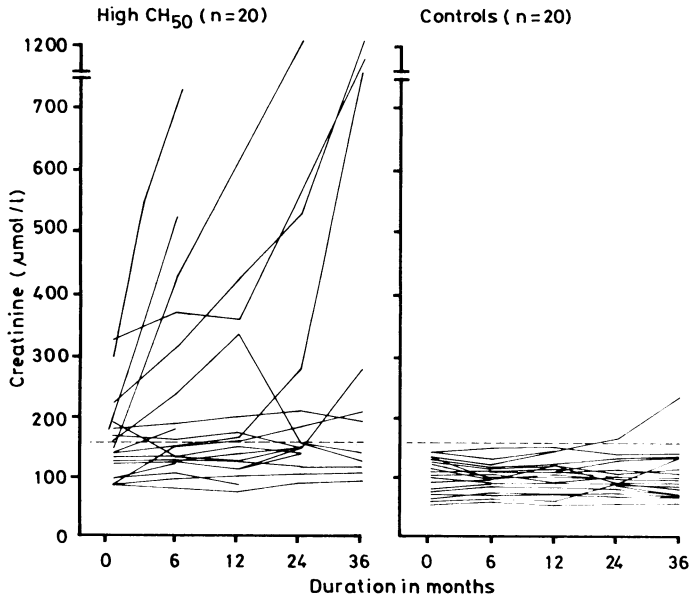

Serial observations of plasma creatinine concentrations in high haemolytic complement (CH_{50}) and control groups during three years of prospective study.

Conversion: SI to traditional units—Creatinine: 1 μmol/l ≈ 0·01 mg/100 ml.

normal during this period. There was a progressive upward trend in CH_{50} activity with rise in plasma creatinine concentration, which did not quite achieve significance. This suggested that CH_{50} activity increases with declining renal function. To test this we studied CH_{50} activity and C3 and C4 concentrations in 20 patients with renal failure due to polycystic kidneys or essential hypertension, all with plasma creatinine concentrations above 600 μmol/l (6·8 mg/100 ml). CH_{50} activity was within normal limits in all, showing that renal failure alone does not affect CH_{50}. C3 and C4 concentrations were also normal in all.

The fluctuations in CH_{50} activity in this group with active nephritis are unexplained. We measured CH_{50}, C3, and C4 values in 10 healthy volunteers daily for five days and monthly for a year. The fluctuations were much smaller than those in our hypercomplementaemic patients, and all remained within the normal range. The wide fluctuations in our high-complement group were therefore an aberration.

Concentrations of C3 and C4 did not differ between our two groups of patients or between the patients and controls. They did not exhibit the same fluctuations as CH_{50}. We found no correlation between raised CH_{50} activity and histological diagnosis, except that no patient with minimal change had raised CH_{50} activity.

Comment

This study confirms the observation of Gabriel *et al*[1] that raised CH_{50} activity is a bad prognostic marker in glomerulonephritis. It probably reflects activity of the disease in some forms of glomerulonephritis and may indicate overproduction of the complement fractions in response to increased catabolism. If this is the case, however, the third and fourth components do not appear to be the ones responsible for the increased total haemolytic complement.

[1] Gabriel R, Glynn AA, Joekes AM. Raised complement in nephritis: prognostic significance. *Lancet* 1972;ii:55-7.
[2] Fischer H. Automatic registration of complement and some applications. *Symposia Series. Immunobiological Standards* 1967;4:221-8.
[3] Mancini G, Carbonara AO, Heremans JF. Immuno-chemical quantitation of antigens by single radial immunodiffusion. *Immunochemistry* 1965;2: 235-54.

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Lecithin treatment in Friedreich's ataxia

The biochemical basis of Friedreich's ataxia is unknown, though associated defects in the pyruvate dehydrogenase enzyme complex suggest that impaired cholinergic mechanisms may contribute to the neurological deficit.[1] This raises the therapeutic possibility of supplementing the diet with precursors of acetylcholine. Encouraging results from trials with lecithin and choline chloride have been reported.[2 3] We report a double-blind cross-over trial of lecithin in 12 patients with Friedreich's ataxia.

Patients, methods, and results

Twelve patients attending neurology clinics in Edinburgh with an established diagnosis of Friedreich's ataxia agreed to participate. Their mean age was 18·8 years (range 11-30 years) and mean duration of illness 7·7 years (range 6 months to 20 years).

Patients were assessed before treatment and at fortnightly intervals thereafter by a battery of clinical tests for dysarthria and ataxia. This included timed handwriting, spiral drawing, and measurement of rapid repetitive finger movements using a simple laboratory cell counter. Each patient was scored for each test on a scale from 0 (normal) to 6 (unable to perform test). Speech was also assessed independently by a speech therapist at monthly intervals. Patients kept daily records of their progress and any side effects.

To disguise the taste and oily nature of lecithin it was incorporated into chocolate bars. Each "active" chocolate bar contained 25 g of 96% pure lecithin (Phospholipon 100, Nattermann) in 100 g chocolate and 40 g porridge oats. Cocoa butter was substituted for lecithin in the placebo bars. The pharmacist randomly allocated patients to lecithin or placebo treatment initially, and a double-blind cross-over procedure was observed over three months. The patient therefore took a chocolate bar daily for the first and third four-week periods, receiving no treatment during the intervening month.

The table shows the mean numerical ataxia scores for grouped arm functions and the total scores. Individual responses varied but no patient showed any consistent substantial change with treatment. Statistical analysis by the Wilcoxon matched pairs signed ranks test failed to show a significant difference between lecithin and placebo ($p > 0·05$). The speech studies similarly showed no significant change. The patients' subjective impressions were of some improvement with lecithin in four cases, with placebo in three, and no change in five. Six patients complained of anorexia and nausea and one noted excessive salivation and motor restlessness while receiving the active preparation.

Mean ataxia scores

Case No	Age (years)	Grouped arm functions		Total score	
		Active treatment	Placebo	Active treatment	Placebo
1	15	16	9	46	45
2	25	36	40	112	116
3	30	23	20	79	76
4	21	15	17	39	41
5	17	11	16	33	42
6	27	17	22	65	74
7	19	15	17	46	53
8	20	9	14	24	33
9	13	7	3	9	4
10	10	22	22	48	49
11	14	33	34	43	44
12	12	30	29	58	54

Comment

The results of this study fail to show any beneficial response to lecithin in 12 patients with Friedreich's ataxia. Barbeau described a 35% mean improvement in 10 patients treated openly with lecithin granules for a mean of 23·9 weeks, with significant improvement after two weeks and maximum response at four weeks,[2] and other workers reported some improvement with choline chloride.[3] A more recent study, however, suggested that performance may actually decline in patients with Friedreich's ataxia treated with lecithin,[4] and animal studies have cast doubt on the idea that increased serum choline concentrations alter the functional activity of acetylcholine at central receptor sites.[5]

Because of the previous reports of early substantial improvement with lecithin[2] and the difficulty of patients in tolerating the large amounts of chocolate necessary for the double-blind study we did not feel justified in embarking on a more prolonged trial. Unless lecithin can be shown to be an effective cholinergic agent there seems no

reason to hope that a longer trial would yield more encouraging results.

We are grateful to the pharmacist, Mrs V Muxworthy; and to Miss M E M Alberti, Mrs M Nash, and Miss R Rozzell and our senior colleagues for allowing us to study their patients.

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[1] Blass JP, Kark RAP, Menon NK. Low activities of the pyruvate and oxoglutarate dehydrogenase complexes in five patients with Friedreich's ataxia. *N Engl J Med* 1976;**295**:62-7.
[2] Barbeau A. Lecithin in movement disorders. In: Barbeau A, Growdon JH, Wurtman RJ, eds. *Nutrition and the brain*. Vol 5. New York: Raven Press, 1979:263-71.
[3] Livingstone IR, Mastaglia FL. Choline chloride in the treatment of ataxia. *Br Med J* 1979;ii:939.
[4] Chamberlain S, Robinson N, Walker J, *et al*. Effect of lecithin on disability and plasma free-choline levels in Friedreich's ataxia. *J Neurol Neurosurg Psychiatry* 1980;**43**:843-5.
[5] Hanin I. Choline and lecithin in the treatment of neurologic disorders. *N Engl J Med* 1979;**300**:1113.

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Predictive value of paired plasma and serum viscosity in early rheumatic conditions

Plasma viscosity and erythrocyte sedimentation rate are established indices of disease activity and inflammation. Both are used as screening tests and monitors of disease activity. Plasma viscosity has important technical[1] and clinical[2 3] advantages over erythrocyte sedimentation rate. Fibrinogen and globulins are the two major plasma components affecting plasma viscosity or erythrocyte sedimentation rate, and a raised value may reflect a rise in either fibrinogen or globulin, or both. Raised fibrinogen values are characteristic of acute tissue necrosis or infection; raised globulin concentrations suggest chronic inflammatory conditions.

As a screening test a raised plasma viscosity/erythrocyte sedimentation rate gives no immediate guide to diagnosis or prognosis because of its inability to differentiate high fibrinogen from high globulin states. Holdstock and Mitchell[4] improved the specificity of the erythrocyte sedimentation rate by measuring it before and after defibrination. Their technique, however, proved time consuming and was often accompanied by haemolysis (which may affect the rate). Serum is fibrinogen-free, and it is simple to measure the viscosity of plasma and serum separately. We investigated the value of paired plasma viscosity and serum viscosity measurements in predicting the development of chronic rheumatic disease in a population with acute symptoms attending a special early-arthritis clinic.

Patients, methods, and results

We investigated 115 consecutive patients attending a clinic specifically for patients with early rheumatic complaints. All had had symptoms for less than three months, and in most cases it was impossible to make a diagnosis at the initial attendance. The group was reassessed at a minimum six-month follow-up and a diagnosis established. Plasma and serum viscosities were estimated at first attendance and then related to the subsequent diagnosis. Blood was collected into two tubes; one plain, the other containing EDTA. Both samples were spun simultaneously and the viscosity of the supernatants measured on a Harkness viscometer under standard conditions. Normal plasma viscosity is 1·52-1·72 mPa s (cP) and normal serum viscosity 1·40-1·60 mPa s (cP).

Plasma viscosity was raised in 72 patients, 35 of whom subsequently developed chronic arthritis (table). The remaining 37 did not develop chronic arthritis but had varied diagnoses, including polymyalgia rheumatica, synovitis associated with infection, etc. Only 29 patients showed raised serum viscosity. Of these, 28 subsequently developed chronic arthritis. The remaining patient had an underlying carcinoma of the bronchus.

Of those patients with chronic arthritis, eight had Reiter's disease and 29 classical or definite rheumatoid arthritis (ARA criteria), of whom five were seronegative. Fifteen patients (eight with an increased plasma viscosity) included in the group with transient synovitis could have been diagnosed as possible rheumatoid arthritis by ARA criteria at presentation, but at six-month follow-up were completely asymptomatic. The diagnosis of infection-association synovitis was based primarily on a strong clinical history and where possible supported by appropriate laboratory tests. On occasions, however, diagnosis was based on a strong history alone, and we suspect that many of the "transient synovitis" group would also have had precipitating infection.

From the clinical standpoint, plasma viscosity was normal in two patients who subsequently developed chronic arthritis, and serum viscosity in eight. Serum viscosity is highly specific in predicting subsequent chronicity but has a higher false-negative rate.

Paired plasma and serum viscosity: 115 patients with early rheumatic disorders

Diagnosis at six-month follow-up	No	Raised plasma viscosity	Raised serum viscosity
Chronic disease			
Rheumatoid arthritis (includes five patients with seronegative disease)	29	28	24
Reiter's	8	7	4
Self-limiting synovitis			
Polymyalgia rheumatica	6	6	0
Infection-associated (proved or highly probable)	18	16	0
Transient synovitis (no definitive diagnosis)	45	11	0
Others (including osteoarthrosis, gout, carcinoma,* ankylosing spondylitis)	9	4	1*
Total	115	72	29

Comment

Plasma viscosity may be increased by raised values of fibrinogen and globulin, serum viscosity only by raised globulin values. Patients with a raised plasma viscosity and normal serum viscosity had acute conditions consistent with a primary increase in fibrinogen—namely, polymyalgia rheumatica and transient synovitis associated with infection. Patients who subsequently developed chronic arthritis had increased globulin concentrations (and possibly fibrinogen as well) and hence an increased serum viscosity.

In our study the serum viscosity very successfully predicted those patients who would develop chronic arthritis from a larger group in which plasma viscosity was increased. A rapid assessment of fibrinogen concentrations can be made from the difference between plasma and serum viscosities. Simultaneous estimation of serum and plasma viscosity improves the value of the latter without appreciable increase in cost or time taken, and compares favourably with the time and cost incurred in estimating globulins and fibrinogen. Moreover, this technique should be applicable to other specialties that deal with chronic inflammatory disease. The advantages of predicting subsequent chronicity at an early stage are self-evident.

[1] Harkness J. Viscosity of human plasma: its measurement in health and in disease. *Biorheology* 1971;**8**:171-93.
[2] Hutchinson RM, Eastham RD. A comparison of the erythrocyte sedimentation rate and plasma viscosity in detecting changes in plasma proteins. *J Clin Pathol* 1977;**30**:345-9.
[3] Bradlow BA, Hagen JM. A comparison of the plasma viscosity and erythrocyte sedimentation rate as screening tests. *S Afr Med J* 1979;**55**:415-20.
[4] Holdstock G, Mitchell JRA. Erythrocyte sedimentation rate before and after in vitro defibrination. *Lancet* 1977;ii:1314-6.

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