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Trabalhos Originais

SOME NEWER APPROACHES TO THE PROBLEMS OF ARTERIOSCLEROSIS

PART I

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There is a growing interest in the problems of aging. Among these the so-called degenerative arterial diseases hold a commanding position. This is particularly true for, the possibly, amenable, premature or pathological aging as contrasted t the involuntary or physiological senescence and senility. Our populace, spared from the ravages of infectious diseases, is moving into the middle age and old age groups. However, the chief source of alarm is that the so-called degenerative disorders are appearing more and more frequently in those below forty years of age. Many individuals are aging organically more rapidly than chronologically. The processes are very insidious. Environmental factors may be contributing especially in those who have hereditary pre-dispositions to early deterioration.

Nothing can be done about the heredity but respect adjust to it. Early recognition and prompt complete and persistent cooperation of the patient may insure postponement of dissolution. This is particularly true of arterial disease processes which play a major role in premature aging. There are several types of arteriopathies but the most common, most serious early process is a subintimal atheromatosis which often develops in strategic positions. The causes of atheromatous formations are not definitely established and the reasons for the dangerous plaque localizations are not known. However, these problems are being vigorously attacked and some facts have been brought to light. The findings and tentative conclusions are of practical

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as well as theoretical value. The problems are still far from solution. Only the grosser factors have been established and attacked up to this time [1 to 14].

The various forms of arteriopathy should be clearly differentiated. The most common sources of serious circulatory troubles, *subintimal atheromatosis*, is mainly a primary disease process which leads to the development of atherosclerosis. In the patients with hypertensive arteriolar disease, atheromatosis is usually secondary, albeit the most serious, involvement or complication. One contributing factor is the strain of augmented intraarterial pressure and the increased turbulence in the blood flow. In malignant hypertension the arteriolar walls become hypertrophic and extreme spasticity produces necrosis of the intima and a fulminating thrombotic clinical picture.

Senile arteriosclerosis is a disease of the media and presents the enlarged, elongated, thickened pipe stem and tortuous peripheral arteries with a tendency to corrugation and calcification. The lumens are usually held widely open and intimal degeneration is uncommon but intimal thickening and secondary subintimal atheromatosis may take place. There are some other rarer forms of inflammatory thrombotic arteritis involving the various coats of the arteries as a result of toxic, allergic or infectious disease processes.

Atheromatosis is by far the most important of the group, and probably the least difficult to study. It is most commonly found in coronary arteries where it produces serious clinical pictures which will be discussed in the third part of this paper. Atheromatosis involves the cerebral retinal and peripheral arteries but especially the aorta at the root, in the arch and most conspicuously in the abdominal portion. It is the most common disease process and most susceptible to investigation. It has been produced in experimental animals not only in herbivora as rabbits, but also in omnivora as chickens, and even in predominately carnivora as dogs under certain special conditions.

In man atheromatosis develops slowly and insidiously yet we know a good deal about its natural history. We have learned to look for evidence of a predisposing or a contributory cholesterol metabolism disorder and make the tentative diagnosis before the symptoms and signs of circulatory obstruction are presented. We have used this evidence in deductive reasoning and recognize certain etiological factors. We try to change the mode of life, remove what we consider certain contributing factors while the conditions may still be amenable to treatment. We cannot hope for complete reversal or reabsorption but we may possibly halt the incrementation of the lesions.

Atheromatosis in most human cases is asymptomatic until advanced anatomic lesions have developed. The intense study of a mass of clinical material from every conceivable point of view and the ap-

plication of deductive reasoning to this has served to establish the probable causative role of several factors. We accept as important the hereditary predisposition, the thickness and nutritional state of the intima, the condition of the vasa vasorum in the media, the condition of the blood, anoxia; very low and high intraarterial pressure; metabolic disturbances, especially hyperthyroidism, with changes in the blood plasma colloids, especially in the lipoids, hypercholesterolemia and fat logged histiocytes, and the permeability of the intima. The degree of vascularization of the wall of the aorta and great vessels according to Schlichter [15] and Paterson et al. [16], must be considered a most important factor. Vascularization is greatest in childhood and decreases with aging of man.

In the experimental animal, vascularization of the aorta has been shown to be greatest in the dog, less in the chicken, and least in rabbits [15]. Rabbits and chickens in our experimental studies, as in those of earlier investigators, are more or less easily overwhelmed with large doses of cholesterol in the feed and there has been reproduced the pathological picture of aortic and coronary artery subintimal atheromatosis quite similar to that seen in the human aorta and coronary arteries. The liver has been found to become very fatty very early and histiocytes laden with cholesterol and cholesterol esters have been demonstrated in the liver and in the aorta by Timothy Leary [9]. The high total blood cholesterol level and liver content of lipoids rise together.

Steiner and Kendall have produced atheromatosis in dogs by the use of thiouracil and cholesterol feeding. In the animals subjected to the feeding experiments, the pathological biochemistry and the histogenesis of the atheromatous lesions in the subintimal tissues have been followed step by step. Just how even the apparently more permeable arterial intima is actually penetrated has not been demonstrated. The wandering macrophages in the subintimal space and locally produced endothelial foam cells in the intima have been incriminated. Cells containing cholesterol and cholesterol esters may penetrate the intima lodging in the subintima where they degenerate and the released fatty substances coalesce.

Simms and Pashley [17] studied the fat formation and depositing mechanism in cultures of fibroblasts from adult chicken aortas in fresh chicken plasma. They concluded that there were lipid precursors ‘’lipfanogens” in the serum which living cells took up and converted into fat globlets and deposited in segments of adult aortas. A heat labile anti-substance was also demonstrated. The ‘’antilipfanogens” were found associated with the serum albumin fraction V of the blood plasma. The pinpoint lesions gradually increase in size by increments of neutral fat, cholesterol and cholesterol esters from the blood, through foam,

cells or histiocytes or by still unknown ways causing atheromatous plaques to develop.

The atheromatous plaque produces pressure in the surrounding cells and irritation and increased irritability of the smooth muscle and a tendency to spasm on slight provocation. Fibroblastic and angioblastic proliferation surround the lesions which seem to degenerate and calcification takes place. The damaged intima may be stretched over the atheromatous plaque and may rupture, precipitating thrombosis. Hemorrhage may develop in the atherosclerotic lesions from the small blood vessels that have arisen in the reparative process and may cause pressure obliteration of the arterial lumens[4].

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