Biochemical and Biophysical Aspects of Collagen

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INTRODUCTION

With some background on the general properties of macromolecules we are now coming to examine some groups of macromolecules that are found in tissues of the animal body, in areas outside the cell. They are, of course, made inside of cells and that is where one must look to learn the details of their biosynthesis. But their major functions and their usefulness to the animal organism seem to lie in their behavior in areas outside the cell, and the properties they impose on the tissues they compose as a whole. These properties are, in part, of a mechanical nature. What is their importance to an animal organism?

Let us first look in a very general way at a parallel situation in single celled organisms. The main fundamental characteristics of living organisms that have often been cited are their abilities to collect, to store, and to transform energy, and to construct organisms like themselves to which they transmit the same pattern of abilities to collect, store, and transform energy. A great many of the biochemical reactions that take place in these processes in living organisms occur in solution and in solution molecules have a way of moving around. Yet a minimum essential requirement of an organism, essential to its persistence and survival, is that its biochemical processes must be highly ordered. A free living organism of any complexity cannot exist entirely in solution, even if the solution is tied up in a bag, as in a cell. Its essential enzymatic reactions cannot occur anywhere in a pool of water inside the cell. Reactions must generally occur at specific sites and be related, in the space of the cell, to specific sites where related prior and subsequent reactions occur. Especially the processes that occur in solution must be segregated in an orderly arrangement and reactants cannot be allowed to diffuse around at random or the organism ceases to exist as a continuing entity. In cells the necessary order or arrangement is imposed by a complex set of containers, pockets, closets, partitions, and tubes. This furniture in the cell is made of water-insoluble materials. An inescapable requirement of a free living organism is a set of water-insoluble barriers to segregate in an orderly way reactions that occur in water. A major component of such barriers seems to be an insoluble protein. Currently work is being directed at isolation and study of the properties of such a protein in the laboratory of David Green.

In multicellular organisms order at still another level is superimposed on the order that exists inside the cells. The individual cells must be constrained to occupy certain areas within the whole organism, some cells must be held together, some must be held apart, some must be allowed a limited freedom of movement. Just as the

furniture inside the cell is necessary to impose order on enzymes for the continuing existence of the cell, so the whole multicellular organism needs a variety of materials with different properties for somewhat similar purposes, to impose order on the relations among the cells. These materials are the connective tissues. The functions these tissues have to perform are largely but not entirely structural and mechanical. In the first place the whole animal organism must be held together, and for this there is a bag, the skin, made up mainly of the derma. But a cell is not just a bagful of enzymes in solution, and an organism is not a bagful of cells. There are bones, joints, pipes, cushions, membranes, and pockets within pockets. Just as the furniture of the cell seems largely made of water-insoluble material, so the connective tissues seem to be largely built around water-insoluble material.

The common insoluble material used for this purpose by most of the vertebrates is the fibrous protein collagen. It is fashioned into fine filaments or coarse fibers, woven into transparent sheets or into thick three dimensional networks. All these insoluble structures are made by connective tissue cells, but the fibers are not part of the cells. The collagen fibers are all outside the cells that made them. This is a structural situation different from that occurring in plants where the fibers are parts of the cells that make them. The formation of collagen fibers outside the cell raises a whole complex set of problems such as how these fibers are set in place, what determines the directions they take, how they are woven into sheets and nets, how they are kept in repair. It is in the disposition of the collagen fibers that the cells lay down the material basis of the organization of the whole animal body.

So we come to some aspects of the biochemistry of collagen that are currently puzzling people who work with this material.

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