Plasma lipid levels in gout

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A number of investigations have previously been carried out to examine inter-relationships between hyperuricaemia, gout, and levels of plasma lipids, usually with particular reference to glycerides and cholesterol. The present study was designed to compare the levels not only of glycerides and cholesterol, but also of phospholipids and free fatty acids, in gout patients with those in a group of very closely matched control subjects; and to determine, in the gout patients, whether there was any relationship between levels of these lipid fractions and the endogenous production of uric acid as measured by urinary levels of uric acid on a low-purine diet.

Plan of study

27 British patients with primary gout (25 men and 2 women) participated in the study. Some of them were on urate-lowering treatment (allopurinol or uricosuric agents) at the time when blood was taken for lipid estimations, but plasma and urinary levels of uric acid had been estimated on a low-purine diet before treatment was started.

A control group of 27 subjects was taken from hospital patients suffering from a wide variety of medical and surgical conditions. None had gout or hyperuricaemia; all were of reasonable social orientation, all were taking normal diets and none was grossly obese. Initial investigations in all subjects, gout and control, excluded predisposing causes for hyperlipidaemia. The control group was matched with gout patients for age, sex, blood pressure, alcohol intake, and the presence of ischaemic vascular disease. The two groups were also matched for ponderal index $\left(\frac{\text{height (in.)}^3}{\text{weight (lb.)}} \right)$, which tends to be lower

in gout patients than in control subjects (Snaith and Scott, 1971), but it was found that the gout patients as a group were heavier (and taller) than the controls (Table I). Both groups were classified with relation to body weight, also for the presence or absence of other factors, namely smoking, social class, and blood group.

Table I Data on 27 gout patients and 27 controls

Data	Gout (mean) patients	Controls (mean)
Age (yrs)	53.6	53.2
Height (in.)	68.4	67.75
Weight (lb.)	184.7	157.4
Ponderal index	12.06	12.51

Venous blood was taken for lipid studies after an overnight fast. Lipids were extracted from plasma by the method of Phillips and Dodge (1967).

Whole plasma cholesterol was measured by a modification of Able's method, using ferric chloride and concentrated sulphuric acid after saponification.

Phospholipids were measured, after digestion, as inorganic phosphorus, using molybdic acid and stannous chloride.

Glycerides and unesterified fatty acids were estimated on the phospholipid-free extract (obtained by using silicic acid) by modifications of the methods of Carlson and Wadström (1959) and Duncombe (1963) respectively.

Plasma and urinary uric acid was determined by an enzymatic spectrophotometric method (Liddle, Seegmiller, and Laster, 1959).

Results

The results of the plasma lipid determinations are given in Table II. Gout patients showed a significant

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Table II Lipids in gout patients and controls

Lipids	Gout patients (mean $\pm$ SD)	Controls (mean $\pm$ SD)	t	P
Cholesterol (mg./100 ml.)	214 $\pm$ 44.0	200 $\pm$ 39.29	1.26	> 0.2, < 0.3
Glycerides (mg./100 ml.)	209.2 $\pm$ 175.5	99.7 $\pm$ 41.4	3.15	> 0.001, < 0.01
Phospholipids (as lecithin mg./100 ml.)	234 $\pm$ 54.5	198.5 $\pm$ 35.3	2.966	> 0.001, < 0.01
Unesterified fatty acids U.F.A. (mEq/litre)	0.725 $\pm$ 0.284	0.451 $\pm$ 0.144	4.530	$\leq$ 0.001

elevation of plasma glycerides, phospholipids, and unesterified fatty acids, but there was no significant difference between plasma cholesterol levels in the two groups.

Although the gout patients as a group showed significantly higher plasma lipid levels than the control subjects (with the exception of cholesterol), no significant correlation existed between plasma uric acid levels and those of any of the lipid fractions, in either group. Among gout patients there was a relationship of marginal significance between obesity and plasma unesterified fatty acids ($0.1 > P > 0.05$), but not other lipids. Among controls, but not among gout patients, there was a significant positive correlation between plasma cholesterol and haemoglobin ($0.05 > P > 0.02$). There was no relation between lipid levels and smoking habits, alcohol intake, hypertension, or social class.

Certain inter-relationships existed between the plasma levels of the different lipid fractions. Both gout patients and controls showed a significant positive correlation between plasma levels of cholesterol and phospholipid ($P < 0.001$), and gout patients also showed correlation between cholesterol and glycerides ($0.01 > P > 0.001$), phospholipids and glycerides ($P < 0.001$), and phospholipids and unesterified fatty acids ($0.01 > P > 0.001$).

Levels of 24-hr urinary uric acid in the gout patients (mean 554 mg./24 hrs; S.D. 233 mg./24 hrs) showed no significant correlation with plasma levels of

cholesterol ($P > 0.1$), or unesterified fatty acids ($P > 0.1$). Regression analysis did, however, show a marginally significant correlation between urinary uric acid and plasma glyceride, though with a very wide scatter (Fig. 1), and a significant correlation between urinary uric acid and plasma phospholipid (Fig. 2).

Discussion

The plasma level of uric acid may be raised in patients with hyperlipoproteinaemia (Harris-Jones, 1957; Strejček and Kučerová, 1968) and elevation of plasma glyceride has been reported previously in patients with primary gout (Berkowitz, 1964; Feldman and Wallace, 1964; Barlow, 1968; Bluestone, Lewis, and Mervant, 1971). The present study confirms this association and shows also in patients with gout an elevation of phospholipids and unesterified fatty acids. Gout patients did not, however, show an elevation of plasma cholesterol, and this study does not therefore lend support to reports of hypercholesterolaemia in gout (Barlow, 1968), or of a relation between plasma levels of uric acid and cholesterol (Salvini and Verdi, 1959; Blahoš and Reisenauer, 1965).

Blood and urine samples for uric acid levels were taken before treatment for gout was started while the patients were taking a standard low-purine diet: samples for lipids were taken at a later date, some-

FIG. 1 Plasma glycerides and urinary acid in gout patients

FIG. 2 Plasma phospholipids and urinary uric acid in gout patients

times when the uric acid levels had been modified by treatment. It is unlikely that probenecid or allopurinol alter lipid levels: Bluestone and others (1971) studied serum glycerides and cholesterol before and during such therapy and found that, although in individual patients there was a rise or fall, no significant overall change was produced.

Urinary levels of uric acid were examined because the 24-hr urinary uric acid on a low-purine diet gives some indication of uric acid production (Scott, Holloway, Glass, and Arnot, 1969), and a graded correlation between plasma lipid levels and urinary levels of uric acid might be taken to indicate that the lipid-uric acid association was one involving production of the latter. A significant relation was found between urinary uric acid and plasma phospholipid levels, but this did not hold with unesterified fatty acids and was only marginal with glycerides.

It is now widely recognized that there are many factors which contribute to the development of hyperuricaemia and gout, a fact which sometimes makes the interpretation of investigations dealing collectively with gout patients difficult. With relation to lipids this point has been well made recently by Emmerson and Knowles (1971), who found that patients with primary gout in Australia had significantly higher plasma glyceride (but not cholesterol) concentration than patients with gout due to chronic lead nephropathy. In the Australian study the mean glyceride level in hyper-excretors of uric acid was slightly but not significantly different from that of

normoexcretors, a finding comparable to the marginal association between urinary uric acid and glycerides found in the present investigation. The nature of the relationship between hyperuricaemia and gout on the one hand, and levels of glyceride, phospholipid, and unesterified fatty acids on the other, remains obscure.

Summary

Plasma lipid levels were investigated in a group of 27 adult patients with gout and in 27 very closely matched controls. No subject had any known predisposing cause for hyperlipidaemia.

No significant difference in plasma cholesterol levels was found between the two groups, but significant increases in both phospholipid and glyceride values and a highly significant increase in unesterified fatty acid levels were observed in the gout patients.

No significant correlation was found in the gout patients between plasma uric acid and plasma lipid levels, or between 24-hr urinary uric acid and plasma cholesterol or unesterified fatty acid levels, but a marginally significant correlation was observed between urinary uric acid and plasma glyceride levels and a significant correlation between urinary uric acid and plasma phospholipids.

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