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THE NUTRITIVE SUPPLY AND NUTRITIONAL VALUE OF SYNOVIAL FLUID

By

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The problem of the nutrition of the articular cartilages has been of current interest ever since the latter half of the nineteenth century, when it was proved by means of morphological investigations that this tissue had no blood-vessels. Two main theories are generally recognised as to the course by which the nutriment reaches the cartilages.

According to the first theory, the articular cartilages are supplied by the blood-vessels of the underlying medullary cavity and bone, as well as from small branches of vessels that radiate from the lines of attachment of the joint-capsule to the most peripheral portions of the articular cartilage (Hunter 1742, Toynbee 1841, Wollenberg 1909).

The second theory states that the articular cartilage obtains its nutriment from the synovial fluid which it is assumed that the synovial membrane and its vessels form (Hildebrand 1896, Schmieden 1900, Bier 1919, Strangeways 1920).

Previously, several authors have been of the opinion that the cartilages receive their nutrition from both these sources (Leidy 1849, Fisher 1922, Ishido 1923, Ito 1924, Axhausen 1924). However these investigations have not taken into consideration such important factors as differences in the facilities for the passage of high- and low-molecular solutions or suspension of particles.

In recent years, the consensus of opinion in medical literature has been that the articular cartilages receive their nourishment from the synovial fluid. In the investigations that Holmdahl, Sääf, Ekholm and myself have lately completed, we have found nothing that in any respect contradicts the accuracy of this view. However, some results were obtained that also suggested the existence of a fluid passing between the medullary cavities of the epiphysis and the articular carti-

lages. As I take it for granted that the first opinion is well known, I shall, in this paper, deal mainly with the second.

It has long been known that the articular cartilages of a joint which is prevented from functioning satisfactorily, i.e. a joint subject to repeated physiological compressions, undergo degenerative changes, in all probability, mainly on account of their unsatisfactory nutrition. Furthermore, it is known that if a cartilage is subjected to pressure by a pelotte, liquid is forced out from the surface of the cartilage in such a way that a number of small drops are formed around the pelotte. (Bär 1926, Hirsch 1944). In spite of the fact that, in this case, it is realised that we are dealing to a certain extent with a non-physiological pressure, the observation nevertheless seems to indicate that the compression of an articular cartilage causes a transference of liquid from the latter into the joint cavity.

This observation gives rise to the question whether repeated compressons of articular cartilages cause a certain reduction of the amount of liquid in the articular cartilages during the function of the joint, a reduction that is not compensated for until the cartilage is at rest or unless the said removal of liquid during the compression is rapidly balanced by a flow into the articular cartilages from somewhere else. In both cases it is of importance to ascertain where the liquid mentioned above originates from.

In connection with other investigations, concerning the physical qualities and functional adaptability of the articular cartilages, the conditions of strain in the joints etc., that have in recent years been completed by Holmdahl, Sääf, Ekholm and myself, these problems have become of very great current interest to us.

Sääf and I therefore made an investigation, published in 1948 in Acta Orthopaedica Scand., where we attempted to study the circulation of liquid in the articular cartilages during movement as well as at rest.

In connection with our earlier investigations of joints we have observed that, in rabbits' as well as those of guinea-pigs', there are portions where the medullary cavity is in contact with the basal parts of the articular cartilage without any intervening bone lamella. We then thought it possible that the articular cartilages might get a supply of liquid from the medullary cavity via these surfaces of contact. In order to investigate this matter, a suspension of rice starch granulated into minute particles was injected into the medullary cavities of the epiphyses of newly killed rabbits. Without opening the joints, the ball and socket were pressed together so as to correspond as far as possible to the way in which the animal runs.

The articular cartilages were then subjected to histological treatment, and at the examination of the sections, grains of starch could be observed in the articular cartilages. It then appeared that joints whose cartilages were not subjected to repeated compressions had grains of starch mainly in their central and basal portions, (every portion being a third of the thickness of the cartilage), but none in the synovial fluid. On the other hand, in joints that had been subjected to repeated compressions, most of the grains of starch were to be found in the upper and medial portions of the articular cartilages. In all these joints, grains of starch were also found in the synovial fluid. The grains of starch found in the articular cartilages could not have passed from the synovial membrane via the joint cavity into the articular cartilages as we were unable to prove the existence of any grains of starch in the articular cartilages, after intra-articular injections of the suspension of starch followed by compressions of the joints were carried out. We considered these observations to imply first, that liquid passes from the medullary cavities of the epiphyses via the surfaces of contact with the articular cartilage, and into the latter, and that a part of it then continues into the joint cavity, and, secondly, that this circulation is more active when the joint is in function than when it is not.

A grave objection to these results may be that we have not here worked under physiological conditions. But when intravenous injections of the suspension of starch were given to live animals, grains of starch were likewise noticed in the articular cartilages. This fact undoubtedly proves the accuracy of the results obtained.

The above mentioned surfaces of contact between the medullary cavities of the epiphyses and the basal parts of the articular cartilages have not before been the object of any particular attention in medical literature. It has been the general opinion that the articular cartilages lie against a homogenous bone lamella without perforations. Writers who have examined and described the surfaces of contact, have usually considered them to be temporary formations existing only during the progressive evolutionary phase of the bones.

Holmdahl and I have therefore studied these conditions somewhat more closely. In a paper now completed, we have examined these problems in rabbits. (A similar investigation of the conditions in man is in progress). Through these investigations it has been proved that all joints have such contacts. These contacts can, without any particular difficulty, be divided into two categories. The one consists of "canal-like" passages with a diameter of about 15 μ (Fig. 1). These, which are filled with vessels, stretch from the medullary cavities via relatively

thick bone lamellae into the cartilage. The other type we have called "wide contacts". They consist of fairly large connecting surfaces between the medullary cavity and the articular cartilage (Fig. 2). Their diameters are on the average about 50 μ. The total relative sur-

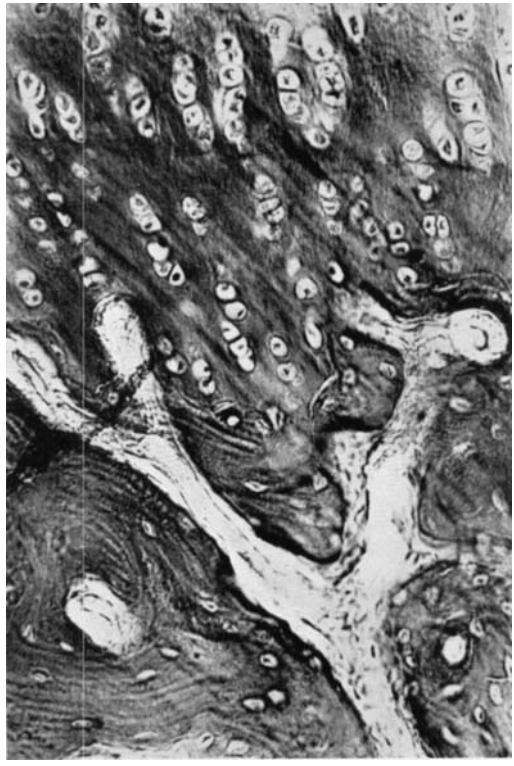

Fig. 1.

"Canal-like contacts" between the medullary cavity and the articular cartilage.

face of these contacts is no less than one per cent and about seven per cent for certain surfaces of the joints.

In the distal end of the femur in rabbits the above conditions are found if the groove between the femoral condyles is examined. Between the distal part of the condyles, where in the normal position of the joint, the patella lies against the femur, there are practically only "canal-like" contacts. The bone lamella that here supports the articular cartilage is thick and relatively compact without any particularly large medullary cavities. More proximally, in the groove

mentioned, the lamella is thin and the number of "canal-like" contacts are very small. On the other hand, here there are numerous large surfaces of contact, a fact which indicates that the bone lamella is perforated to a great degree.

I have examined a great number of different species of mammals,

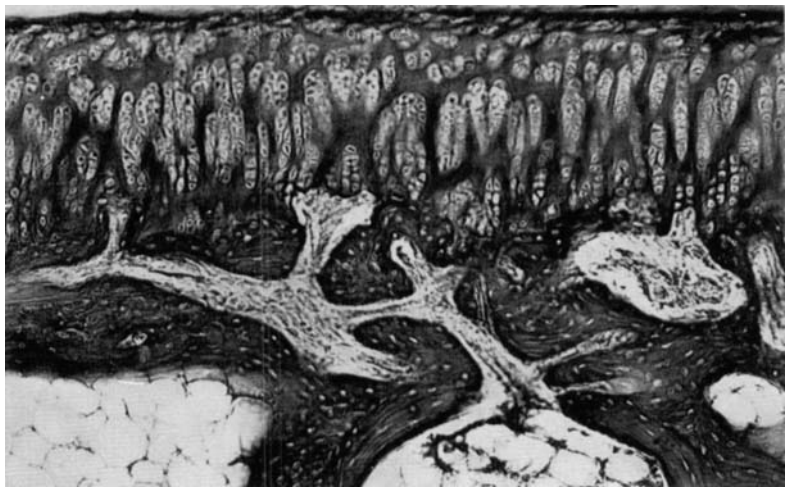

Fig. 2.

"Wide contacts" between the medullary cavity and the articular cartilage.

and I have found that corresponding conditions seem to be applicable to them. In man as well, there is a large amount of such contacts between the medullary cavities of the epiphyses and the articular cartilages.

This fact seems to justify the general conclusion that in mammals there exist possibilities for a passage of fluid from the medullary cavities into the articular cartilages. On the other hand we do not know what factors make the passage possible at the connection between the medullary cavity and the cartilage.

Ekholm and I have made some radiological investigations of the thickness of the articular cartilages in various functional conditions. These investigations have been made on rabbits as well as on man, and we employed a radiological technique which enabled us to determine to a minute degree the total thickness of the cartilages of the femur and the tibia in the knee-joint.

As a result of the examination of the rabbit material (Ingelmark

and Ekholm 1948) we found that the thickness of the articular cartilages decreases at rest, but that function rapidly increases the thickness of the cartilages (Fig. 3). These differences have been statistically proved.

This implies that the thickness of the articular cartilages rapidly increases when they are subjected to repeated compressions and that it decreases when the stress ceases. It is hardly imaginable that such

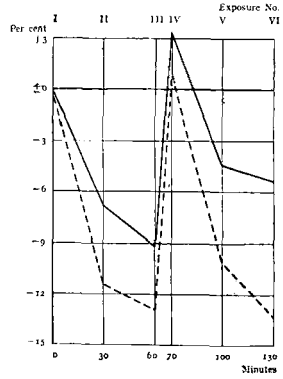

Fig. 3.

I-II. 30 min. rest. II-III. 30 min rest. III-IV. 10 min. function. IV-V. 30 min. rest. V-VI. 30 min rest.

a rapid increase of thickness can be realised in any other way except by the entrance of more liquid into the cartilage. Naturally the investigation does not answer the question from where that liquid originates, nor does it tell us how the fluid is eliminated when the joint becomes inactive. Considering the results of the above briefly-mentioned starch experiment, where, during function of the joints, grains of starch were found consistently and chiefly in the most superficial parts of the articular cartilage and in the synovial fluid, so it is likely that some of the liquid supplied originates from the medullary cavities of the epiphyses.

These results obtained with rabbit material naturally stimulated the investigation to include man as well. The material hitherto studied comprises in all 101 persons without any clinically or radiologically noticeable changes in their knee-joints, 177 suffering from rheumatic polyarthritis and 74 from arthrosis deformans in these joints. The experiments were carried out as follows: The patients were placed in a special training apparatus, in which the leg which was to be exa-

mined could move, so that the knee-joint was exposed to repeated, fairly physiological compressions, such as take place, for example, when a person walks. After an interval of about 30 minutes during which time the subject was not allowed to stand on his legs, exercises were performed for 10 minutes. In about 80 per cent of the cases there occurred an increase of the thickness of the cartilage in all the above three groups. After the work the subject was allowed to rest for

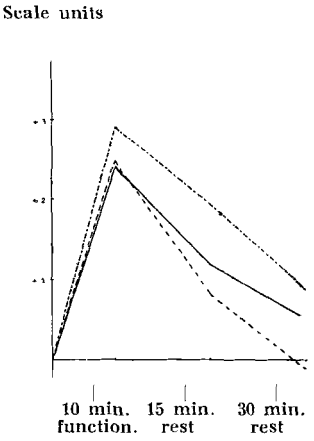

Fig. 4.

———— = Patients with no demonstrable articular disease.
— — — — = Patients with rheumatic polyarthritis.
— · — · — · = Patients with arthrosis deformans.

30 minutes without straining the knee-joint. The thickness of the cartilage was measured after 15 and after 30 minutes. During this time, the thickness of the cartilage gradually decreased. This process also took place in fundamentally the same way in the three groups.

By statistical arrangement of the material hitherto obtained, we have tried to ascertain whether the diseases investigated cause any changes in the increase of thickness of the articular cartilages when in function, and in the decrease of thickness when inactive. Furthermore, we have studied the influence of age on these circumstances.

Figure 4 gives a schematic picture of these conditions. The curve for the cases of arthrosis deformans in every point lies above the one for the patients with rheumatic polyarthritis. The persons not suffering from any disease occupy on the whole an intermediate position. No statistically confirmed differences exist in the isolated points. The aspect and relative position of the curves, however, seem to indicate that in arthrosis deformans the cartilages absorb liquid more easily

during function of the joints, but that they shrink less easily when inactive than in rheumatic polyarthritis.

The average age of the patients suffering from rheumatic polyarthritis is 44 years and 58 years in cases with arthrosis deformans. It might, therefore, easily be suspected that the differences indicated are due to the difference in age. On the basis of their age, the healthy persons have, therefore, been divided into two groups. In the group

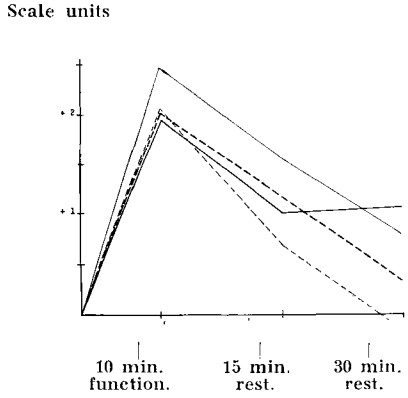

Fig. 5.

——— = Patients with no demonstrable articular disease. Average age 35 years.
– – – – = Patients with no demonstrable articular disease. Average age 55 years.
——— = Patients with arthrosis deformans. Average age 58 years.
— — — = Patients with rheumatic arthritis. Average age 44 years.

where no one was more than 45 years old, the average age was 35. The second group includes subjects older than 45, with an average age of 55. From figure 5 it is clear that no notable differences exist between these groups except in the shrinkage of the cartilage. In the young and in the old subjects the shrinkage is about the same during the first 15 minutes of rest. During the continued period of rest, however, no shrinkage takes place in the young persons, while it continues as before in the old ones. This indicates that in cases of arthrosis deformans the articular cartilage is on the whole congruous with that of the older people who do not suffer from any disease.

Naturally, the curves obtained stimulate further speculations, but at the present stage of the investigation it is, perhaps, more correct to avoid these.

Lately Ekholm has tried to study in more detail the nutritional conditions of the articular cartilage by intravenous injection of radioactive gold in the form of its chloride into rabbits under varying

functional conditions. Thus he works with a substance, foreign to the body and which is, according to available literature, distributed all over the body without special affinity for any tissues. It could, therefore, be assumed that this substance is well suited to give a reliable view of the circulation of fluid in different parts of the body.

By the use of a special training apparatus, allowing exact distribution of the function of the joints, one leg of the animal experimented on was made to work while the other remained inactive. Thus, by comparison of the values from the two knee-joints of one animal, a good picture is obtained of the influence of the exercise on the circulation of fluid in the articular cartilages.

The results hitherto obtained mainly imply a confirmation of those which we have earlier achieved by another method. Thus, the cartilage of joints exercised during 10 to 20 minutes contains considerably more radio-active gold than the cartilage of the unexercised joints of the animals during the same experiment. We have made no observations which contradict the fact that at least part of the gold has come into the articular cartilages from the medullary cavities of the epiphyses.

If we summarize the results of the investigations so far completed on the nutrition of the articular cartilages and its connection with the formation of the synovial fluid, we may express it as follows. By increased function of the joints a certain swelling of the cartilages begins within a few minutes. The swelling gradually disappears during inactivity, but usually the articular cartilages do not resume their normal thickness until half an hour or one hour after the exercise has been completed. This swelling of the cartilage can probably only be explained by an absorption of liquid. As compressions of the articular cartilages must also cause a removal of fluid from the tissue, it can be deduced that physiological function of the joint causes an increased amount of fluid to pass through the cartilage. This fluid may originate from the synovial fluid as well as from the medullary cavities. It is commonly recognized that the first-mentioned alternative prevails, a fact not at all contradicted by the results of our investigations. However, this implies that part of the fluid has been transferred from the medullary cavities of the epiphyses. In all probability the exchange of fluid between the articular cartilages and the medullary cavities takes place through the contacts between them, as described above. Which of these two supplying passages is the quantitatively dominating one during various functional conditions, and whether any qualitative differences exist between them, are problems that we hope to answer by continued investigation.

SUMMARY

The articular cartilages are lacking in blood vessels of their own. Two main theories have been advanced regarding their means of nutrition. According to the one, the articular cartilages are supplied by the blood vessels in the medullary cavities of the joint extremities. According to the other, the articular cartilages receive their nourishment from synovial fluid. The latter theory is the one which has dominated medical literature in recent years. Results of investigations which the writer has carried out in co-operation with D. E. Holmdahl, J. Sääf and R. Ekholm have confirmed the accuracy of this conception. A number of observations have however been made, which argue strongly in favour of the former theory. The most important points are contained in the following:

In certain important areas the basal parts of the articular cartilage lie in direct contact with the medullary bone of the joint extremities, so that the bone lamella, on which the articular cartilage rests, is amply perforated. The medullary bone passes through these perforations for some distance into the basal portions of the articular cartilage. In association with joint function the articular cartilage quickly increases in thickness. This increase must occur as the result of a supply of fluid to the cartilage. Intravenous injections of a suspension of finely granulated rice starch, as well as of radioactive gold, have been made and these have been found to be present in greater quantity in cartilage from a joint which functions, than from one which remains at rest. The distribution of these substances in different layers of the articular cartilages shows that they have partly reached the cartilage from the blood vessels in the medullary cavities of the joint extremities. Thus the results obtained from these investigations argue that the articular cartilages probably receive nutrition from synovial fluid and equally so from the blood vessels of the medullary cavities of the joint extremities.

RÉSUME

Les cartilages articulaires ne possèdent pas leurs propres vaisseaux. Deux théories principales ont été avancées en ce qui concerne leur mode de nutrition. Suivant l'une les cartilages articulaires sont alimentés par les vaisseaux sanguins des cavités médullaires des extrémités de l'articulation. Suivant l'autre, les cartilages articulaires sont alimentés par le liquide synovial. Cette dernière théorie est celle qui a dominé dans la littérature médicale de ces dernières années. Le

résultat d'investigations faites par l'auteur en coopération avec MM. D. E. Holmdahl, J. Sääf et R. Ekholm ont confirmé l'exactitude de cette conception. Toutefois, un certain nombre d'observations parlent en faveur de l'ancienne théorie. En voici les points les plus importants:

Dans certaines étendues, la partie basale du cartilage articulaire est placée en contact direct de la partie médullaire de l'os dans les extrémités de l'articulation, de sorte que la lamelle osseuse sur laquelle repose le cartilage articulaire est fortement perforée. De ce fait la partie médullaire de l'os pénètre dans la partie basale du cartilage articulaire.

Lorsque l'articulation est en fonction, le cartilage articulaire augmente rapidement d'épaisseur. Cette augmentation doit être le résultat d'un apport de liquide dans le cartilage. Des injections intraveineuses d'une suspension finement granulée d'amidon de riz et d'or radioactif ont été pratiquées et l'on a constaté la présence de quantités beaucoup plus élevées de ces substances dans les cartilages d'une articulation en fonction que dans une articulation au repos. La distribution de ces substances dans les différentes couches du cartilage articulaire montre qu'elles sont arrivées au cartilage en partie par les vaisseaux sanguins des cavités médullaires des extrémités de l'articulation.

En conséquence, les résultats de ces investigations indiquent que les cartilages articulaires reçoivent probablement leur nourriture du liquide synovial et également des vaisseaux sanguins des cavités médullaires des extrémités de l'articulation.

1) Note du Prof. Bo E. Ingelmark lue à une conférence de l'Association Orthopédique, à Stockholm, novembre 1949.

ZUSAMMENFASSUNG

Die Gelenksknorpel haben keine eigenen Blutgefässe. Zwei Haupttheorien zur Erklärung ihrer Ernährung sind aufgestellt worden. Nach der einen werden die Gelenksknorpel von den Blutgefässen der Markhöhlen der gelenkbildenden Knochen ernährt. Nach der anderen erhalten die Gelenksknorpel ihre Ernährung von der Synovialfluessigkeit. Die letztere Theorie hat die medizinische Litteratur der neueren Zeit beherrscht. Resultate von Untersuchungen die der Verfasser zusammen mit D. E. Holmdahl, J. Sääf und R. Ekholm ausgeführt hat, haben die Richtigkeit dieser Auffassung bestätigt. Eine Anzahl von Beobachtungen wurden jedoch gemacht, die sehr zu Gunsten der

ersteren Theorie sprechen. Die wichtigsten Punkte sind im Folgenden enthalten:

In gewissen wichtigen Gebieten liegen die basalen Partien des Gelenksknorpels in direktem Kontakt mit der Spongiosa der Gelenksbildenden Knochen, derartig das die Knochenlamellen auf denen der Gelenksknorpel ruht, reichlich perforiert sind. Der Markknochen passiert diese Perforationen fuer eine begrenzte Strecke in die basalen Anteile des Gelenksknorpel. Im Zusammenhang mit der Gelenksfunktion nimmt die Dicke des Gelenksknorpels rasch zu. Diese Zunahme muss das Resultat einer Versorgung des Gelenksknorpels mit Flüssigkeit sein. Intravenöse Injektionen sowohl von feingranulierter Reisstärke als auch von radioaktivem Gold wurden ausgeführt und es wurde gefunden, dass sie in grösseren Mengen in Knorpel von Gelenken mit Funktion, als in solchen, die in Ruhe gehalten wurden, nachzuweisen sind. Die Verteilung dieser Stoffe in den verschiedenen Schichten des Knorpels zeigt, dass sie teilweise den Knorpel von den Blutgefässen der Markhöhlen aus erreicht haben. Die Resultate, die in diesen Untersuchungen erhalten wurden, sprechen deshalb dafür, dass der Gelenksknorpel wahrscheinlich Ernährung von der Synovialflüssigkeit und in gleicher Weise auch durch die Blutgefässe der Markräume der gelenkbildenden Knochen erhält.

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