ATHEROSCLEROSIS UPDATE
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Atherosclerosis and aging of the arterial wall

J. Michael Bowness, PhD

With age, atherosclerotic lesions cover a steadily increasing percentage of the luminal surface of the coronary arteries of human populations.[1] Is this increase caused by the intrinsic and unalterable aging mechanisms in the arterial wall, or is it due, at least in part, to a time-dependent response to risk factors, such as a high blood cholesterol level and hypertension, that can be reversed, arrested or moderated by changes in nutrition or lifestyle?

Although studies in animals have shown that intrinsic aging processes may increase susceptibility to atherosclerosis,[2] there is evidence from chemical analyses of necropsy specimens of the human arterial wall, described below, that changes in the composition of the extracellular matrix associated with normal aging are clearly different from those occurring in the development of advanced atherosclerotic lesions. The primary causes of the latter remain largely undetermined, but likely the progressive development of these lesions represents a time-dependent response to one or more risk factors. Together with the evidence that the blood concentrations of cholesterol and low-density lipoprotein (LDL) and the narrowing of coronary arteries can be decreased by dietary or pharmacologic measures[3] these analyses indicate that atherosclerosis can be dissociated, at least in part, from the intrinsic aging of the arterial wall.

In the extracellular matrix of the normal arterial wall there is a gradual increase with age in the concentration of the chondroitinsulfates found in one type of proteoglycan.[4] This increase is strongly correlated with the age-related increase in levels of intimal cholesterol and apolipoprotein B, which are thought to be derived from the binding of LDL to a chondroitinsulfate proteoglycan and collagen. Binding and passive accumulation of this type, which is postulated to occur in healthy aged intima, cannot account for the concentration of cholesterol in atheromatous plaques; this may be many times the concentration in healthy intima, whereas the concentration of the chondroitinsulfates in plaques is only slightly increased, if at all.[4,5] A similar situation exists for the elastic portion of the aorta: with age the content of polar amino acids in the insoluble elastin fraction increases, apparently independent of the onset and evolution of atheromatous lesions.[6]

Thus, although it seems that normally aged arterial extracellular matrix contains more cholesterol than healthy young matrix, aging alone cannot account for the much greater cholesterol concentration in advanced atherosclerotic plaques. How many other factors are involved is not yet established, but the decrease in coronary artery narrowing demonstrated by angiography in previously hyperlipidemic patients[3] indicates that measures designed to lower LDL concentrations in the blood can influence the process.

References

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Reprint requests to: Dr. J. Michael Bowness, Department of Biochemistry and Molecular Biology, University of Manitoba, 770 Bannatyne Ave., Winnipeg, MB R3E 0W3