above, and to refer to dialysis and transplantation treatment as "extraordinary" is surely an unjustifiable judgment.

At a time when the referral rate to nephrologists clearly indicates that many patients are dying from end-stage renal failure without the benefit of proper assessment, the general medical profession should be clearly aware of the real benefits of renal replacement therapy.

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¹ UK Transplant Annual Report 1977-1978. Bristol, UK Transplant Service, 1978.

Drug treatment of psychiatric patients in general practice

SIR,—A recent survey by Dr Peter Tyrer (7 October, p 1008) of patients seen at his psychiatric outpatient clinic purported to show that many had been prescribed psychotropic drugs incorrectly by their general practitioners. In a subsequent letter (18 November, p 1433) Dr Tyrer confirms that general practitioners received "feedback" about their prescribing habits in the four years covered by his survey and this resulted in less incorrect prescribing during the second half.

As Dr Tyrer and his colleagues responded to psychiatric referrals from the same general practitioners for many years before he started his survey it would be interesting to learn what alteration they made in the contents of their letters to effect a significant change in general practitioner prescribing habits during the survey period. Perhaps he has demonstrated that the standard of general practitioner prescribing in any area alters in accordance with the quality of the advice given by the local specialists.

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SIR,—Dr Peter Tyrer (7 October, p 1008) states that "many general practitioners were unaware that their prescriptions [of antidepressants] were insufficient to produce true antidepressant effects" in his series. The leading article (16 September, p 783) on this topic suggests that plasma concentration might be more important than actual dosage, but even this is debatable. High plasma levels may be ineffectual.

It is a common occurrence to achieve a satisfactory clinical response with small doses of antidepressants. Those doctors who use small doses initially, with increments as required, usually confirm this finding. Such patients are not usually referred to a psychiatrist. On the other hand, if antidepressants are started routinely in large doses, unacceptable side effects may result in the patient's refusing to continue or seeking to place his confidence elsewhere.

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"Lecture Notes on Medical Statistics"

SIR,—I have just read the review (9 December, p 1631) of *Lecture Notes on Medical Statistics* by Aviva Petrie, and the letters by Aviva Petrie and Mr Ian Clarke (23 December, p 1783) and am appalled that your reviewer, although

claiming to be a consultant statistician, appears to have a very prejudiced view of the bread-and-butter methods of applied medical statistics.

The first half of his review appears to be a general criticism of the subject of medical statistics, but the criticisms he makes are unqualified and without rational foundation. For example, he states that small sample sizes are the bane of medical research. How can this statement be defended when a large part of the development of statistical theory in this century has provided solutions to many of the problems that small samples present? For example, the two sample *t* test is a valid test provided that the assumptions of equality of variance and normality are reasonable (the *t* test is, of course, robust to minor departures from normality). Non-parametric tests are valid when used with small samples and make no assumption about the form of the parent distribution.

Does your reviewer really believe that if a patient who survives is scored 1 and a patient who dies is scored 0, the mean of the scores implies that on average the patients are half-dead? Does he not realise that the average of these scores is the proportion of patients who survive? His criticisms of the book are equally absurd. I would be interested to know his specific problems with the example of the *t* test on pp 82-83. The sample sizes are indeed 12 and 13 patients; so what? Are these not the sort of sample sizes which require a *t* test?

On item 4 of Aviva Petrie's letter and the reply concerning whether or not to include Fisher's exact test in an elementary text of medical statistics, I agree with Aviva Petrie but accept that Ian Clarke is entitled to his opinion. The test is certainly very clumsy to perform without a table of logarithms of factorials. However, Clarke's reference to Swinscow¹ is unfortunate. The example used in Swinscow's otherwise good, if brief, book is bad because the decision to perform the test is made *because the results look extreme*.

Ian Clarke's reply to Aviva Petrie's letter gives some excuses and apologies for his wild criticisms but his final paragraph expresses an opinion, stated as a fact, that the book is an inappropriate text for its target audience—a statement with which many experienced medical statisticians would disagree.

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¹ Swinscow, T D V, *Statistics at Square One*. London, British Medical Association, 1976.

Reusing dialysers

SIR,—We are not sure why Dr J M Vandembroucke and his colleagues (18 November, p 1434) reuse the dialyser 10 times and not 15 or 20 times. Limiting factors such as financial gain, rupture rates, dialyser clearance, increasing morbidity, patient acceptance, and nurse and technician times need active consideration before reaching an arbitrary set figure. They do not mention whether they reuse the blood lines and heparin administration sets. In 1975 we described reuse of the Gambro-Lundia dialyser inclusive of blood lines using an automatic rinsing device,¹ which has been further automated, now requiring 15 minutes of rinsing time, and is commercially available. In our experience, considering the labour and time involved, the financial gain achieved in reusing the dialyser more than six times is

negligible. If the blood lines are not reused and the dialyser is reused up to 10 times the cost per dialysis turns out to be more when compared with a dialyser reused up to six times inclusive of blood lines (see table).

Cost comparison of dialyser reuse (Dialyser: Gambro Lundia 1.36 m²: £18.50. Blood lines: Gambro; £3.55)

Reuse	Cost of reuse including blood lines (£)	Cost of reuse exclusive of blood lines (£)
6th	3.67	6.63
7th	3.15	6.19
8th	2.75	5.86
9th	2.45	5.60
10th	2.20	5.40

Finally, we confirm their results concerning pyrogenic reactions and septicaemia but emphasise that the technique of dialyser reuse must be practised only by skilled staff, preferably using an automated dialyser rinsing device, in order to achieve satisfactory results.

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¹ Ahmad, R, and Goldsmith, H J, *Dialysis and Transplantation*, 1975, 4, 29.

Tranquillisers and plasma prolactin

SIR,—The report by Dr S K Majumdar and others of a prolactin-lowering effect of chlor-methiazole (4 November, p 1266) also refers to the wide range of drugs which cause hyperprolactinaemia, including "tranquillisers such as phenothiazines and at least some of the benzodiazepines." While neuroleptic tranquiliser-induced hyperprolactinaemia is well recognised,¹ the effect of benzodiazepines on plasma prolactin is less clear and confusion can arise if the general term "tranquilliser" is used in this context. Patients presenting for investigation of amenorrhoea and hyperprolactinaemia are not infrequently found to be taking or to have recently taken a tranquilliser, most commonly diazepam. Horrobin² maintained that diazepam elevated prolactin secretion in animals but Noel *et al*³ found no increase in plasma prolactin over a 3-h period following intramuscular diazepam in human volunteers. We therefore decided that it was important to establish whether diazepam has any effect on plasma prolactin levels.

We studied basal plasma prolactin levels and the release of prolactin after administration of the dopamine antagonist metoclopramide in 10 women patients before and during treatment with 15 mg diazepam per day.⁴ The patients were selected from a group of hospital in-patients with anxiety symptoms. All were drug-free for at least one week before being studied. After an overnight fast an intravenous cannula was inserted and the patient allowed to settle for one hour to overcome the effects of stress on plasma prolactin levels. Three blood samples were then taken through the cannula at 10-min intervals and the mean of these three values taken as the basal plasma prolactin level. Metoclopramide 2.5 mg was injected intravenously via the cannula and blood samples for plasma prolactin estimation taken 10, 20, 30, 60, 90, and 120 min later. The patients were then started on 15 mg diazepam by mouth per day and the estimations of basal and stimulated prolactin levels

repeated after one week. Four of the patients were postmenopausal; the other six were studied during the same phase of the menstrual cycle on both occasions.

Basal plasma prolactin levels were normal in all patients before and during treatment with diazepam. Metoclopramide produced a marked increase in plasma prolactin levels maximal 30 min after injection. An analysis of variance of the log transforms of the plasma prolactin levels showed no significant difference before and during diazepam treatment. The overall trend was also constant at each time before and during diazepam treatment. It is therefore concluded that diazepam does not affect basal prolactin levels or the release of prolactin in response to the dopamine antagonist metoclopramide. This finding compares with earlier reports, which showed that growth hormone production, pituitary-adrenal function,⁵ and thyroid function⁶ are unaffected by diazepam.

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¹ Sachar, E J, *et al*, *Neuroregulators and Psychiatric Disorders*, p 242. New York, Oxford University Press, 1977.

² Horrobin, D F, *Prolactin: Physiology and Clinical Significance*, p 32. Lancaster, MTP, 1973.

³ Noel, G L, *et al*, *Journal of Clinical Endocrinology and Metabolism*, 1972, **35**, 840.

⁴ Judd, S J, Lazarus, L, and Smythe, G, *Journal of Clinical Endocrinology and Metabolism*, 1976, **43**, 313.

⁵ Havard, C W H, *et al*, *Journal of Endocrinology*, 1972, **52**, 79.

⁶ El-Hazmi, M A F, *Clinica Chimica Acta*, 1975, **63**, 211.

Drug compliance and the elderly patient

SIR,—Recent correspondence and criticism in the press of drugs prescribed for the elderly and the ways in which they are taken have not identified the two most important problems that certainly seem to affect the ways the elderly patients on my list take theirs.

Firstly, the current child-proof container seems also to be elderly-patient-proof as well. Arthritic thumbs make it quite impossible for a substantial minority of my elderly patients to remove the lids from such containers. My own recent investigations of this problem revealed at least six containers of which even I couldn't remove the lid.

Secondly, no more than 45% of 187 elderly patients on my list were able to read the label on the container giving the instructions. The small size of the label and the illegibility of the writing made the job of decipherment difficult. Instructing the chemist to label the containers clearly and in large writing has had no effect. Individual chemists whom I have directly approached tell me that the cost of typing labels would be prohibitive.

Surely the Department of Health and Social Security could recognise that these two problems exist and instruct all chemists to test whether the elderly recipient of the prescription can actually open the container in which the drug has been placed and can actually read the chemist's instructions. These two simple steps would be an excellent starting point in

ensuring compliance. At the moment the situation seems contrived to ensure the opposite.

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Pneumomediastinum in anorexia nervosa

SIR,—We read with interest the report by Drs Anita J Donley and T J Kemple (9 December, p 1604). Recently we saw a similar case in which vomiting seemed an important aetiological factor.

A 16-year-old schoolgirl was referred with primary amenorrhoea, weight loss to 30 kg (height 1.63 m), anorexia, and the psychiatric features of anorexia nervosa. When admitted she was found to have surgical emphysema of the neck, confirmed by chest x-ray, which also showed pneumomediastinum but no pneumothorax. This feature had not been noted at outpatient attendance six days before. A Gastrografin swallow radiograph was normal.

She admitted to feeling nauseated and full after small meals and to one episode of retching and vomiting, perhaps self-induced, following an excessive food intake shortly before she was first seen. In the absence of demonstrable lung disease we feel vomiting to have been the likely precipitating cause of the surgical emphysema and pneumomediastinum.

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Toilet paper and spread of infection

SIR,—Dr R E W Fisher writes (28 October, p 1233) that "tiny sheets of toilet paper are disgusting and insanitary." It is not quite clear whether he objects to the size or the substance.

Several years ago, while I was working in the Middle East, a Moslem medical student followed me into an Armenian general store and saw me buy some rolls of strange pink paper. "Please, Mr Professor, what are those things?" he asked. "Toilet paper," I said. "What are they for?" he inquired politely. Patiently and rather patronisingly I explained that the sheets were used for personal cleansing after defecation. He was shocked in the extreme. "But, Mr Professor," he said, "in Iran we don't even clean our plates by rubbing them with paper?"

Since that time I have never been quite certain that the West was ahead in hygiene. It is worth noting, however, that the East is not particularly famous for the absence of dysentery.

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Rapid diagnosis of *Mycoplasma pneumoniae* infection: a reminder

SIR,—A common problem both in general practice and in hospitals, especially at this time of the year, is infection with *Mycoplasma pneumoniae* (MP), particularly involving the chest. This year has seen a markedly increased number of reports of MP infections in the community.¹

Diagnosis is often made in retrospect by serology when the decision about antibiotics has already been taken, perhaps wrongly.

Tetracycline and erythromycin are known to shorten the MP illness but are not ideal antibiotics for other forms of bacterial pneumonia. Ampicillin or amoxycillin, although often effective against the latter, are useless against MP and in fact may precipitate an exanthem in this infection.²

Agglutinins are found in well over 50% of patients with MP pneumonia, but testing for them is not easily performed, especially in general practice. A cold agglutinin screening test (CAST) done at the bedside has been previously reported as detecting titres of greater than 64.³ In the past three weeks we have seen three patients with lobar pneumonia in whom this simple CAST was positive and allowed us immediately to start appropriate treatment for the MP infections that were later confirmed by serology. This test can most simply be done by adding a few drops of blood to the citrate in a commercial prothrombin tube (making a 50/50 mix) and then placing the tube in the ice tray in the freezing compartment of a refrigerator. After a few minutes the cooled tube is removed, tilted, and rotated, when obvious agglutination will be seen on the wall of the tube if the test is positive. This agglutination goes by warming the tube in one's hand. This test is also ideally suited to general practice, as few homes are without a freezing compartment and prothrombin tubes can be carried by the visiting doctor.

We feel that this test deserves more publicity as an aid to quickly identifying this common and treatable infection and thus reducing morbidity and possible hospital admissions.

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¹ Communicable Diseases Surveillance Centre (PHLS), 1978, unpublished.

² Cherry, J D, Hurwitz, E S, and Welliver, R C, *Journal of Pediatrics*, 1975, **87**, 369.

³ Griffin, J F, *Annals of Internal Medicine*, 1969, **70**, 701.

Intermittent ophthalmoplegia

SIR,—Drs W F Kelly and G F Joplin (2 December, p 1534) rightly stress the difficulty in the differential diagnosis of intermittent ophthalmoplegia and obviously in a short report are unable to supply all the clinical data to enable the reader to assess their statement that the patient was clinically euthyroid, although this appears very likely. However, the possibility that the patient was mildly hypothyroid without clinical signs (obviously closely considered by the writers) appears to remain.

This patient had had a previous partial thyroidectomy, has thyroid antibodies, and in addition a borderline high plasma thyrotrophin (TSH) concentration with an exaggerated response to thyrotrophin-releasing hormone. The "normal" levels of T3 and T4 recorded do not exclude the possibility of mild thyroid deficiency since the normal range is a statistical one and it is now accepted that tissue requirements for thyroid hormones vary from person to person. The findings given appear at least compatible with a patient whose thyroid function is compromised and whose T4 level is maintained at a level below the ideal for this patient but still (just) within the population normal range by an increase in TSH activity.

It is a cornerstone of the treatment of ophthalmic thyroid disease that the patient be