Editorial

Does a Metabolic Barrier to Circulating Cholesterol Protect the Arterial Wall?

ALTHOUGH atherogenesis in man and in experimental animals appears to be associated with an elevation of serum cholesterol, the mechanism relating these two conditions remains obscure. Investigators usually assume that the nondiseased arterial wall exhibits a certain permeability to cholesterol that allows a balance between the influx and removal of this lipid so that no accumulation occurs. It is further assumed that when blood cholesterol levels are elevated the influx of cholesterol increases so much that the removal mechanism lags behind and arterial cholesterol deposits develop. Although this sequence of events is consistent with most of the data at hand, alternate explanations appear possible and should be considered in the light of newer knowledge.

One scheme proposed for consideration is that the healthy aorta presents a metabolic barrier to the influx of circulating cholesterol and that atherogenesis follows the breakdown of this barrier.

The idea of a barrier of some sort is compatible with the results of a large series of experiments showing that arterial injury produced by mechanical or chemical means makes the artery more susceptible to lipid infiltration. It has usually been assumed that this type of arterial injury produces structural modifications of the artery which would facilitate cholesterol influx. This assumption does not explain, however, why cyanide and fluoride when added to normal or atherosclerotic rabbit arteries in vitro markedly stimulate the uptake of labeled cholesterol present in the form of a suspension or as native serum lipoprotein in the incubation medium.

Once one assumes the presence of a metabolic barrier to cholesterol in the arterial wall, several observations make sense: mechanical injury by scraping or freezing as well as chemical poisons or anoxia might increase atherogenesis by affecting enzyme systems involved in maintaining the barrier. Hormones and other humoral agents could modify atherogenesis without necessarily affecting blood lipid levels. It is even possible that dietary cholesterol may play a dual role in the atherogenic process, particularly in animal studies where it is fed in large quantities. This possibility is brought to mind by studies showing that the injection of India ink in rats parabiosed several days after the injection will produce lesions in the noninjected parabiont, presumably the result of a humoral agent. If the uptake of dietary cholesterol by the liver should similarly release a humoral agent which might suppress the metabolic barrier in the artery, this function, as well as its role in producing hyperlipidemia, might make cholesterol the atherogenic agent par excellence.

It would appear that the foregoing considerations warrant a more intense study of metabolic events affecting arterial permeability to lipids.

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References

2. Unpublished observations.
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Circulation. 1966;33:7
doi: 10.1161/01.CIR.33.1.7

Circulation is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
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Print ISSN: 0009-7322. Online ISSN: 1524-4539

The online version of this article, along with updated information and services, is located on the World Wide Web at:
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