13 Occlusive Arterial Disease and Blood Rheology

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13.1 Introduction

A variety of common and important clinical events are thought to arise from organ ischaemia secondary to obstructed blood flow in the major arteries which supply the heart, brain and lower limbs. It is our purpose to review the possible contribution of blood rheology to these events. Recent interest in this topic probably arises for three reasons. In the last decade a number of studies have been reported which associate blood rheology factors with clinical arterial events, not only retrospectively but also prospectively. Secondly, changes in blood viscosity and its major determinants (haematocrit, plasma viscosity, plasma fibrinogen level) have been related to changes in cerebral and limb blood flow in man. Thirdly, alteration of the flow properties of blood appears to be a possible therapeutic approach to problems against which we currently have a very limited armamentarium. Most patients with angina pectoris obtain some relief from glyceryl trinitrate and beta-adrenergic blocking drugs, and arterial reconstructive surgery also gives symptomatic improvement to selected subjects who have angina or transient symptoms of leg or brain ischaemia. There is, however, little evidence that any medical or surgical measures alter the natural history of
occlusive arterial disease — with the exception of stopping cigarette-smoking (Doll and Hill, 1964).

The epidemiology, pathology, and pathogenesis of “occlusive arterial disease” are complex. Patients with different clinical syndromes share certain factors which permit us to group them under this umbrella term. The first of these is a basic pathology, atherosclerosis — non-inflammatory, stenosing or occluding lesions of major arteries which contain smooth muscle, fibrous tissue, fibrinogen, fibrin and low-density lipoprotein. Lesions tend to occur at points of dynamic stress. Atherosclerosis starts early in life, and is progressive and universal. However, post-mortem studies show that persons who experience clinical coronary artery events (sudden death, angina pectoris, or major myocardial infarction) usually have more extensive coronary artery narrowing than do persons who have not suffered these events. Similarly, transient or permanent ischaemia of the lower limbs or brain is usually associated with narrowing of the caudal or the cranial arteries which is of above-average severity. There is also a tendency for the severity of atherosclerosis in one part of the arterial tree (coronary, cranial or caudal) to correlate with the severity of arterial narrowing at the other two sites (Mitchell and Schwartz, 1965).

Epidemiological studies support this pathological concept of arterial occlusion as a systemic disease. Thus, risk associations have been defined which synergically increase the likelihood of a person experiencing clinical arterial events. The major risk factors (increasing age, male sex, cigarette smoking, diabetes, blood pressure and serum cholesterol level) are common to all three major manifestations of arterial occlusion — coronary, cerebral and lower-limb events (Gordon and Kannell, 1972). The link between epidemiology and pathology may be that, in general, autopsy studies suggest that these risk factors also correlate with the extent of atherosclerosis. Whether less important risk factors (oestrogen consumption, obesity, physical activity, blood group, and the negative risk factor of alcohol consumption) are also common to the three main types of arterial event, and whether they also correlate with the extent of atherosclerosis, are questions which require further study.

If the major clinical syndromes of occlusive arterial disease have epidemiological and pathological features in common, they also exhibit dissimilarities. For example, the associations of male sex and cigarette-smoking with ischaemic events in the lower limbs are more pronounced than their associations with coronary or cerebral ischaemia (Gordon and Kannell, 1972). Arterial occlusion is not entirely due to atheroma: platelet-fibrin thrombi, platelet-fibrin emboli, and arterial spasm may all contribute to organ ischaemia, and there is evidence that the relative contribution of these other processes varies in different clinical syndromes. For example, in patients who die suddenly and in patients with “pure” angina there is usually severe coronary atherosclerosis, but not usually an occlusive thrombus (Roberts and Ferrans, 1976). On the other hand, patients who die after sustaining a major cardiac or cerebral infarction commonly have an occlusive thrombus in the appropriate artery (Chandler et al., 1974; Battacharji et al., 1967). Apart from emboli arising from the heart, atheromatous or platelet-fibrin emboli arising from proximal arterial lesions may give rise to transient cerebral or ocular ischaemia (Russell, 1961) and digital ischaemia (Slaney and Hamer, 1973). It has also been suggested that intravascular platelet aggregates might contribute to digital ischaemia (Vreeken and van Aken, 1971) and sudden coronary death (Haerem, 1972). Finally, coronary artery spasm may be associated with some episodes of angina (Oliva et al., 1973).