Interaction Between Cells, Hyaluronic Acid and Collagen.

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During recent years an increasing amount of experimental results published by many investigators suggest that hyaluronic acid interacts with cell surfaces or by other means influences the in vivo and in vitro activities of certain cells. In this review, an attempt will be made to summarize the results of these experiments which were carried out by various research groups including our own. Most of the biological or pharmacological activities of hyaluronic acid described this far show certain specificity in regard to the molecular size and conformation of hyaluronic acid and to the cell type on which the action can be demonstrated. In general, the larger and structurally more "organized" molecules are biologically or pharmacologically more active. Molecules with low molecular size and oligosaccharides show activity seldom.

Most biological action of hyaluronic acid is not directly related to its polyanionic nature because glycosaminoglycans with higher charge density (chondroitin sulfates, heparin) show no similar effects. For example, the phagocytosis and migration inhibitory effect is a specific property of high polymeric hyaluronic acid and is not shared by other polyanionic polysaccharides.

According to the specific effects one can today separate six types of biological activities:

1. Inhibition, in some special cases stimulation, of the phagocytic activity of mononuclear and polymorphonuclear phagocytes.
2. Inhibition of the migration and mitosis of lymphocytes.
3. Inhibition of migration of cells of the lymphomyeloid system.
4. Inhibition of the susceptibility of certain cells to some viruses and prevention of the penetration of sporozoites.
5. Inhibition of interaction between target cells and lymphocytes.

Since all these effects are demonstrated in vitro in solutions that contain hyaluronic acid and in a concentration within the physiological range, one is justified to speculate that this glycosaminoglycan is involved in the regulation of the biological process broadly called inflammation.

A different but related effect of hyaluronic acid was described on the in vitro synthesis of hyaluronic acid and chondroitin sulfate. The former was shown to be stimulated, the latter was inhibited by highly polymeric hyaluronic acid molecules suggesting a regulatory mechanism by a matrix component on the differentiation of connective tissue matrix.

The pharmacological and therapeutic effect of certain hyaluronic acid fractions in arthritis and some eye diseases was extensively studied in the past years. It was shown that very viscous solutions of hyaluronic acid prevent mechanical cell damage and interfere with scar tissue formation. It was hypothesized that the viscoelastic hyaluronic acid solution in the vitreous serves as a shock absorber for the neuroretina, preventing its detachment and dislocation from the retinal pigment epithelium.

The interaction between hyaluronic acid and collagen can be described in two levels: interaction with the collagen macromolecules during fibril formation, and interaction with the fibrils of the collagen gel. The first type of interaction causes an increase in the stability (rigidity) and elasticity of the collagen gel. The second type of interaction may play a role in the development and regeneration of intercellular matrix.