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THE INFLUENCE OF SOME ANTI-INFLAMMATORY DRUGS ON ORIGINAL AND REGENERATING SYNOVIAL TISSUE

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Among other tissues synovium is a target for the damaging effects of the still unknown initiating agent in rheumatoid arthritis. At present the predominating view is that the changes seen in the synovial tissues in rheumatoid arthritis are of the nonspecific inflammatory type (*Kulka* 1959, 1964, 1966). Experimental work—including cold injury, allergic phenomena and lesions obtained by vasospastic agents, hypertension and viral disease—has proved that the response of the mesenchymal tissues is one and the same irrespective of the eliciting agent (*Kulka* 1966). Similar conclusions were reached by *Brånemark et al.* (1967 a) when studying the effects of various inflammation-producing agents on mesenchymal tissues.

This response of the tissue is both vascular and cellular. The vascular reaction appears to precede the cellular. The former is characterized by venular dilation with secondary plasma leakage, fibrinoid necrosis of the vessel wall and formation of thrombi. Arteriolitis is occasionally noted. Based on comparative light microscopic observations the general opinion is that an angiopathy dominates the picture (*Cruickshank* 1954, *Kulka* 1966, *Sokoloff* 1963). In a recent study we (*Brånemark, Ekholm, Goldie* 1967) have, however, suggested that ultra-structural vascular changes are minimal.

As for the cellular behaviour there is a patchy infiltration of lymphocytes often around vessels. There is a scarcity of neutrophils. Fibrinoid

necrosis in the connective tissue may be seen. Besides the interstitial fibrin deposition a connective tissue proliferation is observed. The cellular and intracellular reactions are believed to be secondary to increasing microcirculatory insufficiency (*Kulka 1966*).

It is conceivable that besides general therapeutic measures in rheumatoid arthritis there are also procedures acting more concentratedly on the local articular manifestations. The aim is to reduce the inflammatory reaction. This can be achieved by drugs or by surgery. In the former case anti-inflammatory substances, as *e.g.* steroids and salicylates, are commonly used. The surgical management is directed either to the soft tissue, as *e.g.* synovectomy, or to skeletal structures, as *e.g.* arthroplasties or arthrodeses.

Irrespective of method used the aim is to combat the pain—due to the inflammatory reaction—and malposition and stiffness of joints due to destruction of tissue. In those cases where diseased synovial tissue is locally treated it is of importance to know what the reaction of the tissues lining the joint cavity may be to particular local treatment and its influence on the regenerating tissue after synovectomy.

For this reason we have carried out an experimental study on animals to investigate the influence of some anti-inflammatory drugs on normal synovial tissue and on its regeneration after synovectomy.

MATERIAL AND METHODS

The substances used in this investigation were methyl-prednisoloneacetate (Depomedrone®), prednisolone tertiary butyl acetate (Codelcortone TBA) and 0.2 per cent solution of salicylate. They were injected at regular intervals in doses as described below into the knee joints of dogs and rabbits. In all, seventeen joints were thus injected and in another five the regeneration of synovial tissue after synovectomy was observed.

Methylprednisoloneacetate (Depomedrone®): Four rabbit knee joints were partially synovectomized, leaving the posterior area intact as described in an experimental study by *Lindström (1963)*. On the day of synovectomy and following this at two day intervals the joints were injected with 1.5 ml Depomedrone on two occasions and 0.5 ml on three consecutive occasions. A total of five injections was thus achieved. The animals were allowed to run freely around without any immobilisation. Daily checkings were made of joint mobility and postoperative reaction. The experiment was terminated fourteen days after its initiation.

Prednisolone tertiary butyl acetate (Codelcortone TBA): Four rabbit joints were synovectomized. On the day of synovectomy and at subsequent two day intervals 1 ml prednisolone tertiary butyl acetate was injected totally five injections. Postoperatively the rabbits were freely mobilized and the experiment was ended fourteen days after its initiation.

0.2 per cent solution of salicylate: In this study rabbits and dogs were used.

Rabbits: Four knee joints were synovectomized and 1 ml 0.2 per cent buffered, blood-isotonic solution of salicylate was injected on the day of surgery. Following this the same amount was injected at two day intervals. Five injections were made. The rabbits ran freely around immediately postoperatively. The experiment was terminated after fourteen days.

Dogs: Five dog joints were injected at regular intervals with 0.2 per cent solution of salicylate without any previous synovectomy. The injected joints were freely mobilized. The injections were done at weekly intervals and altogether six injections were made. The experiment was terminated after two months with 2-4 weeks between the last injection and termination.

In all dogs who had solution of salicylate injected into one knee joint the opposite side was synovectomized at the initiation of the experiment. This was done 1) to study synovial regeneration in the dog, 2) to observe if possibly the injected salicylate in the non-synovectomized side may by blood borne conveyance via the capsular-bone-marrow vessels, in any way influence the regenerating synovial tissue.

At the termination of experiments tissues were taken for histologic and electron microscopic study. Haematoxylin-eosin and van Gieson stains were used. A control material consisting of synovial tissues from normal rabbits and dogs were technically processed in the same way.

A microangiographic study was also carried out. The aorta was dissected to the renal arteries and a catheter was introduced distally. To obtain an equilibrium of the intravascular fluid volume a perforation of the inferior caval vein was made distally. The vascular system was then perfused with a contrast solution of 25 per cent Micropaque in physiologic saline. Before the perfusion the animals were heparinized. The perfusion pressure was not measured but excessive pressures could be avoided as the injections were made by hand. In cases of increased resistance this was markedly decreased by intravenous injection of 5 ml 2 per cent Xylocain. The perfusion was interrupted when pure contrast filled the vena cava.

After angiography the specimens were immediately fixed in formalin and after two days all remaining muscles were removed. Following this the specimens were further fixed in 5 per cent neutral formalin with decalcification in formic acid. Finally the samples were embedded in paraffin. The specimens were cut in 800 microns thick pieces.

A Machlett OEG-50 tube was used for the microradiographic study. Exposures were made on Kodak MR plates with a distance of 15 cm at 12 kV, 20 mA and 15 minutes.

Synovial tissue from the dogs were also subjected to electron microscopical examination. For this purpose small pieces of synovial tissue from various parts of the joints were excised and immediately immersed into a fixative consisting of 3 per cent glutaraldehyde buffered at pH 7.2 by sodium cacodylate. Two hours later the tissue pieces were transferred to a second fixative containing 1 per cent osmium tetroxide, buffered at pH 7.2 with Veronal acetate. After postfixation for 1.5-2 hours the tissue was dehydrated in ethanol and embedded in Epon. The sectioning was performed on an LKB Ultratome. The sections were stained with uranyl acetate and lead citrate and examined in a Siemens Elmiskop I.

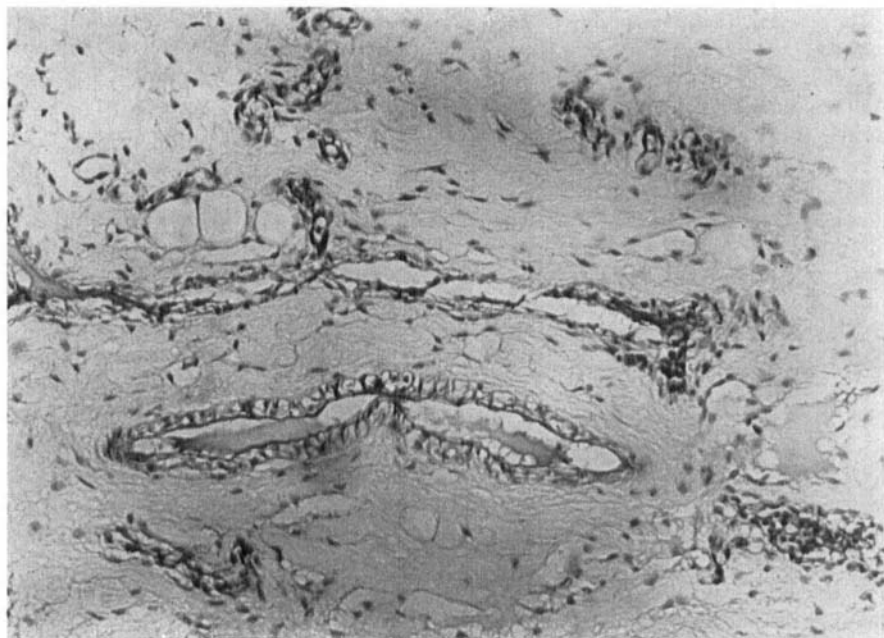


Figure 1. Synovial tissue from rabbit's knee joint treated with methylprednisolone acetate. Quiescent tissue without signs of abnormal cellular or vascular reaction. $\times 150$.

RESULTS

Methylprednisolone Acetate (Depomedrone®)

In the postoperative course no adverse effects were noted. The wounds healed without complications, no articular swelling was observed and motion was unimpaired.

On macroscopic examination of the opened joint at the termination of the experiment the scar tissue in the incision after the previous synovectomy was completely without any pathologic signs. No ruptures, haemorrhages or granulomas were observed. The various layers could with ease be detached from each other. On opening of the joint the cartilage appeared normal, the bone cartilage zone was uninterfered with, the remaining synovium was glossy but not oedematous. There were no signs of retained steroid-like microcrystals or suspension substance in the synovium or in the articular folds. The region where the synovectomy had been performed was normal and small granulation tufts of normal appearance were observed in the bone cartilage zone and along the inner side of the fibrous capsule which previously had

been lined by synovium. There was no excess of joint fluid. The cartilage was intact and on the whole no structural abnormalities were observed.

Histology: There was little reaction in vessels, cellular compartment and intercellular substance. The area of incision showed an increase in collagenous bundles and fibroblasts. Signs of inflammation *i.e.* neutrophils, infiltration of plasma cells, increase in the number of vessels, oedema and minor haemorrhage were not conspicuous (Figure 1). There were no areas of circumscribed necrosis of the fibrinoid type and the vessel walls all remained normal. No thrombi were detected. The granulation tufts in the bone cartilage zone were as expected rich in vessels and histiocytes which were diffusely scattered without any tendency to patchy infiltrations. No foreign body reaction was seen and the general impression was that of a quiescent tissue of normal appearance. Cartilage and bone were normal.

Prednisolone Tertiary Butyl Acetate (Codelcortone TBA®)

This appeared very soon as quite a noxious substance. Within three days following synovectomy the joints were distended with a swollen joint capsule. The patella was in all cases dislocated laterally. The animals refused to bear weight on the injected leg. The wounds tended in all joints to rupture spontaneously; on the fourth to sixth days there was discharge from the joints of thick fluid. Sutures were dislodged. On opening the joint in all animals, it was found that the subcutaneous tissues had ruptures and that the skin was the only covering layer of the joint. Large floccular greyish-white masses were either lodged in the subcutaneous soft tissues or freely floating around in the synovial fluid. This was excessive and of yellowish-grey thick appearance though not purulent. In two cases there were fistulas from the joint cavity ending blindly in the surrounding soft tissues. The joints were all surrounded by thick oedematous tissues. The cartilage of both femur and tibia were in all cases covered by a thin membrane which had a jelly-like appearance. The remaining synovial tissue was oedematous and intensely reddened. It adhered in a gluey fashion to the osseous structures.

Histology: The macroscopic observations were not congruent to the microscopic findings. The most striking feature was oedema. Collagenous bundles and cellular components were split up by a patchy gelatinous substance which apparently did not create any peripheral vascular or cellular reaction. Nevertheless, areas were found with infil-

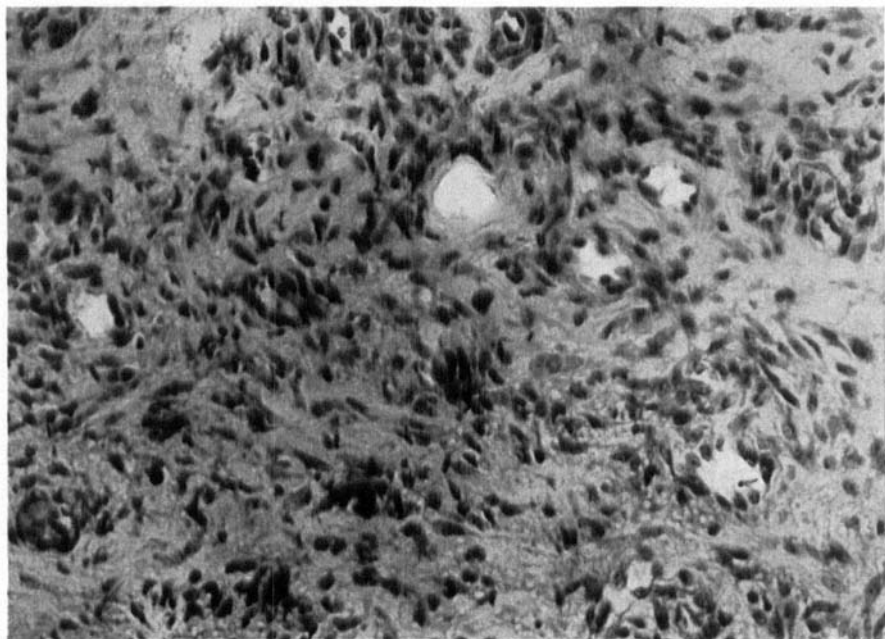


Figure 2. Synovial tissue from rabbit's knee joint treated with prednisolone tertiary butyl acetate. Rich cellular invasion of plasma cells and some neutrophils. There is some hypervascularization, $\times 300$.

trations of plasma cells and neutrophils and in addition some thick-walled vessels of both arteriolar, venular and capillary type (Figure 2). No thromboses were observed. The border zones of the ruptures were richly vascularized and penetrated by numerous mononuclear cells. The cartilage and bone appeared normal. On the whole, the histologic appearance was fairly innocent and did not give the dynamic impression as did the macroscopic findings.

0.2 per cent Solution of Salicylate

Rabbits: Postoperatively all the joints were normal without effusions or other pathologic signs. All animals moved their limbs forcibly and could bear weight without difficulty.

Hostology: No abnormalities were encountered.

Dogs: The joints injected with solution of salicylate were *not* synovectomized prior to injection. All joints appeared normal throughout the observation period of two months. On macroscopic examination of the opened joints at the termination of the experiment all the extra-



Figure 3. Synovial tissue from dog's knee joint treated with salicylate solution. The tissue is in parts areolar without signs of abnormal reaction. Some cellular clusters are observed, but these also occur in normal non-treated tissues. $\times 200$.

articular soft tissue layers were intact. The synovial tissue was slightly oedematous but otherwise without signs of inflammation. There was no synovial effusion. The cartilage appeared normal and the bone cartilage zone did not disclose any abnormalities. In scattered areas the synovial tissues appeared more richly vascularized but the vascular architecture was quite normal.

Histology: In all instances completely normal conditions were present (Figure 3).

Microangiography: As is apparent from Figures 4 a and b the microvascular architecture is normal. The salicylate injections did not leave the impression of interfering with the quantity or quality of the vessels. There was normal distribution and the arborisation did not signify any abnormal response to the injected agent.

Electronmicroscopy: Arterioles, venules and capillaries of the synovial tissue were studied with the electron microscope. It can be stated that these vessels in all respects displayed quite normal ultrastructural features.

The *arterioles* (Figures 6, 7) had, inside an outer layer of collagenous bundles, one or two layers of smooth muscle cells, each of which was enveloped in a basement membrane. The muscle cell cytoplasm had the appearance well known from several earlier studies and characterized by a large number of peripherally localized small vesicles and bundles of myofilaments. The muscle coat was separated from the endothelium by a media which in the larger vessels had a continuous layer of elastic tissue. In the smaller vessels this tissue showed several discontinuities (Figure 6). The endothelial cells were of varying height but generally higher than those of the capillaries. The luminal surface was irregular, displaying variously sized and shaped projections and a few slender villi. The endothelial cells contained normal-looking cytoplasmic components, the most characteristic of which are pinocytotic vesicles and bundles of 70 Å thick filaments (Figure 7).

The *capillaries* and *small venules* were, apart from the calibre, very similar (Figures 8, 9, 10). The endothelial cells had fundamentally the same structure as described above for the endothelium of the arterioles. A difference was, however, that both in capillaries and small venules the endothelium was, within large areas, very thin, measuring only a few hundred Å (Figure 9). However, a cytoplasmic lining did always exist and real pores and fenestrations covered by a thin membrane, the latter of which exist in several tissues (1, 2, 3, 4), were not found in the synovial tissue. The cell junctions did not show any widenings or other changes. The cytoplasmic components, including those most characteristic of endothelial cells—vesicles and filaments—had a normal appearance (Figure 10). The peripheral surface of the endothelium was always covered by a continuous basement membrane. Outside this membrane, there was, according to the size of the vessel, a varying amount of connective tissue elements in the form of collagenous fibrils and fibroblasts with long slender projections.

Figure 4 A. Microangiogram (transverse section through femoral condyle region) of dog's knee joint treated with salicylate solution. Normal vascular architecture with vessels connecting marrow space with synovial tissue via bone substance. Contrast has leaked out in marrow spaces which is due to a disruption of marrow veins during injection. $\times 10$.

Figure 4 B. Sectional enlargement of 4 A. Vessels from the marrow open freely into the cartilage zone, the peripheral limit of which is marked by white dotted line. The vascular appearance is normal as to quantity and individual form and distribution.

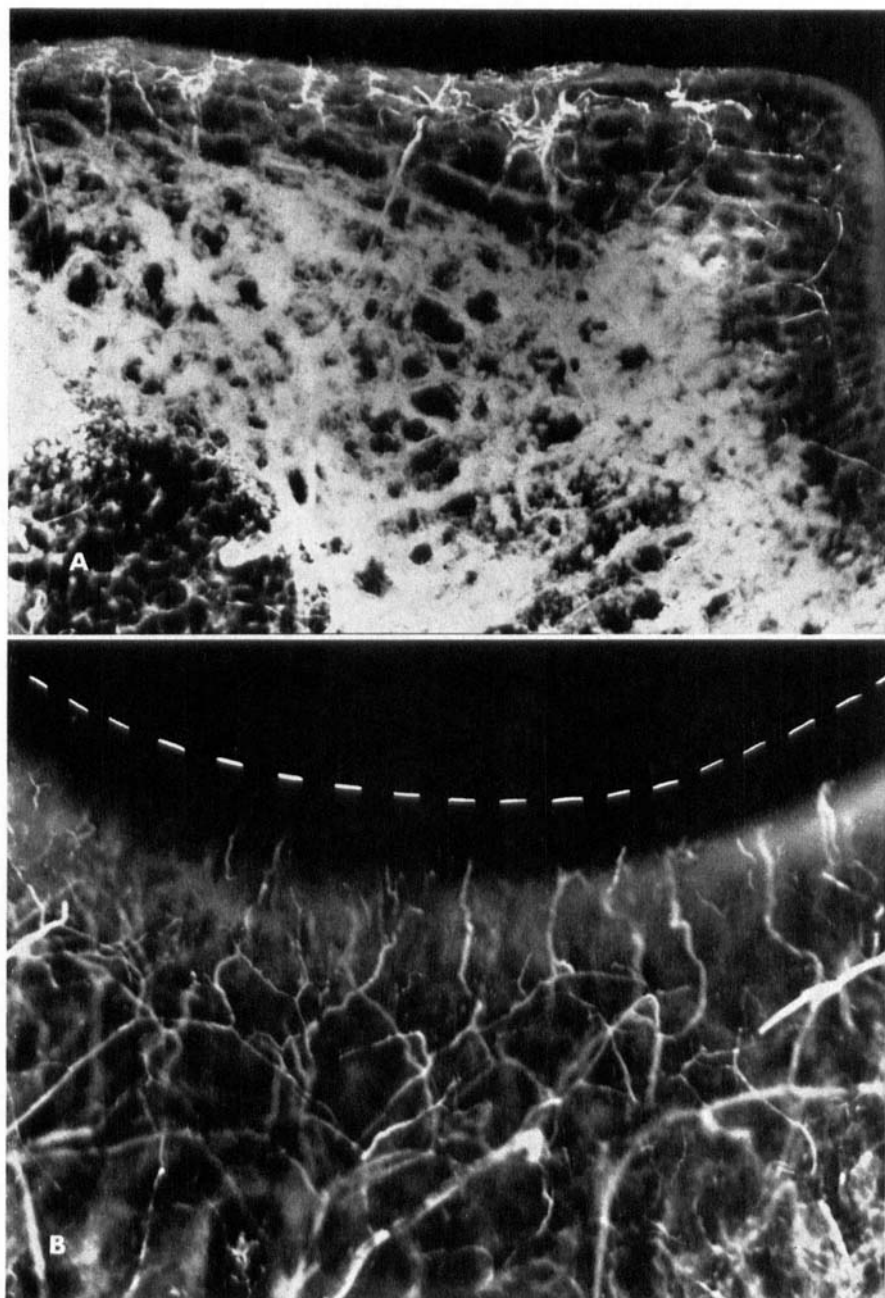


Figure 4.

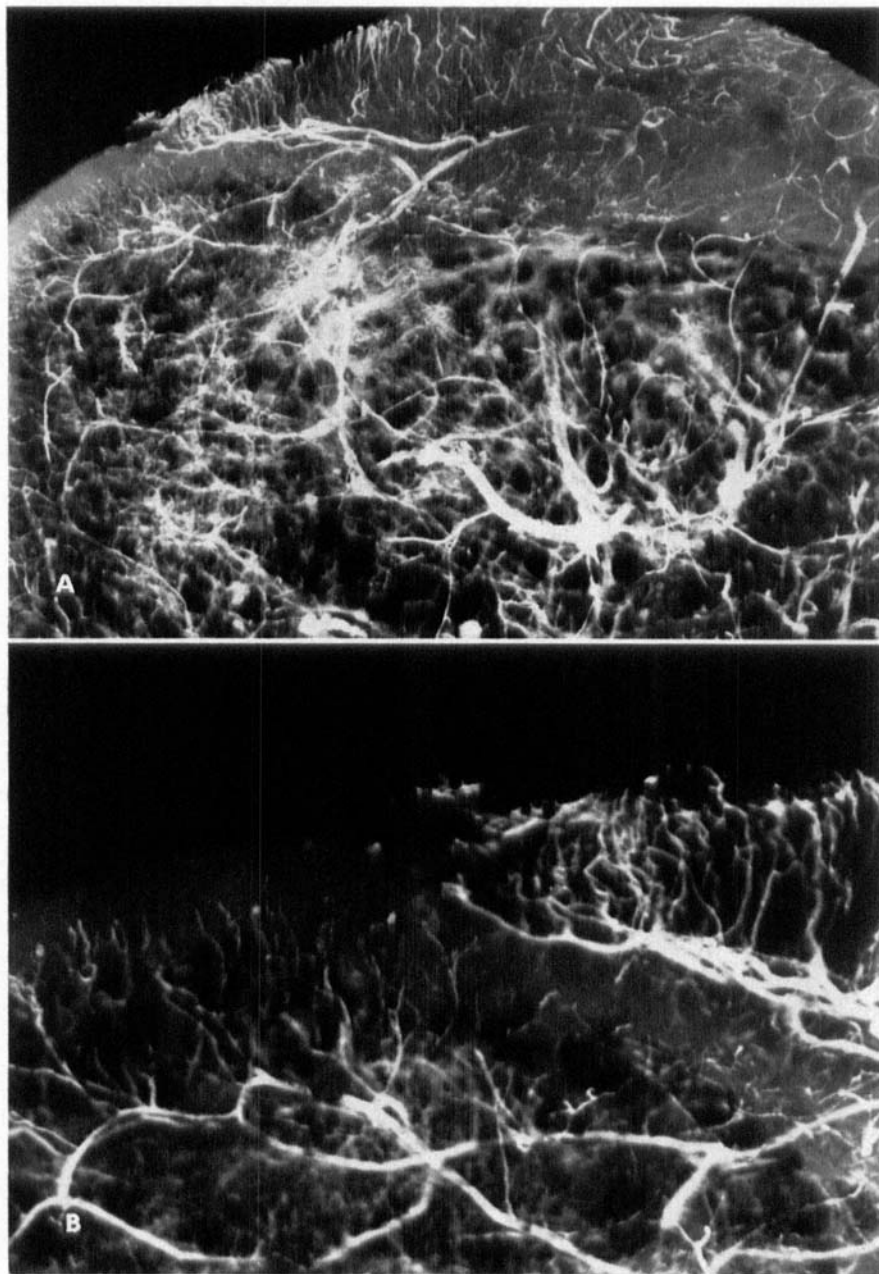


Figure 5 A. Overall view of microangiogram (transverse section through femoral condyle region) from dog's knee joint 2 months after synovectomy. Marrow vessels branch out in rich vascular arborisation in bone cartilage zone where regeneration of synovium occurs. $\times 9$.

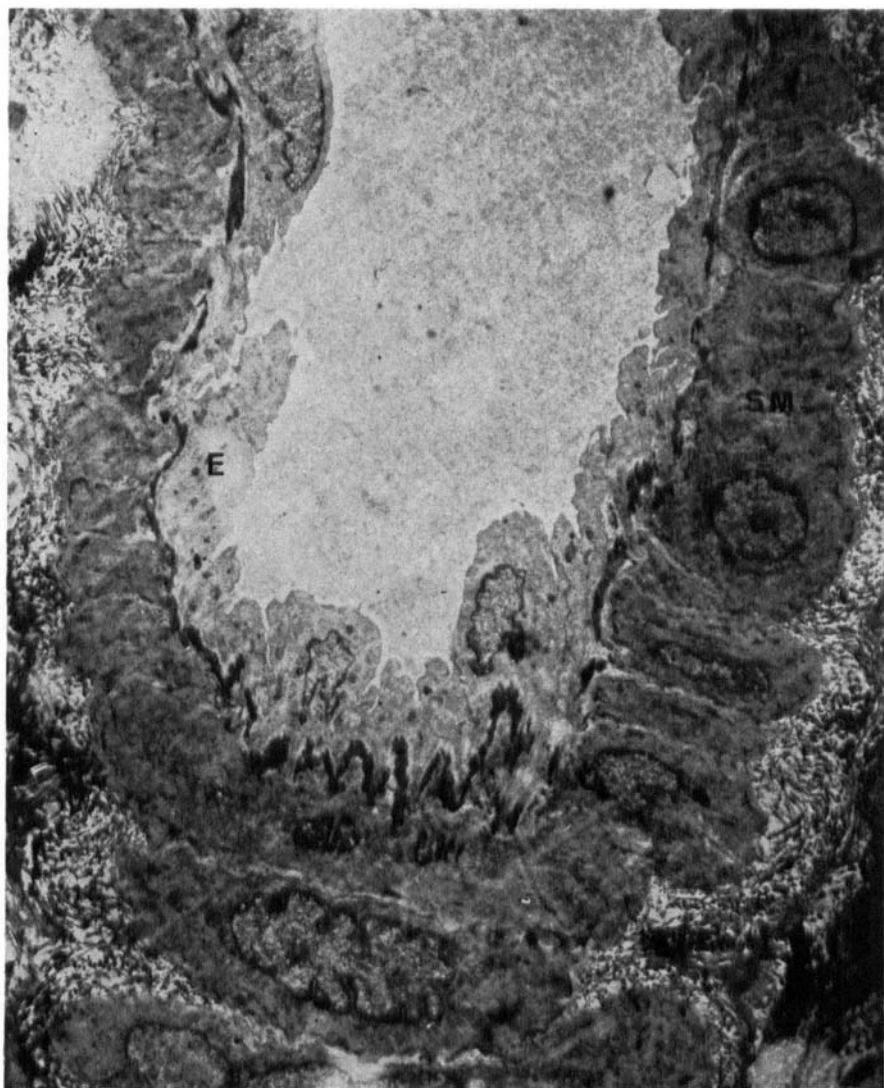


Figure 6. Survey electron micrograph of an arteriole in the synovial tissue from a joint subjected to salicylate injections. The vessel is provided with a single layer of smooth muscle cells (SM) separated from the endothelium (E) by a media containing heavily stained elastic tissue. Note the irregular course of the luminal surface of the endothelium. Outside the muscle layer there are collagenous fibrils running in various directions.—Magnification $\times 45,000$.

Figure 5 B. Sectional magnification of region of hypervascularity in bone cartilage zone where synovium regenerates. The microvasculature is normal for this type of regenerating tissue. $\times 45$.

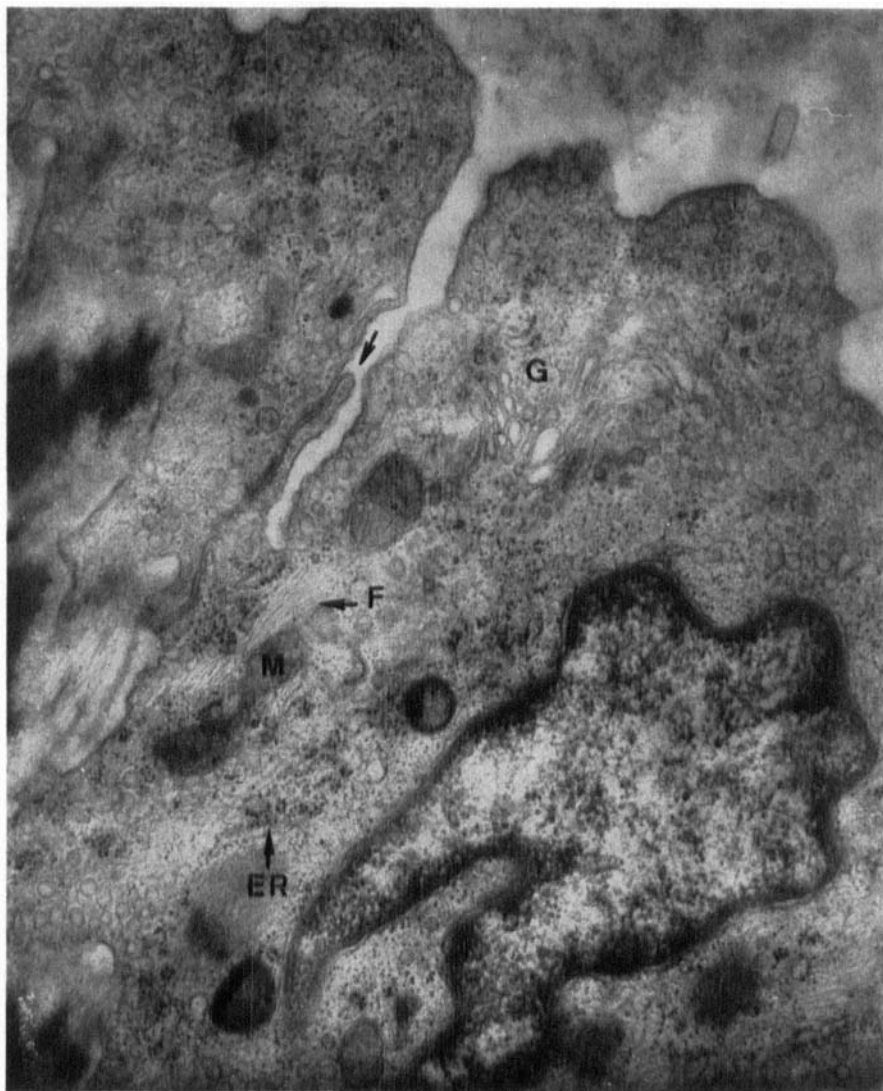


Figure 7. Electron micrograph showing a detail of the endothelium of the arteriole in Figure 6. The endothelial cell cytoplasm contains a few mitochondria (M), a Golgi apparatus (G), endoplasmic reticulum with ribosomes (ER), numerous small vesicles some of which open at the cell surfaces and bundles of fine filaments (F). The arrow points at the junction of two cells. To the left a portion of the media. Magnification $\times 32,000$.

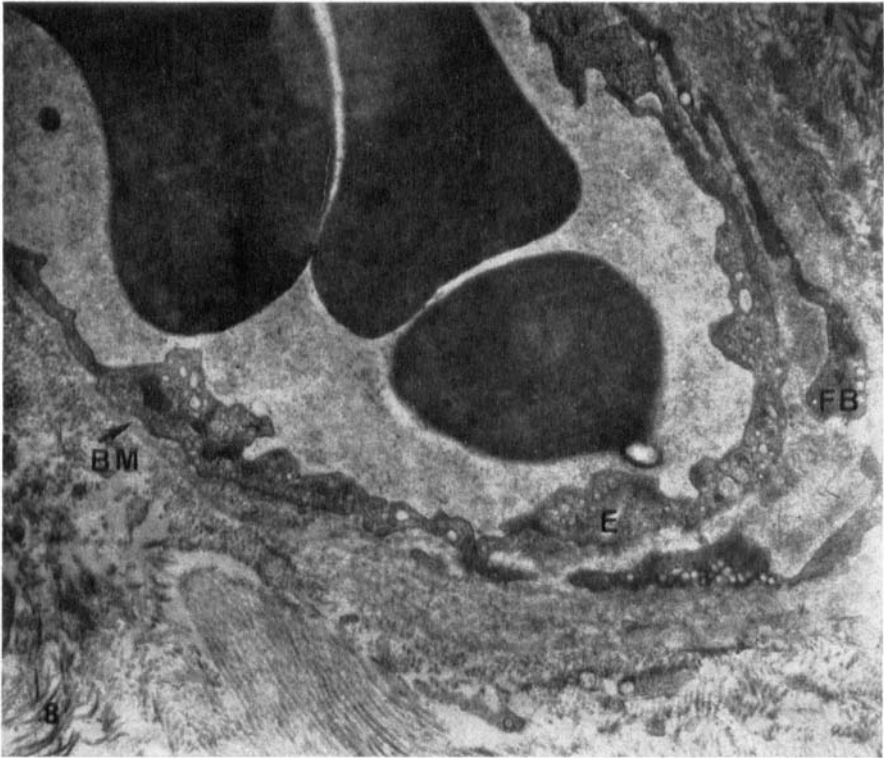


Figure 8. Survey electron micrograph of a capillary in the synovial tissue from a salicylate-treated joint. The endothelium (E) is thinner than in the arteriole (cf. Figure 2). Close to the outer surface of the endothelium there is a basement membrane (BM) and more peripherally several slender projections from fibroblasts (FB) are seen as well as bundles of collagenous fibrils.—Magnification $\times 7,000$.

Regenerated Synovial Tissues in Dog Joints not Subjected to any Injections

In all, the post-operative course was uncomplicated. The joints could be freely moved without impairment or pain. On macroscopic examination at termination of the experiment, two months after synovectomy, the zone of incision was quite reactionfree though the tissues were slightly thicker, harder and more firm than the surrounding tissues. There were no adhesions between the individual layers which were easily separated. The synovial tissue had regenerated and appeared as a very thin glossy membrane without any obvious richness in vessels. The tissue could easily be removed from the femoral condyles and excised as a sac. No oedema was present. No ruptures or other structural

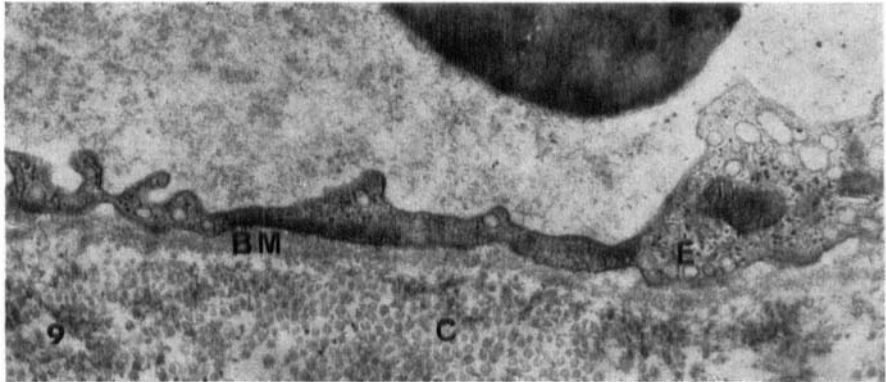


Figure 9. Electron micrograph of a detail of the capillary in Figure 8. Over a long distance the endothelial cell (E) is very attenuated but there are no breaks in the capillary lining. Even the thin portions contain pinocytotic vesicles, a few ribosomes and filaments. The basement membrane (BM) forms a continuous layer along the endothelium. (C) denotes cross-sectioned collagenous fibrils.

Magnification $\times 32,000$.

abnormalities were observed. The cartilage appeared normal. Nothing abnormal was seen in the bone cartilage zone. There was no increase in synovial fluid.

Histology: The microscopic examinations revealed normal synovial tissue. No structural aberrations were noted.

Microangiography: In Figures 5 a and b the vascular pattern is more lively and active indicating a response of repair type. The vessels are smooth but slightly tortuous, but the increase of vessels falls within the normal limits or vascular response to the activity of regenerating tissues.

DISCUSSION

The purpose of this study was to test some anti-inflammatory drugs commonly used in rheumatoid arthritis when administered locally in joints. The question of interest was to what extent these drugs may influence the morphologic structure of the present synovial tissue and if any interference of these could be noted in the regeneration of synovium after synovectomy.

The synovium regenerates within 90 days after synovectomy in normal animal joints (Sumita 1912, Key 1925, Lindström 1963). The regenerated tissue is considered to be structurally and functionally normal. In rheumatoid arthritis, it is claimed that after synovectomy

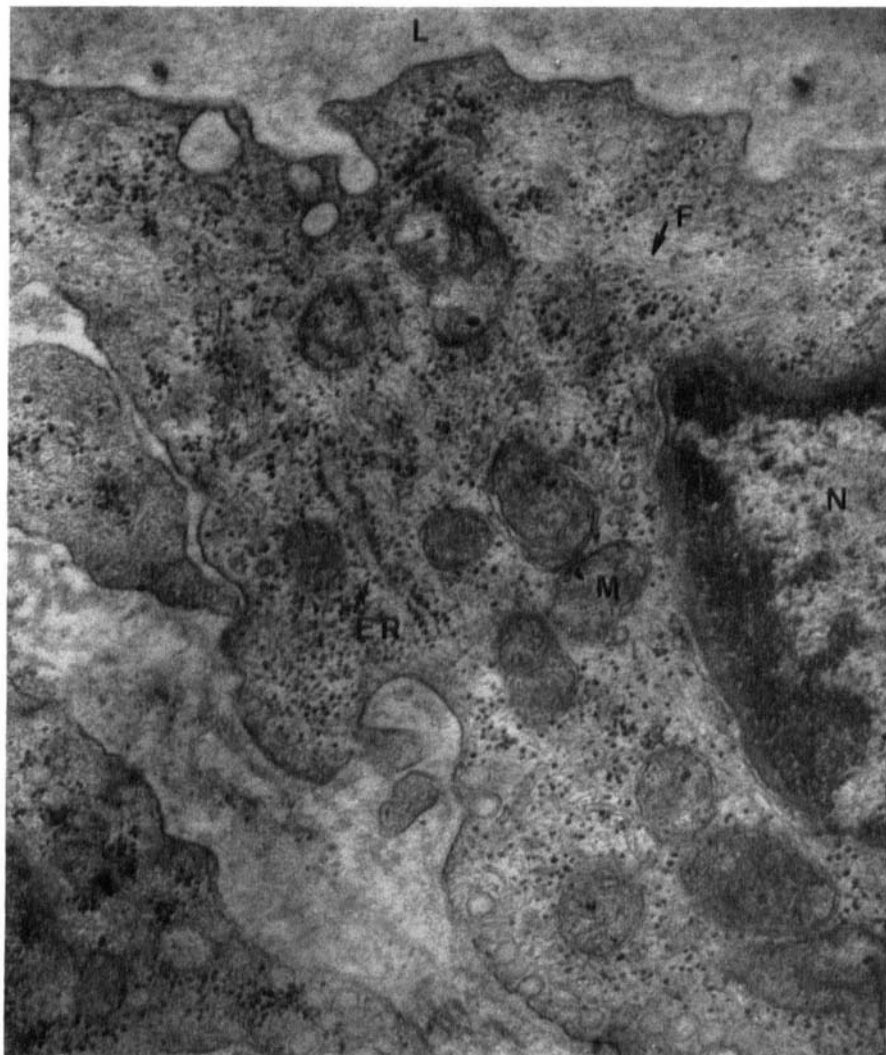


Figure 10. Electron micrograph of a detail of a capillary (salicylate-treated joint) showing a thick portion about the cell nucleus (N) of an endothelial cell. It is clear that there are no essential structural differences between this endothelial cell and that of the arteriole in Figure 7. M—mitochondrion, ER—endoplasmic reticulum, F—filaments, L—capillary lumen.—Magnification $\times 37,000$.

the regenerated synovial tissue also is normal from a morphologic point of view (*Preston 1967, Marmor 1966*). Certain observations made by one of us (*Goldie 1967*) indicate, however, that post synovectomy the regenerated tissue may retain a morphologic appearance similar to that of the original diseased synovium. With that in mind it has been assumed that whatever anti-inflammatory properties the drugs commonly used for local application in rheumatoid arthritis may have, or which could be used in this application, may, on administration immediately after synovectomy, subsequently influence the regenerating tissue to normal appearance and function.

Before engaging on an investigation of this kind, it is, however, essential to establish the innocuousness of the drugs employed.

We have already pointed out (*Brånemark, Goldie & Lindström 1967, Brånemark & Goldie 1967*) that certain steroid preparations contain components in the suspension vehicle which have a deleterious effect on the microcirculation in normal synovial tissues. The retarding effect on healing tissues of steroids is also well-known.

As steroids are used for local therapy in rheumatoid arthritis, it was thought of some interest to investigate their properties in joints with regenerating tissues of normal type. If no adversities were encountered in this procedure it may well be possible to institute an injection therapy following synovectomy. This is of particular interest as own observations (*Goldie 1967*) indicate that the pathologic process appears to accompany the regeneration.

The results in this investigation disclose that certain steroids containing high molecular preservatives of the type sorbitol as does prednisolone tertiary butyl acetate cannot be used because of their tissue destroying properties. Pure steroids do not however cause this damage and it is therefore desirable that they are suspended in vehicles which do not contain tissue destructive components. The use of methylprednisolone acetate has in this investigation yielded no adverse effects. This may therefore be a drug which could be tried as an anti-inflammatory agent following synovectomy.

The analgesic properties of salicylates are well known but little has been investigated on their anti-inflammatory characteristics in local application. *Fremont-Smith & Bayles (1965)* have come to the conclusion that the important action of salicylates is their inhibition of inflammation and secondary to this an analgesia ensues. *Fearnley & Nixon (1965)* have used intra-articular injections of 5 per cent benzylsalicylate in patients with osteoarthritis in the knee. Moderate improve-

ment in the clinical condition was noted and no adverse effects of the locally applied salicylate were observed.

As shown in this investigation, salicylates do not appear to have any deleterious influence on normal regenerating animal synovial tissue either in an early stage or in the later development.

Moreover, it has been shown that human synovial tissues do not react inadvertently to local application of salicylates (*Faernday & Nixon* 1965). The results of synovectomy as such are certainly encouraging but could be improved and it remains desirable that the regenerated tissue should be normal in structure and function after synovectomy. As certain observations indicate that the regenerating synovial tissue holds some pathomorphologic characteristics of the inflammatory type (*Goldie* 1967), these might be combated by the use of anti-inflammatory drugs early in the postsynovectomy phase. The local application of salicylates in this phase may therefore be justified.

SUMMARY

Besides general therapeutic measures in rheumatoid arthritis treatment also includes procedures acting more concentratedly on the local articular manifestations. This can be achieved by anti-inflammatory substances like steroids and salicylates.

It is of importance to know what the reaction of the tissues lining the joint cavity may be to a particular local treatment and its influence on the regenerating tissue after synovectomy. Therefore a study has been carried out on the influence of anti-inflammatory drugs on animal synovial tissues.

Methylprednisolone acetate (Depomedrone), prednisolone tertiary butyl acetate (Codelcortone TBA) and 0.2 per cent of salicylate were used. These were injected into the knee joints of rabbits and dogs.

The rabbit knee joints were synovectomized and following this the substances were injected at regular intervals.

In the dogs one knee joint was injected with salicylate solution without previous synovectomy. The contralateral side was synovectomized without any injections being made.

The results disclosed that rabbit knee joints injected with Depomedrone and salicylate solution showed no pathologic abnormalities. Those injected with Codelcortone TBA showed marked changes with ruptures of operating wounds and granulation tissue formations.

The dogs disclosed nothing abnormal.

Registration of the results was made by ordinary histology, micro-angiography and electron microscopy for particular study of the vessel walls which revealed no pathologic abnormalities.

It has become apparent from this investigation that some drugs with anti-inflammatory properties when locally applied on the whole are substances without obvious noxious effects on individual structural elements in original and regenerating synovial tissues. Local application of these may serve as a therapeutic adjuvant in the postsynovectomy phase in certain patients in whom it appears that the pathologic process accompanies the regeneration of synovial tissues, the pathologic function of which should be combated.

RESUME

A côté de mesures thérapeutiques générales, le traitement de l'arthrite rhumatoïde peut aussi comprendre une action plus concentrée sur les manifestations articulaires locales. Cela peut être réalisé au moyen de substances anti-inflammatoires telles que les stéroïdes et les salicylates.

Il est important de savoir quelle peut être la réaction des tissus revêtant la cavité articulaire à un traitement local particulier et son influence sur le tissu de régénération après synovectomie. C'est pourquoi nous avons étudié l'influence des médicaments anti-inflammatoires sur le tissu synovial des animaux.

L'actate de méthylprednisolone (Depomedrone), l'acétate butylique prednisolone tertiaire (Codelcortone TBA) et une solution de 0.2 pour cent de salicylates ont été utilisés. Ils ont été injectés dans les articulations du genou de lapins et de chiens.

Il a été procédé à une synovestomie de l'articulation du genou des lapins, après laquelle les substances furent injectées à intervalles réguliers.

Dans les articulations du genou des chiens, il fut injecté une solution de salicylates sans synovectomie préalable. Une synovestomie a été pratiquée dans le côté contralatéral sans faire d'injections.

Les résultats révèlent que les articulations du genou des lapins injectés avec Depomedrone et solution de salicylate ne présentent aucune anomalie pathologique. Chez ceux injectés avec Codelcortone TBA on a constaté des altérations marquées avec rupture des plaies d'opération et formations de tissu de granulation.

Chez les chiens rien d'anormal.

L'enregistrement de ces résultats a été fait par histologie ordinaire,

microangiographie et microscopie électronique pour étude particulière des parois des vaisseaux qui n'ont pas révélé d'anomalie pathologique.

Cette étude a fait ressortir que certains médicaments ayant des propriétés anti-inflammatoires sont dans l'ensemble, lorsqu'ils sont administrés localement, des substances sans effet nocif visible sur les éléments structuraux individuels du tissu synovial original ou régénéré. Une application locale de ceux-ci peut servir de thérapeutique adjuvante dans la phase qui suit la synovectomie pour certains malades chez lesquels il apparaît un processus pathologique qu'il convient de combattre, accompagnant la régénération du tissu synovial.

ZUSAMMENFASSUNG

Abgesehen von allgemeinen therapeutischen Massnahmen bei der chronischen rheumatischen Arthritis, schliesst die Behandlung auch Verfahren ein, die konzentrierter auf die örtlichen Gelenksercheinungen wirken. Dies kann mittels entzündungshemmender Stoffe wie Steroide und Salycilate erreicht werden.

Es ist wichtig zu wissen welches die Reaktion der Gewebe, die den Gelenksraum umgeben, gegenüber einer besonderen lokalen Behandlung sein kann und ihren Einfluss auf regenerierendes Gewebe nach Synovectomie zu kennen. Deshalb wurde eine Untersuchung über die Einwirkung von entzündungshemmenden Mitteln auf tierisches Synovialgewebe ausgeführt.

Methylprednisolon Acetat (Depomedrone), Prednisolon tertiäres Butyl Acetat (Codelcortone TBA) und 0.2 Prozent Salycilatlösung wurden verwendet. Diese wurden in das Kniegelenk von Kaninchen und Hunden eingespritzt.

Eine Synovectomie der Kaninchenkniegelenke wurde vorgenommen und nachher wurden diese Substanzen in regelmässigen Zwischenräumen injiziert.

Bei den Hunden wurde ein Kniegelenk ohne vorhergehende Synovectomie mit der Salycilatlösung injiziert. Die kontralaterale Seite wurde synovectomiert ohne dass man Einspritzungen vornahm.

Die Resultate ergaben, dass Kaninchengelenke, die mit Depomedrone und Salycilatlösung injiziert worden waren, keine pathologischen Anomalien aufwiesen. Jene, die mit Codelcortone TBA injiziert worden waren, zeigten bedeutende Veränderungen mit Rupturen der Operationswunden und Bildung von Granulationsgewebe.

Die Hunde wiesen keine Anomalien auf.

Die Einteilung der Ergebnisse wurde mittels gewöhnlicher Histologie, Mikroangiographie und Elektronmikroskopie zwecks besonderem Studium der Gefäßwände, die keine pathologischen Anomalien aufwiesen, gemacht.

Aus dieser Untersuchung geht hervor, dass einige Drogen mit entzündungshemmenden Eigenschaften, wenn örtlich angewendet, im allgemeinen Stoffe sind, die keine augenfällige, schädliche Wirkung auf individuelle Strukturelemente von ursprünglichem und regenerierenden Synovialgewebe ausüben. Lokale Anwendung von diesen kann als therapeutisches Hilfsmittel in der Postsynovektomie-Phase bei gewissen Patienten, bei denen es scheint, dass der pathologische Prozess die Regeneration des Synovialgewebes begleitet, und dessen pathologische Funktion bekämpft werden sollte, dienen.

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