A Review of Symposium on Biochemistry of Connective Tissue  
\textit{in XIIIth International Congress of Rheumatology}  
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The fibreous protein collagen and polysaccharide proteins—systematically named proteoglycans—are known to be the main chemical constituents of cartilage. It became evident from this symposium that a considerable progress was made over the last few years in the chemistry and the metabolism of these substances, but more data are needed for useful application of biochemistry to clinical problems. The following aspects were reported:

(1) The cartilage collagen represents a genetically distinct collagen type consisting of $3\alpha_1$ II chains and thus being different from the skin collagen. Chemically the cartilage collagen is characterized by a higher hydroxylysine and carbohydrate content and its higher resistance to enzymatic degradation. The extracellular cross linking reactions of the collagen are chemically well defined, the reaction mechanism may partially explain the action of drugs such as the effect of D-penicillamine, but little information is available how the cross-links are definitively stabilized and whether abnormalities in cross-linking are involved in the pathogenesis of connective tissue disorders.

(2) The enzymatic degradation of articular cartilage collagen appears to be complex. The synovial collagenase has been shown to degrade the cartilage collagen to a small extent only, but the rate of solubilization may increase markedly by increased temperature as seen in inflammation. Moreover, there is evidence that the collagenase acts in concert with other proteolytic enzymes detected in human cartilage and in the synovial membrane, respectively. Especially in joint diseases—as theumatoid arthritis—protease such as cathepsin D, neutral proteases and the plasminogen may contribute to the degradation of cartilage matrix. Interestingly the neutral protease is inhibited by chloroquine.

(3) The proteoglycans of cartilage have been carefully investigated with respect to their biosynthesis, their macromolecular structure, their enzymatic degradation and to the excretion of their split products in the urine. From available information a proteoglycan molecule consists of a core protein filament with regulary arranged glycosaminoglycan side chains, the molecular weight of it is in the order of $0.5 \times 10^6$ daltons. It turned out, however, that the cartilage proteoglycans represent a family of molecules exhibiting a marked chemical and metabolic heterogeneity. The heterogeneity is indicated by a variation in

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the number and the length of side chains attached to the protein core, by the occurrence of hybrid proteoglycans, where two different glycosaminoglycan types are part of the same molecule and by the detection of different proteoglycan pools having different specific radioactivities when labelled by radioactive precursors. A decrease in the molecular weight of proteoglycans observed with increasing age and in osteoarthritis, resulting from a decreased length and a reduced number of side chains, respectively. Moreover, the proteoglycan research is complicated by the fact that cartilage proteoglycans form aggregates of an unknown but probably highly specific structure the aggregation being mediated by specific glycoproteins, by hyaluronate, by collagen or by macromolecules not yet identified.

The research work to come should draw more attention to the fact that collagen and proteoglycans are not separate entities but closely related to each other and specifically organized in the tissue. There is not doubt, however, that a more detailed knowledge of the chemical and metabolic features of connective tissue will once provide the basis for an interpretation of pathological changes and drug effects on a macromolecular level.