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CHANGES IN THE CHONDROITIN SULPHATE CONTENT AND DISTRIBUTION IN CARTILAGE IN INFECTIVE AND ASEPTIC OSTEOARTHRITIS

BY

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Our knowledge of the physiology and pathology of cartilage is still incomplete. During recent years attention has been directed to the sulphuric acid esters of high molecular weight, which are found in the intercellular substance of cartilage. Now that the technique for studying the distribution of chondroitin sulphates in degenerating cartilage has been perfected, a new method of investigation is available and may lead to a better understanding of certain joint diseases.

The histochemical technique introduced by Lison has been used. It is a metachromatic reaction which allows an exact localisation of the sulphate esters of high molecular weight. Further studies on this staining method have been published by Sylvén and Hirsch.

It has been shown (Hirsch) that in the early stages of cartilage destruction in *non-infective osteo-arthritis*, the content of chondroitin sulphate decreases from the articular surface inwards to deep down in the perpendicular zone; further, a reduction in the content of ester-bound sulphur in the perpendicular zone is never found without accompanying more marked changes in the cartilage nearer the articular surface (tangential and transitional zones). The reasons for this last are obscure, but it seems that mechanical factors are of considerable importance in the distribution of the fluids in

cartilage, and consequently in its nutrition. The cartilage is constructed so that compression is greatest, and consequently the flow of fluid least, near the surface, and this is most marked in those joints or parts of a joint where the pressure per unit area is increased as a result of incongruity of the articular surfaces (Hirsch). Here the flow of tissue fluids and the nutrition will be reduced, and degenerative changes with loss of chondroitin sulphate will occur.

In early cases of osteoarthritis of the hip-joint in young people there is often an incongruity of the joint surfaces following congenital dislocation of the hip, congenital coxa vara, rickets, Perthes' disease or slipped epiphysis. The radiographs of these cases often show that the changes appear first in the lateral part of the joint (Hermodsson). This may be the result of incongruity of the joint surfaces and an increase in pressure per unit area. In osteoarthritis of the hip in elderly people the early changes are more medial or even central.

We do not know the biological processes which lead to the disappearance of chondroitin sulphate. The method of nutrition of cartilage is still not fully understood; little is known about the blood-supply of the border zone between bone and cartilage, and still less about the circulation of fluid in hyaline articular cartilage.

Infections in or near a joint may have various effects on the articular cartilage. Some infections lead to a rapid destruction of the cartilage and ankylosis. This often occurs in gonococcal arthritis (Hirsch, Sylvén). Others, e.g. streptococcal and tuberculous infections, are similarly destructive to the joint cartilage. All types of infective arthritis are alike, in that the chondroitin sulphate does not disappear in the same regular manner as in aseptic necrosis of the cartilage. In specimens taken from various types of infective arthritis it has been possible to demonstrate definite more or less irregular areas where the chondroitin sulphate was considerably reduced. Areas which did not show metachromatic staining were found deep to more superficial layers which gave a normal reaction. This suggests that the process of cartilage destruc-

tion in infected joints is different from that in aseptic osteoarthritis.

Recently Sylvén has stressed the significance of the altered acidity of inflamed tissue, in which the reaction is shifted towards the alkaline side. Since chondroitin sulphate is not stable in an alkaline medium its breakdown might be explained by this shift. On the other hand it is known that certain bacteria can produce substances which break down the polysaccharides (Meyer, Chaffee, Hobby, Dawson, etc.), and, in certain cases, bacterial activity may produce conditions in which the polyester sulphuric acids of the cartilage are broken down.

Since, presumably, at least some of the cartilage's nutrition comes in tissue fluid from the underlying bone it is justifiable to assume that the factors, which in infective conditions, either alone or with other causes, affect the chondroitin sulphate, can act on the deeper layers of the cartilage without reaching the superficial layers. In addition, infective agents can reach the cartilage via the synovial membrane either across the junction between the membrane and the cartilage or in the exudate which is formed in infective arthritis. Theoretically, therefore, one would expect to find a quite irregular picture of the destruction of the hyaline matrix in infective conditions, and this is in fact seen in the histological preparations. One is thus able to determine whether changes in degenerated cartilage are due to aseptic or infective processes by studying the distribution of chondroitin sulphate in it.

In so far as *aseptic necrosis* of cartilage must be attributed to mechanical disproportion our prophylaxis and therapy are presumably limited. One cannot overemphasise the importance of satisfactory correspondence of the joint surfaces in the prevention of osteoarthritis, but so far the technical possibilities in this respect are very limited.

In *infective arthritis* we have not so far had sufficient opportunity to observe the factors which lead to chondrolysis. Sulfonamide and penicillin preparations have enabled us in some cases to eliminate the infection; but our efforts must

also be directed to arresting the process which often leads to a rapid selective breakdown of the chondroitin sulphate.

Chondroitin sulphate holds a key position in our present knowledge of the biology of cartilage. One may perhaps hope that further research on it will lead to better prophylaxis and treatment. Cartilage damage plays a big part in the disabling processes to which mankind is susceptible.

SUMMARY

The author has examined the cartilage from joints which showed osteoarthritis changes of both mechanical and infective origin. He used a histochemical technique described by Lison and was able to show that the content of chrondroitin sulphate is reduced in degenerated cartilage. Further, he was frequently able to determine, by studying the distribution of the chondroitin sulphate in the cartilage, whether the pathological changes were due to aseptic or infective conditions.

RESUME

L'auteur a examiné le cartilage d'articulations dans lesquelles on a constaté des modifications ostéoarthritiques, ayant aussi bien une origine mécanique qu'infectieuse. Il utilise une technique histochimique décrite par Lison et il a pu démontrer que la teneur en chondroïtine est diminuée dans les cartilages dégénérés. D'autre part, il a été fréquemment à même de déterminer, en étudiant la distribution de la chondroïtine dans le cartilage, si les modifications pathologiques étaient de nature aseptique ou infectieuse.

ZUSAMMENFASSUNG

Verfasser hat den Knorpel von Gelenken untersucht, die osteoarthritische Veränderungen sowohl mechanischen wie infektiösen Ursprungs aufwiesen. Er verwendete eine histochemische Technik, die von Lison beschrieben wurde, und

war in der Lage nachzuweisen, dass der Gehalt an Chondroitinschwefelsäure in degeneriertem Knorpel herabgesetzt ist. Ausserdem war er oft imstande, durch Untersuchung der Verteilung der Chondroitinschwefelsäure im Knorpel zu bestmmen, ob die pathologischen Veränderungen aseptischer oder infektiöser Natur waren.

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