nating one ever coming to light is doubtful. A collaborative study with Professor Zuckerman to test his hypothesis would be interesting.

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¹ Beynon, P, *et al*, *Communicable Disease Report* (Public Health Laboratory Service), 1977, 77, 36.

Drug treatment of psychiatric patients in general practice

SIR,—Dr Peter Tyrer (7 October, p 1008) seems to have stimulated a raw nerve with his article on the prescribing of psychotropic drugs in general practice—at least so far as Dr D C Hogg (28 October, p 1228) is concerned. This rather unfortunate response needs to be countered.

Having worked in general practice I know just what Dr Hogg means when he refers to "a horde of chronically depressed and anxious patients who are a constant source of work and difficulty." Surely, however, this can in no sense justify sloppy prescribing habits, which he appears to try to defend. Indeed, if it is the work generated by patients in mental distress to which Dr Hogg objects, then I am surprised that he has chosen to be a general practitioner. He uses shortage of consultation time as one reason for not adopting prescribing patterns which he knows may be the best: all the more reason, therefore, to use scant resources carefully. More time spent listening to patients' troubles often obviates the need to spend extra time with the prescription pad. Of course, in the first instance this usually means greater effort on the doctor's part, for there are no short cuts to good medicine. In the long run, however, it is time well spent. I also find the comment that "innumerable patients... are managed quite well" very telling. Dr Hogg has missed Dr Tyrer's point—namely, that many patients are manifestly *not* managed well by their family doctors so far as psychotropic medication is concerned.

Not that I entirely agree with some of Dr Tyrer's points. For example, his comments about the dosage levels of certain drugs—namely, prescription of neuroleptics being "inadequate" at a level of less than 75 mg chlorpromazine daily or "excessive" at 400 mg of chlorpromazine (or equivalent) daily—are of limited value in the absence of clinical data. I am sure that he is aware of pharmacokinetic studies^{1,2} indicating the great variations in plasma levels of such drugs in individuals on identical dosage regimens, together with considerable differences in clinical response. Furthermore, the picture is made much more complicated by polypharmacy,³ a feature stressed by Dr Tyrer. Added to this is the fact that up to 50% of patients prescribed antidepressants by their general practitioners default within a matter of three weeks or so.⁴ In short, there is no such thing as an "acceptable" dosage range for any psychotropic drug—it depends how it is handled (physically and metabolically) by the patient concerned. In the final analysis, therefore, administration is (or should be) dictated by the clinical response of the patient, not by absolute dosage schedules. Secondly, he suggests that some tricyclic antidepressants had "perhaps" been prescribed for too long. There is evidence⁵ to suggest that in certain cases long-term administration of tricyclics may have a worthwhile prophylactic

effect. Again, without clinical details it is difficult to evaluate Dr Tyrer's case.

Nevertheless, these points are generously outweighed by the remainder of the paper. Dr Hogg accuses Dr Tyrer of "GP baiting" and being destructively critical. This is nonsense: Dr Tyrer draws our attention to inadequacies in the dissemination of impartial information about psychotropic drugs and also to possible shortcomings in the pharmacological training of doctors. None of us is so good at his job that he doesn't need to be reminded to be judicious and vigilant. Dr Hogg's approach is a recipe for mediocrity: if we do not strive for excellence in prescribing habits we shall surely not attain it.

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¹ Curry, S H, *Proceedings of the Royal Society of Medicine*, 1971, 64, 285.

² Sakalis, G, *et al*, *Clinical Pharmacology and Therapeutics*, 1972, 6, 931.

³ Braithwaite, R A, *et al*, *British Journal of Clinical Pharmacology*, 1976, suppl, p 29.

⁴ Johnson, D A W, *British Medical Journal*, 1973, 2, 18.

⁵ Mindham, R H S, *et al*, *Psychological Medicine*, 1973, 3, 5.

Menopausal therapy and endometrial pathology

SIR,—The letter of Professor I L Craft and colleagues (5 August, p 429) showing the protective effect of progestogens on the endometrium in postmenopausal women receiving oestrogen therapy is interesting, supporting our view that it is the duration of progestogen therapy which is important rather than the dose, or indeed the type of oestrogens.

We have updated the Dulwich Hospital's contribution to the paper by Sturdee and others (17 June, p 1575) and can now report the dose schedule and treatment of 34 patients with endometrial hyperplasia. These results are obtained from outpatient Vabra curettage specimens from a total of 530 patients receiving various regimens of hormone replacement therapy. It is not possible to give a precise incidence of individual hormone regimens because treatment was frequently modified during the course of therapy. However, at any time more than half our clinic patients have oestrogen implants and the remainder have oral therapy.

There were 29 patients with cystic glandular hyperplasia but only seven of these occurred in patients receiving any progestogen. Five patients had adenomatous hyperplasia and only one of these had been receiving progestogens. Twelve of the 16 cases which occurred with oestrogen implants were associated with failure to take the prescribed norethisterone each month. No hyperplasia has been found in more than 60 patients taking 5 mg norethisterone for 10 or 15 days with oral or implant oestrogen therapy. The endometrial pathology was reversed to normal by two courses of 15–21 days of 5 mg norethisterone in 28 of the 29 patients with cystic glandular hyperplasia and three of the five patients with adenomatous hyperplasia.

We have had no cases of endometrial carcinoma in patients whose hormone replacement therapy has been initiated and supervised from this clinic, but four cases have been referred from elsewhere. Three of the patients with adenocarcinoma had a history of from 10 to 30 years of continuous high-dose oestrogen ingestion with prolonged intermittent bleeding. The last patient had had

orthodox therapy of nine months of cyclical conjugated oestrogens (Premarin) followed by 50 mg oestrogen implants with five days of norethisterone. Hysterectomy following 15 mg of norethisterone for one month revealed moderate hyperplasia but no carcinoma in the specimen.

These four patients demonstrate well the problems of (a) making an accurate diagnosis of endometrial pathology in a patient taking oestrogen therapy; (b) self-medication without adequate supervision; and (c) unopposed oestrogen therapy without added progestogen, which has in our opinion been responsible for much of the anxiety concerning the apparent carcinogenicity of oestrogens.

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Paracetamol poisoning

SIR,—The letter from Dr A N Hamlyn (14 October, p 1089) commenting on our study of paracetamol overdose fatalities (16 September, p 832) concludes with the question of how 84 deaths before hospital admission can be excluded as being unlikely to have been caused by paracetamol.

As we observed, death due to paracetamol overdose is primarily caused by hepatic failure and occurs some days after ingestion of the overdose. The condition has an insidious onset and death does not occur rapidly but ensues after several days of progressive deterioration. We contend that in England and Wales it is unlikely that a patient with severe hepatic failure will not be admitted to hospital for medical attention. Of the 62 deaths directly attributable to an overdose of paracetamol alone, all but one occurred in hospital, the exception being a patient living alone who reported an overdose but did not receive medical attention and died at home.

The 84 patients referred to had taken at least one other substance in addition to paracetamol and had died at home or were dead on arrival at hospital. In 61 of these patients a fixed combination of paracetamol and the central analgesic dextropropoxyphene had been taken. An overdose of this combination causes early cardiorespiratory depression.¹

We therefore see no reason to modify our opinion that it was unlikely that paracetamol contributed to the deaths of these 84 patients.

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¹ Breckenridge, A, *Prescribers' Journal*, 1978, 18, 49.

Behçet's disease

SIR,—May I reply to the two interesting letters (30 September, p 952) provoked by your leading article (22 July, p 234) on Behçet's disease, in which reference was made to the studies of probands and their first-degree relatives which I have recently undertaken in Yorkshire¹? The form of the study owed much to previous family studies of the seronegative group of arthritides^{2–4} which had been suggested to form a genetically related group. This did not necessarily imply that all these diseases would subsequently all be found to be B27