diabetic whose plasma glucose concentrations were ≥ 11 mmol/l (198 mg/100 ml) were in group 3.

Mortality and clinical findings did not differ significantly between groups 1 and 2 ($p > 0.5$) or groups 3 and 4. Accordingly, groups 1 and 2 and groups 3 and 4 were combined for analysis. The diabetics (groups 3 and 4) showed significantly greater mortality at one week ($\chi^2 = 11.2$, $p < 0.001$) than the non-diabetic patients. All the deaths in the diabetic group occurred within a week of stroke, whereas deaths continued to occur throughout the follow up period in groups 1 and 2 (table).

Admission characteristics and mortality of combined groups

	Non-diabetics (groups 1 and 2) (n = 86)	Diabetics (groups 3 and 4) (n = 14)	Significance
Mean (SD) age (years)	75 (10)	70 (13)	NS
No (%) of men	39 (45)	6 (43)	NS
No (%) of smokers	34 (40)	4 (28)	NS
No (%) being treated for hypertension	35 (41)	5 (36)	NS
No (%) with past ischaemic heart disease/stroke/transient ischaemic attack	34 (40)	8 (57)	NS
Mean (SD) blood pressure on admission (mm Hg):			
Systolic	160 (31)	170 (51)	NS
Diastolic	92 (17)	92 (18)	NS
Mean (SD) packed cell volume	0.43 (0.06)	0.41 (0.04)	NS
No (%) with atrial fibrillation on admission	21 (24)	3 (22)	NS
No (%) with stupor/coma on admission	24 (28)	6 (43)	NS
Median stroke score	15	18	NS
No (%) of deaths:			
At 1 week	14 (16)	9 (64)	$p < 0.001$
At 1 month	27 (31)	9 (64)	$p < 0.05$
At 3 months	33 (38)	9 (64)	NS

Comment

The only previous study of HbA_{1c} concentrations in patients with stroke indicated that 42% of such patients had abnormal concentrations.⁴ The colorimetric assay method used, however, would have been affected by labile adducts, and we suspect that these results were artefacts. By contrast, a clearly abnormal concentration of stable HbA_{1c} determined by isoelectric focusing in patients surviving myocardial infarction appears to be specific for overt diabetes mellitus (with fasting hyperglycaemia) at follow up.³ Accordingly, we consider the prevalence of undiagnosed diabetes mellitus in our patients with acute stroke to have been at least 6%. Diabetes, known and previously unknown, although present in only 14% of the patients, accounted for 39% of the total mortality at one week, giving an early mortality four times greater than that in the patients without diabetes. All deaths of known diabetics and patients in group 3 occurred within the first week, implying that these patients are more prone to extensive infarction or cerebral oedema, or both.⁵

The highly significant relation between plasma glucose and HbA_{1c} concentrations suggests that premorbid abnormal glucose tolerance is a major determinant of the hyperglycaemic response to stroke. Previous observations of poor outcome from stroke in patients with "stress hyperglycaemia" may reflect the clinical course of stroke in diabetics.

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Rheumatoid factors and amyloidosis in rheumatoid arthritis

The precise mechanism of the formation and deposition of amyloid in rheumatic diseases is not known. Important factors appear to be high circulating concentrations of the lipoprotein associated precursor protein serum amyloid A together with altered enzymatic degradation of the precursor and tissue amyloid A protein.¹ Probably there are other factors, however, since only a few patients with these characteristics make amyloid. We have found that in adult rheumatoid arthritis seronegativity—that is, very low values of circulating IgM, IgG, and IgA rheumatoid factors—is strongly associated with the complication.

Subjects, methods, and results

Group 1 consisted of 46 patients (32 women, 14 men; mean age 54.4 years, range 32-84) with definite or classical rheumatoid arthritis complicated by reactive amyloidosis proved by histological examination of renal or rectal biopsy specimens, or both. The mean duration of the rheumatoid arthritis was 16.5 years (range 4-30 years). Patients with the HLA-B27 associated arthropathies ankylosing spondylitis, reactive arthritis, and psoriatic arthritis and those with juvenile onset rheumatoid arthritis were carefully excluded. Group 2 consisted of 47 patients (33 women, 14 men; mean age 53.5 years, range 30-73) with definite or classical rheumatoid arthritis with no clinical signs of secondary amyloidosis. The mean duration of their disease was 15.2 years (range 4-31 years). Patients in the two groups were matched for age, sex, and duration of rheumatoid arthritis. Fifty five healthy blood donors (43 men, 12 women; mean age 37 years, range 21-72) served as controls.

IgM, IgG, and IgA type rheumatoid factors were measured by enzyme immunoassay using swine IgG and specific alkaline phosphatase labelled swine antibodies to human IgG, IgA, or IgM (Orion Diagnostica, Finland). Rheumatoid factor activities were expressed as a change in absorbance at 406 nm over 30 minutes. A value greater than the mean plus two standard deviations recorded in the healthy controls was taken as raised. Statistical evaluation was by χ^2 test and Wilcoxon's ranking test for unpaired data.

IgM, IgG, and IgA type rheumatoid factors in patients with rheumatoid arthritis with or without amyloid

	No of subjects	No (%) with raised values of rheumatoid factors of type:		
		IgM	IgG	IgA
Healthy controls	55	1 (1.8)	1 (1.8)	2 (3.6)
Rheumatoid arthritis	47	38 (80.9)	35 (74.5)	41 (87.2)
Rheumatoid arthritis and amyloid	46	10 (21.7)*	14 (30.4)*	17 (37.0)*

*Compared with rheumatoid arthritis alone: $p < 0.001$.

Patients with rheumatoid arthritis complicated by amyloid had significantly lower values of IgM, IgG, and IgA rheumatoid factors than those without amyloid (table). In neither group did inflammatory activity, as reflected by C reactive protein concentrations, significantly influence the rheumatoid factor value.

Comment

Amyloid was much more common in our subset of patients who had very low values of circulating IgM, IgG, and IgA rheumatoid factors. This confirms the clinical impression based on conventional differential (sheep cell) agglutination tests (which measure only IgM rheumatoid factor) showing that many patients with rheumatoid arthritis complicated by amyloid are seronegative. In this study the subgroup of patients with rheumatoid arthritis not complicated by amyloid were matched with the others for age, sex, and duration of rheumatoid arthritis, so these factors are not likely to have influenced the results. The patient groups were not matched directly for the use of drugs, but review of the clinical records showed that the patients had received the same types of medication, including steroids and gold salts. Since uraemia may be immunosuppressive² it might be inferred that seronegativity in the amyloid group may have resulted from the amyloid state. Many of the patients with amyloid were not uraemic, however, and, based on Waaler-Rose tests, they had been seronegative at an early stage of the disease. Moreover, patients who are clearly seropositive generally remain so, and seronegative patients usually continue to be seronegative regardless of clinical course. We

did not find any relation between inflammatory activity and rheumatoid factor values.

The HLA-B27 associated arthropathies are typically seronegative disorders. We, however, carefully excluded patients with ankylosing spondylitis, reactive arthritis, and psoriatic arthritis, so these arthropathies could not have influenced the results.

The biological role of rheumatoid factors is not known. Although seropositivity at the onset of rheumatoid arthritis suggests a poorer prognosis, several studies have failed to detect a relation between IgM rheumatoid factor titres and disease activity.³⁻⁵ Finding an association of amyloid disease with seronegativity in adult rheumatoid arthritis may be interpreted in favour of some protective role of rheumatoid factors, at least with respect to the development of amyloid; or, more likely, seronegativity and the development of amyloid may be related to similar genetic factors.

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Comparison of three physiotherapy regimens for hands with rheumatoid arthritis

There have been few controlled comparisons of the various physiotherapy techniques for rheumatoid arthritis in the hands. A regimen of standard exercises supplemented by wax is available to most patients and general practitioners. We have compared this simple regimen with two, more elaborate forms of physiotherapy available in hospital departments.

Mean results for each measurement for each treatment

Measurement	Treatment group	Week			
		0	1	2	3
Grip strength (mm Hg)	1	91	99*	111**	111**
	2	66	81**	88**	89**
	3	84	92*	95**	99**
Summed circumference of proximal interphalangeal joints (mm)	1	321	314**	310**	310**
	2	314	308	305**	304*
	3	343	335**	331**	329**
Hand articular index	1	16	11**	8**	6**
	2	13	10*	7**	5**
	3	16	12**	10**	10**
Pain score by visual analogue scale (mm)	1	67	49	39	30*
	2	62	47	30*	29*
	3	71	57*	42**	37**
Range of movement (mm)	1	57	—	—	90**
	2	54	—	—	69*
	3	66	—	—	77
Timed task (s)	1	28	23	20*	18*
	2	30	29	27	25*
	3	25	21**	20**	20*
Activities score	1	6.6	7.8	9.4**	10.2**
	2	6.3	7.7	9.1*	10.0*
	3	7.7	8.2	9.4*	8.7

Compared with baseline: *p<0.05; **p<0.01 (Wilcoxon's rank sum test).

Patients, methods, and results

Thirty inpatients with classical or definite rheumatoid arthritis (American Rheumatism Association criteria) affecting the hands were recruited. All had pain and swelling of the hands and limitation of movement. Patients remained in hospital throughout the three week study period and existing drug regimens and other procedures were continued unaltered. Intra-articular steroid injections were not allowed.

Patients were allocated at random to three groups. Group 1 received wax treatment followed by standard exercises for five days a week. The wax procedure entailed dipping the hands into melted wax 10 times, then wrapping them in greaseproof paper with a blanket which was left on for 20 minutes. Group 2 received ultrasound (3 MHz at 250 W/cm² for six minutes per treatment) followed by standard exercises. Group 3 received ultrasound and faradic hand baths (15 minutes for each hand) followed by standard exercises.

Patients were assessed blindly by an independent observer before treatment and at weeks 1, 2, and 3. Seven assessments were performed at each visit (grip strength, interphalangeal joint circumference, visual analogue scale for pain, articular index confined to the hand, range of movement in the fingers using a method analogous to Schoeber's test, time to dial a six figure telephone number, ability to perform daily activities).

The table gives the results. The groups were well matched initially and all showed significant improvement by week 3 (Wilcoxon's rank sum test: 0.01 < p < 0.05). About half the patients showed significant improvement after only one week of treatment. Statistical comparison between groups was by Kruskal-Wallis one way analysis of variance by ranks. There was no significant difference among treatments at any time for six of the seven assessments, but for activity score there was less improvement in group 3 (p < 0.02). We found no evidence of a difference in performance between dominant and non-dominant hands.

Comment

Although all three physiotherapy methods produced significant improvement, six of the seven clinical assessments failed to disclose a significant difference between methods. We considered that the lack of improvement in activity score observed with faradic hand baths was not clinically important. Ultrasound or faradic hand baths appear to confer no advantage over the simpler wax treatment followed by standard exercises. This has important economic implications: ultrasound and faradic hand baths require referral to a hospital physiotherapy department. Exercises may be supervised at home and wax may be prescribed by general practitioners for patients who can use it safely, and these simple measures are likely to be just as effective in the treatment of rheumatoid arthritis of the hands.

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