Earlier observations had shown that, by implanting specially constructed scaffoldings — made of chemically inert materials, such as glass, plastics, or certain metals — it is possible to produce, at will, tissue growth of a predictable shape and histologic structure in the subcutis of the rat. For example, in a simple, straight glass tube, 30 mm in length and 10 mm in diameter, the two openings are soon closed by round connective tissue discs (“basal plates”), the centers of which immediately become connected by a broad fibrinous bridge. The latter contracts and, within about four weeks, is replaced by a thin but well vascularized thread (about 1 mm in diameter), which consists of parallel bundles of dense, collagenous connective tissue and fibroblasts. This tissue bridge (“growth cord”) is surrounded by a yellow fluid (“growth exudate”) rich in proteins but poor in cellular elements.

Apparently, these cylinders act primarily as “tissue diaphragms” in that they permit growth only in one desired direction. If a parietal hole is made in such a tube, an anastomosis develops, which connects the central growth cord, in a Y- or T-shaped fashion, with the basal plate formed in the additional opening. Cross-shaped growth cords can be constructed by the implantation of cross-shaped tubes, while many-branched, ramifying, dense connective tissue structures are obtained with tissue diaphragms that have a corresponding number of lateral holes in desired positions (SELYE 1959a, b).

Curiously, all these structures tend to degenerate after about two months. In the growth cord there appear histiocytes, containing sudanophilic lipids or iron pigment, as well as cholesterol crystals surrounded by multinuclear giant cells; eventually, first the blood vessels and then the entire cord disintegrate into a brownish, hemorrhagic mass. This

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Induction of bone, cartilage and hemopoietic tissue

process of "degenerative sequestration", or tissue aging, is thought to result from the relative metabolic isolation of the central growth cord, which is separated from the surrounding tissues by the exudate and the wall of the tissue diaphragm itself. If this interpretation were correct, it would imply that the influx of nutrients and the removal of wastes — through the exudate, by diffusion from the basal plates, and through the blood vessels that invade the cord — gradually become insufficient to maintain the structure in a viable condition (Selyle 1959a, b).

Additional studies revealed that in very broad spiral-shaped tissue scaffoldings (having a diameter of 15 mm or more) the organization of the central cavity normally proceeds at an extremely slow rate, but can be greatly accelerated if the lumen is filled with Ringer-Locke solution immediately after implantation. Indeed, any form of tissue scaffolding that can fix water in a connective tissue area exerts a similar growth-promoting effect (Selyle, Prioreschi and Jean 1959).

We need not describe the tissue scaffolding techniques in detail here, but let us add that, by changing the size, shape or surface structure of the implanted objects, and by applying pressure or suction to them, the quality and quantity as well as the life span of the tissue that grows in them can greatly be altered at will. Indeed, it has even been possible to construct tissue diaphragms that fill out with typical adipose tissue, exclusively (Selyle, Jean, Cantin and Lemire 1959).

The object of this communication is to describe the conditions under which ossification, cartilage formation, the growth of lymphatic and hemopoietic tissue, or even of complete tubular bones can be induced under the dorsal skin of the rat merely by implanting a glass tube of suitable size and shape.

Materials and techniques

First, a preliminary series of experiments was conducted to establish the most favorable conditions for the induction of skeletal structures by tissue scaffoldings. It was found that wide but comparatively short glass cylinders (their axis oriented dorso-ventrally) serve best for this purpose, if they are left under the skin for at least two months. It also became evident that topical blockade of the phagocyte system by India ink prevents ossification in such cylinders. Guided by these exploratory observations (which need not be described in detail) we designed the final experiment, on which this communication is based, as follows:

Twenty Sprague-Dawley rats, with a mean initial body weight of 200 gm. (range: 187—230 gm.) were subdivided into two equal groups. On the first day of the experiment, we implanted a cylindrical glass diaphragm under the shaved skin of the mid-dorsal region in each animal in both groups. The operation was performed under ether anesthesia, with the usual sterility precautions. The diaphragm was introduced through a transverse incision (of about 40 mm, from left to right) in the sacral region and pushed forward so that it came to rest on the lower thoracic and upper lumbar fascia of the back, its axis oriented dorso-ventrally. The diaphragm used for this purpose was a short, pyrex glass tube, 20 mm in length.