A COMPARATIVE HISTOPATHOLOGICAL STUDY OF THE EARLY ATHEROSCLEROTIC LESION

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THE early atherosclerotic lesion in human arteries is a raised yellow streak. The nature of this thickening is controversial, some say it is predominantly fatty (Hill, Camps and Rigg, 1961 ; Holman, McGill, Strong and Geer, 1958) others that it is predominantly fibrous (Levene, 1956). This account supports the latter view and illustrates the histological and histochemical similarities of the early lesions in man, rat, rabbit and turkey.

MATERIALS AND METHODS

Human lesions were obtained from subjects in the age group 13–24.

Rat lesions were produced experimentally by feeding 40 per cent Arachis oil, cholesterol, cholic acid and thiouracil (Gresham and Howard, 1960).

Rabbit lesions were produced experimentally by feeding 20 per cent beef fat alone (Gresham and Howard, 1961*a*).

Turkey lesions were obtained from a healthy male bird of a flock in which some birds had died of aortic rupture due to aortic atherosclerosis of the abdominal aorta (Gresham and Howard, 1961*b*).

Fixation was by 10 per cent formal-saline. Frozen sections were examined for fat by means of oil red O staining. Paraffin sections were stained by haematoxylin and eosin, and Weigert's resorcin fuchsin elastin stain. In addition the following histochemical methods were employed.

Acid mucopolysaccharides: Hale's dialysed iron, toluidine blue, alcian blue, the periodic acid Schiff (PAS) (Pearse, 1954), and permanganate paraldehyde fuchsin methods (Gomori, 1950). Sections were also treated with Hyalase (Bengers Ltd., 1000 u./100 ml.) for 12 hr. a 37°.

Protein.—The oxidized tannic acid azo method (Dixon, 1959).

RESULTS

The amount of lipid in the human, rat, rabbit and turkey lesions varied. In the first 3 species lipid was sparse and the lesion was predominantly fibrous (Fig. 1). Fat was more abundant in the lesions in the turkey (Fig. 2), being mainly in the region of the internal elastic lamina but here again, collagen formed a considerable part of the lesion.

The lesion in all four species showed the presence of extracellular material which was found to stain by Dixon's method for protein, Hale's method, alcian blue and metachromatically with toluidine blue (Figs. 3, 4). In the rabbit, rat and turkey the material was diffusely distributed, in the human lesion it was aggregated around clefts which contained a central lipid encrusted nucleus

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(Gresham and Howard, 1961*c*). It did not stain by the PAS method, but stained readily with permanganate paraldehyde fuchsin and was metachromatic with toluidine blue. These tinctorial properties together with the fact that hyalase failed to remove the material suggest that it contained acid sulphated mucopolysaccharide.

DISCUSSION

One of the major problems of research into the aetiology of atherosclerosis is that of relating experimentally induced lesions in animals to those which occur in man. The present work indicates that there are histological similarities between the naturally occurring lesions in man and turkey and those produced experimentally in the rat and rabbit. Such similarities are important because they suggest that the plaques are produced by the same basic mechanism.

In all the 4 species studied, the lesion was predominantly fibrous rather than fatty. It contained acid sulphated mucopolysaccharides which were present in greater amounts than in the adjacent media. The presence of this polysaccharide and also of protein supports the view that collagen formation is taking place as the first step in the formation of these fibrous plaques. Levene (1956) also showed that the earliest indication of atherosclerosis in the coronary arteries was the appearance of fibro-elastic thickenings. The gradual increase in uptake of ^{35}S into mucopolysaccharides with aortae of increasing age (Dyrbye, 1959) is another indication that collagen formation plays an important role in the genesis of the atherosclerotic lesion.

There are of course many fundamental questions as yet unanswered. The nature of the mechanisms which cause fibrogenesis in the arterial intima is unknown. It may be that lipid accumulation in fibroblasts or intimal smooth muscle cells is the first event (Gresham and Howard, 1961*c*). The experimental production of the lesion in the rabbit and rat by feeding large amounts of lipids would certainly indicate the importance of lipids at an early stage in fibrous plaque production.

In the rat, rabbit and man, lesions are present in the aortic arch and coronary arteries, whereas in the turkey they are seen only in the abdominal aorta. The reason for this difference is unknown. Metabolic studies on different parts of the aorta in different species may cast some light on the problem and studies have already been started by Munro and Campbell (personal communication) who showed significant differences in the oxygen uptake of thoracic and abdominal sections in atherosclerotic chick aorta. Such metabolic differences may account for the selective accumulation of lipid in different parts of the aorta which may then trigger off the atherosclerotic process. A continuation of these comparative studies of naturally occurring and experimentally induced arterial disease may lead to a solution of many of these problems.

EXPLANATION OF PLATE

FIG. 1.—Early human atherosclerotic lesion (Oil red O × 50.)
FIG. 2.—Plaque in abdominal aorta of turkey. (Oil red O × 66.)
FIG. 3.—Fibrous plaque in coronary artery of rabbit. (Hale's method × 50.)
FIG. 4.—Fibrous plaque in aorta of rat. (Alcian Blue × 66.)

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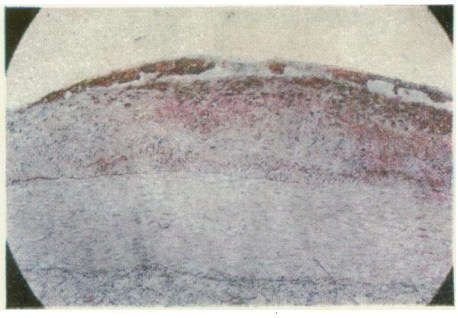

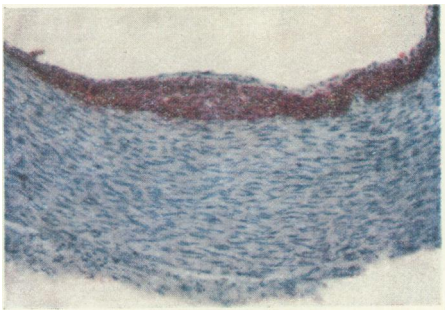

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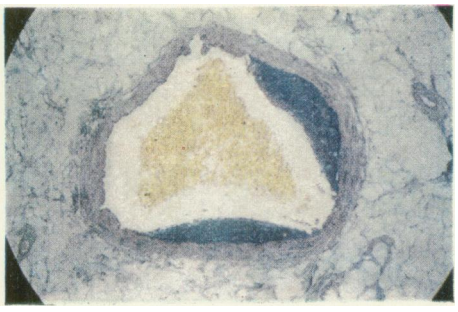

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SUMMARY

A histochemical investigation has been made of naturally occurring early atherosclerotic lesions in man and the turkey and experimentally induced plaques in the rat and rabbit. In all cases, the lesion was predominantly fibrous and only in the turkey did it contain much lipid. The presence of extracellular material which stained for acid mucopolysaccharide and protein suggested that the lesions were active sites of collagen production, and were produced by the same basic mechanism.

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