LETTERS TO THE EDITOR

The time of blood sampling for osteocalcin determinations

Sir: We have read the interesting article by Pietschmann *et al* about the serum osteocalcin concentrations in patients with rheumatoid arthritis.[1] In their work there was no mention of the time at which blood samples were taken for osteocalcin determination.

Several studies have shown a circadian rhythm of serum osteocalcin in normal adults, with peak values during the night and a nadir during the morning hours.[2 3] Therefore, in our opinion, if osteocalcin is used as a marker in clinical investigations of bone metabolism it is important to mention the time at which blood was collected for its measurement. Otherwise, interpretation of results may be difficult and comparison with values obtained in other studies impossible.

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Sir: We agree with Drs Nolla and Rozadilla that in applying serum osteocalcin measurements it is important to take account of the diurnal variations of serum osteocalcin concentrations. In a recent study (Pietschmann *et al*, unpublished data) in patients with postmenopausal osteoporosis we found a diurnal rhythmicity of serum osteocalcin concentrations similar to that described by Gundberg *et al* in normal subjects.[1] In contrast, Guillemant and Guillemant did not find circadian fluctuations of serum osteocalcin concentrations in patients with primary or secondary hyperparathyroidism.[2] In our study on serum osteocalcin concentrations in patients with rheumatoid arthritis[3] blood for osteocalcin measurements was collected from all patients and controls between 8 00 and 9 00 am.

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Anticardiolipin antibody negative occlusive vascular retinopathy in systemic lupus erythematosus

Sir: A strong association has recently been reported between the presence of anticardiolipin antibody and occlusive ocular vascular disease in patients with systemic lupus erythematosus (SLE).[1 2] We now wish to report a patient with SLE who developed bilateral central retinal artery occlusion and in whom anticardiolipin antibody was not detected despite several other features suggesting the presence of antiphospholipid antibodies.

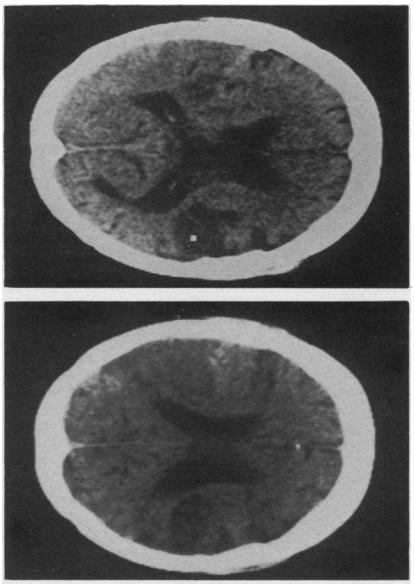
The patient, a 30 year old nursing sister, was diagnosed as having SLE[3] in 1982. She had a history of two spontaneous abortions. In January 1986 she had a 'flare' of SLE, which resolved after one month's treatment with steroids (prednisone 50 mg daily) and chloroquine (200 mg daily). The lupus remained quiescent, both clinically and serologically, for the ensuing 10 months during treatment with prednisone (10 mg alternate days) and chloroquine (200 mg daily).

In November 1986 she developed sudden complete loss of vision in the left eye. Two days later a similar visual deficit developed in the right eye. She was admitted to Kalafong Hospital 20 hours later and ophthalmoscopy disclosed a pale fundus with a bright red fovea bilaterally. The arteries were attenuated and apparently bloodless. Foci of retinal ischaemia ('soft exudates') were evident. An ophthalmologist affirmed the appearances were pathognomonic of central retinal artery occlusion. No other clinical evidence of active lupus or other predisposing factors for central retinal artery occlusion were present. Relevant investigations showed thrombocytopenia of 34×10^9/l, a prolonged activated partial thromboplastin time (APTT) of 50–76 s (control <40 s), and positive antinuclear antibody titre of 1/40. The erythrocyte sedimentation rate, anti-DNA antibody, serum complement, and gammaglobulin concentrations, white cell count, haemoglobin, urine analysis, and echocardiogram were all normal. She declined further hospital treatment.

In February 1987, six days after being admitted to hospital for social reasons, she developed a mild transient ischaemic attack. Again there were no other clinical or laboratory features of active lupus. The APTT was now 37 s, the rapid plasma reagin test was negative, and an enzyme linked immunosorbent assay (ELISA) (The Rayne Institute, St Thomas's Hospital, London) showed absence of anticardiolipin antibody. She again declined further hospital treatment.

Three months later she was readmitted after having developed loss of consciousness abruptly five hours earlier. She was comatose with dilated pupils, which reacted sluggishly to light. She had a right hemiparesis. A computed tomographic brain scan was performed within a few hours after admission. This showed multiple areas of low attenuation in both hemispheres consistent with infarctions. The lateral ventricles were mildly dilated and several cortical sulci appeared unduly prominent (figure). The platelet count was 52×10^9/l and APTT 76 s. Anticardiolipin antibody was once more not detected and the rapid plasma reagin test was again negative. Antibodies to Ro and La were negative but antibodies to RNP and Sm were positive. She was initially anticoagulated with heparin and subsequently with warfarin. High doses of cyclophosphamide, prednisone, and aspirin were also prescribed, but her clinical state remained unchanged and she died six weeks later. Permission for necropsy was not granted.

Recurrent fetal loss, occlusive stroke, thrombocytopenia, and a prolonged APTT—all features that existed in our patient—have been associated with the presence of antiphospholipid antibodies.[4] The failure in this case to detect anticardiolipin antibody is therefore noteworthy. In our recent study of SLE in black South Africans clinical features were found to be little different from those described in series from other parts of the world.[5] Four of the 30 patients had a history of cerebrovascular accidents. Of these, three were tested for the presence of anticardiolipin antibody and the levels were found to be normal in each (Dessein PH, Gledhill RF, Asherson RA, unpublished). Moreover, of the 12 other patients tested, only one was found to have a raised anticardiolipin antibody level and this patient had no clinical features of the antiphospholipid syndrome.[4] It is our impression that the incidence of antiphospholipid antibodies may be significantly less in Africans with SLE. Our patient is another example of anticardiolipin antibody negativity in the presence of probable lupus anticoagulant positivity, a finding observed by other investigators.[6 7]



Computed tomographic brain scan showing multiple infarcts and cerebral atrophy.

Although occlusion of both central retinal arteries in rapid succession, such as appeared in this patient, seems an exceptional circumstance, the observation by Stafford-Brady *et al*[2] that retinopathy in SLE may be a marker of poor prognosis for survival is shown only too well by our case.

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Beneficial effects of reduced intake of polyunsaturated fatty acids in the diet for one year in patients with systemic lupus erythematosus

Sir: We have investigated the effects of dietary changes in patients with systemic lupus erythematosus (SLE) in an open study. Patients were treated with a diet reduced in polyunsaturated fats and enriched in saturated fat for 12 months. This approach was inspired by a report by Hurd, who showed that such a diet markedly prolonged survival and reduced all manifestations of disease in NZB/W mice—that is, an experimental model of SLE.[1 2] Both deficiencies and excesses in macronutrients and micronutrients seem to affect the immune response. It has also been shown that other changes in dietary fatty acid composition have a beneficial effect on mouse strains which spontaneously develop manifestations of autoimmune disease, such as NZB/W and MRL/L.[3 4]

Nineteen patients (17 female) with a mean age of 37 years (range 18–52) and an average disease duration of 13 years (range 1–26) were included in the study. All patients fulfilled at least five of the New York revised criteria for the diagnosis of SLE.[5] The activity or inactivity of their disease was judged at the start and end of the diet period. Active and inactive SLE were defined according to the doctor's and patients' estimates of appearance or absence of new symptoms of the disease or aggravation of earlier symptoms. Patients with symptoms of atherosclerosis, with diabetes mellitus or arterial hypertension, treated with β blockers, were excluded.

Patients were initially admitted to the day centre at the department of rheumatology for one week in groups of four. A detailed dietary history was taken by a dietician. During the admission week the patients were instructed by a dietician in the theory and practical aspects of following a diet in which the ratio of polyunsaturated to saturated fatty acids was reduced from an average of 0·3 to 0·1. They were told not to change their total energy intake. During the study the patients saw the dietician every three months to monitor dietary adherence. A dietary history for each patient was recorded after nine to 12 months.

Laboratory analyses and clinical examinations were performed at the start and every three months throughout the study. Compliance was monitored by diet counselling and by analysis of fatty acid percentage composition. The percentage content of linoleic acid was already significantly reduced after three months and continued to drop throughout the treatment period in plasma triglycerides, cholesterol esters, and phospholipids ($p<0·01$ for all three). After 12 months the linoleic acid percentage was reduced in adipose tissue ($p<0·01$). These findings indicate that the patients complied with the diet regimen. Serum and low density lipoprotein cholesterol increased (both $p<0·05$) but remained within the normal limits. High density lipoprotein 2 cholesterol increased ($p<0·05$) and high density lipoprotein 3 decreased ($p<0·05$).

The number of patients with active SLE was reduced from 11 to three by the end of the study ($p<0·05$). The prednisolone consumption was reduced from 10·1 to 7·0 mg/day ($p<0·01$). The total amount of drugs used by patients, including antimalarial and immunosuppressive drugs, was estimated at the start and at the end of the diet period. It was reduced for 14 patients and remained unchanged for the other five. The table gives detailed information about drug use before and after one year of the diet treatment. There were no significant changes in routine laboratory tests or other laboratory indices measured at the end of the year, including anti-DNA antibodies and complement levels. In general, the patients tolerated the treatment well and no significant side effects were noted.

Our results indicate that substitution of polyunsaturated for saturated fats in the diet may reduce inflammatory metabolites, probably derived from polyunsaturated fatty acids which would explain the reduced disease activity despite reduced drug treatment. Spontaneous improvement and placebo effects cannot be excluded, however, as this was an open study with no control group. Each patient served as his/her own control. These results highlight a possible supplementary, non-pharmacological approach to treatment of patients with SLE by the alteration of dietary fats to reduce intake of the omega six series of polyunsaturated fatty acids.

Patient characteristics and treatment before and after one year of treatment

Patient No	Age	Disease duration (years)	Before diet			After one year		
			Active (A) or inactive (I)	Prednisolone dose (mg)	Drug treatment*	Active (A) or inactive (I)	Prednisolone dose (mg)	Drug treatment
1	39	19	A	10	AM	I	6·25	AM
2	41	15	I	2·5	AM	I	2·5	AM
3	52	20	A	7·5	IS	A	6·25	IS
4	43	8	I	12·5	IS	I	7·5	IS
5	33	17	A	20	IS	A	17·5	IS
6	50	11	I	15	IS	I	7·5	—
7	31	14	I	3·75	IS	I	1·25	—
8	43	17	A	10	—	I	0	—
9	35	11	A	7·5	AM	I	6·25	—
10	36	2	A	12·5	—	I	12·5	—
11	31	2	A	25	IS	I	13·75	—
12	38	13	A	10	AM	I	10	AM
13	47	21	I	5	—	I	3·75	—
14	37	18	I	0	—	I	0	—
15	21	1	A	5	AM	I	7·5	—
16	34	14	I	7·5	AM	I	7·5	—
17	34	15	A	10	AM	A	10	AM
18	18	2	I	20	AM	I	7·5	—
19	28	26	A	7·5	AM	I	5	AM

*AM=antimalarial drug; IS=immunosuppressive drug.
The patients were female apart from Nos 8 and 16.

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Peyronie's disease in systemic sclerosis

Sir: Peyronie's disease is a localised fibrotic disorder involving the covering sheaths of the corpora cavernosa of the penis. Histological analysis shows a fibrous plaque firmly attached to the penis tunica albuginea.[1 2]

The cause of this disorder is unknown, but it is included among the localised fibrotic diseases (Riedel's struma, Dupuytren contracture, plantar fasciitis, orbitary pseudotumour, sclerosis cholangitis, and retroperitoneal fibrosis) or described as a form of localised systemic sclerosis or connective tissue disease with local collagen accumulation.[3 4] Recently, Gualdieri and coworkers described the first two cases of Peyronie's disease in systemic sclerosis.[5] A review of our series of patients with scleroderma has brought to light a new case.

A 63 year old man was admitted to our centre in 1985. There was a history of bilateral Dupuytren's disease and he had had an operation on his left hand in 1976.

Six months before this admission he had developed arthralgia involving several small and medium sized joints. There was morning stiffness, decreased sensitivity and paraesthesia of the left side of the face, Raynaud's phenomenon, and cutaneous hyperpigmentation. Physical examination showed hypopigmented and hyperpigmented areas in the upper thorax and arms, clubbing, and proximal cutaneous induration in both arms. A chest x ray showed bilateral lower lobe interstitial infiltrates, and the spirometry readings were consistent with a moderate restrictive process with impairment of carbon monoxide diffusion. The laboratory results showed an erythrocyte sedimentation rate of 97 mm/h, a positive 1/16 Waaler-Rose test, a 1/3200 positive antinuclear antibody test by indirect immunofluorescence with a speckled pattern and negative anti-DNA, extractable nuclear antigens, and anticentromere and Scl-70 antibodies. A gallium-67 lung scan and bronchoalveolar lavage examinations