roentgenogram* shows a concavity in the outline of the subchondral bone. At the bottom of the concavity there is a separate density in the cartilage shadow (Fig. 13).

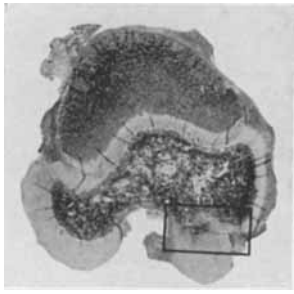


Fig. 11

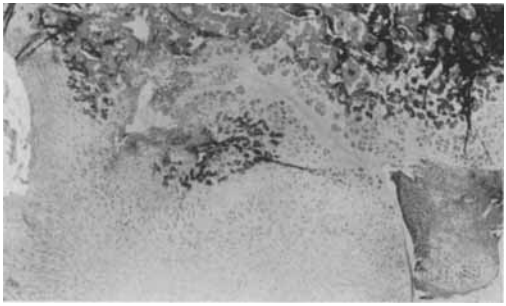


Fig. 12

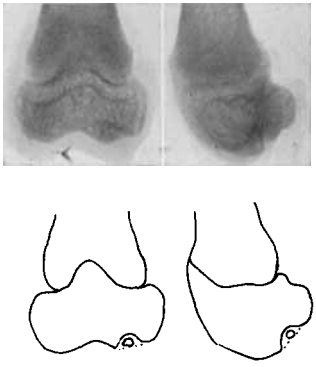


Fig. 13

Stage 5 (series A)

This stage is represented by an animal sacrificed 13 days after operation.

Microscopic findings. The fragment lies in its concavity (Fig. 14). Most of the cleavage between fragment and concavity is clearly visible and contains both vascular granulation tissue rich in cells and hyalinized connective tissue (Fig. 15). Medially the cleavage is bridged by vascular connective tissue originating in the perichondrium. The ossification of the epiphysis has proceeded so far that the hinge is in part ossified (Fig. 15). Within the cartilage of the fragment there is a separate centre of ossification with marrow cavities filled with blood vessels and connective tissue (Fig. 15). This separate ossific centre is supplied by blood vessels coming from the spongy bone of the epiphysis via the vascular granulation tissue in the cleavage (Fig. 15). In the cartilage adjacent to this vascular communication, osteoid tissue is seen.

The *roentgenogram* shows a concavity in the outline of the subchondral bone. At the bottom of the concavity a separate bone shadow is seen (Fig. 16).

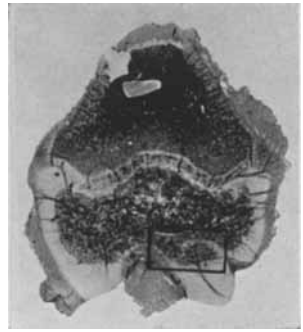


Fig. 14

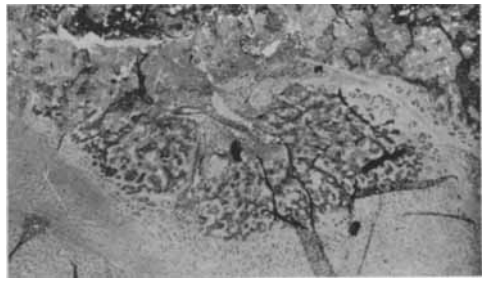


Fig. 15

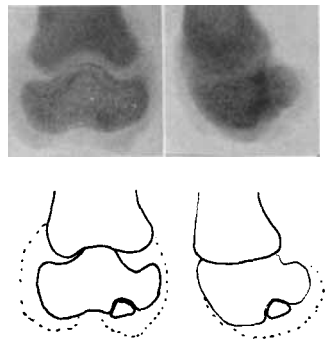


Fig. 16

Stage 6 (series A)

This stage is represented by an animal sacrificed 22 days after operation.

Microscopic findings. The fragment lies in its concavity. Ossification of the epiphysis has proceeded to near the concavity, and the spongy bone is separated from the latter by a thin layer of hyaline cartilage. In the zone of ossification a corresponding concavity is thus formed (Fig. 17). In the fragment a separate bony nucleus is seen, which has a biconvex shape in cross-section in the frontal plane. The centre of ossification is covered by hyaline cartilage, which is thick in the aspect facing the joint and thin in the aspect facing the concavity (Figs. 17 and 18). Most of the cleavage between fragment and concavity is visible. Medially it is bridged by dense connective tissue originating in the perichondrium. Laterally it is filled with primitive cartilage, which in some parts shows a gradual transition into older cartilage, while in other parts there is a clear line of demarcation (Fig. 18). The vessels in the separate centre of ossification in the fragment communicate with the vessels in the intercondyloid fossa. This communication runs through the cartilage of the hinge (Fig. 18). At the same site there is also a vascular connection with the epiphyseal spongy bone.

The *roentgenogram* shows a concavity in the outline of the subchondral bone of the medial condyle. In the concavity a separate bone shadow is seen (Fig. 19).



Fig. 17

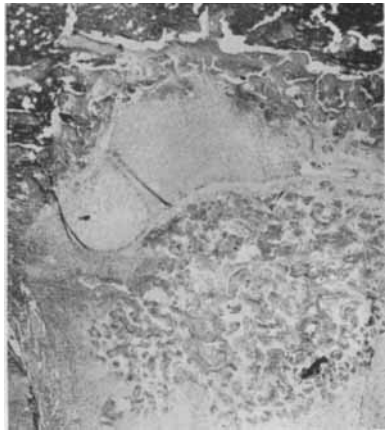
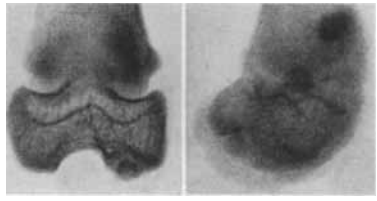


Fig. 18



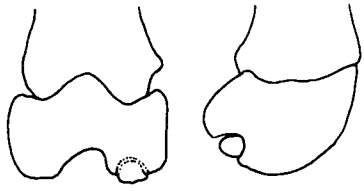


Fig. 19

Stage 7 (series A)

This stage is represented by an animal sacrificed 32 days after operation.

Microscopic findings. The fragment lies in its concavity. The central portion consists of living bone, which on the aspect facing the concavity is covered by a layer of hyaline cartilage. This is thicker than the corresponding layer of the lateral condyle (Fig. 20). Towards the concavity the bony portion of the fragment is covered by hyaline cartilage with cartilage cells in large clusters (Fig. 22). The bony portion of the fragment and the rest of the epiphyseal bone are united by the ossified hinge (Fig. 21). The cleavage is visible only partially. It contains hyaline cartilage rich in cells. In some parts this shows cystic degeneration, in others signs of ossification (Fig. 21).

The *roentgenogram* shows a concavity in the outline of the bone of the medial condyle. The concavity is completely filled by a separate bone shadow. At the bottom of the concavity the line of demarcation between the latter and the separate bone shadow is indistinct (Fig. 23).

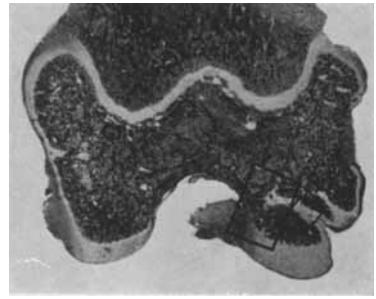


Fig. 20

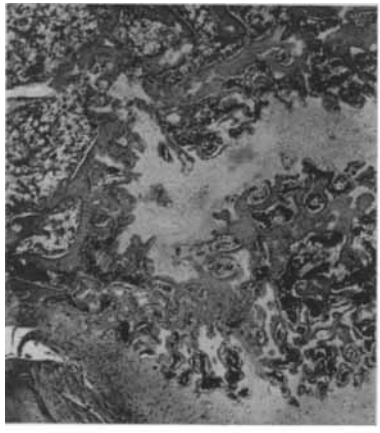


Fig. 21

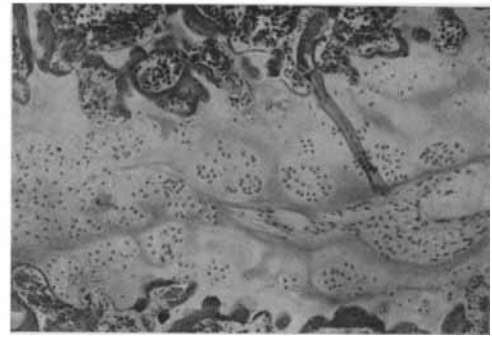


Fig. 22

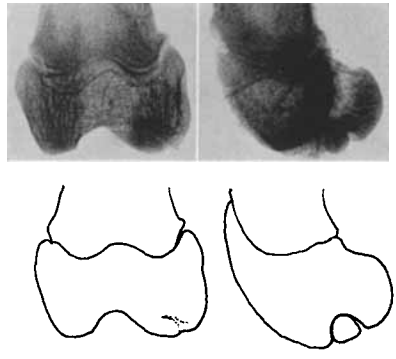


Fig. 23

Stage 8 (series A)

This stage is represented by an animal sacrificed 23 days after operation.

Microscopic findings. The joint cartilage of the medial condyle is thicker than that of the lateral condyle (Fig. 24). The bone of the medial condyle is penetrated by a transverse curved streak of cartilage and osteoid tissue (Fig. 25). In the continuation of this streak, near the aspect of the condyle facing the intercondyloid fossa, there is an island of hyaline cartilage within the spongy bone (Fig. 25, arrow). Medially the streak consists of a protruding wedge of two layers of hyaline cartilage with highly vascular granulation tissue between them (Fig. 25).

The *roentgenogram* shows a crescent-shaped indistinct line of demarcation crossing the bone of the medial condyle (Fig. 26).



Fig. 24



Fig. 25

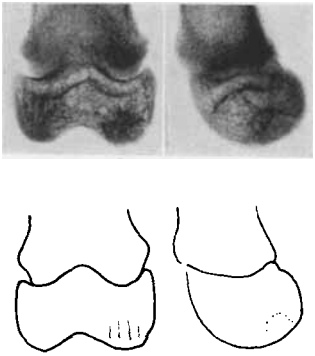


Fig. 26

Stage 9 (series A)

This stage is represented by an animal sacrificed 55 days after operation.

Microscopic findings. A section made in the sagittal plane shows at the site of the former cleavage between fragment and concavity a discontinuos streak of hyaline cartilage penetrating into the spongy bone (Fig. 27). At the site of the former cleavage in the plane of the joint surface there is a portion where the cartilage cells are irregularly arranged as compared with the structure of the adjacent cartilage (Figs. 28, 29 and 30). In the plane of the joint surface the border of the former fragment is in some parts even, in others it is characterized by a shallow indentation (Fig. 27). The streaks of hyaline cartilage which penetrate into the spongy bone show signs of enchondral ossification (Fig. 28).

The *roentgenogram* shows an incomplete line of demarcation between a concavity in the outline of the subchondral bone and a bone shadow filling this concavity (Fig. 31).

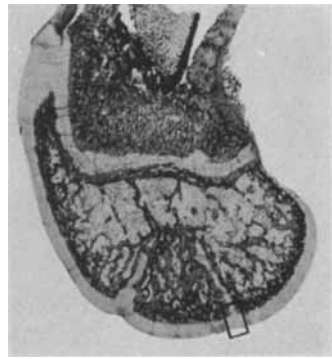


Fig. 27

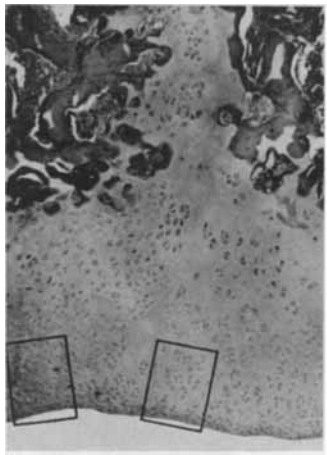


Fig. 28

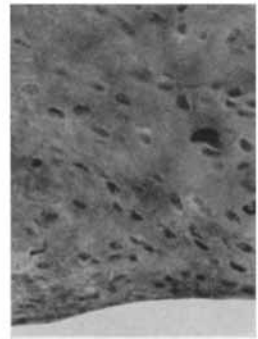


Fig. 29

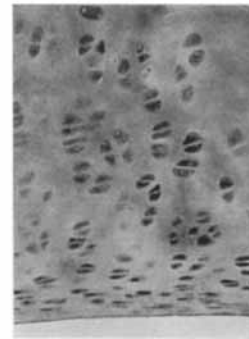


Fig. 30

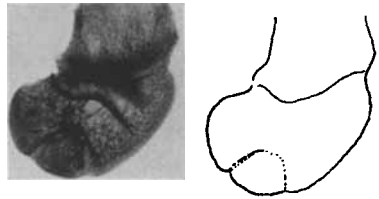


Fig. 31

Stage 10 (series A)

This stage is represented by an animal sacrificed 91 days after operation.

Microscopic findings. A section made in the sagittal plane shows that the structure of the subchondral bone is normal, in the main. At one site in the joint cartilage there is at right angles to the joint surface a cleavage, which penetrates for some distance into the subchondral spongy bone. The cleavage is lined with layers of hyaline cartilage, which become thinner towards the bottom of the cleavage. In these layers the cells are mainly arranged parallel with the cleavage and perpendicularly to the joint surface (Figs. 32 and 34). More ventrally, at the site of the former cleavage, there is joint cartilage with cells irregularly arranged, as compared with the adjacent cartilage, in which the cells are arranged in clusters (Figs 33, 35 and 36). The structure of the underlying bone does not deviate from that of the control side.

The *roentgenogram* shows that the medial condyle is somewhat deformed. In the lateral view an indistinct streak penetrates into the subchondral bone (Fig. 37).

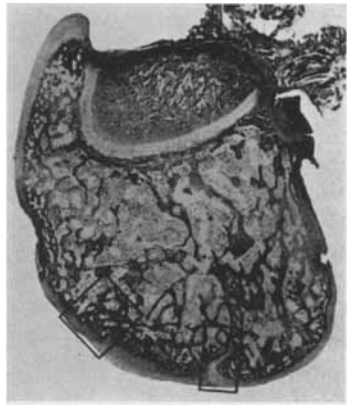


Fig. 32



Fig. 33



Fig. 34



Fig. 35



Fig. 36



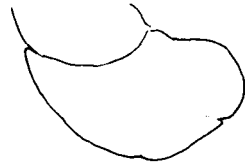


Fig. 37

Summary of the results in series A

In all animals in this series the course of development was that described in the foregoing as stages 1—10 (see Plates I—III). The figures in the plates (denoted a) are contour drawings of micrographs and roentgenograms with corresponding numbers shown in connection with the description of the various stages.

Where the cartilaginous fragment was partially detached, a concavity was formed in the subchondral zone of ossification (stages 1—3). In the fragment a separate centre of ossification developed, which grew and finally fused with the rest of the condyle (stages 4—10).

The fragment grew as a part of the condyle and at the same rate as this. The bony nucleus of the fragment was supplied by vessels coming from the spongy bone of the remaining epiphysis via highly vascular granulation tissue in the cleavage between the fragment and the concavity, and by vessels originating in the ligament tissue in the intercondyloid fossa.

In the cleavage between the fragment and the concavity the following structures succeeded each other: highly vascular granulation tissue, hyalinized connective tissue, primitive cartilage and hyaline cartilage. Gradually the cleavage disappeared and was replaced by a solid wall of hyaline cartilage, which was divided into fragments by enchondral ossification and which finally ossified completely. In the plane of the joint surface the cleavage between the fragment and the concavity persisted in some places, while in others the edges of the cleavage united by the formation of hyaline cartilage of irregular structure.

PLATE I

Stage 1

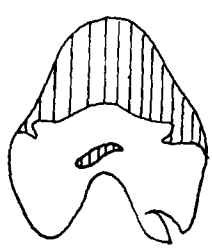


Fig. 1 a



Fig. 2 a

Stage 2

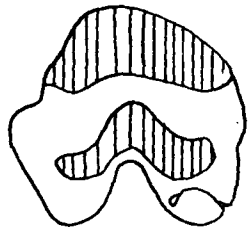


Fig. 3 a

Stage 3

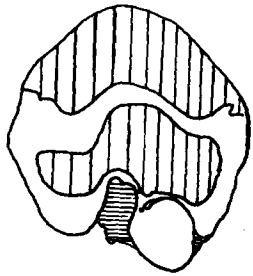


Fig. 7 a

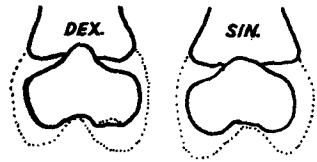


Fig. 10 a

Stage 4

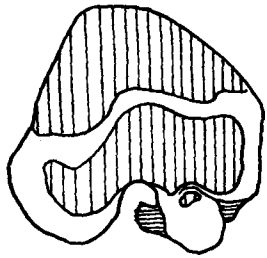


Fig. 11 a

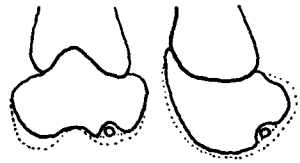


Fig. 13 a

PLATE II

Stage 5

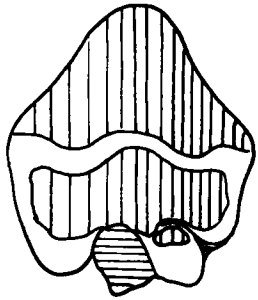


Fig. 14 a

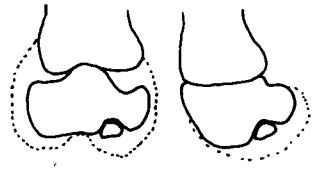


Fig. 16 a

Stage 6

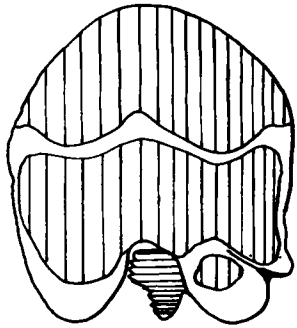


Fig. 17 a

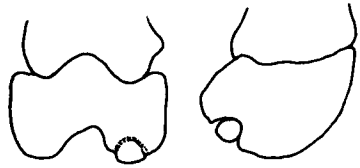


Fig. 19 a

Stage 7

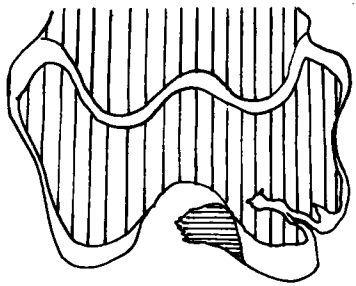


Fig. 20 a

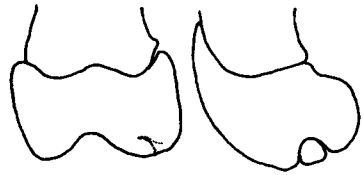


Fig. 23 a

Stage 8

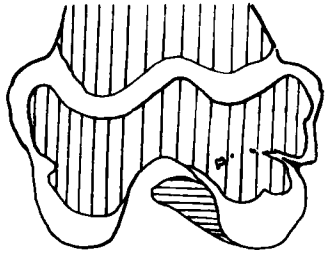


Fig. 24 a



Fig. 26 a

PLATE III

Stage 9

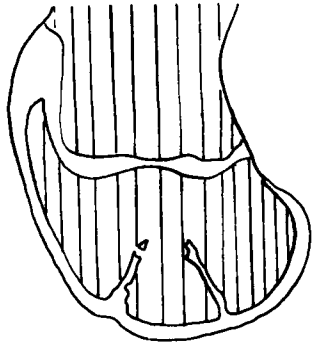


Fig. 27 a



Fig. 31 a

Stage 10

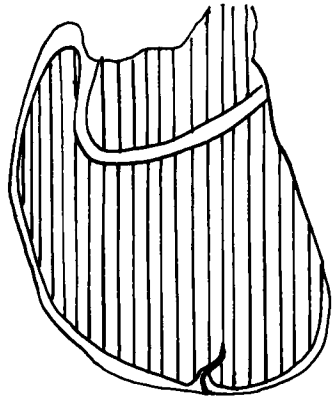


Fig. 32 a

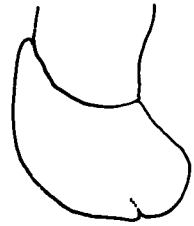


Fig. 37 a

Series B «small fragment«

Stage 1 (series B)

This stage is the situation immediately after operation. For details see page 22 and Fig. 38.

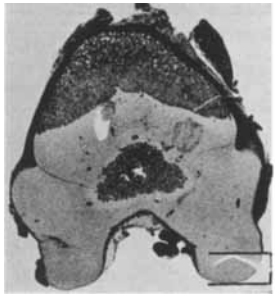


Fig. 38

Stage 2 (series B)

This stage is represented by an animal sacrificed 53 days after operation.

Microscopic findings. The fragment lies in its concavity (Fig. 39). The cleavage between fragment and concavity is distinctly visible. Medially it is bridged by vascular connective tissue originating in the periosteum (Fig. 41). The lateral portion of the cleavage contains primitive cartilage rich in cells. In some places this shows an indistinct transition into the surrounding cartilage, while in others there is a sharp line of demarcation (Fig. 40). The ossification of the epiphysis has proceeded so far that the hinge and the proximate parts of the fragment have ossified. The primitive cartilage in the lateral portion of the cleavage shows signs of ossification (Fig. 40).

The *roentgenogram* shows a concavity in the outline of the subchondral bone (Fig. 42).

The *macroscopic findings* are shown in Fig. 43.

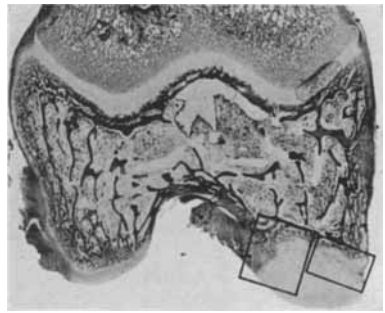


Fig. 39

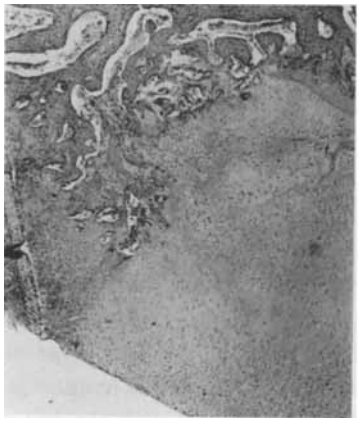
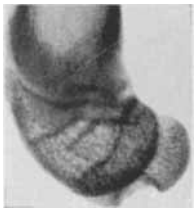


Fig. 40



Fig. 41



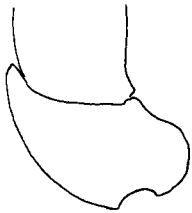


Fig. 42

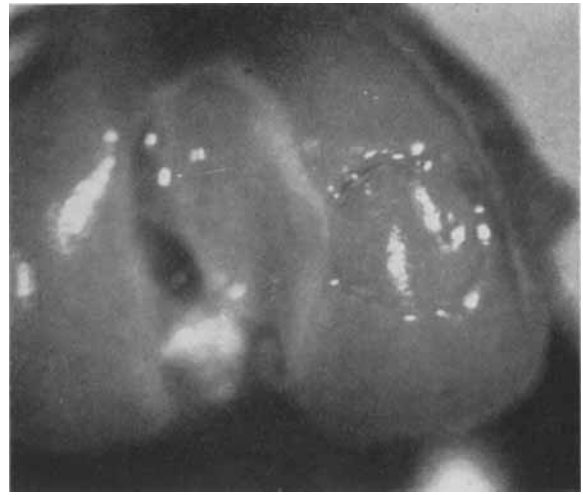


Fig. 43

Stage 3 a (series B)

This stage is represented by an animal sacrificed 82 days after operation.

Microscopic findings. The fragment lies in its concavity and the cleavage between fragment and concavity is distinctly visible. Medially it is bridged by vascular connective tissue originating in the periosteum (Fig. 44). The subchondral zone of ossification is separated from the cleavage by a thin layer of hyaline cartilage. Laterally there is a portion where the bone trabeculae are covered only by vascular connective tissue, rich in cells. The vessels of this tissue anastomose with the vessels of the underlying spongy bone (Fig. 45, note arrow). In the zone of ossification a concavity corresponding to the experimental lesion is formed. In the medial portion of the fragment there is a bony nucleus (Fig. 45) with marrow cavities containing erythrocytes, living bone trabeculae and osteoid tissue. The trabeculae are well stained and unbroken, the lacunae contain cells, the walls of the blood vessels are intact. This centre of ossification is supplied via the vascular connective tissue which has *developed postoperatively* and bridges the medial portion of the cleavage (Fig. 45).

The *roentgenogram* shows a concavity in the outline of the bone and in this there is a separate bone shadow (Fig. 46).

The *macroscopic findings* are shown in Fig. 47.

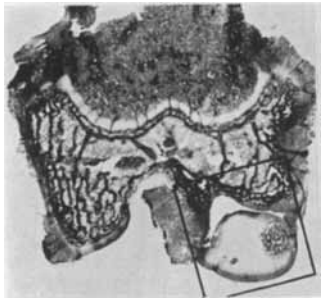
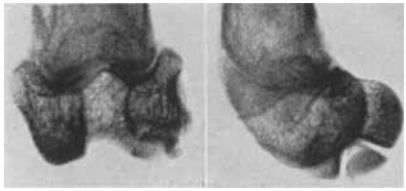


Fig. 44



Fig. 45



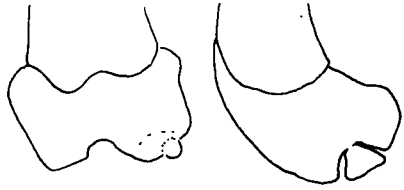


Fig. 46

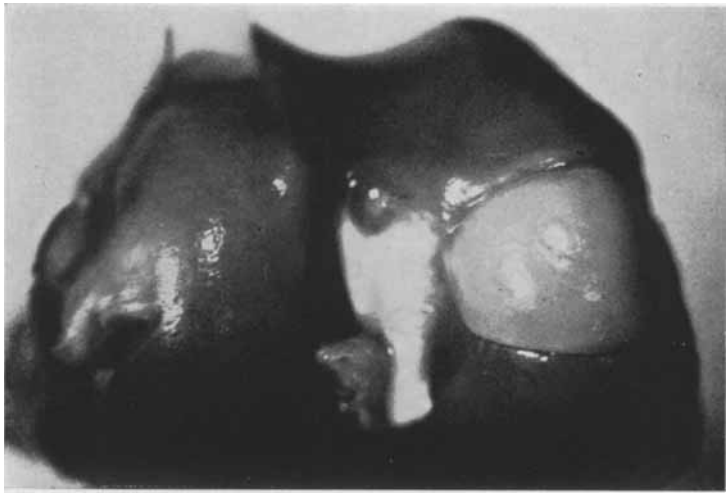


Fig. 47

Stage 3 b (series B)

This stage is represented by an animal sacrificed 109 days after operation.

Microscopic findings. The fragment lies in its concavity and the cleavage is distinctly visible. It is lined with hyaline cartilage. In the zone of ossification a concavity is formed under the fragment (Fig. 48). To its major portion the fragment has ossified, and its bone tissue is directly connected with the rest of the epiphyseal bone via the ossified hinge. The bone structure of the fragment is dense, with thick trabeculae and narrow marrow cavities. The latter contain erythrocytes. There are no cells in the lacunae (Fig. 49). The bone tissue seems necrotic.

The *roentgenogram* shows a concavity in the outline of the subchondral bone. In this a separate bone shadow is seen (Fig. 50).

The *macroscopic findings* are shown in Fig. 51.



Fig. 48

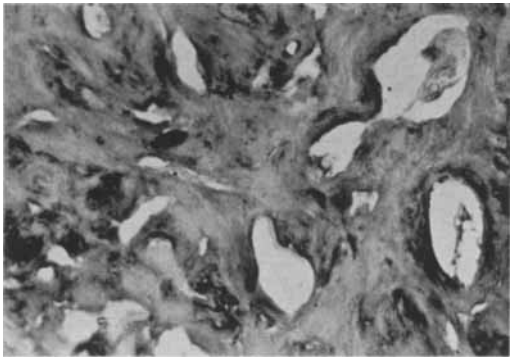


Fig. 49



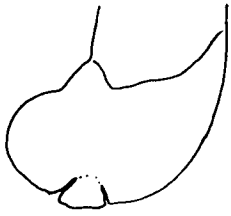


Fig. 50



Fig. 51

Stage 4 a (series B)

This stage is represented by an animal sacrificed 112 days after operation.

The fragment is hanging from a pedicle of ligamentous tissue in the intercondyloid fossa (Fig. 56).

Microscopic findings. In the fragment a centre of ossification is situated eccentrically, near the point of attachment of the ligamentous peduncle (Fig. 52). The cells in the lacunae of the ossific centre are well stained in some parts, while in others they are indistinct. The marrow cavities contain erythrocytes and osteoblasts. The bone and osteoid trabeculae are whole. Thus, the bony nucleus of the fragment shows slight signs of decreased vitality, although necrosis is not demonstrable (Fig. 54). In the subchondral zone of ossification of the medial condyle a shallow concavity is seen. This is covered by hyaline connective tissue, the deeper layers of which show a gradual transition to primitive cartilage. The latter is in some parts separated from the subchondral zone of ossification by a thin layer of hyaline cartilage, the cells of which are arranged in dispersed clusters (Fig. 53). Both these cartilaginous structures show signs of enchondral ossification.

The *roentgenogram* shows a concavity in the outline of the bone of the medial condyle. In this a separate bone shadow is seen (Fig. 55).

The *macroscopic findings* are shown in Fig. 56.

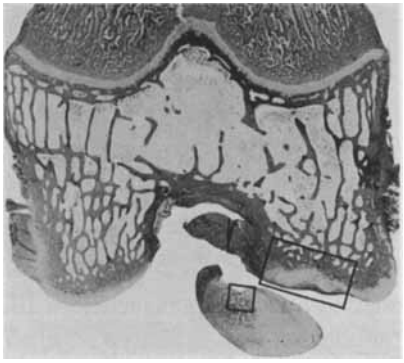


Fig. 52

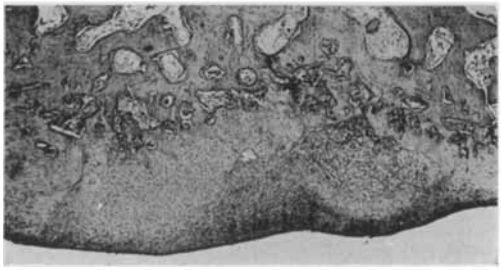


Fig. 53

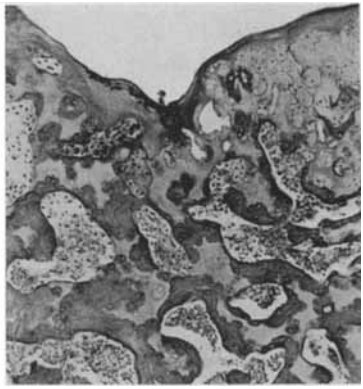
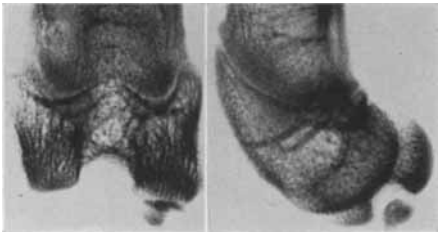


Fig. 54



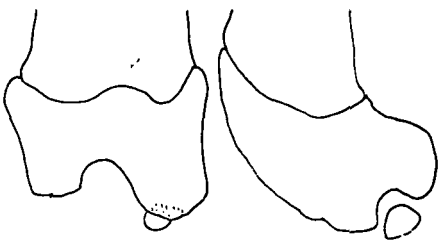


Fig. 55

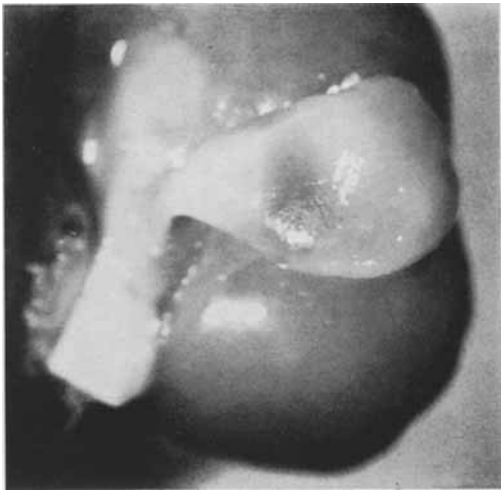


Fig. 56

Stage 4 b (series B)

This stage is represented by an animal sacrificed 132 days after operation.

The fragment is found as a detached loose body in the joint cavity, as is seen in Fig. 61 (note arrow), which is a roentgenogram of the knee joint of the animal *in vivo*.

Microscopic findings. The fragment consists of bone surrounded by hyaline cartilage. The lacunae and marrow cavities are empty, and the bone trabeculae are broken, which suggests that the bone tissue is necrotic. The structure is dense (Figs. 59 and 60). The medial condyle shows a concavity involving both the joint cartilage and the underlying bone. In the lateral portion of the concavity, the bone is covered by a thick layer of hyaline cartilage (Fig. 57). More medially the bone trabeculae are in some places covered with a fragmentary layer of hyaline cartilage, in others by primitive cartilage, towards the surface showing a gradual transition to hyaline connective tissue. At the medial border of the concavity the bone trabeculae are covered only by fibrous connective tissue (Fig. 58).

The *roentgenogram* shows a concavity in the outline of the bone of the medial condyle and a fragment with distinct bony structure separated from the concavity (Fig. 61).

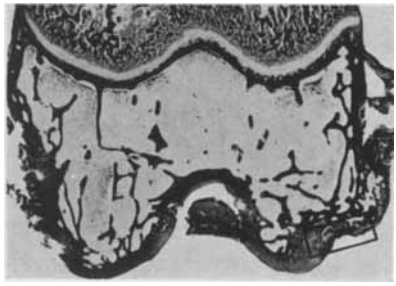


Fig. 57

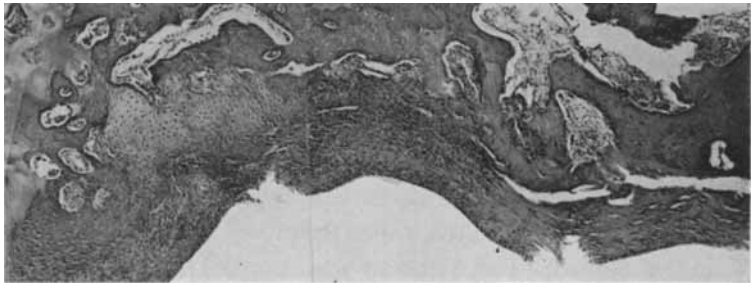


Fig. 58

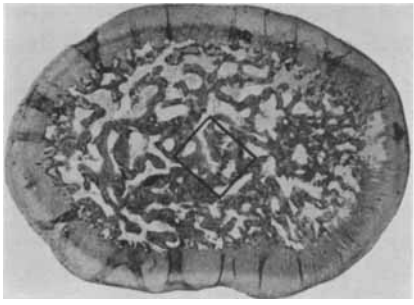


Fig. 59

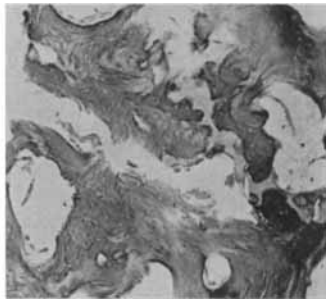
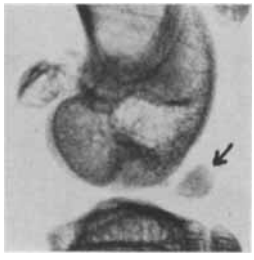


Fig. 60



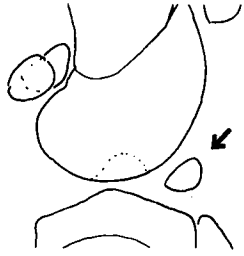


Fig. 61

Summary of the results in series B

The experimental lesion showed a uniform course of development in the 12 animals first killed (up to 53 days postoperatively) of the total number of 40 in this series. This initial phase is described as stages 1 and 2.

In the remaining 28 animals, sacrificed at various intervals from 57 to 200 days postoperatively, three different lines of development seemed to be discernible.

1. The fragment ossified, but was detached so that a pedunculated or non-pedunculated loose body resulted, which contained a bony nucleus. This was either living or necrotic. The fragment was supplied either via the hinge left at operation or via a connective tissue bridge which developed postoperatively over the medial portion of the cleavage. In some cases the bony nucleus of the fragment showed a strikingly dense structure. The concavity in the medial condyle was covered in part by hyaline cartilage, in part by primitive

PLATE IV

Stage 1

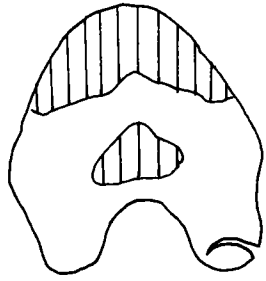


Fig. 38 a

Stage 2

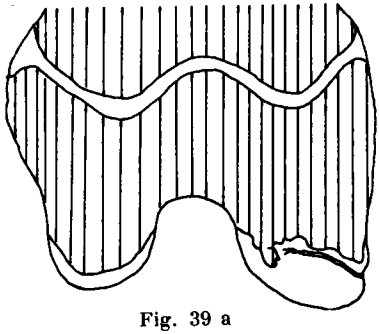


Fig. 39 a



Fig. 42 a

Stage 3 a

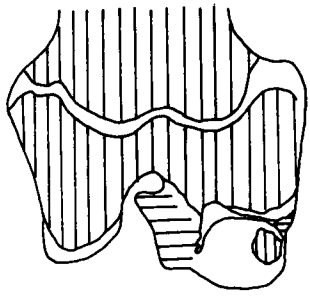


Fig. 44 a

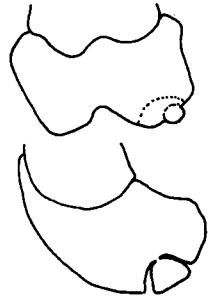


Fig. 46 a

Stage 3 b

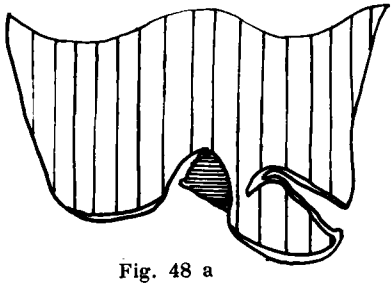


Fig. 48 a

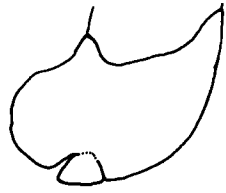


Fig. 50 a

cartilage showing a gradual transition to hyaline cartilage, and in part by fibrous connective tissue alone. These layers of cartilage underwent enchondral ossification. This line of development was observed in 5 animals and was described as stages 3 a, 3 b, 4 a and 4 b.

2. The fragment ossified and fused with the underlying bone. This line of development was not illustrated by examples, since the course was the same as in series A »large fragment». This group seemed to comprise 8 animals.

3. The fragment did not ossify, but was detached and formed a loose body in the joint cavity, consisting entirely of cartilage. No examples from this group were described, since the course was the same as in series D »loose fragment.» This group seemed to comprise 15 animals.

See Plates IV and V. The figures in the plates (denoted a) are contour drawings of micrograghs and roentgenograms with corresponding numbers shown in connection with the description of the various stages.

PLATE V

Stage 4 a

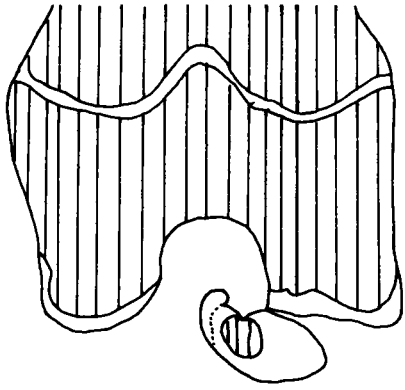


Fig. 52 a

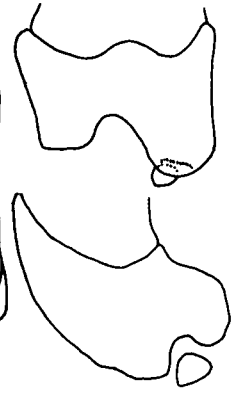


Fig. 55 a

Stage 4 b

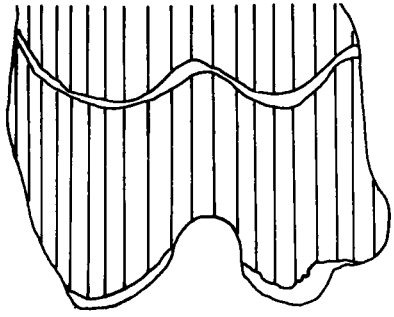


Fig. 57 a

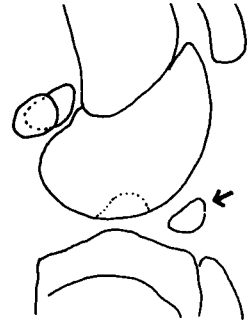


Fig. 61 a

Series C «hinge of ligament tissue«

Stage 1 (series C)

This stage is the situation immediately after operation. For details see page 22 and Figs. 62 and 63.

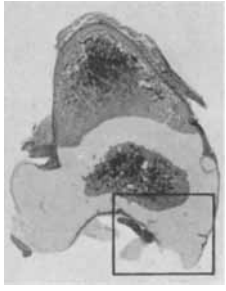


Fig. 62



Fig. 63

Stage 2 (series C)

This stage is represented by an animal sacrificed 22 days after operation.

Microscopic findings. The subchondral zone of ossification is similarly arched in the medial and lateral condyles. The fragment hangs upon its hinge of ligamentous tissue (Fig. 64). The cartilage cells stain identically throughout the fragment (Fig. 65). At the former site of the fragment in the medial condyle a concavity is formed, at the bottom of which a layer of primitive cartilage with closely packed cells is seen. This is separated from the underlying normal cartilage by a narrow zone of cartilaginous matrix devoid of cells (Fig. 65).

The *macroscopic findings* are shown in Fig. 66.

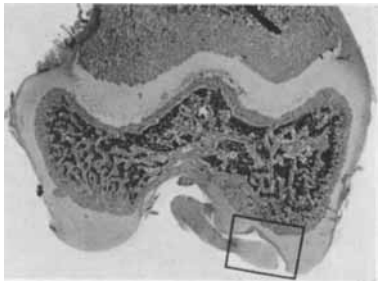


Fig. 64

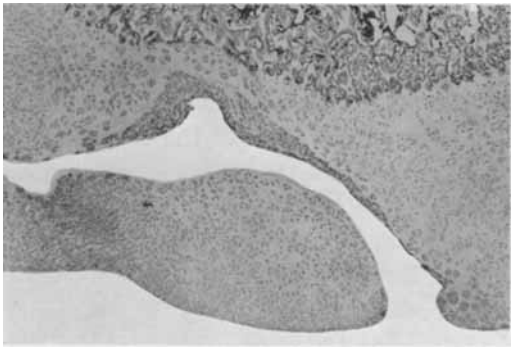


Fig. 65

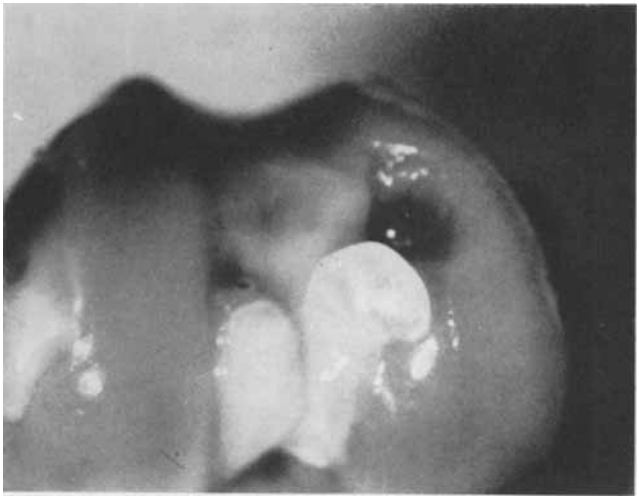


Fig. 66

Stage 3 a (series C)

This stage is represented by an animal sacrificed 63 days after operation.

Microscopic findings. The ossification of the condyle has proceeded so far that a concavity has formed in the subchondral bone at the former site of the fragment (Fig. 67). In the joint surface a corresponding concavity is seen. The bottom of the latter consists of cartilage, which here and there in the proximity of the subchondral zone of ossification shows dispersed clusters of cartilage cells. Other parts of the concavity are lined with primitive cartilage rich in cells. Both types of cartilage show signs of enchondral ossification (Fig. 68).

The fragment hangs from a hinge of ligament tissue. In the centre of the cartilaginous fragment, there are distended cells with relatively small nuclei, and an abundance of faintly stained matrix is seen. The superficial parts of the fragment have a normal appearance (Fig. 68).

The *roentgenogram* shows a shallow concavity in the outline of the bone of the medial condyle (Fig. 69). The fragment gives a weak shadow, indicating calcium content but lack of bony structure.

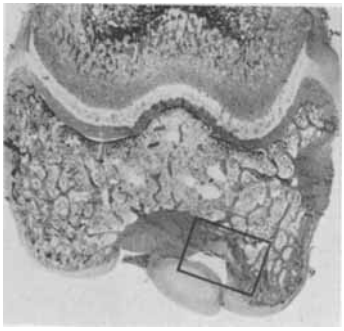


Fig. 67

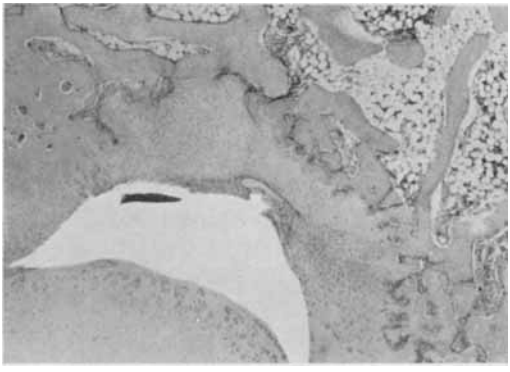


Fig. 68



Fig. 69

Stage 3 b (series C)

This stage is represented by an animal sacrificed 172 days after operation.

The fragment hangs from a hinge of ligament tissue attached to the intercondyloid fossa (Fig. 75, the arrow indicates the concavity).

Microscopic findings. In the operated condyle the subchondral zone of bone shows a shallow concavity at the former site of the fragment (Fig. 70). Over this the joint cartilage is thin and hyaline and shows an irregular structure with densely arranged cells. At this site the joint surface is uneven. In the proximity of the intercondyloid fossa the bone trabeculae are covered by a thin layer of fibrous connective tissue (Fig. 72). In the cartilage of the fragment, near the point of attachment of the ligamentous peduncle, a bony nucleus is seen (Fig. 71). In the lacunae of the latter there are well-stained bone cells, and the marrow cavities contain erythrocytes. The cartilage of the fragment shows degenerative changes and is covered very superficially by a layer of fibrous connective tissue (Fig. 73).

The *roentgenogram* shows that the two condyles have similar, curved outlines. The fragment gives rise to a shadow, which laterally is indicative of bony structure (Fig. 74).

The *macroscopic findings* are shown in Fig. 75.

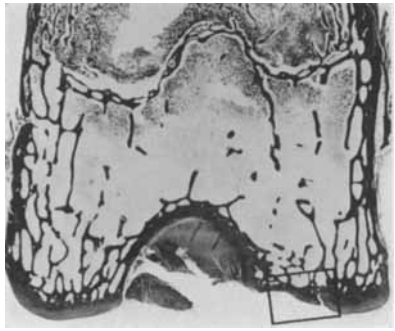


Fig. 70

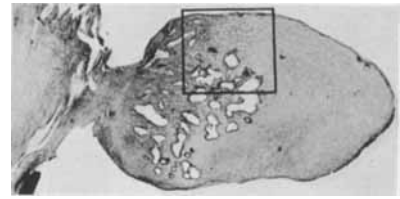


Fig. 71

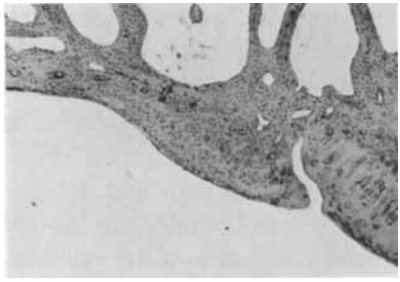


Fig. 72

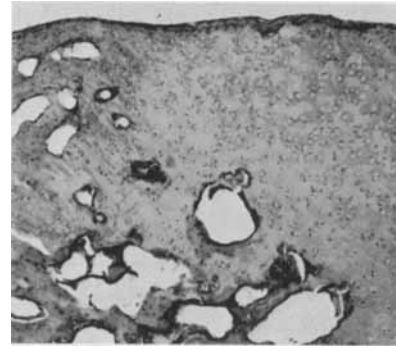


Fig. 73



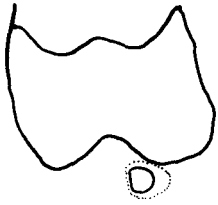


Fig. 74



Fig. 75

Summary of the results in series C

In 17 of the 18 animals in this series the lesion seemed to develop as was described in the foregoing (stages 1—3 a).

During the course of development the fragment was dislocated from its crater. Under the latter a corresponding concavity was formed in the zone of ossification. The crater was incompletely filled with primitive cartilage, which later was replaced by hyaline cartilage of somewhat irregular structure. Most of this cartilage ossified, so that the concavity in the subchondral zone of bone was in part levelled out. The operated condyle remained deformed, as compared with the intact condyle.

The fragment grew, hanging from its ligamentous peduncle. On the surface, its cartilage maintained a normal structure, in the middle it showed degenerative changes, and at the end of the observation time it was calcified. The fragment was surrounded by a thin capsule of connective tissue. It remained attached to its peduncle of ligament tissue.

In one case a living bony nucleus was found in the pedunculated fragment. It was supplied by vessels in the ligamentous pedcile (stage 3 b).

See Plate VI. The figures in the plate (denoted a) are contour drawings of micrographs and roentgenograms with corresponding numbers shown in connection with the description of the various stages.

PLATE VI

Stage 1

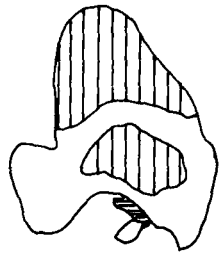


Fig. 62 a

Stage 2

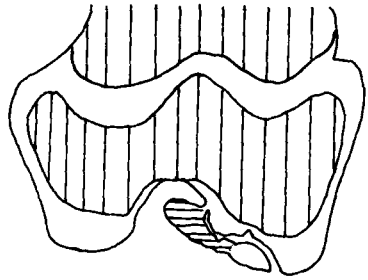


Fig. 64 a

Stage 3 a

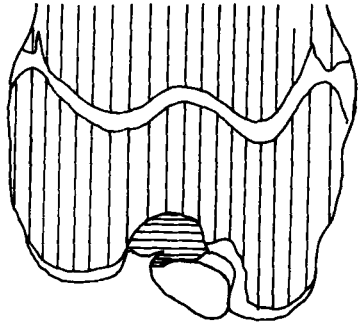


Fig. 67 a

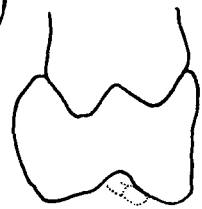


Fig. 69 a

Stage 3 b

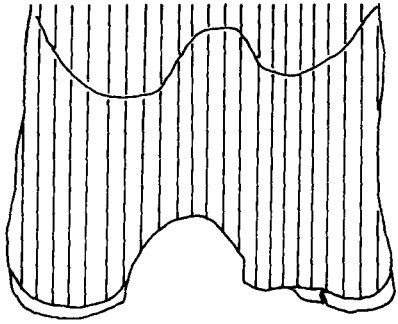


Fig. 70 a

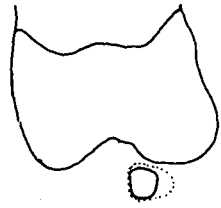


Fig. 74 a

Series D «loose fragment«

Stage 1 (series D)

This stage is represented by an animal sacrificed 8 days after operation. (For details regarding the experimental lesion see page 22.)

Microscopic findings. In the cartilage of the condyle a defect is seen (Fig. 76). The joint cartilage in the proximity of the concavity shows ill-stained cartilage cells.

The fragment, which lies as a loose body in the joint cavity, shows well-stained cartilage cells of normal size and shape in all parts of the cross-section. Its periphery consists of a single layer of flat connective tissue cells (Fig. 77).

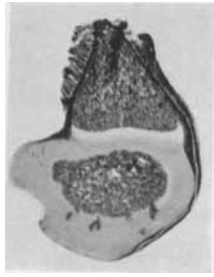


Fig. 76

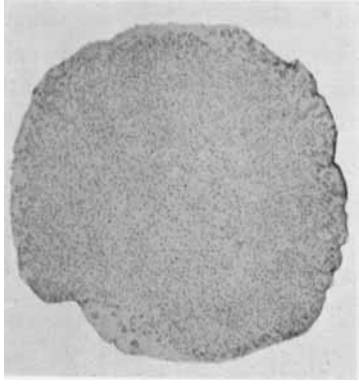


Fig. 77

Stage 2 (series D)

This stage is represented by an animal sacrificed 26 days after operation.

Microscopic findings. There is a concavity in both the joint surface and the underlying zone of ossification (Fig. 78). In the concavity of the joint surface a layer of primitive cartilage, rich in cells, is seen. This shows no signs of enchondral ossification. The transition to normal joint cartilage is in some parts indistinct, in others distinct and characterized by a streak of ill-stained cartilage cells (Fig. 80).

Most of the fragment, which lies as a loose body in the joint cavity, consists of normal-looking cartilage. In the centre of the fragment there are occasional cells lacking nuclei. On its extreme periphery, the fragment is surrounded by a thin capsule of fibrous connective tissue, and under this there is a layer of cartilage of irregular structure, rich in cells (Figs. 79 and 81).

The *roentgenogram* shows a concavity in the outline of the bone of the operated condyle (Fig. 82). The fragment gives no shadow.

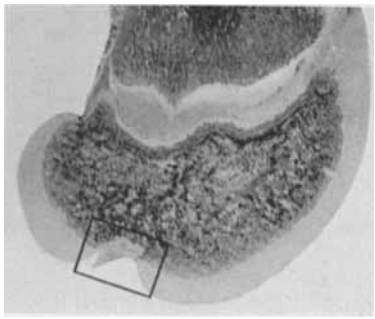


Fig. 78

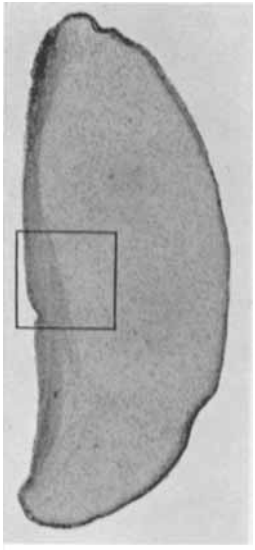


Fig. 79

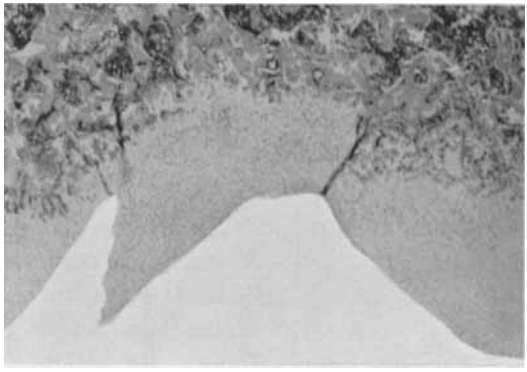


Fig. 80

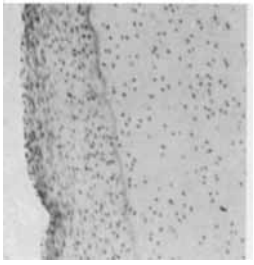


Fig. 81





Fig. 82

Stage 3 (series D)

This stage is represented by an animal sacrificed 48 days after operation.

Microscopic findings. On the joint surface there is a shallow concavity. At the same site in the subchondral zone of bone a corresponding concavity is seen (Fig. 83). This is covered by an uneven layer of hyaline cartilage showing an abundance of irregularly arranged cells and here and there striated intercellular substance. This cartilage shows definite signs of enchondral ossification (Fig. 85) and is distinguishable from the surrounding normal joint cartilage by a more intensely stained streak in the matrix without any cells in the proximity (Fig. 85).

The fragment is found as a loose body in the joint cavity. At the centre of the fragment there are large ill-stained cells, some of which have pyknotic nuclei, while others have no nuclei. The peripheral parts of the fragment exhibit normal structure, and superficially there is a layer of fibrous connective tissue (Figs. 84 and 86).

The *macroscopic findings* are shown in Fig. 87, which is a view of the medial condyle without any loose fragment.



Fig. 83

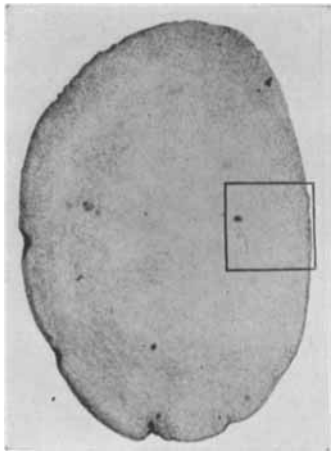


Fig. 84

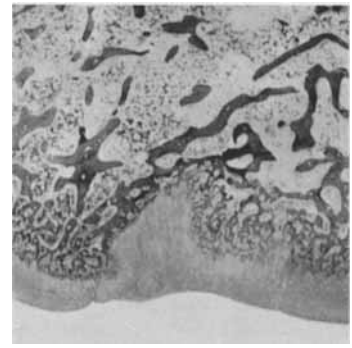


Fig. 85

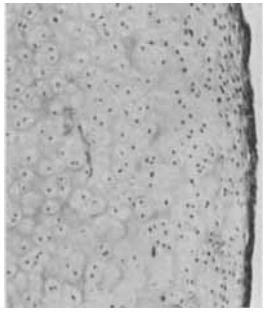


Fig. 86



Fig. 87

Stage 4 (series D)

This stage is represented by an animal sacrificed 103 days after operation.

Microscopic findings. Where the fragment has been gouged out a shallow concavity is seen in the joint surface and in the subchondral zone of bone (Fig. 88). The joint cartilage in the concavity consists of an uneven layer of hyaline cartilage with irregularly arranged cells in abundance and a striated matrix (Fig. 90). The transition to the surrounding normal joint cartilage is characterized in parts by a more intensely stained streak in the matrix without any cells in the proximity, in parts by a cleavage filled with a picrinophilic substance, while in still other parts the transition is indistinct.

At the centre of the fragment, which is found as a loose body in the joint cavity, there are large, faintly stained cartilage cells. At the periphery, there is a layer of cartilage of irregular structure, bounded superficially by a layer of connective tissue cells (Figs. 89 and 91).

The *roentgenogram* shows that the medial condyle is deformed. The fragment gives a diffuse shadow indicating calcium content (Fig. 92).



Fig. 88

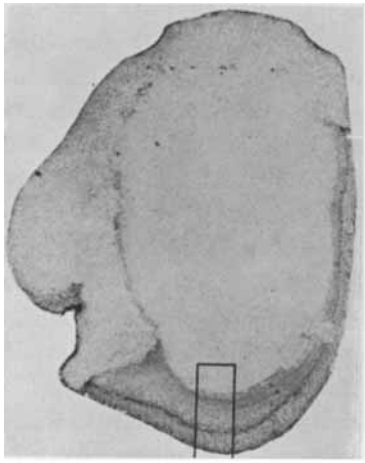


Fig. 89



Fig. 90

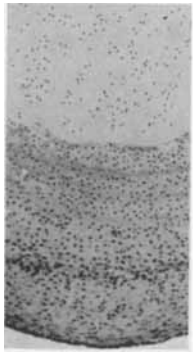


Fig. 91





Fig. 92

Summary of the results in series D

In all the 16 animals of the series the course of development seemed to be that which was described in the foregoing as stages 1—4.

The concavity in the cartilage was incompletely filled out with primitive cartilage, which was later replaced by hyaline cartilage of irregular structure. This cartilage ossified slowly, so that a concavity was initially formed in the subchondral zone of ossification. As ossification proceeded, this concavity was levelled out. At the end of the observation time the condyle was somewhat deformed, inasmuch as it showed a shallow concavity at the site where the fragment had been gouged out. The cartilage at the centre of the fragment degenerated and calcified, while at the end of the observation time the peripheral parts still showed signs of vitality and, at certain sites, an irregular structure and densely packed cells. Most superficially the fragment was surrounded by a thin connective tissue capsule, which may suggest that the increase in volume of the fragment in part, at least, was due to appositional growth.

See Plate VII. The figures in the plate (denoted a) are contour drawings of micrographs and roentgenograms with corresponding numbers shown in connection with the description of the various stages.

Plate VII

Stage 1

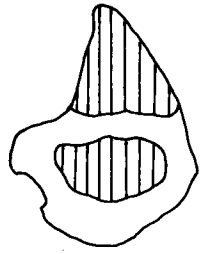


Fig. 76 a

Stage 2

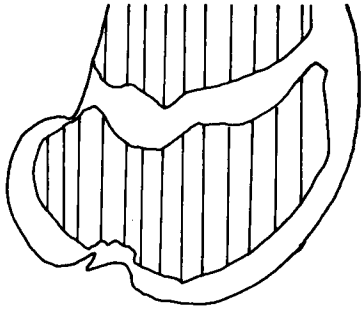


Fig. 78 a



Fig. 82 a

Stage 3

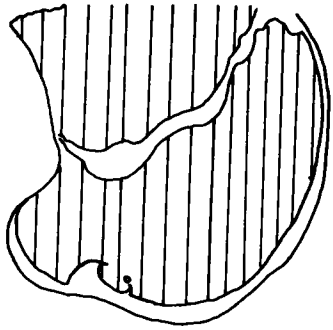


Fig. 83 a

Stage 4

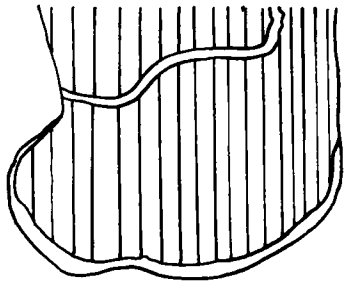


Fig. 88 a



Fig. 92 a

Series E «intracartilaginous cleavage«

Stage 1 (series E)

This stage is the situation immediately after operation. For details see page 22 and Figs. 93 and 94.

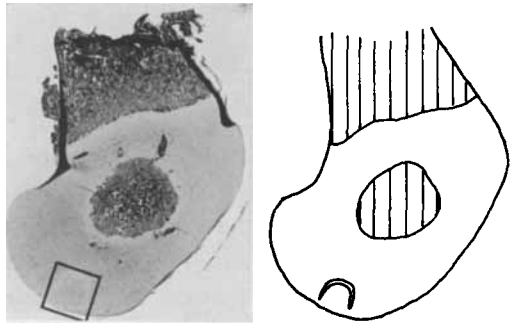


Fig. 93

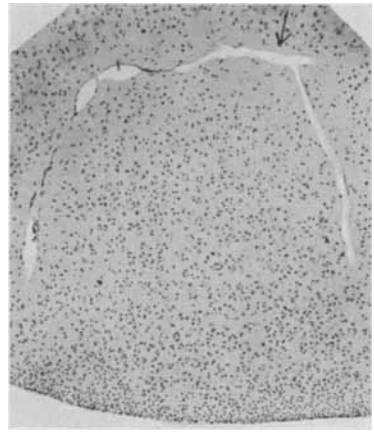


Fig. 94

Stage 2 (series E)

This stage is represented by an animal sacrificed 32 days after operation.

Microscopic findings. The ossification of the epiphysis has proceeded so far that a concavity has formed in the subchondral zone of ossification at the site of the intracartilaginous cleavage (Fig. 95). The cleavage is almost completely filled by primitive cartilage, which in some parts is separated from its surroundings by a more intensely stained streak in the matrix without any cells in the proximity, and which in other parts shows a gradual transition (Fig. 96). In certain places, the cleavage is visible. At these, the cartilage of the separated piece and the thin layer of cartilage covering the zone of ossification meet (Fig. 96). The cartilage cells at the centre of the separated piece are distended and their nuclei are pyknotic (Fig 96.).

The *roentgenogram* shows a concavity in the outline of the bone of the medial condyle (Fig 97).

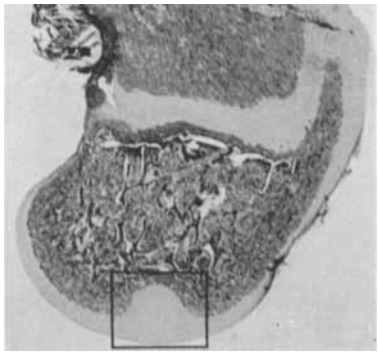


Fig. 95

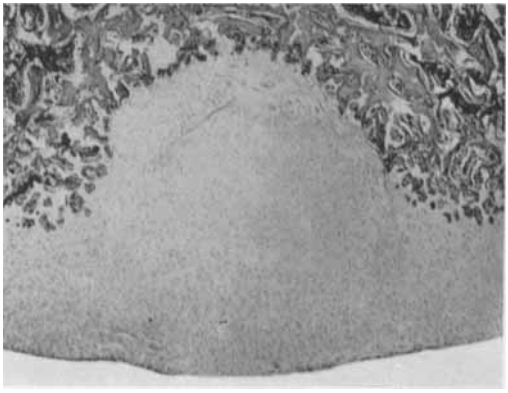


Fig. 96

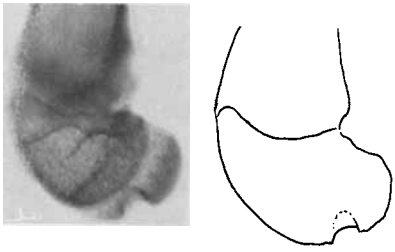


Fig. 97

Stage 3 (series E)

This stage is represented by an animal sacrificed 35 days after operation.

Microscopic findings. In the zone of ossification of the medial condyle, a concavity is seen. In the piece separated by the intracartilaginous cleavage there is a living bony nucleus (Fig. 98). The cleavage contains some granulation tissue, the vessels of which anastomose with the vessels of the separate bony nucleus and with the vessels of the spongy bone of the epiphysis. The bony nucleus of the separated piece is surrounded by a layer of hyaline cartilage, which in some places narrows to a thin border of cartilaginous matrix containing scattered clusters of cartilage cells. The cleavage is almost completely filled by an irregular layer of hyaline cartilage with scattered cells. In some places, the cleavage is visible and contains a picrinophilic structureless substance. The zone of ossification of the concavity is lined with a layer of more intensely stained cartilaginous matrix with scattered clusters of cartilage cells (Fig. 99).

The *roentgenogram* shows a concavity in the outline of the subchondral bone. In the concavity there is a separate bone shadow, which in part is clearly distinguishable from the surroundings (Fig. 100).

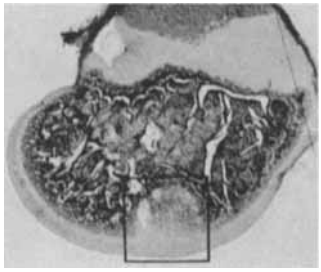


Fig. 98

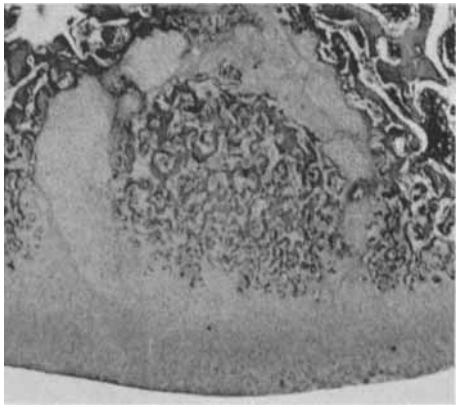


Fig. 99

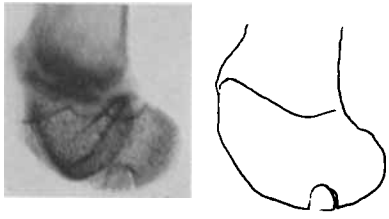


Fig. 100

Stage 4 (series E)

This stage is represented by an animal sacrificed 64 days after operation.

Microscopic findings. In the spongy bone of the medial condyle a transverse, curved streak of indeterminate structure is seen. In this and in its surroundings osteoid tissue is observable (Figs. 101 and 102). As a continuation of the streak, under the medial periosteum of the condyle, there is thickened hyaline cartilage (Fig. 101). Around the streak of osteoid tissue the bony structure is dense, as compared with that of the lateral condyle (Fig. 101).

The *roentgenogram* shows minor irregularities in the bony structure of the operated condyle (Fig. 103).

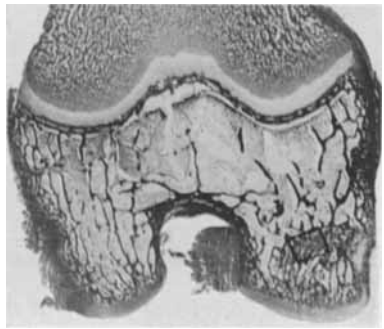


Fig. 101

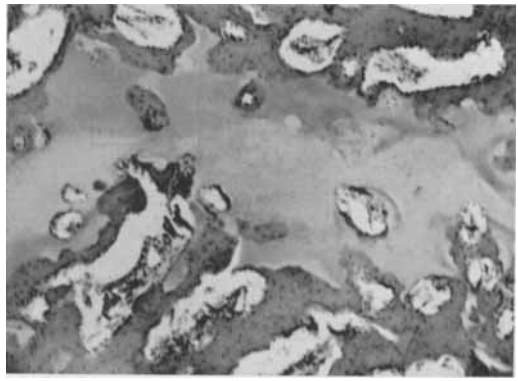


Fig. 102



Fig. 103

Summary of the results in series E

In all the 18 animals of this series the course of development of the experimental lesion seemed to be as described in the foregoing as stages 1—4.

In the intracartilaginous cleavage primitive cartilage was formed, which later was succeeded by hyaline cartilage. At the site of the experimental lesion ossification was arrested, so that a concavity was formed in the zone of ossification. At the centre of the cartilaginous piece, which was separated by the intracartilaginous cleavage, degenerative changes, and later a separate bony nucleus, developed. The latter was supplied in part by vessels which originated in the perichondrium (the periosteum) and bridged the medial opening of the cleavage, in part by vessels which reached the separated piece via granulation tissue present at the bottom of the cleavage.

By enchondral ossification the hyaline cartilage which developed in the cleavage was divided into fragments. Thus islands of hyaline cartilage were formed in the spongy bone. These islands, too, underwent enchondral ossification, and in the course of development a normal bony structure was re-established, although at the end of the observation time the operated condyle was somewhat broader than the non-operated condyle.

See Plate VIII. The figures in the plate (denoted a) are contour drawings of micrographs and roentgenograms with corresponding numbers shown in connection with the description of the various stages.

PLATE VIII

Stage 1

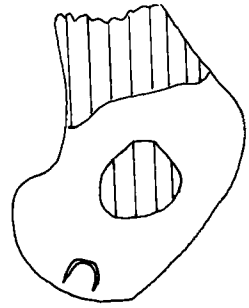


Fig. 93 a

Stage 2

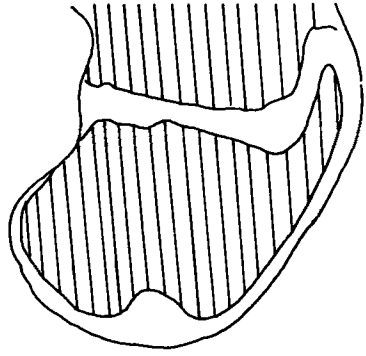


Fig. 95 a

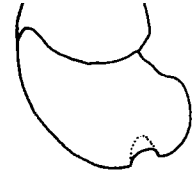


Fig. 97 a

Stage 3

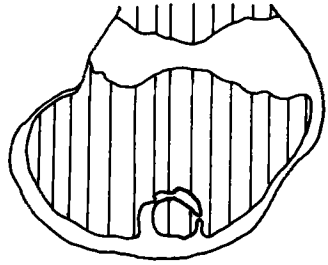


Fig. 98 a

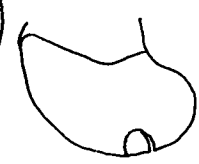


Fig. 100 a

Stage 4

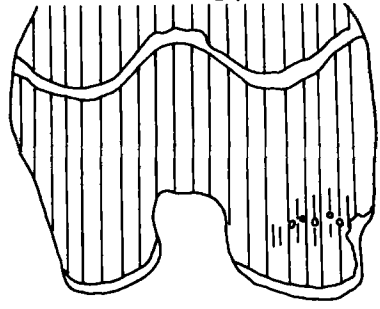


Fig. 101 a



Fig. 103 a

DISCUSSION AND CONCLUSIONS

The present results in the light of the relevant literature

In series A »large fragment» the cleavage between fragment and concavity initially contained fibrin, then granulation tissue, then hyaline connective tissue succeeded by primitive cartilage, and finally hyaline cartilage. This is in agreement with the observations made by SHANDS (1931), who performed experiments on dogs (probably adult dogs, the age was not indicated). The origin of the regeneration observed is not revealed by the present study. RAO (1954) and GIBSON (1955) stated that hyaline cartilage regenerates in three different ways: 1) by proliferation of chondrocytes, 2) by proliferation of vascular connective tissue originating in the perichondrium and 3) by invasion of vascular connective tissue from the subchondral bone. It appears that in an attempt to account for the present results the first two alternatives may be considered, but not the third alternative, since the subchondral bone was left intact at operation. On the other hand it is probable that the vessels in the joint cartilage were injured, and it is possible that the regeneration originated in the endothelium of these.

It appears that in series A the ossification of the fragment originated in vessels penetrating from the granulation tissue present in the cleavage between fragment and concavity. It is also possible, however, that the ossification of the fragment was due to the penetration of vessels from the intercondyloid fossa. These vessels may have existed before operation and remained intact. (Cf series A, stage 3, Fig. 9.)

Figs. 28 and 33 in series A, stages 9 and 10, showed that the superficial layer of the joint cartilage regenerated in such a way that the cleavage was filled with hyaline cartilage, which was distinguishable from the surrounding normal cartilage only by a somewhat irregular arrangement of the cartilage cells. This tallies with the observations made by GIES (1883), NAGURA (1937), NAGURA & KOSUGE (1938) and CARLSON (1957).

After incision and subchondral infraction, respectively, of epiphyseal bone in growing rabbits NAGURA (1938) and BURCKHARDT (1948) observed

that the subchondral defect was filled with a cartilage-like tissue. This tissue showed very slow enchondral ossification and may, perhaps, be compared with the primitive cartilage which in the present study was found in the cleavage between fragment and cartilage and ossified much later than the cartilage of the fragment. (Cf series A, B and E.)

In growing rats BRASHEAR (1959) created a transverse fracture through the cartilage of the epiphyseal plate at the distal end of the femur. At some distance from the fracture the ossification of the portion of the epiphyseal plate situated proximally to the fracture was arrested for a long time. In the portion of the epiphyseal plate which was distal to the fracture a secondary bony nucleus developed after vascularization. Only later did the portions of cartilage bordering on the fracture line undergo ossification. Although this experiment involved the epiphyseal plate, it has certain features in common with the results in series A and E in the present study. In both cases a cleavage was made in cartilage which normally ossifies, and in both cases a separate bony nucleus developed distally to this cleavage.

In series A and B it appeared that the fragments ossified first at the site where the invading vessels penetrated into the fragment, and not at the site where the cartilage cells could be assumed to be oldest, *i. e.* proximately to the bottom of the concavity. Proximately to the cleavage between fragment and concavity the cartilage ossified relatively late. This was correspondingly observed in series E »intracartilaginous cleavage». This phenomenon shows features in common with those noted by BRASHEAR (1959). Why the cartilage bordering on the cleavage ossified relatively late remains an open question.

EHRENBORG, ENGFELDT and OLSSON (1961) tore the ligamentous attachment to the cartilaginous tibial tuberosity in 1-month-old dogs. In one case a radiopaque tissue fragment was observed separately from the apophyseal bony nucleus of the tibial tuberosity, which exhibited a defect corresponding to the fragment. It may be supposed that this phenomenon was analogous to those demonstrated in this study in series A, B and E.

According to STRANGEWAYS (1920), FISHER (1922) and LANDELLS (1957), articular cartilage is supplied by the synovial fluid. LANDELLS stated that »cartilage may live, grow and calcify (but not ossify) when completely detached from bone, provided it has free access to the synovial fluid». This theory is substantiated by the present results in series D »loose fragment», inasmuch as none of the cartilaginous fragments which were initially completely detached from their concavities ossified. They grew,

showed signs of vitality and calcified. In series B »small fragment» it was found that the fragment was sometimes vascularized and ossified via the hinge of cartilage and ligament tissue which was left at operation *or* via a connective tissue bridge which developed *postoperatively* and originated in the periosteum at the medial margin of the condyle and bridged the medial portion of the cleavage. This finding contradicts LANDELL's assertion to some extent, since it implies that growing articular cartilage may live, grow and calcify and, in the presence of a vascular connection, also ossify although the cartilage is completely separated from bone. (Cf. DANIS & LABARRE 1957 and LACROIX 1959, see below).

DANIS & LABARRE (1957) and LACROIX (1959) excised a piece of cartilage from the head of the radius of a new-born monkey and from fracture callus, respectively, and implanted the fragment into the eye or under the renal capsule in adult animals. The fragments ossified. The implantation of costal cartilage in a similar way brought about only slight and retarded ossification. Under normal conditions joint cartilage from a new-born animal and cartilage from fracture callus ossifies, while costal cartilage does not ossifly The cartilaginous fragments, too, which in the present study were partially detached from the joint surface and which ossified, would also normaly. have ossified. This shows that cartilage which normally ossifies during the course of development may also maintain a tendency towards ossification when detached from direct continuity with its original surroundings. (See series A, B and C.)

In series B it was found that some fragments contained a bony nucleus showing a denser structure than normal (cf. Figs. 48 and 59). BOBECHKO & HARRIS (1960) detached the head of the femur in adult rabbits, severed the round ligament and nailed the head of the femur into place again. Initially they observed necrosis of the bone trabeculae in the head of the femur, and subsequently apposition of new bone to the necrotic trabeculae, corresponding to a diminution of the marrow cavities and a denser shadow in the roentgenogram. Similar observations were made by GAMBIER & VENTURINI (1959) and by RUTISHAUSER, RÖHNER & HELD (1960). It is possible, therefore, that the dense structure of the spongy bone observed in certain fragments in the present study was due to poor nutrition, necrosis of the bony portion of the fragment and reossification as in the experiment described by BOBECHKO & HARRIS.

In the available literature the author has not encountered any report except LANGENSKIÖLD's (1955) to the effect that a partially detached piece of joint cartilage in a growing individual may result in a pedunculated joint-

mouse with a nucleus of necrotic or living bone, as was found in the present study, series B. In this, a similar lesion gave rise also to a completely loose joint-mouse, with a nucleus of necrotic bone.

In series B certain fragments fused with the surrounding bone tissue at the site from which they had been gouged out, just as in series A. Others ossified and were then detached, still others were detached without foregoing ossification. In series A all fragments underwent bony union with their beds. This difference may be due to the fact that in series A the fragments were relatively deeper (1.4—1.8 mm) in relation to their extension in the plane of the joint surface than in series B (0.7—1.2 mm). Hence, it would seem that the mechanical conditions for the fragment remaining in the concavity were more favourable in series A than in series B. On the other hand, in series A the lesion extended more deeply towards the bony nucleus of the epiphysis than in series B. Hence, the risk was probably greater that the vessels in the cartilage (which probably are more abundant near the bony nucleus than near the surface) would be injured in series A. It is possible that granulation tissue originating in injured vessels in the cartilage contributed to the fixation of the fragment to its bed.

In series D »loose fragment» it was found that during the course of development the fragment degenerated at the centre and showed signs of proliferation peripherally. The fact that towards the end of the observation time the fragment gave a relatively dense shadow in the roentgenogram suggests that calcium had been deposited. Around the fragment a thin capsule of connective tissue was formed. All these findings are in agreement with the observations made by GIES (1882), STRANGEWAYS (1920), PHEMISTER (1924), BENNET, BAUER & MADDOCK (1932) and LANDELLS (1957).

In series D, the cartilage bordering on the operatively created defect showed cartilage cells with markedly diminished stainability soon after operation. A similar observation was made by CARLSON (1957), who detached a small chip of cartilage from the joint surface of the patella in growing rabbits.

The defect in the joint cartilage created in series D was filled by primitive cartilage, which later was succeeded by hyaline cartilage with a partially striated matrix. BENNET, BAUER & MADDOCK (1932) reported that after an analogous operation on adult dogs the end result was fibrous cartilage.

BENNET, BAUER & MADDOCK (1932) and BUCHER (1955) gouged out a fragment of cartilage together with a piece of underlying bone. The tissue filling the concavity (fibrous cartilage, according to BUCHER) ossified in its deeper portions. In the present series D a concavity developed in the

zone of ossification at the site of the experimental lesion (see Fig. 78, page 77), before the cartilage which filled the concavity in the cartilage ossified in its deeper layers (see Fig. 83, page 79 and Fig. 88, page 81).

In series C »hinge of ligament tissue» the results were in agreement with the results in series D »loose fragment» with regard to the development of both the fragment and the concavity. In one case, however, in series C a bony nucleus developed in the fragment (Fig. 71, page 71). Obviously this bony nucleus was supplied by vessels in the ligamentous peduncle, but when it developed is less obvious. The concavity in the joint cartilage at the former site of the fragment was partially levelled out and covered by hyaline cartilage, which only differed slightly from intact articular cartilage. Hence it may be concluded that the fragment had been dislocated from the concavity relatively early. In addition, the bony nucleus was relatively small in relation to the whole fragment, and its osteoid trabeculae were relatively narrow and contained living cells (Fig. 72, page 71). This seems to suggest that the centre of ossification had developed relatively late. The implication would be that *the centre of ossification developed after the fragment had been dislocated from its bed.* This hypothesis is not, however, substantiated by any observations reported in the literature, nor does it account for the fact that no bony nucleus developed in any other fragments in this series.

In the available literature no data were found concerning experiments involving an intracartilaginous cleavage in growing joint cartilage. In series E »intracartilaginous cleavage» the course was practically the same as in series A, although in series E the superficial layer of the joint cartilage had been left intact. The results in series E showed that an intracartilaginous cleavage, too, in growing joint cartilage may later give rise to a separate centre of ossification.

Ribbing (1951), Caffey, Madell, Royer & Morales (1958) and others have emphasized the occurrence of accessory bony nuclei *e. g.* in the distal femoral epiphysis in children. The same phenomenon has been observed in other epiphyses by Roche & Sunderland (1959). These accessory bony nuclei were so common that the last-mentioned writers claimed that they should be regarded as normal. Caffey *et al.* (1958) detected accessory bony nuclei in the distal femoral epiphysis in children aged between 4 and 12 years in 19 cases out of 147. Ribbing (1951) and Smillie (1960) suggested that some of these accessory centres of ossification are precursors to juvenile osteochondritis dissecans. The results in the present series E showed that an accessory bony nucleus in a growing individual may result from an intra-

cartilaginous cleavage sustained at an earlier age. Whether a condition resulting from a previously sustained cleavage in cartilage was involved in some of the cases of accessory bony nuclei in children described by the above-mentioned writers remains an open question.

The present results as compared with the pathological anatomy of osteochondritis dissecans

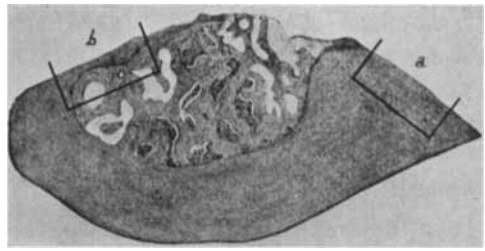
ROBERTS (1957) stated with regard to osteochondritis dissecans: »No hard and fast criteria can be laid down as being necessary to justify the diagnosis but it is usually accepted that the diagnosis can be properly applied to any case in which a portion of articular surface, not necessarily containing bone, separates or attempts to separate by a process of gradual and 'dissecting' extrusion.» Since in the present study both completely loose and pedunculated joint-mice, some of them containing a bony nucleus and others not, were experimentally created, there seems to be a resemblance between the present results and osteochondritis dissecans, if ROBERT's definition of this condition is accepted.

A common finding in osteochondritis dissecans is that the border of the bony nucleus is surrounded by hyaline cartilage extending for some distance between the fragment and the concavity (LEB 1924, LEHMANN 1925, LACROIX 1941, BIANCHI *et al.* 1955). A similar observation was made in several experiments in the present study (Fig. 22, page 37, Fig. 25, page 39, Fig. 34, page 43 and Fig. 54, page 57).

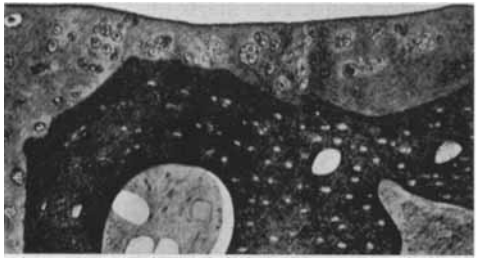
LACROIX (1941) described a case of osteochondritis dissecans in which the outer surface of the fragment was coated with normal cartilage, which at the margin included the periphery of the underlying bony nucleus (Fig. 104). On the aspect facing the concavity, the bony nucleus was covered by what LACROIX called young cartilage, which was characterized by the arrangement of cells in clusters (Fig, 104 b). In stage 7, series A, of the present study (Fig. 22, page 37) and in stage 4 a, series B (Fig. 54, page 57) a similar finding was made at the corresponding site of the fragment.

In the case described by LACROIX the cartilage cells at the margin of the fragment were arranged in rows at right angles to the articular surface and parallel with the cleavage (Fig. 104 a). A similar finding was made in series A, stage 10 (Fig. 34, page 43).

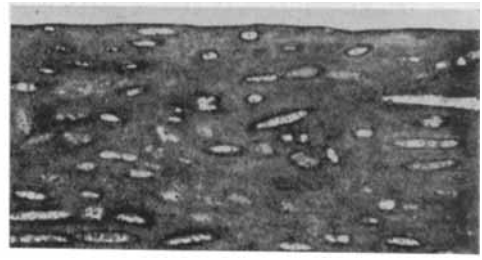
PHEMISTER (1924), LEHMANN (1925) and BIANCHI *et al.* (1955) described cases of osteochondritis dissecans in which the spongy bone of the frag-



*) Fig. 104

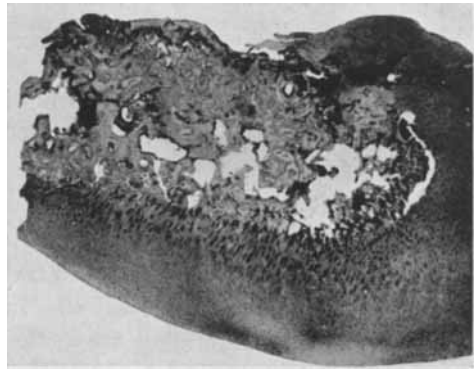


*) Fig. 104 b



*) Fig. 104 a

ment showed a strikingly dense structure (Fig. 105). There was a similar finding in series B of the present study, stage 3 b (Fig. 49, page 55) and stage 4 b (Figs. 59 and 60, page 59).



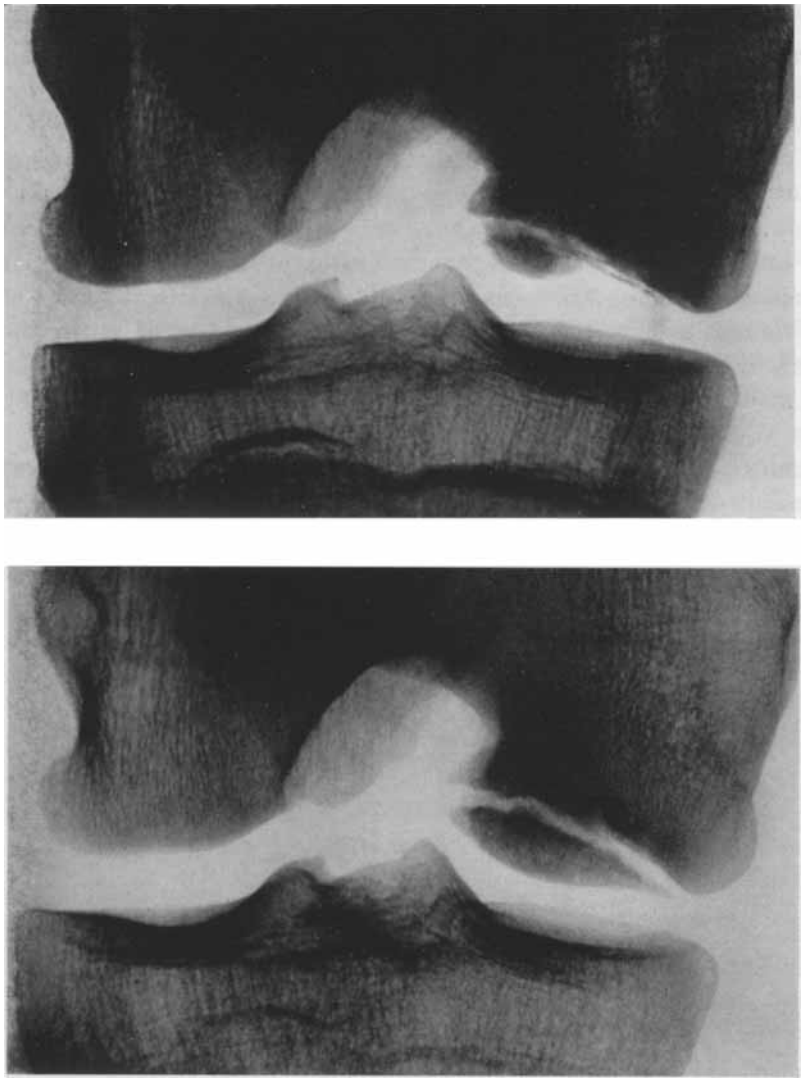
**) Fig, 105

In series A and B many of the separate fragments united with their beds. Analogously in series E this was consistently the case. Spontaneous

*) (With the courtesy of P. LACROIX).
**) (With the courtesy of J. C. LEHMANN).

healing of the lesion in osteochondritis dissecans has been reported by WIBERG (1943), NOVOTNY (1951, 1952), PICK (1955) and others.

On roentgenological follow-up of patients with osteochondritis dissecans FREIBERG (1923) and SCHELLER (1960) observed that the shadow of the



A.

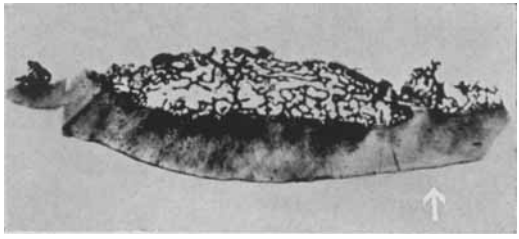
B.

Fig. 106. A. -A roentgenogram of the knee of a 16-year-old boy with osteochondritis dissecans. B. -The same knee two years later. Note the growth of the fragment. (A. LANGENSKIÖLD unpublished observations)

fragment grew. In the Orthopaedic Hospital of the Invalid Foundation growth of the fragment has been observed in several cases of osteochondritis dissecans (A. LANGENSKIÖLD unpublished observations). See Fig. 106. That growth of the fragment occurred in the present study, series A, could be inferred from some of the micrographs (Fig. 11, page 31, Fig. 14, page 33 and Fig. 17, page 35). SCHELLER explained his observation as »not an expression of authentic growth but of increased calcium content in the lesion which is therefore visualized more distinctly on the roentgenogram». It is also possible, however, that the roentgenological finding reported by FREIBERG, SCHELLER and LANGENSKIÖLD may be the manifestation of a process analogous to that described in the present series A, *i.e.* to authentic growth.

PHEMISTER (1924) and FAIRBANK (1933) pointed out that in osteochondritis dissecans, fragments which originated in the lateral margin of the condyle and remained pedunculated by ligament and synovial tissue, contained living bone and showed signs of bone formation. A similar finding was made in the present study, series B, stage 4 a (Fig. 54, page 57) and series C, stage 3 b (Fig. 71, page 71).

LEHMANN (1925) described a case of osteochondritis dissecans in which downward protrusion of the joint cartilage marked the border between the fragment and its surroundings (Fig. 107, note arrow). A similar finding



*) Fig. 107

was made in the present series A, stage 9 (Fig. 28, page 41). In addition, LEHMANN observed islands of hyaline cartilage at the border between the fragment and its bed. A similar feature was observed in the present study, series A, stages 8 and 9 (Fig. 25, page 39 and Fig. 27, page 27).

Several authors (see page 19) have shown that the bony nucleus of the fragment was viable in osteochondritis dissecans. Living bone in the separate fragment was also observed in many cases in the present study.

*) (With the courtesy of J. C. LEHMANN).

LEHMANN (1923), FAIRBANK (1933) and others have reported that the concavity remaining in the articular surface after separation of the fragment was lined with fibrous connective tissue, fibrous cartilage or hyaline cartilage In the present study a similar finding was repeatedly made at the corresponding site (Fig. 45, page 53, Fig. 48, page 55, Fig. 53, page 57, Fig. 58, page 59 and Fig. 73, page 71).

The present results as compared with the data on experimentally induced imitations of osteochondritis dissecans

As mentioned in the survey of the literature, many investigators have tried to create osteochondral joint-mice in laboratory animals by detaching pieces of cartilage and bone completely or partially from the joint surface and replacing them in their beds. The fragments united with the joint capsule, with the site from which they had been gouged out, with the synovial tissue or the periosteum, or were completely resorbed.

In order to study the uptake of radioactive sulphur in loose joint-mice, BAILEY & SELLE (1959) excised a fragment (probably consisting of cartilage and bone) from the surface of the knee joint in 4- to 8-week-old rabbits and placed it in the intercondyloid fossa. After 2 to 6 months the fragments were found as loose bodies with necrotic bony nuclei surrounded by fibrous connective tissue. The concavity at the site from which the fragment had been excised was covered by fibrous connective tissue. These writers performed no experiments in which the fragments were replaced in their beds.

By repeated blunt trauma of the joint surface REHBEIN (1950) brought about necrosis of the cartilage and the underlying bone. The necrotic area was separated from the surroundings by a streak of loose tissue. At the proximal side of this, bone formation was seen, at the distal side, resorption of bone. Loose bodies did not result.

By incision or infraction of articular cartilage and the underlying bone in growing rabbits NAGURA (1938) and BURCKHARDT (1948) brought about the development of a streak of hyaline substance, which underwent slow enchondral ossification. In this way NAGURA succeeded in separating a piece of the subchondral bone of the patella. Loose bodies did not result.

In this connection the following statements by DE PALMA (1954) concerning the etiology of osteochondritis dissecans may be cited: »Critical assessment of the varied theories advanced by numerous investigators fails to provide an explanation for the origin of loose bodies under discussion,

which is supported by indisputable clinical and scientific observation. Although most investigators feel that trauma, in some form or manner, plays a significant role, no foolproof mechanism has yet been conceived . . .».

In the present study both completely loose and pedunculated joint-mice, both with and without a living or necrotic bony nucleus, were created. Furthermore, a marked resemblance could be demonstrated between these results and the pathological anatomy of osteochondritis dissecans. It may, perhaps, be stated therefore that these results imitate osteochondritis dissecans more obviously than any previously reported in the literature. Thus the hypothesis formulated in A. LANGE»SKIÖLD's paper of 1955, »Can osteochondritis dissecans arise as a sequel of a cartilage fracture in early childhood?», seems to be justified.

SUMMARY

In order to study more closely the development of the post-traumatic condition resembling osteochondritis dissecans described by A. LANGENSKIÖLD in 1955, mechanical lesions of articular cartilage were created in a total of 114 rabbits aged from one to 12 days. On the basis of the type of experimental lesion induced, the material was divided into the following five series:

Series A »large fragment». From the cartilage of the medial femoral condyle a fragment, 1.4—1.8 mm deep, was gouged out with a sharp scoop, a hinge of cartilage and ligament tissue facing the intercondyloid fossa excepted (Figs. 1 and 2, page 25).

The series comprised 20 animals killed at different intervals up to an age of 102 days.

Series B »small fragment». The same operation was made as in series A, but the fragment was made only 0.7—1.2 mm deep (Fig. 38 page 49).

The series comprised 40 animals killed at different intervals up to an age of 200 days.

Series C »hinge of ligament tissue». The operation was performed as in series A, but the hinge left consisted of ligament tissue alone (see Fig. 62, page 65).

The series comprised 18 animals killed at differet intervals up to an age of 200 days.

Series D »loose fragment». The same operation was performed as in series A, but the fragment was completely detached and replaced in its bed.

The series comprised 16 animals killed at different intervals up to an age of 120 days.

Series E »intracartilaginous cleavage». Using a special instrument an intracartilaginous cleavage was created in the cartilage of the medial femoral condyle. The cleavage separated a piece of cartilage from the underlying

tissue, excepting the most superficial layer of the joint cartilage, which was left intact (see Fig. 93 and 94, page 85).

The series comprised 18 animals killed at different intervals up to an age of 150 days.

The specimens obtained were studied macroscopically, microscopically and roentgenologically. In the different series the following findings were made:

Series A »large fragment«. During the course of growth a concavity was formed in the subchondral zone of ossification (Fig. 7, page 29). In the fragment a separate centre of ossification was formed, which grew (Fig. 11, page 31, Fig. 14, page 33 and Fig. 17, page 35). In the cleavage between the fragment and the concavity the following structures succeeded each other: granulation tissue, hyalinized connective tissue, primitive cartilage and hyaline cartilage. The cleavage disappeared and was replaced by a solid wall of hyaline cartilage (Fig. 20, page 37) which was divided into fragments by enchondral ossification (Fig. 27, page 41) and subsequently disappeared, so that the previously separate bony nucleus fused with the rest of the epiphysis. In the plane of the joint surface the cleavage persisted partially, while partially its margins were united by hyaline cartilage showing an irregular structure (Fig. 28, page 41, Figs. 33 and 34, page 43).

Series B »small fragment«. Three different lines of development were discernible.

1. The fragment ossified and fused with its bed, the course being mainly the same as in series A.

2. The fragment ossified (Fig. 44, page 53 and Fig. 48, page 55) and became detached, so that a completely loose (Fig. 59, page 59) or pedunculated joint-mouse (Fig. 52, page 57) resulted, which contained a necrotic or living bony nucleus. The concavity was covered by fibrous connective tissue, primitive cartilage or hyaline cartilage. The two last-mentioned tissues showed signs of ossification (Fig. 53, page 57 and Fig. 58, page 59).

3. The fragment did not ossify, but became detached and formed a completely loose joint-mouse. The course was the same as in series D.

Series C »hinge of ligament tissue«. The fragment was dislocated from its bed. Corresponding to the latter a concavity was formed in the zone of ossification (Fig. 67, page 69). This concavity was partially filled by primitive cartilage, which later was replaced by hyaline cartilage of somewhat irregular structure. Most of this cartilage ossified, so that the concavity in the outline of the bone was levelled out. The condyle remained deformed (Fig. 70, page 71). The fragment grew, while remaining attached to the ligamentous peduncle. On the surface its cartilage maintained its

normal structure. It was surrounded by a thin capsule of connective tissue. The central portions of the fragment degenerated and calcified. In one case the fragment contained a living bony nucleus (Fig 71, page 71).

Series D »loose fragment». The concavity in the cartilage was incompletely filled by primitive cartilage (Fig. 79, page 77), later by hyaline cartilage of irregular structure (Fig. 84, page 79). This cartilage ossified slowly, so that a concavity initially was formed in the subchondral zone of ossification (Fig. 79, page 77). Later this concavity was levelled out (Fig. 88, page 81). The condyle remained deformed (Fig. 92, page 81). The fragment grew, degenerated at the centre and calcified. Its peripheral parts remained viable.

Series E »intracartilaginous cleavage». In the intracartilaginous cleavage primitive cartilage, and later hyaline cartilage, was formed. A concavity developed in the subchondral zone of ossification (Fig. 96, page 87). In the separated cartilaginous fragment a separate bony nucleus developed (Fig. 99, page 89). Later the cartilage which had been formed in the cleavage ossified (Fig. 101, page 91), and in the course of development normal conditions were re-established, apart from the fact that the operated condyle remained broader than the intact one.

The results were assessed in the light of the relevant literature and compared with the data on the pathological anatomy of osteochondritis dissecans. Striking resemblances were found. The results of the present study seem to support the hypothesis formulated by A. LANGENSKIÖLD in 1955: »Can osteochondritis dissecans arise as a sequel of a cartilage fracture in early childhood?»

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