be simply written off as a "primitive and mutilating procedure." In these times, when balancing the cost benefit equation is increasingly important, to introduce an expensive new treatment for a common condition when an equally effective one already exists cannot be justified unless its benefits are fully examined.

A study of male attitudes to castration as a treatment for cancer is needed and this could well be funded by the drug companies introducing these new preparations.

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Olfactory hallucinations

SIR,—Dr N E F Cartlidge states in Any Questions (23 January, p 278) that the commonest cause of olfactory hallucinations is epilepsy. While this may be so in purely neurological practice it is not true in general. The most frequent causes are depression and schizophrenia. In a series of patients with olfactory hallucinations drawn from both neurological and psychiatric clinics a third were depressed, a quarter were schizophrenic, a quarter had an olfactory reference syndrome, and only 8% had epilepsy.¹

In depression the hallucination is typically of a foul odour, and two thirds of patients believe this to arise from their own bodies. There are seldom any other sensory abnormalities. The depression is usually endogenous with retardation, depressed mood, and morbid thoughts. Olfactory hallucinations are common in schizophrenia but are often subordinate to hallucinations in other modalities. In late onset paranoid schizophrenia, however, they may be the dominant complaint. Such patients believe the smells are being forced on them and take "reasonable" steps to prevent this by, for example, blocking up chimneys or complaining to the police. In the olfactory reference syndrome the complaint of smell is usually of a true hallucination which the patient believes emanates from himself. It occurs without prior depression of mood and leads to excessive washing of hands, changes of clothes, and avoidance of other people.

In these conditions there is often secondary delusional interpretation, whereas in temporal lobe epilepsy the olfactory hallucinations are almost always recognised by the patient as a subsidiary part of the illness. Patients who present with olfactory hallucinations need careful neurological and mental state examination. The presence of delusions points to a psychiatric syndrome, but the clinician should not lightly dismiss organic causes in patients who have psychiatric symptoms.

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1 Pryse-Phillips W. An olfactory reference syndrome. *Acta Psychiatr Scand* 1971;47:484-509

Transporting critically ill patients by ambulance

SIR,—Dr J F Bion and colleagues (16 January, p 170) suggest that blood pressure should be

monitored during transfer of very ill patients. We would be interested to know how they do this.

Measurement of blood pressure in a moving ambulance is not easy. Automatic measurement of blood pressure by invasive and non-invasive methods requires a still patient. Auscultation of Korotkoff sounds in an ambulance is awkward and frequently impossible. Oscillotonometers are inaccurate in the presence of vibration. The most satisfactory method of measuring systolic blood pressure is by the use of a mercury sphygmomanometer and a finger on the pulse. In the presence of hypotension even this technique is inadequate.

We confess that we are frequently unaware of the precise blood pressure of our patients in transit. Often it is a case of knowing whether or not the patient actually has a blood pressure.

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AUTHOR'S REPLY—We made it clear in our article that no monitoring was employed during transport of the 50 patients in the study. The results suggest that blood pressure monitoring would be a useful aid during ambulance transport of the critically ill, but space did not allow us to elaborate on possible methods.

Intra-arterial blood pressure measurement is the ideal¹ but requires medical staff competent at inserting cannulas; a cheap and satisfactory monitor is the simple Tycos gauge which displays mean arterial pressure. Non-invasive methods suitable for the critically ill are still at the development stage: the Copal semiautomatic sphygmomanometer (Andrew Stephens Co, Blackpool), the Omega (Vickers), and the Dinamap (Critikon) are available in portable form but overestimate at low pressures.² The Finapres (Ohmeda) represents an important development in accurate and continuous non-invasive pressure measurement, but the device is not yet portable.

Until these problems are resolved critically ill patients should not be transported until they are physiologically stable,³ and they should be attended by staff properly trained in resuscitation; intra-arterial cannulation is the most reliable method, and the Tycos gauge the cheapest monitor.

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The future of teaching in district general hospitals in the NHS

SIR,—Professor Harold Ellis (16 January, p 152) casts doubt on the ability of private medicine to provide the basic requirements for teaching senior house officers and registrars.

I have just resigned from the NHS to go into the private sector 15 years before my due date of retirement as a result of the draconian cuts which have been forced on us in the Bromsgrove and Redditch District. These cuts have reduced our senior house officers by one and have completely swept aside a training post in knee surgery which

had been set up as part of the training rotation from the Robert Jones and Agnes Hunt Hospital at Oswestry.

The job description for the "fellow in knee surgery" had created a timetable in which the incumbent trainee was exposed to a maximum amount of knee surgery, including arthroscopic surgery, and spent most of his time in outpatients dealing with new and follow up cases of knee problems. This arrangement has now become impossible owing to the drastic cuts in funding in our district and the closure of our specialist orthopaedic hospital at Hill Top, Bromsgrove. The concomitant reduction in senior house officer staffing levels has meant that the teaching post has now become a common or garden NHS senior house officer post.

Furthermore, owing to the changes in staffing levels of registrars and senior house officers after the recommendations in *Achieving A Balance* we are now left with one registrar, four senior house officers, and no junior house officers to deal with about 1000 elective major orthopaedic cases a year and roughly the same number of emergencies and minor cases. This in effect means that the senior house officers spend nearly all their time clerking patients on the ward while the registrar and consultants deal with outpatients on their own and there is no time left at all for teaching or for instruction in operative technique.

The monetary restrictions have also prohibited the purchase of several items of diagnostic and therapeutic importance in knee surgery which would improve both the quality of teaching and the experience of the senior house officers during their six month sojourn in trauma and orthopaedics.

A far better deal can be offered in the private sector for the senior house officer or junior registrar who wants six months' training in a surgical or medical specialty. The junior would be attached full time to one or at the most two consultants and would deal in depth with a small number of inpatients (between five and 10 a week) and a similar number of outpatients.

Sophisticated modern equipment is what the private patient today expects in a specialist knee service, where there is no question of not being able to afford computed tomography, arthrograms, video recorded arthroscopies, routine clinical photographs, and so on. Theatre time is far more available, and emergencies are dealt with in the private sector by the consultant with help from his junior.

All this is good grist to the teaching mill, and the consultant in private practice should be encouraged to advertise for top quality juniors with the assurance that with very little effort the full time private surgeon has more to offer than the overworked and underfunded NHS consultant.

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Fraud in medicine

SIR,—Dr Stephen Lock's leading article (6 February, p 376) suggests two lessons to be learnt from the many accounts of fraudulent publication: the close supervision of young researchers, and the rethinking of the emphasis placed on number of publications. The latter seems likely to be the most effective. Faced with the enormous pressure, not just on juniors but on entire departments, to keep up a "good"—bulky—publications record, it is difficult to see close supervision as a satisfactory solution. The way in which Slutsky managed to involve those who should have been monitoring him shows this.¹

I have suggested that the most effective solution is to alter the pressure on researchers, so that they are encouraged to publish small quantities of good work rather than just large quantities of publications regardless of quality.² May I suggest that the BMA recommend to the Medical Research Council, the medical charities, and clinical and academic organisations responsible for staff appointment, tenure, and promotion that they should alter the section on their application forms which currently reads "Publications (continue on attached sheet(s) if necessary)" to read "List not more than 6 of your publications by which you would wish your application to be judged."

If a few major organisations would take the lead on this I am convinced that researchers would soon change their publishing patterns to try to produce publications which would stand up to exhaustive scrutiny, rather than, as at present, desperately trying to fill out attached sheets of paper with anything they can get their name on to.

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Drug points

Mefenamic acid nephropathy—acute renal failure in overdose

Drs A J TURNBULL, P CAMPBELL, and J A HUGHES (Gastrointestinal Laboratory, Rayne Institute, St Thomas's Hospital, London SE1 7EH) write: The nephrotoxic effects of mefenamic acid in medium to long term use are well known. We describe a case of acute renal failure after a single overdose.

A 30 year old man, previously well and taking no regular medication, was admitted collapsed, having taken about fifty 250 mg mefenamic acid tablets (12.5 g). He was restless and agitated, had a depressed level of consciousness, and had a blood pressure of 110/80 mm Hg. He was paralysed and intubated and gastric lavage performed. He rapidly developed generalised tonic-clonic convulsions requiring intravenous diazepam and, later, chlormethiazole. Serum biochemistry values on admission were normal, and neither salicylate nor paracetamol was detected. Twenty four hours later he developed bloody diarrhoea, abdominal pain, and vomiting lasting 18 hours. He remained well hydrated and normotensive and received intravenous fluids and oral antacids. Twenty four hours after admission the serum creatinine concentration rose to 366 µmol/l, peaking at 804 µmol/l five days after the overdose and subsequently falling steadily to 221 µmol/l over the following week. The serum urea concentration rose to a maximum of 21 mmol/l. Creatinine clearance four days after admission was 15 ml/min, rising to 54 ml/min 11 days after the overdose. Neither casts nor myoglobin was present in the urine and the serum creatine phosphokinase value peaked at only 248 U/l (normal <110 U/l).

Conservative treatment for acute renal failure was started and dialysis was not required. Four days after admission he developed severe bilateral loin pain and microscopic haematuria. Renal ultrasound showed no evidence of obstruction and intravenous urography showed normal kidneys. Serial mefenamic acid measurements showed a peak of 46 mg/l on admission, falling to 4 mg/l 21 hours later and becoming undetectable within 27 hours. Expected therapeutic concentrations are up to 10 mg/l.

Mefenamic acid is an increasingly common problem in analgesic poisoning.¹ Court and Volans reported one case of acute renal failure after consumption of 15 g mefenamic acid over four to five days,² but acute

renal failure has not been reported in association with a single overdose.

Nephrotoxic effects of mefenamic acid in medium to long term use include acute renal failure, interstitial nephritis, the nephrotic syndrome, and papillary necrosis.³ In 1980 six cases were reported of elderly women developing non-oliguric acute renal failure after two to six weeks' treatment at therapeutic doses.⁴ The authors suggested that inhibition of renal prostaglandin synthesis reduced renal blood flow, resulting in ischaemic papillary necrosis, the effects being enhanced by dehydration. Subsequent reports indicate acute interstitial nephritis as the cause, renal biopsy showing interstitial inflammatory cell infiltrate.⁵

The abdominal pain and microscopic haematuria of the patient reported on here suggested renal tract obstruction, though we found no evidence of this. In the absence of other causes of acute renal failure, such as dehydration or myoglobinuria, we conclude that the nephrotoxicity of mefenamic acid may also be manifest in acute overdose. Such patients must remain adequately hydrated and their renal function must be monitored closely.

We thank the Poisons Unit, New Cross Hospital, for performing the mefenamic acid assays.

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Convulsive seizures after treatment with praziquantel

Drs JOSE L BADA, BEGOÑA TREVIÑO, and JUAN CABEZOS (Department of Microbiology, Universidad Autónoma, Barcelona, Spain) write: Praziquantel is considered to be a major advance in the treatment of schistosomiasis as well as other trematode and cestode infections because it is taken by mouth, usually as a single dose, and lacks apparent serious toxicity. Several studies confirm the absence of serious side effects after oral administration in short courses over 24-48 hours. Transient dizziness, headache, drowsiness, abdominal pain, nausea, and vomiting have been reported¹ and, in a few patients, fever, dysenteric stools, epistaxis, and urticaria.^{2,3} We report on a 32 year old Spanish man who was diagnosed as suffering from grand mal epilepsy at the age of 13. He was treated with diphenylhydantoin, phenobarbitone, and clonazepam and had had no seizures for the past seven years. An electroencephalogram taken in March 1986 during waking state was normal, but during stages I and II of slow wave sleep it showed paroxysmal generalised deep irritative manifestations. In November 1985 he travelled to north and west Africa, and in April 1986 he complained of high fever with shivering. *Plasmodium vivax* was seen in the blood. He was treated with chloroquine and primaquine at standard doses. A serological test for schistosomiasis was positive (indirect haemagglutination positive at 1/640), and *Schistosoma mansoni* eggs were found in the stools in June. He was treated with two doses of 20 mg praziquantel/kg 12 hours apart. About 12 hours after the second dose he suffered one tonic-clonic convulsive seizure with loss of consciousness and biting of the tongue, which was repeated two hours later. A neurological examination, electroencephalography, and computed topography performed several days later yielded normal results. No further seizures have been reported.

The convulsive seizures in this patient were probably due to praziquantel: the patient had had no attacks for seven years, there was no change in medication, no precipitating factor preceded the convulsion, and there was no seizure during a previous malaria attack, when fever reached 41°C. In cerebral cysticercosis praziquantel can precipitate fits, but we believe the patient's seizures were not a manifestation of cerebral schistosomiasis; this effect of praziquantel has not

been proved in cerebral schistosomiasis,⁴ and neurological signs and symptoms suggestive of central nervous system disease were absent before and after treatment with praziquantel.

To the best of our knowledge, this complication has not been reported as a side effect of praziquantel, although among 25 693 patients with *S. japonica* treated with this drug it was found that eight epileptic patients had seizures more frequently during and several days after praziquantel treatment.⁵ We recommend caution when praziquantel is used in patients with convulsive disorders.

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Is inosine pranobex contraindicated in autoimmune disease?

Drs A J CHUCK, J K LLOYD JONES, N A DUNN (Department of Rheumatology, Harlow Wood Hospital, Nottinghamshire), and R J POWELL (Department of Immunology, University Hospital, Nottingham) write: A 27 year old woman developed muscle pain and weakness, preceded for two years by arthralgia and for 12 months by extensor tendon nodules. Needle muscle biopsy confirmed active polymyositis. She responded to prednisolone 30 mg daily, which was gradually reduced. Extensive flat topped plane warts (human papillomavirus III by deoxyribonucleic acid hybridisation) later appeared on the face and limbs. These proved too numerous for treatment by podophyllin and cryotherapy, and inosine pranobex (Imunovir) 1 g four times daily was given. One week later muscle pain worsened accompanied by profound weakness. Inosine pranobex was withdrawn and prednisolone increased. The warts remained unchanged. The polymyositis deteriorated further when steroids were reduced. Antibodies to Jo-1 were present. Azathioprine 150 mg daily was started: the polymyositis improved rapidly and the warts disappeared over a period of two months. Prednisolone was gradually withdrawn.

Polymyositis is an autoimmune disease in which T cells sensitised to muscle predominate in the inflamed muscles; any drug which further enhances these T cell activities might exacerbate the disease. Inosine pranobex has been reported to potentiate IL-2 production¹ and thus to stimulate sensitised T lymphocytes. The detrimental effect of inosine pranobex might therefore have been predicted. Inosine pranobex has been used in small trials in treating a variety of other autoimmune diseases, including rheumatoid arthritis² and diabetes mellitus³ with no obvious detrimental effect; a single case report of a beneficial effect in systemic lupus erythematosus has recently been published.⁴ It could be suggested that B cell activation is more prominent in rheumatoid arthritis and in diabetes mellitus than in polymyositis; this alone, however, is unlikely to explain the apparent dichotomy of clinical effects because T cell activation is integrally implicated in B lymphocyte differentiation.

We are unaware of a previous report of the use of inosine pranobex in polymyositis. We believe that this drug was implicated here in the deterioration of the polymyositis and it should therefore be used with caution in this and other autoimmune diseases.

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