

patients with severe depressions, and the expectation is that those patients with elevated 2-7 patterns will show more antidepressant responses to lithium than those with lower 2-7 patterns, our findings suggest that obsessional thinking might be as important as depression as a discriminator variable of antidepressant responses to lithium. For example, when scale 7 was used alone, our results approximated the 2-7 hit rate found by House and Martin (74% v 80%, respectively) for the responders, suggesting that response to lithium is almost equally dependent on high scores on obsessional thinking almost as much as on depression.

These suggestions from several studies seem worthy of further investigation, given the interest being taken in attempts to find patient subgroups and potential responders prior to the weeks of treatment usually required to evaluate response or non-response to psychoactive drugs.

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Nebulised salbutamol in life-threatening asthma

SIR,—I was pleased to read that Dr P Bloomfield and others (31 March, p 848) were able to confirm our findings¹ that nebulised salbutamol was as effective as intravenous salbutamol in the treatment of acute asthma and was free of the side effects associated with the intravenous route. However, it was disappointing to find that they used intermittent positive-pressure respiration (IPPR) from a respirator in delivering the nebulised drug and by implication advocate this form of therapy.

It is 23 years since Leslie *et al*² showed there to be no advantage in using IPPR in nebuliser therapy and since then there have been numerous reports confirming this finding.³⁻⁶ An editorial in *Chest*⁷ states, "Not a single well designed study has shown convincingly that a bronchodilator or any other drug delivered by this method [IPPR] is more effective than inhalation of the same aerosol delivered by a powered or hand held bulb nebuliser." Indeed, a recent study has shown that in patients with chronic bronchitis 32% less aerosol was deposited in the lungs with IPPR than during quiet breathing.⁸ Unfortunately, there are still many doctors who seem to think that without a mechanical respirator they cannot give their patients the full benefit of nebuliser therapy. It is unfortunate that papers such as that by Dr Bloomfield and his colleagues tend to confirm this erroneous view, and the position is not helped by the fact that the manufacturers of salbutamol refer to their product as "respirator solution." How can we get across the message that respirators for nebuliser therapy are quite unnecessary? They are much more costly and difficult to maintain than a simple £1.0 semi-disposable nebuliser. Surely this is one area where we can move away from

high technology to something simpler, less frightening, and at least as effective.

We advocate that the dose (5-10 mg of salbutamol) be diluted in 10 ml of saline or water so that delivery is prolonged over a 40-minute period. This has the merit that the initial portion of the drug will be having a bronchodilator effect by the time the last portion is being inhaled. This last portion is thus able to reach parts that the initial drug was not able to reach.

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New approach to treatment of recent stroke?

SIR,—I am afraid Mr D R Gifford (2 June, p 1491) has missed the point. At no stage in my letter (12 May, p 1283) did I indicate that I believed the two patients described in the manufacturer's literature had been part of Dr A K Admani's double-blind trial. What I did say, on the basis of the same literature, was that these patients "would not have qualified for the trial in the first place." Why then choose them, as examples of the alleged efficacy of the drug, rather than trial patients?

Mr Gifford's point about the date of printing of the brochure is equally irrelevant. If later criticism (10 February, p 412) of the trial is accepted by his company (and they have not attempted to answer these criticisms) why not subsequently withdraw the promotional literature, even if it is already printed?

The ethics of this particular case are now being assessed by the Association of the British Pharmaceutical Industry, and I await their comments with interest.

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Antibiotic-induced interstitial nephritis?

SIR,—I was interested to read the short report by Squadron Leader D Saltissi and others (5 May, p 1182) concerning antibiotic-induced interstitial nephritis as the patient they describe was under my care during the first two episodes of renal failure.

The patient originally had a cystoscopy as an outpatient and returned home. His symptoms thereafter were of septicaemia rather than drug reaction, but renal biopsy showed acute interstitial nephritis and so I treated him with high doses of steroids. One month later he was admitted for elective prostatectomy but developed fever, and *Escherichia coli* was grown on urine culture. He was treated with gentamicin but the serum creatinine concentration was not measured until several days later, when it was found to be 557 $\mu\text{mol/l}$ (6.3 mg/100 ml). During this time the patient was symptomless and had a good urinary output.

Repeat biopsy showed interstitial nephritis and I considered the possibility of this being due to gentamicin. However, the histopathologist was adamant that the biopsy showed resolving interstitial nephritis by comparison with the first biopsy one month earlier and did not show convincing evidence of new interstitial nephritis. As the patient had received normal doses of gentamicin one month after suffering acute renal failure it is very likely that toxic levels of gentamicin occurred despite the implication in the report that serum concentrations were kept within recommended limits, which they were not.

I was eager to report this as the first case of gentamicin-induced interstitial nephritis but concluded that the evidence was too weak and that the alternative explanation of gentamicin nephrotoxicity in a damaged kidney could not be excluded. The third episode of renal failure is attributed to co-trimoxazole on very flimsy grounds—one wonders at the curious reluctance of the patient even to admit that he was taking it.

This is an interesting case of recurrent renal failure but the evidence does not merit the conclusion that each episode was caused by antibiotic-induced interstitial nephritis, and in the case of gentamicin the actual evidence is against it.

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Treatment of tinnitus

SIR,—May I add the following practical point to your leading article on tinnitus (2 June, p 1445)? Tinnitus is a well-recognised feature of aspirin overdose, but may occur as the sole complaint at low dosages in susceptible individuals. Patients on a daily aspirin dose of only four tablets (1.2 g) may have troublesome tinnitus, which responds to withdrawal of the drug. In view of the widespread self-medication with aspirin-containing proprietary medicines it seems wise to exclude this ubiquitous drug as a cause of tinnitus.

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Dialysis and transplantation in young children

SIR,—In your recent leading article "Dialysis and transplantation in young children" (21 April, p 1033) you mentioned that the number of those treated is significantly less than the estimated requirement (0.7 v 1.3 per million). Similarly, "by the end of 1977 of a total of 288 children who had ever been treated in Britain only five had been aged under 5 at the start." These figures reflect the many problems encountered with the management of these patients, especially the very young ones, and the inability of inexperienced centres to cope with these problems.

The introduction of continuous ambulatory peritoneal dialysis (CAPD)¹ provides an alternative treatment that has many advantages and can be easily applied to children, even the very young. It is less traumatic, does not require a machine, allows more independence and an almost free diet, and promotes home dialysis.

We have recently treated with CAPD four children for periods of 3 to 11 (average 6)

months. Three of them had had unsuccessful kidney transplants before CAPD and the fourth, a 3-year old, had Wilms's tumours. Although our experience is still too short to allow us more generalised conclusions, we are convinced that the availability of CAPD increases the therapeutic armamentarium in the management of children with end-stage renal disease.

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¹ Oreopoulos, D G, *Dialysis and Transplantation*, 1979, 8, 460.

History of an improvement

SIR,—I was interested to read Dr C J Levy's letter "History of an improvement" (26 May, p 1426).

In 1976 the Coventry anaesthetic department decided that all operating theatres in the Coventry area should be equipped with anaesthetic gas scavenging facilities, and this has now been done. When the work started there were not many other such systems from whose designers we could gain experience. Not surprisingly, we had several problems initially; but thanks to a very helpful area works department, some fine work by the hospital engineers, and useful constructive criticism by members of the anaesthetic department we overcame them. With the systems now in daily use the improvement in working conditions is commented on by all who have to work in the operating suites. We hope that there may also be more successful pregnancies among female operating theatre staff than there were before the scavenging systems were introduced.

In summary, I fully agree with Dr Levy that "complicated physics" demands the services of experts, and that engineering works that can affect patients must not be undertaken unilaterally. I strongly disagree with his Hutber's Law stating that "improvement means deterioration."

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Doctors and children's teeth

SIR,—We are much obliged to Dr A J S Waterston (2 June, p 1487) for drawing attention to fluoride tablets, but we think he may be giving a wrong impression by suggesting that a child should start on tablets at 2 years.

In accordance with Dr Benjamin Spock's suggestion, we advise that an expectant mother should take them in the last six months of pregnancy and the child from birth up to the early teens. An American dentist has demonstrated that dental caries can be almost entirely prevented by this method.¹

Taking tablets does not restrict their use to the most dedicated parents. For some 20 years Austria has had a nationwide fluoride tablet distribution scheme, which has resulted in the children in the 6-14 age group having just half as many teeth in need of treatment as children

in Britain. In this country Birmingham has achieved the same success through having a very efficient water fluoridation scheme since 1964.

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¹ Glenn, F B, *Journal of Dentistry for Children*, 1979, 46, 17.

Cimetidine for hypertrophic prostate?

SIR,—The antiandrogenic effect of cimetidine has been demonstrated recently in both animal and human studies.^{1,2} In the former atrophy of the prostate has also been shown. One wonders if there is any place for the use of the product in benign hypertrophy of the prostate in man. The age at which it would be used would give little concern about reduction in sperm count.

We do not as yet know enough about the long-term use of cimetidine, or the optimal dosage for this type of effect, but it would be interesting to know if anyone had considered the feasibility of such a study.

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¹ Winters, S J, *et al*, *Gastroenterology*, 1979, 76, 504.

² Van Thiel, D H, *et al*, *New England Journal of Medicine*, 1979, 300, 1012.

The dilated upper urinary tract

SIR,—Your leading article on this subject (26 May, p 1382) was a timely focus on a clinical problem of increasing importance to urologists. It was unfortunate therefore that it contained several inaccuracies; we hope you will afford us the courtesy to correct these and update your account.

Firstly, it was stated that "the Manchester group believe that obstructed and non-obstructed dilated systems can be distinguished by comparing renograms in the dehydrated and hydrated states." Nothing could be further from the truth. What the diuresis renogram compares is renography in the normally hydrated patient with that performed during a brisk frusemide-induced diuresis, which increases the urine flow rate across the site of suspected obstruction to 10 ml/min or more—a situation similar to that artificially induced during urodynamic perfusion studies but without the coincidental invasion. We ourselves have stressed the pitfalls associated with dehydration renography, which can produce an obstructive pattern even in normal subjects.¹

Secondly, it is stated that "others who have compared the Manchester method with dynamic studies have found that even renography on hydrated patients can overdiagnose obstruction in those with greatly dilated upper tracts and underdiagnose it in those with early obstruction but minimal dilatation." A 1975 reference is given in support of this statement² yet our technique was first reported in 1978.³ To our knowledge no one has yet compared the technique with perfusion studies (although our own current work in this context shows good correlation). Your comments surely refer to standard, unmodified renography and describe the very reason for the development of our technique, which overcomes these deficiencies.

Thirdly, you state that the accuracy of the procedure has been compared only with operative findings. Twelve months ago we reported the results of a further study correlating the diuresis renogram with objective morphological changes in the renal pelvis of patients with idiopathic hydronephrosis removed at Anderson-Hynes pyeloplasty and examined by light and electron microscopy.⁴ Of 26 examinations, there was accurate correlation between our functional dynamic isotope procedure and the morphological changes in 24 and equivocal results in two, providing further evidence for the accuracy of the technique.

I trust you will record these important details so that any misconceptions may be corrected for the benefit of those clinicians wishing to continue using a simple, non-invasive, and accurate technique for the assessment of the dilated upper urinary tract while reserving more complex and invasive procedures for the small group of patients in whom the findings remain equivocal.

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² Whitaker, R H, *British Journal of Urology*, 1975, 47, 377.

³ O'Reilly, P H, *et al*, *British Journal of Urology*, 1978, 50, 76.

⁴ Lupton, E W, *et al*, *British Journal of Urology*, 1979, 51, 10.

Biochemical testing for acute medical emergencies

SIR,—To do as Drs B T Williams and R A Dixon (19 May, p 1313) suggest and have an external advisory service in clinical biochemistry would, as I see it, take away from consultant chemical pathologists their raison d'être. But my chemical colleagues need have no fear, for Drs Williams and Dixon are quite naive when they talk of the "pooled experience of acknowledged experts."

Firstly, this would mean that the two groups of acknowledged experts, clinicians and biochemists, would physically have to come together, and this they simply do not do. Over the past three years I can think of only one scientific meeting to which both groups have been invited. And on this occasion they were as different as chalk and cheese, with little in common. Secondly, it assumes that you can get experts to agree. For many years now international experts in clinical enzymology have been wrangling over what is the best temperature to assay enzymes and have still not come up with an agreed figure. What hope is there for agreement on what tests are best in a given clinical situation?

So as not to appear totally destructive, may I propose a solution to some of the problems highlighted in this paper and many others? It is formulated on the premise that, just as clinicians consider themselves experts in clinical medicine, biochemists should also consider themselves experts in clinical biochemistry. My proposal is that clinicians, when requiring the assistance of clinical biochemistry for their diagnosis, simply submit a request stating the clinical details or the differential