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SKIN ARTHROPLASTY

IN THE LIGHT OF ANIMAL EXPERIMENTS WITH SPECIAL REFERENCE TO

FUNCTIONAL METAPLASIA OF CONNECTIVE TISSUE

BY

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PREFACE

The subject for the present study was suggested by Professor K. E. Kallio, my esteemed teacher and principal, Chief of the Orthopaedic Clinic of the University of Helsinki. As a resident at the Clinic, I have received from Professor Kallio ready advice, encouragement and inspiring criticism, which were an invaluable help for my work. I am happy to have this opportunity to express my deep gratitude to Professor Kallio.

The microscopical part of the study was carried out at the Institute of Forensic Medicine, University of Helsinki, Chief Professor U. Uotila, who kindly placed the laboratories of the Institute at my disposal. The interest he took in my work and his stimulating criticism have been invaluably helpful. For all this I am deeply grateful to my esteemed teacher.

My gratitude is due to my colleagues Dr Kaj Karlsson and Dr Kalevi Pyörälä, for help and criticism given in the historadiographical and histochemical examinations included in the study and to Dr Erkki Kallio who made available to me the follow-up records he had collected of skin arthroplasties carried out at the Orthopaedic Clinic.

To Docent Lauri Saxén, M.D., M.A., I am indebted for many hours of helpful discussion over details in the manuscript to this study.

I offer very sincere thanks to Miss Annikki Kinosmaa, my right hand and untiring technical helpmate during the whole of the work, to Miss Marianne Ejder and Mrs. Anja Roos for technical help in connection with operations, and to Miss Elisabeth Bismarck and Miss Eeva Kaprio, who helped me with the microscopic preparations.

My thanks are also due to Lector Aune Tuomikoski, Mag. Phil., for her translation of the MS into English.

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Helsinki, January 1958

Kauko O. Kettunen

CONTENTS

I. INTRODUCTION

At the Orthopaedic Clinic, University of Helsinki, animal experiments and clinical investigations have been made since 1952 with the view of developing and extending the use of skin in reconstructive surgery. In 1952 Professor KALLIO assigned Dr KIVILAAKSO to undertake a general experimental study on changes in the whole-thickness skin graft used as replacement of tissue defects. This study was published as a supplement to Acta Orthopaedica Scandinavica in 1955.

In the spring of 1954, as known, Professor KALLIO began to use a full-thickness autogenous skin graft as interposition material in arthroplasties. The results obtained with this method looked from the first promising, and skin arthroplasty has become a routine procedure at the Clinic. To this day skin has been used as interposition material in 103 arthroplasties performed in different joints. No infection has occurred in any of the cases treated at the Clinic, and the follow-up results which will be published by Dr ERKKI KALLIO stand comparison with those obtained by alloplastic methods.

Because of favourable clinical experience Professor KALLIO entrusted me with the task of elucidating by means of animal experiments the changes undergone by the fresh full-thickness autogenous skin graft with subcutaneous fatty tissue when used as interposition material in arthroplasties.

II. SURVEY OF LITERATURE ON SOFT PART INTERPOSITION ARTHROPLASTIES

A. EARLIER EXPERIMENTAL STUDIES ON THE USE OF FASCIA LATA, FAT AND MUSCLE AS INTERPOSITION MATERIAL IN ARTHOPLASTIES

The first arthroplasties were carried out in the later half of past century; VERNEUIL (1860) and HELFERICH (1894) published reports on a surgical procedure which conforms with what is understood by arthroplasty today. Their operations consisted of resection of an anchylosed temporo-mandibular joint, and to prevent anchylosis from recurring they inserted a pedicled muscle flap between the bone surfaces.

Before long surgeons began to use other soft parts, especially fascia lata and fatty tissue as interposition material (KIRSCHNER 1909, PAYR 1910, HELFERICH 1913, RÖPKE 1913, LEXER 1916). This procedure, called soft part interposition, soon gained ground and results obtained by its use were published at a number of surgical centres (MURPHY 1913, KIRSCHNER 1913, 1927, PAYR 1914, LEXER 1925, 1931, FALTIN 1927, LANGENSKIÖLD 1944).

While the clinical literature on arthroplasty is fairly extensive, comparatively few reports have been brought out on experimental work attempting to elucidate the fate of the soft parts used as interposition material. MURPHY (1905) inserted fat and fascia between freshened articular surfaces on two dogs and noted that the changes in the interposition material led to the development of a new joint resembling a bursa or a hygroma. SUMITA (1912) performed interposition arthroplasties with muscle, fat and fascia in the knee joint of dogs. In all types of tissue a fibrous transformation of the interposition material was found to occur at an early stage. Only a slight degree of tissular necrosis was noted. No cartilaginous regeneration was revealed, on the contrary, pieces of articular cartilage which had remained in the joint, underwent transformation into fibrotic tissue. A layer of dense connective tissue, firmly attached to its base, partly originating in the interposition tissue, partly in transformed remains of the

articular cartilage, was seen macroscopically. No appreciable difference could be noted in the results depending upon whether the interposition material was muscle, fat, or fascia. ALLISON and BROOKS (1913) and PHEMISTER and MILLER (1918) made arthroplasties on dogs. They used as interposition material either pedicled fascia flaps or a free fascial transplant and also carried out a series of arthroplasties without any interposition material. These authors believed that the interposition material was of secondary importance only in the formation of the new joint, because in their experiments most of the interposition material necrosed in the weight-bearing area of the joint. The end results were on the whole in agreement in the different experimental series. What they found more important was the new connective tissue growing from the freshened bone surface, which covered the non-weight-bearing areas of the joint. The connective tissue disappears from the weight-bearing area and a naked bony surface is left. The fascia used in these experiments was thin, muscular fascia, while SUMITA in his used considerably thicker grafts of fatty-fascia. PAYR (1934) believed that the differences in the quality and amount of the interposition material accounted for the discrepancies in the results obtained in the experiments. HOHMEIER and MAGNUS (1914) performed arthroplasties on the knee joint of the rabbit inserting soft parts between freshened bone surfaces. They did not see any cartilaginous development. The articular surfaces were invested with fibrotic connective tissue. In the control series, in which no interposition material was used, granulation tissue grew up from the naked bone surface, covering the articular surface. There was no appreciable difference on this point between the experimental and the control series. RÖPKE (1913) showed by animal experiments that fat produced »einen derben bindegewebigknorpeligen Überzug» between the articular surfaces.

EISLEB (1916) performed fat interposition arthroplasties in the knee joint of the rabbit. In histological specimens the fat was found to become transformed in the weight-bearing area into more or less differentiated connective tissue with a structure favourable to articular function.

B. HISTOLOGICAL STUDIES OF FASCIA LATA, FAT AND MUSCLE INTERPOSITION ARTHROPLASTIES PERFORMED ON THE HUMAN BEING

Clinical cases in which it has been possible to obtain a histological specimen at operation or at autopsy from a joint in which a soft part interposition arthroplasty has been made earlier are of special interest.

LEXER (1917) opened a knee joint operated upon 13 months before, in which fat had been used as interposition material. Both joint surfaces were covered by a light, smooth tissue resembling cartilage; no intra-articular adhesions occurred. In the weight-bearing area of the joint was solid fibrous connective tissue, deeper down in the process of being transformed into cartilage and bone. In those areas, on the other hand, where the interposition material was not subject to loading was fatty tissue attached by means of connective tissue to its base and presenting a normal appearance.

PUTTI (1917) opened a joint with a fascia lata interposition arthroplasty of three years' standing and saw in the weight-bearing area tissue which was histologically fibrous, in part hyaline type cartilage. No metaplasia of this kind occurred in the non-weight-bearing area.

BIER (1919) mentions a case in which a fat interposition arthroplasty in the knee, of two years' standing, was opened. Here connective tissue, partly transformed into fibrous and partly into hyaline type cartilage was seen on the articular surface.

KALIMA (1921) reported on two cases of fat and fascia interposition arthroplasty in the elbow joint, which were subjected to autopsy. In one, observed during four weeks, the fat had become partly transformed into connective tissue. In the other, which was under observation for 2 years, the inserted tissue had become transformed into solid connective tissue where the fibrils were running a course parallel with the joint surface. No regeneration of cartilage was noted. PAYR (1934) opened a joint, in which arthroplasty with fascia interposition had been made earlier, seeing a satiny joint surface which was histologically hyaline connective tissue. BOYD (1956) described seven cases in each of which a joint treated with fascia interposition arthroplasty was opened in connection with another operative measure. He stated that »after arthroplasty a joint is developed in which function is restored to a practical degree. There is a definite joint cavity containing a lubricating fluid. This cavity, including the articular surface, is invested by a stratum of fibrous tissue which will after the lapse of years be supplanted through function adaption by a permanent investment of fibrocartilage. The typical hyaline cartilage of a normal joint, however, is not restored.»

As seen, the results obtained in animal experiments were not in agreement. In one animal experiment formation of cartilaginous tissue was noted. In some experiments the interposition material was transformed into fibrotic tissue while a few among the workers saw extensive necrosis of the interposition material, concluding that it was only of secondary

importance in the development of the new joint. Clinical observations mainly revealed a concurrent trend. In a number of clinical cases cartilage of a fibrous or hyaline type formed in the weight-bearing area of the joint.

C. ON THE CLINICAL USE OF SKIN AS INTERPOSITION MATERIAL IN ARTHROPLASTIES

In the course of his attempts to develop a new biological method of arthroplasty KALLIO, in 1954, began to use an autogenous whole-thickness skin graft comprising fatty tissue as interposition material in arthroplasty. Before the clinical use of skin for this purpose, KIVILAAKSO had carried out at the instigation of KALLIO an experimental study on changes in the whole-thickness skin graft used as replacement of tissue defects (1955), which showed that when a whole-thickness skin graft is used, the organism destroys or isolates in it the tissue which is ectodermal in origin and transforms the tissue which has developed from the mesoderm into an organic part of itself.

The skin arthroplasty method when applied in the hip joint is characterized by the following features. »The operation is most conservative. The length of the femoral neck and head can be preserved and the operation need not weaken the mechanical strength of the bone, which renders it less liable to wear. Owing to the ideal plasticity of the skin it is also possible to preserve the shapes of the articular surfaces so that the original adaptation of the head in the acetabulum can be left as such, and in case the statics of the joint is correct, the result is a feeling of a natural joint in walking» (K.E.KALLIO 1955, 1956, 1957). Because of the plasticity of the skin, the method is easily adaptable for use in other joints. Since 1954 it has actually been used in 103 cases of arthroplasty in different joints while within the same time the number of alloplastic procedures applied at the Clinic is 118. As to the clinical results of skin arthroplasty, the follow-ups which were undertaken after observation periods of 2—1 years showed that the results achieved by skin arthroplasty compared not infavourably with those obtained by alloplastic methods (E. KALLIO 1958).

When KALLIO first began to use skin as interposition material in arthroplasties in 1954, he had not happened to meet any mention in the literature of the use of skin in arthroplasties nor had he personally seen such operative measures carried out. It was not until making a closer study of literature on the use of skin in reconstructive surgery that I found that even earlier, in some few cases, skin had been employed as interposion material in mobi-

lizing stiffened joints. Yet the method had not so far been put to any systematical use in clinical surgery.

The first written report I have met on the subject is from 1929, when LOEWE used de-epithelized skin between freshened bone surfaces in mobilizing stiffened joints. He describes a knee joint stiffened into a faulty position by rheumatism, in the mobilization of which he applied de-epithelized skin instead of fascia as interposition material, as well as two stiffened hip joints in which he carried out subtrochanteric osteotomy, inserting between the bone surfaces a pedicled de-epithelized skin strip. Loewe found skin a serviceable material for reconstructive surgery in all cases where fascia could be used. But although a number of arthroplasties were performed in the 1920'ies and 1930'ies, skin, quite likely because of fear of infection, did not find favour as interposition material. In other reconstructive surgery, e.g. in hernia operations, de-epithelized skin began to be widely used on the initiative of LOEWE and REHN (LOEWE 1913 and REHN 1914, 1919, 1931).

It is only after 1948 that the use of skin in arthroplasty is mentioned occasionally in the literature. PAIS made three arthroplasties for the mobilization of stiffened finger joints, applying free full-thickness skin flaps as interposition material. LOGROSCINO (1950) mobilized a hip joint stiffened by a fracture using as interposition material skin. BÄTZNER (1951) described seven and PASQUALI (1951) three cases of osteoarthritis of the hip joint, in which the remodelled femoral head was invested with a stratum of full-thickness skin.

FIUME (1952) and DELCHEF (1955) both reported on one case each of skin arthroplasty in the hip joint. LOEFFLER (1956) likewise mentions that he had used skin in arthroplasties, but neither describes the character nor gives the number of his operations. MCGRAW (1956) reported on four cases of cutis arthroplasty in the knee joint. The cases were under observation for 6—2 ½ years and the results were good. In one case a sample was later obtained for histological study from the non-weight-bearing area of the joint in connection with another operative measure, in which the interposition material was seen to have become transformed into a membrane resembling synovia. In conclusion it should be mentioned that SANCHIS-OLMOS (1954) used homoplastic skin obtained from a dead body and preserved in »Mertiolate», for repair of ligaments and as interposition material in arthroplasties.

D. EARLIER EXPERIMENTAL STUDIES ON THE USE OF SKIN AS INTERPOSITION MATERIAL IN ARTHROPLASTIES

In the literature I have been able to find only two investigations in which the fate of skin used as interposition material has been elucidated by means of animal experiments.

PEREGALLI (1951) carried out experiments in the elbow joint of the rabbit. He freshened the articular surfaces and invested the humeral head with a whole-thickness skin flap. The series consisted of 13 laboratory animals and the period of observation was from 7 to 150 days. The investigations revealed that the skin prevented proliferation of connective tissue and formation of adhesions in the new joint so that a joint with a clinical capacity of function was formed. The transplanted skin, still distinguishable as late as 100 days after the operation, merges with the granulation tissue which is subchondral in origin. The articular surfaces were covered by fibrous connective tissue which here and there showed characteristics of fibrocartilaginous tissular structure. PEREGALLI considered himself justified in excluding with certainty the possibility of the formation of hyaline-type cartilage in the new joint. The epidermal cells were on the way of disappearance. According to PEREGALLI, in animal experiments the skin proved an excellent interposition material for arthoplasties.

DE MARCHI and CAMBIER (1953) experimented on five dogs inserting whole-thickness skin between freshened articular surfaces in the knee joint. The period of observation was from the 15th to the 150th postoperative day. The vitality of the skin seemed good. As late as 100 days after the operation the graft was distinguishable. The transplanted skin assimilated with the originally subchondral granulation tissue and the articular surface was invested by continuous fibrous connective tissue. Even in this case no cartilaginous formation could be noted in the interposition material.

The authors also describe two clinical cases in which a sample was obtained from the knee in connection with another operative measure. In one of these a skin arthroplasty had been made 4 months and in the other 8 months earlier. The histological appearance was in agreement with the results obtained in the animal experiments, and these authors found skin a very suitable interposition material. The vitality of the skin exceeded that of other soft parts and the skin seemed effective in preventing the formation of adhesions in the new joint.

III. PROBLEMS

Growing interest, as we saw, has been manifested in recent years in the development of a biological method of arthroplasty. Skin has so far been used only tentatively, in some isolated cases, as interposition material. The explanation must perhaps be sought in the fact that the scientific background of these procedures has not yet been adequately elucidated by experimental work.

The purpose of the present study has been to provide an answer to the following questions:

— What is the macroscopic and x-ray picture presented by the skin arthroplasty joint?

— What is the fate of the epidermis of the full-thickness skin graft used as interposition material?

— Does functional metaplasia take place in the full-thickness skin graft used as interposition material?

— If metaplastic development takes place, what changes manifest themselves in the occurrence of metachromasia and P. A. S. positive material in the ground substance of the connective tissue in the course of the process?

— Are any changes brought out by historadiography in the distribution of the dry substance or mass of connective tissue during cartilaginous metaplasia?

— Is anything indicative of ossification of the interposition material demonstrable?

— What are the macroscopic, x-ray and microscopic pictures presented by the arthroplasty joint in cases without interposition material?

IV. MATERIAL AND OPERATIVE TECHNIQUE

Adult healthy cats were used for the experiments, during which they were kept in well-lighted spacious boxes, one animal in each. The animals were given adequate normal food. The series comprised 37 cats in all. A skin interposition arthroplasty was made in the hip joint of 30 cats. In nine of these cases partial or complete dislocation of the femoral head was noted in the operated joint at the end of the period of observation. In these cases the interposition material was only partly or not at all exposed to the pressure and function of the joint. These 9 cases were likewise included among the series because in them the importance of articular pressure and function to the development of the metaplasia was clearly revealed. Seven cats constituted a control series, subjected to the corresponding operation without interposition of skin. The length of the periods of observation and the number of the laboratory animals in the experimental and control series appear from Table 1.

In earlier animal experiments arthroplasties had been performed either in the knee or the elbow joint. Only MURPHY (1905) used the hip joint of the dog. In my preliminary experiments I found that the elbow and knee joints were poorly suited for arthroplastic studies: the animals when walking kept the joint operated upon in an almost stiff position so that it was exposed to only slight postoperative function. In this respect the hip joint proved much more serviceable.

I my preliminary animal experiments the operation was carried out by investing the head of the femur with skin. Because of the shortness of the cat's femoral neck, attachment of the skin cap round the caput proved difficult. When, on the other hand, the attachment was effected through holes bored in the femoral neck, blood supply often became disturbed in the caput and an aseptic necrosis of the bone followed. The operative technique was therefore modified in the animal experiments. One operation was carried out in the left hip joint of each of the animals. Preoperatively the animals were kept fasting for 6 hours. The operations were carried out under aether narcosis (MARCOWITZ 1949). In the operative area the fur was first cut with scissors and then shaved with a razor. The skin was then

TABLE 1.

Time in days	Number	
	Experimental Series	Control Series
7	1	—
10	1	—
15	1	—
20	1	—
25	1	—
30	1	1
35	—	1
40	1	1
50	2	—
60	2	1
70	2	—
75	1	—
80	1	—
85	1	—
90	4	1
100	1	—
105	1	—
110	1	—
115	1	—
120	1	1
130	1	—
150	1	1
180	2	—
240	1	—
Total	30	7

cleaned with a solution of alcohol and iodine. The operations were performed under aseptic conditions.

The experimental animal lying on its right side an incision was made over the left trochanter major which was exposed. The insertion of m. gluteus maximus was detached from the trochanter. The capsule of the hip joint was exposed and split (LEACH 1952). While the extremity was rotated forcefully outwards, the ligamentum teres was cut off and the femoral head was dislocated from the acetabulum. With a sharp scoop the articular cartilage was carefully removed from the acetabulum. The articular cartilage of the femoral head was left intact. A full-thickness skin graft with subcutaneous fatty tissue was cut off from an area in the animal's left flank from which the fur had been shaved. The skin graft with its fatty tissue was inserted in the acetabulum so that the epidermis faced the naked bone surface. The skin transplant was attached with a few silk sutures to the margins of the acetabulum and the femoral head was reduced.

A hole was drilled through the trochanter major of the femur and a firm silk thread was fastened through it subperiostally to the surface of the pelvis anteriorly of the acetabulum. This supportive thread presses the head against the bottom of the acetabulum preventing rotation of the femur and dislocation of the femoral caput. The supportive thread proved essential in preventing the postoperative dislocation of the femoral head. The gluteus maximus muscle was attached to its insertional place and the tissue was closed. The animals were given 200 000 units of procaine penicillin intramuscularly. The extremity was immobilized with tensoplast under the belly (OBEL 1949). The immobilization was removed 14 days after the operation and the animals were allowed to move freely.

V. METHODS OF INVESTIGATION

The experimental animals were sacrificed by deepening the aether narcosis down to exitus. The visual observations were made while the joint operated upon was being opened. The radiographic appearance of the operated joint was compared with that of the other hip joint. For histological studies the whole of the acetabulum of the joint was detached. On some of the animals in the series two tissue samples were obtained of the interposition material from the articular surface of the acetabulum, one of which was fixed in 10 % neutral formalin and the other in fresh 4 % lead acetate solution. These samples were used for histochemical and historadiographic studies.

The acetabulum was fixed in 10 % neutral formalin and decalcified in 5 % trichloro-acetic acid (ROMEIS 1948). The decalcified acetabulum was mounted in paraffin and specimens of 5μ thickness were made. The cross section was placed so as to pass through the weight-bearing area of the joint. The tissue samples were stained by the Weigert-van Gieson haematoxylin method (ROMEIS 1948).

Histochemical methods: In the present work, for examination of the ground substance of the connective tissue, toluidine blue metachromasia staining and the periodic-acid-Schiff (P.A.S.) oxidation method were used.

The toluidine blue staining was carried out according to Bunting: After being fixed in 4 % basic lead acetate the tissue was stained by toluidine blue in an aqueous 0.05 % solution at pH 4.5—5.0 for 20 hours. The sections were then agitated successively for 4 seconds each in solutions of 95 % and absolute ethyl alcohols, placed directly in xylol and mounted in paraffin.

The exposure to alcohol almost constantly converts to the blue or orthochromatic colour any purple or dimerized dye from the staining solution, which may simply be retained in the tissue section, without materially altering the dye that has combined with and been polymerized by such substances as the acid mucopolysaccharides (BUNTING 1950).

The hyalurodinases decompose acid mucopolysaccharides. In the present study toluidine blue staining was also carried out on specimens which had

first been treated with testicular hyaluronidase (RONDASE, Evans Medical Supplies Ltd, 18 mg/100 cc phosphate buffer at pH 6.5). The tissue samples were kept in a thermostate at 37° C for 18 hours (LILLIE 1954). The control series was treated in the same way but without any enzyme, and the specimens were stained together with those treated with an enzyme.

A series of tissue samples were treated similarly with testicular hyaluronidase before the P.A.S. staining, with the purpose of ascertaining whether the P.A.S. positive material in the ground substance was resistent to hyaluronidase.

The periodic-acid-Shiff (P.A.S.) staining was carried out according to MCMANUS (1948). The results were checked in two ways. If the periodic acid oxidation was omitted, no recolouring of reduced fuchsin by tissue aldehydes occurred. The colour reaction obtained with the Schiff reagent after periodic acid oxidation disappeared in 0.1 N NaOH and was restored with 0.1 N HCl (OSTER 1944).

Because glycogen produces a P. A. S. positive reaction, a series of samples was treated with a malt diastase enzyme (Nutritional Biochemicals Co.) before staining with P.A.S. The samples were treated for 18 hours in a phosphate buffer solution at pH 6.5, containing 0.5 % malt diastase enzyme, at 37° C. The control series was treated similarly, without any enzyme.

To bring out possible areas of ossification in the connective tissue undergoing metaplasia, the specimens obtained from tissue samples fixed in 10 % neutral formalin were stained with von Kossa's silver staining (LILLIE 1954).

Historadiography: Microradiography, as is known, is a procedure in which an absorption X-ray picture on the scale 1: 1 is obtained of the sample under examination, and then magnified under the microscope. If the substances under examination contain biological material, the method is usually called historadiography and the picture a historadiogram (ENGSTRÖM 1955). Historadiographical studies were made of tissue samples, 5μ thick, obtained from connective tissue undergoing metaplasia on the articular surface of the acetabulum.

The historadiograms were taken either by the method developed by LINDSTRÖM (1955), with exposure values at 3 kV, 35mA and the exposure time at 4 min., or the historadiography was carried out with the midget x-ray tube developed by ENGSTRÖM and LUNDBERG (1957). In this case 1.2 kV tension, a 2 mA anode current and a 20 min. exposure were applied (Fig. 1).

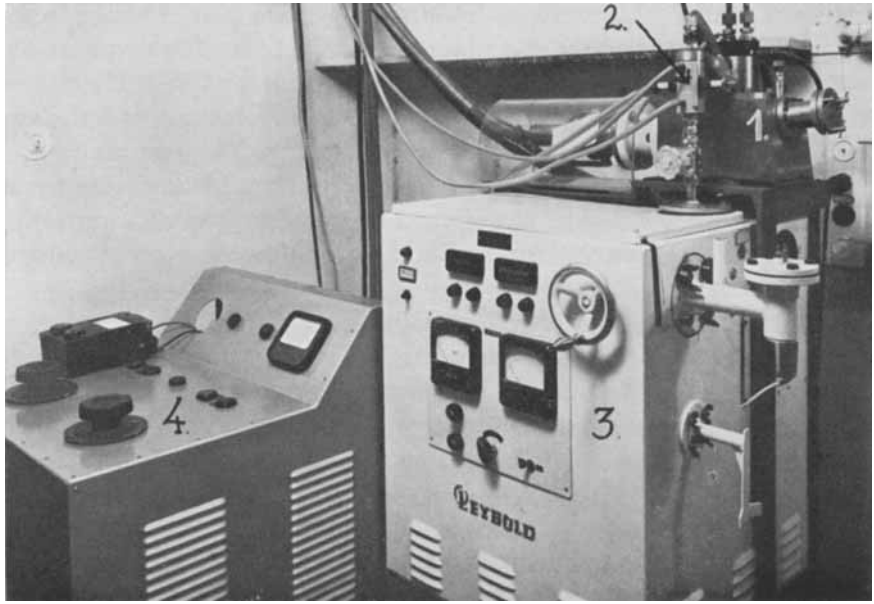

Fig. 1. Photograph of the roentgen tubes (1 and 2), the vacuum system (3), and the high voltage supply (4) used in the historadiographic studies.

VI. ARTHROPLASTY WITHOUT INTERPOSITION MATERIAL—CONTROL SERIES

A. EARLIER STUDIES

Side by side with soft-part interposition arthroplasty, mobilization operations were carried out without interposition material in the first half of the present century (SCHMERTZ 1916, 1919, SCHEPELMAN 1917). The development of the new joint was also elucidated, in cases without application of interposition material, by means of some few animal experiments and clinical observations. ALLISON and BROOKS (1913) and PHEMISTER and MILLER (1918) made animal experiments using soft-part interposition in the knee joint of dogs. They also operated on a control series performing arthroplasties without interposition in the knee joint of dogs. They found in the controls that new connective tissue grew from the freshened bony surface in the absence of articular weight. A naked bone surface formed in the weight-bearing area of the joint. Because in their experiments the interposition material largely necrosed, the authors believed that the interposition substance was of secondary importance in the development of the new joint: the granulation tissue growing from the freshened bony surface was more important. The results obtained by HOHMEIER (1914) in his investigation tallied with this. SCHMERTZ (1916, 1919) both carried out animal experiments and made clinical observations of operations in which no interposition material had been used. From the joint surface grew granulation tissue which filled in irregularities present. But the new connective tissue was not strong enough to carry the weight of the joint, and histologically the joint surface was partly naked bone, partly connective tissue. The latter revealed signs of cartilaginous regeneration. KROMPECHER (1938, 1947, 1956) studied physical factors affecting the development of the cartilage and the joint. He removed the cartilage from the knee joint of the rabbit and noted in the granulation tissue growing from the freshened articular surface formation of cartilage which was due to articular weight and function. Yet, in case of heavy and too early loading, the new connective tissue becomes destroyed.

As is seen from the foregoing, it has been possible to prove in animal experiments and clinical studies that the granulation tissue growing from

the freshened bone surface promotes the development of a new joint and that articular loading may give rise to formation of cartilage in the granulation tissue. Yet the granulation tissue is capable of carrying only slight articular loading and tends to degeneration in the weight-bearing area of the joint. In these cases the articular surface mainly consists of naked bone surface.

B. AUTHOR'S INVESTIGATIONS

1. MACROSCOPIC AND ROENTGENOGRAPHIC OBSERVATIONS

In the controls as well as in the experimental series later the visual observations were made at the opening of the joint. Here attention was paid to the passive mobility of the joint, the formation of the articular capsule and the articular fluid, and the character of the joint surface.

For a complete roentgenologic picture, roentgenograms were taken in both the control and the experimental series of the hip joints of the experimental animals. In the roentgenograms notice was paid to the formation of the articular space in the operated joint as compared with the non-operated one and to the possible presence of osteophytes. The macroscopical and x-ray findings in the control series are shown in Table 2.

In the control series the passive mobility of the joint operated upon was found to be good in all except two cases in which, when the joint was moved, crepitation could be felt at the point of the joint. After a month's period of observation the development of the articular capsule was completed. The joint fluid appeared at the beginning of the second month of observation. In 4 cases the amount of the joint fluid was pathological so that abundant hydrops was revealed when the joint was opened. In one joint a strong adhesion was present between the remnant of ligamentum teres and the surface of the acetabulum. Macroscopically the joint surface consisted of a bare partly uneven bone surface. In two laboratory animals connective tissue was seen on the surface of the acetabulum. In one of these cases, 40 days after the operation, the tissue had the appearance of connective tissue, while in the other, on the 120th postoperative day, the tissue resembled cartilage. In both cases the tissue was in the bottom part of the acetabulum, where it was not exposed to any considerable loading.

In roentgenograms of the control series the joint space in the operated joint was clearly narrowed in five cases. In two the joint space had disappeared in parts. In one experimental animal clear osteophytic formation was seen in the margin of the acetabulum (Figs 2, 3 and 4).

TABLE 2.

Macroscopical Findings							X-ray Findings	
No	Time	Passive Mobility	Joint Capsule	Joint Fluid	Adhe-sions	Joint Surface	Joint Space	Osteophytes
1	30	Good	Formed	None	None	Naked bone surface	Almost completely disappeared	None
2	35	Good	Formed	Yes	None	Naked bone surface	Narrowed	None
3	40	Good	Formed	Hydrops	None	Mainly naked bone surface, at the bottom of acetabulum an area with connective tissue	Narrowed	None
4	60	Crepitation	Formed	Hydrops	None	Naked bone surface	Partly disappeared	Osteophytes on the margin of acetabulum
5	90	Good	Formed	Hydrops	None	Naked bone surface	Narrowed	None
6	120	Good	Formed	Yes	Yes	Mainly naked bone surface, at the bottom of acetabulum an area with cartilaginous tissue	Narrowed	None
7	150	Crepitation	Formed	Hydrops	None	Naked bone surface	Narrowed	None

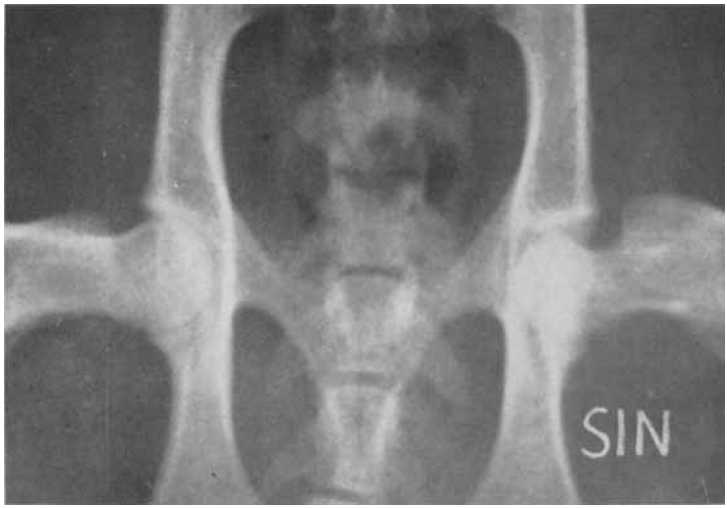

Fig. 2. Control series. 40 days from the operation. The articular space in the left joint operated upon has narrowed in comparison with the non-operated side.

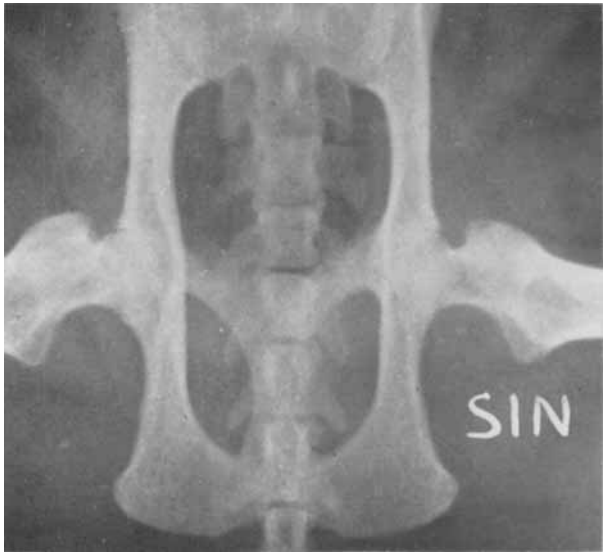

Fig. 3. Control series. 150 days from the operation. In the left operated joint the articular space has narrowed compared with the non-operated side.

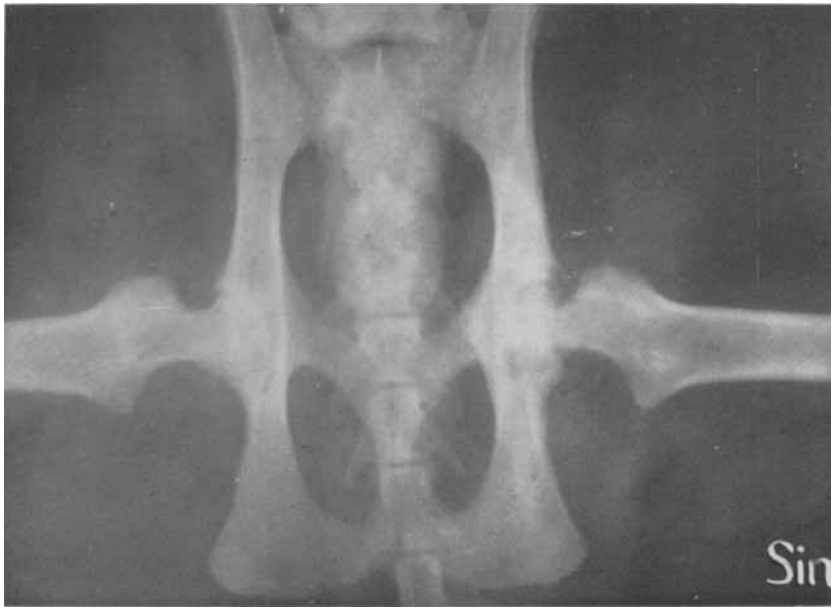

Fig. 4. Control series. 60 days from the operation. The articular space has narrowed and partly disappeared in the operated joint. Osteophytes in the margin of the acetabulum.

2. MICROSCOPIC FINDINGS

In the control series the joint surface of the acetabulum mainly consisted of naked bone surface (Fig. 5). In the hollows formed in the bone surface in connection with the removal of the joint cartilage of the acetabulum, new connective tissue growing from the freshened bony surface could be seen; it partly filled in the irregularities in the joint surface. Connective tissue occurred in places which were out of the range of the pressure effect of the femoral head (Fig. 6). Yet the amount of connective tissue was so small that no extensive continuous tissue layer substituting the articular cartilage was observable on the surface of the acetabulum.

During the two first months of observation no signs of cartilaginous metaplasia were visible in the new connective tissue. Towards the end of the third month beginnings of this process were seen in the islets of connective tissue on the surface of the acetabulum. However, cartilage which had undergone metaplasia, either fibrous or hyaline in type, occurred only in the form of small islets in irregularities of the joint surface and formed no extensive continuous cartilaginous layer on the surface of the new joint (Fig. 7).

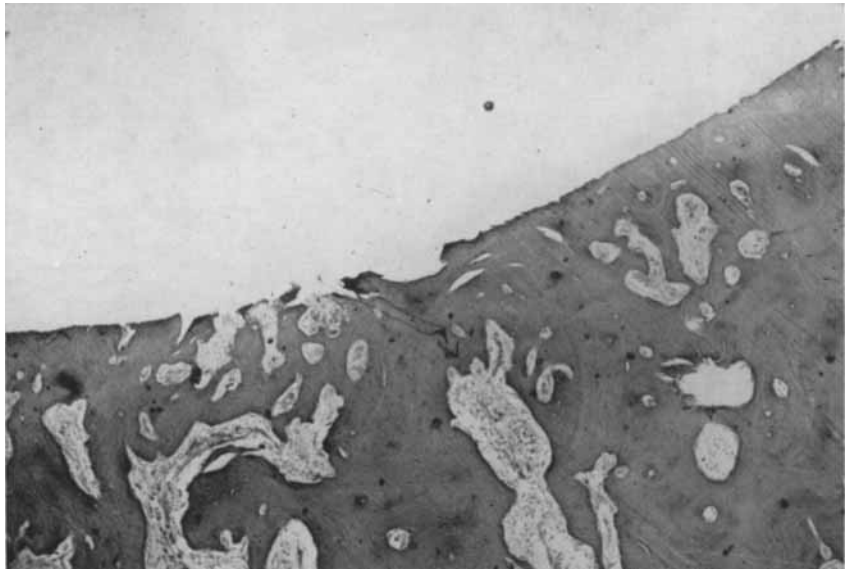

Fig. 5. 150 days from the operation. In the control series the articular surface mainly consisted of a naked partly uneven bone surface. Weigert-van Gieson staining. × 20

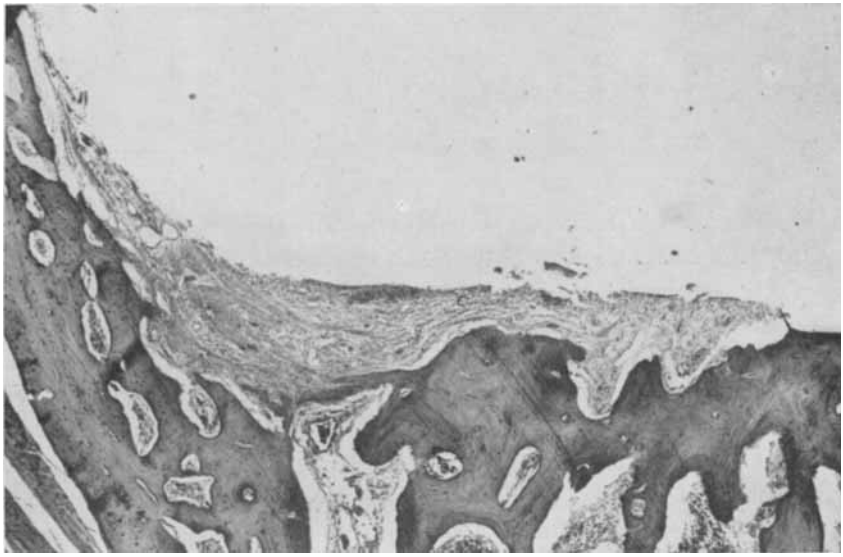

Fig. 6. 35 days from the operation. A thin layer of granulation tissue fills the hollow formed in connection with the removal of the joint cartilage in the bony surface, which was partly out of the range of the loading effect of the femoral head. Weigert-van Gieson staining. × 20.

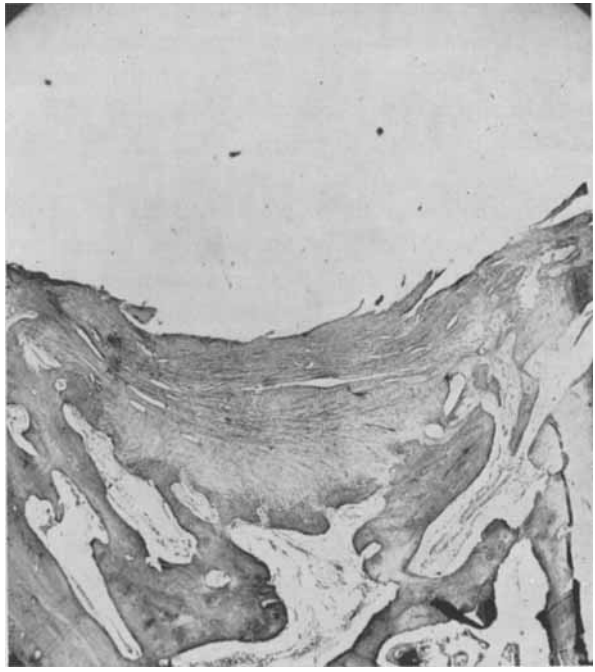

Fig. 7. Control series. 90 days from the operation. Islet of connective tissue persisting in the hollow formed in the articular surface at the removal of the articular cartilage. Incipient cartilaginous metaplasia in the part of connective tissue closest to the bone surface. Weigert-van Gieson staining. × 20.

VII. MACROSCOPIC AND ROENTGENOLOGIC OBSERVATIONS OF THE SKIN ARTHROPLASTY JOINT

The macroscopic observations were made with the unaided eye in connection with the opening of the joint. Notice was paid to the following points: What is the passive mobility of the operated joint like? At what stage do the joint capsule and the joint fluid develop? Do intra-articular adhesions occur? Is the interposition material distinguishable and what kind of appearance does the joint surface present? The macroscopic observations are seen in Table 3. The nine cases in which the femoral head had become dislocated after the operation, either completely or partly, were not entered in the table. In one case, likewise omitted from the series, intra-articular infection was noted.

For studies of the x-ray appearance of the skin arthroplasty joint x-ray films were taken of those hip joints of the experimental animals which were under observation for more than 20 days. In the analysis of the x-rays notice was paid to the joint space compared with that of the non-operated side and to possible osteophytic formation. The x-ray findings are shown in Table 3.

As we see from the Table, the passive mobility of the operated joint was good in all the cases. The joint capsule had formed within about 3 weeks and macroscopically normal joint fluid was seen towards the end of the first month of observation. Intra-articular adhesions did not occur in any of the cases. During the first month of observation and at the beginning of the second the skin transplant was clearly distinguishable in the joint surface. Towards the end of the second month of observation the interposition material was developing into tissue resembling fascia to the naked eye. At the beginning of the third month of observation the joint surface was covered by a layer of tissue resembling cartilage macroscopically. In two cases the graft was seen to have disappeared partly in the weight-bearing area of the joint, in the margin of the acetabulum, where the articular surface consisted of naked bony surface.

X-rays revealed that in 11 of the cases the joint space of the operated joint had been well preserved compared with the non-operated side (Figs

TABLE 3.

Macroscopical Findings							X-ray Findings	
No.	Time	Passive Mobility	Joint Capsule	Joint Fluid	Adhe-sions	Joint Surface	Joint Space	Osteophytes
1	7	Good	None	None	None	Graft covers joint surface	—	—
2	10	Good	None	None	None	Graft covers joint surface	—	—
3	15	Good	None	None	None	Graft covers joint surface	—	—
4	20	Good	Formed	None	None	Graft covers joint surface, interposition material has partly disappeared from the weight-bearing area of the joint	Narrowed	None
5	25	Good	Formed	Yes	None	Graft covers joint surface	Good	None
6	30	Good	Formed	Yes	None	Graft covers joint surface	Narrowed	None
7	40	Good	Formed	Yes	None	Graft covers joint surface, interposition material has partly disappeared from the weight-bearing area of the joint	Narrowed	None
8	50	Good	Formed	Yes	None	Joint surface covered by tissue resembling fascia	Good	None
9	60	Good	Formed	Yes	None	Joint surface covered by tissue resembling fascia	Narrowed	None
10	70	Good	Formed	Yes	None	Joint surface shiny, covered by tissue resembling cartilage	Good	None
11	75	Good	Formed	Yes	None	Joint surface shiny, covered by tissue resembling cartilage	Good	None
12	90	Good	Formed	Yes	None	Tissue resembling cartilage in the weight-bearing area of the joint, elsewhere the graft distinguishable	Good	None
13	90	Good	Formed	Yes	None	Joint surface shiny, covered by tissue resembling cartilage	Good	None
14	105	Good	Formed	Yes	None	Joint surface covered by thin cartilaginous layer	Narrowed	None
15	110	Good	Formed	Yes	None	Joint surface covered by thin cartilaginous layer	Narrowed	None
16	120	Good	Formed	Yes	None	Joint surface covered by thin cartilaginous layer	Good	None
17	130	Good	Formed	Yes	None	Joint surface covered by thin cartilaginous layer	Good	None
18	150	Good	Formed	Yes	None	Joint surface covered by thin cartilaginous layer	Good	None
19	180	Good	Formed	Yes	None	Joint surface covered by thin cartilaginous layer	Narrowed	None
20	180	Good	Formed	Yes	None	Joint surface covered by thin cartilaginous layer	Good	None
21	240	Good	Formed	Yes	None	Joint surface covered by thin cartilaginous layer	Good	None

8—9) while in the 7 other cases the joint space had clearly narrowed in comparison with the non-operated side (Fig. 10). No osteophytic process was noted in any of the operated joints in the experimental series.

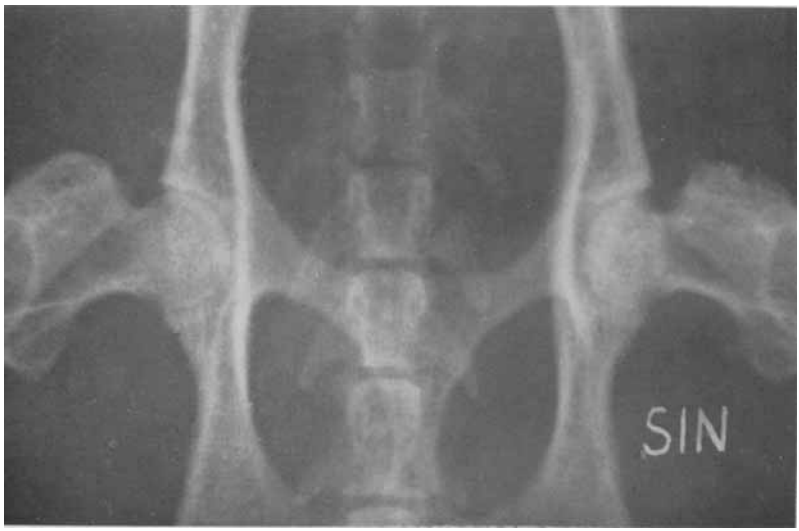

Fig. 8. 240 days from the operation. The articular space of the operated joint (sin) has persisted well compared with the non-operated side.

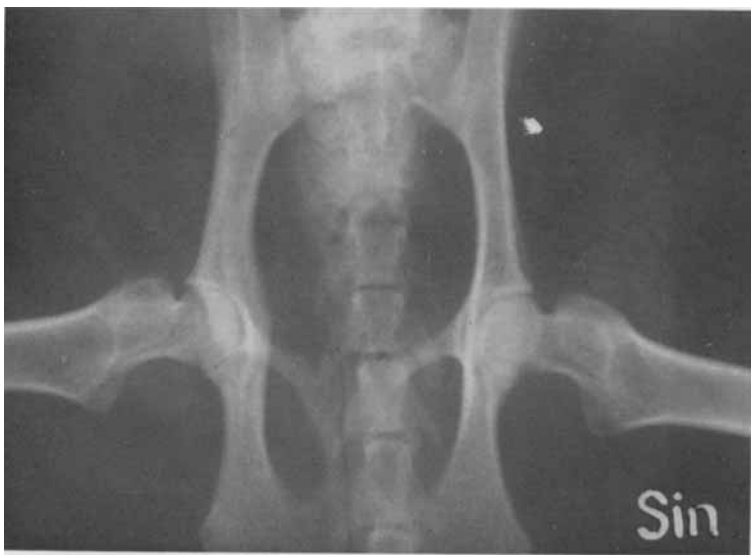

Fig. 9. 120 days from the operation. Left side has been operated upon. The articular space has persisted well compared with the non-operated side.

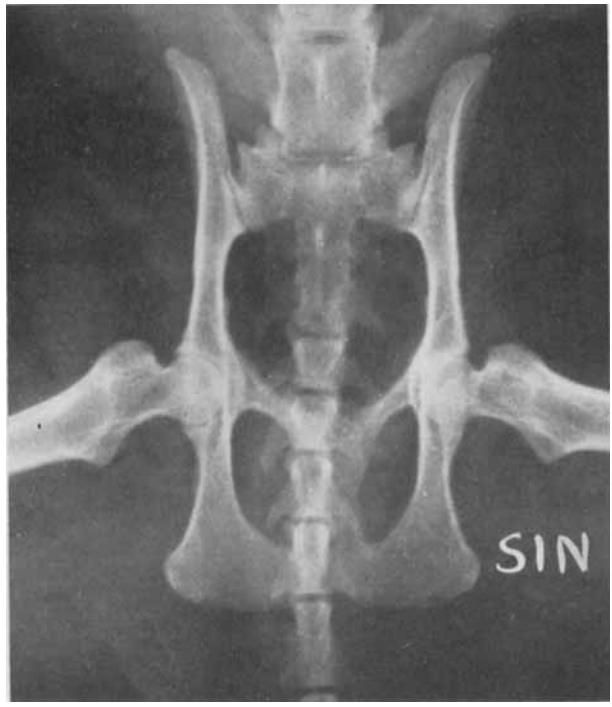

Fig. 10. 105 days from the operation. A case in which the joint space of the operated joint (sin) has narrowed compared with the non-operated side.

VIII. MICROSCOPIC OBSERVATIONS OF THE SKIN ARTHROPLASTY JOINT

1. FATE OF THE EPIDERMIS

During the first two weeks of observation islets of epidermis with signs of necrosis of the epidermal cells were revealed in the granulation tissue which had formed between the skin graft and the bone surface of the acetabulum. In the same areas accumulations of inflammatory cells and formation of giant cells could be seen. The epidermal cells had been preserved best in the neighbourhood of the root sheaths of hairs (Fig. 11).

During the third and fourth weeks of observation the epidermal cells necrosed in the area of the joint and were supplanted by accumulations of

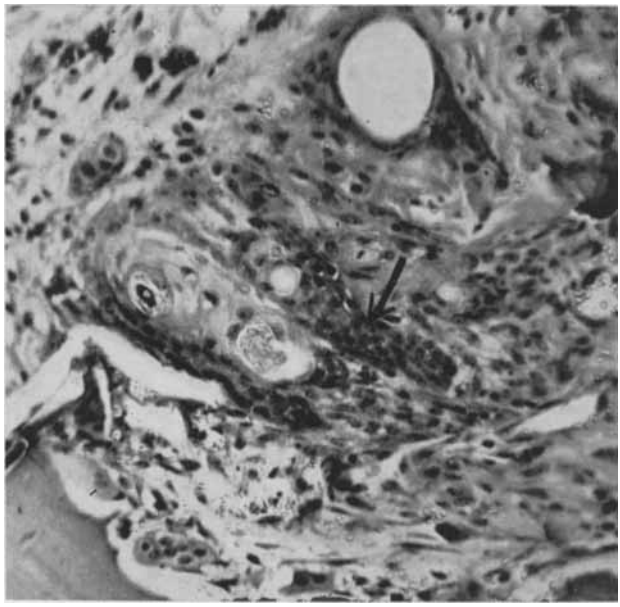

Fig. 11. 10 days from the operation. Islets of epidermal cells (arrow) surrounded by granulation tissue. Close by transverse section of a hair sheath. Some of the epidermal cell nuclei stain poorly and exhibit signs of degeneration. — Weigert-van Gieson staining. × 160.

inflammatory cells. In the periphery of the joint, where the skin is not subject to pressure from the joint, better preserved islets of epidermal cells are seen, and a small epidermal cyst here and there (Fig. 12). After a month's observation epidermal cells usually no longer occur. The accumulations of inflammatory cells likewise disappear and are replaced by new connective tissue (Fig. 13). No epidermal cysts are present in the area of the joint. Remnants of skin hairs and colour pigment still occur in the converted connective tissue even after some months.

In cases in which the head of the femur was dislocated postoperatively so that the skin had not been subjected to articular loading, the epidermal cells had been preserved markedly longer and had here and there developed epidermal cysts. Most of the epidermal cells had however disappeared even in these cases and had been replaced by inflammatory cells.

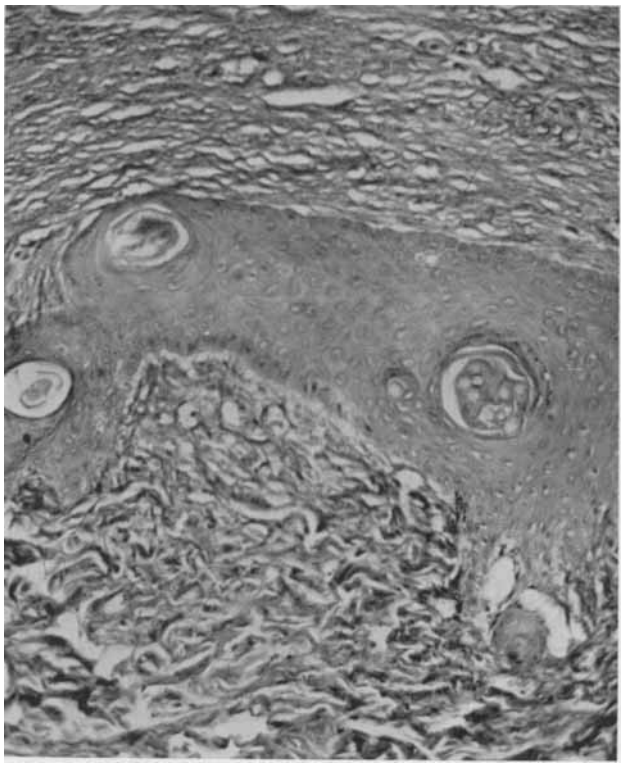

Fig. 12. 50 days from the operation. The Fig. shows the periphery of the joint in which the articular loading has not been fully effective. Islet of epidermal cells has persisted and formed small epitheliat cysts. Weigert-van Gieson staining. x 100.

It may therefore be established that the epidermis of the full-thickness skin graft used as interposition material in arthroplasty becomes destroyed through articular weight and function and no epithelial cysts form.

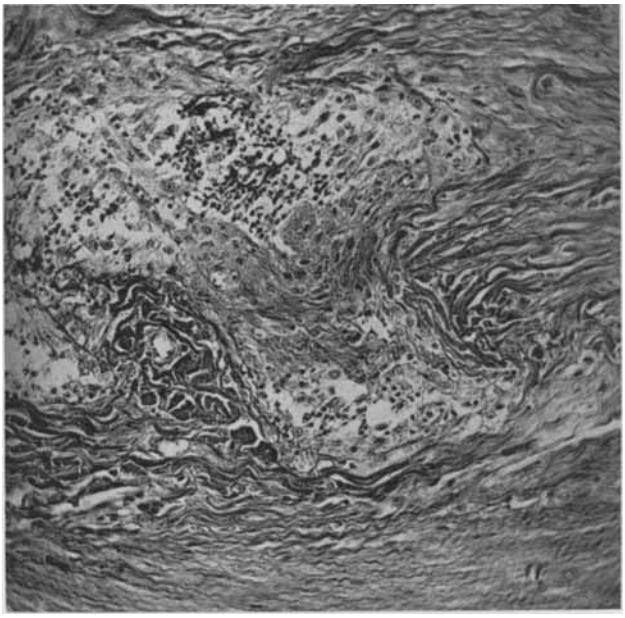

Fig. 13. 30 days from the operation. Islet of degenerating epidermal cells surrounded by connective tissue, partly replaced by inflammatory cells and a partially new connective tissue. Weigert-van Gieson staining. × 120.

2. CHANGES IN CONNECTIVE TISSUE AND IN SUBCUTANEOUS FATTY TISSUE

At 7—14 Days from the Operation

A stratum of granulation tissue with abundant vascularity forms between the skin graft and the freshened bone surface of the acetabulum, penetrating between the bunches of collagen in the connective tissue of the skin and attaching the transplanted skin to its base (Fig. 14). In the area of the islets of degenerating epidermal cells accumulations of inflammatory cells and formation of giant cells is seen. Osteoclasts are revealed in the bony surface of the acetabulum. On the whole no necrosis is present in the cutis and subcutaneous fatty tissue of the graft (Fig. 15).

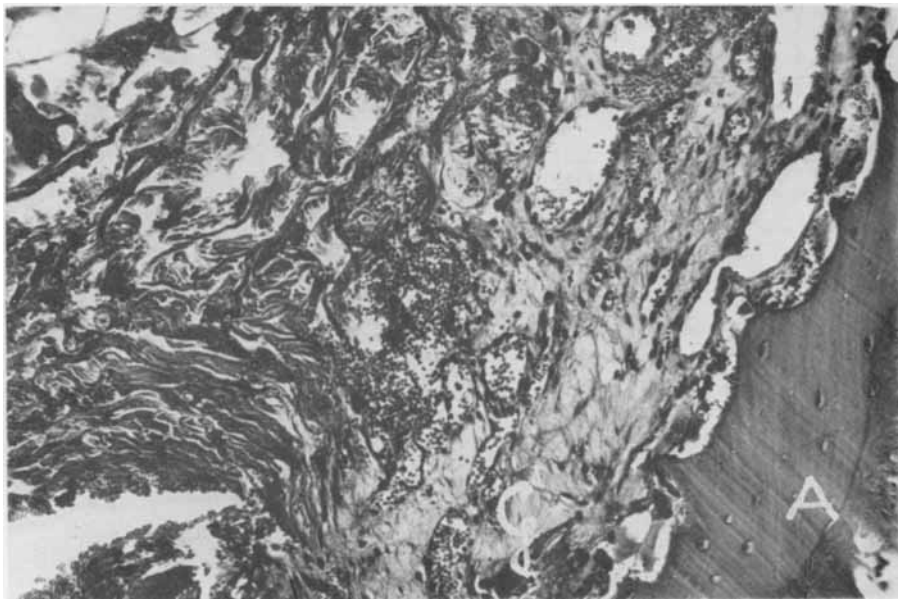

Fig. 14. 10 days from the operation. Well vascularized granulation tissue (G) between the surface of the acetabulum (A) and the skin graft. On the left the graft. Weigert-van Gieson staining. × 120.

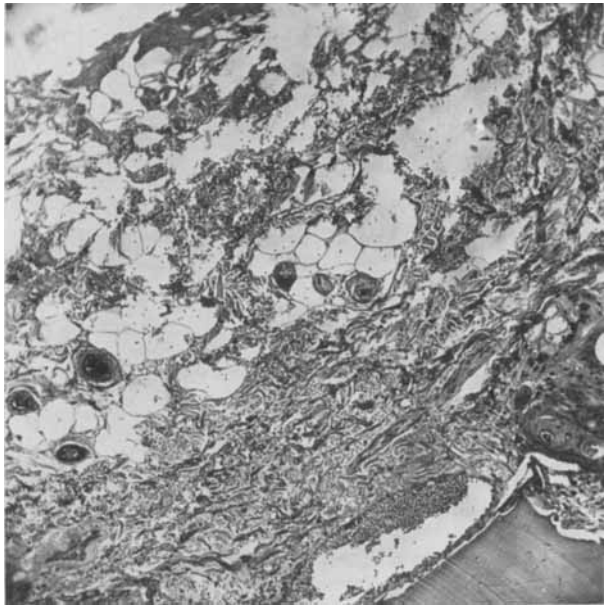

Fig. 15. 10 days from the operation. On the left above subcutaneous fatty tissue in which the fatty cells have remained unchanged. On the right below connective tissue of the transplanted skin and the acetabulum. Weigert-van Gieson staining. × 100.

At 15—30 Days

The fibrils of the granulation tissue become stronger and partly line up parallel with the outline of the joint surface (Fig. 16). Even the cutis of the skin graft here and there reveals signs of collagenous fibrils rearranging themselves so as to follow the same direction. The margin between the granulation tissue and the skin graft becomes diffuse and in places new connective tissue is seen to grow into the cutaneous connective tissue. The subcutaneous fatty tissue degenerates and is substituted by new connective tissue. No epitheloid or giant cell formation could be noted in the preparations. The joint surface begins to take shape (Fig. 17).

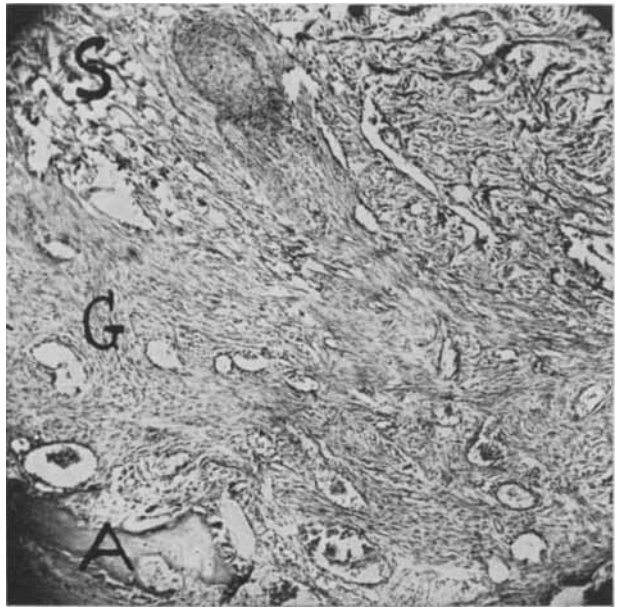

Fig. 16. 20 days from the operation. Below is seen some bony surface of the acetabulum (A), in the centre granulation tissue (G) and above part of the skin graft (S). The border between the graft and the granulation tissue has become more diffuse. The fibrils of the well vascularized granulation tissue have lined up partly parallel with the bone surface of the acetabulum. Weigert-van Gieson staining. × 100.

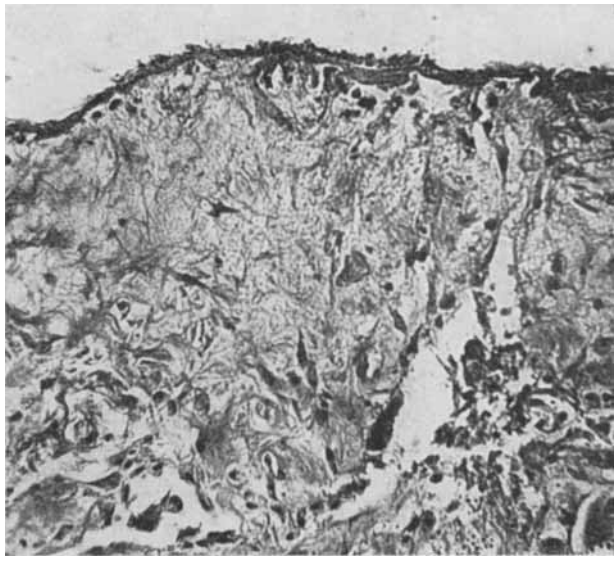

Fig. 17. 20 days from the operation. The cells of the subcutaneous fatty tissue are degenerating and being replaced by new connective tissue. In the centre degenerating fatty cells, foam cells. Below new connective tissue. Weigert-van Gieson staining. x160.

At 30—60 Days

During the second month of observation the orientation of the fibrillary structure of the connective tissue so as to follow the outline of the joint surface is brought out clearly both in the area of the cutis and that of the granulation tissue (Figs. 18—19). The reorganization of the fibrils begins and preponderates in the weight-bearing area of the joint. Abundant vascularity is seen in the new connective tissue and the cutaneous connective tissue. The accumulations of inflammatory cells have disappeared and have been replaced by new connective tissue. Towards the end of the second month of observation increase of the homogenous ground substance and breaking up of collagen bundles is revealed in the connective tissue nearest to the articular surface, in the weight-bearing area of the joint (Fig. 20).

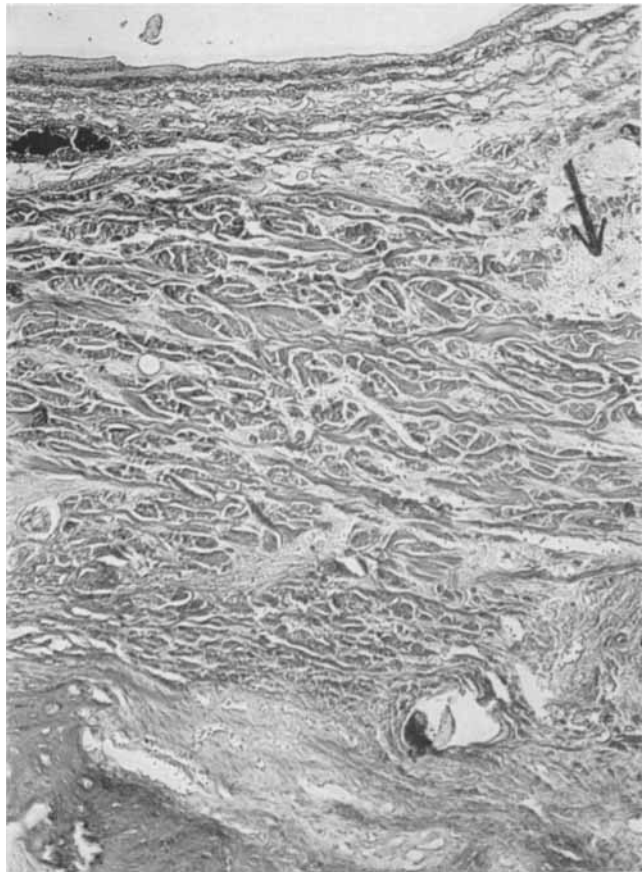

Fig. 18. 50 days from the operation. The connective tissue of the skin graft has been converted into dense fibrous connective tissue the fibrils of which have lined up parallel with the articular surface. Between the collagenous bundles here and there new connective tissue (arrow) which has replaced accumulations of inflammatory cells. The articular surface is seen above. Weigert-van Gieson staining. × 60.

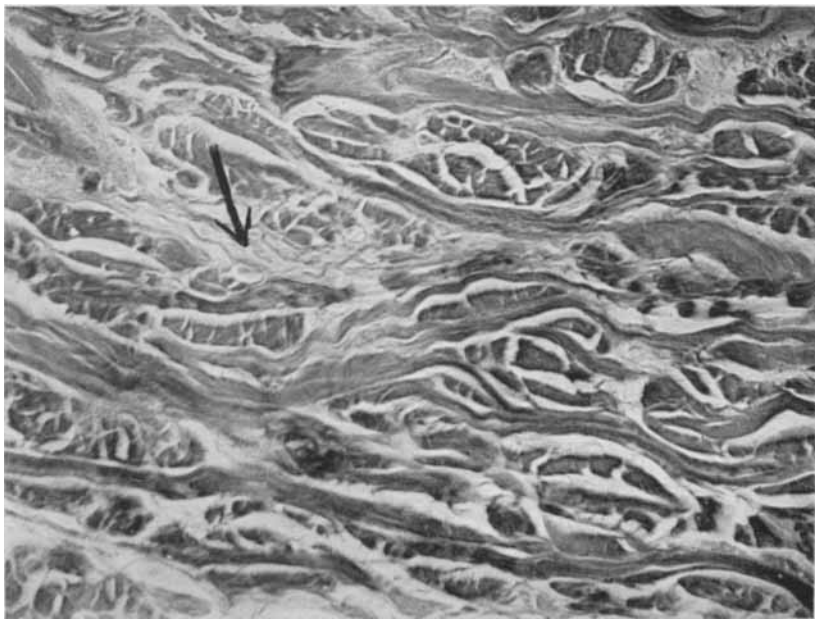

Fig. 19. Same specimen as in Fig. 18. Connective tissue of the cutis by larger magnification. The reorganization of the collagsnous fibres of the connective tissue so as to run parallel with the articular surface is brought out clearly. New connective tissue (arrow) is seen here and there between the collagenous bundles. Weigert-van Gieson staining. × 200.

Fig. 20. 50 days from the operation. Joint surface from the weight-bearing area of the joint. The collagenous bundles have broken up into thin undulating fibrils. The homogenous ground substance of the connective tissue has increased. Weigert-van Gieson staining. × 150.

At 60—90 Days

In the course of the third month of observation clear cartilaginous metaplasia is observable in the connective tissue. In the first phase of the conversion the homogeneous ground substance of the connective tissue increases. Strong bundles of collagen push farther away from each other and break up into thin undulating fibrils which seem to disappear into the ground substance. At the same time an abundance of cells microscopically resembling slightly differentiated connective tissue cells appear in the ground substance. These cells are especially frequent in the close vicinity of the joint surface. Slightly differentiated cells of the same type occur here and there around the capillaries of the connective tissue undergoing metaplasia (Figs 21 and 22). Along with an increase of the ground sub-

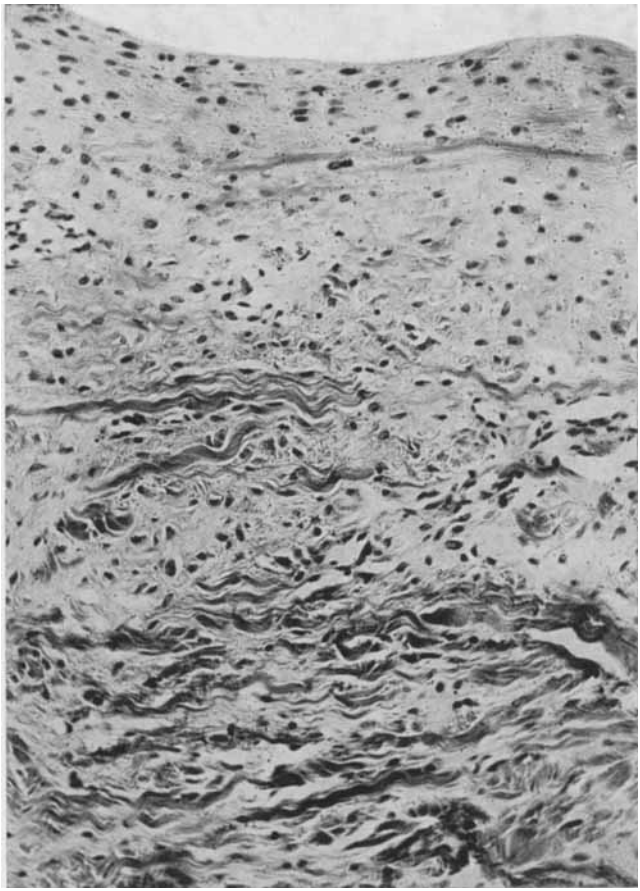

Fig. 21. 75 days from the operation. The homogenous ground substance of the connective tissue has increased. The collagen bundles are pushing apart from each other and breaking up into thin undulating fibrils. Closer to the articular surface the ground substance has increased more and the connective tissue fibrils have disappeared almost completely. An abundance of slightly differentiated connective tissue cells are seen in the ground substance of the connective tissue, likewise around the capillaries of this tissue. The articular surface is above. Weigert-van Gieson staining. × 120.

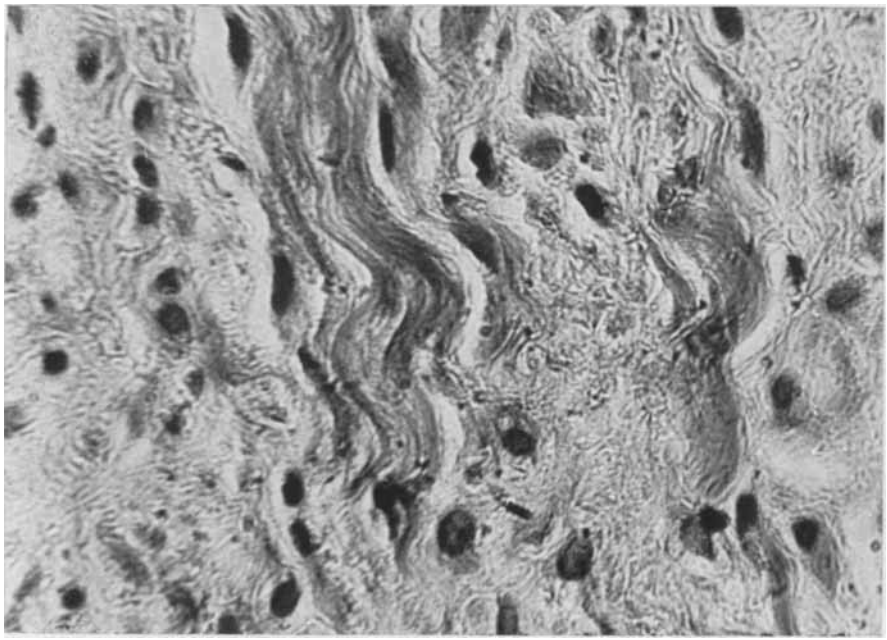

Fig. 22. Same specimen as in Fig. 21. Connective tissue undergoing metaplasia, by larger magnification. Between collagenous bundles which have broken up into undulating fibrils an increased amount of ground substance containing an abundance of slightly differentiated connective tissue cells. Weigert-van Gieson staining. × 600.

stance of the connective tissue a lacunar formation characteristic of chondrocytes is seen round the new cells. Microscopically the connective tissue cells have thus developed into cartilage cells (Figs. 23—24). First these cells occur in the ground substance as isolated cells, but with further development of the metaplasia groups of some cartilaginous cells are formed. The metaplastic changes first appear in the weight-bearing area of the joint. The process begins in the joint surface and / or from the direction of the new connective tissue which has developed between the skin graft and the surface of the acetabulum (Fig. 25). Along with the increase of the metaplasia the vascularity of the connective tissue decreases.

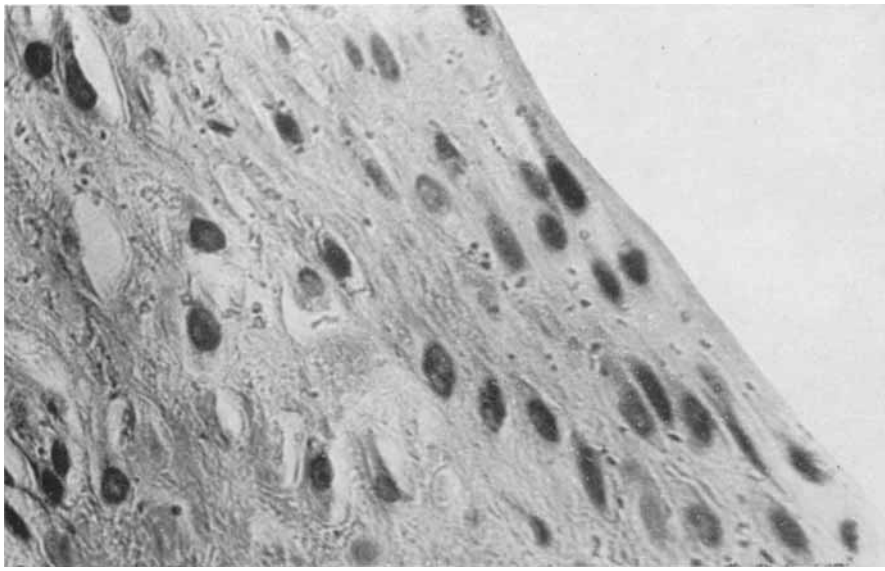

Fig. 23. Same specimen as in Fig. 21. Articular surface by larger magnification. The ground substance is homogenous and the connective tissue fibrils have disappeared almost completely. An abundance of slightly differentiated connective tissue cells in the ground substance. Incipient lacunar formation characteristic of chondrocytes is seen around some of the cells. Weigert-van Gieson staining. × 600.

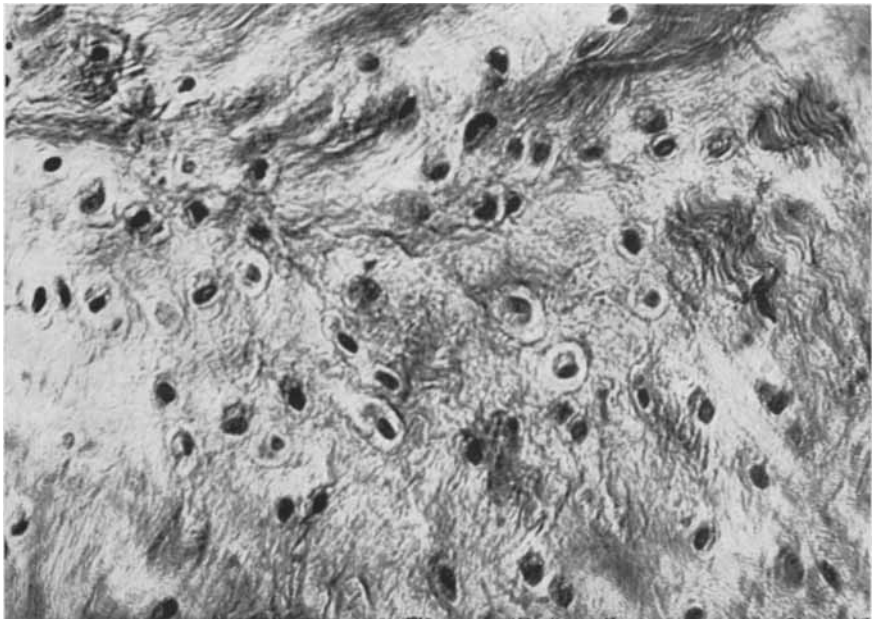

Fig. 24. 80 days from the operation. Connective tissue undergoing metaplasia. The collagenous bundles have broken up into thin undulating fibrils. In the ground substance slightly differentiated connective tissue cells, some of which have been transformed so as to have the appearance of cartilage cells. Weigert-van Gieson staining. × 270.

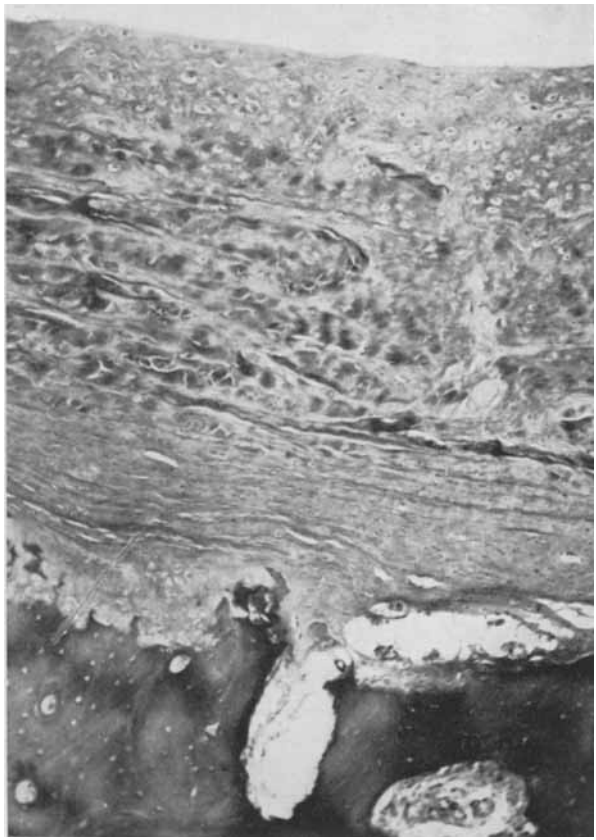

Fig. 25. 70 days from the operation. Cartilaginous metaplasia beginning from the direction of the articular surface. Higher up in the Fig. articular surface and new metaplastic cartilage. The connective tissue nearer to the bony surface of the acetabulum is dense tendon-like tissue, so far manifesting no signs of a metaplastic process. Lower down in the Fig. acetabulum. Weigert-van Gieson staining. × 80.

At 90—240 Days

After the third month of observation metaplastic cartilage occurs in all the specimens. The metaplastic process is particularly evident in the weight-bearing area of the joint. The converted cartilage is partly fibrillary with fibrils in the ground substance (Fig. 26). In places the cartilage has the appearance of hyaline cartilage while the ground substance is more homogeneous (Figs. 27—28), yet not of as complete homogeneity as normal joint cartilage. The cartilage cells nearer the joint surface are usually flattened along the outline of this surface.

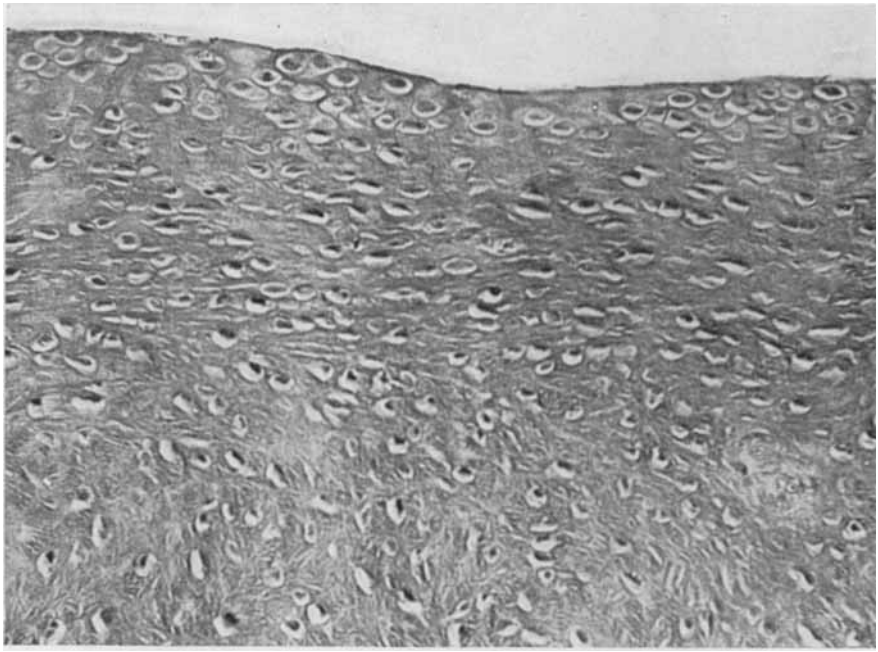

Fig. 26. 115 days from the operation. New metaplastic fibrous cartilage. Nearer to the articular surface the cartilage cells are flattened along its outline. Above in the Fig. articular surface. Weigert-van Gieson staining. × 120.

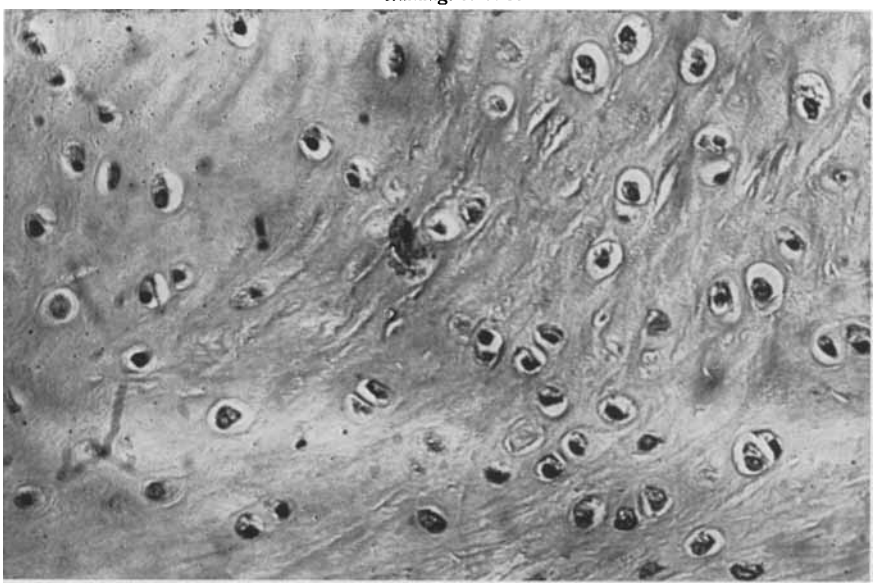

Fig. 27. 110 days from the operation. Metaplastic cartilage of hyaline type. Weigert-van Gieson staining. × 270.

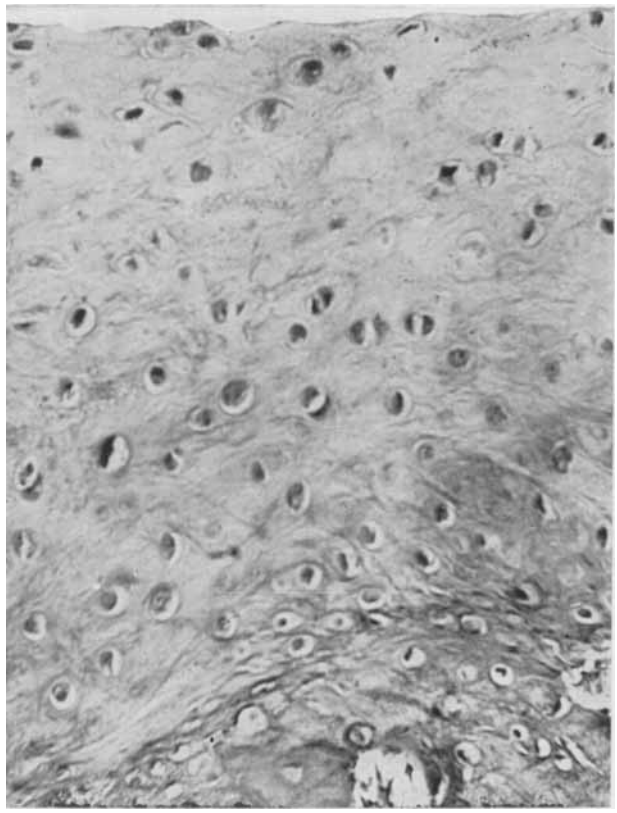

Fig. 28. 115 days from the operation. Metaplastic hyaline cartilage. Articular surface above, acetabulum below. Weigert-van Gieson staining. × 200.

In the non-weight-bearing area of the joint the cartilaginous metaplasia is slighter or the connective tissue there is dense and fibrous. The connective tissue undergoing metaplasia is vascularised while no blood vessels occur in the new completely converted cartilage.

In cases with partial or complete dislocation of the femoral head after the operation in which the graft had not been subjected to articular weight and function, no signs of cartilaginous metaplasia were revealed. In these cases the connective tissue of the cutis had remained unchanged (Fig. 29).

To sum up the changes which took place in the connective tissue and the subcutaneous fatty tissue the following may be stated:

Within the two first weeks of observation a layer of richly vascularized granulation tissue forms between the skin graft and the freshened bone surface of the acetabulum, attaching the graft to its base. The cutis remains

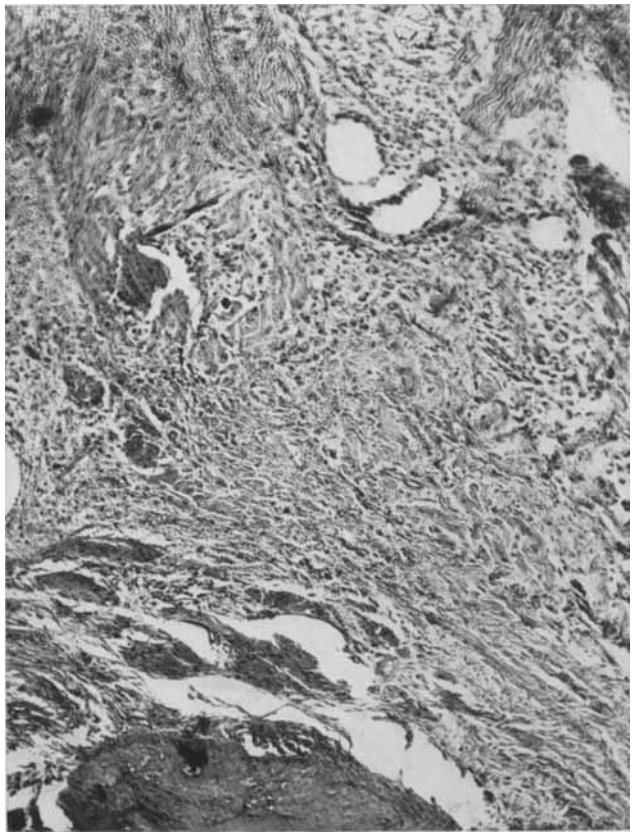

Fig. 29. 100 days from the operation. A case in which the femoral head has postoperatively become dislocated from the acetabulum. In the absence of articular weight and function no metaplasia has taken place in the connective tissue. Below, the acetabulum, in the centre and above connective tissue. Weigert-van Gieson staining. × 60.

unchanged. During the third and fourth weeks of observation the fibrils of the granulation tissue strengthen and under the effect of the loading of the joint line up parallel with the outline of the joint surface.

The subcutaneous fatty tissue degenerates and is substituted by new connective tissue. The new connective tissue also replaces the inflammatory cell accumulations which form in the area of the degenerating epidermal cells.

During the second month of observation clear reorganization of the fibrillary structure of the connective tissue to follow the outline of the joint surface is seen. The cutis has thus developed into a dense fibrous

connective tissue in which the collagenous fibres have lined up parallel with the surface of the joint and which microscopically, in places, has the appearance of tendon tissue.

At the end of the second month of observation and the beginning of the third the earliest signs of incipient cartilaginous metaplasia are to be seen in the interposition material. The process begins in the joint surface in the weight-bearing area of the joint and/or from the direction of the new connective tissue forming between the skin transplant and the surface of the acetabulum. Along with the incipient metaplasia the ground substance of the connective tissue increases, the collagenous fibres push apart from each other and break up into thin fibrils. Slightly differentiated connective tissue cells appear in the ground substance around which lacunar formation characteristic of cartilage cells takes place in the homogeneous ground substance. The metaplastic cartilage is either fibrous or hyaline in type.

In the absence of articular weight and function no cartilaginous metaplasia takes place.

3. PRESENCE OF METACHROMASIA AND P.A.S. POSITIVE MATERIAL IN THE GROUND SUBSTANCE OF THE CONNECTIVE TISSUE UNDERGOING METAPLASIA

The presence of metachromasia:

The staining method used in the experiments produced no metachromasia in the normal ground substance of the cutaneous connective tissue of the cat. The cutaneous epidermis, hair sheaths, and mast cells contained metachromatically staining substances.

Slight metachromasia occurred during the first weeks of observation in the granulation tissue developing between the skin graft and the surface of the acetabulum and where a new connective tissue replaces islets of degenerating epidermal cells. In the ground substance of the connective tissue of the skin transplant no metachromatically staining substances were seen until the end of the second month of observation.

At the turn of the second and third months, when the cartilaginous metaplasia began in the connective tissue, increasing metachromasia was revealed in the ground substance. In areas with increase of ground substance, where the collagenous fibres break up and cartilage cells make their appearance, metachromatically staining substances are formed. Metachromasia is especially abundant in the vicinity of chondrocytes, so

that a metachromatically staining ring is often visible around these cells (Fig. 30). With the progress of metaplasia the intensity of metachromasia increases. Areas with cartilage of hyaline type are characterized by quite intensive metachromasia. Yet in the ground substance of the cartilage resulting from metaplasia less metachromasia is present and its distribution is more irregular than in normal joint cartilage.

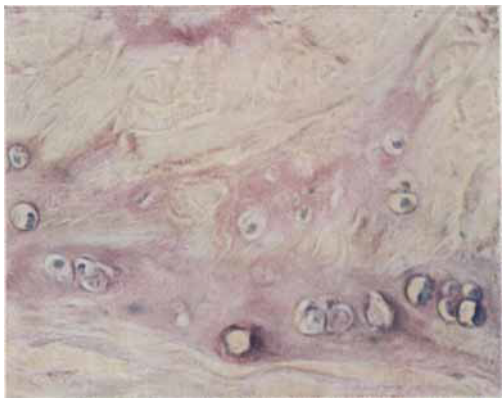

Fig. 30. 90 days from the operation. Connective tissue undergoing metaplasia. Metachromatically staining material around chondrocytes in the ground substance. Toluidine blue staining. × 270.

Testicular hyaluronidase decomposed the metachromatically staining material in the ground substance (Figs. 31 and 32). In some of the specimens only, with intensive metachromasia, slight metachromasia was still present even after treatment with enzymes.

Mast cells occurred in the connective tissue of the transplant and in the new connective tissue during the first days of observation. Later no mast cells were seen in the connective tissue subject to metaplasia.

The occurrence of P.A.S. positive substances:

By the method used in the experiments, no substances staining with the Schiff reagent were revealed in the ground substance of the connective tissue of the cat's skin. Part of the connective tissue fibrils were P.A.S. positive.

During the two first months of observation the P.A.S. positivity of the ground substance of the new connective tissue was slight. In the ground substance of the connective tissue of the skin graft positivity to this reagent manifests itself early in the third month of observation, with the beginning of the cartilaginous metaplasia. Along with an increase of the ground

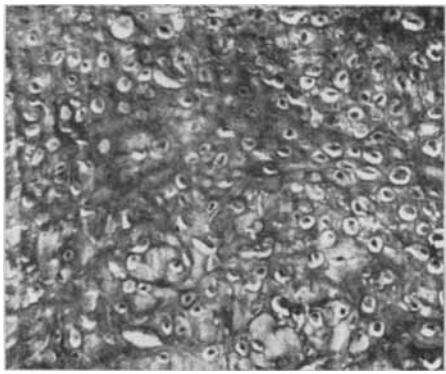

Fig. 31. 90 days from the operation. Metaplastic hyaline type cartilage. Intensive metachromasia in the ground substance. Toluidine blue staining. × 270.

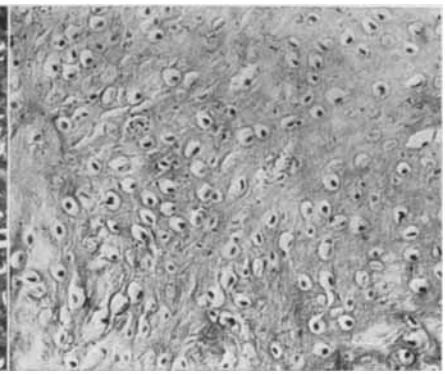

Fig. 32. Same specimen as in Fig. 31. The specimen has been treated with testicular hyaluronidase before staining. Treatment with an enzyme has decomposed the metachromasia. Toluidine blue staining. × 270.

substance of the connective tissue, the breaking up of collagenous fibres and the appearance of cartilaginous cells in the ground substance, clear P.A.S. positivity was noted. (Fig. 33) With the progress of metaplasia the P.A.S. positivity of the ground substance increased. Yet it is slighter in the metaplastic cartilage than in normal joint cartilage.

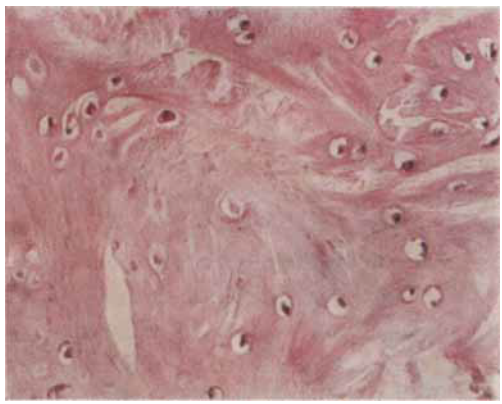

Fig. 33. Connective tissue undergoing metaplasia. P.A.S. positively staining material in the ground substance. Periodic-Acid-Schiff staining. × 270.

Treatment with testicular hyaluronidase did not destroy the P.A.S. positivity from the ground substance of the metaplastic cartilage. Nor did the malt diastase enzyme decompose substances staining positively with P.A.S.

To sum up from the foregoing:

In the first stage of cartilaginous metaplasia, material staining metachromatically and P.A.S. positively manifests itself in the ground substance of the connective tissue. With the advance of the metaplasia its amount increases.

Treatment with testicular hyaluronidase removed the metachromasia of the ground substance. The P.A.S. positive material was resistent both to testicular hyaluronidase and malt diastase. No mast cells were revealed in the connective tissue undergoing metaplasia.

4. HISTORADIOGRAPHIC OBSERVATIONS OF THE DISTRIBUTION OF THE MASS OF THE CONNECTIVE TISSUE DURING CARTILAGINOUS METAPLASIA

Histologically, during cartilaginous metaplasia, the strong collagenous fibres of the connective tissue were seen to break up into thin fibrils, which seemed to disappear into the ingreasing ground substance. Histochemically, on the other hand, it could be demonstrated that metachromatically staining and P.A.S. positive material makes its appearance in the ground substance of the connective tissue during cartilaginous metaplasia. From these findings I thought it possible that in the course of the metaplastic process changes may take place in the distribution of the amount of the dry substance or mass of the connective tissue. For the verification of these changes historadiography was used.

The fibrillary mass of the connective tissue was visually compared, in historadiograms taken of tissue samples obtained at different stages of the metaplastic development, with the mass of the ground substance of the same specimen. It could likewise be noted histochemically that in the ground substance of the metaplastic cartilage the distribution of metachromasia was less regular than in the normal joint cartilage. By comparing the historadiogram of the converted cartilage with that taken of normal joint cartilage the extent of the difference in the distribution of the mass between normal cartilage and in cartilage which had undergone metaplasia could be established.

The historadiograms were obtained at different stages of the metaplasia, 25, 50, 75, 90, 120, 150 and 180 days after the operation. Historadiograms were likewise taken of the normal skin and joint cartilage of the cat.

In normal cutaneous connective tissue of the cat the mass is mainly localised in the fibrils of the connective tissue while in the ground substance the amount of mass is appreciably smaller (Fig. 34).

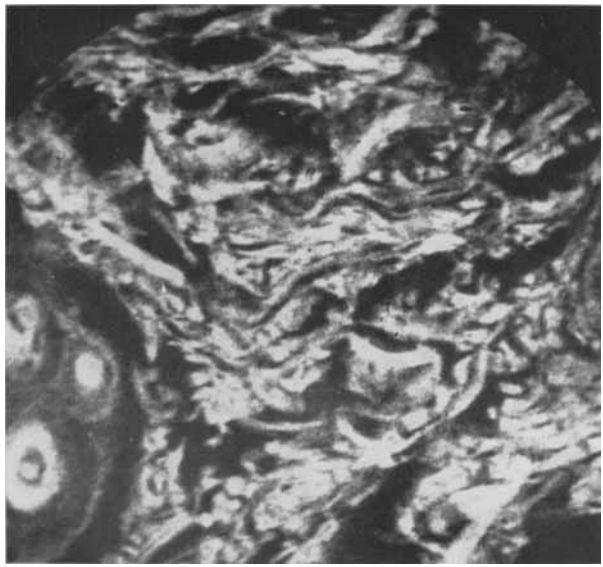

Fig. 34. Historadiogram of normal cutaneous connective tissue of the cat. The mass mainly localizes in collagenous bundles while the ground substance contains less mass. Registered at 3 kV, 35 mA. × 300.

In the normal joint cartilage of the cat's hip joint the mass distributes itself comparatively homogenously in the ground substance of the cartilage. The historadiogram showed the amount of the mass of cartilage cells to be smaller than that of the ground substance (Fig. 35).

During the two first months of observation no essential changes occurred in the distribution of the mass of the interposition material. The mass of the connective tissue fibrils still exceeded that of the ground substance considerably.

At the beginning of the third month of observation, when the beginnings of the cartilaginous metaplasia could be seen histologically, the first signs of changes in the distribution of the mass of the connective tissue were revealed. The difference between the mass of the ground substance of the connective tissue and that of the fibrils diminishes. The mass of the

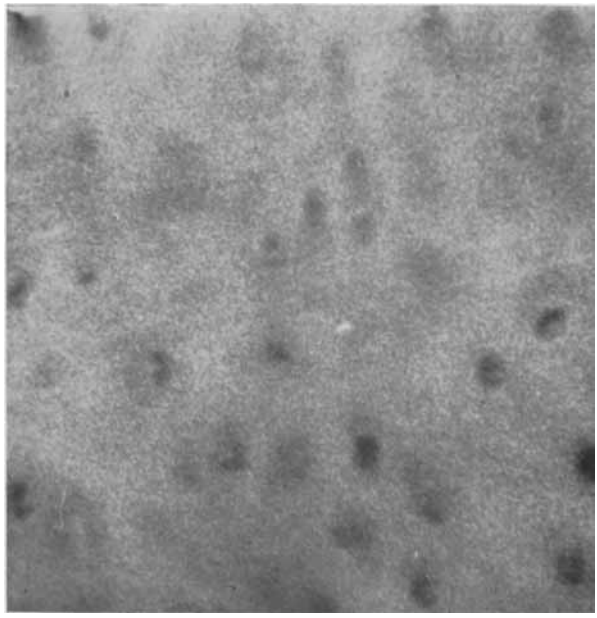

Fig. 35. Historadiogram of normal hip joint cartilage of the cat. The mass distributes itself relatively homogeneously in the ground substance. Less mass in cartilage cells than in the ground substance. Registered at 3 kV, 35 mA. × 300.

connective tissue fibrils breaks up and merges with that of the ground substance. The tendency in the distribution of the mass of the connective tissue is thus towards homogenization (Figs 36, 37 and 38). In areas where the connective tissue developed into fibrous cartilage, the fibrillary distribution of the mass is still faintly visible (Fig. 39). On the other hand, wherever the metaplastic cartilage is of hyaline type, the distribution of the mass in the ground substance is more homogeneous (Fig. 40). Yet the homogeneity of the distribution of the mass is less complete in the new metaplastic than in normal joint cartilage. The chondrocytes contained less mass than the ground substance.

As a summary of the historadiographic observations the following may be stated:

In the historadiogram of normal connective tissue the mass localizes mainly in the connective tissue fibrils while much less mass is present in the ground substance. In normal joint cartilage the mass distributes itself in the cartilaginous ground substance comparatively homogeneously and the mass of the cartilage cells is less than that of the ground

substance. In the course of the cartilaginous metaplasia the distribution of the mass in the connective tissue becomes more homogeneous. The difference between the fibrillary mass and that of the ground substance diminishes so that in the hyaline type cartilage developed through metaplasia the mass distributes itself relatively evenly in the cartilaginous ground substance. Historadiographically the metaplastic cartilage is either fibrous or hyaline in type.

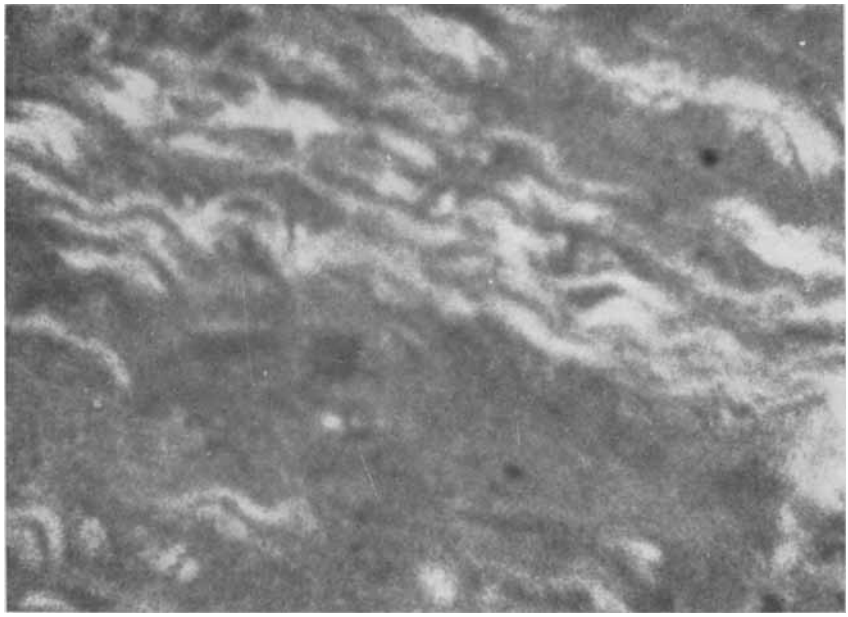

Fig. 36. 75 days from the operation. The mass of the ground substance of the connective tissue has increased compared with that of fibrils. Breaking up of the mass of collagenous fibres can also be noted. Registered at 3 kV, 35 mA. × 360.

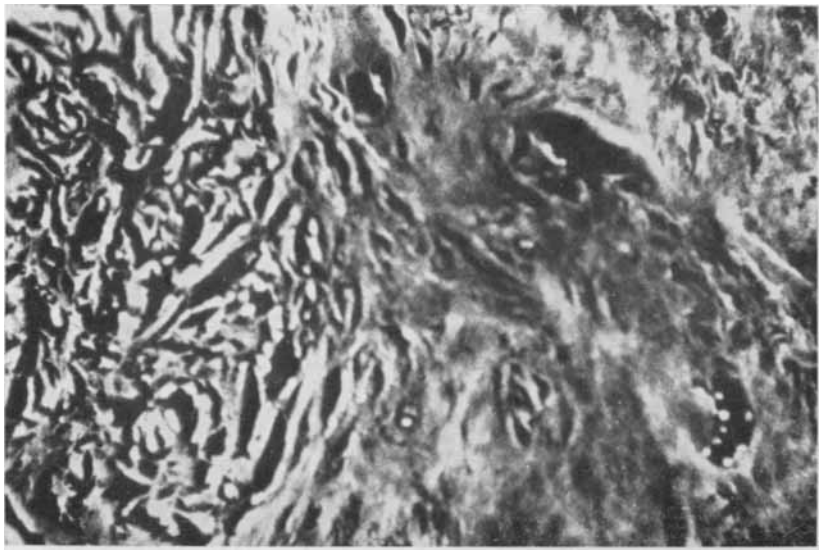

Fig. 37. Historadiogram of connective tissue undergoing metaplasia, 120 days after the operation. In the centre of the Fig. an area with incipient metaplasia. The distribution of the mass in the ground substance has clearly homogenized. On the left non-metaplastic connective tissue with fibrillary distribution of the mass Registered at 1,2 kV, 2 mA. × 360.

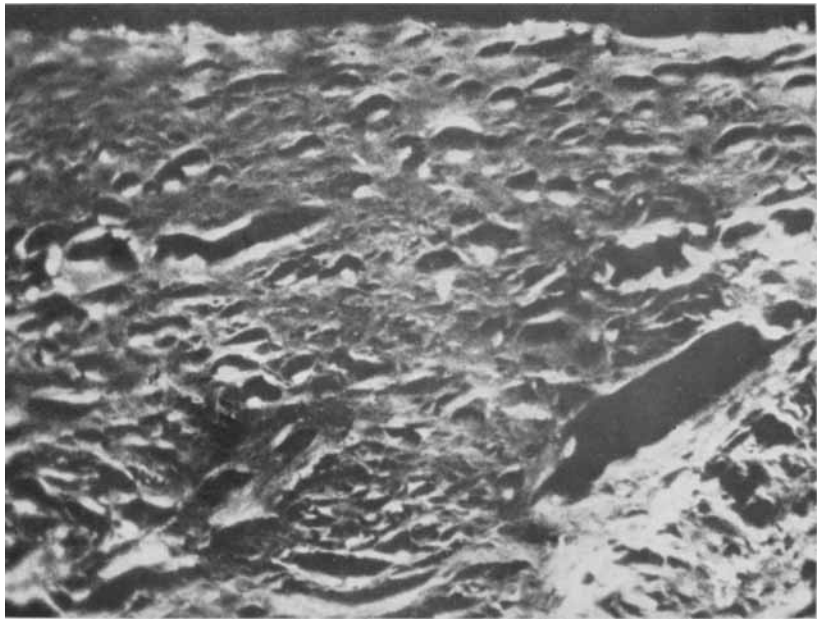

Fig. 38. Historadiogram 120 days after the operation. Above in the Fig. articular surface and close to it metaplastic cartilage. Lower down fibrous connective tissue. In the cartilaginous area the distribution of the mass is more homogeneous than in the connective tissue. Less mass in chondrocytes. Registered at 1,2 kV, 2 mA. × 280.

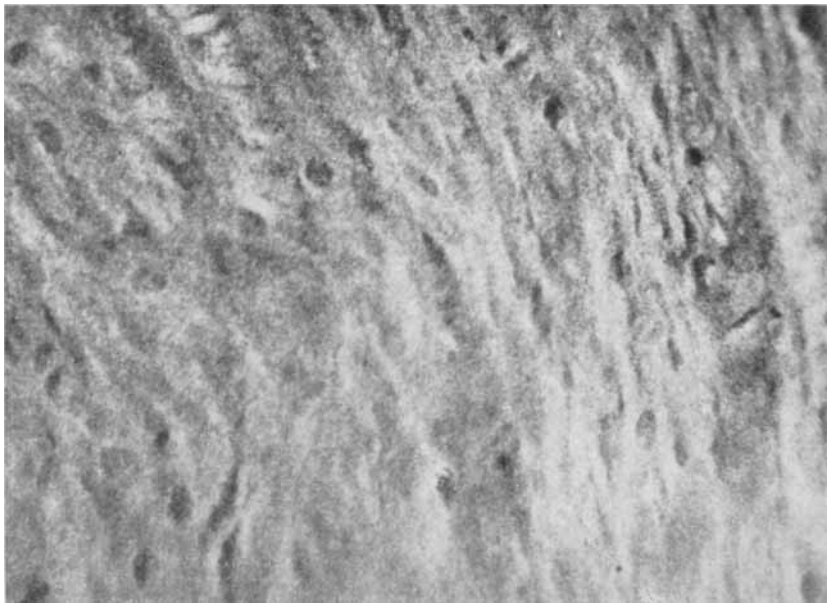

Fig. 39. 150 days from the operation. Historadiogram of metaplastic fibro-cartilage. Fibrillarity still visible in the distribution of the mass. Registered at 3 kV, 35 mA. × 360.

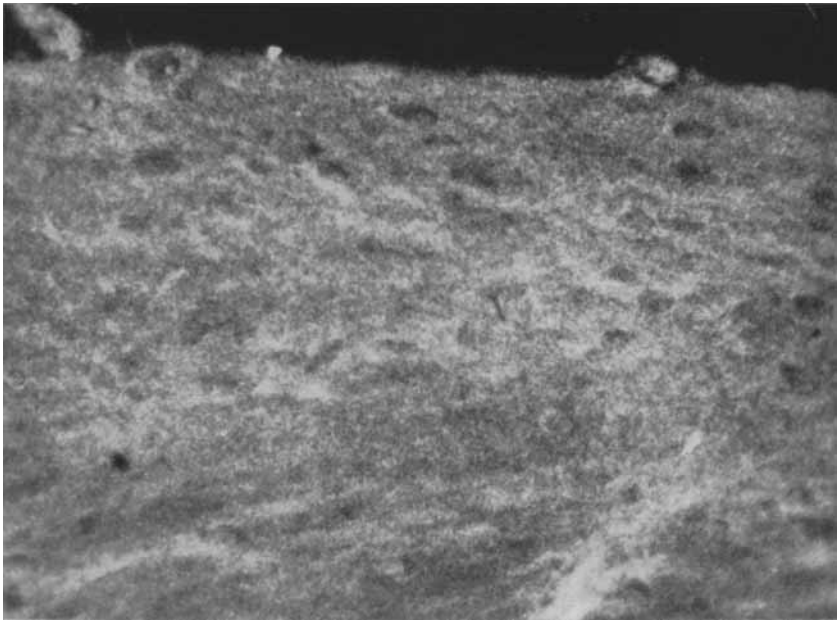

Fig. 40. 150 days from the operation. Historadiogram of metaplastic hyaline type cartilage. Distribution of mass in the ground substance comparatively homogeneous, less mass in the chondrocytes than in the ground substance. Registered at 3 kV, 35 mA. × 300.

5. OCCURRENCE OF OSSIFYING PROCESSES IN THE INTERPOSITION MATERIAL

Along with the ossification of the cartilage, calcium phosphates accumulate in its ground substance (HAM 1955). To bring out possible ossified areas in connective tissue which has undergone metaplasia I used VON KOSSA's silver staining. The positivity of this method is based on the presence of phosphates and carbonates, not of calcium salts, in the tissue. Yet in an animal organism insoluble phosphates and carbonates nearly always occur in combinations with calcium so that VON KOSSA's staining may be considered almost specific in demonstrating calcium salts in animal tissue (PEARSE 1954).

To reveal possible bone formation in the bony surface of the acetabulum and in the new metaplastic cartilage WEIGERT VAN GIESON stains prepared from decalcified samples of tissue were also used.

In the tissue samples obtained from cartilage which had undergone metaplasia no areas of ossification were revealed by VON KOSSA's silver staining.

Reparative new ossification was noted in the bony surface of the acetabulum in the decalcinated samples of tissue. Its purpose was obviously to fill in the incongruities resulting in the bone surface in connection with the removal of the joint cartilage and thus to remodel the bone surface of the acetabulum to a shape serviceable for articular function.

In the area of the metaplastic cartilage which bordered on the surface of the acetabulum, ossification of cartilage was to be seen here and there. The ossification, however, was restricted to the deepest parts, those closest to the bone surface, and manifested no tendency to extend to the articular surface. In one case only was an ossified area noted in the cartilage which had undergone metaplasia (Fig. 41).

It therefore seems that the metaplastic cartilage shows no marked tendency to ossification and that the ossification which takes place in the surface of the acetabulum and in the cartilaginous area bordering on it has a reparative purpose to remodel the articular surface to suit joint function.

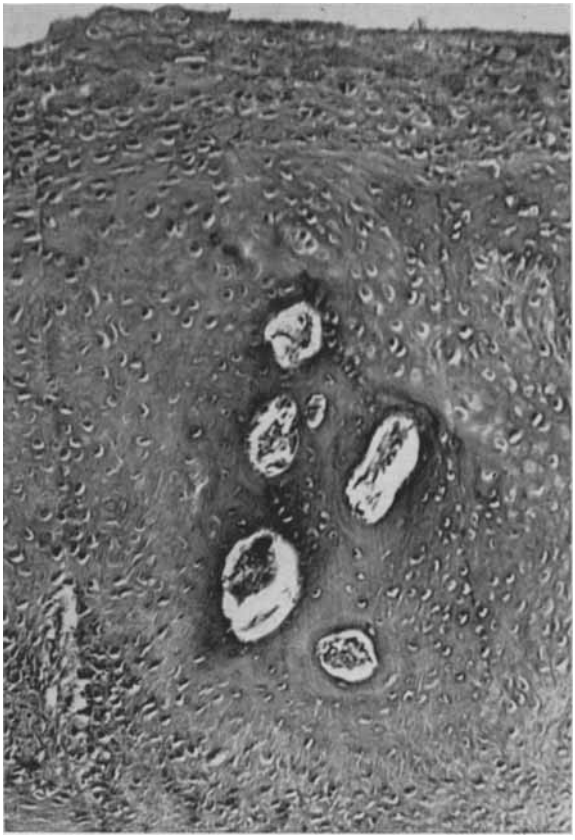

Fig. 41. 115 days from the operation. Specimen in which an ossification centre is seen in the metaplastic articular cartilage. Ossified cartilaginous area in the centre. Weigert-van Gieson staining. × 100.

IX. DISCUSSION AND CONCLUSIONS

As could be seen from the experiments carried out, exposure of the interposition material to articular weight and function apparently is essential for the development of cartilaginous metaplasia. These two factors promotive of the metaplastic process were allowed sufficient scope in the experimental method used. The hip joint was favourable in view of function and the operative technique used increased the pressure affecting the interposition material.

Possibly this may account for the fact that in the present study the connective tissue used as interposition material underwent cartilaginous metaplasia although in some earlier work carried out by PEREGALLI and DEMARCHI no metaplastic development occurred.

The organism was found to tolerate the full-thickness skin graft inserted in the joint well. As could be seen in earlier animal experiments (KIVILAAKSO 1955) and clinical follow-ups (K. E. KALLIO 1957) the insertion of the full-thickness skin graft in tissue or in the joint did not cause postoperative infection. In the present series only one instance of intra-articular infection occurred.

In the animal experiments the skin proved an excellent interposition material. As early as the beginning of the second month of observation a well-shaped joint capsule and a joint cavity were established macroscopically. The vitality of the skin graft proved remarkably good. At an early stage the interposition material is more prone to necrosis, and excessive articular pressure directly after the operation may cause some disintegration of the transplant in the weight-bearing area of the joint (KETTUNEN 1956).

The macroscopical examinations showed a clear difference between the experimental and the control series. In the controls the arthroplasty joint achieved was less valuable functionally than in the experimental series. In the control series the articular surface consisted mainly of bony surface. The presence of hydrops in the operated joint in more than half of the control cases is indicative of some intra-articular irritation.

The macroscopical observations thus showed that the interposition material promotes the formation of a functionally valuable joint and that a better result is obtained with than without interposition material.

X-ray findings seem to point in the same direction. In the experimental series the articular space of the joint operated upon was on the whole better preserved than in the control series. According to the clinical follow-ups no osteophytic formation occurred in skin arthroplasty joints while osteophytes did occur in vitallium cup and replacement arthroplasties (E. KALLIO 1958). As a biological material skin acts less as an irritant conducive to the formation of osteophytes than alloplastic materials. In the experimental series of the present work not a single one of the joints operated upon exhibited osteophytes. In the control series osteophytes occurred on the edge of the acetabulum in one case. It seems that the interposition of skin may have an effect counteracting osteophytic development. The elucidation of this point, however, will have to be left to further investigation.

KIVILAAKSO (1956) showed in his animal experiments that the organism tended to destroy or to isolate the epidermis of a full-thickness skin graft embedded in tissue and that the tension to which the graft becomes subject promoted epidermal degeneration. PEER (1955) likewise stated that, when epidermal structures are buried and not allowed to breathe, they usually degenerate and disappear. In the present work the epidermis of the skin used as interposition material was found to degenerate in the articular area within the first weeks of observation; no epidermal cysts formed. The same observation was made by PEREGALLI and DE MARCHI in animal experiments.

In areas where the skin is not subject to pressure the epidermal cells may be preserved longer but even there the organism tends to isolate or to destroy them.

In some earlier experimental studies on arthroplasty the significance of granulation tissue, which is of subchondral origin, in the formation of the new joint has been emphasized and the interposition material has been ascribed secondary importance only (ALLISON and BROOKS 1913, PHEMISTER and MILLER 1914, SCHMERTZ 1919). Yet it seems apparent that the new granulation tissue does not alone tolerate any considerable loading caused by the joint but becomes necrosed so that a naked bony joint surface results. In the present study granulation tissue was found to develop between the freshened bone surface and the graft. The new connective tissue is well vascularized and clearly contributes in an important way towards the preservation of the vitality of the interposition material.

On the other hand the interposition material serves as a protection to the granulation tissue so that this multipotent tissue, favourable in view of metaplasia, is preserved from destruction. In the control series it was in fact clearly brought out that articular weight has the effect of causing extensive necrosis of the granulation tissue, which retained its vitality only where the weight of the joint was slight.

RÖPKE (1913) and REHN (1914) noted that in fatty tissue arthroplasties the interposition material became transformed into connective tissue through wear and tear of the joint. In the present study the skin graft used as interposition material also comprised some subcutaneous fatty tissue. When subjected to loading the subcutaneous fatty tissue degenerated and was replaced by new connective tissue. This new connective tissue, apparently, like the granulation tissue forming between the skin graft and the bony surface and the connective tissue replacing islets of degenerating epidermal cells, is of the multipotent type favourable in view of metaplasia.

Many investigators believe that certain cells persist in the adult organism with the potency of undifferentiated mesenchymal cells (HAM 1953, PEER 1955), a point confirmed convincingly by MAXIMOW (1926, 1927) in his work. According to Maximow, when mesenchymal cells are differentiated into different types of connective tissue, part of the cells stay on a less differentiated stage. Thus a number of less differentiated cells are always present in the connective tissue. MAXIMOW believes that of the different types of connective tissue the loose subcutaneous kind resembles mesenchymal tissue most closely.

Under the influence of certain stimuli these undifferentiated cells may undergo progressive development and furnish new cell types (MAXIMOW 1952, PEER 1955). LEVANDER (1946, 1949) injected some alcohol extract of osseous tissue intramuscularly into the experimental animal thus causing cartilaginous and osseous formation. He believed that there is every reason for thinking that this factor will ultimately be identified as a definite chemical substance. LEVANDER's investigations, however, have been adversely criticized and HEINEN (1949) among others proved that a mere solvent was capable of acting osteo- and cartilagogenetically and believed that the existence of a specific osteogenetic substance in extracts of skeletal tissue could not be accepted as proved. Mechanical factors, likewise, such as weight and tension, have been shown to participate in cartilago- and osteogenetic processes (KROMPECHER 1938, 1947, 1956, GLÜKSMANN 1939). Of the effect of external factors on tissular differentiation HAM (1953) writes as follows: »The environment of cells plays a very important role in

affecting their differentiation. So, if some new potent environmental influence appears in a special kind of connective tissue, it may induce the mesenchymal cells that remain in that tissue to differentiate along a different pathway from their customary one, and the cells of different type that arise in this way may gradually replace those of former tissue thus giving the impression that the previous type of tissue has changed into another type. Actually it has been replaced by another. This process in connective tissue is known under the name of metaplasia.»

The full-thickness skin graft used as interposition material in arthroplasties, the granulation tissue growing from the freshened bone surface and the new connective tissue replacing degenerating epidermal cells and fatty tissue come under the influence of new environmental factors in the joint. Joint function may then induce metaplasia of the slightly differentiated connective tissue cells into a new mesenchymal tissue, cartilage, which gradually replaces the differentiated connective tissue.

The question as to the origin of the multipotent connective tissue cells which at the inception of metaplasia increase and change into cartilage cells is a very interesting one. Do they originate in the multipotent cells of granulation tissue or are the islets of mesenchymal cells in the skin graft another source of the metaplastic process? In the present work considerable evidence seemed to speak for the view that the metaplasia had a twofold origin: in the slightly differentiated cells of the transplant and in the multipotent cells of the new connective tissue. In a number of histological specimens the process could be seen arising both in the articular surface, i.e. the loose subcutaneous connective tissue of the skin, which according to MAXIMOW is slightly differentiated tissue, and in granulation tissue, while no metaplasia was under way at the time in the fibrous more differentiated connective tissue of the transplant. On the other hand, in some of the histological specimens, the granulation tissue originating in the bone marrow and growing from the freshened bony surface was seen penetrating into the connective tissue of the transplant. It is perhaps not impossible that the multipotent cells of the granulation tissue might penetrate deep into the skin transplant and as far as the articular surface where the metaplastic development begins. The skin graft would thus act as a kind of culture medium for the new connective tissue undergoing metaplasia, which would gradually replace and assimilate into itself the connective tissue of the transplant. A full elucidation of these problems falls outside the scope of the present study. Supplementary work will be necessary for their solution.

In the present study the importance of articular loading and function

for the development of cartilaginous metaplasia was clearly demonstrated, a point which KROMPECHER (1938, 1947, 1956) was the first to bring out in his investigations. The cartilaginous metaplasia began and had reached the most advanced stage in the weight-bearing area of the joint. If no pressure effect was present, no metaplasia occurred. It therefore seems to me fully justifiable to speak of functional metaplasia of the connective tissue.

In embryonal development of cartilage the mesenchymal cells are seen to grow globular and secrete around them a layer of cartilaginous ground substance. The collagenous fibres push apart from each other and disappear into the ground substance (MAXIMOW 1952, ROBB-SMITH 1954). The mature cartilage regenerates very slowly and poorly (CARLSON 1957). Yet in cases in which new connective tissue replaces the cartilaginous defect, more rapid development of new cartilage may occur. If for instance a cartilaginous defect involves the articular surface as far as the subchondral bone, it soon fills up with new connective tissue. Subject to articular function the cells of the new connective tissue may be transformed into cartilaginous cells, the ground substance of the cicatric tissue and fibrils become homogenized and the connective tissue has thus undergone cartilaginous metaplasia in the fully-developed organism (BENNETT 1931, HALDEMAN 1938, MAXIMOW 1952). The phases of cartilaginous metaplasia here described could be verified in the course of the present work when the connective tissue used as interposition material underwent metaplasia into cartilage.

During the progress of the cartalaginous metaplasia increasing metachromasia was revealed in the ground substance. The metachromatically staining substance in question is apparently chondroitin sulphate A, which is the main mucopolysaccharide component of hyaline cartilage. Treatment with testicular hyaluronidase decomposed this metachromatically staining substance, just as it is known to decompose chondroitin sulphate A (MEYER 1951, 1954).

Chondroitin sulphate is believed to play a central part in the biology of joint cartilage. Diminished or absent metachromasia of articular cartilage is evidence of degenerative changes resulting from reduced chondroitin sulphuric acid content (HIRSCH 1944, SYLVEN 1947). The intensity of the metachromasia may be taken as a criterion to the biological value of the joint cartilage. On the other hand, contrary to SYLVEN's suggestion (1947), no definite conclusions can be drawn from the intensity of the metachromasia and changes in this intensity as to the chondroitin sulphate concentration of the joint cartilage. The changes in staining capacity, besides possibly being due to changes in the amount of the substance itself, may

also result from alterations in the polymerization of mycopolysaccharides or changes in their binding to other components of the ground substance, especially to proteins (GROSS 1953). In the metaplastic cartilage the metachromasia was less intensive than in normal joint cartilage, and quite probably the chondroitin sulphate concentration may likewise have been below normal. The cartilage developing by metaplasia must in fact be set down as either fibrous or hyaline in type. This inference was supported by the histological and historadiographic findings. Yet it should be kept in mind that cartilaginous metaplasia is a comparatively slow biological process. The chondroitin sulphate concentration of the cartilage quite possibly increases with the lengthening of the period of observation and the biological value of the new cartilage likewise.

ASBOE-HANSEN (1951) saw a close interrelation between the occurrence of hyaluronic acid and mast cells in connective tissue and believes that the mast cells secrete hyaluronic acid. On the other hand, he found no interrelation between the occurrence of mast cells and chondroitin sulphate, which is one of the components of the mucous ground substance. In the present study no mast cells were revealed in the connective tissue undergoing metaplasia so that apparently they play no role in the formation of metachromatically staining substances.

The ground substance of hyaline cartilage is rich in P.A.S. positively staining material. This P.A.S. positivity of the cartilaginous ground substance is not due to chondroitin sulphate A, since it is known to react negatively to P.A.S. and since testicular hyaluronidase does not decompose P.A.S. positive substances (LEBLOND 1950, GLEGG 1952, PYÖRÄLÄ 1958). GLEGG (1954) believed that the P.A.S. positive substances are neutral mucopolysaccharides. In the present study the P.A.S. positive material developing during metaplasia in the ground substance was resistent to testicular hyaluronidase, and therefore may have been some neutral mucopolysaccharide, as GLEGG thought, and not chondroitin sulphate A. The P.A.S. positivity of this material, which was not decomposed by treatment with malt diastase, could not be due to the glycogens present in the tissue.

The homogenization of the distribution of the mass in the connective tissue undergoing metaplasia may be due, on the one hand, to the breaking up of the fibrillary mass, and on the other to increase in the mass of the ground substance. The latter increase apparently is ascribable to the formation of histochemically demonstrated mucopolysaccharides in the ground substance.

From the animal experiments which were carried out it seems justifiable to draw the following conclusions:

1) The full-thickness autogenous skin graft with fatty tissue is an excellent interposition material for arthroplasties. The organism tolerates the full-thickness skin graft as interposition material in the joint well and the procedure results in a functionally highly valuable joint.

2) The epidermis of the full-thickness skin graft used as interposition material degenerates when subject to loading and function of the joint. No epithelial cysts form.

3) Owing to loading and function of the joint the connective tissue of the skin graft used as interposition material and the granulation tissue growing from the freshened articular surface undergo metaplastic development into cartilage. The cartilage which results is either fibrous or hyaline in type. In the absence of articular weight and function no cartilaginous metaplasia takes place.[1])

4) In the course of the metaplasia both metachromasia and the P.A.S. positive material increase in the ground substance.

5) Historadiograms reveal homogenization of the distribution of the mass of the connective tissue in the course of the metaplastic process. This is effected by the increase in the mass of the ground substance of the connective tissue and also by the breaking up of the mass of the connective tissue fibrils.

6) The metaplastic cartilage manifests no tendency to ossification.

7) If interposition of skin is omitted, the loading and function of the joint easily destroy the granulation tissue growing from the freshened articular surface, which consequently mainly consists of naked bony surface.

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[1]) While the present study was in press the author had an opportunity to verify histologically, in clinical material, the cartilaginous metaplasia in tissular samples obtained from a knee joint in which skin arthroplasty had been performed about 6 months earlier. The case will soon be published in Ann. chir. et gynec. Fenniae.

SUMMARY

The purpose of the animal experiments carried out was to elucidate the changes which take place in an autogenous full-thickness skin graft when used as interposition material in arthroplasties in the hip joint of cats.

Thirty-seven adult cats in all were used for the experiments, on 30 of which, comprising the experimental series, a skin interposition arthroplasty was made in the left hip joint. In the operation the joint cartilage of the acetabulum was removed and a full-thickness skin graft was inserted into the acetabulum so that the epidermis faced the freshened articular surface. The control series consisted of seven cats subjected to the same operation as was carried out in the experimental series, but without interposition. The periods of observation ranged between the 7th and 240 days from the operation.

The joints operated upon were under observation macroscopically and by roentgenography. The fate of the interposition material was studied by histological, histochemical and historadiographical examinations.

The results obtained in the experiments may briefly be summed up as follows:

In the control series, in which no skin interposition was used, the articular surface mainly consisted of naked bone surface. Roentgenographically the articular space in the joint operated upon had either narrowed or partly disappeared. Microscopy showed that the granulation tissue growing from the freshened articular surface became destroyed through the effect of articular weight and function and that the new connective tissue was only preserved in areas where the articular weight was slight. Under the influence of loading and function the preserved connective tissue underwent metaplastic development into cartilage. Yet the cartilage formed no continuous extensive layer to replace the articular cartilage but occurred in the form of small islets in hollows of the uneven articular surface.

In the experimental series the autogenous full-thickness skin graft proved a very suitable material for interposition in arthroplasties. The organism tolerated the full-thickness skin graft as interposition material

in the joint very well. During the two first months of observation the graft was still distinguishable. In the course of the third month of observation the interposition material was transformed into tissue which macroscopically had the appearance of cartilage; the articular surface became covered by a thin continuous layer of cartilage. The inserted skin exhibited a good vitality and tolerated the loading due to the joint well. Both macroscopically and in x-ray films the skin arthroplasty joint exhibited a development to a joint with functionally highly valuable characteristics.

Microscopically the epidermis of the skin graft was seen to degenerate owing to wear and tear of the joint and no epithelial cysts formed.

From the freshened articular surface of the acetabulum granulation tissue grew between the graft and the bone surface. The new connective tissue also replaced the disintegrating islets of epidermal cells and the degenerating subcutaneous fatty tissue. Both in the cutis and in the new connective tissue the fibrils line up parallel with the outline of the articular surface owing to the weight of the joint, during the two first months of observation. At the beginning of the third month a process of cartilaginous metaplasia manifests itself in the connective tissue used as interposition material. The metaplasia begins and reaches its most advanced stage in the weight-bearing area of the joint. At the initial stage of the process the ground substance of the connective tissue increases, the collagenous fibres break up into thin undulating fibrils which seem to disappear into the ground substance. At the same time slightly differentiated connective tissue cells may be seen in the increased ground substance, gradually transforming themselves into cartilage cells. The cartilage resulting from the metaplastic development is histologically of either fibrous or hyaline type. In the absence of loading and function of the joint no cartilaginous metaplasia takes place.

In the course of the metaplasia both metachromasia and the P.A.S. positive material increase in the ground substance. The substance staining metachromatically which was decomposed by the testicular hyaluronidase enzyme, is chondroitin sulphate A. The P.A.S. positive material was resistent to testicular hyaluronidase and malt diastase and very likely is one of the neutral mucopolysaccharides.

In historadiography the mass of the normal connective tissue mainly localizes in tissular fibrils while considerably less of ground substance mass is seen. In the connective tissue undergoing metaplasia homogenization of the distribution of the mass was apparent. This may be accounted for, on the one hand, by the increase in the mass of the ground substance,

on the other by the breaking up and merging with the ground substance of the mass of the connective tissue fibrils.

The new metaplastic cartilage showed no appreciable tendency to ossification.

The author concludes that the autogenous whole-thickness skin graft with subcutaneous fatty tissue is eminently suitable as interposition material. The epidermis of the skin is destroyed by the weight and function of the joint and the connective tissue acting as interposition material undergoes functional metaplastic development into cartilage. If no interposition material is used, articular weight and function tend to destroy the granulation tissue growing from the freshened articular surface so that in these cases the articular surface consists of naked bone.

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