

In the six control cases in this present study, spontaneous regression was not observed. The number of cases is obviously too small to warrant the conclusion that such regression never occurs.

THERAPY IN ATHEROSCLEROSIS

Several forms of therapy have proved effective in inhibiting the development of atherosclerosis in animals subjected to cholesterol feeding. Cessation of cholesterol feeding is followed by some regression of lesions as previously mentioned. Desiccated thyroid has been shown to inhibit atherosclerosis in cholesterol-fed rabbits.¹¹ Cortisone,¹² alloxan,¹³ and heparin¹⁴ all have the same beneficial effect. Oestrogen therapy, while promoting atherosclerosis in the chick aorta, exerts a sparing effect on the coronary arteries of the same animal.¹⁵ Finally certain wetting agents have been shown to protect the artery from hypercholesterolaemia.¹⁶

Recently it has been shown that ascorbic acid deficiency in guinea-pigs is followed rapidly by atherosclerosis without cholesterol feeding.¹⁷ Parenteral ascorbic acid has a protective effect against atherosclerosis in the cholesterol-fed guinea-pig.¹⁷

In searching for a feasible form of therapy for atherosclerosis in man, the results in experimental animals have naturally been the guide. Many of the forms of therapy described can be discarded at once because of undesirable side effects. Low cholesterol diets are at present very popular. The rationale for their use is based upon the fact that cholesterol feeding with subsequent hypercholesterolaemia results in atherosclerosis in some animals. However the hypercholesterolaemia and reticulo-endothelial lipid deposits have no counterpart in the usual case of atherosclerosis in man.¹⁸ An objective assessment of the efficacy of the low cholesterol diet in human atherosclerosis has not yet been reported.

Heparin has been tried in atherosclerosis, again because of its value in the cholesterol-fed animal. It does not produce regression of lesions in the rabbit but does inhibit their development.¹⁴ This treatment is not without its side effects¹⁹ and studies in man based upon symptomatic relief in angina pectoris have shown no improvement.²⁰

Ascorbic acid therapy has been combined with rutin in an uncontrolled study of atherosclerosis

in man and the results based on symptomatic grounds were favourable.²⁰

The rationale for ascorbic acid therapy is based upon studies of the pathogenesis of atherosclerosis.^{21, 22} Gross depletion of ascorbic acid has been demonstrated to be frequent in human arteries at autopsy.²² Ascorbic acid deficiency in guinea-pigs is accompanied by rapid deposit of lipid in the intima of arteries morphologically identical to human atherosclerosis.¹⁷ These lesions occur at normal plasma cholesterol levels and are not accompanied by lipid deposits in the reticulo-endothelial system. The concept of atherosclerosis as a lesion of the intimal ground substance localized at points of mechanical stress, as suggested by Virchow and Aschoff,²³ is incorporated in the atherosclerosis of ascorbic acid deficiency.²² Finally the lipid accumulation in the arteries would seem to be related to the increased rate of incorporation of C¹⁴ acetate into cholesterol which occurs in ascorbic acid deficiency.¹⁶

Ante-mortem ascorbic acid therapy is capable of making good the ascorbic acid deficiency observed in the arteries at routine hospital autopsies.²² Although parenteral ascorbic acid therapy is considerably more potent in inhibiting the atherosclerosis of cholesterol-fed guinea-pigs,¹⁷ it has certain practical drawbacks. For this reason oral therapy for long term studies was employed. No toxic effects have been reported from the use of oral ascorbic acid, nor were any observed in this study. The dose chosen was based upon the studies of ascorbic acid absorption and saturation as described by Faulkner *et al.*²⁴ and Todhunter *et al.*²⁵ The aim was to ensure continuous saturation of tissues with ascorbic acid.

The results in this present study of ascorbic acid therapy in human atherosclerosis as followed by serial arteriography are encouraging. Once again it must be pointed out that the series is small and that final conclusions must await studies carried out for a longer time with more cases added. This is being done, and the present review is to be considered as a preliminary report.