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An analysis of cholesterol values
by usual hospital laboratory methods in 1,700
patients with atherosclerotic disease re-
vealed no definite correlation between
serum cholesterol levels and the nature
and extent of atherosclerotic disease.
Eight out of ten patients had cholesterol
values below 300 mg/100 ml, the upper
limits of normal for the procedure em-
ployed. Associated diseases such as di-
abetes mellitus and arteriosclerotic heart
disease, age, and anatomical location and
extent of atherosclerotic disease did not
significantly alter the distribution of
cholesterol values. Although an elevated
cholesterol level may be a factor in ab-
normal lipid metabolism and associated
atherosclerotic disease, the majority of
patients in this group had serum chole-
sterol values within the accepted normal
range for Americans.

ELEVATED SERUM CHOLESTEROL values are sometimes found in patients, including
those with uncontrolled diabetes, myxedema, ne-
plasia, xanthomatosus, and idiopathic hypercho-
lersterolemia. Atherosclerotic disease is usually present
at an early age in these patients. In populations
relatively free of atherosclerotic disease, serum chole-
sterol values are usually low and are well below
the average values found for Americans, who
have an alarming degree of atherosclerosis. From
these and other epidemiologic studies, it has been
postulated that the serum cholesterol level, as an
index of altered lipid metabolism, may be related
to the incidence of atherogenesis in various popu-
lations. Current efforts at reduction and control of
blood cholesterol levels by means of dietary restric-
tion or drugs, or both, are based on this
concept.

However, reports of serum cholesterol levels in
patients with atherosclerotic heart disease and
cerebral infarction have appeared which indicate
poor correlation between the occurrence of athero-
sclerotic disease and the observed serum chole-
sterol level.

The purpose of this report is to summarize
serum cholesterol data obtained for 1,200 patients
with a degree of atherosclerotic disease sufficient
to require surgical treatment, and to determine
the relationship between the observed cholesterol
values and the anatomical type and extent of vas-
cular lesions. Evidence was also sought for the
effect of certain associated diseases on this
relationship.

Method of Study
Serum cholesterol determinations were done in
the Methodist Hospital Laboratory for patients
with vascular disease admitted to the surgical ser-
vice. The method of Pearson and associates was
used for the determination. This method has been
found to be suitable for routine analysis, it gives
consistent and reproducible results with a minimum
degree of preparation of the sample. Values ob-
ained in this study are approximately 12% higher than those
obtained by the Aabell method. A strict quality
control system is imposed in the laboratory. Stand-
ard serum samples are checked frequently and
allowed a maximum variation of two standard
deviations (17 mg/100 ml). Serum cholesterol
determinations were also carried out in the Lipid
Research Laboratory, using the technique of Creech
and Sewell on 200 of the blood samples in which
cholesterol determinations have been done in the
hospital laboratory. The method of Creech and

Sewell employs a silicic acid column for the separation of free and esterified cholesterol, and is more specific for cholesterol than the routine hospital methods. The cholesterol determination method was that of Hanel and Dan.

Values which were determined by this technique were found to be from 20 to 30 mg/100 ml below the values of the hospital laboratory.

Blood samples were obtained on the morning following admission and prior to any diagnostic arteriography. The venous tourniquet was removed within two minutes to eliminate sampling error.

The patients were divided into groups according to the site and nature of the atherosclerotic lesions. All patients with arteriosclerotic heart disease manifested by either angina pectoris or history of myocardial infarction. The majority of patients were admitted to a single site were considered to have arteriosclerosis of limited extent. Patients with an involvement of two or more separate areas were considered to have moderately extensive disease, and patients with atherosclerotic lesions involving three or more separate anatomic areas were classified as having extensive vascular damage. Thus, a patient with an aneurysm of the abdominal aorta but no other lesion of clinical importance was classified in the first group. A patient with an aneurysm of the abdominal aorta and arteriosclerotic heart disease as well was placed in the second group. A patient with an aneurysm of the abdominal aorta, arteriosclerotic heart disease, and associated extracranial occlusive disease or superficial femoral artery occlusive disease was considered to have extensive involvement.

Results

Included in this study were 1,700 patients with arteriosclerotic lesions whose nature was defined by angiography and during surgery. There were 1,416 (83%) males and 284 (17%) females, and their ages ranged from 20 to 85 years (Fig 1). Fifty-six percent of the patients had arteriosclerotic occlusive disease and 44% had aneurysmal disease produced by atherosclerosis. Seventy-eight percent of all patients had serum cholesterol values below 300 mg/100 ml (hospital values) (Fig 2), the upper limits of normal for this procedure. Patients with aneurysmal and occlusive disease were studied separately; the serum cholesterol levels for the groups are recorded in Fig 3.

The results of the analysis of patient data according to the extent of disease are given in the Table. The disease was localized in one or two areas in 96% of the patients. Serum cholesterol values were below 300 mg/100 ml in more than 80% of these patients. In patients with involvement of three or more areas, the cholesterol levels were below 300 mg/100 ml in 70% of the group. Sixteen percent of patients with disease localized in one area and 15% of patients with involvement of two or more areas had cholesterol values below 200 mg/100 ml.

Overdoses of the patients were present in 7% of the patients and 75% of the diabetic patients had cholesterol values below 300 mg/100 ml (Fig 4). Arteriosclerotic heart disease characterized by angina pectoris or a history of previous myocardial infarction was present in 28% of the patients. Eighty percent of this group had cholesterol values below 300 mg/100 ml (Fig 5).

Serum cholesterol values for 200 patients who were chosen at random were determined by the method of Cooper and Sewell. These data are on curve C in Fig 6.

Patients aged 31 to 50 and 51 to 70 years were studied separately to compare cholesterol values in the relatively young and relatively old patients with significant atherosclerotic disease. The results are recorded in Figs 7 and 8.

Comment

The determination of serum cholesterol values is subject to many errors even with rigid control of the patient environment and of laboratory procedures. Therefore, when attempts are made to correlate this measurement with a disease process. Nevertheless, similar blood sampling and estimation methods are followed in many hospitals, and serum cholesterol values for patients under study and treatment for arteriosclerotic disease are always recorded and evaluated. The procedures used to obtain the data for this study are comparable to those used in other hospitals and laboratories.

The purpose of this study of patient data was to determine if the nature and extent of the atherosclerotic lesions observed during surgery were associated with variations in age, sex, associated diseases, or serum cholesterol levels for the patient. The marked association of both occlusive and aneurysmal disease with males, as compared with females, is evident from Fig 1. The belief that clinical manifestations of arteriosclerotic disease occur predominantly in males is widely accepted, and these data are in accord with this view. Within the group of male patients, occlusive disease tended to be the most likely form of arterial damage ob-
In the present study, in order to compare the cumulative frequency distribution of serum cholesterol values for the patient group with corresponding distributions observed under other circumstances, 200 cholesterol determinations were made by the method of Creech and Sewell from the same blood samples used for the hospital laboratory determinations and were taken without selection of patients. These values may be compared with the most recent data from two other sources.** Fig 6 shows the cumulative frequency distribution of serum cholesterol values for this group (curve C) compared with values for a group of "normal" Finnish males, aged 36 to 65 years (curve B), for a group of male Finnish patients with coronary heart disease (curve A), and average values for a group of Minnesota business and professional men observed during 1956-1962 (curve D). Values for American and Finnish subjects are compared in detail by Niskila and Pelkonen, respectively. Curves A and B are based on an estimation procedure that gives slightly high values, but, with a correction factor estimated at 0.9, it is evident that the patient group has a cumulative frequency distribution that is higher than that observed for the Minnesota businessmen, although lower than that observed for Finnish patients with coronary disease; and not very different from that observed for "normal" (blood donors) Finnish males aged 36 to 65 years.

An age trend towards increasing serum cholesterol levels was found in the Minnesota study and in the Finnish study, and an age trend in the occurrence of clinically defined vascular damage is evident from Fig 1. However, an analysis of cholesterol values in a relatively young group of our patients (31 to 50 years of age) and an older group (51 to 70 years of age) reveals little difference in the distribution of values (Fig 7).

The cumulative frequency distribution of these values within our group of patients is, then, different from those found for a group of "normal" males in one study,** but not from those found in another.** The values for patients in our series with widespread atherosclerotic disease were not remarkably different from those among patients in this series whose disease was of more limited distribution (Table). These observations support the judgment that, at best, the basal cholesterol level in an individual patient is a valid predictive factor with regard to the likelihood of coronary disease only when placed in relation to other and perhaps more consequential factors; they suggest also that extension of studies which focus on determination of basal serum cholesterol levels to the exclusion of other possible determinants of atherosclerosis carry only the remote likelihood of contributing additionally or significantly to solution of the problem of the etiology of occlusive and aneurysmal disease.

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References


