Prevalence of Atheroma

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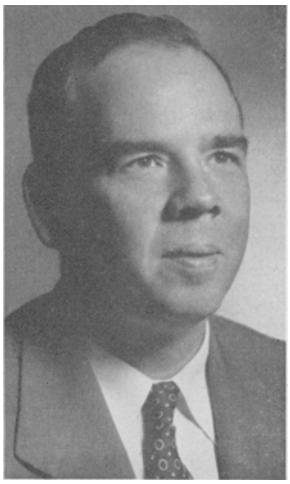
MUCH OF THE detailed data presented at the symposium on Fats in Nutrition and Health has recently been published (1) or is in the process of being published (2). Rather than repeat these data the following synopsis of the paper is presented.

The anatomic changes related to atherosclerosis in more than 1,200 aortas from necropsies on individuals, aged 1 to 40, performed in seven geographic areas (New Orleans, Spain, South Africa, England, Puerto Rico, Guatemala, and Costa Rica) have been studied qualitatively, quantitatively, and topographically before and after staining them with Sudan IV (to bring out in sharp contrast the early fatty streaks that constitute the first change).



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Our studies to date have indicated that atherosclerosis develops by definite sequential stages: fatty streak, fibrous plaque, complication (*e.g.*, thrombosis or hemorrhage), and clinical disease and that each stage is a necessary precursor to the following one. The factors responsible for succeeding stages may be, and probably are, different from those that initiated the first stage (atherogenesis). Thus intelligent therapy must take cognizance of these different stages because that which may be effective against one stage may be ineffective or even contraindicated against another stage.

Most of our studies to date have been directed toward the first stage, fatty streak, as we are convinced that prevention or retardation of this stage will prevent or retard all subsequent stages. NO FATTY STREAK, NO FIBROUS PLAQUE; NO FIBROUS PLAQUE, NO COMPLICATIONS; NO COMPLICATIONS, NO CLINICAL DISEASE. If each link in this chain of pathogenesis is sound, NO FATTY STREAK, NO CLINICAL DISEASE.

Several findings of interest have emerged from these studies in this age group up to 41 years.

a) Every child beyond the age of three years in all parts of the world thus far sampled, despite the widely varying genetic and environmental backgrounds represented by the seven geographic areas studied, has shown some degree of sudanophilic fatty streaking of the aorta, and this has been confirmed by histologic and histochemical studies. This has raised serious fundamental questions about the definition of "normal" and about the relationship of diet to atherogenesis.

b) The degree of fatty streaking of the aorta in cases of sudden accidental death (automobile accidents, gun-shot wounds, etc) has been as great or greater than it has been in cases of death due to natural causes. Thus the terminal illness is not the determining factor.

c) In all parts of the world that have been studied thus far, a rapid increase in fatty streaks (expressed as percentage of the inner surface of the aorta that stains red with Sudan IV) has occurred between the ages of 8 and 18 years. This has suggested a relationship of atherogenesis to the hormonal changes of puberty.

d) Some evidence for reversibility of early fatty streaks has been obtained, but the limits of this reversibility have not been defined.

e) An interval of approximately 15–20 years lapses before any of the fatty streaks is converted to a fibrous plaque. No evidence for reversibility of fibrous plaques has been obtained.

OTHER STUDIES related to race, age, sex, principal cause of death, and associated findings, such as hypertension, hypercholesterolemia, diabetes, weight gain or weight loss are in progress and will be reported as sufficient data for statistical analyses become available. The findings to date however are sufficient to warrant certain tentative conclusions.

The tempo of the natural history of atherosclerosis is in terms of months, years, and decades—not that of 3 meals per day. Our anatomic studies are more easily interpreted in the light of increased local formation of lipide (by mesenchymal cells in the inner layer of the arterial wall) and/or decreased local removal of lipide than they are in the light of filtration of lipide from the blood. The evidence from our studies substantiates that from other sources in indicating that the arterial wall normally forms and turns over to the body economy (metabolic pool and fat depots) certain lipides not unlike those that are normally found in the blood and that local accumulation of these lipides in the arterial wall results from some breakdown in this normal turn-over mechanism.

If diet plays a role in atherogenesis—and there is ample evidence that it does—it does so not by flooding the filtering capacity of the arterial wall with cholesterol, chylomicrons, or lipoprotein complexes but by upsetting some of the safety valves (hormones? enzymes?) that normally protect the arterial wall.

The early age of onset and the long period of 15 or more years during which fatty streaks remain in a potentially reversible stage recommend the problem of prevention of atherosclerosis to the pediatricians.

REFERENCES

1. Holman, R. L., McGill, H. C. Jr., Strong, J. P., Griffin, O. R., Geer, J. C., Transactions of the Life Insurance Medical Directors of America, *XL*, 86–114 (1956).
2. Holman, R. L., McGill, H. C. Jr., Strong, J. P., Geer, J. C., Transactions of the Western Metabolic Conference, Palm Springs, Calif., Feb. 14–17, 1957, vol. 2.