1034

THE EPIDEMIOLOGY OF HAEMOSTATIC AND OTHER VARIABLES IN CORONARY ARTERY DISEASE. T.W. Meade. MRC Epidemiology/Medical Care, Northwick Park Hospital, Harrow, U.K.

The increase in the clinical manifestations of coronary artery disease (CAD) since the 1920s cannot be explained solely in terms of atheroma. Another major process such as thrombogenesis must also be involved. Pathological studies show that thrombosis contributes not only to myocardial infarction but to nearly all cases of sudden coronary death as well. Epidemiologically, it is the coagulation system rather than platelet function that has so far been more rewarding in attempting to identify characteristics of the haemostatic system that are associated with the subsequent risk of CAD. In particular, two clotting factors - factor VII coagulant activity, VIIc, and fibrinogen - may be involved. Factor VII has several characteristics that are required for a system to secure rapid haemostasis after injury. The question is whether an exaggeration of the physiological state of readiness implied by these features may predispose to thrombosis. There are at least four pathways through which high fibrinogen levels, however they are determined, may operate to increase the risk of CAD - involvement in atherogenesis, determination of blood and plasma viscosity, effects on platelet aggregability and an influence on the amount of fibrin formed. The prospective Northwick Park Heart Study (NPHS) has shown an association between high VIIc levels and an increased risk of CAD. NPHS and three other prospective studies have also demonstrated a clear association between high levels of plasma fibrinogen and an increased risk of CAD, this association generally being stronger than for more familiar markers of risk such as the blood cholesterol level. There may well be an interaction between fibrinogen and blood pressure, the occurrence of high levels of both increasing CAD or stroke risk to a greater extent than would be expected from the sum of their separate effects. Several pathological and clinical observations support a "hypercoagulable state" not simply as a concept but as a demonstrable abnormality in which characteristics of the circulating blood influence the course of events. These include the effects of anti-thrombotic agents (particularly oral anticoagulants) on re-infarction rates and the likelihood that high VIIc levels lead to increased levels of thrombin production. The general epidemiology of VIIc and fibrinogen is consistent with the view that high levels of each are of pathogenetic significance. Thus, increasing age, obesity, oral contraceptive usage, the occurrence of the menopause and diabetes are all associated with high levels of VIIc and fibrinogen and with an increased risk of CAD. Psychosocial influences may increase the risk of CAD through effects on the plasma fibrinogen level. There is strong evidence that dietary habit, particularly the consumption of fat, is a leading determinant of the VIIc level. A substantial proportion of the relationship between cigarette smoking and CAD is probably mediated through the plasma fibrinogen level. The most radical implication of a "hypercoagulable state" is for the pharmacological prophylaxis of CAD which, it may turn out, is better approached by anti-thrombotic measures than by the use of lipid-lowering agents.