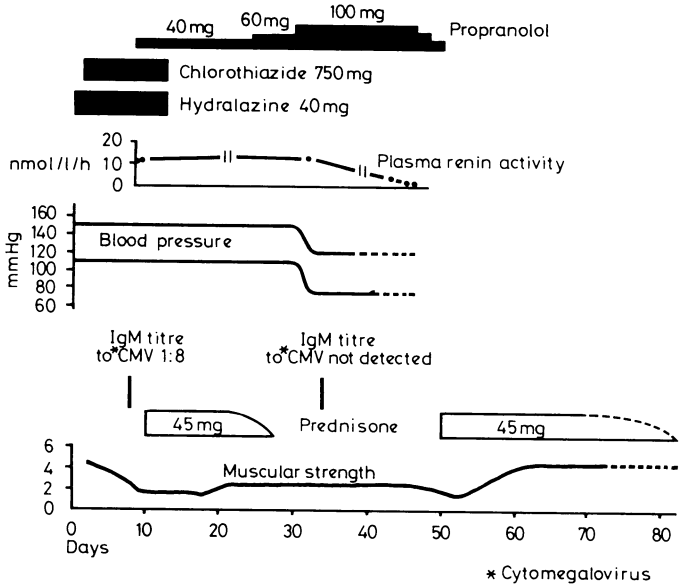
Prednisone treatment was started. The figure shows the patient's course of recovery. A relapse occurred after 45 days, which also responded to prednisone.

Before the onset of paresis and throughout the course of the disease diffuse headache was prominent and sometimes debilitating. Chlorothiazide and hydralazine were ineffective in relieving the symptoms. The patient's hypertension and concomitant headache were controlled with propranolol. Plasma renin activity was raised throughout the course (range 13·0-14·8 nmol/l/h (16·9-19·2 ng/ml/h)) and eventually returned to normal (1·5 nmol/l/h (2·0 ng/ml/h)) after high doses of propranolol. Serum catecholamine concentration (150 ng/ml) and urine excretion of vanillylmandelic acid (<5·0 mg/g creatinine) were normal. During this period propranolol was stopped for 12 hours and severe headache and hypertension recurred.

Six months after admission the patient had a normal vital capacity and no signs of residual muscle weakness or hypertension.



Flow chart of clinical progress and treatment.

Conversion: SI to traditional units—Plasma renin activity: 1 mmol/l/h ≈ 1·3 ng/ml/h.

Comment

Symptoms related to disease of the autonomic nervous system are common in patients with the Guillain-Barré syndrome.[1] It is unlikely, however, that adrenergic overactivity was responsible for the hypertension in our patient, since no tachycardia, hyperhidrosis, or peripheral vasoconstriction were noticed. In addition, no raised values of blood catecholamines or urinary excretion of vanillylmandelic acid, as observed by Mitchell and Meilman,[2] were found. The presence of the hypertension was closely associated with the raised plasma renin activity. Propranolol, which inhibits renin biosynthesis by the juxtaglomerular apparatus, proved particularly effective in controlling the headache and reduced the blood pressure and plasma renin activity. Only one similar case has been reported.[3]

We suggest that plasma renin activity should be measured in all patients with the Guillain-Barré syndrome and hypertension, and that propranolol should be the drug of choice in the hypertension of the Guillain-Barré syndrome.

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Serum ferritin and rheumatoid disease

All inflammatory conditions affect iron kinetics. In rheumatoid arthritis this is reflected by anaemia, with variables suggestive of iron deficiency but normal iron stores within the bone marrow and excess iron within the inflamed synovial membrane. The synovial reticuloendothelial cell stores iron as ferritin[1] within the protein envelope of apoferritin. The production of ferritin by the reticuloendothelial cell and concomitant rise in serum ferritin concentration may reflect the cell's attempt to protect itself from the toxic consequences of excess free intracellular iron.

Estimation of serum ferritin concentration is useful in assessing the degree of inflammation in juvenile chronic polyarthritis[2] and in many other inflammatory conditions. Because of suggestions that disturbance of iron metabolism may directly affect the inflammatory process[3] we studied the role of serum ferritin concentration in patients with rheumatoid synovitis and systemic rheumatoid disease.

Patients, methods, and results

Serum ferritin concentration was measured by radioimmunoassay (Gammadab ^{125}I ferritin kit, Travenol Lab). Two studies were performed: A cross-sectional study of 47 patients with rheumatoid synovitis and 13 with systemic complications of their disease and a longitudinal study of 150 patients presenting with early rheumatoid synovitis (total duration less than six months) and continued for 18 months through exacerbation and remission of their disease. In the first study serum ferritin concentration was correlated with two measures of inflammatory activity: *clinical*, Ritchie articular index (joint pain index) and duration of morning stiffness; *laboratory*, haemoglobin concentration, white cell count, platelet count, IgM rheumatoid factor, plasma viscosity, erythrocyte sedimentation rate, C-reactive protein, putative immune complexes (% C1q binding activity), and complement components C3 and C4. There was no significant correlation between serum ferritin concentration and any of these variables (Spearman rank correlation coefficient $r \leqslant 0{\cdot}2$ in each case). Mean serum ferritin concentration in the 13 patients with systemic complications, however, was three times that in the 47 patients with pure synovitis (240 *v* 80 μg/l; $p < 0{\cdot}001$).

In the longitudinal study serum ferritin concentrations were raised during episodes of active synovitis and fell with remission. Changing concentrations mirrored changes in plasma viscosity and levels of circulating immune complexes. High concentrations ($\geqslant$300 μg/l) were found in eight out of 10 patients who presented with, or developed, systemic manifestations and severe disease. None of the five patients with low initial concentration ($\leqslant$15 μg/l) developed such complications and all had mild disease, often seronegative. A single estimation of serum ferritin concentration was no help in assessing the degree of inflammation unless contrasted with an estimation performed during a period of remission, which accounts for the lack of correlation in the cross-sectional study.

Comment

Serum ferritin concentrations fluctuate during episodes of inflammation, the percentage change within the individual rather than the absolute concentration reflecting the degree of inflammation. Consequently serum ferritin concentration may be used to monitor inflammatory activity only if serial measurements are made. An initial high concentration in patients presenting with early rheumatoid arthritis is a poor prognostic index associated with either the presence of, or development of, systemic complications and severe disease.

That iron may have a direct role in worsening the inflammatory process is supported by the observations that high ferritin concentrations are associated with systemic disease and that patients with low concentrations do not appear to develop such complications. Iron may promote inflammation by catalysing free oxygen radical production,[3] which may adversely affect reticuloendothelial metabolism. Genuine iron deficiency reflected by a low serum ferritin concentration may therefore protect against such complications. This may explain why men, with their greater iron stores, are more likely to develop the most severe systemic complications of this disease, which have recently been suggested to be due to reticuloendothelial cell dysfunction.[4] Intravenous iron infusion in patients with established rheumatoid inflammation may be associated with exacerbation of the disease.[5]

Iron in the development of systemic rheumatoid disease merits further investigation.

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High-density lipoprotein and other risk factors for coronary artery disease assessed by angiography

Total blood cholesterol and low-density lipoprotein cholesterol concentrations are well-established risk factors for the development of coronary artery disease,[1] whereas high-density lipoprotein cholesterol constitutes a negative risk factor for coronary disease[2]—that is, may exert a protective effect. The Framingham study[1] showed that the ratio of high-density lipoprotein cholesterol to total cholesterol may be an even more powerful negative risk factor. As neither the presence nor severity of coronary artery disease can be determined accurately by clinical or electrocardiographic examination, our study compared the serum total cholesterol and total high-density lipoprotein cholesterol concentrations and the ratio of high-density lipoprotein cholesterol to total cholesterol with the degree of coronary artery disease assessed angiographically.

Patients, method, and results

We studied 160 consecutive patients undergoing coronary angiography for the investigation of chest pain or assessment of valvular heart disease. The angiograms were reported independently by a consultant radiologist. Lesions were graded visually from 0 to 4: 0=normal, 1=25% stenosis, 2=50% stenosis, 3=75% stenosis, and 4=total occlusion.

A coronary index was calculated using the method designed by Balcon *et al*[3] which takes into account the site, severity, and effect of multiple lesions in the coronary circulation. The index ranges from 0 to 1, where 0=total occlusion of all vessels and 1=normal coronary circulation. Twenty-four hours before catheterisation the serum total cholesterol and high-density lipoprotein cholesterol concentrations were measured after a 12-hour fast. Cholesterol and triglyceride concentrations were measured by semiautomated fluorometric techniques, Technicon method N77 and Liebermann-Burchard's reagent being used for cholesterol and Cramp and Robertson's method for triglyceride. High-density lipoprotein cholesterol was measured as for plasma cholesterol after precipitation with heparin (250 units in 50 μl) and manganese chloride (50 μl 1M solution).

The 160 patients were divided into quartiles on the basis of mean serum cholesterol and high-density lipoprotein cholesterol concentrations and the ratio of high-density lipoprotein cholesterol to total cholesterol. The coronary indices of the patients in the top and bottom quartiles for the respective lipid profiles were determined for comparison. Also, patients with normal coronary arteries were compared with an equivalent number of patients with the severest coronary artery disease for differences in lipoprotein concentrations. Other risk factors such as age, the number of cigarettes smoked daily, and systolic and diastolic blood pressures were also considered. The Mann-Whitney U non-parametric test was applied in all statistical analyses.

The table gives clinical details of the patients and the coronary indices, and shows significant differences between the groups.

Comment

Jenkins *et al*,[4] in a study similar to ours, showed a significant inverse relation between high-density lipoprotein concentrations and the severity of coronary artery disease assessed angiographically, This association was not found in the present study ($p < 0.11$). Total cholesterol, however, was significantly associated with severity of coronary artery disease, and the ratio of high-density lipoprotein cholesterol to total cholesterol was inversely related to the severity of coronary disease. Of these two variables, the inverse relation of the ratio was slightly stronger ($p < 0.001$ and $p = 0.01$ respectively).

Apart from a significant age difference between the two quartiles with high and low concentrations of high-density lipoprotein cholesterol ($p = 0.05$), there were no significant differences in age, number of cigarettes smoked daily; and systolic and diastolic blood pressures between the upper and lower quartiles. When the data were analysed by comparing patients with the severest coronary occlusion (coronary index < 0.42) with those with no occlusion, however, those with the severest occlusion were found to be older ($p = 0.04$) and heavier smokers and to have higher blood pressure ($p = 0.02$), as well as having a lower ratio of high-density lipoprotein to total cholesterol ($p < 0.01$).

These results support the suggestion of Williams *et al*[5] that the ratio of high-density lipoprotein cholesterol to total cholesterol should be included in any coronary risk screening profile.

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Clinical details, lipid measurements, and coronary indices (expressed as means ± SD) of patient groups analysed by quartiles

Patient group	Sex		Age (years)	Blood pressure (mm Hg)		No of smokers	Mean No of cigarettes smoked daily	Plasma cholesterol (mmol/l)	Plasma high-density lipoprotein cholesterol (mmol/l)	High-density lipoprotein cholesterol: total cholesterol	Coronary index
	M	F		Systolic	Diastolic						
Cholesterol:											
Upper quartile	33	7	54·4 ± 8·8	144 ± 23	89 ± 12	16	22·9	8·0 ± 0·88			0·5 ± 0·31
Lower quartile	27	13	54·9 ± 8·4	144 ± 22	85 ± 12	18	20·0	4·8 ± 0·51			0·71 ± 0·32‡
High-density lipoprotein cholesterol:											
Upper quartile	23	17	57·4 ± 8·4	141 ± 22	85 ± 12	15	15·6		1·4 ± 0·51		0·71 ± 0·33
Lower quartile	34	6	53·4 ± 7·7*	136 ± 23	85 ± 12	20	26·9		0·67 ± 0·09		0·58 ± 0·32
High-density lipoprotein cholesterol: total cholesterol:											
Upper quartile	26	14	55·7 ± 8·6	141 ± 23	85 ± 14	15	18·5			0·24 ± 0·04	0·78 ± 0·34
Lower quartile	36	4	52·9 ± 8·8	140 ± 24	86 ± 13	23	22·1			0·1 ± 0·01	0·52 ± 0·28§
Patients with coronary index of:											
1	33	23	52·9 ± 9·9	136 ± 22	85 ± 13	27	18·0	5·9 ± 1·2	1·05 ± 0·28	0·18 ± 0·06	1·0
< 0·42	49	7	56·1 ± 6·3*	145 ± 25†	89 ± 13	36	26·0	6·7 ± 1·6‡	1·0 ± 0·29	0·15 ± 0·05‡	0·25 ± 0·1

Significance of differences (Mann-Whitney U test): *$p = 0.04$; †$p = 0.02$; ‡$p < 0.01$; §$p < 0.001$.
Conversion: SI to traditional units—Cholesterol: 1 mmol/l ≈ 38·7 mg/100 ml.