treat local swelling with oral antihistamines. A patient with any systemic manifestations should be given a Medihaler-Epi as well as antihistamine tablets, although it is doubtful if any medication will be absorbed by the gastric mucosa after a sting.

Although there may be few actual fatalities from insect stings, the number of near-fatalities and of incidents terrifying to patients and their relatives must, to judge by the number seen at our clinic, be high. Some attempt should therefore be made to protect acutely sensitive patients. The best method available at present is hyposensitisation and the pure venom extracts mentioned in your article should become available in a few weeks.

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¹ Lawrence, D R, *Clinical Pharmacology*, 4th edn, pp 6 and 59. Edinburgh, Churchill Livingstone, 1973.

Back pain—what can we offer?

SIR,—Your leading article Back pain—what can we offer? (17 March, p 706) points out that since routine lumbar radiographs are not helpful in evaluating spinal disease in the absence of clinical pointers of serious causes many thousands of pounds would be saved by the NHS weekly if such investigation were avoided. Few would disagree.

It therefore seems strange that in the same editorial you suggest that certain laboratory screening tests are justified at the initial assessment of any patient with back pain. You include the erythrocyte sedimentation rate, serum calcium, phosphate, alkaline phosphatase, and acid phosphatase as well as plasma proteins, with electrophoresis. The many thousands of pounds that you claim that the NHS would save by not doing routine radiological evaluation would quickly be spent on this large battery of "screening tests."

In the absence of a formal study to demonstrate the clinical usefulness of these tests, it seems appropriate to recommend that patients should be so evaluated only if symptoms persist despite appropriate management, or a more sinister disease is suggested by the history and examination.

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Amitriptyline plasma concentration and clinical response

SIR,—The letter of T R Norman and others (31 March, p 894) raises the recurrent problem of correlating plasma tricyclic antidepressant levels with clinical response. They suggest that one source of variation between studies of this relationship may be the method of analysis used for drug estimations.

This department has initiated an antidepressant external quality control scheme¹ similar to its established anticonvulsant quality control scheme.² Spiked serum samples containing amitriptyline and nortriptyline or imipramine and desipramine (in concentrations of 50–200 ng/ml) are sent to participating laboratories. The methods of analysis used are gas liquid chromatography, radioimmunoassay, thin-layer chromatography, high-pres-

sure liquid chromatography, and gas chromatography-mass spectroscopy.

The coefficient of variation of returned results has ranged from 10% to 34%, larger than the coefficients of variation reported for the different methods of analysis (usually <10%). One measure of the quality of performance of an individual laboratory is the variation index (VI).³ A tenfold difference in VI was found between laboratories using similar or different methods of analysis. Those laboratories known to assay routinely these drugs tended to have low VIs, indicating a better quality of performance.

The scheme indicates that the skill of the analyst is an important factor in the precision and accuracy of determinations of antidepressant plasma levels and may partly explain the diverse findings of several groups concerned with plasma levels and clinical response. We shall be pleased to hear from others who wish to participate in the antidepressant external quality control scheme.

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¹ Jones, S, *et al*, to be published.

² Richens, A, *British Journal of Clinical Pharmacology*, 1978, 5, 285.

³ Whitehead, T P, *et al*, *Journal of Clinical Pathology*, 1973, 26, 435.

The drug of choice for major seizures?

SIR,—The following two statements about the treatment of major generalised seizures have appeared in recent issues of the *BMJ*: "Sodium valproate is the first choice in new patients" (leading article, 3 March, p 576), and "Phenytoin is now generally regarded as the anticonvulsant of first choice" (Drs D F Smith and J C Mucklow, 14 April, p 1000). My own first choice is carbamazepine.¹

The only conclusion to be drawn must be that any statement to the effect that drug X is generally regarded as the drug of first choice in major generalised seizures should be generally regarded as being wrong.

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¹ Addy, D P, *British Medical Journal*, 1978, 2, 811.

Difficulties in diagnosing meningococcal meningitis

SIR,—Drs V A Spagna and R B Prior (7 April, p 953) make bold but unrealistic claims for the limulus assay. The assay requires a scrupulously endotoxin-free system (I have found strongly positive gelation with distilled water). Ambient temperature, agitation, and time all affect the end-point. In practice, Gram-positive infection is not distinguished from Gram-negative.¹

When one suspects meningitis, the finding of a cloudy cerebrospinal fluid is confirmatory, subject to microscopy. Specific diagnosis once required Gram stain and culture, but counter-immunoelectrophoresis (CIE) has the many advantages pointed out by Drs L G Evans-Jones and Anthony Bryceson (31 March, p 892). Limulus gelation gives no useful information.

Problems arise when one finds a clear CSF, and indeed this carries a poorer prognosis in

meningococcal disease.² In the ABU Hospital, Zaria, Nigeria (lacking many facilities found in district general hospitals of the overdeveloped world), specific diagnoses are made confidently at a rate of 20 or more per day during epidemics.³ A rapid slide latex agglutination test (akin to the familiar pregnancy test) distinguishes pneumococcus, *H influenzae*, and group A and group C meningococcus in three minutes, pending the more sensitive CIE in one hour. Limulus assay added no useful information in patients with confirmed acute meningococcaemia and clear CSF.² Contrast this with the specificity, sensitivity in spite of antibiotics, and prognostic value of CIE, which enables specific treatment and also specific vaccination or prophylaxis when indicated. No test is infallible. But CIE on serum can rapidly diagnose those patients with meningococcaemia² (groups A and C at least) who would not survive long enough for CSF changes to occur.

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¹ Stumacher, R J, Kovnat, M J, and McCabe, W R, *New England Journal of Medicine*, 1973, 288, 1261.

² Lewis, L S, *Archives of Disease in Childhood*, 1979, 54, 44.

³ Greenwood, B M, Whittle, H C, and Dominick-Rajkovic, O, *Lancet*, 1971, 52, 320.

Saxophonist's diverticulosis

SIR,—The letters on occupational hazards (7 October, p 1023; 4 November, p 1295) prompt me to write of an interesting patient.

An 18-year-old saxophonist in the college band presented with a sudden onset of cramping abdominal pain and haematochezia. Sigmoidoscopy, colonoscopy, barium meal with follow-through, and technetium scan revealed no source for the bleeding. Barium enema indicated extensive diverticulosis coli. The patient noted that he could generate oral pressures of 5.6 kgf/cm² (80 lbf/in²) while playing his saxophone. We thus assumed that the extensive diverticulosis was due to the increase in intraluminal and intra-abdominal pressures generated from horn playing.

Incidentally, he has also required several root canals—a further complication of his avocation.

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Paget's disease in a treadle machine operator

SIR,—We were interested to read Dr L R Soloman's recent short report (7 April, p 931) of Paget's disease occurring in the fingers of a billiard player. We would like to describe a similar case where Paget's disease may well be related to previous repetitive localised physical exercise.

In 1966 a 73-year-old lady presented with pain in the right leg and on examination was found to have classical Paget's disease of the right tibia with anterior bowing. Radiology revealed osteitis deformans of the right innominate bone, lower end of the right femur, and the uppermost two-thirds of the right tibia. The left leg was normal and there was no radiological evidence of disease in the left side of the pelvis.

Since 1915 she had had a part-time occupation making the wrist bands for gloves, a well-known local industry. The work entailed using a treadle

machine which she peddled with her right foot using her left foot to work the brake. This machine was installed in her home during the first world war and she continued to produce wrist bands in this manner until the early 1950's.

The absence of Paget's disease in her left leg and, indeed, the rest of her skeleton strongly suggests that the recurrent physical trauma associated with some 40 years of peddling her treadle machine has predisposed the right leg and right side of the pelvis to this disease. Subsequently she has developed severe osteoarthritis of the right hip necessitating a total hip replacement and a degree of high-output heart failure secondary to the Paget's disease.

We therefore concur with the hypothesis that repeated physical trauma predisposes to the onset of Paget's disease in the affected limbs.

My thanks are due to Dr C Romer for drawing my attention to this case.

T M GASPER

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Epilepsy

SIR,—I was interested to read the article on epilepsy (14 April, p 1000) and especially interested to note the tragic fate of the unfortunate patient—suffocation in his pillow during a major seizure.

For some years I have been advocating the use of a special pillow in cases of grand mal epilepsy—especially in teenage and young epileptics.¹ Such tragic deaths are not uncommon. This is the tenth case of which I have personal knowledge, adding one more to the eight reported in July 1978 and another about whom I learned in August 1978.

The only manufacturers of such pillows are Melco Products Ltd, of Tottington, Near Bury, Lancashire.

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¹ Wilson, J B, *British Medical Journal*, 1978, 2, 200.

Mercury battery ingestion

SIR,—The ingestion of mercury batteries probably occurs more frequently than is documented and Mr D T Reilly in his report (31 March, p 859) recommended early operation to avert potentially fatal poisoning. Our experience with one such case raises several questions.

A 1-year-old girl swallowed a mercury battery (Mallory Px 625 dry cell, contents similar to those described in the report). She was observed, appeared to develop an upper respiratory tract infection, and vomited 12 hours later. She began passing dark grey stools 24 hours later and at this stage an x-ray revealed an intact battery lying within the stomach. A laxative was given to hasten the passage of likely intoxicants released from the battery. Reassurance from the makers was obtained by telephone that the battery was inert and ought to resist dissolution but that, should this occur, the contents were unlikely to form toxic components. Vomiting was episodic and at 48 hours a second x-ray showed the battery had separated into two discs, one still in the stomach, the other having progressed to the ascending colon. Maxolon was administered and Isogel was given to increase bulk and hopefully to "encase" the now sharp-edged discs, which could have lacerated the pylorus and gut wall. The baby ceased vomiting, developed colic, and continued to pass dark grey stools; and by 72 hours one half of the battery appeared, followed shortly by the second. Neither serum nor urine levels of mercury had been checked. After a week of anorexia and some lassitude an apparently

total recovery followed, and now at the age of 6 she is normally developed, active, and intelligent.

Several points deserve comment. Firstly, it must be emphasised that these batteries are in increasing use in cameras, fancy key-ring flashlights, etc, and must be kept well out of reach of children. Secondly, the nickel-plated casing would not have corroded sufficiently quickly to account for stool discolouration, which simply suggests release of battery contents, as confirmed by the in-vitro test described in the report. Radiological evidence of an "intact" battery is therefore unreliable. According to information received, the amount of mercuric chloride formed would decrease with increasing usage of the battery, as discharge of the dry cell reduces the amount of mercuric oxide available to form the chloride.

Absorption of mercury was not monitored in the case described here and, although all is well, one is left with an abiding concern that toxic damage to various organs might have occurred over the three-day period. If this is so, can it be confirmed, quantified, and the likely long-term consequences predicted? The possibility of poisoning and the mechanical difficulty of negotiating a tiny pylorus would certainly indicate operative removal. However, in Mr Reilly's report the absence of toxicity over a period exceeding 24 hours and in our case the clinical normality six years later, despite ample opportunity for intoxication, may in fact permit a conservative approach to be adopted.

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Differences between Leeds fractures and London fractures?

SIR,—Drs R Wootton and J Reeve (14 April, p 1017) have questioned the statistical validity of the difference in plasma 25-hydroxy vitamin D (25-OHD) level between our femoral neck fracture patients and controls and they suggested that we should apply a logarithmic transformation to our data (3 March, p 589). Unfortunately, this is impossible because of the zero values in both our groups. The non-parametric Wilcoxon sum rank test is appropriate, however, and its application to the data yields a P value of less than 0.00001. This compares with P values of <0.001 with the Student's *t* test and <0.0001 by the χ^2 test. Your correspondents can therefore rest assured that the difference between the two groups, which is so apparent to the naked eye, is statistically valid.

As to why the data from Northwick Park are so unlike those from Leeds, the most likely explanation is in the choice of controls. We are not given details of the elderly subjects admitted for cold orthopaedic surgery to Northwick Park Hospital but they are likely to include a high proportion of relatively immobile subjects with joint disease whose exposure to sunlight is restricted. Our controls, on the other hand, were randomly selected from a random sample of the population of Leeds living in their own homes. As over 90% of our fracture patients were also admitted from their homes, the two groups are comparable.

In this connection, it may be relevant that, whereas our control data are almost normally distributed, the Northwick Park data are, in your correspondents' own words, "skewed." This in itself suggests that their control series

is not in fact a normal group but, like their and our fracture groups, pathological.

As Drs Wootton and Reeve say, our data are compatible with the hypothesis that vitamin D deficiency contributes to fractured neck of femur in the elderly in Leeds; we cannot accept that they have provided evidence to the contrary in London.

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Microscopic words

SIR,—Dr B J Freedman in his letter (14 April, p 1021) reveals himself as the erudite author of your enjoyable feature "Words." Unfortunately, however, he perpetuates a common error in restricting Robert Hooke's use of the word "cell" to the empty variety that makes up cork. As I pointed out in the original version of my letter, which was published abridged in "Points" (24 February, p 559), Hooke¹ described not only the dead cells of cork, but also the living entities, "for, in several of those Vegetables, whilst green, I have with my *Microscope*, plainly enough discover'd these Cells or Poles (sic) fill'd with juices, and by degrees sweating them out."

Clearly Hooke's "cells" fulfilled Dr Freedman's stringent criteria for the use of the word in its modern biological sense.

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¹ Hooke, R, *Micrographia: or some Physiological Descriptions of Minute Bodies made by Magnifying Glasses*, p 116. London, The Royal Society, 1665.

Unusual reaction to monoamine oxidase inhibitor

SIR,—I had an outpatient who was an industrial chemist involved in devising new dressings or fillers for paper, and was therefore exposed to vapour, mist, or spray from his reagents. He had become despondent about his progress, and I prescribed phenelzine, 15 mg three times a day. He understood the dietary restrictions, and disclosed that cheese did not agree with him anyway. This may have been an unheeded warning to me. When seen again he was very well, his research being successful.

He had been so drug-compliant that he had observed dietary restrictions for a full 24 hours before his first and only dose, but within minutes he felt malaise and nausea. Half an hour later he must have been shocked, his wife remarking how grey and pale he looked; four hours later he had a "blinding headache," which passed off. He did not contact any doctor, and so the opportunity of checking on his clinical state, urinary metabolites, and serum enzymes was lost.

Reflecting that this reaction suggested that all his metabolic amine detoxification systems must be saturated, and that his research might have utilised higher amines for their known antiseptic and surface tension activity, I asked about his reagents. He wrote that one of them was a substituted propane diamine acetate, the second a tertiary amine, and the third a substituted imidazoline acetate.

I suggest that in unusual circumstances