

ulcer has shown that admission for perforation in the years 1973-6 was as common among black as among white patients at the Johannesburg General Hospital.¹ The type of complication occurring was also similar in the two population groups, perforation and haemorrhage being common, in contrast to the greater frequency of stenosis reported in many studies from rural areas in Africa.²

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¹ Cooke, S A R, *British Journal of Surgery*, 1977, **64**, 791.

² Tovey, F I, and Tunstall, M, *Gut*, 1975, **16**, 564.

Choosing an antidepressant

SIR,—The letter from Mr G W Lewis (25 February, p 510) implies that 98% of a dose of viloxazine is eliminated unchanged in urine. This is incorrect. Viloxazine is very well absorbed following oral administration and 98% of the dose is excreted via the kidneys. However, it is extensively metabolised and only about 12% of the eliminated material is unchanged drug.¹ As viloxazine is metabolised to inactive metabolites it does, of course, fulfil the first criterion for the selection of an antidepressant proposed in the letter cited.

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¹ Case, D E, and Reeves, P R, *Xenobiotica*, 1975, **5**, 113.

Schumann's hand injury

SIR,—May I add two small postscripts to the fascinating paper on Schumann's hand injury by Drs R A Henson and H Urich (8 April, p 900)? Firstly, their paper has practical importance to pianists in finally dispelling the myth that gruelling finger-stretching exercises, such as those by Joseffy and Dohnanyi, are intrinsically dangerous and may cause permanent injury. Secondly, I wonder whether Schumann's composition technique may have been specifically adapted to minimise the effect of his own physical disability. In many of his technically difficult passages he appears to avoid undue use of his affected right middle finger; most of his Op 7 toccata, for example, can be played without this finger, although it is a formidable exercise for the other three digits and thumb. Is this a manifestation of his posterior interosseous palsy?

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GP obstetrics

SIR,—It was kind of Mrs Jean Fedrick and Professor N R Butler (25 March, p 763) to comment so favourably, albeit paradoxically, on the obstetric results emanating from our general practice (15 October 1977, p 1004) in the midst of an article aiming to substantiate from somewhat dated statistics that care in consultant obstetric units carries less risk of death to the fetus. It is this paradox which points the way to further obstetric improvement. Overall figures such as theirs contain good and bad results from consultant units as

well as general practices. The challenge for the future is for those units and practices producing mediocre figures either to improve or to phase out of the obstetric scene.

They are right to highlight the importance of enthusiasm for obstetrics as being a sine qua non for the achievement of good results from general practice. This practice, however, is not alone in having enthusiasm, and we are well aware of many other practices with similar attitudes. Dr M J V Bull in Oxford (25 March, p 788) has reported provisionally on most excellent general practice care from that city. Furthermore, as a teaching practice we are passing on our enthusiasm year in, year out to our trainee general practitioners. Nevertheless, the sad chronicle of Mr B V Lewis and others (25 February, p 484) of the declining general practitioner obstetrics in Watford, apparently culminating now in over 50% of women choosing epidural anaesthesia in a specialist unit as their delivery method of choice, is becoming unfortunately prevalent in Great Britain. I still maintain that the ideal situation and the best results will emerge from areas where enthusiastic general practitioners are encouraged to "normalise" the majority of obstetric care and delivery by enthusiastic and open-minded specialists, who can then concentrate their expertise on a small number of high-risk and problematic patients who truly require it.

It must be borne in mind that the more recent statistics emerging from specialist units indicate that the price many mothers are paying for the tiny improvement in the overall perinatal mortality rate is a labour directed by virtually unknown doctors, in a highly abnormal and artificial setting, with increasing mechanisation, increasing use of drugs and drips (for example, see Dr R J Rowlatt's plea (15 April, p 985) for less diazepam for the neonate), considerable interference in the natural father-mother-child bonding (probably of great importance in preventing future family morbidity), and far, far too little orientation towards the behavioural aspects of the intranatal period. A good general practitioner unit "specialising" in normal labour with personal care under the same roof but not necessarily under the same ceiling as a quality, not overworked, specialist unit appears to offer the best of both worlds. Results from this practice substantiate that claim.

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Diseases of the respiratory system

SIR,—In her article in the Today's Treatment series Dr Margaret E Hodson (15 April, p 971) says: "The most important aspect of medical treatment [of bronchiectasis] is regular postural drainage of the affected segments or lobes. . . . The patient should maintain the appropriate posture for 10-15 minutes night and morning. . . . If possible, a relative or friend should be shown how to percuss the chest to aid expectoration. . . . If a pathogenic bacterium is found then appropriate antibiotics should be given. . . . Patients with large volumes of purulent sputum in whom simpler measures have failed should be admitted to hospital for intensive treatment. They should have intensive (four to six times daily) physiotherapy and [an antibiotic]. . . . Sepsis in the paranasal sinuses and teeth should be eliminated."

As bronchiectasis is a chronic malady the main object of treatment is to give long-term benefit. No doubt there are grounds for believing that regular postural drainage lessens the volume of sputum, but otherwise is there any evidence that any of these measures achieve this goal? In particular, is there evidence that percussing the chest aids expectoration or that intensive physiotherapy four to six times daily is beneficial? Moreover, what is "intensive physiotherapy"?

Throughout my medical career I have read an endless series of articles in which authorities have made ex-cathedra statements about treatment, all unsupported by evidence. Rest was repeatedly said to be of "fundamental importance" for all manner of maladies, diets were laid down in the fussiest detail, and numerous activities were "forbidden." In recent years we have become more critical and it has been accepted that, when dealing with variable and recurrent conditions, controlled trials are needed to evaluate drug and operative treatment (except when these are overwhelmingly and consistently successful, as for tuberculosis). But, as Dr Hodson's article illustrates, we still tend to be uncritical of such general measures as rest and physiotherapy.

May I finally suggest that you, Sir, are more critical of your contributors' articles? They should always be asked to provide evidence to support their recommendations about treatment, and in particular should distinguish between treatment based on evidence and treatment based on theory.

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Lithium toxicity

SIR,—Some time ago Professor S R Hirsch discussed with me the paper he wrote with Dr Jean Speirs on lithium toxicity (1 April, p 815). However, I should be glad if I could add some further comments in the light of new data.

It is difficult to explain the increased requirement for lithium in this case. It may be mundane, but the most likely causes for this are poor compliance or inadvertent intake of lithium on the morning of the test. It is desirable to know how an individual patient is going to handle lithium before starting treatment in order to predict the most appropriate dosage. This can be done either by performing a renal lithium clearance test¹ or by taking a 24-hour blood sample after a lithium loading dose.² In the case described we would then have known whether or not the lithium clearance had changed during the treatment.

The cause of the patient's becoming comatose is difficult to determine. The surprising thing is that he developed coma one week after lithium was stopped. The lithium level at that time was not indicated, but it would be extremely surprising if it was anywhere near the toxic range, as the mean biological half life of this drug is 13 hours.³ It does, however, seem likely that the patient had had lithium levels well above the toxic range for seven months before admission. He was then receiving lithium carbonate in the form of Priadel at a dosage of 2000 or 2400 mg per day. Analysis of bioavailability data by a curve-peeling technique⁴ in volunteers receiving Priadel, with a mean age one year less than the patient described, shows that the mean serum lithium level would rise to a peak of

2.36 mmol/l (1.6 mg/100 ml) if the 12-hour steady-state serum lithium level was maintained at 1 mmol/l.^{5,6} The mean dosage of Priadel required to maintain this level would be 1643 mg. Comparison of these results suggests that the peak serum lithium level would be certainly above 2 mmol/l (1.4 mg/100 ml) and probably considerably above this in the patient described, as the patient was receiving a higher dosage of lithium. If the blood samples were taken just before administration of the whole dose of lithium, the peak serum lithium level would be even higher than this.

We still do not know how best to give lithium to maintain prophylaxis, but in view of the recent reports of renal damage following lithium toxicity^{7,8} it is prudent to give lithium in such a way as to avoid levels in the toxic range. The majority of patients should receive lithium in at least a divided dose schedule.

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- ¹ Schou, M, et al, *British Journal of Psychiatry*, 1970, **116**, 615.
² Cooper, T B, Bergner, P-E E, and Simpson, G M, *American Journal of Psychiatry*, 1973, **130**, 601.
³ Amdisen, A, *Danish Medical Bulletin*, 1975, **22**, 277.
⁴ Bergner, P-E E, et al, *British Journal of Pharmacology*, 1973, **49**, 328.
⁵ Tyrer, S P, in *Lithium in Medical Practice*, eds N F Johnson and S Johnson, p 395. Lancaster, Medical and Technical Publishing, 1978.
⁶ Tyrer, S P, *American Journal of Psychiatry*, in press.
⁷ Hestbech, J, et al, *Kidney International*, 1977, **12**, 205.
⁸ Hansen, H E, et al, *Proceedings of the European Dialysis and Transplant Association*. London, Pitman Medical, 1977.

Endometrial assessment

SIR,—We have profound reservations about the conclusions drawn by Dr J D Hutton and his colleagues (15 April, p 947). Endometrial cytology is notoriously difficult to assess, and whereas most experienced cytologists would be happy to differentiate between normal endometrial cells and the cells of adenocarcinoma this would not apply to the subtle changes described in cystic hyperplasia and adenomatous hyperplasia. The degree of experience required to grade these changes is considerable and could be provided only in a few centres. One can easily understand these problems, as pathologists may have difficulty in differentiating between the various hyperplasias, and they have much more tissue to examine.

The endometrial cell sampler may have a limited place as a screening procedure in postmenopausal women before they are given oestrogen therapy. In this group of patients satisfactory endometrium for histological examination is obtained in only about 12% of cases, whether the endometrium is obtained by dilatation and curettage¹ or by Vabra aspiration.²

They also comment that the endometrial cell sampler is almost painless in comparison with the Vabra. Although accepting that the Vabra may be a little more painful, it is probably not significantly so. In a series of 348 Vabra aspirations performed at either Dulwich Hospital or the Birmingham and Midland Hospital for Women, 46 (13%) were painless, 267 (77%) had minimal or moderate pain, and only 35 (10%) had severe pain. Although not strictly comparable, these results differ very little from Dr Hutton's series.

We would therefore urge caution before the

endometrial cell sampler is used in the monitoring of postmenopausal patients on oestrogen therapy.

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- ¹ McBride, J M, *Journal of Obstetrics and Gynaecology of the British Commonwealth*, 1954, **61**, 691.
² Sturdee, D W, et al, *British Medical Journal*, in press.

Demeclocycline in congestive cardiac failure

SIR,—Dr D Zegers de Beyl and colleagues (25 March, p 760) demonstrated increased urine volume and sodium excretion with the use of demeclocycline in congestive cardiac failure intractable to conventional diuretics. Their explanation for this diuresis, based on experimental studies, suggests inhibition of antidiuretic hormone activity. Their data show a fall in urine osmolality commensurate with increasing urine volume, but urine osmolality remained hypertonic so that free water excretion was not apparently increased.

In congestive cardiac failure natriuresis from demeclocycline may be striking, even when urinary diluting capacity is inhibited by simultaneous "loop" diuretic administration, suggesting that natriuresis may be independent of free water excretion (see figure). Frusemide probably acts by blocking active chloride reabsorption in the thick ascending limb of the loop of Henle,² simultaneously preventing free water formation and passive sodium reabsorption at their site. Metolazone blocks active sodium transport in the distal tubule. With combined use of frusemide and metolazone in the case shown in the figure, urine volume was maintained between 2 and 3 litres per day, presumably by inhibiting sodium reabsorption in the loop of Henle and the

distal tubule respectively. The addition of demeclocycline to these diuretics produced a sustained rise in urine volume, and a considerable natriuresis with associated fall in body weight. A proximal site of action for demeclocycline may be speculated on.

The 1200 mg starting dose of demeclocycline used by Dr Zegers de Beyl may be excessive, as in our patient, a 60-year-old man with congestive heart failure, resistant oedema, and hyponatraemia. Sodium depletion resulted and was accompanied by a further fall in serum sodium concentration. Urine osmolality rose slightly during natriuresis, indicating that this was predominantly a solute diuresis. We now employ a starting dose of 150 mg of demeclocycline per day, when conventional diuretics are simultaneously given, and increase the dose by 150 mg every fifth day. This regimen has proved a satisfactory adjunct to diuretic therapy in intractable congestive heart failure.

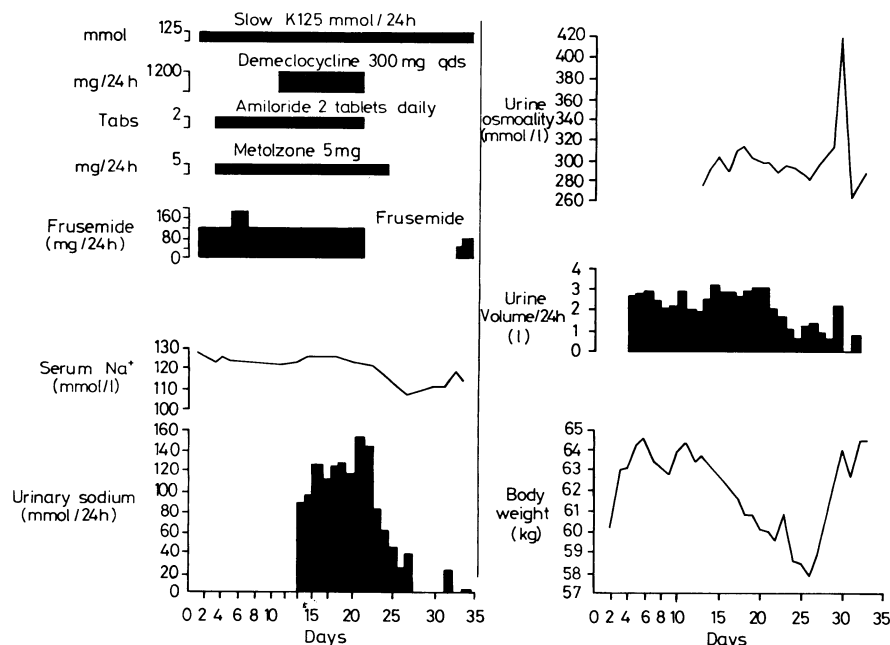
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- ¹ Burg, M B, and Green, W, *American Journal of Physiology*, 1973, **224**, 659.

Aortography in infantile coarctation

SIR,—Adequate demonstration of the hypoplastic segment of aortic arch in infants with preductile coarctation and intraventricular septal defect frequently requires arteriotomy, with its inherent risk to subsequent growth of that limb and other complications.

The use of a balloon angiocatheter floated anterogradely from the pulmonary artery through the patent ductus arteriosus into the aorta permits the affected segment to be easily demonstrated. After inflating the balloon with carbon dioxide or dilute contrast medium so as to completely occlude the descending aorta contrast is immediately injected into the aorta proximal to the balloon and retrograde filling of the aortic arch permits angiograms of high quality to be obtained. No adverse effect has



Conversion: SI to traditional units—Sodium: 1 mmol = 1 mEq. Osmolality: 1 mmol = 1 mosmol.