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MATTERS ARISING

Relation between fractional urate excretion and serum triglyceride concentrations

A recent letter in the journal reported that after a dietary intervention 15 hyperuricaemic-hyperlipidaemic subjects showed considerably decreased triglyceride and cholesterol concentrations and increased renal excretion of uric acid.[1] This observation is of interest since patients with hyperlipidaemia often suffer from hyperuricaemia and vice versa.[2] Furthermore, evidence for an uricosuric effect of fenofibrate and for a lipid lowering effect of benzbromarone has been reported.[3] Therefore, correlations between fractional urate excretion (calculated from urate and creatinine levels measured in serum and in morning untimed urine specimens[4]) and serum cholesterol and triglyceride concentrations have been studied in 4057 consecutive adult subjects (2010 women), under unrestricted diet, from Renzetti Hospital, Lanciano (Chieti, Italy). Fifty four per cent of the females and 49% of the males were outpatients.

Morning blood and urine samples were taken after an overnight fast. The biochemical tests were performed by an autoanalyser (Monarch, Instrumentation Laboratory) using standard methods. Only patients with a fasting blood glucose concentration less than or equal to 110 mg dl^{-1} were considered since serum urate levels are significantly related to development of glucose intolerance[5] and in diabetic subjects glycosuria can affect uric acid excretion.[6] Using these selection conditions, the number of patients decreased to 3058 subjects.

The mean age values (SD) were 55.56 (17.03) years in men and 53.24 (17.13) years in women. Serum urate levels were higher in men than in women, at 5.54 (1.70) *v* 4.30 (1.63) mg dl^{-1}, while fractional urate excretion was higher in female subjects than in their male counterparts: 12.40 (9.97) % *v* 10.11 (13.41) %. The mean serum triglyceride concentration was 141.55 (113.26) mg dl^{-1} in men and 121.39 (93.26) mg/dl^{-1} in women. As shown in the table, in both sexes serum triglyceride concentration was inversely correlated with fractional urate excretion as obtained by simple and multiple linear regression analyses performed using age, serum cholesterol, and serum triglyceride as predictors of fractional urate excretion (dependent variable). The association was highly significant ($P < 0.001$).

Acute elevation of serum triglyceride did not modify uric acid excretion or serum urate levels in previous studies.[7 8] However, these data are not conclusive since infused triglycerides have a different composition and metabolic origin from endogenous triglycerides. In addition prolonged elevation might have effects not elicited from these acute experiments. Regardless of the mechanism—perhaps involving structural components of very low density lipoproteins[9]—the present data from a large cross sectional study show an inverse relation between renal excretion of uric acid and serum triglyceride concentration.

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Should patients with recent onset of rheumatoid arthritis be offered genetic screening?

We would like to compliment Dr Symmons and her colleagues on their paper in the journal,[1] which reviews the evidence for the role of genetic factors in the progression of rheumatoid disease. A slight area for disagreement would be that the authors suggest that we have used genetic factors to screen patients for early rheumatoid arthritis. The term "screening" is normally applied to populations at risk of disease, whereas the suggestion we have made is that genetic factors may be of use as one of the several factors that are capable of aiding in the prediction of poor prognosis. Thus we use it as part of the second stage of a two stage process. Patients who have already fulfilled stage 1 have developed the markers of persistence, that is, symmetrical small joint arthritis of a certain duration.

Genetic factors have the particular advantages that they are present from onset (which will become increasingly important the earlier patients are studied) and are unchanged by treatment. In our previous prospective study of patients fulfilling ACR criteria,[2] testing this hypothesis we showed a 13-fold relative risk for possession of rheumatoid factor or the shared epitope. This is clearly of predictive value. Furthermore, with radical new treatments which may profoundly alter the outcome of rheumatoid arthritis, it produces information on what might have happened if the natural course of the disease had been followed, for example it is known that most hospital based populations of patients with rheumatoid arthritis possess rheumatoid factor in around 70% of cases and have a shared epitope in 70-80%, which rises to over 90% in those with severe disease. A major deviation from this frequency would suggest that milder patients are being treated. Several longitudinal studies of patients who have been tissue typed are now being analysed, and these should provide good information on the relation between genetic factors and outcome in clinical practice.

We wholeheartedly agree with the final suggestion that establishing well designed clinical outcome studies of rheumatoid arthritis stratified by HLA DRB1 genotypes would be of value. We have already done this in Yorkshire from a population of several million where for the last 18 months new patients with inflammatory arthritis have been routinely tissue typed. Controlled intervention studies based on this information are nearing the completion of recruitment, and data should soon be available. Until that time it is inappropriate to use tissue typing other than as an adjunct to clinical diagnosis. We would certainly agree that at present it is not justifiable to use this outside major research centres.

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Authors' reply

We would like to thank Professor Emery and his colleagues for their interest in our paper. The purpose of the paper was to review the current published evidence that screening of patients with recent onset rheumatoid arthritis for the shared epitope or other genetic markers could be used to guide treatment decisions. All the papers which we included had examined the prognostic value of genetic markers in patients who satisfied classification criteria for rheumatoid arthritis.

Table 1 Association between fractional urate excretion and age, serum cholesterol, triglyceride levels in 1511 men and in 1547 women as determined by simple and multiple linear regression analysis

		Age	*Serum cholesterol*	*Serum triglyceride*
Simple linear regression analysis	Men	0.102***	−0.067**	−0.119***
	Women	−0.083**	0.017(NS)	−0.092***
Multiple linear regression analysis	Men	0.095***	−0.011(NS)	−0.118***
	Women	−0.069**	0.068*	−0.106***

Results are standardised β coefficient and significance.
All variables were normalised by logarithmic transformation except age.
Significance level: *** $P < 0.001$; ** $P < 0.01$; * $P < 0.05$; (NS) $P > 0.05$.