SLE precipitated by antibiotics in Sjøgren's syndrome

SIR,—In his letter (17 January, p 152) about the recent article on this subject by my colleagues and myself (15 November, p 385) Dr J R Sewell makes four main points: (1) Our case of systemic lupus erythematosus (SLE) did not meet current diagnostic criteria for SLE; (2) neither LE cells, abnormalities in DNA binding, nor pericarditis are specific to SLE; (3) the abnormalities in DNA binding we reported might have been due to treatment with an anti-inflammatory drug; and (4) the patient's second disease exacerbation was a consequence of pneumonia. We wish to make the following comments in reply.

(1) Our patient has shown the following disease features at some time in the course of her illness: polyarthritis without deformity, Raynaud's phenomenon, rash, pericarditis, more than two classical LE cells in a blood film, and DNA binding of 60%. The first five of these are included in the preliminary criteria for the classification of SLE proposed by the American Rheumatism Association (1971), four of which were considered necessary for diagnosis. In a "short report" we were of necessity succinct, and the Raynaud's phenomenon and rash were not specifically mentioned in the article.

(2) We would certainly agree with Dr Sewell that neither pericarditis, nor the finding of LE cells in a blood film, nor an abnormal DNA binding are specific to SLE—we did not suggest that they were.

(3) Before the patient's later disease exacerbation she had been taking ibuprofen and this was continued subsequently when she was well apart from her joint symptoms and DNA binding was normal. Thus the 60% DNA binding in her blood could not be explained by anti-inflammatory drug administration, although co-trimoxazole, as we stated in the article, may well have precipitated the two exacerbations of her disease.

(4) The confusion, pyrexia, and weakness in the second episode described in our patient responded only to the administration of high-dose steroids, and this clinical improvement occurred in parallel with change in DNA binding and fall in antinuclear factor titre. Had the clinical features been the result of pneumonia this would have been the case.

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High plasma calcitonin levels in breast cancer

SIR,—Dr R C Coombes and his colleagues (25 October, p 197) report increased levels of immunoreactive calcitonin in the plasma of 23 out of 28 patients with metastatic carcinoma of the breast. We have recently completed a similar study[1] and are pleased to be able to confirm their findings.

In our laboratory 44 women aged 30-91 years with histologically proved breast cancer were studied; 29 had widespread metastatic involvement and the others had localised disease. Three-quarters of the patients with metastatic disease who were not receiving current therapy had high plasma calcitonin values (up to 1070 ng/l; normals <260 ng/l). Interestingly, patients recently treated with irradiation or chemotherapy had normal values. Only one patient with apparently localised disease had a high value. It appears that the measurement of calcitonin may have important diagnostic, therapeutic, and prognostic indications as a marker in breast cancer.

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[1] Silva, O L, Chisholm, R C, and Becker, K L, *Clinical Research*, 1975, **28**, 596A.

Tryptophan and depression

SIR,—The report of a double-blind multicentre study from four Scandinavian hospitals,[1] with its subsequent elaboration by Dencker at the symposium held recently at the Royal College of Physicians (leading article, 31 January, p 242) is a remarkable development in the evolution of the psychopharmacological role of the amino-acid tryptophan. Encouraged by this, we are making a preliminary report on a comparative evaluation of L-tryptophan and imipramine using a randomised double-blind design.

So far 16 inpatients with depressive illness, broadly selected on the criteria adopted by the Clinical Psychiatry Committee of the Medical Research Council,[2] have completed the trial successfully. The second and the third of these criteria were modified to the extent that the previous duration of the illness should not be less than four weeks and that the patient should not have received any specific treatment for the present episode of illness. The Hamilton rating scale for depression was used to quantify the depression on admission to the trial and at the end of four weeks. All patients received a fixed regimen of medication—either six 25-mg tablets of imipramine daily and 12 tablets of L-tryptophan placebo or six tablets of imipramine placebo and 12 tablets of L-tryptophan, each containing 0·5 g of the amino-acid together with 5 mg of pyridoxine hydrochloride and 10 mg of ascorbic acid. Thus each patient received a total of six tablets three times a day. To ensure further the double-blind nature of the trial the patients were instructed to discuss the possible side effects with a staff member other than the rater, as we observed initially that the subjects taking genuine imipramine could reveal themselves because of their common anticholinergic side effects.

As can be seen in the accompanying table our results are consistent with those of Jensen and his colleagues.[1] It was shown that there was no statistically significant difference between the two groups and that L-tryptophan and imipramine were equally effective in the treatment of these cases of depression. Our trial differs from that carried out by Jensen and his colleagues in that they used L-tryptophan without added vitamins. Winston[3] has postulated that the good results of a recent trial[4] of L-tryptophan in depression may have been due to the fact that in that study pyridoxine was omitted from the commercially available tablet. Our own results suggest that pyridoxine does not detract from the antidepressant properties of L-tryptophan.

We thank Mr Jack Desty of Cambrain Chemicals Ltd for supplying the L-tryptophan tablest (Optimax) and other trial materials and we are grateful to the other staff members of our department for their co-operation.

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[1] Jensen, K, *et al*, *Lancet*, 1975, **2**, 920.
[2] Clinical Psychiatry Committee of the Medical Research Council, *British Medical Journal*, 1965, **1**, 881.
[3] Winston, F, *Lancet*, 1975, **2**, 868.
[4] MacSweeney, D A, *Lancet*, 1975, **2**, 510.

Hamilton rating scale scores before and after treatment with L-tryptophan and imipramine

Time of rating	L-Tryptophan (n = 9)			Imipramine (n = 7)			*t* value of intergroup differences
	Mean	*t* value	Significance	Mean	*t* value	Significance	
On admission	25·33			22·86			0·77 (NS)
After four weeks	4·67	8·58	P<0·01	3·00	18·73	P<0·001	0·28 (NS)

Warfarin and Distalgesic interaction

SIR,—A 28-year-old woman who had developed a venous thrombosis after a Pott's fracture was referred to this laboratory for supervision of anticoagulant therapy. On 31 December 1975 her prothrombin ratio (BCR) was 3·2 and the dose of warfarin was lowered to 6 mg daily. On 7 January her BCR was 1·54 so the dose was increased to 7 mg. On 19 January BCR was 3·35 and warfarin was omitted for a day. She denied either any change in dietary habits or taking any drugs except for two Distalgesic tablets in the evening of 18 January. On 20 January she presented with haematuria and loin pain and had taken "a few more" Distalgesic tablets on 19 January. BCR was 5·2 and 2 mg of vitamin K_1 was given intravenously. The haematuria and pain ceased on 21 January.

I had been unable to explain why she had gone out of control, but in the light of the communication from Dr M Orme and others (24 January, p 200) I now assume that it was because of warfarin and Distalgesic interaction.

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Myasthenic syndrome during treatment with practolol

SIR,—We wish to report an apparent complication of practolol therapy.

The patient, born in 1921, was a wheezy bronchitic hypertensive whose blood pressure in 1969 was persistently elevated (220-195/120-105 mm Hg). Practolol was given in increasing doses, with bendrofluazide 5 mg and Slow-K 600 mg daily. His blood pressure on practolol 2400 mg daily had fallen to 140/70 mm Hg and he remained well until October 1972, when he presented with an eight-month history of double vision on watching football matches or long films, culminating in a two-day episode of bilateral ptosis. All the above symptoms were relieved by rest. There was no evidence symptomatically or on examination of