

LETTERS TO THE EDITOR

Worsening of Felty's syndrome with methotrexate

Sir: Drs Hughes and Abdulla recently reported a favourable response to low dose oral methotrexate treatment in a patient with Felty's syndrome,¹ confirming earlier reports.^{2,3} In contrast, we found such treatment failed, with worsening of neutropenia.

A 55 year old man had had rheumatoid arthritis since 1980. He had received second line drug treatment, including gold compounds and D-penicillamine, which were discontinued because of proteinuria and inefficacy respectively. Haematological signs of toxicity were not noted with these treatments. A diagnosis of Felty's syndrome was established in 1988 when he developed a splenomegaly associated with polyarthritis and was found to have neutropenia (white blood cells $2.41 \times 10^9/l$; neutrophils $0.72 \times 10^9/l$). Prednisone treatment 30 mg daily was started, then decreased to 20 mg/daily. In December 1989 he presented with acute polyarthritis and low peripheral neutrophils at $1.76 \times 10^9/l$. The erythrocyte sedimentation rate was 45 mm/h. Methotrexate 7.5 mg weekly was introduced, together with 15 mg prednisone daily. After one month no marked amelioration of clinical condition was seen, the spleen was unchanged, white blood cells control showed a drop of neutrophils to $1.036 \times 10^9/l$ (WBC $2.8 \times 10^9/l$, platelets $231 \times 10^9/l$). Methotrexate was discontinued. Further follow up showed that after one month neutrophils had increased and stabilised. Treatment with corticosteroids was continued alone.

In this patient methotrexate treatment failed to improve Felty's syndrome, and, on the contrary, induced a transient worsening of neutropenia. His condition was well defined,⁴ and no previous history of toxic neutropenia was found. He was not receiving any other neutropenic drug. His condition did not apparently differ from those of other patients who improved with methotrexate treatment.¹⁻³ Our data suggest individual sensitivity to methotrexate treatment in Felty's syndrome, and further studies are needed to define the characteristics which would predict a positive response.

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Lymphoedema complicating rheumatoid arthritis

Sir: I read with interest the report of Dacre,



Wrist radiographs taken in two planes.

Scott, and Huskisson on lymphoedema as an extra-articular feature of rheumatoid arthritis.¹ The phenomenon of lymphoedema of a limb complicating rheumatoid arthritis is well recognised, and I have successfully treated two patients with unilateral hand and forearm swelling with daily compression methods (Flowtron apparatus).

The article also reminded me of another interesting patient seen a few years ago with an identical appearance of one hand and wrist to that seen in the illustration accompanying the article. This patient had a wrist arthrogram performed, and the films show the resulting radiographs taken in two planes, clearly

showing the dye penetrating the marrow cavity of the radius. This patient's oedema was rather refractory to treatment. I am unaware of this marrow penetration phenomenon being previously reported.

I thank Dr J D Jessop, University Hospital of Wales, Cardiff, for permission to reproduce the radiographs.

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- Dacre J E, Scott D L, Huskisson E C. Lymphoedema of the limbs as an extra-articular feature of rheumatoid arthritis. *Ann Rheum Dis* 1990; 49: 722-4.

Smoking and back pain

Sir: The recent study by Symmons and coworkers¹ confirms previous work showing an association between smoking and back pain. The authors also (for the first time) show a similar association between back pain and oral contraceptives. These two findings might have a common mechanism as both smoking and oral contraceptives lead to disturbances in the flow properties of blood. Blood viscosity is a suitable ex vivo parameter for measuring this. It is roughly 50% higher in non-smokers than in heavy smokers (23.3 (SD 8.0) v 31.2 (9.7) mPa.s).² When oral contraceptives (levonorgestrel) are taken by young healthy women for three cycles blood viscosity increases on average by 3 mPa.s.³ One might therefore speculate⁴ that this alteration in blood rheology leads to a malnutrition of the highly bradytrophic intervertebral disc, rendering it more vulnerable to injury. This would be an attractive explanation of the fact that these cardiovascular risk factors are also related to back problems. It seems tempting to test this speculation in more detail—for example, by reanalysing some of the numerous epidemiological studies on cardiovascular disease in terms of back problems.

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Rheumatology in Dar-es-Salaam, Tanzania

Sir: May I commend and support the views expressed by Dr Adebajo.¹ During a spell teaching at Muhimbili Hospital, Dar-es-Salaam, Tanzania, I found a dearth of rheumatological experience amidst a wealth of clinical material. The table shows those disorders encountered during two weeks, mainly by scouting through clinics and wards. Good-

Rheumatic disorders at Muhimbili Hospital, Dar-es-Salaam, Tanzania, March 1990

Septic arthritis	Polyarthritits		Miscellaneous		
	Acute	Chronic			
<i>Staph aureus</i>	1	Reiter's disease	1	Frozen shoulder	1
Pneumococcus	1	HIV	2	Fibromyalgia	1
Gonococcus	1	SBE*	1	Osteosclerosis	1
Tuberculosis	3	Gout	1	Osteoporosis	3
		Rheumatic fever	1	Primary hypertrophic arthropathy	1
		Unknown	3	Leprosy	1
		Pseudo gout	1		

*SBE=subacute bacterial endocarditis.

ness knows what would be the response to opening a rheumatic clinic.

Like their brethren world wide, general physicians and orthopaedic surgeons cheerfully acknowledge their fumbling ineptitude when faced with locomotor disease of this variety and magnitude. Ours is a 'low tech' discipline compared with most these days, and our clinical skills and experience remain paramount. Elements can be taught at all levels of medical and paramedical practice, however, with some expectation of benefit to patients. South of the Sahara and north of Zambesi there lies a rheumatological abyss. The International League Against Rheumatism (ILAR) has recently established an African regional group (AFLAR),² which expects to hold an inaugural congress in Cairo in 1991. This may prove a catalyst to re-establishing medical links between Britain, Europe, and Africa sundered in the post-independence era. From Africa and its peoples we may learn how to husband meagre resources, stifle the demands of minor ailments, and perhaps, through appropriate research, explore the link between environmental and genetic factors in a variety of rheumatic disorders.

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Increased serum cytidine deaminase activity in gout and articular chondrocalcinosis

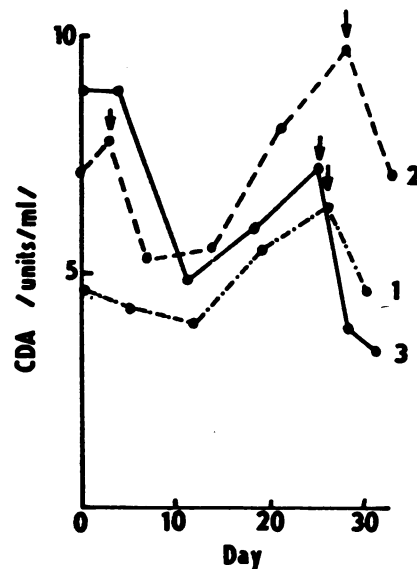
Sir: Thompson *et al* studied the activity of cytidine deaminase in serum and synovial effusions of patients with rheumatoid arthritis,¹ the activity after withdrawal of non-steroidal anti-inflammatory treatment,² and the circadian rhythm of serum cytidine deaminase activity.³ Increased activity of cytidine deaminase was found in serum and synovial effusions of patients with rheumatoid arthritis. The authors assumed that cytidine deaminase released from damaged neutrophils diffuses

from all inflamed joints into the blood, so that serum cytidine deaminase activity may provide an integrated measure of joint inflammation more specific than traditional measures, such as the erythrocyte sedimentation rate.

Increased granulocyte turnover and activation are involved in the inflammatory process connected with crystal induced arthritis. This prompted us to study the changes of serum cytidine deaminase in gout and articular chondrocalcinosis. Measurements of cytidine deaminase activity were carried out with cytidine as a substrate, and the ammonia liberated was determined by a modified Berthelot reaction.⁴

Fifty four patients with gout aged 32-57 years (mean 49), seven patients with chondrocalcinosis aged 56-69 years (mean 63) with proved crystals of sodium urate and calcium pyrophosphate dihydrate in synovial effusions, and 32 healthy controls aged 29-60 years (mean 47) were studied. Subjects with liver damage and increased serum creatinine were excluded.

Serum cytidine deaminase activity was significantly higher in patients with gout than in healthy controls (mean (SD) healthy 2.5



Changes of serum cytidine deaminase activity (CDA) during the gouty attack in three inpatients. Gouty attack is indicated by an arrow. The days indicate the time from admission to hospital.

(0.7) units/ml, patients with gout 5.4 (2.9) units/ml, $p < 0.005$). In three hospital inpatients the cytidine deaminase activity reflected a gouty attack (figure). The patients were receiving a purineless diet without treatment or they were receiving non-steroidal anti-inflammatory drugs (tiaprofenic acid, diclofenac). Patient No 2 had two attacks, following each other. Cytidine deaminase activity increased before the attack with the maximal value occurring during the attack and a subsequent decrease. Regardless of the basal values the appearance of acute arthritic syndrome in gout was preceded by an increase of cytidine deaminase. The patients with the primary hereditary form of chondrocalcinosis,⁵ and who developed secondary arthrosis, came from Velká Mača, a village located in southern Slovakia. Their serum cytidine deaminase values were significantly higher (5.3 (1.8) units/ml) than those of healthy controls ($p < 0.001$). The highest values of cytidine deaminase (7.5 and 7.7 units/ml) were found in two patients with active arthritic syndrome (on knees, metacarpophalangeal joints, and wrists).

Our observations indicate that serum cytidine deaminase reflects the inflammatory activity not only in rheumatoid arthritis and other autoimmune, bacterial, and viral inflammatory diseases¹ but also in crystal induced arthritides, such as gout and chondrocalcinosis. Higher cytidine deaminase values were present in these patients with no evidence of arthritic syndrome, but the cytidine deaminase activity increased further with the appearance of acute arthritic syndrome. Phagocytosis by neutrophils of monosodium urate and calcium pyrophosphate dihydrate microcrystals can cause the release of lysosomal enzymes, as well as a higher turnover of neutrophils; damage and breakdown of these cells would cause increased cytidine deaminase activity. Our results correspond with the investigation of Thompson *et al*¹ and extend their findings, showing that higher cytidine deaminase activities are also present in gout and chondrocalcinosis.

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