

Relationship between the blood levels of cholesterol, mucoproteins, and fibrinogen in ischaemic heart disease

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SYNOPSIS Serum cholesterol, serum mucoproteins, and plasma fibrinogen levels were estimated in 60 male patients with ischaemic heart disease. No correlation was found between the levels of these blood components.

The levels of a number of substances have been shown to be frequently raised in the blood of patients with ischaemic heart disease and other conditions associated with the intimal lesions of atherosclerosis. The most widely recognized and investigated of these substances is cholesterol; many investigators have shown that atherosclerosis is associated with a raised total serum cholesterol level (Keys, 1951; Oliver and Boyd, 1953; Gofman *et al.*, 1956). It has also been observed that atherosclerotic subjects have a higher serum mucoprotein level than normal subjects (Antonini and Salvini, 1957; Schwartz and Gilmore, 1958) and plasma fibrinogen levels have been shown to be increased in patients with ischaemic heart disease (McDonald and Edgill, 1957; Merskey, Gordon, Lackner, Schrire, Kaplan, Sougin-Mibashan, Nossel, and Moodie, 1960; Egeberg, 1962).

The present investigation was undertaken to determine whether any relationship exists between the serum cholesterol, serum mucoproteins, and plasma fibrinogen levels in patients with ischaemic heart disease.

METHODS

SERUM CHOLESTEROL The total serum cholesterol was estimated on a Technicon AutoAnalyzer as described by Green, Inman, and Thorp (1963). Although there is some disagreement about the maximum serum cholesterol level in health we consider that values over 275 mg./100 ml. are undoubtedly abnormal.

SERUM MUCOPROTEINS Serum mucoproteins were estimated by the method of Winzler, Devor, Mehl, and Smyth (1948). The factor 23.8 was used to convert

milligrams tyrosine to milligrams mucoprotein. The range in 22 control subjects was 80-130 mg./100 ml. (mean 107 mg./100 ml.; S.D. 12) (Ogston, 1962).

PLASMA FIBRINOGEN Plasma fibrinogen was estimated by a modification of the method of Nilsson and Olow (1962). The range in 20 control subjects was 250-410 mg./100 ml. (mean 336 mg./100 ml.; S.D. 46).

SUBJECTS

PATIENTS WITH ISCHAEMIC HEART DISEASE Sixty male patients aged between 36 and 69 were studied. All had electrocardiographic evidence of myocardial infarction at the time of their admission to hospital four to 81 months before this investigation. All were receiving long-term anticoagulant therapy (phenindione), the Quick one-stage prothrombin time being maintained at two and a half to three times the control.

Therapeutic doses of phenindione do not affect the levels of serum cholesterol (Herbert, Beamish, and Perry, 1959; Watson, Buchanan, and Dickson, 1963), serum mucoproteins (Ogston, 1962), or plasma fibrinogen (Merskey *et al.*, 1960).

CONTROL SUBJECTS; These subjects were mainly healthy men aged between 40 and 69; a few male patients in the convalescent ward were also included. Care was taken to ensure that members of this group gave no history of angina pectoris or calf claudication, and had no evidence of atherosclerosis on clinical examination.

Infections result in a rise in plasma fibrinogen (Eastham and Morgan, 1963) and in serum mucoproteins (Lockey, Anderson, and Maclagan, 1956). Transient respiratory infections were not uncommon in the patients studied and those who gave a history of recent infection and had a raised erythrocyte sedimentation rate (above 12 mm. in the first hour) were excluded from the main study. The mucoprotein and fibrinogen levels of these patients are presented in Figure 2.

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RESULTS

Table I summarizes the data for the group of 60 patients with ischaemic heart disease while the scatter and distribution of the individual cholesterol, fibrinogen, and mucoprotein levels is shown in Figure 1. For each of these blood components a number of patients had levels above the normal ranges as defined above. Twenty-one patients had a raised plasma fibrinogen, 18 a raised serum cholesterol, and 13 a raised serum mucoprotein level.

TABLE I

RESULTS FOR PATIENTS WITH ISCHAEMIC HEART DISEASE

Age Group	No. in Group	Mean Fibrinogen (mg./100 ml.)	Mean Mucoprotein (mg./100 ml.)	Mean Cholesterol (mg./100 ml.)
30-39	2	378	119	273
40-49	7	390	119	231
50-59	33	396	114	272
60-69	18	390	115	254
All ages	60	393	115	262

Figure 2 plots the fibrinogen levels against the mucoprotein levels in the 60 patients with ischaemic heart disease and in 11 patients with an additional intercurrent infection. Although there is no correlation between the fibrinogen and mucoprotein levels in the patients with ischaemic heart disease alone, both rise in the presence of infection.

Figures 3 and 4 plot the serum cholesterol levels against serum mucoprotein and plasma fibrinogen

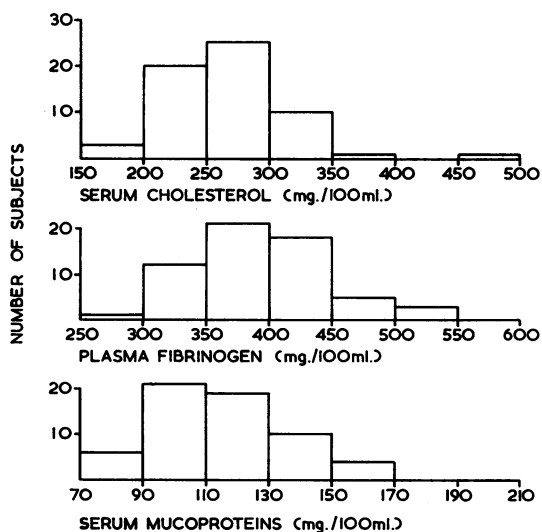


FIG. 1. Serum cholesterol, serum mucoproteins, and plasma fibrinogen levels in patients with ischaemic heart disease.

TABLE II

COEFFICIENTS OF CORRELATION

	Coefficient of Correlation (r)	Significance (p)
Fibrinogen and mucoproteins	+0.012	>0.1
Cholesterol and fibrinogen	+0.104	>0.1
Cholesterol and mucoproteins	-0.099	>0.1

respectively. Table II presents the coefficient of correlation (r) for fibrinogen with mucoprotein, fibrinogen with cholesterol, and cholesterol with mucoprotein. It can be seen that there is no correlation between these measurements when the complete group is analysed.

In order to determine whether a correlation was present between elevated levels the subjects with an elevation of one parameter were examined separately for an associated elevation of a second para-

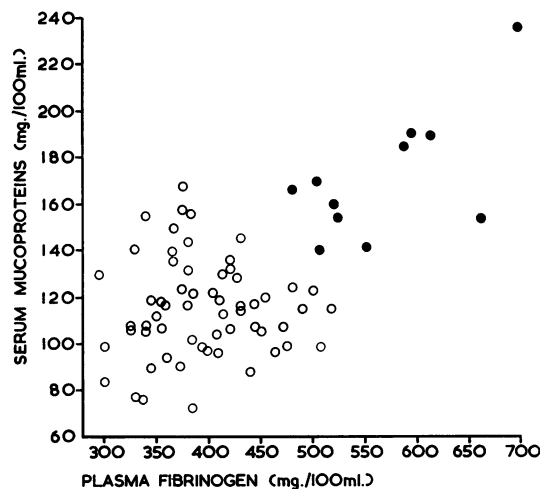


FIG. 2. Plasma fibrinogen related to serum mucoproteins. ○ Patients with ischaemic heart disease. ● Patients with ischaemic heart disease and a superadded infection.

meter. Twenty of the 60 patients had a normal level of all three parameters studied. Twenty-eight of the remaining 40 patients had an elevation of one parameter only, and 12 had an elevation of two of the parameters. No patient had an elevation of all three. There was an associated elevation in serum cholesterol and plasma fibrinogen in six patients, in serum cholesterol and serum mucoproteins in four patients, and in plasma fibrinogen and mucoproteins in two patients. It is apparent that elevation of more than one of these parameters is seldom found in patients with ischaemic heart disease.

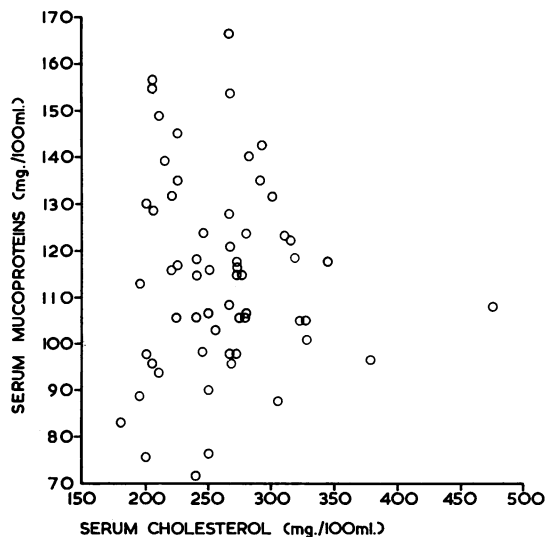


FIG. 3. Serum cholesterol level related to serum mucoproteins.

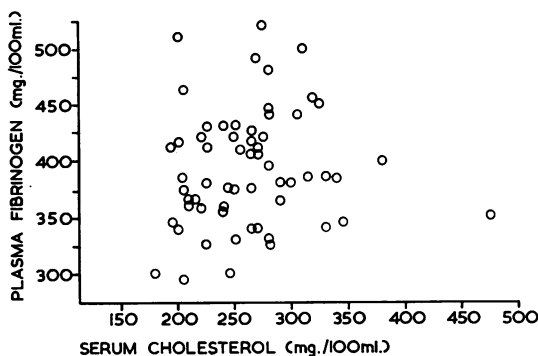


FIG. 4. Serum cholesterol level related to plasma fibrinogen.

DISCUSSION

There is now general agreement that coronary artery disease has an association with a high level of blood cholesterol. Cholesterol, along with other lipids and fibrin, is the substance which accumulates in the walls of arteries. The suggestion has been made that the rise in serum cholesterol may be causally associated with the intimal lesion.

Attention has been drawn to alterations in the mucopolysaccharides in vessels with atherosclerosis and it has been suggested that deposition of lipids follows a primary change in the mucopolysaccharide in the arterial wall (Noble, Boucek, and Kao, 1957).

Arterial wall mucopolysaccharide depolymerization was suggested as the cause of the raised serum mucoprotein level found in atherosclerosis (Schwartz and Gilmore, 1958) although Dorfman (1959) has stated that it is unlikely, on chemical grounds, that the blood mucoproteins arise from such a source.

The cause of raised plasma fibrinogen levels in patients with coronary artery disease is unknown. It has been suggested that it might be a result rather than a preceding factor in the disease (Merskey *et al.*, 1960).

We have found no correlation between serum cholesterol, serum mucoproteins, and plasma fibrinogen levels in patients with ischaemic heart disease. This suggests that there is no common cause for the increased blood levels of these substances in many patients with ischaemic heart disease. One possible explanation, however, for this lack of correlation may be that the maximum elevations of these blood components occur during different phases of the disease process. Proof of this hypothesis would require serial measurements of cholesterol, mucoproteins, and fibrinogen at different stages in the development of the atherosclerotic lesion.

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