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RÔLE OF SURGICAL INTERVENTIONS OF THE HIP JOINT IN THE AETIOLOGY OF ASEPTIC NECROSIS OF THE FEMORAL HEAD

EXPERIMENTAL STUDY

BY
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PREFACE

The subject of this work was suggested by my highly respected teacher and present principal, Professor K. E. KALLIO, M.D., Chief of the First Surgical Clinic of the Central Hospital, University of Helsinki, the Clinic for Orthopaedics and Traumatology, and Surgeon-in-Chief of the Töölö Hospital. He has not spared his advice, encouragement and constructive criticism in the different stages of my work, and I am very happy of this opportunity to express my deep gratitude for his attention.

The microscopic work and the special investigations involved in my studies were carried out in the Department of Forensic Medicine, University of Helsinki. Its Chief, my former teacher, Professor U. UOTILA, M.D., has given me most valuable aid in the form of ample advice and unfailing criticism. My sincerest thanks are due to him for this and for the use of the Department's facilities.

The interest shown towards my work by University Lecturer R. KÖHLER, M. D., has enabled me to make the required x-rays in the Roentgenological Department of the Surgical Clinics of the University of Helsinki. My inclination towards scientific research was first inspired by University Lecturer S. VAINIO, M.D., at the time I was working under him. I feel greatly obliged to them both.

The English translation of my manuscript was made by Mr. U. ATTILA, M.Sc., and read by Miss ELVI KAUKOKALLIO. In the compilation of references from the pertinent literature I have been aided by Miss AINO NIKUPAAVO, M.A., and by Mrs. EEVA KIHLBERG, M.A. Assistance in the technical aspects of the work was given by Mr. J. SALORANTA, M.Sc. in Eng., who also drew the diagrams reproduced here. Mr. H. LAINE, B.M.S., assisted me in the operations on the rabbits and in the x-ray work, and Mr. A. TAMMINEN in the microradiographic technique. The histologic preparations were processed by Mrs. LISBETH SCHWANCK, and Mr. P. KORHONEN of the Photographic Department of the University of Helsinki made the micrographs. All these persons are deserved of my sincere thanks.

The operation room nurses of the First Surgical Clinic have placed at my disposal the equipment and materials needed in the operations, while

the nurses of its Roentgenologic Department assisted me in the x-ray procedure. I wish to express my gratitude to them, as well as to all others, not specifically mentioned here, who have aided my work in various ways.

To my wife, AILA ROKKANEN, Lic.Med., I am deeply thankful for her loving help and understanding throughout the progress of the work.

This work has been partially aided by an institutional grant from the SIGRID JUSÉLIUS Foundation, Helsinki, to the Department of Forensic Medicine, University of Helsinki.

Helsinki, May, 1962.

Pentti Rokkanen

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INTRODUCTION

GENERAL CONSIDERATIONS

Regardless of the method that may be applied, arthroplasty of the hip joint involves opening of the joint, division of the ligamentum teres, dislocation of the femoral head, and even capsulectomy. It is only natural that in a clinic which applies its own method, skin arthroplasty, and in which much reconstructive work is also otherwise done on the hip joint, there is a desire to penetrate into fundamental factors for such surgical interventions. Accordingly, I was advised in the autumn of 1958 by my present principal, Professor K. E. KALLIO, M.D., to find out by means of animal experiments whether the above mentioned operations might produce aseptic necrosis of the bone of the femoral head. In the course of the work it turned out to be worth while to investigate whether the cancellous circulation might also be affected by other expedients. This is the background against which the present work has taken shape.

SOME OBSERVATIONS ON THE BLOOD SUPPLY OF BONE AND ITS DISTURBANCES

Clinical investigations. — An early observation concerning the circulation of the femoral head was made by HUNTER (1743), who found that the blood vessels, prior to entering the bone, are anastomosed in the subsynovial layer, constituting the so-called circulus articuli vasculosus. Numerous investigations (PALLETTA 1820, COOPER 1823, SAPPEY 1869, LANGER 1875) were carried out in the last century also concerning the blood supply of the femoral head, although they were mainly macroscopic in character, with no tracing of the circulation within the bone in greater detail being done. LANGER (1875) already showed that bones have their main arteries, but awareness of the circulatory disturbances of bones and joints was slow in developing. It is certainly true that VOLKMANN (1864) described multiple, suppurating infarcts in bones in connection with septic endocarditis. KÖNIG (1888) characterized osteochondritis dissecans as an independent disease, attributing it to contusion with a subsequent necrotic

process and inflammatory sequestration of a bone fragment, but he was not able to explain the origin of the necrosis. The first observation relating to aseptic disturbance of circulation of the bone was made in association with bone transplantation. This was when BARTH (1893) observed that the transplanted bone tissue dies and is later replaced with new bone.

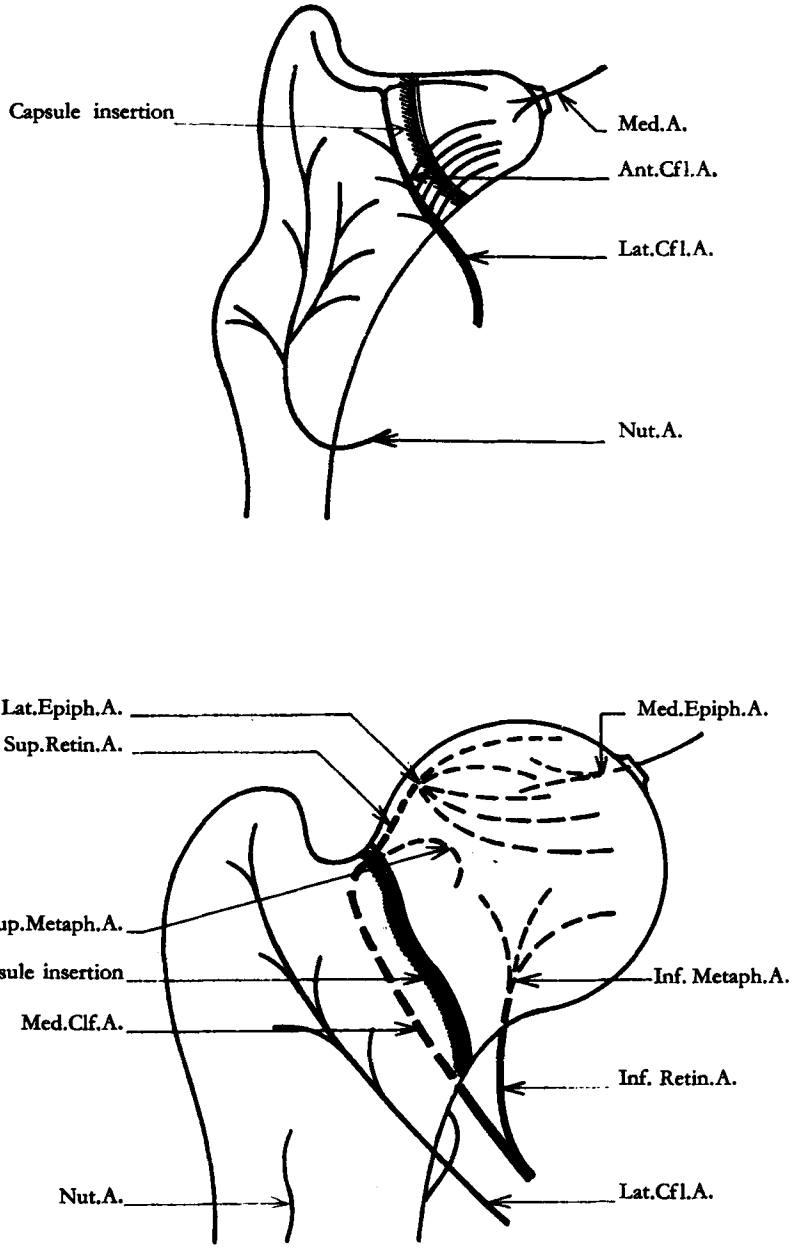
Aseptic necrosis of bone will occur in a place where the blood supply of the bone has been disturbed to a sufficient degree. It is most readily produced in the epiphysis of the bone. Accordingly, the most numerous observations in earlier times were made in connection with so-called spontaneous epiphyseal necrosis. Here, we have reason to mention AXHAUSEN, who has studied the bone necrosis problem already since 1911 and who created in 1922 the actual concept of avascular necrosis of the bone, by clarifying its histologic picture and combining the concepts of osteochondritis dissecans and spontaneous epiphysitis. He described, in a patient aged 16, necrosis of the bone after a ten-months-old fracture of the neck of the femur, in which he found total necrosis of the spongy bone, bone marrow and epiphyseal cartilage, and partial necrosis of the articular cartilage.

It has been realized later that traumata, such as fracture of the neck of the femur and dislocation of the femoral head, may cause necrosis of the bone on the basis of circulatory disturbance. Also contusion may result in necrosis of the bone. According to PHEMISTER (1931), JACKSON and BICKELL (1948) and BLOUNT (1956), necrosis of the bone subsequent to fracture of the trochanter is rare. Furthermore, necrosis of the bone is encountered in the caisson disease (*e.g.* MCCALLUM *et al.* 1954) and in certain forms of anaemia (*e.g.* TANAKA *et al.* 1956). Moreover, BOYD (1957) has described the so-called coronary disease of the hip.

Necrosis of the bone occurs also in connection with arteriosclerosis. For instance, MÜLLER (1927) observed in four, JAFFE and POMERANZ (1934) in seven, and SHERMAN and SELAKOVICH (1957) in ten patients subjected to amputation on account of circulatory disturbance a deranged blood supply and necrosis of the bone, particularly in the intermediate lamellae. Also in connection with normal aging arteriosclerosis, and thus necrosis of the bone, occurs physiologically already, just as connective tissue degenerates as it becomes older (RISSANEN 1960).

We thus see that the states are numerous in which aseptic necrosis of the bone plays a central part in orthopaedic surgery, even apart from the bone necrosis phenomenon encountered in connection with normal repair of a fracture. In his extensive monograph, HÄUPTLI (1954) has reviewed the chondro-osteonecroses.

Fig. 1. Anterior view of the blood supply of the femoral head in adult rabbit and man



TRUETA and HARRISON (1953) and after them JUDET *et al.* (1955), in respect of adults, and TRUETA (1957), in respect of children, were the first to clarify the blood supply in the femoral head and neck in persons of different age and to show that it changes in the course of time. Fig. 1 is a schematic presentation of this blood supply in the femoral head of a human adult, according to TRUETA, and, for comparison, that in the head of the rabbit femur, according to LEMOINE (1957). Not until this normal anatomy was clarified was a basis established for investigation of circulatory disturbances and necrosis of the bone and for their understanding in various clinical conditions relating to the head of the femur.

Animal experiments. — Numerous experiments have been arranged to produce necrosis of the bone in animals and to clarify its clinical and histological picture. CORNIL and COUDRAY (1904) showed that in bone fractures in the rabbit necrosis of the cortex ensues at some distance from the line of fracture, and that this is followed by replacement of the dead bone with new bone. The importance of the epiphyseal line was pointed out by an observation made by JACKSON (1913). When he attempted to induce experimental arthritis in rabbits by intravenous injection of pyrogenic organisms, wedge-like infarcts of bone were produced, which were located in the metaphyses immediately under the epiphyseal cartilage. This indicated that the main arteries of the epiphysis may be obstructed by emboli. Later investigations have also shown that the epiphysis may act as an obstruction preventing blood flow to the head of the bone (HARRIS and HOBSON 1956).

AXHAUSEN (1914) produced necrosis of the bone by application of heat, cold, and tincture of iodine. ELOESSER (1917) observed that sectioning of a nerve of a certain kind without sympathectomy produced articular changes resembling Charcot's disease. BANCROFT (1922) introduced croton oil into the dog's humerus by intramedullary injection, obtaining necrosis and rapid involucrum formation, as well as swift healing. He stressed the importance of the blood supply in bone regeneration. Using radium, PHEMISTER (1926) produced necrosis of bone in the humerus and knee joint of dogs. BRUNSCHWIG (1930) found that detachment of the periosteum in young dogs caused extensive necroses in the femur and tibia. In the head of the metatarsus of a growing dog, SACERDOTE (1931) produced marked necrosis and deformity by detaching the periosteum from the fractured segment. Either removal of the periosteum or fracture resulted in a much lesser degree of vascular changes and attendant necroses.

CORBIN (1937) studied the question in experiments with 15 cats, finding that section of lumbal and sacral nerve roots produced considerable ar-

thritic changes although also sympathectomy had been performed: the cartilage degenerated, was destroyed, and the spongiosa became sclerosed. THOMASEN (1939) investigated the humerus and femur of six-months-old pigs weighing about 66 kg; he found changes in five bones out of 2203 of the latter kind and in 62 out of 1482 (4 %) of the former. They were resemblant of infarct situated subchondrally, with the base towards the cartilage. Microscopic examination revealed fibrous tissue, abundant cells and new blood vessels in the cancellous spaces, but no signs of osteoblasts or osteoclasts, nor any of actual necrosis. All the same, he considered the changes most nearly like those of osteochondritis juvenilis.

Remarkable were also the clinical as well as experimental studies carried out by NAGURA (*e.g.* 1937, 1938, and NAGURA and KOSUGE 1938) in his investigation of the similarity in aetiology between osteochondritis dissecans and so-called spontaneous epiphyseal necrosis. With a hammer blow he induced a blunt trauma at the upper and lower ends of the femur in young rabbits and followed the resulting changes histologically; in addition to the immediately ensuing demolition and rebuilding process also another secondary such process took place (the so-called phenomenon of NAGURA). According to him, in every avascular bone necrosis the primary occurrence is a small, subchondral fracture, and the bone necrosis is produced traumatically. BURCHARDT (1948) repeated NAGURA's work with rabbits of 5—7 weeks' age, confirming his findings.

RUTISHAUSER and MAJNO (1949) resected part of the radius in dogs, producing osteonecrosis in the ulna, on the basis of an overexertion phenomenon. The same investigators (RUTISHAUSER and MAJNO 1951) also paid increased attention to the changes of various kinds occurring in the osteocyte itself and in the ground substance in conditions of bone necrosis. TRUETA (1954) performed experimental investigations of the regeneration of bone in rabbits and found that the presence of dead bone was important, though not indispensable, in order that regeneration of the bone might take place. The sequel of the reaction caused by dead bone was hyperaemia, according to HARRISON *et al.* (1953).

SOME SPECIAL INVESTIGATIONS FOR CLARIFICATION OF THE BLOOD SUPPLY OF BONE

By the usual clinical means, futile attempts have been made to elucidate the circulation of the femoral head in various traumatic conditions.

At roentgenologic assessment of avascular necrosis of bone one has to observe, according to the clinical and experimental work of LACHMAN and WHELAN (1936), that the loss of calcium must amount at least to 20 per cent before the change in density becomes obvious in the x-ray.

According to WATSON-JONES and ROBERTS (1934), increased density in an avascular bone is merely a secondary phenomenon when the adjacent, living bone is hyperaemic and decalcified. This occurs because calcium cannot be mobilised from the dead fragment and the density therefore remains unchanged. Admittedly, many investigators are of the opinion that the bone is not really dead but that rather there occurs transient reossification, with new bone being apposited on the surface of the dead bone trabeculae, producing so-called creeping substitution (*e.g.* PHEMISTER 1935, 1939, DE HAAS and MACNAB 1956, and BONFIGLIO and BARDENSTEIN 1958).

Thus bone may, in likeness with other dead tissues, take up calcium salts from its surroundings and the density will increase also by this mechanism. This provides indeed an explanation for the trabecular structure and for the increased density at the point in question in the x-rays. Moreover, it should be noted that ossified intercellular matter does not change immediately even in the roentgenologic respect. As AXHAUSEN (1922) has observed, dead bone (the avascular organic matrix) gradually loses its strength and resistance so that it will collapse and the density will in fact increase. BOBECHO and HARRIS (1960) observed in the course of repair of bone necrosis experimentally induced in rabbits that in the fifth week the new cancellous cavities were smaller in size in comparison with those existing before, and the density was thus indeed due to reossification. They furthermore corroborated their result by autoradiography with radio-calcium. They also reported that the density began to be observable at 3 weeks, but with certainty only at 8 weeks, after inception of the bone necrosis. Since in man the corresponding change takes place mostly at an even slower rate, it is evident that this method, too, is slow and judgment of its results is difficult.

As a means to obtain results more rapidly, arteriography has been applied by, *e.g.*, ROOK (1953) and MÜSSBICHLER (1956) in attempts to clarify the blood supply of the femoral neck in fractures. However, the investigation renders mainly a picture of the circulatory disturbances that occur outside the bone. Microangiography (BARCLAY 1951) has not been developed for elucidation of man's intraosseal circulation in clinical conditions. HULTH (1956, 1958, 1958) suggested venography as a method by which in connection with operation an idea of venous damage and indirectly also of trauma to the parallel artery can be obtained, and he considered that in this manner the extent of the avascular bone necrosis to be expected might be inferred. BENASSY and LAMARE (1956), for instance, have also employed venography in their investigations on coxarthroses.

There have been attempts to clarify the blood supply of bones with the aid of radioactive isotopes. In England, TUCKER (1950) was the first to apply radio-phosphorus clinically, after preliminary tests with rabbits, in order to determine the circulation in the femoral head in 13 patients who had a fractured neck of the femur. Similarly, in a series of 45 patients with fractured neck of the femur, ARDEN and VEALL (1953) took bone specimens from the femoral head and from the trochanteric region, examining their radioactivity and comparing the relative values indicating the blood supply of the femoral head. They considered their results encouraging. BOYD *et al.* (1955) investigated this question with 15 dogs in which avascular necrosis had been produced by division of the ligamentum teres, inflicting damage to the capsule and, furthermore, performing in some instances osteotomy on the neck of the femur. In addition, they studied 53 clinical cases. LAING *et al.* (1957) administered radio-phosphorus to ten rabbits by intravenous injection and took bone specimens at different points. They stressed the importance of the time when the specimens are taken. LAING and FERGUSON (1959) produced in 33 dogs dislocation of the femur in connection with damage caused to the lig. teres and to other blood vessels; in addition, they studied avascular bone necrosis with the aid of radioactive sodium. They were well satisfied with their results.

In contrast with the preceding report, ARDEN (1960), after having assembled 100 clinical cases with an observation period exceeding two years, noted a primary error percentage of 40 per cent, while one-fifth of the remaining results were doubtful. He placed weight on the significance of the point of measurement, that is, on its equivalent location, because the radioactivity is high close to the lig. teres owing to its still active circulation, while it is low in the neighbourhood of the fracture itself. He considered additional studies to be necessary before the method might be adopted for general use. Also STEVENS (1960) arrived at a similar result in his experiments with rats. NORDBY (1960) reported the successful use of radioactive iodine to establish unilateral cases of necrosis of the femoral head. In experimental studies autoradiography with various isotopes has also been employed as a means to clarify the vascularization of bone, as has been described by FITZGERALD and ENGSTRÖM (1952) and by BOYD (1955). However, owing to their inconvenience the methods have not found their way into everyday clinical usage.

HULTH (1961) employed microradiography in four cases in his investigation of aseptic necrosis of the femoral head. He said that the trabecular bone structure was well preserved and that the hypersclerosis was due to revitalization of bone.

We may thus state that it has not been possible so far to observe any positive signs of necrosis of the bone other than the lack of nucleus in the osteocyte, which was demonstrated by AXHAUSEN (1922, 1926, 1928) and by AXHAUSEN and BERGMANN (1937) and which they considered absolutely reliable. It is certainly true that the phenomenon takes place at a slow rate. Although the bone can be considered dead already 4—5 days after its blood supply has been arrested, disappearance of the nucleus in the osteocyte does not occur until after 2—3 weeks, as was shown by WOLLENBERG (1928) in his experiments with white mice. The increase of fibrous tissue in the cancellous spaces furnishes an indication of incipient regeneration and subsequent metaplasia, with simultaneous replacement of the dead bone by new bone; a phenomenon which PHEMISTER (1926) has named creeping substitution, as stated above.

Chemicals and dyes, such as *e.g.* fluorescein, have also been employed for the purpose of demonstrating necrosis of the bone, but the methods have been rejected because of failure to elicit sensitive response.

The facts emerging from this review seem to justify another attempt at clarification, by means of animal experiments, of questions relating to the aetiology of aseptic necrosis of bone.

PROBLEMS

The purpose of the present work was to elucidate the following questions associated with arthrotomy:

1. What signs of aseptic necrosis, either macroscopic or roentgenologic, are produced in the femoral head by arthrotomy of the hip joint, division of the lig. teres and temporary luxation of the femoral head in rabbits 6—7 months of age?

2. What changes are produced in the femoral head when it has been subjected to similar dislocation by operative interference and subsequently left in a luxated state?

3. What changes are produced in the femoral head by arthrotomy and capsulectomy?

4. What changes are produced in the femoral head by nearly total osteotomy of the neck of the femur?

5. What changes are produced in the femoral head by tight ligation of the neck of the femur with steel wire?

6. What changes are produced in the femoral head by the mere ligation of the deep femoral artery and the obturator artery?

7. Does such aseptic necrosis as may be called forth by the above mentioned interferences present a correlation with the changes in the articular cartilage?

8. How is aseptic necrosis of bone demonstrated histologically, autoradiographically and microradiographically?

MATERIAL AND METHODS

EXPERIMENTAL ANIMALS AND OPERATION TECHNIQUES

The experimental animals were rabbits, which were mostly white, and of both sexes. During the experiments they were kept in well-lighted, roomy cages, each animal in its own compartment. Postoperatively, the animals were kept in the animal stables of the clinic for a period of 1—2 weeks and then transferred to the stables of a pharmaceutical factory, where they received the same kind of care. The rabbits received the routine diet of the stables, *i.e.*, water *ad libitum*, dry hay and bread or oats and in the stables of the clinic also very frequently vegetables, such as carrots, cabbage and swedes. In the animal stables of the pharmaceutical factory they were given, in addition to the routine feed, fresh field grass in summer and compressed concentrates and mixed meal in winter.

Altogether 155 animals were used in the experiments, divided into six groups. Only one operation was made on the left hip of each animal, while the right hip served as control. The periods of observation and the distribution of the animals among the different experimental groups are seen from Table 1. Ten rabbits died under anaesthesia and four others (Nos. G IV 60, G VI 10, 20 and 25) of unknown cause. No specimens were taken from these animals, but replacements were provided for the first mentioned and subjected to the same operation.

In preliminary experiments, some rabbits were operated by anterior approach to the joint, but all of them sustained subsequent luxation and this procedure had to be abandoned. Immobilization of the operated extremity was attempted in the preliminary experiments by tying it to the body with elastic adhesive tape, or in other cases by tying both lower extremities together. These measures, too, caused luxations as well as untidiness of the animals, and for this reason no immobilization of any kind was employed in the experimental series proper. Altogether 12 rabbits were used in the preliminary experiments, of which two developed infection, four sustained luxation, two died of unknown cause and four died under anaesthesia.

TABLE 1. *Plan of experiments*

Group	Surgical interference	Number of experimental animals																									Studies performed						
		Total	Time of examination, days since operation																								X-Ray	Histologic				Autoradiography	Microradiography
			5	10	15	20	25	30	35	40	45	50	60	70	80	90	100	110	120	130	140	150	180	240	360			Weigert-van Gieson	Alcian blue	Pentachrome II	P.A.S.		
I	Arthrotomy, Division of lig. teres, Temporary luxation of femoral head	22	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	—	41	22	7	—	5	—	—
II	Arthrotomy, Luxation of femoral head without reduction	22	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	—	41	22	7	1	5	2	2
III	Arthrotomy, Capsulectomy	22	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	—	41	22	7	—	5	1	1
IV	Arthrotomy, Nearly total osteotomy of neck of femur	21	1	1	1	1	1	1	1	1	1	1	—	1	1	1	1	1	1	1	1	1	1	—	39	21	9	4	5	2	2
V	Arthrotomy, Tight ligation of neck of femur with steel wire ..	22	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	—	1	41	22	9	2	5	2	2
VI	Ligation of deep femoral artery and obturator artery	19	1	—	1	—	—	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	—	36	19	7	—	5	1	1

The operations were performed in the operating room of the clinic's animal stables under careful asepsis. An undiluted solution »Diminal» of Astra (Sweden) was used as anaesthetic. During operation the animal was kept lying freely on its right side, with no restraining bands. From the area to be operated, the hairs were cut with scissors and it was cleaned with »Iodopax» of Ferrosan (Sweden).

The left hip was explored through a posterolateral incision, following the course of the musculature. The posterior surface of the joint was reached after the sciatic nerve had been pulled to one side. The joint capsule was opened in all other cases except in those of Group VI.

Thereafter, in Group I, the ligamentum teres was divided after the joint space had been rendered more wide by pulling the extremity ventrally and rotating it inwards. The femur was luxated backwards and kept in this position for a while, after which it was repositioned in the acetabulum. The capsule was not sutured, but the margin of the muscle was drawn up to cover it, and the wound was closed by layers with thin catgut. Two separate applications of »Nobecutan» plastic film spray of Bofors (Sweden) were made in the sutured wound.

In Group II the extremity was left permanently in its luxated position.

In Group III the operation described above was supplemented with capsulectomy during the phase of luxation, which invariably resulted in heavy haemorrhage from the ventral capsule.

In Group IV, osteotomy of the neck of the femur was performed in connection with the luxation, applying an electric saw so that the osteotomy surface was equivalent to at least two thirds of the diameter of the neck. This osteotomy was made in the middle of the neck of the femur, starting from its caudal margin. The femoral head was then repositioned and the wound closed in the usual manner.

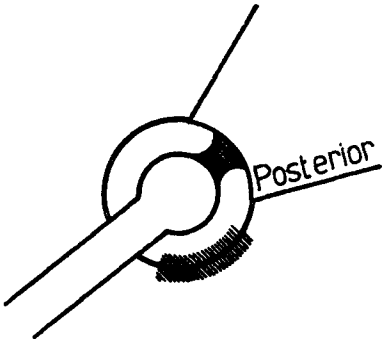
In Group V the neck of the femur was ligated with a tightly applied steel wire while the femoral head was held luxated. For attachment of the wire, the greater trochanter was pierced with an electric drill and the end of the steel wire was passed through the hole. The steel wire thus formed a double loop.

In Group VI the joint was not entered at all, but the large vessels which branch off later into the joint, *i.e.*, the deep femoral artery and the obturator artery, were ligated. During this operation the muscles attaching to the greater trochanter were cut off temporarily.

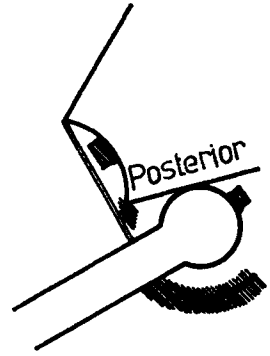
The different operations that were performed are shown in the schematic diagrams in Fig. 2.

Each rabbit received postoperatively 100,000 I. U. of procaine peni-

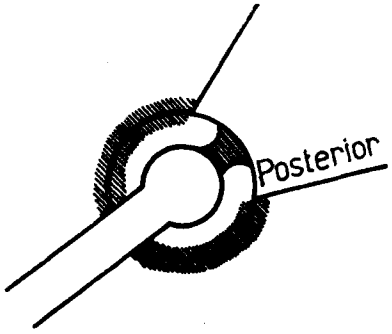
Fig. 2. Operations performed



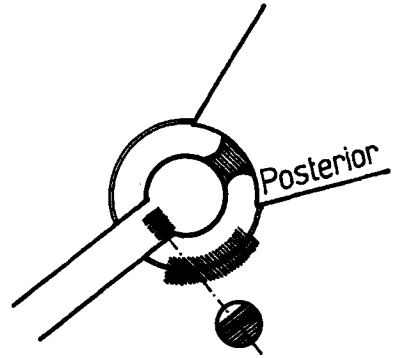
GROUP I
Arthrotomy,
Division of lig. teres, Temporary luxation of the femoral head



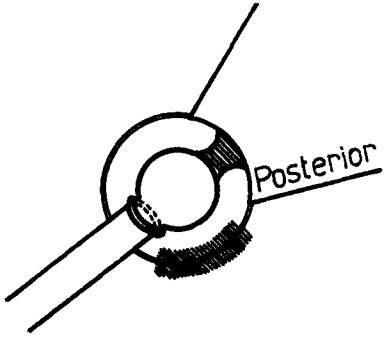
GROUP II
Arthrotomy,
Luxation of the femoral head without reduction



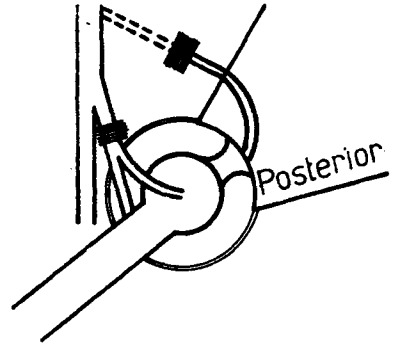
GROUP III
Arthrotomy,
Capsulectomy



GROUP IV
Arthrotomy,
Nearly total osteotomy of the neck of the femur



GROUP V
Arthrotomy,
Tight ligation of the neck of the femur with a steel wire



GROUP VI
Ligation of the deep femoral artery and the obturator artery

cillin intramuscularly and was transferred to its cage while still under anaesthesia. In one instance distinct infection was observed in the joint, and another animal was operated to replace the subject.

The individual rabbits were marked according to a systematic key, in which, for instance, the notation G I 5 refers to the animal treated in Group I and sacrificed on the fifth postoperative day.

METHODS OF EXAMINATION

The experimental animals were put to death by injection into the ear vein of a lethal dose of an anaesthetic intended for intravenous use.

Visual observations were made when both hip joints were being exposed and the femoral heads were being excised.

As a rule, two x-ray examinations were made of each experimental animal, one being done a few days after the operation and the other immediately after sacrificing. If the animal was scheduled to be sacrificed on the 5th to 15th postoperative day, only the latter x-ray was made. For x-raying the rabbit was placed in a special fixture and strapped down by its trunk. The hind legs were held by hand in a symmetrical position while the exposure was made on non-screen »Kodirex» (Kodak) film with the tube at 2 m distance and settings at 105 mAs and 65 kV. In the x-rays the operated and the intact hip were compared, as well as the status with respect to radiologic density of the bone after operation and after sacrificing. Attention was also paid to narrowing of the joint space, to establishment of a new socket in the luxated cases, and to changes in the pelvic bones.

Both femoral heads of the rabbit, including part of the neck, were taken as specimens for histological examination. The specimens were fixed in neutral 10 per cent formalin and decalcified with 32 per cent (vol./vol.) EDTA (ethylene-diamine-tetra-acetic acid, disodium salt) solution of pH 7.2—7.4 at about 37°C. Upon decalcification, the samples were dehydrated by passing them through a series of baths with increasing alcohol content (50, 70, 80, 95 per cent and absolute alcohol) and transferred through benzene into paraffin in the usual manner. Subsequently they were kept in paraffin at about 63° C in an incubator for about one week. This is a good though slow procedure.

Sectioning was done with a standard microtome. The femoral head was split through the middle in the frontal plane so that the ligamentum teres fell into the plane of cleavage. According to the histologic findings this was succesful in all instances. The basic stain was Weigert-van Gieson's haematoxylin. In addition, Pentachrome staining was used.

Pentachrome I and II staining (Movat 1955) is a method by which all connective tissue elements, also the acid mucopolysaccharides of the ground substance, can be made visible in one and the same section. It is a combined staining method composed of Weigert's iron-haematoxylin for nuclei, woodstain scarlet-acid fuchsin or orange G for cytoplasm, resorcin-fuchsin for elastic tissue, saffron or diphenyl fast red for collagen and Alcian blue for the ground and cementing substances. The bone acquires an intensive red stain with Pentachrome II, hyaline cartilage a bluish or blue-green stain and fibrous cartilage a greenish yellow or brown stain. Fibrous tissue is stained red or brownish red, the cytoplasm of blood cells yellowish, the nucleus black, and the elastic fibres of the vascular walls are stained dark red.

Assessment of the articular cartilage included examination of its surface smoothness, thickness of the layer, number of cells, their size and distribution in the depth dimension, cell agglomerations and nucleation of the cells. Separate attention was paid to the subarticular spongeous bone and to the nucleation of the osteocytes situated at greater depth, to the occurrence of osteoblasts and osteoclasts, and in the bone marrow to vascularization and content of cells, and above all to the presence of granulation tissue and its place and extent of occurrence. The ossification of the epiphyseal cartilage was studied in the operated and unoperated extremity in respect of ossification, column width, arrangement of cells and nucleation of the cells.

The histochemical methods employed in this work for investigation of the ground substance in the connective tissue were the Alcian blue stain and the periodic acid-Schiff (P.A.S.) oxidation method.

Alcian blue is a selective stain for acid polysaccharides devised by STEEDMAN (1950). LISON (1954) reports on the usefulness of this new method, stating that it is also particularly well suited for investigation of cartilage and especially of ossification; it seems, according to him, that stainability with Alcian blue is proportional to the chondroitin-sulphuric acid content of the cartilage. It imparts a bluish green stain to the ground substance of cartilage and to certain types of tissue, purplish blue to the nucleus, red to collagen and bone, and a pale yellow to cytoplasm and muscle. In the present work LISON's technique was employed, in which Chlorantine Fast Red 5 B is added to the basic stain.

The P.A.S. staining was done according to MCMANUS (1948). This is a histochemical reaction in the first stage of which the tissue polysaccharides are converted to polyaldehydes under periodic acid treatment. In the second stage these polyaldehydes are made visible by fuchsin-sulphuric

acid, which is a carbonyl reagent. Cartilage responds with the heaviest violet stain, because cells and nuclei are both stained. In the bone matrix an intensive stain is clearly visible upon decalcification. The stain demonstrates the general presence of carbohydrates, without being more specific.

Autoradiographic examinations were carried out in eight cases. An injection of 3.0 millicuries of P^{32} in the form of phosphate (from the Radiochemical Centre, Amersham, England) was given intravenously to the anaesthetized animals two hours before they were sacrificed. After splitting of the femoral head through the middle in the frontal plane with an electric saw, one of the halves was fixed in 75 per cent alcohol and treated by the methyl metacrylate procedure without decalcification. The specimens were ground down to 100 μ thickness. Autoradiographs were then prepared according to the contact method on Kodak Fast Autoradiographic Stripping Plates AR 50. The contact plates were exposed and developed in Kodak DX-80 Developer. The time of exposure, six days, had been determined in preliminary tests.

In order to obtain a histologic reference series for those cases in which autoradiography was undertaken, the other split half of the femoral head was decalcified as usual and fixed and stained with Weigert-van Gieson's haematoxylin.

Microradiography is a procedure by which an absorption roentgenograph is obtained with x-rays in 1:1 scale of the specimen under investigation. The roentgenogram is then examined under the microscope. Microradiographs were here prepared of bone specimens ground down to 100 μ thickness. Because the specimens contain biologic material, this investigation is referred to as historadiography (Engström 1955). The present historadiographs were made with a Philips X-ray Apparatus Type 11704, using x-ray tube No. 25293/32. The specimen was placed 10 cm from the copper anode and the film was exposed for 2 minutes at 20 kV and 15 mA. The sensitive material was Kodak's Spectroscopic Plate 649-GH, which was developed during 5 minutes (experimentally determined) in Kodak D.19 b developer.

The different studies that were made are tabulated in Table 1.

The results of the macroscopic, roentgenologic and microscopic examination are presented in connection with each group of experimental animals in Tables 2—7, and according to method of examination in Tables 8—10 in the discussion. This duplication was thought to be helpful to the reader.

ARTHROTOMY, DIVISION OF LIGAMENTUM TERES AND TEMPORARY LUXATION OF THE FEMORAL HEAD

EARLIER INVESTIGATIONS

Clinical investigations. — To a great extent, the investigations have reference to the blood vessels passing through the ligamentum teres and to their significance in various age periods and in various situations. KOLODNY (1925) found that this ligament was significant only in children and that it goes to the centre of ossification, while NUSSBAUM (1924, 1926) claimed the direct opposite, as did also WALMSLAY (1915) and WOLCOTT (1933).

Numerous subsequent investigations show that in children as well as in adults the vessels of lig. teres are in function in most instances (CHANDLER and KREUSCHER 1932, SCHWEIGERT 1936, NORDENSON 1938, VEREBY 1942, TUCKER 1949, HOWE 1950, CHEYNEL 1954 and JUDET *et al.* 1955). Some investigators (LANGER 1875, WALMSLEY 1915, LANG 1916, KOLODNY 1925, CHEYNEL 1947, and ETIENNE and GRANEL 1949) arrived at the result that with age the blood vessels decrease in number, but this has been contradicted by others (HEINE 1926 and BENNETT *et al.* 1942).

WALDENSTRÖM (1934) stated that in the treatment of epiphysiolysis of the femoral head either operatively or by reposition, necrosis of the femoral head is due to damage of the lig. teres.

Animal experiments. — ZEMANSKY and LIPPMAN (1929) divided the lig. teres and part of the capsule of two-weeks-old rabbits and observed after 6—35 days levelling of the femoral head and avascular changes, but no regeneration. In three rabbits of seven weeks' age, which were operated to serve as controls, no corresponding changes could be found. GRAHAM (1930) divided the lig. teres of young goats, producing flattening of the femoral head and partial necrosis. STEWART (1933) divided the lig. teres of young and adult rabbits and of adult dogs. He sacrificed the animals after 7—120 days and observed slight changes of bone in the young as well as old animals. By division of the lig. teres in cats, dogs and rabbits of various ages CELLA (1934) obtained changes in the femoral head in those aged 1—10 days, while no changes developed in animals 40 days to 5 months

old. KISTLER (1934, 1936) observed that division of lig. teres caused necrotic foci and deformities in young rabbits; no changes occurred in the few adult animals included in his experiments. BURROWS (1941) divided the lig. teres of rabbits less than five weeks of age, producing aseptic necrosis and observing its subsequent healing. The same finding was reported by LACROIX (1942). WOLCOTT (1943) elicited no changes on division of lig. teres in young dogs of 30—60 days' age.

SMITH *et al.* (1958) subjected six dogs aged 3—5 weeks merely to arthrotomy of the hip joint, pushing the femoral head into its socket immediately upon division of the lig. teres and dislocation of the head. The recorded changes were quite scanty, or no changes ensued at all. LEMOINE (1957) obtained no changes by division of lig. teres. HOOVER and COVENTRY (1961), in their skin arthroplasty experiments with adult dogs, performed with three dogs in the control series only arthrotomy, division of lig. teres and momentary luxation finding that no changes ensued.

The traumatic and degenerative processes of cartilage have also been investigated. For instance, HALDEMAN (1938) found with rabbits that a lesion of the articular cartilage which does not extend to the bone will not heal. On the other hand he observed that experimental fractures of cartilage which extend to the underlying bone heal by the formation of fibrous tissue, which is transformed in the course of months into cartilage resembling articular cartilage. CARLSON (1957), in his histologic study of defects of the patellar cartilage in rabbits, found that regeneration was more rapid in young animals, but that healing as a rule only took place in the course of months.

OWN INVESTIGATIONS

Although the literature, accordingly, contains reports on the effects exerted by arthrotomy, division of lig. teres and temporary luxation of the femoral head, such investigations have mainly been carried out with young animals. On account of this fact, and because this particular operation constitutes the basic framework for the operations performed in the other groups in this work, investigation of this question with older animals was considered appropriate.

The macroscopic, roentgenologic and microscopic findings in the experiments with arthrotomy, division of lig. teres and temporary luxation (Group I) are shown in Table 2.

Macroscopic changes. — Very slight changes only were found in the femoral head at 5, 10 and 15 days. Only traces of haemorrhage were observed in the joint and in its surroundings. In the later specimens the region of

TABLE 2.

Arthrotomy, division of lig. teres and temporary luxation (Group I): Examination results

Time of examination, days since operation	Macroscopic findings				Roentgenologic findings			Microscopic findings					
								Cartilage		Bone			
	Unevenness of articular surface	Adhesions	Dislocation	Lig. teres reattached	Narrowed joint space	Changed form of femoral head	Increased density of femoral head	Unevenness	Degeneration	Granulation tissue	New bone	Necrosis	Epiphysis
5													+
10				+				+					+
15								+	+		+		+
20													
25				+				+					+
30								+		+			+
35								+					+
40	+							+	+			+	
45													
50													+
60													+
70													
80								+					
90									+			+	
100		+		+	+	+	+	+		+		+	
110		+		+				+					
120								+					
130								+					
140					+	+	+	+	+	+	+	+	
150								+					
180					+	+		+					
240								+					
360	No specimen												

the joint was fully comparable to that of the intact side, the sole difference consisting of insignificant scar formations. At 40 days, but not in any other specimen, unevenness was noted in the articular cartilage. Owing to the small size of the hip joint of the rabbit, it is not possible actually to speak of the quantity of articular fluid; at its most one may distinguish a moist condition of the joint. Thus macroscopic comparisons in this respect appeared too inaccurate. The lig. teres had become reattached in four instances, *i.e.*, at 10, 25, 100 and 110 days.

Roentgenologic changes. — As a rule no changes were visible. In contrast with this, however, 100 days after the operation there could be seen, in addition to subluxation, an increased density of the head of the left femur, greater translucency close to the articular cartilage, and sclerosis at the upper margin of the acetabulum (Fig. 3).

At 140 days similar changes were observed: the femoral head showed increased density, the sclerosis in the upper part of the acetabulum was

Fig. 3. X-ray, 100 days after arthrotomy, division of lig. teres and temporary luxation of the femoral head. In addition to subluxation, there is increased density of the head of the left femur, greater radiolucency close to the articular cartilage, and sclerosis at the upper margin of the acetabulum.

accentuated and the entire acetabulum presented a confused structure. A distinct spot of greater translucency was observed in the distal part of the femoral head. At 180 days after the operation the joint space appeared to be narrower on the left side (Fig. 4).

Microscopic changes. — 5 — 15 days. In the specimen of the 5th day the articular cartilage was thin, but its surface was smooth. In that of the 10th day the articular surface was uneven and frayed in spots. The specimen taken on the 15th day presented a fairly smooth articular cartilage, but it had been destroyed and was replaced by fibrous tissue in the peripheral part near the epiphysis (Fig. 5). A somewhat similar change was also seen in the periphery on the other side. At the corresponding points of the femoral head, osteoblasts were seen in the spongeous bone adjacent to the destroyed articular cartilage.

15 — 45 days. In the specimen of the 25th day the articular surface was uneven and frayed in spots. There were no bone changes. In the specimen

Fig. 4. X-ray, 180 days after arthrotomy, division of lig. teres and temporary luxation of the femoral head. The joint space appears to be narrower on the left side.

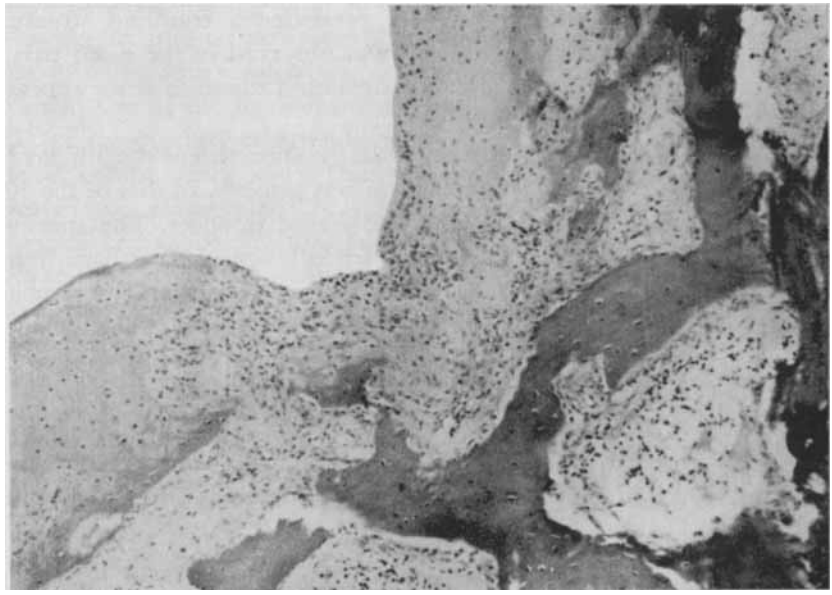


Fig. 5. Micrograph, 15 days after arthrotomy, division of lig.teres and temporary luxation of the femoral head. In the peripheral part of the articular cartilage on the side of the epiphyseal cartilage the articular cartilage seems to be destroyed and replaced with fibrous tissue. — Alcian blue × 100.

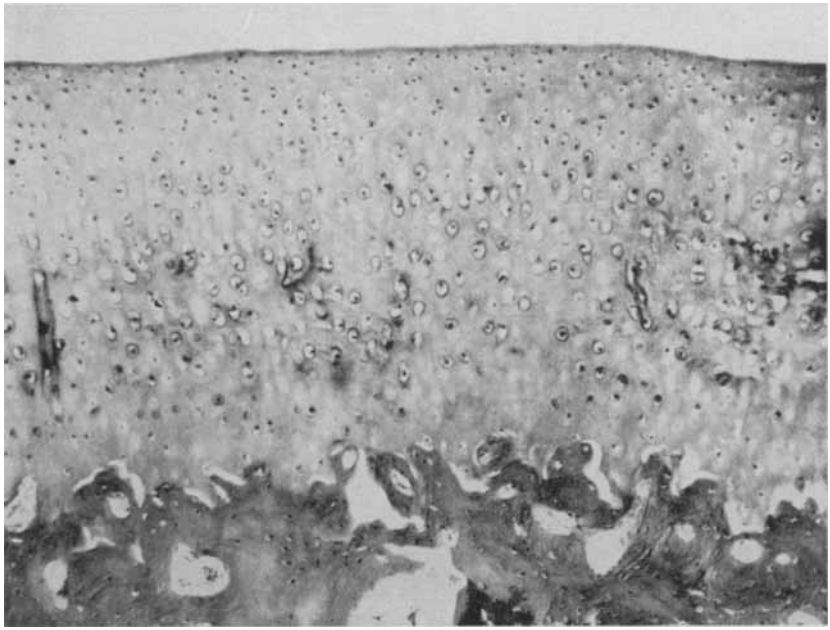


Fig. 6. Micrograph, 35 days after arthrotomy, division of lig. teres and temporary luxation of the femoral head. The articular cartilage is normal in thickness on one margin. — Weigert-van Gieson × 100.

taken on the 30th day granulation tissue was present in the cancellous spaces under the ragged articular cartilage, but there was no osteogenesis. In the specimen of the 35th day the articular cartilage was of normal thickness on one margin and replaced by fibrous tissue on the other. Also elsewhere was it uneven and frayed (Figs. 6 and 7). No bone changes were noted, however. In the specimen of the 40th day the articular cartilage had vanished over a large portion and was replaced by fibrous tissue and fibrous cartilage. In the spongeous bone Alcian blue revealed lighter areas in which no nuclei were visible, while the nucleated areas stained a brighter red.

45—90 days. In the specimen of the 80th day the articular cartilage was uneven and frayed here and there. At 90 days poorer staining of the nuclei was observed over an extensive area on the inner side of the articular cartilage, and the cells in the bone marrow were few in number.

90—240 days. In the specimen of the 100th day the articular surface was here and there uneven and frayed. The bone presented a few areas poor in nuclei. The cancellous spaces were normal elsewhere, but there was granulation tissue in two or three spaces near the articular cartilage. In the specimens taken at 110, 120 and 130 days some slight unevenness of the articular cartilage was observed, but nothing abnormal in the bone. In the specimen of the 140th day the articular cartilage was uneven and frayed in spots and it was disrupted at one point in the periphery. Beneath it there was granulation tissue, and areas poor in nuclei were found in the bone itself, in addition to which occasional osteoclasts and osteoblasts were seen (Figs. 8 and 9).

In the specimen taken 150 days after the operation the articular cartilage was replaced at one point by tissue resembling fibrous and hyaline cartilage (Fig. 10).

In the specimen of the 180th day the articular surface was uneven and frayed in spots, but no bone changes were observed. The specimen of the 240th day presented an articular cartilage of partly faultless surface but lightly frayed at one margin; in addition, lacunae were noted, each containing several cartilage cells, although these cells usually occurred singly, in pairs or in threes in the areas of normal cartilage. There were no bone changes.

Of the above mentioned specimens those taken at 10, 25, 100 and 110 days exhibited reattachement of the lig. teres.

Epiphyseal cartilage was observed in seven instances among the specimens taken 5—50 days after the operation and only once subsequently, namely, in the specimen of the 60th day. In the specimen of the 5th day

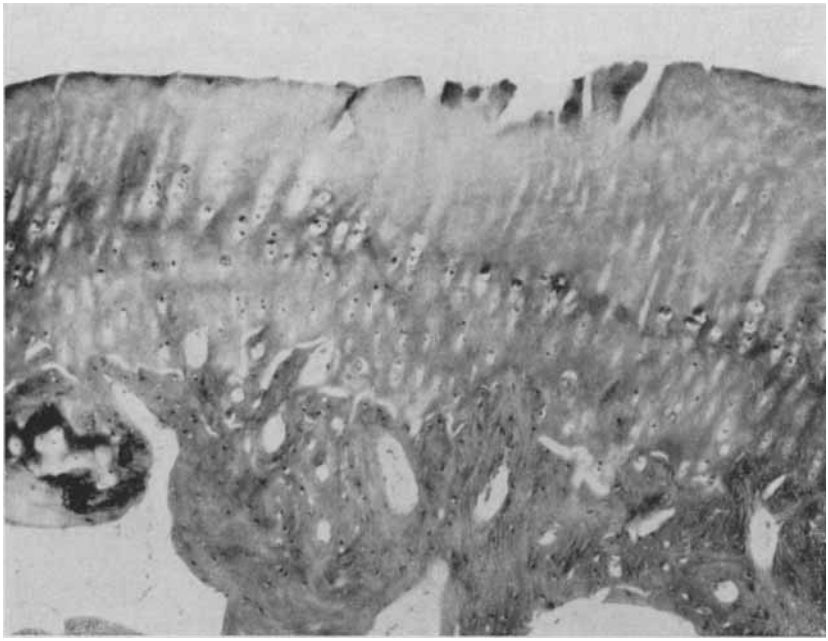


Fig. 7. Micrograph, 35 days after arthrotomy, division of lig. teres and temporary luxation of the femoral head, of the other margin of the same specimen as in Fig. 6, showing articular cartilage of frayed structure, poor in cells and less intensively staining. — Weigert-van Gieson × 100.

Fig. 8. Micrograph, 140 days after arthrotomy, division of lig. teres and temporary luxation of the femoral head. The articular cartilage has subsided and the bone under it is destroyed, but partly replaced by granulation tissue. The articular surface is uneven. — Weigert-van Gieson × 100.

Fig. 9. Detail of the same micrograph as in Fig. 8, showing bone in the process of destruction; beside it, osteoclasts and more in the center, incipient formation of new bone, osteoblasts and granulation tissue. — Weigert-van Gieson × 500.

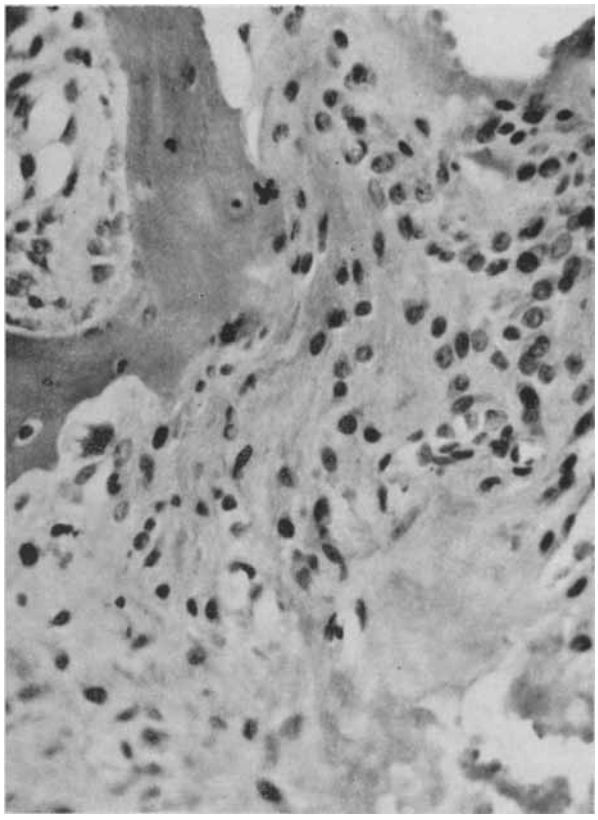
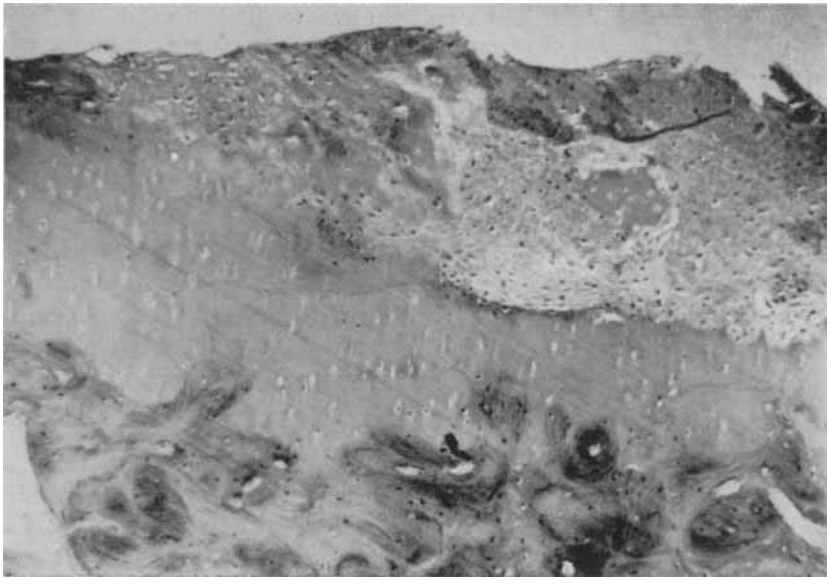


Fig. 10. Micrograph, 150 days after arthrotomy, division of lig. teres and temporary luxation of the femoral head. The articular cartilage has been destroyed at one point and replaced by cartilage resembling fibrous and hyaline cartilage. — Weigert-van Gieson × 100.



ossification of the epiphysis was found to be farther advanced in the operated hip.

Necrosis of the bone was found in 4 instances among the 22 operated rabbits.

COMMENTS

In earlier investigations, distinct changes were induced in the femoral head and articular cartilage of very young rabbits and other experimental animals already by the performance of arthrotomy and division of lig. teres, while little or no changes resulted in older animals. In the present investigation, unevenness of the surface of the articular cartilage was found microscopically in 15 instances. In the specimen taken 15 days after operation the degenerative changes in the articular cartilage were marked, and in the same specimen there was also granulation tissue in the subcartilaginous bone. According to the literature, a much longer time is required for degeneration and necrosis of cartilage and its replacement to occur (HALDEMAN 1938, CARLSON 1957). One might therefore suspect that in this case the change had been present already prior to operation. However, no equivalent changes were visible in the control specimens.

The other changes observed in the cartilage may in part have been outright artefacts produced by instrumental interference, or they may have been caused traumatically by a slight change in position of the femoral head due to the arthrotomy and division of lig. teres itself. Rather exceptionally, in four instances, necrotic changes occurred in the bone. They were concomitant in three cases with degenerative changes in the cartilage. It would thus seem that the bone reacts rapidly to changes in the cartilage, possibly with the aim of strengthening the static condition of the femoral head at such a point, or of enhancing the regeneration of cartilage by this means.

However, no alterations were observed in the articular cartilage at 90 days, although in an extensive area of the bone, adjacent to the articular cartilage, poorer staining of the nuclei and scantiness of cells in the bone marrow were noted. In this case it may have been a question of degeneration of bone on a circulatory basis, encountered in connection with the normal aging of bone, which has previously been demonstrated by, *e.g.*, MÜLLER (1927), JAFFE and POMERANZ (1934) and SHERMAN and SELAKOVICH (1957). It is a fact, at least, that no subchondral fracture as described by NAGURA (1937, 1938) was observed, which would have accounted for such a change. On the other hand, the change was of such extent that one would expect some other factor, for instance operative

trauma of exceptional magnitude, to have accelerated in this case the process that led to necrosis of the bone.

After reattachment of the lig. teres, the specimens differed in no way from other virtually simultaneous specimens.

In two instances, increased roentgenologic density was encountered, which was then correlated with the necrotic changes found in the bone. However, a comparatively long time had passed since the operation in both cases and it is therefore not possible to speak of a roentgenologic early diagnosis.

Summarizing what has been stated above, it can be said that the macroscopically observed changes in the femoral head were fairly insignificant. Increased roentgenologic density was noted twice at the femoral head, and in these cases granulation tissue was histologically observable in the cancellous spaces, in addition to which there were areas poor in nuclei in the femoral head itself. Numerous specimens revealed microscopically unevenness of the articular cartilage and its slight destruction and replacement with fibrous cartilage or fibrous tissue, with granulation tissue reaction in the corresponding underlying area. An actual change indicative of partial necrosis of the bone was found in four instances. In these cases the areas poor in nuclei took a lighter red stain with Alcian blue.

On the strength of the investigations carried out in the present connection, my opinion is that the observed changes in the articular cartilage had mainly occurred as a consequence of direct trauma. Furthermore, they were insignificant in magnitude, since they were rarely accompanied by granulation tissue reaction. Some correlation with simultaneous changes in the bone was noted.

ARTHROTOMY AND LUXATION WITHOUT REDUCTION

EARLIER INVESTIGATIONS

Clinical and experimental investigations. — Scattered clinical observations were reported already before MÜLLER (1924) experimentally demonstrated that luxation produces also avascular necrosis of bone and described it histologically. However, it was only later that several investigations were carried out, including some studies of considerable extent. POTTS and OBLETZ (1939) described five cases of their own, stressing the importance of a primary lesion, while BANKS (1941) reported on nine cases of his own and 42 cases collected from the literature, calling attention to the significance of the lig. teres and of the capsular vessels. In contrast with these authors, HABERMAIER (1955) arrived at the result that necrosis was a sequel to direct damage suffered by the femoral head; in likeness with STEWART and MILFORD (1954), he placed weight on early reduction. According to the last mentioned authors, all cases in which reposition had been performed 24 hours after the accident terminated in aseptic necrosis, which otherwise only occurred in 27 per cent. In his experiments with 29 cadavers, in which he produced luxation by means of a special compression device, BÖHLER (1957) observed that a depression was caused in the bone, which reverted to normal, but he demonstrated the significance of a primary trauma in the first place and creation of a disturbance in nutrition in the second place only.

The following figures are stated in the literature for the incidence of aseptic necrosis of bone in connection with luxation and fracture with associated luxation: PFAB (1939), 8.3 per cent; WATSON-JONES (1942), 30 per cent in fresh and 100 per cent in inveterate cases; URIST (1947), 6.6 per cent in common fractures and (1948) 7.4 per cent in fractures with associated luxation; ARMSTRONG (1948), 2.3 per cent in fractures with associated luxation; PAUS (1951), 1.7 per cent and in central luxations 100 per cent; D'AUBIGNÉ (1953), 20 per cent; STEWART and MILFORD (1954), 21.2 per cent; THOMPSON and EPSTEIN (1951), 55 per

cent; TROJAN and PERLSCH (1956), 2.9 per cent in common fractures and 19.4 per cent in fractures with associated luxation; BANCROFT and MURRAY (1945), degenerative changes ensuing in 50 per cent; and D'AUBIGNÉ (1956), 64 per cent. WALLER (1955) noted that in dashboard fractures avascular bone necrosis occurred in 16.6 per cent and traumatic arthritis in 44.8 per cent. These figures refer to varying lengths of observation period and to different degrees of severity of the original trauma, but they serve to indicate the general trend and they bear evidence of the importance of bone necrosis.

Animal experiments. — MÜLLER (1924), who investigated traumatic luxation of the hip joint in animals of various ages and who was the first to clarify the histologic features encountered in this connection, observed that luxation of the joint caused necrosis of cartilage only in adolescent animals during an observation period of 6—40 days, whereas in adult animals he found fibrous tissue in the cancellous spaces and areas poor in cells in the bone.

BERGMAN (1927) produced closed luxation in two adolescent rabbits, observing in one of them, which was sacrificed after two months, that part of the bone trabeculae under the articular cartilage stained poorly and that the articular cartilage was interrupted in many places. LANGENSKIÖLD and SARPIO (1958) luxated the hip joint in rabbits a few days old, observing after a few weeks, in addition to dysplasia of the acetabulum, hypoplasia of the epiphysis of the femoral head. SMITH *et al.* (1958) produced operative luxation of the hip joint in 16 young dogs aged three to five weeks, obtaining considerable coxa vara and reduced anteversion. They sacrificed the animals after closure of the epiphysis, and no histologic examination was carried out.

In their investigation of the influence excerted on the articular cartilage by functional activity of the joint in rabbits, EKHOLM and NORBÄCK (1951) observed that already after a short time of activity the cartilage cells were more rounded in the surface layer, owing to a greater quantity of fluid. INGELMARK (1950) studied the value of the joint fluid in the supply of nutrition and inclined towards the opinion that the principal nutrition comes by way of the bone and not from the articular fluid. This had also been indicated earlier by the experiments of INGELMARK and SÄÄF (1946). On the other hand, BROWER *et al.* (1962) observed in their experiments with rabbits that 0.5 per cent neutral red solution entered the cartilage by way of the articular fluid. KETTUNEN (1958) noted in his studies of skin arthroplasty in cats the significance of function with regard to the metaplasia of fibrous tissue into cartilaginous tissue.

TABLE 3.

Arthrotomy and luxation without reduction (Group II): Examination results

Time of examination, days since operation	Macroscopic findings				Roentgenologic findings			Microscopic findings					
								Cartilage		Bone			
	Unevenness of articular surface	Adhesions	Dislocation	Lig. teres reattached	Altered joint space	Changed form of femoral head	Increased density of femoral head	Unevenness	Degeneration	Granulation tissue	New bone	Necrosis	Epiphysis
5			+		+			+					+
10		+	+		+			+		+			+
15		+	+		+					+		+	+
20	+	+	+		+			+		+			
25	+	+	+		+								
30	+	+	+		+	+	+	+		+			
35	+	+	+		+	+	+	+	+	+	+	+	+
40	+							+					+
45	+	+	+		+	+	+	+		+			+
50	+	+	+		+	+		+	+	+			
60	+	+	+		+	+	+	+	+	+		+	
70	+							+	+	+		+	
80	+	+	+		+	+	+	+	+	+	+	+	
90	+	+	+		+	+	+	+	+	+	+	+	
100	+	+	+		+	+		+	+	+	+	+	
110	+	+	+		+	+	+	+	+	+			+
120	+	+	+		+			+	+	+			+
130	+	+	+		+	+	+	+	+	+	+	+	
140	+	+	+		+	+	+	+	+	+			
150	+	+	+		+	+	+	+	+	+	+	+	
180	+	+	+		+	+	+	+	+	+	+	+	
240	+	+	+		+	+	+	+	+	+	+	+	
360	No specimen												

OWN INVESTIGATIONS

Rather few animal experiments have been carried out on this subject and the following study therefore seemed called for.

The macroscopic, roentgenologic and microscopic findings in the experiments with arthrotomy and luxation without reduction (Group II) are shown in Table 3.

Macroscopic changes. — Unevenness of the surface of the articular cartilage was observed in nearly all specimens. The changes were distinct already 20 days after the operation; the articular cartilage had lost its normal gloss, a new capsular sheath had been formed of the surrounding tissue and the femoral head had begun to grind a new socket for itself in the pelvic bones, dorsal and cranial to the original acetabulum. At later times the changes were more massive, and the femoral head had also lost its normal shape and hardness. The femoral head had returned into its original socket in two instances, namely, in the specimens taken at 40 and 70 days. In these cases the changes in the surroundings were rather insignificant.

Roentgenologic changes. — Twice (in the animals sacrificed at 40 and 70 days) the femoral head was seated in its proper socket. At 30, 35, 45 days (Fig. 11), 50, 60, 80, 90, 100, 110 days (Fig. 12), 130, 140, 150, 180 and 240 days after the surgical interference increased density was noted in all the femoral heads and small areas of greater radiolucency, now and then in the femoral head but also in the neck of the femur. In most cases there also were observed a distinctly altered shape of the femoral head and degenerative changes in the pelvic bones. It was found that the femoral head had hollowed for itself a new socket cranial and dorsal to the initial acetabulum. In these cases the joint space displayed slightly greater width in nearly all X-rays.

Microscopic changes. — 5 — 15 days. At 5 days the articular cartilage was found to be uneven and frayed, but there were no bone changes. In the specimen taken at 10 days were noted unevenness of the articular cartilage, and at one point fibrous tissue on the articular surface, and some granulation tissue in the cancellous spaces at the margin of the femoral head (Fig. 13). In the specimen of the 15th day no changes were seen in the articular cartilage, but there was some granulation tissue in the cancellous spaces and slight occasional scantiness of cells and disappearance of nuclei in the spongeous bone itself.

15 — 45 days. On the 20th day the articular cartilage was found to be uneven and frayed, and there was granulation tissue in the cancellous

Fig. 11. X-ray, 45 days after arthrotomy and luxation of the femoral head, without reduction. The luxated femoral head has ground a new socket for itself cranial to the original acetabulum. The femoral head appears to be of considerably greater density on the operated side.

Fig. 12. X-ray, 110 days after arthrotomy and luxation of the femoral head, without reduction. Extensive degenerative changes not only in the femoral head, but also in the pelvic bones and the trochanteric region on the left side; increased density as well as areas of greater radiolucency in spots.

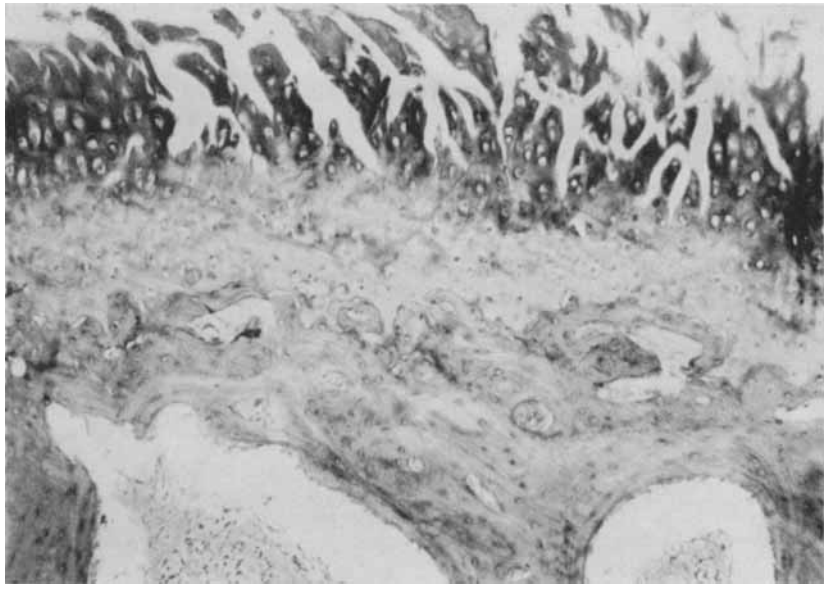


Fig. 13. Micrograph, 10 days after arthrotomy and luxation of the femoral head, without reduction. At one point, the articular cartilage has been deeply cleft into fringes. — Alcian blue ×100.

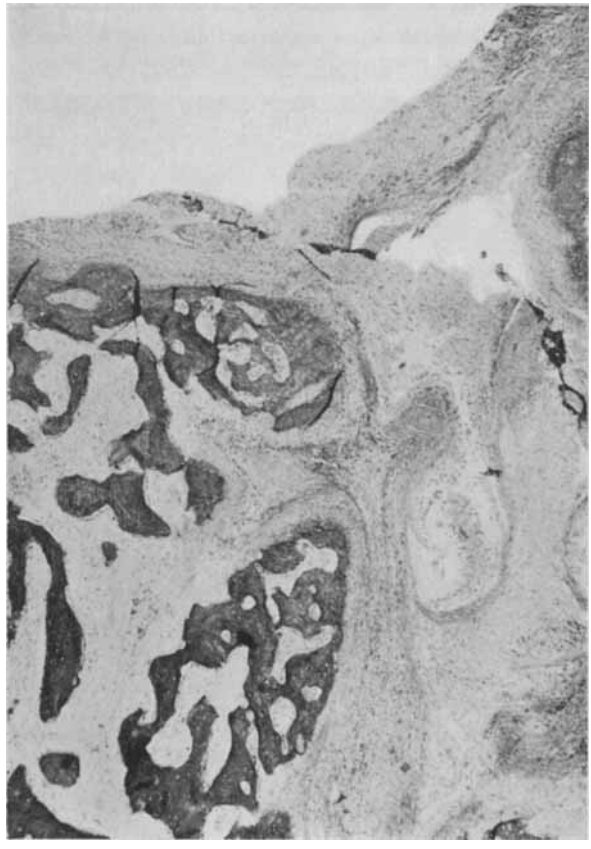


Fig. 14. Micrograph, 100 days after arthrotomy and luxation of the femoral head, without reduction. The articular cartilage has almost entirely been replaced by fibrous cartilage and fibrous tissue. In the underlying cancellous spaces there is abundant fibrous tissue and osteogenesis. — Weigert-van Gieson ×40.

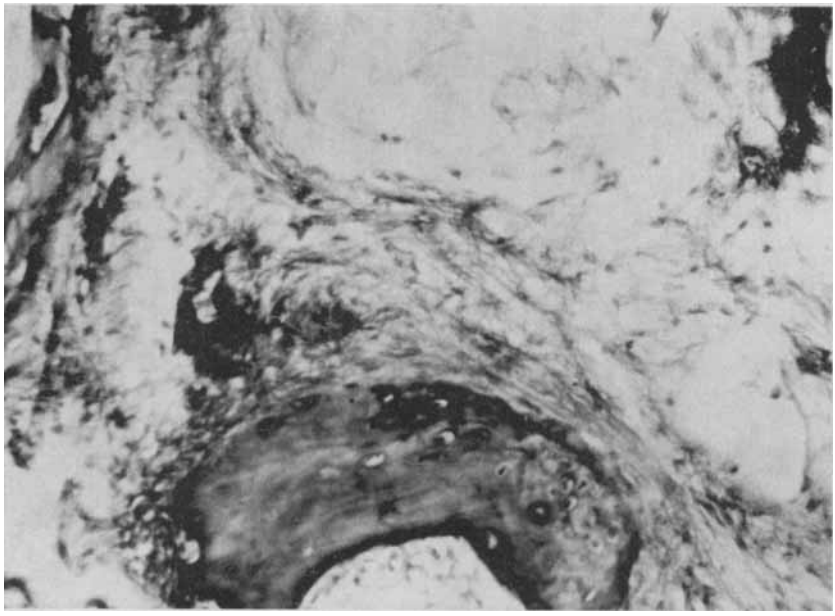


Fig. 15. Micrograph, 100 days after arthrotomy and luxation of the femoral head, without reduction. Large cancellous spaces contain abundant granulation tissue, and osteogenesis. — Alcian blue ×280.

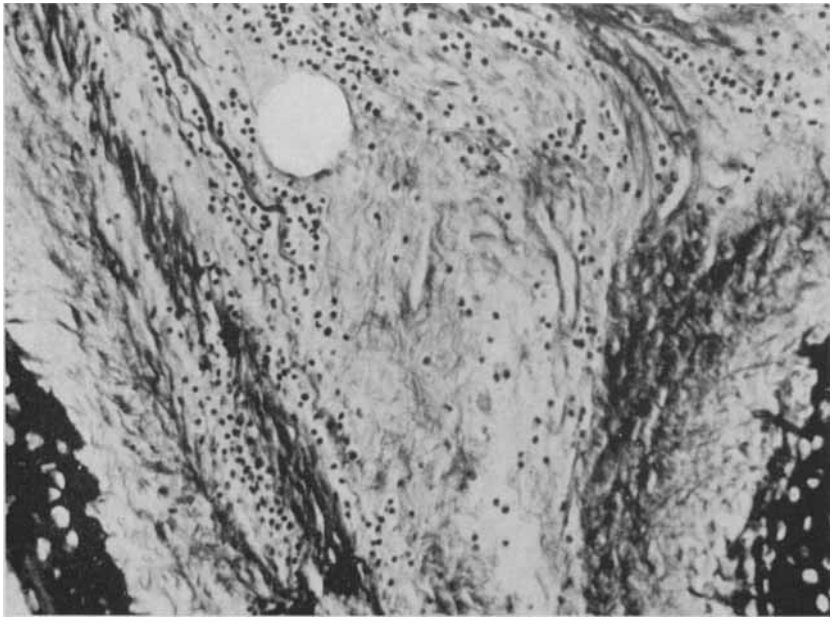


Fig. 16. Micrograph, 240 days after arthrotomy and luxation of the femoral head, without reduction. Abundant granulation tissue in the cancellous spaces, and osteogenesis. — Alcian blue ×280.

spaces. In the specimen of the 30th day the articular cartilage was worn down and thin; it was completely absent in spots, and granulation tissue was observed in the cancellous spaces. Examination of the specimen of the 35th day revealed, in addition to the foregoing, areas of articular cartilage and granulation tissue in the cancellous spaces. The spongeous bone was poor in cells and osteoblasts and foamy degeneration of fat cells were encountered in the cancellous spaces in the middle of the specimen. In the specimen of the 40th day the articular cartilage was very slightly uneven and a couple of smaller particles had become detached from it, but no bone changes were observed. At 45 days the articular cartilage was found to be uneven and frayed, and the cancellous spaces contained granulation tissue.

45—90 days. In the specimen taken at 50 days, most of the articular cartilage had disappeared and was replaced by fibrous tissue. Granulation tissue was seen in the cancellous spaces under the articular cartilage, on one side. The specimen of the 60th day had an articular cartilage that was even in some places but it was absent and replaced by fibrous tissue in others; the spongeous bone under the articular cartilage was poorer in cells and there was granulation tissue in the cancellous spaces. In the specimen of the 70th day the articular cartilage was mostly destroyed and replaced either by fibrous tissue or, in spots, by cartilage with hyaline content. Granulation tissue was highly abundant in the cancellous spaces, while the spongeous bone itself was sparse in quantity and contained areas poor in cells or displaying lack of nuclei. The articular cartilage in the specimen of the 80th day was very narrow and frayed and cell agglomerations were observable in it. The articular cartilage was not compressed. The femoral head, on the other hand, was found to be flattened throughout; very abundant granulation tissue and profuse osteogenesis, osteoclasts and osteoblasts were seen in the cancellous spaces. The spongeous bone contained extensive areas without nuclei and numerous areas poor in nuclei. In the specimen of the 90th day the articular cartilage had disappeared almost completely and was replaced by fibrous cartilage and fibrous tissue. Large cancellous spaces rich in granulation tissue and extensive areas of anuclear bone tissue were also noted. Osteoclasts and osteoblasts were abundant. The areas poor in nuclei stained a lighter red with Alcian blue, while new bone was a brighter red. In the P.A.S.-stained slides the areas where no nuclei were seen were a lighter violet in colour.

90—240 days. Changes of extraordinary degree were observed in the specimens referring to the period of 100—180 days. Only fragments were left of the articular tissue, embedded in fibrous tissue, and at numer-

ous points the articular cartilage had been replaced by tissue resembling hyaline cartilage or by fibrous cartilage. The changes in the cancellous spaces and in the spongeous bone in the specimens taken at 100 days (Figs. 14 and 15) and at 110, 120, 130, 140 and 150 days were similar in kind. In the specimen of the 120th day, furthermore, the femoral head appeared flattened. In the specimen of the 180th day granulation tissue was observed in particular abundance and osteoclasts and osteoblasts in profuse quantity in the entire femoral head. In the specimen of the 240th day some larger portions of the articular cartilage were still comparatively well preserved, but they were covered with fibrous cartilage. The greater part of the articular cartilage, however, was destroyed and fibrous tissue and fibrous cartilage occupied its place. The changes in the cancellous spaces and in the spongeous bone were like those in the preceding specimens (Fig. 16). In the preparations stained with Alcian blue the new bone was bright red, but also less intensively stained, anuclear areas were seen.

Epiphyseal cartilage was observed in six instances among the specimens referring to periods of observation between 5 and 50 days, and twice thereafter, namely, in the specimens of the 110th and 120th days. In the specimens of the 35th, 40th and 45th days ossification of the epiphyseal

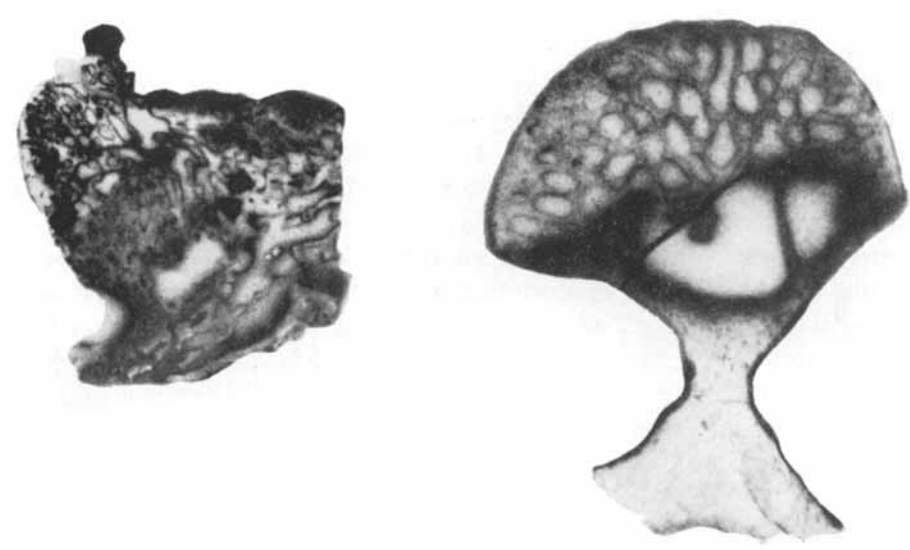


Fig. 17. Contact autoradiographs, 90 days after arthrotomy and luxation of the femoral head, without reduction. Uniform uptake of radio-phosphorus on the intact right side (control) and uneven distribution on the operated side with greater deposition in the area of osteogenesis and scantier deposition where necrosis of the bone was observed.

line was found to be farther advanced in the operated hip, whereas it was less strongly ossified in the specimen taken on the 5th day.

Autoradiographic changes. — Two specimens, namely, those of the animals sacrificed 90 and 240 days after the operation, were subjected to autoradiographic study. Comparison of the specimens from both hips in the first mentioned case revealed (Fig. 17) that the structure was distinctly reproduced in the autoradiograph of the control side (right hip) where the radioactive phosphorus (P^{32}) was uniformly taken up by the bone tissue, while the deposition on the operated side was less uniform. More radio-phosphorus was observed in the area where osteogenesis occurred,

Fig. 18. Microradiograph, 90 days after arthrotomy and luxation of the femoral head, without reduction. Distinct differences observable between granulation tissue (1), tissue in the process of osteogenesis (2) and normal bone (3). Likewise, necrotic bone (4) displays stronger x-ray absorption, producing a lighter area in the radiograph.

and less in the region with necrosis of the bone. There was no uptake of radioactive substance by the articular cartilage on the control side. In the specimen from the left side the articular cartilage was destroyed. — In the specimen taken at 240 days a non-radioactive band was visible at the site of the articular cartilage on the right (control) side but not on the left side. On the whole the specimen from the right side was more uniform than that from the left. In the latter the uptake of radioactive phosphorus was greater in the area where osteogenesis occurred than in any other part of the bone tissue.

Microradiographic changes. — Microradiographic examination was carried out with the same two specimens of which autoradiographs were prepared, namely, those taken 90 and 240 days after the operation. Clear differences could be observed in both specimens as regards the concentration of mass of the granulation tissue within the cancellous spaces, of the substance in the process of osteogenesis, and of already formed bone: compared with normal bone tissue the mass was distinctly less in new bone and greater in the necrotic portions (Fig. 18).

Necrosis of the bone was observed in 11 of the 22 operated rabbits.

COMMENTS

Comparison of the changes after permanent luxation with those produced by arthrotomy, division of lig. teres and temporary luxation of the femoral head revealed that the changes subsequent to the first mentioned interference were massive both macroscopically, roentgenologically and microscopically. STEWART and MILFORD (1954) reported from their clinical investigations that all cases in which luxation had been present longer than 24 hours terminated in aseptic necrosis. The result obtained in the present investigation is not equally categorical, but also here half of the cases developed aseptic necrosis.

MÜLLER (1924) observed necrosis of cartilage upon luxation in adolescent animals only. In the present investigation with adult rabbits, extensive changes were seen both macroscopically and roentgenologically in the articular cartilage of nearly all specimens. Also microscopically, degenerative changes in the articular cartilage were encountered almost regularly from the very beginning onwards. They were invariably accompanied by increased granulation tissue in the cancellous spaces, which has also been noted by HALDEMAN (1938), and by degeneration and necrosis of bone. It was evident that the cartilage responded more rapidly to degenerative

factors than bone, but on the other hand its repair was slower. It should be noted, however, that the articular cartilage was in a less favourable position in the present experiments than the bone. The effect of pressure, the altered statics and the direct trauma all acted directly on the articular cartilage and less on the bone protected by the cartilage and supplied with nutrition by the cancellous circulation.

According to EKHOLM and NORBÄCK (1951) the function of the joint is an essential factor in the aetiology of changes occurring in the cartilage. Lack of function in itself may cause necrosis of the cartilage. KETTUNEN (1958) observed in his experimental investigation with skin arthroplasty in cats that metaplasia of cartilage took place in the grafted connective tissue only under the influence of function. As in the present work the extremities had not been immobilized in any manner, there can be no question of lack of function at least in the initial stage. On the contrary, seeing that the unprotected articular cartilage had been forced to grind a new socket, the contribution of trauma was obviously considerable indeed. The nutrient effect of the articular fluid was insignificant. It has in fact been suggested that the articular cartilage receives its principal nutrition from the bone (INGELMARK and SÄÄF 1946, INGELMARK 1950), though there also are reports that it receives its nutrition by mediation of the articular fluid according to the investigations of BROWER *et al.* (1962). The comminution of the articular cartilage causes a regenerative reaction in the underlying bone, with increasing granulation tissue, as could be seen in the course of 60 days.

After 70 days the extensive changes in the articular cartilage were supplemented not only by an increase of granulation tissue but also by the occurrence of osteoblasts, osteoclasts and necrosis of bone, particularly in the middle portion of the femoral head. Obviously the pressure, the changed statics and the reduced function also exerted their influence on the bone so that the spongeous bone, which had become superfluous, disappeared and was replaced by new bone tissue that was formed at a more expedient point.

According to HARRISON *et al.* (1953), hyperaemia plays an important part in the aetiology of osteoarthritis. On the other hand, RUTISHAUSER (1956) and HULTH (1958) claimed that osteoarthrosis may develop on the basis of venous stasis. It is obvious that pressure, changed statics, direct trauma and reduced function are essential agents in producing necrosis of cartilage and, by reflectory response, necrosis of bone. These factors are also present in osteoarthrosis. BÖHLER (1957) also observed in his experimental investigation of luxation the essential significance of direct,

specifically of acute, trauma as a primary circumstance in the aetiology of necrosis of the bone.

It was found that the onset of cartilaginous changes occurred rapidly after luxation. In the two cases in which the femoral head had returned again into its socket, the changes in the specimen taken at 40 days were very few, and the reposition had obviously occurred within a rather short time after the luxation, whereas in the specimen of the 70th day there were copious changes and the luxated condition had apparently persisted for a long time in this instance.

The autoradiographic studies with P^{32} revealed that bone in necrosis took up less phosphorus than living bone. On the other hand, more phosphorus was deposited in newly formed bone. In the x-rays, as was also the case in microradiography, the changes were also of a kind associated with the reaction of bone necrosis, so that after a longer period the necrosis of bone itself caused distinctly increased density.

Summarizing what has been stated above, it can be said that abundant macroscopic changes were observed in the femoral head and in its articular cartilage; also, with the exception of one single case, there was a new socket, and in two instances spontaneous reposition of the femoral head in its socket. Roentgenologically, too, the changes were quite distinct. In addition to changes in the joint space and those relating to displacement of the femoral head, there were roentgenologically distinct degenerative changes in the femoral head itself in cases in which the histologic picture displayed necrosis in the bone in addition to strong granulation tissue reaction. However, fibrous tissue reaction in the cancellous spaces alone did not produce any roentgenologically observable changes, as could be noted in four instances. Among the microscopic findings, degenerative changes in the articular cartilage were dominant initially, and the cartilage had frequently disappeared almost entirely. In addition to changes of the articular cartilage, granulation tissue reaction was observed in the cancellous spaces and, excepting only two cases, actual necrosis of bone was not encountered until beginning on the 60th day, the histologic picture being governed even then by extraordinarily strong granulation tissue reaction and abundance of osteoclasts and osteoblasts.

Necrosis of the bone was found in altogether 11 instances. The autoradiographic changes showed up a clear difference between the two sides in respect of regularity of structure, the bone structure of the intact, control side being clearly visualized. On the operated side powerful deposition of radio-phosphorus in the area of osteogenesis was noted,

in contrast to poor uptake at the point where necrosis occurred. In the microradiographs, the mass of the necrotic bone tissue was greater than that of the surrounding bone tissue.

It is my opinion that the observed profuse changes in the articular cartilage with the associated granulation tissue reaction are due to direct trauma. Later, the pressure, changed static conditions and reduced function also affect the bone, in which, in addition to degenerative changes, abundant regeneration is observed.

ARTHROTOMY AND CAPSULECTOMY

EARLIER INVESTIGATIONS

Clinical and experimental investigations. — It has already been pointed out in the foregoing that luxation of the femur frequently causes aseptic necrosis of bone. Arthroplasty, of whatever kind it may be, always necessi-in the foregoing that luxation of the femur frequently causes aseptic necrosis of bone. Arthroplasty, of whatever kind it may be, always necessi-tates luxation of the joint. In describing, in CAMPBELL's textbook of operative orthopaedics (1956), different methods of opening the hip joint, Knight only once mentioned possible vascular lesion in this connection, namely, in his account of Ollier's lateral U incision, where he cautioned against damaging the capsular branch of the medial circumflex artery. In numerous other connections only the direction of the capsular incision is mentioned. For instance, MARCY and FLETCHER (1954) and LUCK (1955) said nothing about the capsular vessels, whereas *e.g.* MCFARLAND and OSBORNE (1954) reminded of the branch of the medial circumflex artery behind the trochanter and of that of the lateral circumflex artery in the neighbourhood of the vastus lateralis.

PHEMISTER (1930) described a case of necrosis in the femoral head five months after arthroplasty performed with the aid of the fascia lata in a man aged 28. SMITH-PETERSEN (1949), in describing the incision employed by him in his cup arthroplasty, warned against causing distal damage to the capsule. JAKOBSEN (1957) stated in his investigation concerning the same operation that vessels may be damaged in any of the following ways: by injury to small vessels where they penetrate the bone at the osteophyte ring when the femoral head is being scraped, by excessive radical resection of the lateral part of the articular capsule whence the main blood supply comes, or by detaching the greater trochanter and thereby destroying the greater part of the vessels supplying the trochanter and the neck of the femur. Since atrophy has rarely been encountered in osteoarthrosis, this has to be considered a postoperative complication resulting from the above described vascular lesion. JAKOBSEN stated that there was, roent-

genologically, atrophy in 16 per cent of cases postoperatively, and that in one such reoperated case total necrosis of the femoral head and of the neck of the femur was seen.

JUDET *et al.* (1955) studied in cadavers the blood supply of the femoral head and neck by Trueta's method. At first they performed on eight bodies the arthroplastic operation devised by themselves; subsequently, on examination of the blood supply, they observed that particularly drilling of the centre and shaping of the stump produced serious disturbances of circulation within the bone and in the medial inferior arteries, respectively. Examination of the lesions produced in connection with opening of the hip joint in 15 cadavers revealed that no disturbances of metaphyseal or epiphyseal vascularization are caused even by T capsulectomy. If the point of attachment of the capsule to the bone is not disturbed, not even complete anterior or posterior capsulectomy will cause reduction of the blood supply to the neck of the femur, but it will reduce the blood supply to the femoral head. If the attachment of the capsule is destroyed, disturbances follow also in the epiphysis. The authors studied Hueter's anterior approach in seven cadavers and Gibson's posterolateral incision in eight, finding that they carried no significance in respect of vascular lesions unless excessively distal capsulectomy was performed or the arteries on the upper surface of the neck of the femur were damaged.

Also the medial and lateral circumflex arteries could be ligated without incurring any noteworthy changes. Likewise, the point of origin of the deep femoral artery and of the circumflex arteries could be ligated without causing marked reduction of the blood flow in the femoral head or neck. Neither was any change caused by ligation of the circumflex arteries and the quadriceps artery and superficial femoral artery 10 cm below the point of origin of the deep femoral artery, or, on the other hand, by ligation of the deep femoral artery below the origin of the circumflex artery and simultaneous ligation of the superficial femoral artery 2 cm below the origin of the deep femoral artery.

LAURENT (1953) stated, in connection with discussion of the operative treatment of congenital dislocation of the hip in children, that the capsule must not be divided at the point of lateral insertion, as haemorrhage will occur from the capsular branch of the femoral circumflex artery if the capsule is opened in its ventral-distal part. In a later report (LAURENT 1959) he pointed out that in conservative as well as operative orthopaedic treatment of congenital dislocation of the hip care should be taken not to cause epiphyseal damage, which is the major reason for poor results. PYLKKÄNEN (1960) stressed the importance of avoiding damage to the

capsular vessels in connection with operations of the hip, particularly in children.

Animal experiments. — KISTLER (1934) ligated the lig. teres and caused injury to the vessels in the trochanteric region in rabbits aged 3 weeks to 2 years. On sacrificing the animals after periods of 1—150 days he found changes simulating osteochondritis juvenilis in young animals, but in the older rabbits lesion of the lig. teres alone produced no such changes unless the vascularization of the trochanteric region was simultaneously damaged. No other references to investigations with a bearing on total capsulectomy have been found in the literature.

OWN INVESTIGATIONS

Although the significance of the capsule and its preservation have been commented upon in considerable extent in the literature, relatively little experimental work with animals has been done on this aspect. For this reason it was thought to be appropriate to undertake in the present work an investigation of this particular question.

The macroscopic, roentgenologic and microscopic findings in the present experiments with arthrotomy and capsulectomy (Group III) are shown in Table 4.

Macroscopic changes. — In the specimens taken 5, 10 and 15 days after the operation a considerable haematoma was found in the joint and its neighbourhood. Macroscopically, a tissue resembling the synovialis had partially developed already ten days after the operation; at the later examinations the surroundings of the articular capsule consisted of hard, cicatrized tissue. In the specimen of the 110th day the joint was luxated. In those taken 120, 130 and 240 days after the interference, there was unevenness of the articular cartilage itself. In the animal sacrificed after 100 days the lig. teres had become reattached. No changes were observed in any of the other cases. From 120 days onwards the joint had a restricted range of motion.

Roentgenologic changes. — Only two of the cases displayed changes observable in the x-rays, namely, luxation after 110 days, with a femoral head of considerably smaller size and greater density than the control on the other side, and increased density of the femoral head 130 days after the operation.

Microscopic changes. — 5 — 1 5 d a y s. The specimen taken after 15 days contained granulation tissue in the cancellous spaces.

1 5 — 4 5 d a y s. Granulation tissue was found in the cancellous spaces in the specimens of the 20th and 25th days, located centrally to the site of

TABLE 4.

Arthrotomy and capsulectomy (Group III): Examination results

Time of examination, days since operation	Macroscopic findings				Roentgenologic findings			Microscopic findings					
								Cartilage		Bone			
	Unevenness of articular surface	Adhesions	Dislocation	Lig. teres reattached	Narrowed joint space	Changed form of femoral head	Increased density of femoral head	Unevenness	Degeneration	Granulation tissue	New bone	Necrosis	Epiphysis
5													+
10													+
15										+			+
20		+								+			+
25		+								+			+
30		+											+
35		+								+		+	+
40		+											
45		+											
50		+											
60		+											
70		+											
80		+											
90		+											
100		+		+									
110		+	+			+	+	+					
120	+	+						+		+		+	
130	+	+					+	+		+		+	
140		+								+		+	
150		+								+			
180		+										+	
240	+	+						+		+			
360	No specimen												

attachment of the lig. teres and in the central portion of the femoral head, respectively. Notable features in the specimen of the 35th day, as compared with the other side, were small size, rich content of granulation tissue of the cancellous spaces in the femoral head, and flattening of the head itself. Areas poor in nuclei were encountered in the spongeous bone.

45—90 days. No changes worth mentioning.

90—240 days. In the specimen of the 110th day there was fibrous cartilage and fibrous tissue here and there on the surface of the articular cartilage. In the specimen of the 120th day the articular cartilage was uneven over an extensive area; it was thin and contained cell agglomerations. In the bone under the articular cartilage there were areas poor in nuclei and granulation tissue occurred in scanty quantity in the cancellous spaces. The articular cartilage of the specimen taken on the 130th day was slightly frayed. At one point in the specimens of the 130th and 140th days granulation tissue was found in the cancellous spaces and a few areas poor in nuclei in the spongeous bone. The specimen of the 150th day had granulation tissue in the cancellous spaces. In the specimen of the 180th day were found nucleus-poor areas in the bone and scanty bone marrow (Fig. 19). The specimen of the 240th day revealed occasional unevenness of the articular cartilage and granulation tissue in the cancellous spaces.

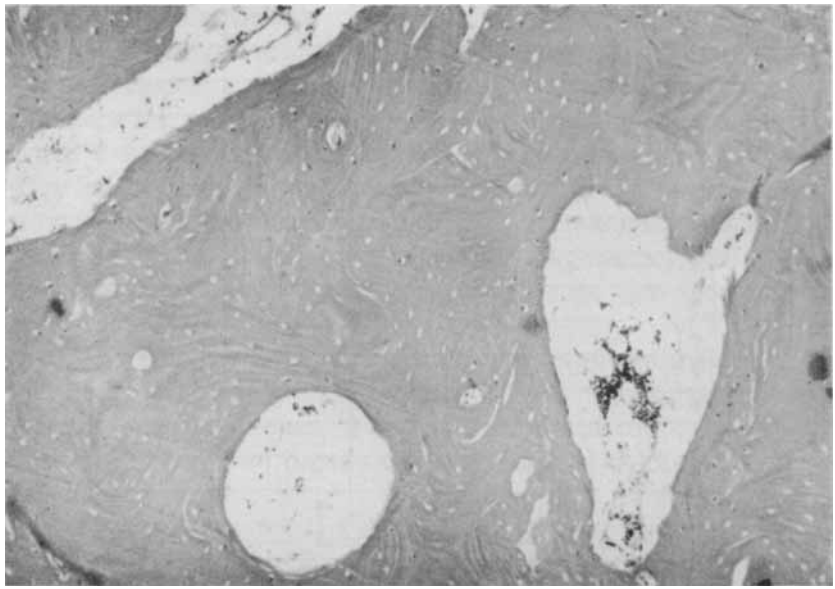


Fig. 19. Micrograph, 180 days after arthrotomy and capsulectomy. Areas poor in nuclei in the bone, and scanty quantity of bone marrow. — Weigert-van Gieson × 100.

Epiphyseal cartilage was observed in seven instances among the specimens from the period of 5—50 days and not once after 50 days. On the 20th, 25th, 30th and 35th postoperative days, ossification of the epiphyseal line was found to be farther advanced on the operated side than in the corresponding control.

Autoradiographic changes. — One specimen, 240 days after the operation, was subjected to autoradiographic study. It revealed uniform deposition of radio-phosphorus in the bone tissue and in the richly vascularized granulation tissue, as was distinctly seen in the specimen of the operated left side at the point where granulation tissue was present in the cancellous spaces.

Microradiographic changes. — Microradiography was also applied to the specimen examined by autoradiography, *i.e.*, that derived from the animal sacrificed after 240 days. It was found to contain only normal bone.

Necrosis of the bone was recorded in 5 of the 22 operated rabbits.

COMMENTS

Comparison of the results elicited in this group by capsulectomy with those in the basic experiments consisting of arthrotomy, division of lig. teres and temporary luxation of the femoral head (Group I) revealed that necrosis of the bone developed here at a much later time and occurred only once more frequently. Changes in the articular cartilage were considerably less frequent than in Group I.

Rather little experimental work has been done on the effect of capsulectomy in experimental animals, although it is true that KISTLER (1934 and 1936) observed degenerative changes in the bone caused by this interference in young animals. In the present investigation such changes were noted only once in the initial stage, but they were distinctly present at a later time, between the 120th and 180th days. The low incidence of bone necrosis particularly in the early stage is thought to imply that the cancellous circulation carries greater significance in rabbits.

According to the clinical investigations of BANKS (1941) and of STEWART and MILFORD (1954), damage to the capsular vessels has an important role in the development of necrosis of the bone following luxation. Ample reference has also been made to their significance in fractures of the neck of the femur. In the present work, however, there is much evidence to the effect that, in rabbits at least, the capsular circulation is not an essential factor, seeing that necrosis of the bone was encountered infrequently only.

If any significance is to be attributed to it, this will be only later when the new capsule hardens and increases in thickness with increasing age and, moreover, produces distinct impairment of function.

Summarizing what has been stated in the foregoing, it can be said that the macroscopic changes were rather insignificant, with the exception of haematoma in the surroundings and of later cicatrization. The roentgenologic changes were likewise negligible, apart from one instance of luxation of the femoral head and of increased density observed in two cases. Neither were any marked microscopic changes noted even in the case presenting luxation. The luxation must therefore have occurred relatively late. Unevenness of the articular cartilage was microscopically established in four instances. The granulation tissue reaction of the cancellous spaces was low in intensity, and indications of necrosis of the bone were not encountered before 120—180 days had passed from the operation, altogether in four instances (except once already on the 35th day). The autoradiographic study showed uniform deposition of radio-phosphorus in the normal bone tissue. The structure of normal bone tissue was visible in the microradiograph.

Changes occurred, in my opinion, in surprisingly small numbers in this experimental group. Observations worth noting are that, with the exception of the fairly rapidly developing granulation tissue reaction, the changes in the bone did not begin until after 110 days, showing then some correlation with the changes in the articular cartilage. This was obviously attributable to the reduced functional activity due to hardening of the new capsule.

ARTHROTOMY AND NEARLY TOTAL OSTEOTOMY OF THE NECK OF THE FEMUR

EARLIER INVESTIGATIONS

In the experimental group to be considered next, the neck of the femur was subjected to osteotomy, stopping short of its complete division. But this operation is virtually equivalent to complete fracture of the neck, seeing that according to LEMOINE (1957) the point chosen for the osteotomy involves essentially all vasculature supplying blood to the femoral head in rabbits, and it seems appropriate to review also the literature referring to such fractures. It was technically preferable to leave a narrow bridge between the fragments of the femoral neck because fixation would have been less secure if the bone had been completely divided.

Clinical and experimental investigations. — In respect of fractures of the neck of the femur, the following incidences, among others, have been reported for aseptic necrosis as complication of these fractures in spite of operative treatment: EYRE-BROOK and PRIDIE (1941), 14.7 per cent; WATSON-JONES (1942), 30 per cent with operative reduction and 15 per cent with extraarticular nailing; D'AUBIGNÉ and HERTZOG (1943), 11.5 per cent; LINTON (1944), 39.5 per cent and 9.3 per cent with nailing according to SMITH-PETERSEN and according to NYSTRÖM, respectively; BOYD and GEORGE (1947), 33.6 per cent and (1948) 32.6 per cent; BADO (1948), 24 per cent and 22 per cent with fixation by means of a three-winged nail and by means of a screw, respectively; RUSSE (1952), 26 per cent; BÖHLER and ENDER (1953), 33.85 per cent; SCAGLIETTI (1953), 42.3 per cent with fixation by screw; CHRISTOPHE *et al.* (1953), 17.8 per cent; D'AUBIGNÉ (1953) 70 per cent in subcapital and 30 per cent in collum fractures; NYSTRÖM (1954), 25 per cent; and WEIS and MÜLLER (1954), 25 per cent. The figures vary according to the length of follow-up period and the type of fracture, but they serve to emphasize the remarkable significance of aseptic necrosis as a complication after such fractures.

For conservatively treated (repositioned and immobilized) fractures of the same kind, equivalent and even higher incidences have been reported: PHEMISTER (1934), 65 per cent; SANTOS (1930), 60 per cent; SCAGLIETTI

(1953), 41.5 per cent; and CARRELL and CARRELL (1941), 25 per cent in children.

Although the figures are of the same order of magnitude, it has been suggested that the presence of metal would contribute to the risk of necrosis of the bone. BRODETTI (1960) and CLAFFEY (1960) studied this question in 16 and 12 cadavers, respectively, performing in them SMITH-PETERSEN's nailing and investigating the cancellous circulation by means of transversal specimens and microangiography. They concluded that the metal nails contributed little to the occurrence of aseptic necrosis of the bone if the upper posterior quadrant of the femoral head was avoided when the nails were placed. A similar observation of the insignificant detrimental effect of the nail was already reported in a single case by WISE (1941).

Several investigators, *e.g.* LANGE (1951) and DUBOIS (1953), stress the importance of circumstances associated with the fracture itself in the aetiology of aseptic necrosis, while MCELVENNY (1960) still placed particular weight on the essential significance of careful and accurate nailing, as did the above mentioned and other authors in recent years. Moreover, he suggested that the sole true blood supply to the avascular femoral head comes from the cancellous part of the bone, while most of the other authors stress the important part played by the capsular and periosteal circulations.

Animal experiments. — BONN (1923) produced in six adult dogs fracture of the medial neck of the femur, which he fixated by means of a plaster cast. The animals were sacrificed 35—100 days later. Complete necrosis of the bone was found in two cases, partial necrosis in two others, coxa vara in one, and complete bony repair of the fracture in one case. Total necrosis developed when also the lig. teres had been completely divided. HENRY (1931) performed on 15 dogs proximal osteosynthesis after complete intracapsular, transverse osteotomy. In one instance avascular necrosis resulted in the femoral head.

COMPERE and WALLACE (1942) instituted a comparison between different therapeutic procedures in fractures of the neck of the femur in 38 dogs; they examined 21 of the animals and found in 33.3 per cent avascular necrosis if the fracture had been reduced and fixated well, otherwise in 66.6 per cent, and in untreated cases in 75 per cent. TOVEE, as cited by GALLIE (1956), produced subcapital fracture in dogs, cut off the blood supply and fixated the fracture by means of a screw, obtaining a good result in 100 per cent.

BONFIGLIO (1954) investigated in 15 adult dogs the repair of subcapital fracture of the neck of the femur and the influence exerted on it by bone

transplantation. The animals were sacrificed after periods from 3 weeks to one year. He found that fixation produced bony consolidation but did not reduce the occurrence of avascular necrosis. Necrotic areas were still encountered in the bone after 3—4 months, although the fracture itself had already healed. As occurs also in bone transplants, the bone died in a few days but did not lose its osteocytes until 2—3 weeks after transplantation.

HARRIS and HOBSON (1956), using male rabbits aged 5—6 weeks, performed operative epiphyseolysis, which they refixated with a Kirschner wire. The first series comprised 45 rabbits, which were sacrificed after 1—6 weeks. The authors reported avascular necrosis of the bone and deformation of the femoral head. In another series they detached the epiphysis, and observed more rapid revascularization. LANGENSKIÖLD and SARPIO (1960) removed the medial epiphysis of young rabbits, obtaining coxa vara.

BOBECHO and HARRIS (1960) used adult rabbits in their investigation of the comparability of the histologic and roentgenologic findings in aseptic necrosis. They produced necrosis of the bone in 80 rabbits by exploration of the hip through a posterolateral incision and division of the lig. teres, in addition to which they divided the neck of the femur with an electric saw. The fracture was then fixated with a Kirschner wire. Necrosis followed already in four days. Repair of the fracture occurred within 10—20 days, the femoral head being regenerated so that degeneration of the articular surface or collapse of the femoral head did not occur in a single instance.

MÜLLER (1924) studied traumatic epiphyseolysis in young dogs, cats and rabbits, eliciting only transient changes. The animals were sacrificed after 7—47 days and no regeneration had come under way during this period. LAURENT (1959) removed the greater trochanter of some five-day-old rabbits, producing typical valgus deformity of the femur.

It is seen that by inflicting various kinds of injury to the epiphyseal cartilage, aseptic changes of bone have been produced in the femoral head in young animals and that by experimental fracture of the neck of the femur, variable changes of the bone of a corresponding kind have been induced in adult animals.

OWN INVESTIGATIONS

This part of the present investigation has also been considered indicated, for the reason that the operation involved here damaged the cancellous circulation more directly than any other procedure employed in this work.

TABLE 5.

Arthrotomy and nearly total osteotomy of the neck of the femur (Group IV): Examination results

Time of examination, days since operation	Macroscopic findings				Roentgenologic findings			Microscopic findings					
								Cartilage		Bone			
	Unevenness of articular surface	Adhesions	Dislocation	Lig. teres reattached	Narrowed joint space	Changed form of femoral head	Increased density of femoral head	Unevenness	Degeneration	Granulation tissue	New bone	Necrosis	Epiphysis
5								+	+			+	+
10													+
15												+	+
20													+
25					+	+						+	+
30								+		+	+		+
35						+	+			+			+
40						+	+	+		+			+
45		+								+			+
50								+	+	+		+	
60	No specimen												
70						+	+			+			+
80						+	+	+		+		+	
90								+		+			
100								+		±			+
110		+											
120								+		±			
130				+									
140													+
150													
180													
240					+	+							
360	No specimen												

The results of the macroscopic, roentgenologic and microscopic examinations in the experiments with arthrotomy and nearly total osteotomy of the neck of the femur (Group IV) are shown in Table 5.

Macroscopic changes. — Very slight changes were observed here, merely greater than normal firmness of the articular capsule and its environment being noted. In one instance, 130 days after the operation, the lig. teres was reattached. On cutting samples with the electric saw, the neck of the femur was found to be of normal hardness. Distinct infection of the joint was observed once, and the femoral head was entirely destroyed in this case. This experimental animal was discarded and another was operated to replace it. Complete fracture was recorded once, after 25 days, and distinct pseudoarthrosis of the neck of the femur was seen on the 240th day.

Roentgenologic changes. — Dislocated fracture of the neck of the femur was seen 25 days after the operation (Fig. 20).

The head of the femur appeared equal in density to that on the intact right side. In the animals examined 35, 40, 70 and 80 days after the operation the femoral head was increased in density, in addition to which it was flattened on the 35th day. On the 240th day, pseudoarthrosis of the neck of the femur was noted on the left side, and the femoral head appeared less dense (Fig. 21).

No changes were observed in any other x-rays in this group.

Microscopic changes. — In this connection the report shall be limited to changes that occurred in the femoral head itself, disregarding those seen at the point of fracture or associated with the repair of the fracture.

5 — 15 days. In the specimen of the 5th day the articular cartilage was uneven; the nuclei were absent at many points. The femoral head was flattened, the bone marrow poor in cells, and in the bone itself there were areas poor in nuclei (Fig. 22). The specimen of the 15th day displayed a thin articular cartilage and areas poor in nuclei in the spongeous bone (Fig. 23).

15 — 45 days. In the specimen of the 25th day the articular cartilage was thin; the nuclei were fewer in some areas of the spongeous bone and entirely absent in others. In the specimen of the 30th day the articular cartilage had almost entirely disappeared and was replaced by fibrous tissue and fibrous cartilage. The bone tissue was broken in structure, the cancellous spaces were rich in granulation tissue and osteoclasts and osteoblasts were encountered in abundance. After 35 days, foamy degeneration of fat cells and some giant cells were present in the bone marrow, but

Fig. 20. X-ray, 25 days after arthrotomy and nearly total osteotomy of the neck of the femur. Dislocated fracture of the neck of the femur. The femoral head appears equal in density to that on the right (control) side.

Fig. 21. X-ray, 240 days after arthrotomy and nearly total osteotomy of the neck of the femur. Pseudo-arthrosis in the neck of the left femur. The head of the femur is less dense in comparison with the right side.

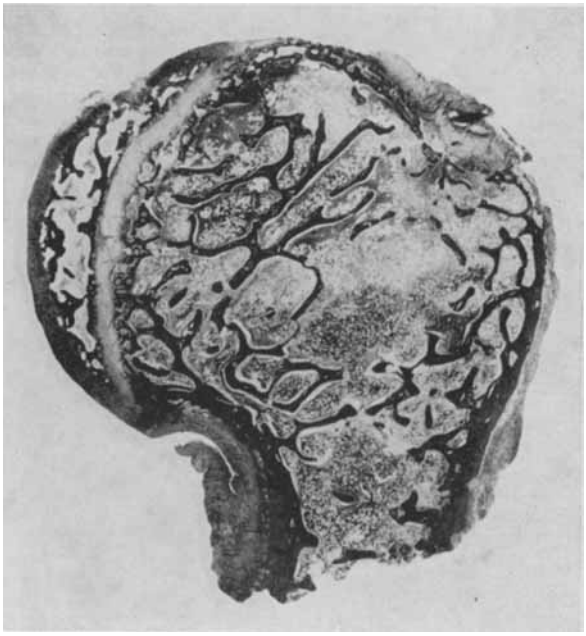


Fig. 22. Micrograph, 5 days after arthrotomy and nearly total osteotomy of the neck of the femur. The femoral head is flattened, the bone marrow poor in cells, and in the bone itself there are some cell-poor areas. — Weigert-van Gieson ×10.

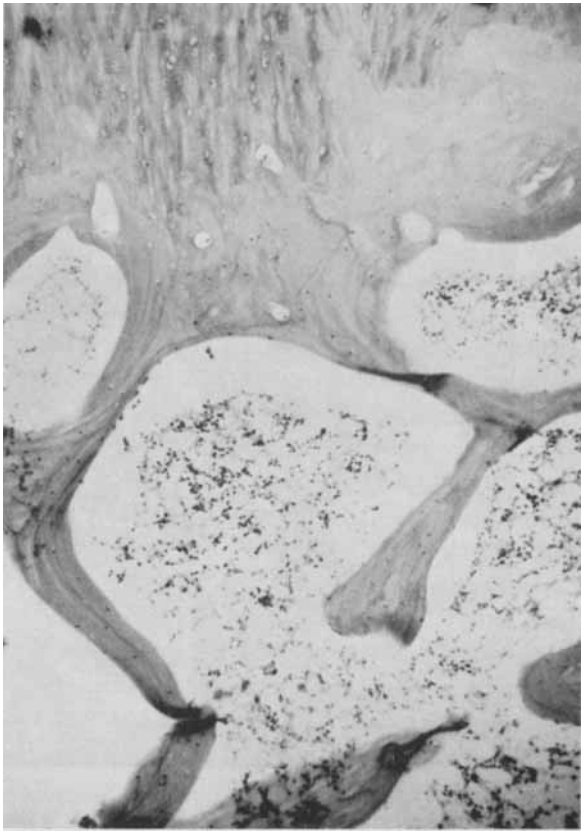


Fig. 23. Micrograph, 15 days after arthrotomy and nearly total osteotomy of the neck of the femur. Areas poor in nuclei are present in the bone under the articular cartilage. — Weigert-van Gieson ×100.

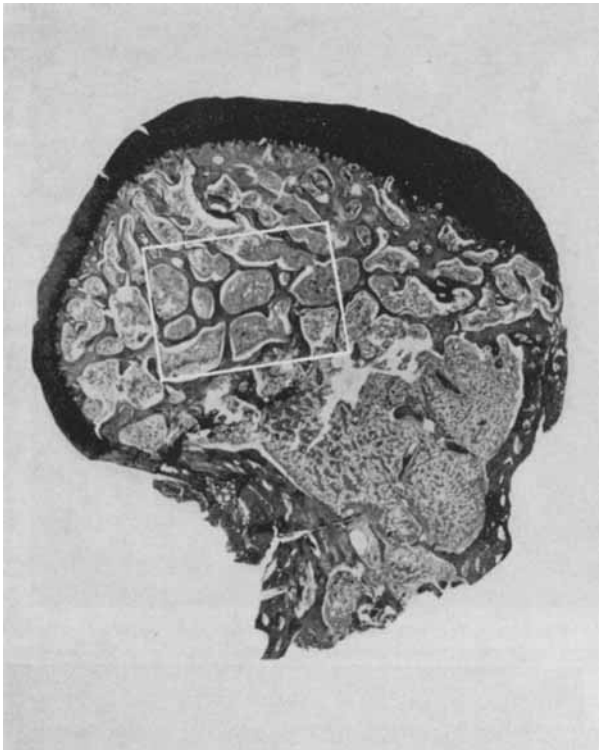


Fig. 24. Micrograph, 50 days after arthrotomy and nearly total osteotomy of the neck of the femur. The cancellous spaces are filled, mainly with granulation tissue; there is slight occasional depletion of nuclei in the spongeous bone. — P.A.S. ×10.

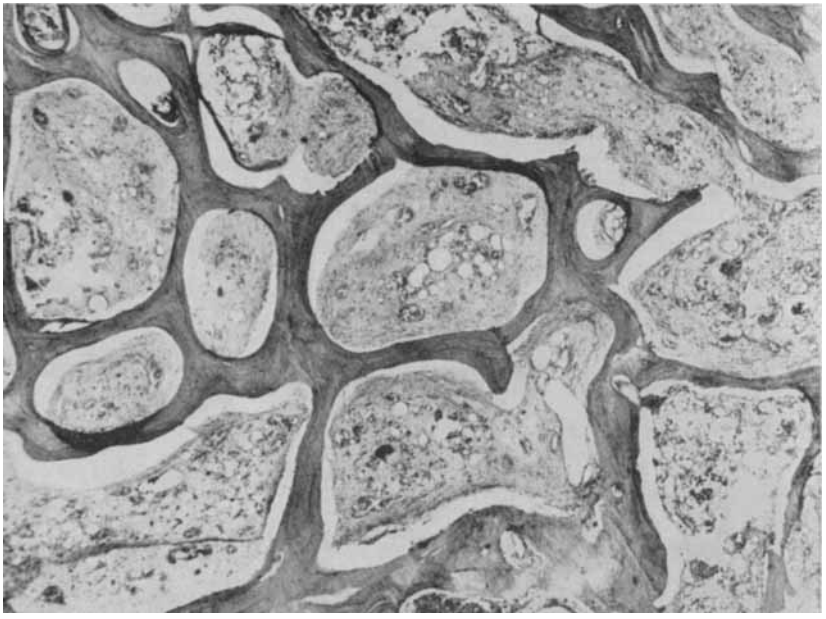


Fig. 25. Detail of the micrograph in Fig. 24. Cancellous spaces very rich in granulation tissue, but no osteogenesis. — P.A.S. ×50.

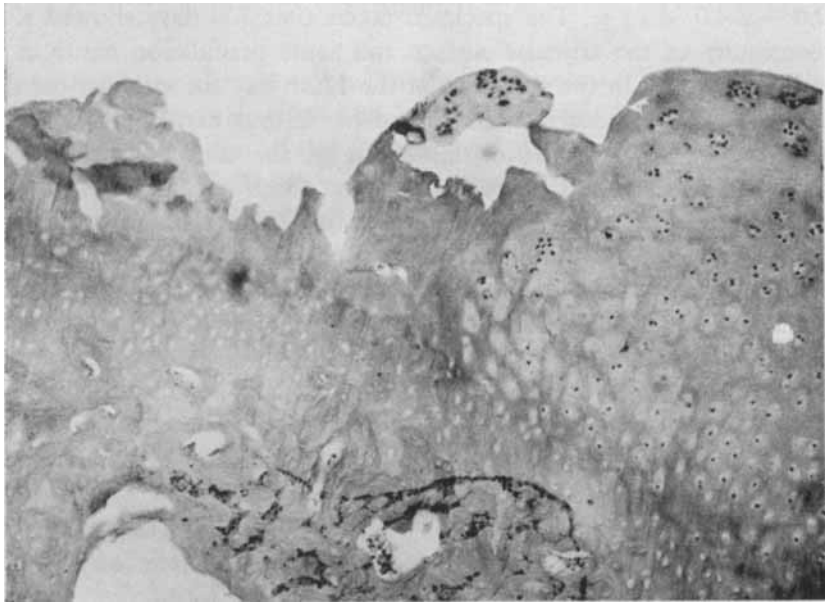


Fig. 26. Micrograph, 80 days after arthrotomy and nearly total osteotomy of the neck of the femur. The articular cartilage is mostly worn off down to the bone. Scantiness of nuclei is observed in the underlying bone. — Weigert-van Gieson ×100.

there were no changes in the articular cartilage. In the specimen taken on the 40th day the articular cartilage was frayed in spots and its surface was poor in cells. There was some granulation tissue at a few points in the cancellous spaces, as was also in the specimen of the 45th day, but the latter showed no changes in the articular cartilage.

45—90 days. The articular cartilage in the specimen of the 50th day was frayed and thin, worn down in some places, and poor in cells. The cancellous spaces were well-filled, rich in granulation tissue, and there was slight depletion of nuclei at some points in the bone (Figs. 24 and 25). In the specimen of the 70th day no changes were observed in the articular cartilage, but there was some granulation tissue in the cancellous spaces on one side of the femoral head. The articular cartilage in the specimen of the 80th day was mostly worn off, but only a small quantity of granulation tissue was encountered in the cancellous spaces. There was scantiness of nuclei in the bone underlying the articular cartilage (Fig. 26). The specimen of the 90th day revealed slight unevenness of the articular cartilage and some granulation tissue in the cancellous spaces on one side of the femoral head, but no osteogenesis and no necrosis of bone.

90—240 days. The specimen taken after 100 days showed slight discontinuity of the articular surface and some granulation tissue in the cancellous spaces. In the specimen of the 120th day the articular cartilage was largely broken down and replaced by fibrous cartilage and fibrous tissue; there was little granulation tissue in the cancellous spaces. No changes were noted in the specimen of the 130th day, in which the lig. teres had become reattached, nor in any of the later specimens.

Epiphyseal cartilage was observed in nine of the animals sacrificed on the 5th to the 50th day and in three later instances, namely, 70, 100 and 140 days after the operation. On the 10th and 15th days there was less ossification of the epiphyseal line on the operated than on the control side, but the opposite was observed on the 140th day.

Autoradiographic changes. — An autoradiographic study was made in two instances, namely with the animals sacrificed on the 90th day (Fig. 27) and on the 150th day. Comparison of the autoradiographs obtained from both sides with the specimen of the 90th day showed a uniform distribution of radio-phosphorus on both sides. In the specimen of the 150th day the radio-phosphorus accumulated along the sides of the cancellous spaces and in the bone tissue itself; no difference was observed between the two sides. This is quite natural, seeing that also microscopically no osteogenesis and no necrosis of bone were observed.

Microradiographic changes. — The two specimens subjected to autoradiography were also studied by microradiography. No differences in the distribution of the mass were observed between the specimens (90th and 150th days).

Necrosis of the bone was recorded in 5 instances among the 22 operated rabbits.

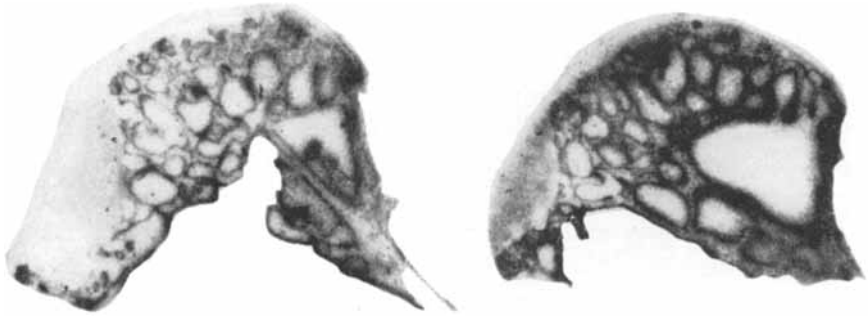


Fig. 27. Contact autoradiographs, 90 days after artbrotomy and nearly total osteotomy of the neck of the femur. Comparison of the operated (left) side and the control reveals that deposition of radio-phosphorus seems to have been uniform on both sides.

COMMENTS

Comparing the changes found in this experimental group with those obtained after the basic operation, *i.e.*, arthrotomy, division of lig. teres and temporary luxation of the femoral head (Group I), the changes were found to be lesser in degree in the group now under discussion, though necrosis of the bone was encountered once more in this group. In this group, necrosis of the bone occurred at an earlier time and the later specimens contained granulation tissue, indicating regeneration. The changes in the articular cartilage, too, were less marked in this group.

In experiments carried out previously with adult dogs, aseptic necrosis of bone followed fractures of the neck of the femur in equal frequency as in man (*e.g.*, BONN 1923, HENRY 1931, and COMPERE and WALLACE 1942). According to some investigators (BONFIGLIO 1954, TOVEE 1956, and BOBECHO and HARRIS 1960), aseptic necrosis was a transient phenomenon, as also KISTLER (1936) has shown with a few adult rabbits. In the present investigation, repair of the osteotomy failed to occur in two cases only, although it has to be kept in mind that the osteotomy performed here, while certainly comprising the most essential portion of the femoral neck as regards the blood supply of the femoral head, was not complete. Of course, this investigation did not aim at a study of the repair of osteotomized bone but rather at an understanding of the changes of bone and articular cartilage occurring in the femoral head.

Necrosis of bone and also degeneration of the articular cartilage were observed at a comparatively early stage. In the later specimens, on the other hand, the histologic picture was dominated by the occurrence of granulation tissue, indicative of regenerative ability. Thus, in these instances the necrosis of bone, encountered 5 times, was a transient phenomenon associated with the repair of the fracture, as was already shown by BARTH (1893).

As a rule, authors have stressed damage caused to the capsular vessels as an agent producing necrosis of bone in fractures of the neck of the femur, but MCELVENNY (1960) constitutes an exception in stating, in his clinical studies, that the cancellous circulation is more important. The present investigation with rabbits supports his opinion. The blood vessels supplying nutrition were severed in the operation, but as the osteotomized fragments were satisfactorily retained in their proper positions, a cancellous circulation was rapidly established and good consolidation of the osteotomy ensued with exception of the case in which the femoral head became detached and complete necrosis of the bone followed within 25 days. In

the case with pseudoarthrosis, after 240 days no bone changes were observed.

The regenerative power of the bone tissue in the experiments of this group was nicely demonstrated also by the fact that hardly any scantiness of cells was noted in the bone marrow even when there were changes in the bone. Although the blood supply of the femoral head had been destroyed, the slight changes in the bone healed rapidly because, apart from the direct instrument-induced trauma, no pressure effect, altered static conditions or remarkable reduction of function were present in this experiment.

The decrease in the articular changes with time finds its explanation in the mere operative trauma, seeing that no actual degenerative changes occurred simultaneously with necrosis of the bone except in the very first specimens. Owing to the more radical operative intervention, the direct trauma was heavier here than in the preceding groups. After five days, degenerative changes were noted in the cartilage as well as in the bone, but also BOBECHO and HARRIS (1960) have been able to observe such rapid changes. Further corroboration of this is the fact that necrosis of bone had already fully developed in the specimen of the 15th day.

The roentgenologic changes observed in this group show no fully convincing correlation with the histologic picture, inasmuch as the roentgenologically noted increased density of the femoral head, which occurred in six instances, was concomitant with microscopically observed necrosis of the bone in one case only.

Summarizing what has been stated in the foregoing, it seems justified to say that the macroscopic changes were insignificant, with the exception of one completely dislocated fracture of the neck of the femur and one case of pseudoarthrosis. The changes were also visible roentgenologically. Moreover, increased density was revealed by the x-rays in four specimens, while the changes otherwise were insignificant in amount. Only the first specimen showed the osteotomy on macroscopic examination. The said four specimens had granulation tissue in the cancellous spaces, though in scanty amount.

Microscopically, degenerative changes in the articular cartilage itself were noted between the 30th and the 120th day; simultaneously a distinct, though mostly slight granulation tissue reaction could be noted in the cancellous spaces. Necrosis of the bone was encountered only 5 times in the early specimens of the group and showed an obvious transient character. The autoradiographic changes were equal on both sides, revealing

deposition of radio-phosphorus in the bone but not in the articular cartilage. No differences between the left (operated) and right (control) hips were observed in the microradiographs.

On the strength of the present experiments it is my opinion that the changes of an obviously transient character encountered in this experimental group were mainly associated with the general phenomenon of fracture repair and give evidence of the regenerative power of bone tissue.

ARTHROTOMY AND TIGHT LIGATION OF THE NECK OF THE FEMUR WITH STEEL WIRE

EARLIER INVESTIGATIONS

Animal experiments. — Without actually injuring the bone, NUSSBAUM (1923, 1923) excised the synovialis of the neck of the femur in young dogs and divided the lig. teres, producing a histologic picture resembling that of chondrosis coxae juvenilis. BERGMAN (1927) repeated the experiments of NUSSBAUM (and of MÜLLER, 1924) with a few rabbits, confirming the previous findings.

BENTZON (1926) injected alcohol close to the upper epiphysis of the femur in young rabbits and obtained a histologic condition resembling coxa plana. INTROZZI (as cited by LERICHE 1934), produced in 44 rabbits aged 3½ to 4 weeks flattening and local necrosis of the femoral head by various means, such as injection of alcohol and ammonia, and injury to the lig. teres.

MILTNER and HU (1933) repeated BENTZON's and INTROZZI's experiments but were unable to confirm their results. On the other hand, in eleven rabbits aged 2½ months, which were sacrificed after observation periods of 2½—4½ months, they observed necrosis of cartilage and necrotic changes in the underlying bone after ligation of lig. teres, peeling of the periosteum and application of a silk ligature to the neck of the femur.

STEWART (1933) peeled the neck of the femur in young and adult rabbits and in adult dogs, sacrificing them after 7—120 days, and found levelling of the femoral head and necrosis of the bone. However, he did not consider these changes resemblant of coxa plana. KISTLER (1936) applied a silk ligature to the neck of the femur in rabbits aged 4 and 30 days, obtaining changes indicative of necrosis of the bone in the first mentioned but not in the latter.

JAKOBSEN (1957) observed in connection with cup arthroplasties, which he performed also in rabbits, that total atrophy of the head and neck of the femur resulted in four cases out of ten. KETTUNEN (1958) mentioned in a report on his preliminary tests concerning skin arthroplasty with cats

that he had to abandon the practice of drilling holes through the neck of the femur, intended to achieve attachment of the skin flap, because aseptic necrosis followed from it. HOOVER and COVENTRY (1961) observed in their skin arthroplasties in dogs that aseptic necrosis developed only twice in 57 operations although the neck of the femur was loosely ligated for attachment of the skin flap.

OWN INVESTIGATIONS

From the above it is noted particularly that, as a rule, only very young experimental animals have been studied in the respect in question. Older animals have been used only for reference in single instances. In view of this, the present investigation was thought to be appropriate.

The macroscopic, roentgenologic and microscopic findings in the experiments with tight ligation of the neck of the femur with steel wire (Group V) are shown in Table 6.

Macroscopic changes. — Slight unevenness of the femoral head was observed in the specimens taken 10, 20, 25, 30, 35, 40, 45 and 120 days after the operation. The steel wire passed through the trochanter was covered by a thick mass of scar tissue in all except the specimens of the 5th, 10th and 20th days. The steel wire had also produced a strong callus reaction in the neck of the femur (Fig. 30). When the specimen was being detached with the electric saw, the neck of the femur was invariably found to be quite soft. Luxation of the femoral head was noted in two instances, namely, in the animals sacrificed on the 100th and 120th days.

Roentgenologic changes. — 10 days after the operation the left femoral head had a denser appearance than that on the right (control) side. On the 40th day it was flattened and of greater density than the control, as also was the case on the 45th day. On the 60th day a distinct, radiolucent cavity was observed in the centre of the femoral head. At 70, 80 and 90 days slight increases in density and deformities were noted in the femoral heads. In the specimens of the 100th and 120th days the femoral head was luxated and the steel wire had almost sheared off the femoral head, which was of greater density than that on the control side. There was osteoporosis in the neck of the femur 110 days after the operation, and the femoral head appeared less dense (Fig. 28). No changes were observed in any other x-rays.

Microscopic changes. — 5 — 15 days. In the specimen of the 10th day the articular cartilage was more poorly stained in spots, and it had lost its nuclei. The margins of the spongeous bone under the articular car-

TABLE 6.

Arthrotomy and tight ligation of the neck of the femur with a steel wire (Group VI): Examination results

Time of examination, days since operation	Macroscopic findings				Roentgenologic findings			Microscopic findings					
								Cartilage		Bone			
	Unevenness of articular surface	Adhesions	Dislocation	Lig. teres reattached	Narrowed joint space	Changed form of femoral head	Increased density of femoral head	Unevenness	Degeneration	Granulation tissue	New bone	Necrosis	Epiphysis
5													+
10	+						+		+	+	+		+
15													+
20	+							+	+	+	+		+
25	+	+						+	+			+	+
30	+	+						+	+	+	+	+	+
35	+	+						+	+	+		+	
40	+	+				+	+	+	+	+	+	+	+
45	+	+				+	+	+	+	+		+	
50		+								+	+	+	+
60		+				+	+	+		+	+		
70		+			+	+		+				+	
80		+				+	+					+	
90		+				+	+					+	
100		+	+		+	+	+	+	+	+	+	+	
110		+				+		+	+			+	
120	+	+	+		+	+	+	+	+	+	+	+	
130		+						+		+		+	
140		+											
150		+											
180		+											
240	No specimen												
360		+						+	+			+	

Fig. 28. X-ray, 110 days after ligation of the neck of the femur with steel wire. On the operated side there is osteoporosis in the femoral neck, and the head of the femur also appears to be less dense.

tilage contained granulation tissue, osteoblasts and new bone (Fig. 29).

15—45 days. The specimen taken on the 20th day showed unevenness of the articular cartilage, which was thin and poor in cells along one margin (Figs. 30, 31 and 32). In the cancellous spaces, in the middle of the femoral head, there was granulation tissue, as well as osteoblasts and osteoclasts (Fig. 33). In the specimen of the 25th day the cells in the basal part of the articular cartilage were anuclear for the greater part. The same changes were observed in the specimen of the 30th day, where furthermore the articular cartilage was frayed and worn off in spots, as also was the case after 35 days.

In the specimen of the 40th day the hyaline cartilage was partly converted into fibrous cartilage and its surface was uneven. At the boundary between bone and cartilage the cartilage cells were fairly large in size. At 45 days the articular cartilage was uneven and here and there worn off down to the bone, in addition to which it had been replaced in some places by fibrous tissue and fibrous cartilage. Elsewhere it was thickened, with confuse arrangement and greater number of cells. Extensive necrosis of the bone was present in all other specimens of this group.

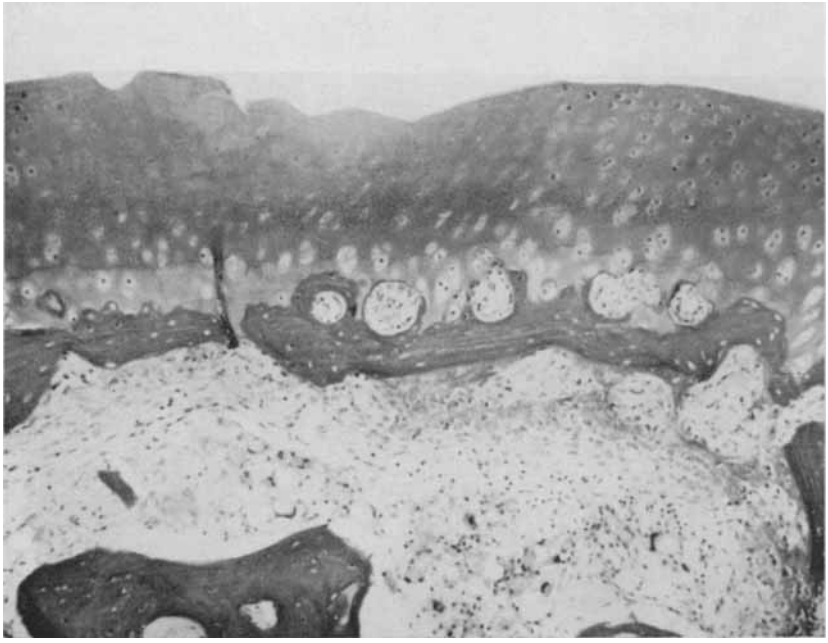


Fig. 29. Micrograph, 10 days after ligation of the neck of the femur with steel wire. The articular cartilage has lost its nuclei at certain points and is uneven. Beneath it, on one side, are seen osteoblasts and already new bone. — Weigert-van Gieson ×100.

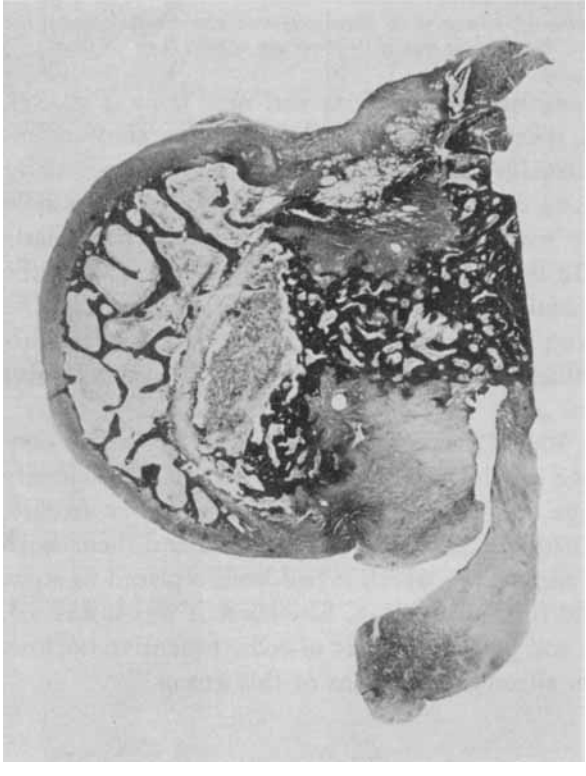


Fig. 30. Micrograph, 20 days after ligation of the neck of the femur with steel wire. The steel wire has penetrated deep into the neck of the femur and produced a strong callus reaction in its neighbourhood. — Weigert-van Gieson ×10.

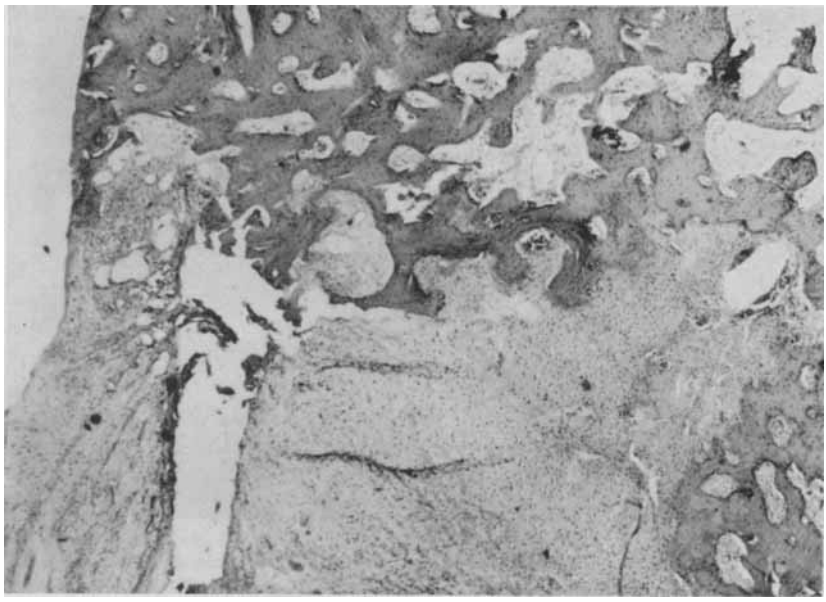


Fig. 31. Micrograph, 20 days after ligation of the neck of the femur with steel wire (same specimen as in Fig. 30). Abundant callus tissue around the steel wire, and granulation tissue in the adjacent cancellous spaces. — Weigert-van Gieson ×40.

Fig. 32. Micrograph, 20 days after ligation of the neck of the femur with steel wire (same specimen as in Fig. 30). Thin articular cartilage, poor in cells. — Weigert-van Gieson ×40.

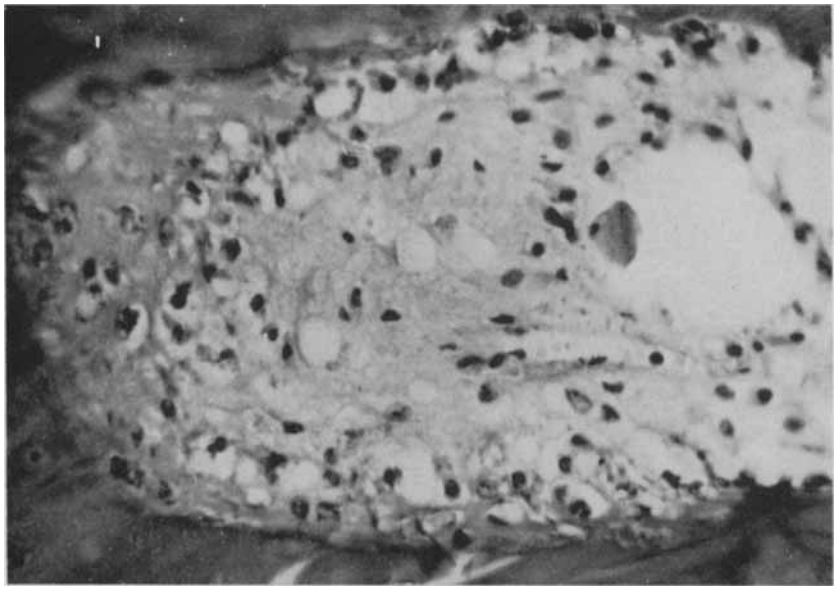


Fig. 33. Micrograph, 20 days after ligation of the neck of the femur with steel wire (same specimen as in Fig. 30). In the cancellous space, granulation tissue and incipient formation of new bone. On the left, new bone is apposited on the old bone and osteoblasts are seen in abundance. — Weigert-van Gieson $\times 500$.

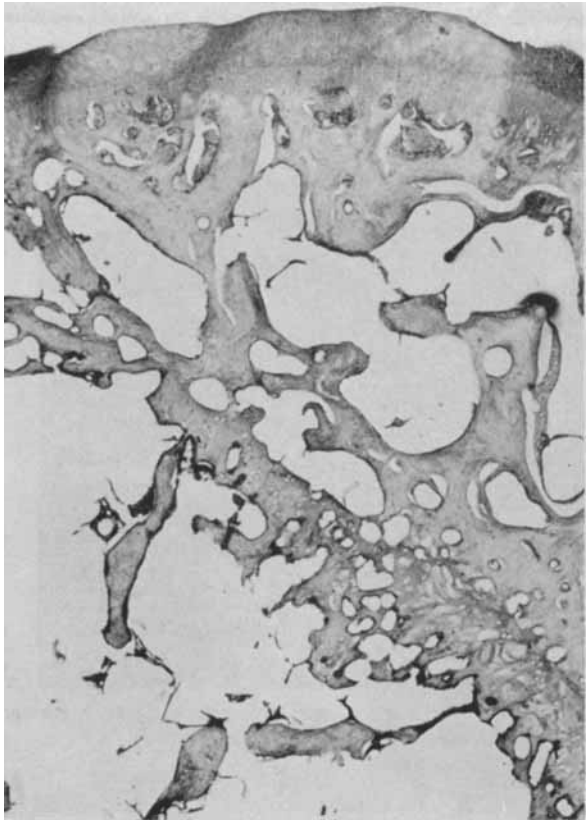


Fig. 34. Micrograph, 25 days after ligation of the neck of the femur with steel wire. Uneven articular surface and empty cancellous spaces; the bone tissue and epiphyseal cartilage are anuclear. — P.A.S. $\times 40$.

Fig. 35. Micrograph, showing specimen from the right (control) side of the same animal as in Fig. 34. No signs of degenerative changes in the cartilage or bone. — P.A.S. × 40.

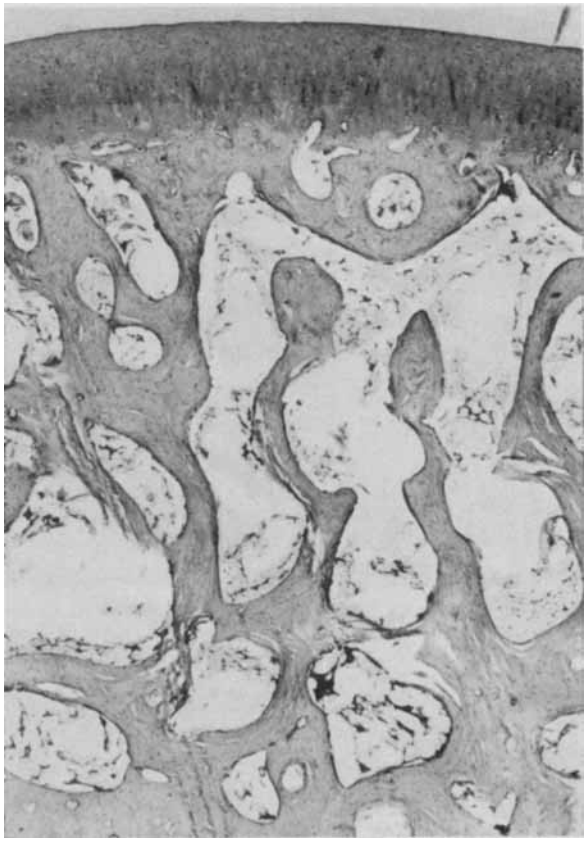
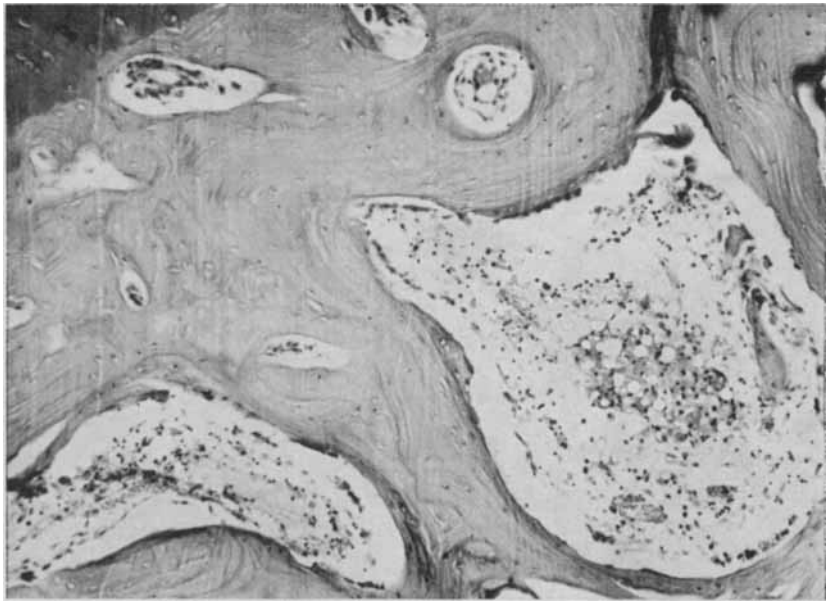


Fig. 36. Micrograph, 30 days after ligation of the neck of the femur with steel wire. The spongeous bone is poor in nuclei in spots, and granulation tissue is present in the cancellous spaces. — P.A.S. ×100.



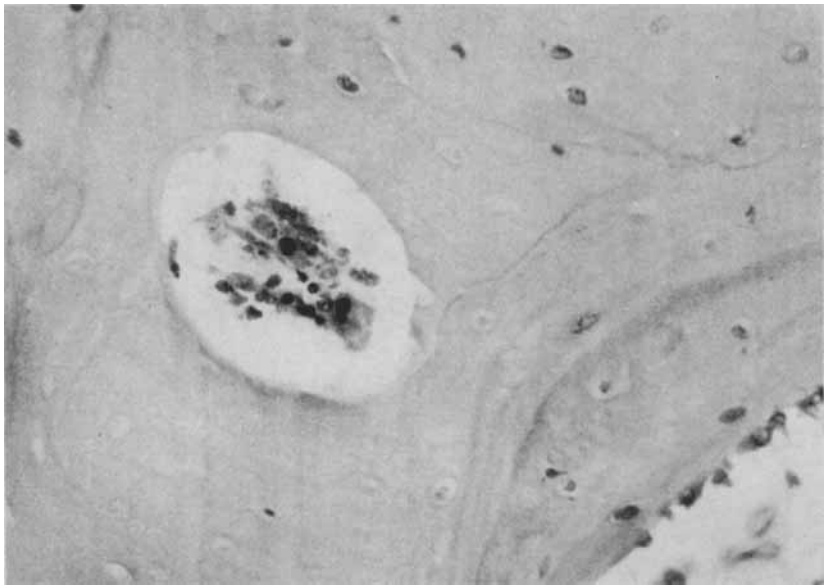


Fig. 37. Micrograph, 30 days after ligation of the neck of the femur with steel wire (same specimen as in Fig. 36). The bone tissue poor in nuclei has taken a less intensive stain than the tissue rich in nuclei. — P.A.S. ×500.

Fig. 38. Micrograph, 30 days after ligation of the neck of the femur with steel wire (same specimen as in Figs. 36 and 37). Granulation tissue and osteogenesis. — Alcian blue × 100.

Fig. 39. Detail of the micrograph in Fig. 38. Osteoblasts and new bone are fairly abundant. — Alcian blue ×500.

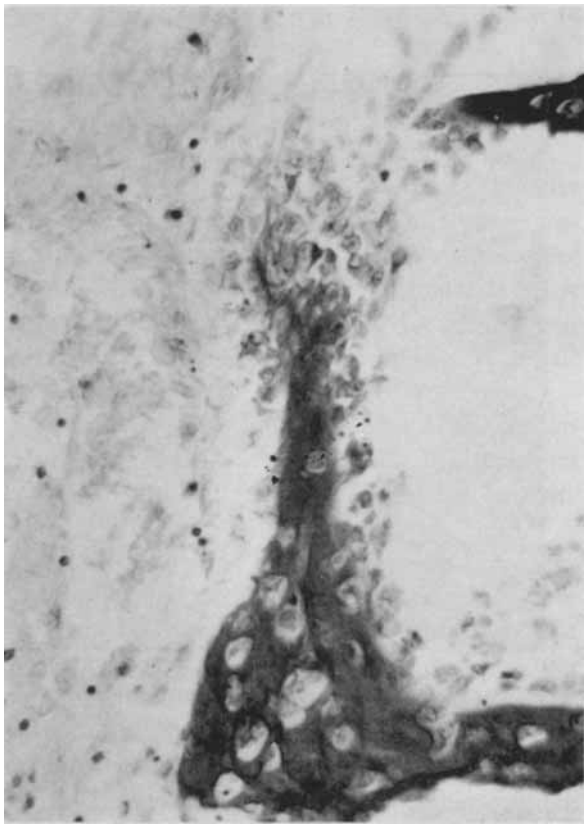
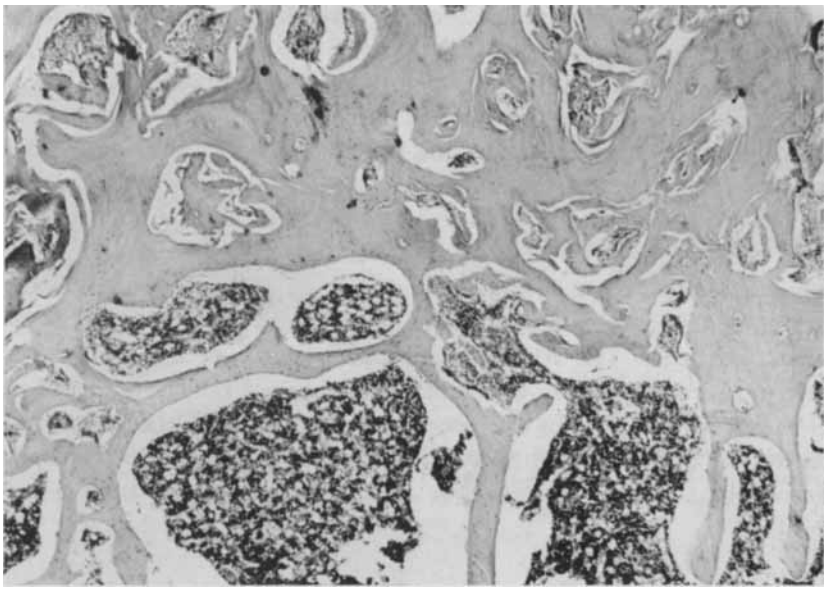


Fig. 40. Micrograph, 130 days after ligation of the neck of the femur with steel wire. In the upper part of the micrograph is seen necrotic bone with unstained nuclei; abundant granulation tissue in the cancellous spaces. — P.A.S. ×100.



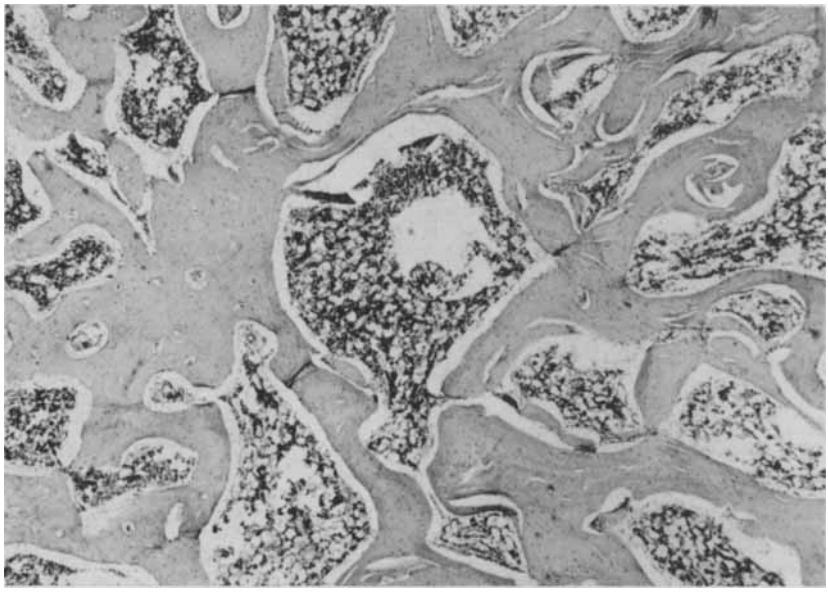


Fig. 41. Micrograph of the control side opposite to the operated side in Fig. 40. The spongeous bone is nucleated and the number of cells in the bone marrow is normal. — P.A.S. × 100.

In the specimen of the 25th day the cancellous spaces were empty and the bone tissue itself was poor in cells (Figs. 34 and 35), but in the specimens of the 30th day (Figs. 36—39) and of the 35th, 40th and 45th days granulation tissue was noted in the cancellous spaces in considerable quantity. In those of the 30th and 40th days there were, moreover, osteoblast and osteoclast agglomerations at several points, and scantiness of nuclei in the bone tissue.

45—90 days. In the specimen of the 50th day extensive anuclear, necrotic areas of bone were seen, but no changes in the articular cartilage. The granulation tissue had increased in the cancellous spaces and incipient osteogenesis was seen here and there. The specimen taken on the 70th day showed occasional unevenness and wear of the articular cartilage, but in the specimens of the 80th and 90th days the articular cartilage was fairly smooth. In these specimens areas poor in nuclei were encountered in spots in the spongeous bone, but no granulation tissue and no osteogenesis was seen. The Alcian blue-stained sample of the 90th day contained numerous anuclear areas that had acquired only a light red stain.

90—360 days. In the specimens derived from the animals sacrificed on the 100th and 120th days, in which also the effect of luxation was present, the articular cartilage was found to have largely been worn off

or replaced by fibrous cartilage or fibrous tissue. In the corresponding samples of the cancellous spaces, granulation tissue was found in abundance, and there were osteoblasts, osteoclasts and areas without nuclei.

The specimen of the 110th day presented a particularly broken articular surface with a top layer poor in cells and areas poor in nuclei in the underlying spongeous bone. In the specimen of the 130th day, the articular cartilage was uneven and the nuclei were absent in the spongeous bone over an extensive area. The cancellous spaces were rich in granulation tissue (Figs. 40 and 41). In the specimens taken on the 140th, 150th and 180th days, again, no changes were observed.

The specimen of the 360th day had a bone tissue that was broken up and poor in nuclei; the articular cartilage was occasionally even, but its greater part was destroyed and replaced by fibrous tissue or fibrous cartilage.

Epiphyseal cartilage was observed in eight instances among the specimens from the period between the 5th and 50th days, but not at any later time. In the specimens of the 5th and 25th days, ossification of the epiphyseal line was farther advanced on the operated side.

Autoradiographic changes. — An autoradiographic study was made of the two specimens taken on the 80th and 90th days. In the first mentioned instance the distribution of radio-phosphorus was found to be less uniform on the left (operated) side, but it indicated considerably greater deposition. In the specimen of the 90th day the radio-phosphorus was distributed over the entire area of bone tissue also on the left side, however so that less deposition had occurred in the areas of necrotic bone (Fig. 42).

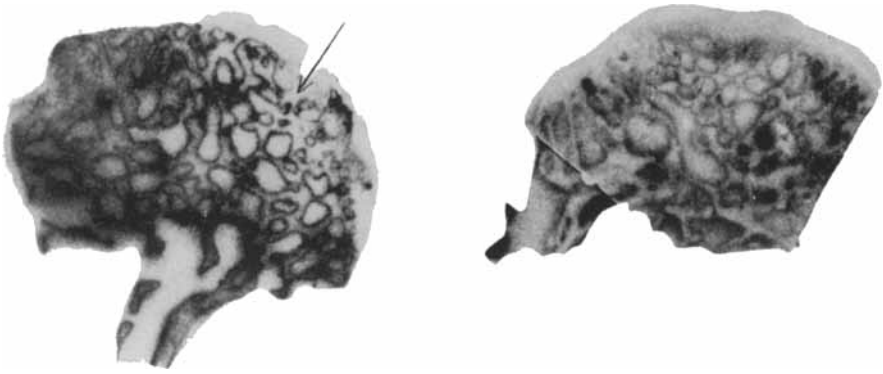


Fig. 42. Contact autoradiographs obtained with radio-phosphorus of the specimen taken 90 days after arthrotomy and ligation of the neck of the femur with steel wire. Comparison shows apparently less deposition at the point of bone necrosis (indicated by an arrow) on the operated left side.

Microradiographic changes. — The same specimens which were used for autoradiographic studies were also subjected to microradiographic examination, that is, the specimens of the 80th and 90th day. A slight difference was noted here between the two sides with respect to lower x-ray absorption by the surrounding areas than by necrotic bone.

Necrosis of the bone was observed in 14 instances among the 22 operated rabbits, although in two of them also the effect of luxation was present.

COMMENTS

When the effects of the basic operation, that is, of arthrotomy, division of lig. teres and temporary luxation (Group I), are eliminated from the results reported above, it will be seen that the degenerative changes in the cartilage and the necrotic changes in the bone encountered in this experimental group were of a very high degree, exceeding those in any other group concerned in this work.

As has been learned from earlier investigations, necrosis of the bone can be produced in the femoral head by causing damage to the neck of the femur in various ways. MILTNER and HU (1933) employed the method described here, but their experimental animals were young rabbits of 2½ months' age. KISTLER (1936), too, obtained the most marked changes of bone necrosis in his experiments with rabbits by this procedure, although also his animals were young. In the present work already at a comparatively early stage, after ten days, a change was found in the articular cartilage, from which also the nuclei had partially disappeared.

According to previous reports, the change develops at a fairly slow rate in the articular cartilage (HALDEMAN 1938, CARLSON 1957) and it may therefore be one of preoperative origin. This is not likely, however, seeing that not a single one of our cases presented a similar change on the other side which served as control.

Degeneration of the cartilage occurred twice although no necrosis of bone was observed, and the opposite was noted to have occurred five times. It is conceivable that in the first mentioned instances the change is visible sooner in the cartilage, while the bone also has obviously been in the process of necrosis, though it is not yet anuclear. The necrosis of bone was then already evident in the subsequent specimens. When necrosis of bone was observed 25 days after the operation and the cancellous spaces were at the same time found to be empty, this was a sign of fairly complete necrosis of the bone. The regenerative ability, however, was

strong enough so that granulation tissue could be seen already in the following specimens between anuclear areas of bone. The time at which necrosis of the bone became demonstrable was also in this experimental group fully consistent with observations in earlier investigations (AXHAUSEN 1922, 1926, 1928, WOLLENBERG 1928, AXHAUSEN and BERGMAN 1937).

In the specimen taken on the 80th day no change of the cartilage was encountered. Obviously no change had been produced in them, the synovial fluid and functional activity of the joint maintaining a normal conditon of the cartilage; or regeneration had already occurred before the specimen was taken.

In the specimens of the 100th and 120th days, in which also the effect of luxation was present, massive necrosis of bone and destruction of the cartilage had taken place. Consequently, owing to the combined effect, these specimens cannot be used as representatives of this group in comparisons with the other groups. In the specimens taken on the 140th, 150th and 180th days, in which no changes were observed, the cancellous blood supply of the bone obviously played already an essential part and the changes that would have been noted at an earlier time had already been repaired.

In also this group the autoradiographic studies with radio-phosphorus furnished indications to the effect that the uptake of phosphorus is greater by new bone than by normal bone, which inferentially implies that more active metabolism and also more profuse vascularization exists there, as has been quite generally observed. Microradiography confirmed the results obtained in the roentgenographic examinations in respect of distribution of the mass, making it possible to observe the reaction in the areas adjacent to the necrotic bone.

In every case in this group a strong reaction of the surrounding tissues and formation of cartilaginous callus at the point involved had been caused by the pressure atrophy produced by the wire. Considering the investigations of LEMOINE (1957), this in itself may have impeded the circulation at the surface of the bone, and the cancellous circulation was not able to compensate for this loss until at a later time.

Summarizing what has been stated in the foregoing, it may be said that, in addition to the scar tissue that had been formed around the wire, the macroscopic findings consisted of the observation that the neck of the femur was softer than normal. Roentgenologically, increased density of the femoral head was noted in eight instances, and osteoporosis of the neck of the femur, or greater radiolucency, in two cases.

The microscopic changes were great already in the specimen taken after 20 days. In the articular cartilages the examination revealed, in addition to degenerative changes, also extensive wear in many specimens. In the spongeous bone itself and in the cancellous spaces abundant degenerative changes and fairly complete necrosis of bone developed as early as by the 25th day and in altogether 14 cases. This included, it is true, two cases in which the effect of luxation also was present.

Granulation tissue reaction and osteoblasts and osteoclasts in profuse numbers were observations associated with the preceding; in the Alcian blue staining the new bone was found to acquire a more intensive red stain, while necrotic bone showed a lighter red hue than normal spongeous bone. In the P.A.S. stain necrotic bone responded less strongly to the staining agent than living bone tissue, which stained violet.

Autoradiography revealed a distinct difference in the concentration of radio-phosphorus in the bone on the operated left side and on the right side serving as the control. The effect correlated well with the histologic and microradiographic pictures in that more phosphorus was deposited in the area of osteogenesis, and less in necrotic areas, than in normal bone.

According to my observations the changes were greater in this group than in any other experimental group, the wire causing considerable pressure atrophy, followed by degeneration and necrosis in the neck of the femur, which the cancellous circulation naturally was unable to prevent. The correlation with the changes in the articular cartilage was distinct, with mainly simultaneous effects.

LIGATION OF THE DEEP FEMORAL ARTERY AND THE OBTURATOR ARTERY

EARLIER INVESTIGATIONS

Animal experiments. — BENASSI (1931) ligated the femoral artery and the iliac artery, both with and without simultaneous venous ligature, in rabbits of varying age, but he did not note any alterations in the bone. PEARSE (1928) excised the entire femoral artery of six dogs with no noteworthy detriment, a strong collateral circulation having developed within two weeks. OLOVSON (1942) ligated the femoral artery and iliac artery of 23 rabbits and examined the circulation at various times between 24 hours and nine months. He found that collateral paths had been established.

BERGMAN (1927) in his experiments with 13 dogs succeeded by injection of metal powder into the femoral artery in producing necrosis of the bone in the diaphysis of the long bones in six cases, but not in the epiphysis. KAHLSTRÖM *et al.* (1939) made unsuccessful attempts to produce necrosis of bone in seven dogs by injection of air into the artery and by keeping the animals in the Trendelenburg position. COLONNA and JONES (1948) showed experimentally with 12 rabbits that necrosis of the bone was produced when a vacuum acted on the bone marrow itself, setting free the nitrogen that was present there.

LEMOINE (1957) carried out investigations with 60 rabbits, five of them adult, clarifying the normal circulation in the rabbit hip by microangiography and by means of impediment caused in different ways to the blood supply of the femoral head. He found that surgical ligation of the most important capsular vessel, the anterior circumflex artery, resulted in young rabbits in changes resembling osteochondritis juvenilis in man. On the other hand, no corresponding change was elicited in three adult rabbits, which were sacrificed after 35, 42 and 90 days. He also noted that regeneration takes 90 days in young rabbits and that the actual hypovascularization phase in the femoral head lasts 15 days.

JUDET *et al.* (1955), using autopsy material, have carried out experimental studies including ligation of the above mentioned arteries. These experi-

TABLE 7.

Ligation of the deep femoral artery and of the obturator artery (Group VI): Examination results

Time of examination, days since operation	Macroscopic findings				Roentgenologic findings			Microscopic findings						
								Cartilage		Bone				
	Unevenness of articular surface	Adhesions	Dislocation	Lig. teres reattached	Narrowed joint space	Changed form of femoral head	Increased density of femoral head	Unevenness	Degeneration	Granulation tissue	New bone	Necrosis	Epiphysis
5													+
10	No specimen												
15													
20	No specimen												
25	No specimen												
30													
35													
40													+
45								+					
50													
60													
70													
80													
90													
100													
110													
120													
130													
140													
150													
180													
240													
360	No specimen												

ments have been reviewed in the chapter dealing with the effects of capsulectomy, on p. 51.

OWN INVESTIGATIONS

This part of the investigation was undertaken entirely for an experimental purpose, to serve as a reference series.

The macroscopic, roentgenologic and microscopic findings in the experiments with ligation of the deep femoral artery and of the obturator artery (Group VI) are shown in Table 7.

Macroscopic changes. — No changes were observed in the articular cartilage. In the musculature of the trochanteric region there were extensive cicatricial strictures. The specimens of the 5th and 15th days showed fairly massive haematomata.

Roentgenologic changes. — No changes were observed.

Microscopic changes. — On the 45th day the articular cartilage was broken up at one point. In the other specimens it was even and no pathologic changes were present in it nor were there noteworthy changes in the spongeous bone or in the bone marrow.

Epiphyseal cartilage was recorded in two instances among the specimens taken between the 5th and 50th days but not thereafter.

Autoradiographic changes. — One specimen, taken 90 days after the operation, was subjected to autoradiographic study. The distribution of radiophosphorus was similar on both sides and it was observed that the deposition in the bone was uniform (Fig. 43).

Microradiographic changes. — One specimen, which also was subjected to autoradiography (specimen of the 90th day), was examined by micro-

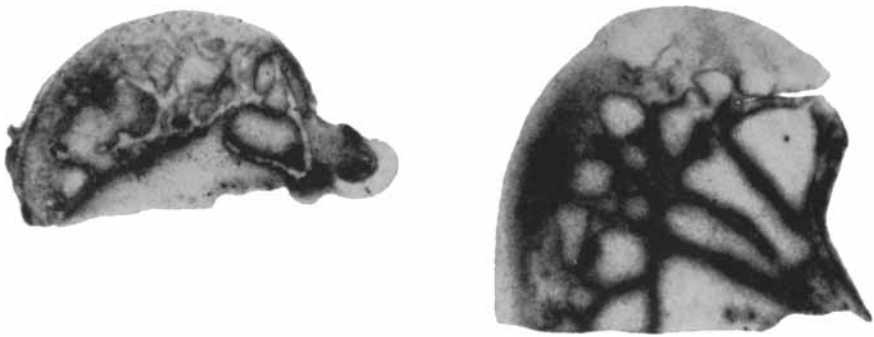


Fig. 43. Contact autoradiograph obtained with radio-phosphorus of the specimen taken 90 days after ligation of the deep femoral artery and the obturator artery. The deposition is uniform and equal on both sides.

radiography. There was no difference between the two sides in respect of distribution of the mass.

COMMENTS

In conformity with earlier investigations, no changes were seen in the femoral head after ligation of the large arteries. Obviously, in order that necrosis of bone might be produced by this interference, the ligation should be quite local, as was that applied by LEMOINE (1957), and the subjects should furthermore be young individuals.

The subject's age and possibly the metabolic processes in the bone are important factors in vascular lesions. A disturbance no doubt results more easily in necrosis in young subjects, but on the other hand, as is well known, regeneration is more rapid in them.

As has been shown by earlier research (COLONNA and JONES 1948), necrosis of bone can be produced by obstructing the blood flow, for example by means of air, but also then the interference must have immediate reference to the internal circulation.

Summarizing what has been stated above, it may be said that the macroscopic, roentgenologic, histologic, autoradiographic and microradiographic changes following ligation of the deep femoral and the obturator arteries in the femoral head were practically nonexistent.

DISCUSSION

Each surgical interference concerned in this work is an entity in itself and the results elicited in the respective experiments have therefore been considered separately and in relation to each other in the foregoing. In the following shall be presented the thoughts and inferences which have emerged from my investigation. For the reader's convenience the results of the macroscopic, roentgenologic and microscopic examinations are shown once more in Tables 8, 9 and 10, grouped by the methods of investigation.

Cartilage and bone are derivatives of connective tissue. One would therefore be inclined to expect that, although they possess additional properties owing to their specialization, they would respond in the manner of connective tissue and of other living tissues. For instance, they respond slowly to various factors that produce degeneration, to the extent that regenerative phenomena, such as the formation of granulation tissue, may become evident sooner than the actual necrosis itself.

It is well known that a great variety of traumatic, circulatory, external and internal factors may exert a degenerative and even a necrotic effect on connective tissue, which responds by regeneration. Cartilage and bone are not static tissues; it is a known fact that continuous destruction and rebirth of cells takes place in them. These phenomena are greatly affected by, among others, hormonal factors, but also topical influences such as altered static conditions, direct trauma, reduced functional activity and circulatory conditions have a considerable bearing in this respect.

In the present investigation evidence has come forth to the effect that internal disturbances in the blood supply of bone are able to produce changes in the bone and the cartilage, as for example in connection with osteotomy, but at the same time this material reveals that such changes are also brought about by the trauma and altered static conditions resulting from dislocation, and by the reduced functional activity consequent on capsulectomy. Pressure applied by means of a steel wire also causes marked changes. Degeneration and necrosis are thus a result of the action of various factors. The literature cites a great number of other factors which

TABLE 8. *Macroscopic findings in the different experimental groups*

Time of examination, days since operation	Arthrotomy, Division of lig teres, Temporary luxation of femoral head				Arthrotomy, Luxation of femoral head without reduction				Arthrotomy, Capsulectomy				Arthrotomy, Nearly total osteotomy of neck of femur				Arthrotomy, Tight ligation of neck of femur				Ligation of deep femoral artery and obturator artery		
	Unevenness of articular surface	Adhesions	Dislocation	Lig. teres reattached	Unevenness of articular surface	Adhesions	Dislocation	Lig. teres reattached	Unevenness of articular surface	Adhesions	Dislocation	Lig. teres reattached	Unevenness of articular surface	Adhesions	Dislocation	Lig. teres reattached	Unevenness of articular surface	Adhesions	Dislocation	Lig. teres reattached	Unevenness of articular surface	Adhesions	Dislocation
5							+																
10				+		+	+										+				No specimen		
15						+	+																
20					+	+	+			+							+				No specimen		
25				+	+	+	+			+							+	+			No specimen		
30					+	+	+			+							+	+					
35					+	+	+			+							+	+					
40	+				+					+							+	+					
45					+	+	+			+				+			+	+					
50					+	+	+			+								+					
60					+	+	+			+			No specimen					+					
70					+					+								+					
80					+	+	+			+								+					
90					+	+	+			+								+					
100		+		+	+	+	+			+		+						+	+				
110		+		+	+	+	+			+	+			+				+					
120					+	+	+		+	+							+	+	+				
130					+	+	+		+	+						+		+					
140					+	+	+			+								+					
150					+	+	+			+								+					
180					+	+	+			+								+					
240					+	+	+		+	+													
360	No specimen				No specimen				No specimen				No specimen					+			No specimen		

TABLE 9. *Roentgenologic findings in the different experimental groups*

Time of examination, days since operation	Arthrotomy, Division of lig. teres, Temporary luxation of femoral head			Arthrotomy, Luxation of femoral head without reduction			Arthrotomy, Capsulectomy			Arthrotomy, Nearly total osteotomy of neck of femur			Arthrotomy, Tight ligation of neck of femur			Ligation of deep femoral artery and obturator artery		
	Narrowed joint space	Changed form of femoral head	Increased density of femoral head	Altered joint space	Changed form of femoral head	Increased density of femoral head	Narrowed joint space	Changed form of femoral head	Increased density of femoral head	Narrowed joint space	Changed form of femoral head	Increased density of femoral head	Narrowed joint space	Changed form of femoral head	Increased density of femoral head	Narrowed joint space	Changed form of femoral head	Increased density of femoral head
5				+														
10				+											+	No specimen		
15				+														
20				+												No specimen		
25				+						+	+					No specimen		
30				+	+	+												
35				+	+	+					+	+						
40											+	+		+	+			
45				+	+	+								+	+			
50				+	+													
60				+	+	+				No specimen				+	+			
70											+	+	+	+				
80				+	+	+					+	+		+	+			
90				+	+	+								+	+			
100	+	+	+	+	+								+	+	+			
110				+	+	+		+	+					+				
120				+									+	+	+			
130				+	+	+			+									
140	+	+	+	+	+	+												
150				+	+	+												
180	+	+		+	+	+												
240				+	+	+				+	+							
360	No specimen			No specimen			No specimen			No specimen						No specimen		

TABLE 16. *Microscopic findings in the different experimental groups*

Time of examination, days since operation	Arthrotomy, Division of lig. teres, Temporary luxation of femoral head						Arthrotomy, Luxation of femoral head without reduction						Arthrotomy, Capsulectomy						Arthrotomy, Nearly total osteotomy of neck of femur						Arthrotomy, Tight ligation of neck of femur						Ligation of deep femoral artery and obturator artery					
	Cartilage		Bone				Cartilage		Bone				Cartilage		Bone				Cartilage		Bone				Cartilage		Bone				Cartilage		Bone			
	Unevenness	Degeneration	Granulation tissue	New bone	Necrosis	Epiphysis	Unevenness	Degeneration	Granulation tissue	New bone	Necrosis	Epiphysis	Unevenness	Degeneration	Granulation tissue	New bone	Necrosis	Epiphysis	Unevenness	Degeneration	Granulation tissue	New bone	Necrosis	Epiphysis	Unevenness	Degeneration	Granulation tissue	New bone	Necrosis	Epiphysis	Unevenness	Degeneration	Granulation tissue	New bone	Necrosis	Epiphysis
5						+	+					+						+	+	+			+	+						+						+
10	+					+	+		+			+						+						+		+	+	+		+	No specimen					
15	+	+		+		+			+		+	+			+			+					+	+					+						
20							+		+						+			+						+	+	+	+	+		+	No specimen					
25	+					+									+			+					+	+	+	+			+	+	No specimen					
30	+		+			+	+		+									+	+		+	+		+	+	+	+	+	+	+						
35	+					+	+	+	+	+	+	+			+		+	+			+			+	+	+	+		+							
40	+	+			+		+					+							+		+			+	+	+	+	+	+	+						+
45							+		+			+									+			+	+	+	+		+		+					
50						+	+	+	+										+	+	+		+				+	+	+	+						
60						+	+	+	+		+								No specimen						+		+	+							
70							+	+	+		+										+			+	+				+						
80	+						+	+	+	+	+								+		+		+						+						
90		+			+		+	+	+	+	+								+		+								+						
100	+		+		+		+	+	+	+	+								+		±			+	+	+	+	+	+	+						
110	+						+	+	+			+	+								±				+	+				+						
120	+						+	+	+			+	+		+		+		+		±				+	+	+	+	+	+						
130	+						+	+	+	+	+		+		+		+								+		+		+							
140	+	+	+	+	+		+	+	+						+		+							+												
150	+						+	+	+	+	+				+																					
180	+						+	+	+	+	+						+																			
240	+						+	+	+	+	+		+		+																					
360	No specimen						No specimen						No specimen						No specimen						+	+			+		No specimen					

are able to produce changes of this kind and which have not been considered in the present investigation, such as heat, cold, various chemicals, and irradiation with x-rays.

In my opinion the present results also point to the possibility that aseptic necrosis of the bone may not in itself be detrimental under all conditions but that it may be a natural phenomenon conducive to the occurrence of regenerative processes, for example in the repair of osteotomized bone.

Even interferences as radical as the ligation of blood vessels, capsulectomy, division of the lig. teres, and temporary luxation of the femoral head in connection with arthrotomy in rabbits seemed to have comparatively insignificant and transient consequences. This would seem to justify the opinion that the cancellous blood supply of the femoral head and neck plays an important role. This is understandable enough, seeing that the growth of granulation tissue and the regenerative processes commence just in the cancellous spaces. It would thus seem that in surgery of the femoral head and the neck of the femur attention should be paid to promotion of the cancellous blood supply. This principle has indeed been applied in the therapy of pseudoarthrosis after fracture of the neck of the femur. It is also obvious, on the other hand, that great weight should be placed on the static conditions, which should be rendered as favourable as possible since the bone and cartilage which are being formed are greatly dependent on prevailing static conditions.

These facts are probably largely responsible for the benefit derived from osteotomy in the treatment of pseudoarthrosis. Furthermore, the present investigation may be taken to indicate that various traumata may produce degenerative changes and even necrosis of bone and cartilage.

It was observed in this work that the degenerative changes in the cartilage and bone and those resulting in necrosis are so correlated that when the cartilage is more directly subjected to trauma, as after dislocation, it will be damaged first and similar changes in the bone will follow later. When the disturbance of the blood supply to the bone is obviously the primary occurrence, such as it was when the neck of the femur was tightly ligated with a steel wire, both kinds of changes develop nearly simultaneously.

The present experiments serve to confirm, for their part, the prevalent opinion that necrotic bone absorbs x-rays more strongly than normal bone in x-ray examinations and that new bone has less mass than normal tissue. Recognition of necrosis of the bone by autoradiography has proved a difficult problem. In the present work, too, the best indications of degeneration and necrosis of the bone were found to be the degenerative

changes in the nucleus of the osteocyte and its karyolysis, which already were described by AXHAUSEN in 1922. To be sure, occurrence of granulation tissue or emptiness of the cancellous spaces already before this may constitute signs of incipient necrosis of the bone.

The observation was made in the histochemical examinations in the present experiments that living bone tissue yields a stronger positive reaction to P.A.S. stain than dead, anuclear bone tissue. According to RISSANEN (1960), the histochemically demonstrable quantity of mucopolysaccharides in connective tissue is reduced in the process of degeneration, and in the present work this was found to hold true also for cartilage and bone tissue. On the other hand, bone tissue in the process of being formed gives a more intensive P.A.S. reaction, as also reported by MCMANUS (1948) and HOTCHKISS (1948). Alcian blue staining reveals similar changes, and by this method new bone acquires a more intensive red stain owing to its higher collagen content. Moreover, irregularity of structure was noted in necrosis of the bone of longer duration.

It may be worth while to contemplate continued investigation of the degenerative changes of bone and cartilage by means of enzyme-chemical methods, which give a rapid reaction, as observed by, *e.g.*, RAEKALLIO (1961). Even in a contusion wound, for instance, they reveal clearly observable changes in the distribution of acid phosphatase and leucine aminopeptidase as early as a few hours after infliction of the wound.

The practice of referring to the phenomena considered here as avascular necrosis of the bone receives little encouragement from what has been found in the present work. It seems in my opinion that the name employed in the title of this book, *aseptic necrosis of bone*, should be preferred, as it better calls attention to the numerous factors of various kinds responsible for such necrosis.

SUMMARY AND CONCLUSIONS

The purpose of the present experimental study of the hip joint of the rabbit was to clarify the contribution of various surgical factors to the development of necrosis of the bone.

A total of 155 rabbits were used, divided into six groups subjected to the following surgical interferences:

— Arthrotomy by posterolateral approach, division of lig. teres, and temporary luxation of the femoral head;
— As the preceding group, but without reduction of the luxation;
— Arthrotomy and capsulectomy;
— Nearly total osteotomy of the neck of the femur by arthrotomy approach;
— Arthrotomy and tight ligation of the neck of the femur with a steel wire;
— Ligation of the deep femoral artery and the obturator artery, without arthrotomy.

In each case the left hip of the rabbit was subjected to the surgical interference, while the right hip served as control. The periods of observation ranged from 5 to 360 days, one animal in each group being sacrificed at each specified date. In addition to macroscopic and roentgenologic examination of the operated and control hips, specimens were taken from both hips for histologic examination and stained by Weigert-van Gieson's haematoxylin method and in some cases with Pentachrome II. Alcian blue and periodic acid-Schiff staining after EDTA decalcification were also used. In eight instances autoradiographs were made by the contact method, using radio-phosphorus, and the same specimens were also examined by microradiography.

Following *arthrotomy, division of lig. teres and temporary luxation of the femoral head* quite insignificant macroscopic, roentgenologic and microscopic changes were observed. However, partial necrosis of the bone developed in 4 out of 22 rabbits and numerous specimens revealed unevenness of the articular cartilage and its destruction and replacement by fibrous cartilage and fibrous tissue.

In the rabbits operated similarly but with *permanent luxation* there were, on the other hand, in addition to definite macroscopic and roentgenologic changes, distinct destruction of the articular cartilage from the very beginning and granulation tissue in the cancellous spaces of the underlying bone. Sixty days and more after the operation there was necrosis of the bone in altogether 11 out of 22 cases. Even then the histologic picture was dominated by granulation tissue reaction and osteoclast and osteoblast activity.

After arthrotomy and *capsulectomy* only insignificant macroscopic and roentgenologic changes were encountered. The articular cartilages showed slight unevenness. The necrotic changes in the bone itself were fairly insignificant, occurring in 5 out of 22 cases.

When *nearly total osteotomy of the neck of the femur* by the arthrotomy approach was performed, repair took place within 10—20 days and there were slight macroscopic and roentgenologic changes. Histologically, degenerative changes in the articular cartilage itself were seen between the 30th and 120th days after the interference. Simultaneously a distinct but scanty granulation tissue reaction was present in the cancellous spaces. Necrosis of the bone was only encountered transiently in 5 out of 22 cases.

Tight *ligation of the neck of the femur* with a steel wire in connection with arthrotomy produced, in addition to massive macroscopic changes, increased roentgenologic density of the femoral head between the 40th and 120th days after the operation. The microscopically observable changes were great. By the 20th day the degenerative changes in the articular cartilage were supplemented by complete necrosis of bone in the femoral head, with its accompanying regenerative phenomena. Necrosis of the bone resulted in altogether 14 out of 22 cases, although this includes two cases in which also the effect of luxation was present.

Following *ligation of the deep femoral artery and of the obturator artery* without arthrotomy there hardly were any changes.

The macroscopic and roentgenologic changes were well correlated with the microscopic findings. When the articular cartilage degenerated or was destroyed, a granulation tissue reaction was produced in the cancellous spaces of the underlying bone. Necrosis of the bone was a frequent consequence; it was slow in developing upon luxation but rapid and complete after ligation of the neck of the femur in connection with arthrotomy. The greater changes were also roentgenologically demonstrable.

The autoradiographic studies with radio-phosphorus revealed ample deposition of phosphorus in the bone, particularly in the new bone, while

necrotic areas of the bone took up phosphorus poorly, as also did the cartilage. Microradiography revealed that new bone has less mass than normal bone; in actual necrosis of the bone the reduction of the mass is difficult to demonstrate and rather tends to be apparent in its surroundings.

A great variety of causes were deemed to be responsible for the disturbances resulting in degeneration and necrosis of the bone. Parallel to circulatory disturbances, an influence in this respect is exerted at least by direct trauma, pressure effect on the articular cartilage and on the neck of the femur, altered static conditions, and reduced functional activity. The cancellous circulation was found to surpass the capsular circulation in importance.

Owing to the retained structure of the collagen, living bone tissue acquired a distinctly more intense stain than aseptic, anuclear bone tissue in the P.A.S. and the Alcian blue stainings, but the only really reliable sign of aseptic necrosis of the bone was the lack of nuclei in the osteocytes. This was usually preceded by scantiness of cells or occurrence of granulation tissue in the cancellous spaces. However, clarification of the early diagnostics of bone necrosis will require further investigation.

The following conclusions seem to emerge from the present investigation:

1. The greatest degenerative and necrotic changes in the cartilage and the bone occurred when the neck of the femur was tightly ligated with a steel wire, *i.e.*, as a result of pressure by and reaction to the wire, and when in addition to arthrotomy and division of lig. teres the femoral head was left in its luxated position, *i.e.*, as a result of direct trauma and later of pressure, altered static conditions and reduced functional activity. A number of factors were thus responsible simultaneously for the changes.

2. In all other instances the changes were less marked. No changes at all ensued following only ligation of the deep femoral artery and the obturator artery. The regenerative ability of the bone tissue was distinctly evident, particularly upon nearly total osteotomy of the neck of the femur.

3. Aseptic necrosis of the bone could be demonstrated by histopathologic, autoradiographic (using radio-phosphorus), microradiographic and roentgenologic methods. The best indications were found to be the degenerative changes in the nucleus of the osteocyte and the karyolysis of this cell, although the occurrence of granulation tissue even before this stage or emptiness of the cancellous spaces might be considered to be signs of incipient necrosis of the bone.

4. The practice of speaking of avascular necrosis of the bone is inconsistent with the present results. Aseptic necrosis of the bone is suggested as a preferable term for the phenomenon, on the grounds that it better implies the presence of numerous factors conducive to such necrosis.

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