Mobility, end-plate defects, and disc degeneration in the lower spine. By R. C. HILTON and J. BALL (*University of Manchester, Department of Rheumatology*)

Because of the paucity of data on the mobility and morbid anatomy of the lower spine, we have systematically studied the T10-S1 region in 50 post-mortem specimens covering the age range 13-96 years.

Patients with cancer, bone diseases, and disorders likely to cause the latter were excluded. The flexion-extension mobility of the fresh specimen was measured radiologically. Serial slab sections of vertebral bodies were examined radiologically, and selected blocks studied histologically, with particular reference to lesions at the disc-bone border (rim and cartilage end-plate) and disc degeneration. Spinal bone density was assessed by measuring the weight/volume ratio of a complete central slab of L3.

Mean mobility fell progressively from L5/S1 to T10/11, but this smooth pattern of movement was seen mainly in those aged <50. More often the pattern was irregular indicating that maldistribution of stress may be common in the lower spine *in vivo*. In the lumbar spine mean overall mobility was less in those aged 50+ than in the <50 age group, especially in females, and the difference was largely due to a fall in mobility at the L5/S1 level.

Defects of the cartilage end-plate (Schmorl's nodes) were found in 76% of cases with similar frequency in the <50 and 50+ age groups and some, but not significant, preponderance in males. They were characteristically localized in the posterocentral part of the end-plate and were usually found at more than one level. They were not related to bone density and were significantly more severe and more frequent in the upper (T10-L1) region than in the lower (L2-S1) region. In those aged 50+ there was a significant relation between end plate defects and disc degeneration in the upper region but not in the lower region.

Reference

SCHMORL, G., AND JUNGHANN, H. (1971) 'The human spine in health and disease'. 2nd American edition translated by E. F. Besemann from the 5th German edition 1968. Grune and Stratton, New York and London

The musculoskeletal features of Wilson's disease: a clinical, radiological, and serological survey. By D. N. GOLDING and J. M. WALSH (*Department of Rheumatology, Princess Alexandra Hospital, Harlow; Department of Clinical Investigations, Addenbrooke's Hospital, Cambridge*)

Twenty-six patients with established Wilson's disease (hepatolenticular degeneration) have been reviewed with regard to musculoskeletal abnormalities. This is a preliminary report of the clinical and radiological findings.

There were 12 males and 14 females, ages ranging from 7 to 36 years (median 20 years). The majority were having penicillamine therapy at the time of review. All but four had one or more locomotor abnormality considered to be significant. The following principle clinicoradiological syndromes were identified: (a) A syndrome resembling premature osteoarthritis of the knees, characterized by pain (sometimes severe), stiffness and 'gelling', and radiological evidence of loss of joint space and osteophytes (7 patients). (b) Spinal pain and stiffness, often with radiological appearances resembling active or healed vertebral osteochondritis (5 patients). (c) Episodes of acute

or subacute polyarthritis (5 patients). (Some may relate to penicillamine therapy, which is known to cause occasionally an LE-like disturbance.) (d) Clinical and radiological features indistinguishable from rheumatoid arthritis (2 patients).

Other features of interest with regard to the musculoskeletal system were recurrent painful nodules about MCP joints 1, muscle cramps 8, tenosynovitis 3, painful feet 2, paraesthesiae of hands/feet 2.

Other radiological features of probable or possible significance were generalized osteoporosis 16, prominent periosteal reaction (fluffy spurs) in relation to trochanters 4, premature OA of hips 4, premature OA of wrists carpal joints 2, premature OA of spine 1, premature OA of ankles 1, 'squaring' of vertebrae 3, osteochondritis dissecans 3, multiple tongue-like osteophytic protrusions 2, and chondrocalcinosis 1.

Terminal phalangeal osteosclerosis. By W. HALIM, J. K. VAN DER KORST, H. A. VALKENBURG, and P. P. VAN ELTEREN (*Division of Rheumatology, Catholic University, Nijmegen, and Department of Epidemiology, Erasmus University, Rotterdam, The Netherlands*). Published in full in the *Annals*, 1975, 34, 82.

Plasma zinc in rheumatoid arthritis. Its relationship to corticosteroid therapy and osteoporosis. By A. C. KENNEDY, P. LEE, W. CARSON DICK, and W. W. BUCHANAN. (*Centre for Rheumatic Diseases, the University Department of Medicine, Royal Infirmary, Glasgow*)

Plasma zinc concentrations were determined in 47 male and 68 female patients with definite or classical rheumatoid arthritis, including 17 males and 24 females who were receiving corticosteroid therapy.

The mean $\pm$ SD for the noncorticosteroid-treated groups was 85.7 ± 19 (females 93.6 ± 23.6 $\mu\text{g}/100$ ml; males 82.6 ± 15.2 $\mu\text{g}/100$ ml), which was lower than normal controls (99 ± 11 $\mu\text{g}/100$ ml). The corticosteroid-treated group had a lower mean zinc level (females 83.4 ± 11.5 $\mu\text{g}/100$ ml; males 78.9 ± 26.1 $\mu\text{g}/100$ ml), which was significantly lower than the nonsteroid-treated group ($+ = 2.01$; $P < 0.05$). In addition, 5 patients with confirmed vasculitic skin ulcers also had a lower mean plasma zinc level (74.8 ± 8.5 $\mu\text{g}/100$ ml) which was significantly lower than the corticosteroid-treated group ($+ = 6.24$; $P < 0.001$).

The plasma zinc levels were also correlated against other clinical and laboratory indices. It was found that there was a correlation coefficient between plasma zinc and an index of osteoporosis (metacarpal index) in the corticosteroid-treated group of 0.47 ($+ = 2.15$; $P = < 0.05$) and also in the nonsteroid group of 0.45 ($+ = 2.1$; $P < 0.05$).

It is well recognized that collagen synthesis requires the presence of zinc, and the results of this study appear to confirm this. The results also suggest that zinc deficiency may play a role in the pathogenesis of osteoporosis in rheumatoid arthritis, especially that induced by corticosteroid therapy.

Single daily dose of allopurinol. By I. D. L. BREWIS, W. Y. LOEBL, and J. T. SCOTT (*The Mathilda & Terence Kennedy Institute of Rheumatology, Bute Gardens, Hammersmith, London, W.6*)

The most common dosage schedule for the xanthine oxidase inhibitor allopurinol is 100 mg taken 3 times a day,

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*

<i>Steroid-treated culture supernatants</i>	<i>Percentage stimulation of migration $\pm$ SEM</i>
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*

<i>Steroid-treated culture supernatant</i>	<i>Percentage stimulation of migration $\pm$ SEM</i>
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 spondylitics 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