but it would obviously be more convenient for the patient if the drug could be given as a single dose once in the morning. Robin, Tolchin, and Rodnan (1973) found that the average decrement in serum uric acid was similar whether allopurinol was given as a single 300 mg dose or as 100 mg 3 times a day. However, in that study the serum uric acid was measured only once during 24 hours, whereas the critical fact is to know whether serum uric acid levels are as well controlled throughout the 24 hours by once daily as by divided dosage, since rapid fluctuations in serum uric acid levels can precipitate attacks of gout.

Three subjects were studied in detail. After equilibrium on one or other of the regimens, blood was taken every 6 hours and urine collected over continuous 6-hour periods for 3 days. They were then taken off treatment and later re-equilibrated on the other dosage regimen, urine and blood being again collected 6-hourly over the final 3 days. The serum uric acid was equally well controlled throughout the 24 hours on either regimen, and there was little difference in urinary levels.

It is therefore evident that allopurinol may be given once daily, a considerable advantage in patients on long-term therapy for gout.

Reference

ROBIN, J. A., TOLCHIN, S., AND RODNAN, G. P. (1973) *Arthr. and Rheum.* 16, 128

Stimulation of polymorph migration by a factor produced by steroid-treated monocytes. By R. D. STEVENSON (*University Departments of Medicine and Pathology, Western Infirmary, Glasgow*)

Human mononuclear leucocytes cultured in the presence of hydrocortisone produce a supernatant factor which markedly stimulates the *in vitro* migration of allogenic polymorphs. The mononuclear leucocytes used in the above experiments consisted of lymphocytes and monocytes, and the present study was undertaken to determine the relative roles of these difference cell types.

As shown in Table I polymorph migration was stimulated marginally by both steroid-treated lymphocyte supernatants and by hydrocortisone alone. On the other hand, approximately five times greater stimulation of migration was induced by supernatants both from steroid-treated mixed mononuclear cultures and from steroid-treated monocyte cultures. The monocyte, therefore, is the cell responsible for this effect, and the lymphocyte is not involved.

Table I *Stimulation of polymorph migration by supernatants of various steroid-treated leucocyte cultures*

Steroid-treated culture supernatants	Percentage stimulation of migration $\pm$ SEM
Mixed mononuclear leucocytes*	44 $\pm$ 3.46
Monocytes	36 $\pm$ 4.17
Mixed mononuclear leucocytes†	34 $\pm$ 4.13
Lymphocytes	6 $\pm$ 2.59
Hydrocortisone alone	7 $\pm$ 1.47

* Cultured as controls for monocytes.

† Cultured as controls for lymphocytes.

Table II *Effect of various steroids on the production of polymorph migration stimulator*

Steroid-treated culture supernatant	Percentage stimulation of migration $\pm$ SEM
Glucocorticoids (10 μ g/ml)	
Hydrocortisone	62 $\pm$ 1.06
Prednisolone	79 $\pm$ 1.81
Corticosterone	30 $\pm$ 0.77
Mineralocorticoids (10 μ g/ml)	
Hydrocortisone	34 $\pm$ 0.89
Aldosterone	11 $\pm$ 0.35
Desoxycorticosterone (DOC)	-5 $\pm$ 0.16
Sex steroids (10 μ g/ml)	
Hydrocortisone	44 $\pm$ 1.16
Progesterone	5 $\pm$ 0.13
Oestradiol	8 $\pm$ 0.25
Testosterone	3 $\pm$ 0.14

The polymorph migration stimulator was produced principally by glucocorticoids, prednisolone being more potent, and corticosterone less potent than hydrocortisone. Of the mineralocorticoids, aldosterone stimulated migration to a minor degree, whereas desoxycorticosterone was inactive, as were the sex steroids (Table II).

Monocytes also produce a substance known as colony-stimulating factor which stimulates *in vitro* growth of granulocytes. This factor may be a physiological mediator of granulopoiesis *in vivo* and may be related to the polymorph migration stimulator described above. In support of such a relationship, corticosteroid administration to man is known to induce a peripheral blood leucocytosis which is accompanied by a rapid disappearance of monocytes from the circulation.

It is postulated, therefore, that polymorph production and subsequent kinetic behaviour may be controlled by the monocyte under the influence of the glucocorticosteroid hormones of the adrenal cortex.

Raised levels of complement inactivation products in ankylosing spondylitis. By R. D. STURROCK, A. J. BARRET, J. VERSEY, and P. RENNOLDS (*Departments of Rheumatology, Haematology, and Chemical Pathology, Westminster Hospital, Dean Ryle Street, London, S.W.1*)

Activation of the complement system and utilization of complement is associated with the production of smaller fragments known as complement 'inactivation products'. Versey, Hobbs, and Holt (1973) have reported raised levels of C3 and C4 inactivation products in rheumatoid arthritis and noted some correlation with disease activity. Using a semiautomated two-dimensional immunoelectrophoretic method previously described (Versey, 1971), C3 and C4 levels and their inactivation products were measured in 31 patients with ankylosing spondylitis and 21 patients with osteoarthritis. Raised levels of C3 and C4 inactivation products were detected in 19 patients (61%) with ankylosing spondylitis and in only 2 patients (9.5%) with osteoarthritis ($\chi^2 = 13.9$; $P < 0.01$). The highest levels of C3 and C4 inactivation products were found in spondylitis with severe disease but there was no correlation with the ESR level. There was a wide range of total C3 and C4 levels in both groups of patients with the mean C4 level being higher in the spondylitic group.

The presence of raised complement 'inactivation

products' in ankylosing spondylitis denotes complement consumption and may represent an altered immune response to a persistent antigen in this disease.

References

VERSEY, J. M. B. (1971) 'An automated system of two-dimensional immuno-electrophoresis' in 'Protides of the Biological Fluids Proc. 19th Colloquium, Bruges 1971', ed. H. Reeters, Pergamon Press, Oxford.
—, HOBBS, J. R., AND HOLT, P. J. L. (1973) *Ann. rheum. Dis.*, 32, 557 (Complement metabolism in rheumatoid arthritis. I. Longitudinal studies)

Lymphocyte proliferation to artery antigen as a positive diagnostic test in polymyalgia rheumatica. By B. L. HAZLEMAN, I. C. M. MACLENNAN, and M. M. ESIRI (Oxford). Published in full in the *Annals*, 1975, 34, 122.

Evidence of impaired cell mediated immunity in the sero-negative arthritides. By R. D. STURROCK, K. FROEBEL, R. N. M. MACSWEEN, and W. C. DICK (Centre for Rheumatic Diseases, Royal Infirmary and Department of Pathology, Western Infirmary, Glasgow)

Lymphocyte responses to plant mitogens have previously been reported to be depressed in ankylosing spondylitis (Escanilla, Alepa, and Reeve, 1970). In view of this, lymphocyte responses to phytohaemagglutinin (PHA), Concanavilin A (Con A), and poke-weed mitogen (PWM) have been studied in twenty patients with ankylosing spondylitis, twelve patients with Reiter's disease, and eleven patients with psoriatic arthritis*. The results were compared with a group of fourteen normal controls and twenty patients with osteoarthritis. Skin testing was performed using 40 units streptokinase-streptodornase varidase and dinitrochlorobenzene sensitization. The Table summarizes the effect of the plant mitogens on lymphocytes from the various groups. PHA responses at a submaximal dose were significantly depressed in the ankylosing spondylitic and Reiter's groups and occurred particularly in those patients with clinically severe disease. An increased response occurred in the psoriatic group at higher doses of PHA and a similar effect was observed in response to PWM among the Reiter's patients. No correlation was found between *in vivo* skin testing and *in vitro* lymphocyte response, and the pattern of skin

* None of these patients were on anti-inflammatory treatment at the time.

reaction to dinitrochlorobenzene and streptokinase-streptodornase varidase was similar in all groups tested.

It is concluded that the impaired lymphocyte responsiveness to the plant mitogens tested may reflect an alteration of lymphocyte function in this group of diseases. Further work is necessary to establish whether this is a quantitative or qualitative defect.

Reference

ESCANILLA, F., ALEPA, P. F., AND REEVE, W. (1970) *Arthr. and Rheum.*, 13, 314

A serial study of eosinophilia and raised IgE antibodies during gold therapy. By P. DAVIS and G. R. V. HUGHES (Post-graduate Medical School, Hammersmith Hospital, London)

Gold therapy is known to be effective therapy for rheumatoid arthritis (RA) but to be associated with a high incidence of mucocutaneous side effects (Empire Rheumatism Council, 1961). Little is known about the mechanism of gold reactions nor is there a satisfactory method of monitoring gold reactions. A recent report has shown that patients with gold reactions also have raised levels of IgE antibodies (Davis and others, 1973) and that this was usually associated with raised eosinophil counts. The aim of this study was to perform serial IgE levels and eosinophil counts in patients receiving gold for arthritis and to correlate raised levels with gold reactions.

Case and methods 47 patients with RA and 3 patients with psoriatic arthritis have been studied. All patients were receiving gold in a standard regimen and had normal eosinophil counts and IgE levels before starting their therapy. Patients with a known atopic history were excluded. Eosinophil counts were measured by routine full blood counts and IgE levels by the radioimmuno-sorbent technique.

Results 14 patients developed a reaction to their gold therapy, i.e. rash, pruritus, or mouth ulcers. 11 of these patients had concurrent eosinophilia which preceded the side effect in 6 instances. In addition, a further 9 patients had eosinophilia without clinical side effect. IgE levels were raised in 22 of the 50 patients receiving gold therapy, the relationship to eosinophilia and clinical side effect is shown in the Table.

Table Lymphocyte responses to PHA, PWM, and Con A found to be significantly different ($P < 0.05$) from normal

	Ankylosing spondylitis	Psoriatic arthritis	Reiter's	Osteoarthritis	Normals
PHA (2.5 µg/ml)*	$\bar{x} = 15928 \pm 3479$ $\dagger t = 2.84$ $P < 0.05$		$\bar{x} = 19473 \pm 4007$ $t = 2.098$ $P < 0.05$		$\bar{x} = 31370 \pm 4175$
PHA (500 µg/ml)*		$\bar{x} = 32921 \pm 4461$ $t = 5.12$ $P < 0.005$	$\bar{x} = 33268 \pm 3991$ $t = 2.947$ $P < 0.01$		$\bar{x} = 21397 \pm 1604$
Con A (250 µg/ml)*				$\bar{x} = 13641 \pm 2099$ $t = 2.416$ $P < 0.005$	$\bar{x} = 30130 \pm 6847$
PWM (1:10)*			$\bar{x} = 28138 \pm 3601$ $t = 3.218$ $P < 0.01$		$\bar{x} = 16015 \pm 1632$

* The concentration of the stock solution of mitogen. The final concentration in the culture medium is 10% of the stock solution.
† The mean dpm per culture for the group $\pm$ SEM.
‡ The values of t and P are derived using Student's 't' test.