Some Comments on Atheromatosis and Thrombosis

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There is an intimate relationship between atheromatosis and thrombosis. Where the arterial intima is the seat of atheromatous changes, secondary deposition of fibrin is apt to occur, and development of thrombi may result. In the opinion of some workers (Duguid, Astrup), the deposition of fibrin is the primary phenomenon which gives rise to atheromatosis through subsequent organization and deposition of cholesterol and calcium. Thrombosis is also promoted by arterial and venous congestion.

Whatever the views on the development of atheromatosis, disturbances of the clotting mechanism – in the form of increased coagulability and presumably also reduced fibrinolysis – must be considered an important pathogenic factor.

Investigations into the clotting mechanism in arteriosclerotics as well as in elderly individuals have not so far thrown much light on such disturbances. The fibrinogen level of the blood is stated to increase somewhat with advancing age, whereas the clotting time changes but little. Determinations of the recalcification time of blood plasma in elderly persons at “De Gamles By” (the Geriatric Hospital, Copenhagen) have shown a considerably greater dispersion of the values than in young healthy subjects, but it was striking that low values were more common among the aged persons. It must be borne in mind, however, that the elderly persons were patients in a geriatric department and are therefore not applicable as a basis for comparison in studying pure changes of ageing. According to various investigators (Schulz) fibrinolysis decreases with advancing age.

The methods available for determining alterations in coagulation and fibrinolysis are rather rough and unreliable for clinical

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use, and it must be the object of medical biochemistry to develop methods permitting a more exact determination. As a rule, however, major variations in these processes are not to be expected in elderly persons. Thus, a greatly shortened clotting time would be disastrous to the human body, since it might easily lead to generalized thrombosis. The clotting mechanism with its promoting and inhibitory factors takes up a state of equilibrium which may be altered temporarily, but to which the body tries to return. In studying the clotting mechanism it would seem to be more fruitful to consider the individual factors, promoting as well as inhibitory, since disturbances of the quantitative ratio between these factors is probably more easily demonstrable than is disturbance of the overall result, i.e. the clotting time. During old age, when the ability to maintain a state of equilibrium (homeostasis) is reduced, any changes are far more serious than at an earlier age. Often, they may be disastrous, since increased coagulability for any length of time

must lead to deposition of fibrin on the intima of the arteries at sites where they are damaged (atheromatosis, mechanical stress) and on the intima of the veins in the presence of phlebitis. To this day, many aspects of the aetiology of atheromatosis remain unelucidated, but it seems to be an established fact that disturbances of the cholesterol metabolism constitute the main factor. Hypercholesterolaemia must be interpreted as an important indication of metabolic disturbances of this nature, and the connection between a high serum cholesterol level and the development of atheromatosis is evident. This applies to essential, familial hypercholesterolaemia (xanthomatosis) which sooner or later results in coronary sclerosis and coronary thrombosis [Müller-Harbitz disease). It is different with the moderately high and high serum cholesterol levels (200–300 mg per 100 ml). Recent investigations by Keys and his associates have shown a clear correlation between a high serum cholesterol level and the development of atheromatosis and coronary disease. These authors consider the dietary content of animal fat, especially milk fat, to be definitely atherogenic, whereas vegetable oils, especially corn oil, sunflower oil, and soya oil with a high content of unsaturated fatty acids, appear to inhibit the development of atheromatosis. According to the most recent investigations by Malmros and Wigand, this disease is simply caused by a deficient supply of the essential unsaturated fatty acids. It must be mentioned, however, that factors such as hypertension, stress, excessive cigarette smoking, and other partly unelucidated factors must be assumed to play a role as well.

Lober has shown that the atheroma in the coronary arteries rapidly increases from childhood up to about 60 years of age, after which the rate of increase slows down. He demonstrated an unmistakable correlation between the level of the blood pressure and the degree of atheromatosis. The same findings have been reported by Faber, studying aortic atheromatosis. Against the causal role of hypertension, it has been stated that in Japan hypertension is common, whereas coronary sclerosis and coronary thrombosis are rare and the serum cholesterol level is low. This apparent incongruity, however, seems to be explicable by the assumption that hypertension can only give rise to atheromatosis if the serum cholesterol has reached a relatively high level. The hypertension proper must be presumed to involve minor injuries to the intimal wall of the arteries which then become the seat of cholesterol, calcium, and fibrin deposits. Post-mortem examinations of aged persons have frequently shown a striking discrepancy between the extent of atheromatosis in the coronary arteries and in the aorta. Pronounced atheromatosis of the aorta despite low-grade coronary sclerosis is not an uncommon finding, but the reverse is more often encountered. It has been stressed by Duguid that the changes in the coronary arteries represent a special syndrome which he calls “coronary disease”. Repeated depositions of fibrin with subsequent organization lead to narrowing of the arterial passage, and this promotes thrombosis. True, recanalization will create new passages but still the circulation has to contend with an extremely narrow lumen.

As a rule, the risks of a high-fat diet are believed to be an unwanted increase in serum cholesterol and a consequent deposition in the intima of the arteries. This is more complicated than generally assumed, since cholesterol is probably synthesized in the vascular wall. Less attention has been paid to an apparently equally serious property of the animal fats, especially of milk fat with a high content of saturated fatty acids, viz. that it promotes coagulation and inhibits fibrinolysis (O'Brien, Maclagan and Billimoria, Sinclair). Large, high-fat meals appear to increase the frequency of thrombosis, especially in elderly and particularly predisposed persons (Greppi's

thrombophilic type). Accordingly, Geill, From Hansen and Lund have demonstrated that in a large group of geriatric hospital patients

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kept for some length of time on a diet low in milk fat and dripping but high in corn oil and soya oil, the incidence of arterial and venous thrombosis was only one-quarter of that found in a corresponding control group on ordinary hospital diet. The two groups did not differ in body weight, blood pressure, age, or other factors that might explain the difference in the incidence of thrombosis.

It must be one of the goals of geriatrics to arrive at a diet that may reduce the present high incidence of atheromatosis and thrombosis. Prevention and treatment of a number of diseases and habits, such as hypertension, obesity, hormonal insufficiency (myxoedema, diabetes mellitus, hypogonadism, etc.), excessive cigarette smoking, and inactivity must form an important part of the therapeutic effort.

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