Prevalence of hyperlipoproteinaemia in apparently healthy men

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Lipoprotein typing was carried out on 4385 apparently healthy male subjects at work in the Glasgow conurbation of the West of Scotland. Subjects were fasting and the investigations undertaken were cholesterol, triglyceride, lipoprotein paper electrophoresis, and preparative ultracentrifugation when necessary. 29·5 per cent of subjects were normal in terms of history, weight, blood pressure, electrocardiogram, and all smoked less than 5 cigarettes daily.

The overall prevalence of hyperlipoproteinaemia was 15·3 per cent and consisted of 12 per cent type IV and 3·3 per cent type II hyperlipoproteinaemia. Type IIa abnormality occurred more frequently than type IIb.

There was a significantly higher prevalence (17·6%, P<0·01) of type IV abnormality in the obese group.

In normal subjects the prevalence of type II abnormality was 3·1 per cent, whereas that of type IV hyperlipoproteinaemia was 7 per cent.

In 1971 there were 17,656 deaths from ischaemic heart disease in Scotland. This accounted for 28·6 per cent of all deaths, 1 in 3 male and 1 in 4 female deaths in the country (Registrar General, 1972).

Epidemiological studies have indicated that hyperlipidaemia as shown by raised cholesterol or raised triglyceride, either singly or in combination, hypertension, and heavy cigarette smoking are among the major risk factors in the development of coronary heart disease (Blackburn, 1970; Carlson and Böttiger, 1972; Kannel *et al.*, 1964). Advances in the study of hyperlipidaemia have led to the concept of the hyperlipoproteinaemias and to the development of lipoprotein typing systems, such as described by Fredrickson, Levy, and Lees (1967). There is, however, as yet little knowledge of the frequency with which lipoprotein abnormalities occur in the population in this country.

This study was, therefore, undertaken to investigate the prevalence of lipoprotein abnormalities in apparently healthy male subjects at work in the Glasgow conurbation of the West of Scotland, an area where there is a high incidence of coronary heart disease.

Methods

Sample and response

The sample consisted of apparently healthy men, either self-employed or on the staff of professional or industrial groups. The survey comprised 4477 men (a response rate of 77%). They were mainly between the ages of 35 and 59 years and were in employment as shown (Table 1). There were 2346 (52·3%) non-manual and 2131 (47·7%) manual workers. Before attending the screening unit, each subject was asked to complete a

TABLE I *Health survey in the West of Scotland: sample subgroups with individual numbers of respondents and response rates*

Group	No.	Response rate (%)
A: Non-manual		
Faculty of Procurators in Glasgow	275	69
British Rail (executive and clerical)	1047	88
Civil Service	1024	83
B: Manual		
Weir-Pacific Valves Ltd.	103	81
British Steel Corporation	225	54
Prestcold Scotland Ltd.	274	91
I.C.I.	648	78
Caterpillar Tractor Co. Ltd.	881	70

questionnaire containing standardized questions on history of chest pain (Rose and Blackburn, 1968a), smoking habits, and bronchitis (M.R.C., 1965). At the screening unit, the questionnaire was individually checked. Subsequently the procedure was as described by Hawthorne, Gillis, and MacLean (1972), with height, weight, blood pressure (Rose and Blackburn, 1968b), a 6-lead electrocardiogram (3 standard and 3 unipolar limb leads), and chest radiograph being recorded.

Venous blood, 10 ml, was withdrawn from subjects who had been asked to fast for at least 9 hours before sampling. Plasma was separated and, when necessary, stored at 4°C. Plasma total cholesterol and triglycerides were measured by autoanalyser techniques (Annan and Isherwood, 1969; Kessler and Lederer, 1966).[1] Plasma lipoprotein electrophoresis was carried out on each sample using albuminated barbitone buffer (Lees 'and Hatch, 1963). The age related upper normal limits used for cholesterol and triglyceride were those suggested by Fredrickson *et al.* (1967). Subjects who had probable postprandial hypertriglyceridaemia on the basis of chylomicrons detected on the electrophoretogram were reinstructed about the need for fasting, and sampling was repeated. Subjects with increases in both cholesterol and triglyceride were recalled in the fasting state, and a 35 ml venous blood sample was obtained. The cholesterol content of each of the major lipoprotein fractions was determined following ultracentrifugation at 114,000*g* for 16 hours (Fredrickson *et al.*, 1967) and heparin and manganese precipitation of all lipoproteins other than high density lipoprotein (Burstein, Scholnick, and Morfin, 1970). Electrophoresis of the ultracentrifuged fractions at D < 1·006 and at D > 1·006 was also done. Following these investigations, the results were classified as follows.

1) Normal lipoproteins on the basis of normal total cholesterol and triglyceride and normal electrophoretogram.
2) Type IIa hyperlipoproteinaemia, as defined by a raised total plasma cholesterol, a normal total triglyceride, and a pronounced beta band on the electrophoretogram. Type IIb hyperlipoproteinaemia (Beaumont *et al.*, 1970) as defined by a raised low density lipoprotein cholesterol and a raised total triglyceride value.
3) Type IV hyperlipoproteinaemia, as defined by a raised triglyceride, a normal total cholesterol, and a distinct pre-beta band on the electrophoretogram.

Types I, III, and V hyperlipoproteinaemia were not encountered in this study.

Normal and abnormal participants

The total population examined (4477) was divided into two subgroups designated 'normal' and 'abnormal'. The abnormal group contained subjects with any of the following conditions which were present in the proportion shown in Table 2.

[1] Laboratory techniques standardized with lipid standardization laboratory, Centre for Disease Control, Atlanta, Georgia, U.S.A.

TABLE 2 *Health survey in West of Scotland men*

Classification	Percentage
Normal	29·5
Cigarette smoking	59·0
Obese	28·0
Hypertension	7·4
Abnormal electrocardiogram	4·9
Possible angina	5·0

The following definitions were used: Cigarette smoking – 5 or more cigarettes daily. Obesity – more than 10 per cent above predicted ideal weight. Hypertension – systolic blood pressure of more than 170 mmHg and/or diastolic blood pressure of more than 100 mmHg at time of study. Electrocardiographic abnormalities were those summarized as categories I and II in the Minnesota code. (*Minnesota code I*: major Q wave or left bundle-branch block, groups 1·1 or 1·2 or 7·1. *Minnesota code II*: Minor Q wave, group 1·3, or ST depression groups, 4·1 or 4·2 or 4·3, or T wave abnormality, groups 5·1 or 5·2 or 5·3.) A history of possible angina was obtained from the questionnaire.

Of the total group, 29·5 per cent were defined as normal using the above criteria.

Data analysis

Variables such as mean and standard deviations were calculated by conventional methods. Student's 't' test or χ^2 analysis was used as appropriate for calculation of levels of significance.

Results

Results for fasting cholesterol and triglyceride values were available from 4385 subjects (1296 normal and 3089 having one or more abnormality as previously defined). Three subjects above 60 years of age were not included in the analysis. Obesity was the sole abnormality in 539 subjects There were 255 non-obese and non-cigarette smoking subjects who were found to have one or more of the other abnormalities defined above. There were 89 subjects from the 4474 who attended, in whom, for technical reasons, results were not obtained.

Cholesterol and triglyceride values for these subgroups are shown in Table 3. There is no significant difference in cholesterol values between the groups. Values tend to be lower in subjects less than 39 years but little change occurs thereafter. Triglyceride levels are significantly higher at all age groups in the obese group. There is, in general, no tendency for triglyceride values to increase with age. Normal levels appeared to decrease in the over 40 age groups. When subjects are considered who have an abnormality other than obesity or cigarette

TABLE 3   *Plasma total cholesterol and triglyceride values (mg/100 ml) in normal subjects, those with an abnormality other than smoking or obesity, and those who are obese but otherwise normal (mean ± SD are shown)*

Age (yr)	Normal			Abnormality other than smoking or obesity			Obesity as sole abnormality		
	No.	Chol.	TGL	No.	Chol.	TGL	No.	Chol.	TGL
<39	238	216 ± 39	102 ± 76	32	226 ± 39	117 ± 73	82	218 ± 32	135 ± 119*
40–44	365	227 ± 38	112 ± 68	49	237 ± 52	116 ± 84	119	226 ± 41	157 ± 128*
45–49	282	233 ± 39	110 ± 53	54	233 ± 40	118 ± 61	132	237 ± 40	132 ± 66*
50–54	249	234 ± 38	105 ± 48	71	241 ± 45	127 ± 68	114	225 ± 37	131 ± 139*
55–59	162	232 ± 38	104 ± 44	49	242 ± 42	114 ± 48	92	229 ± 38	136 ± 72*

* P < 0·01 when compared to normal.

TABLE 4   *Prevalence of types of hyperlipoproteinaemia in total population studied*

Age (yr)	No.	Type II		Type IV	Per cent abnormal
		a	b		
<39	654	30	1	93	19·0
40–44	1057	38	4	160	19·1
45–49	1034	43	4	142	18·2
50–54	939	17	0	74	9·6
55–59	701	13	1	52	9·4

smoking, triglyceride levels are intermediate between those of the normal and obese groups.

Data in Table 4 indicate that type IV hyperlipoproteinaemia occurs more frequently than type II abnormality. It has an overall prevalence of 12·0 per cent compared to the 3·3 per cent found for type II hyperlipoproteinaemia. In type II hyperlipoproteinaemia, it was found that type IIa occurred more frequently than type IIb. Possible reasons for this are discussed below. When the normal and abnormal subgroups were compared (Table 5) little difference was found between the groups with

respect to type II hyperlipoproteinaemia. There was a significantly higher prevalence (P < 0·01) of type IV abnormality in the obese group. This was not present among subjects who had an abnormality other than obesity or cigarette smoking.

The overall prevalence of hyperlipoproteinaemia in an apparently healthy male group at work was therefore 15·3 per cent and was predominantly type IV abnormality.

Discussion

The frequency of hypercholesterolaemia and hypertriglyceridaemia in a community depends on an arbitrary choice of values for the upper limits of normal. At present, there is no widespread agreement as to what these limits should be. Indeed, both plasma cholesterol and triglyceride may represent graded risks at all levels, there being no clearcut separation into low risk and high risk groups (Fredrickson, 1971). Furthermore, studies of 'normal' populations have the disadvantage that many of the apparently normal individuals may have latent coronary atherosclerosis. At present, it is customary to choose upper fixed values for chol-

TABLE 5   *Percentage prevalence of hyperlipoproteinaemia in normal subjects, those with an abnormality other than smoking or obesity, and those who are obese but otherwise normal*

Age (yr)	Normal			Abnormality other than smoking or obesity			Obesity as sole abnormality		
	II	IV	Total	II	IV	Total	II	IV	Total
<39	3·8	8·8	12·6	3·1	6·3	9·4	6·1	22·0*	28·1*
40–44	3·9	11·1	15·0	8·2	10·2	18·4	2·5	25·2*	27·7*
45–49	5·7	7·2	12·9	1·9	11·1	13·0	5·3	17·3*	22·6*
50–54	1·2	3·6	4·8	5·6	5·6	11·2	1·8	7·0*	8·8*
55–59	3·1	3·1	6·2	2·0	8·2	10·2	1·1	15·2*	16·3*

* P < 0·01 when compared to normal.

esterol and triglyceride so that comparison of the prevalence of hyperlipidaemia can be made within a country and also between various countries.

The present study indicates a high prevalence of hypercholesterolaemia in the Glasgow conurbation whether the cut-off point is taken at 240 or 275 mg/100 ml. These cut-off points reveal prevalence rates of 38·3 per cent and 13·3 per cent, respectively. Oliver (1969) has reported a corresponding rate of 8 per cent using the cut-off point of 260 mg/100 ml in a study of 2672 male subjects between 30 and 59 years in Edinburgh, while Veitch (1970), using manual methods, found that 21·4 per cent of male blood donors in the North of Scotland had a plasma cholesterol above 275 mg/100 ml. In a Californian study, Wood *et al.* (1972), using similar cut-off points to those in the present investigation, found prevalence rates of 19 per cent above 240 mg/100 ml and 4·5 per cent above 275 mg/100 ml. These various investigations are not directly comparable in that the Glasgow study consisted of men at work in manual, clerical, and professional occupational groups, while the North of Scotland study consisted of samples from volunteer blood donors. The Californian data were obtained from volunteers for a community health programme. None the less, the data may be useful in suggesting national and international trends.

Hypertriglyceridaemia also has a high prevalence in the West of Scotland. The cut-off points of 150 or 200 mg/100 ml for upper limits for normal values reveal prevalence rates of 24 per cent and 10 per cent, respectively. No comparable figures for other areas of Scotland or the United Kingdom have so far been published, but comparison with studies elsewhere suggests that plasma triglyceride values may be higher in California (Wood *et al.*, 1972) and Stockholm (Carlson and Lindstedt, 1969).

Age-related plasma cholesterol and triglyceride values in subjects selected as normal on the basis of the same criteria in Glasgow as used in Stockholm show similar trends. The higher levels in California may be partly due to the fact that their subjects were non-fasting (2 slices of dry toast and fruit juice before venous sampling) and that obese subjects were not excluded from their normal group. Obesity has a considerable influence on the prevalence of hypertriglyceridaemia. Table 4 shows that the mean plasma triglyceride values for obese, but otherwise normal individuals, are 20 to 30 mg/100 ml higher than for non-obese, normal subjects. Obesity does not appear to affect plasma cholesterol levels. Comparison with other investigations is, therefore, difficult unless normal, non-obese subjects have been studied. The apparent increase in triglyceride levels in California as compared to

Glasgow and Stockholm can thus perhaps be related to the inclusion of obese subjects in their normal group.

The classification of hyperlipidaemia in terms of the hyperlipoproteinaemias has given a fresh stimulus to the study of the relation between plasma lipids and vascular disease. At present there is no general agreement as to the best method of classification, or what should be regarded as the upper limits of normal for the major plasma lipoprotein fractions (high density lipoprotein, low density lipoprotein, and very low density lipoprotein). Agreement as to classification and levels of normality are needed for consistency in determination of the prevalence of hyperlipoproteinaemias in the community and for comparison with results obtained elsewhere. In addition, there are major technical and methodological problems which contribute to the relative scarcity of published data regarding the prevalence of the hyperlipoproteinaemias. Various reports have, however, appeared. Thus, Wood *et al.* (1972) using age related upper normal limits for cholesterol and triglyceride reported overall prevalence rates in a 'normal' group (which did not exclude obese individuals) of 2·8 per cent for type II and 13 per cent for type IV hyperlipoproteinaemia. In the Glasgow group the overall prevalence rate of type II abnormality was 3·3 per cent, and 12 per cent for type IV abnormality. When, however, the normal group is considered separately, then the prevalence rates remain at around 3·1 per cent for type II abnormality and fall to 7 per cent for type IV abnormality. The apparent decrease in the prevalence of the hyperlipoproteinaemias in the older age groups may well be related to the fact that the upper limits for normal cholesterol values reported by Fredrickson *et al.* (1967) for a group of American men are higher than those found in the West of Scotland. It is likely that the prevalence of plasma lipoprotein disorders in the community can be adequately studied only when normal values, based on quantitative measurements, are determined.

In assessing these results it should be emphasized that this is not a random sample of the general population, though it does represent an important economic group in the community. In addition, the use of total plasma cholesterol levels in the classification of type IIa hyperlipoproteinaemia may underestimate the prevalence of this abnormality. The measurement of low density lipoprotein cholesterol would be more accurate. Though quantitative lipoprotein typing is difficult and time consuming when large numbers of subjects are studied, it must be done before accurate prevalence rates can be determined. The results based on only semi-

quantitative techniques underestimate the prevalence of lipoprotein abnormalities, especially type II, since an abnormally high low density lipoprotein cholesterol can be found in association with a normal total plasma cholesterol (Carlson and Lindstedt, 1969).

Thus in an area where there is a high incidence of coronary heart disease, there is also a high prevalence of lipoprotein abnormalities in apparently healthy men. Type IV is the commonest abnormality and is related in part to obesity. This does not occur with type II abnormality. These data suggest that dietary factors, such as total calorie or carbohydrate intake, may be important. A detailed community dietary survey is indicated to elucidate the contribution of diet to lipoprotein disorders in the West of Scotland area. Such a survey would also help to suggest what dietary factors might need to be controlled in the management of hyperlipoproteinaemia.

It must also be conceded that a high prevalence of hyperlipoproteinaemia in an area where there is a high incidence of coronary disease does not mean that they are causally related. Their clinical significance could best be determined by large scale, long-term prospective studies of 'at risk groups' or by demonstrating that the correction of lipoprotein abnormalities results in a reduction in the clinical manifestations of coronary heart disease in the community.

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