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# Gout and its relation to lipid metabolism

## II. Correlations between uric acid, lipid, and lipoprotein levels in gout

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Beaumont and Schwartz (1964), Benedek (1967), and Barlow (1968) studied the correlations between the serum lipid and uric acid levels in normal populations. The investigations were extended to gouty patients by Feldman and Wallace (1964), Günther, Herbst, and Knapp (1967), Günther, Knapp, and Siller (1968) and Darlington and Scott (1972). The findings of these authors do not always agree. The first part of this study (Mielants, Veys, and de Weerdt, 1973) reported an increase in the triglycerides, cholesterol, free-fatty acids, and phospholipids in gout, and suggested that the disturbances in the lipid and purine metabolism in gout were due to an enzyme defect common to the two processes. This paper reports a study of the relations between uric acid, lipids, and lipoproteins in gouty patients and in a control group.

### Methods and material

The investigations are based on the same biological determinations of serum uric acid, lipid, and lipoprotein levels, in the same 31 gouty patients and 31 normal subjects.

### Results

Since the frequency distributions of serum uric acid, triglyceride, cholesterol, FFA, and phospholipid levels and of the percentages of lipoprotein fractions are of the log normal type, log-log plots are executed to consider the possible correlations between the parameters.

Regression curves were calculated on the log-log plots for each pair of serum levels in the control group. Table I shows that this investigation revealed an absence of significant correlation ($2\alpha < 0{\cdot}05$) in the majority of cases. A log-log correlation was, however, found between the triglyceride levels and cholesterol, and the $\alpha$-and the $\beta$-lipoprotein levels. We were also able to demonstrate a statistically significant correlation between the cholesterol levels and the phospholipids, the $\alpha$- and the $\beta$-lipoprotein levels. On the other hand, serum uric acid concentrations correlated only with the $\alpha$- and the $\beta$-lipoprotein values. In gouty patients log-log correlations were found between all lipids, lipoproteins, and uric acid levels, in sharp contrast to the data reported above. Exception must be made for cholesterol, which correlates only with the triglycerides and the phospholipids (Table II).

In the control group, the uric acid levels did not correlate with any lipid value, in contrast to the gouty group, in which the uric acid concentration correlates with all these values except for cholesterol. In the gouty patients, practically all lipids and lipoproteins were found to be in correlation with each other. In the Figure the regression lines between uric acid and lipids in gout are plotted; there is an obvious parallelism between the uric acid/pre-$\beta$-lipoprotein and uric acid/triglyceride curves (respective slopes 0·1442 and 0·1460) and of the uric acid/$\alpha$-lipoprotein and uric acid/$\beta$-lipoprotein curves (respective slopes $-0{\cdot}1870$ and $-0{\cdot}1608$).

The interpretation of the regression lines, calculated according to the method described by Armitage (1971), are shown in Table III (overleaf). The uric acid/phospholipid curve differs significantly from the uric acid/triglyceride curve and from the uric acid/pre-$\beta$-lipoprotein curve, but the uric acid/FFA curve, however, does not differ. The Figure (overleaf) shows that a greater increase in the triglyceride, as compared to the phospholipid level, corresponds to an identical increase in the serum uric acid (from 0·60 to 0·80 for example).

By plotting each lipid and lipoprotein fraction against each other, we obtained similar curves to those shown in the Figure. In comparing the regression

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**Table I** *Correlation between uric acid, lipid levels, and lipoprotein percentages in the control group (r = correlation coefficient calculated on the logarithms of the serum levels)*

| | *Triglycerides* | *Free fatty acids* | *Phospholipids* | *Cholesterol* | *α-lipoproteins* | *pre-β-lipoproteins* | *β-lipoproteins* | *Uric acid* |
|---|---|---|---|---|---|---|---|---|
| *Triglycerides* | //////////////////// | – | – | + | + | + | – | – |
| | //////////////////// | $r = -0.05$ | $r = +0.27$ | $r = +0.44$ | $r = -0.58$ | $r = +0.61$ | $r = +0.11$ | $r = +0.26$ |
| | //////////////////// | $2\alpha > 0.1$ | $2\alpha > 0.1$ | $2\alpha < 0.05$ | $2\alpha < 0.001$ | $2\alpha < 0.001$ | $2\alpha > 0.1$ | $2\alpha > 0.05$ |
| *Free fatty acids* | – | //////////////////// | – | – | – | – | – | – |
| | | //////////////////// | $r = +0.08$ | $r = -0.05$ | $r = +0.12$ | $r = -0.02$ | $r = -0.13$ | $r = +0.08$ |
| | | //////////////////// | $2\alpha > 0.1$ | $2\alpha > 0.1$ | $2\alpha > 0.1$ | $2\alpha > 0.1$ | $2\alpha > 0.1$ | $2\alpha > 0.1$ |
| *Phospholipids* | – | – | //////////////////// | + | – | – | – | – |
| | | | //////////////////// | $r = +0.62$ | $r = -0.17$ | $r = -0.04$ | $r = +0.24$ | $r = +0.17$ |
| | | | //////////////////// | $2\alpha < 0.001$ | $2\alpha > 0.1$ | $2\alpha > 0.1$ | $2\alpha > 0.1$ | $2\alpha > 0.1$ |
| *Cholesterol* | + | – | + | //////////////////// | + | – | + | – |
| | | | | //////////////////// | $r = -0.47$ | $r = +0.10$ | $r = +0.34$ | $r = +0.15$ |
| | | | | //////////////////// | $2\alpha < 0.01$ | $2\alpha > 0.1$ | $2\alpha < 0.05$ | $2\alpha > 0.1$ |
| *α-lipoproteins* | + | – | – | + | //////////////////// | N.D. | N.D. | + |
| | | | | | //////////////////// | | | $r = -0.44$ |
| | | | | | //////////////////// | | | $2\alpha < 0.05$ |
| *Pre-β-lipoproteins* | + | – | – | – | N.D. | //////////////////// | N.D. | – |
| | | | | | | //////////////////// | | $r = +0.23$ |
| | | | | | | //////////////////// | | $2\alpha > 0.1$ |
| *β-lipoproteins* | – | – | – | + | N.D. | N.D. | //////////////////// | + |
| | | | | | | | //////////////////// | $r = +0.44$ |
| | | | | | | | //////////////////// | $2\alpha < 0.05$ |
| *Uric acid* | – | – | – | – | + | – | + | //////////////////// |
| | | | | | | | | //////////////////// |
| | | | | | | | | //////////////////// |

**Table II** *Correlation between uric acid, lipid levels, and lipoprotein percentages in gout*

| | *Triglycerides* | *Free fatty acids* | *Phospholipids* | *Cholesterol* | *α-lipoproteins* | *pre-β-lipoproteins* | *β-lipoproteins* | *Uric acid* |
|---|---|---|---|---|---|---|---|---|
| *Triglycerides* | //////////////////// | + | + | + | + | + | + | + |
| | //////////////////// | $r = +0.57$ | $r = +0.72$ | $r = +0.37$ | $r = -0.55$ | $r = +0.78$ | $r = -0.83$ | $r = +0.40$ |
| | //////////////////// | $2\alpha < 0.001$ | $2\alpha < 0.001$ | $2\alpha < 0.05$ | $2\alpha < 0.01$ | $2\alpha < 0.001$ | $2\alpha < 0.001$ | $2\alpha < 0.05$ |
| *Free fatty acids* | + | //////////////////// | + | – | + | + | + | + |
| | | //////////////////// | $r = +0.48$ | $r = +0.28$ | $r = -0.43$ | $r = +0.52$ | $r = -0.56$ | $r = +0.61$ |
| | | //////////////////// | $2\alpha < 0.01$ | $2\alpha > 0.1$ | $2\alpha < 0.05$ | $2\alpha < 0.01$ | $2\alpha < 0.01$ | $2\alpha < 0.001$ |
| *Phospholipids* | + | + | //////////////////// | + | + | + | + | + |
| | | | //////////////////// | $r = +0.40$ | $r = -0.59$ | $r = +0.65$ | $r = -0.64$ | $r = +0.53$ |
| | | | //////////////////// | $2\alpha < 0.05$ | $2\alpha < 0.001$ | $2\alpha < 0.001$ | $2\alpha < 0.001$ | $2\alpha < 0.01$ |
| *Cholesterol* | + | – | + | //////////////////// | – | – | – | – |
| | | | | //////////////////// | $r = -0.24$ | $r = +0.29$ | $r = -0.11$ | $r = +0.11$ |
| | | | | //////////////////// | $2\alpha > 0.1$ | $2\alpha > 0.1$ | $2\alpha > 0.1$ | $2\alpha > 0.1$ |
| *α-lipoproteins* | + | + | + | – | //////////////////// | N.D. | N.D. | + |
| | | | | | //////////////////// | | | $r = -0.35$ |
| | | | | | //////////////////// | | | $2\alpha < 0.05$ |
| *Pre-β-lipoproteins* | + | + | + | – | N.D. | //////////////////// | N.D. | + |
| | | | | | | //////////////////// | | $r = +0.48$ |
| | | | | | | //////////////////// | | $2\alpha < 0.01$ |
| *β-lipoproteins* | + | + | + | – | N.D. | N.D. | //////////////////// | + |
| | | | | | | | //////////////////// | $r = -0.37$ |
| | | | | | | | //////////////////// | $2\alpha < 0.05$ |
| *Uric acid* | + | + | + | – | + | + | + | //////////////////// |
| | | | | | | | | //////////////////// |
| | | | | | | | | //////////////////// |

lines, identical findings are observed (Table II): a parallel variation of the pre-β-lipoproteins and triglycerides and of the α- and β-lipoproteins. No parallelism was observed between the FFA and triglyceride curves, but their variation was always equally important. The slope of the phospholipid curves is always significantly steeper than that of the triglyceride curves.

## Discussion

In the normal population we found a log-log correlation between triglycerides and cholesterol, α- and pre-β-lipoprotein; we also reported a log-log correlation between cholesterol and phospholipids, α- and β-lipoproteins and between uric acid and α- and β-lipoproteins. The correlation between trigly-

**Table III** *Statistical approach to uric acid/lipid regression curves in gout*

| *Uric acid* | *Triglycerides* | *Free fatty acids* | *Phospholipids* | *α-lipoproteins* | *pre-β-lipoproteins* | *β-lipoproteins* |
|---|---|---|---|---|---|---|
| | //////////////////// | − | + | + | − | + |
| *Triglycerides* | //////////////////// | t = −1·54 | t = −2·01 | t = 2·84 | t = 0·02 | t = 3·18 |
| | //////////////////// | P > 0·05 | P < 0·05 | P > 0·005 | P > 0·05 | P < 0·005 |
| | | //////////////////// | − | + | − | + |
| *Free fatty acids* | − | //////////////////// | t = −1·05 | t = 3·93 | t = 1·65 | t = 4·36 |
| | | //////////////////// | P > 0·05 | P < 0·0005 | P > 0·05 | P < 0·0005 |
| | | | //////////////////// | + | + | + |
| *Phospholipids* | + | − | //////////////////// | t = 3·73 | t = 2·11 | t = 3·90 |
| | | | //////////////////// | P < 0·0005 | P < 0·05 | P < 0·0005 |
| | | | | //////////////////// | + | − |
| *α-lipoproteins* | + | + | + | //////////////////// | t = −3·00 | t = −0·21 |
| | | | | //////////////////// | P < 0·005 | P > 0·05 |
| *Pre-β-lipoproteins* | − | − | + | + | //////////////////// | + |
| | | | | | //////////////////// | t = 3·43 |
| | | | | | //////////////////// | P < 0·005 |
| | | | | | | //////////////////// |
| *β-lipoproteins* | + | + | + | − | + | //////////////////// |
| | | | | | | //////////////////// |

cerides and cholesterol was also found by Beaumont and Schwartz (1964). Benedek (1967) described this correlation as being found only in the age group 19 to 50 years. The correlation we found between triglycerides and pre-β-lipoproteins is to be expected, since the pre-β-fraction essentially consists of triglycerides.

The correlations between uric acid and serum lipids, reported in the literature, are inconstant and discrepant. Barlow (1966) found a correlation between serum uric acid triglycerides in normal female subjects, but Beaumont and Schwartz (1964) reported this correlation in males as well as females, and they also found a correlation between uric acid and cholesterol. Benedek (1967) restricted these findings to the 19 to 50-year age group. We must stress that the comparison of our data with the results reported in the literature is rather difficult, since most authors did not take the log normal frequency distribution into account.

In gout we found a correlation between uric acid and triglycerides, FFA, phospholipids, α-, β-, and pre-β-lipoproteins. We did not find a correlation between uric acid and cholesterol. Our data partly disagree with the results reported by Günther and others (1967) and Günther and others (1968). These authors found that serum uric acid is correlated to the triglycerides and the FFA, but not to the phospholipids and cholesterol. Darlington and Scott (1972) found correlations between phospholipids and cholesterol, phospholipids and unesterified fatty acids, phospholipids and glycerides, and cholesterol and glycerides in gouty patients. In the gouty patients the only absent correlations are those related to cholesterol. Furthermore, the slopes of the uric acid/triglyceride and uric acid/pre-β-lipoprotein regression curves are remarkably similar. The parallel course of these curves was to be expected, since 50 per cent of pre-β-lipoproteins consists of triglycerides.

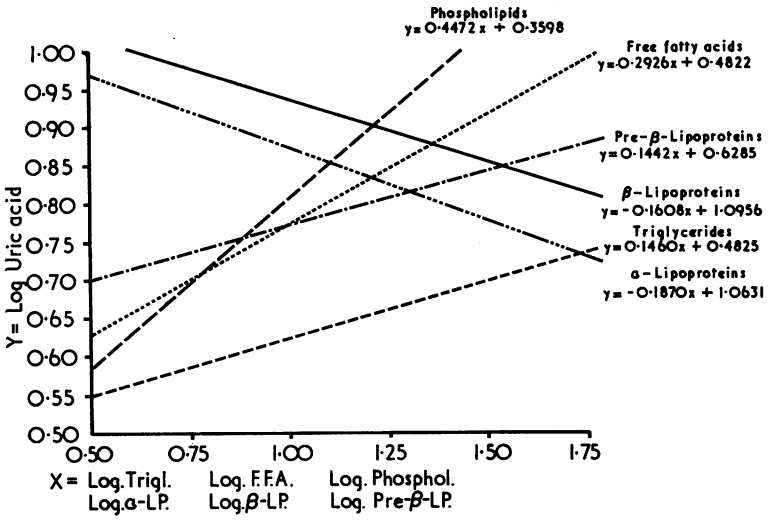


FIGURE *Uric acid/lipid uric acid/lipoprotein log-log correlation curves in gout. The regression lines are presented on the same diagram to facilitate the comparison*

The uric acid $\alpha$- and $\beta$-lipoprotein curves decrease in a parallel way, which allows us to conclude that the percentual rise of the pre-$\beta$-lipoproteins is caused by an equal percentual fall of the $\alpha$- and $\beta$-lipoproteins. For identical variations in the uric acid level however, we observe a larger increase of triglycerides than of phospholipids. We found that in fact, the triglycerides showed the largest relative increase in this disease.

Since an elevation of triglycerides, FFA, phospholipids, and pre-$\beta$-lipoprotein levels was found in gout, we have postulated in the first part of this study that, in gout, the strong relationship between lipid and purine metabolism is due to a genetic linkage, based on a hypothetical common enzyme defect.

In the second part of the study, we discovered, in the gouty patients, correlations between uric acid, lipids, and lipoproteins, which were absent in the control group.

We think that these data can be interpreted in the context of the same hypothesis, and we emphasize the necessity of a thorough knowledge of the enzyme sequences in lipid and purine metabolism, including the possible interaction of the two cycles.

**Summary**

The same biological determinations of serum uric acid, lipid and lipoprotein levels as in the 31 gouty patients and 31 normal subjects, reported in the first part of this study were used. Regression curves are calculated in this way on the log-log plots of these data.

In the control group, uric acid levels do not correlate with any lipid value, whereas in gouty patients log-log correlations are found between all lipid, lipoprotein and uric acid levels, except for cholesterol, which only correlates with the triglycerides and the phospholipids. These findings indicate the existence of a simultaneous disturbance in lipid and purine metabolism in gout.

Although all lipid levels are found to be elevated in gout, a larger relative increase of triglycerides is reported.

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