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

associated—as is now becoming apparent. Indeed, the situation with regard to both B27 and B5 associations may vary in different parts of the world. In our patients with Behçet's triad, two out of four are B5 positive and one out of four is B27 positive. Of those with "definite" Behçet's disease (by the criteria of Mason and Barnes²), two out of 11 are B5 positive and only one out of 11 is B27 positive. The connection with the B5 antigen seems less strong than in Turkey but further work is necessary to clarify the position.

The criteria of Mason and Barnes are valuable in indicating some measure of diagnostic certainty. Patients with the triad of symptoms undoubtedly have Behçet's syndrome. But some patients satisfy their criteria at the "definite" level without the concurrence of mouth and genital ulceration which I would now regard as obligatory. Nor would I attach much importance to the presence or absence of a family history.

Thus the stated prevalence rate of 0.064 per 10 000 can be only an estimate of the disorder's prevalence: it may be a slight overestimate. In any event it contrasts markedly with the Japanese finding of 1 in 10 000.⁶

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¹ Chamberlain, M A, *Annals of the Rheumatic Diseases*, 1977, **36**, 491.

² Macrae, I, and Wright, V, *Annals of the Rheumatic Diseases*, 1973, **32**, 16.

³ Haslock, I, *The Arthritis Associated with Crohn's Disease: A Family Study*. MD thesis, University of Edinburgh.

⁴ Moll, J M H, *A Family Study of Psoriatic Arthritis*. DM thesis, University of Oxford.

⁵ Mason, R M, and Barnes, C G, *Annals of the Rheumatic Diseases*, 1969, **28**, 95.

⁶ Aoki, K, Fujioka, K, and Katsumata, H, *Japanese Journal of Clinical Ophthalmology*, 1971, **25**, 2239.

Burn hazard with cement

SIR,—The article by Mr M W Flowers (13 May, p 1250) contains some inaccurate and misleading statements about the lime content and caustic properties of Portland cement and concrete that require correction.

Mortar containing lime or hydraulic cement has been used by humans since ancient times and its characteristic of being an alkaline or caustic material has always been present. Some persons seem to be particularly sensitive to skin reactions with caustics while others have more tolerance to contact. Lime is a product of universal distribution, used for many purposes, and knowledge of its properties is widespread.

Portland cement is a hydraulic product, which means that the constituents will react with water and in so doing it becomes a hydrated material. Water reacts with the silicates, aluminates, and any free lime which is sometimes present in small quantities. As a result of this reaction with water calcium hydroxide (hydrated lime) is formed. This is responsible for giving a cement mortar or concrete its alkaline or caustic property. Hydrated quicklime is the same material as this reaction product.

There is no "free calcium oxide" in hydrated Portland cement concrete. When the concrete is fresh and plastic, calcium hydroxide is present and is the reason for "burns" when proper protective measures are not followed. It is only necessary for the worker to avoid contact on exposed skin for any prolonged length of time. The use of watertight boots, gloves, and clothing will prevent this contact, while any accidental splash landing on exposed skin must be promptly washed away.

After concrete loses its plasticity and becomes

hard any calcium hydroxide residing on the surface rapidly reacts with carbon dioxide from the atmosphere and becomes a relatively inert material that is no longer caustic. Hardened concrete will probably contain only 15% Portland cement and the remainder will be combined water, sand, and coarse aggregates (possibly limestone in this instance). Of the 15% cement in the concrete, about 25% of calcium hydroxide will ultimately be generated; this means that the maximum content of calcium hydroxide will be 15% × 25% = 3.75%, which is 10% of the value quoted in Mr Flowers's report. With reference to the statement in the article that hardened concrete contains "37% by weight of free calcium oxide," it must be assumed that this refers to the total calcium oxide in the concrete as reported in the customary manner for chemical constituents and therefore includes the calcium in the aggregate. Thus it does not mean that free calcium oxide actually exists in the concrete, but is simply the quantity of calcium, expressed as the oxide, in the entire mass.

Since some persons will use this material without regard to warnings or without knowledge of the product it would be most helpful if medical personnel could easily recognise the symptoms and provide the proper attention. It is common practice in the United States for manufacturers of Portland cement to place warning notices on sacked cement.

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Thyroid disease and pregnancy

SIR,—A paper on "Myxoedema in young women" that I published in 1963¹ would appear to be relevant to your leading article (7 October p 977). That paper described four women between 25 and 37 years old who showed good evidence of subhypothyroidism when seen 3–20 months after normal confinements.

Their thyroid glands could not be felt or were very small. They all returned to full health on thyroid treatment by mouth and became pregnant again between three months and five years later and had healthy babies. One developed lupus erythematosus, which responded well to treatment, but she died from a florid systemic form of it in 1976. The others have remained well on permanent oral thyroxine.

In April 1968 two other striking cases were seen within 10 days. Women 23 and 22 years old were referred by their general practitioners for investigation of suspected myxoedema. The clinical picture was frank but not florid, their thyroid glands were very small or impalpable, and test results confirmed the diagnosis—namely, low basal metabolic rate, high blood cholesterol concentration, delayed ankle and knee jerks, and low-voltage electrocardiograms. The first gave negative tests for thyroid antibodies. She had a son nearly 3 years old, the other had sons of 22 months and 8 months. Both returned to normal on oral thyroid and one had a baby girl after 14 months, the other a baby girl after two years.

In May 1977 Ginsberg and Walfish² reported from Toronto on "postpartum transient thyrotoxicosis with painless thyroiditis." Of their five patients (whose thyrotoxicosis resolved within four months), four later developed transient hypothyroidism and one of these developed permanent myxoedema. They

thought that painless subacute thyroiditis was probably the underlying condition in most of their patients. They referred to the 1976 paper by Amino *et al*³ from Osaka, which also described transient hypothyroidism occurring 3–6 months after delivery. In 1963 the BMA librarian could trace no references to myxoedema following pregnancy; and another search completed in August 1977 revealed only the three papers that I have mentioned.

The observation of this group of cases in Hartlepool has always left a suspicion that they represent the tip of an iceberg, as proved to be the case with Hashimoto's disease after 1956.⁴ To find other cases all women should be briefly seen six months after delivery to determine if there are any symptoms of subhypothyroidism (especially puffiness of the face) and to feel whether the thyroid gland is abnormally small, abnormally large, tender, or firm. In my opinion this condition is due to postpregnancy hyperinvolvement of the thyroid.

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¹ Cooke, R T, *Journal of the College of General Practitioners*, 1963, **6**, 626.

² Ginsberg, J, and Walfish, P G, *Lancet*, 1977, **1**, 1125.

³ Amino, N, *et al*, *Journal of Clinical Endocrinology and Metabolism*, 1976, **42**, 296.

⁴ Luxton, R W, and Cooke, R T, *Lancet*, 1956, **1**, 105.

Clinical information on x-ray and pathologist requests

SIR,—Dr B Golberg's Personal View on x-ray examinations (7 October, p 1017) includes a *cri de coeur* common to pathologists as well as radiologists. His solution is to include "imaging" as a subject in the undergraduate and postgraduate curriculum. May I suggest another?

Personal contact between radiologist and clinicians is an unrivalled opportunity for exchange of information. How often does Dr Golberg share his coffee break and lunch with junior clinical medical staff? Informal social exchange at this level may be worth more than many periods of formal education.

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Beta-blockade in subarachnoid haemorrhage

SIR,—In their study of patients with subarachnoid haemorrhage (SAH), Mr G Neil-Dwyer and others (7 October, p 990) have demonstrated that treatment with propranolol and phentolamine has a highly significant cardioprotective effect. The cardiac lesions seem to be related to excess catecholamines and beta-blockade therefore appears to be the crucial therapeutic factor. We have recently had a patient with SAH in whom treatment with oxprenolol failed to prevent ECG changes, which were so grossly abnormal that we were concerned that the patient might have additionally sustained a silent myocardial infarction.

The patient, a fit 62-year-old man, had been maintained on oxprenolol 80 mg thrice daily for hypertension, which was thus well controlled. However, shortly after his admission with SAH (confirmed by lumbar puncture) his blood pressure rose to levels of about 180/105 mm Hg and oxprenolol was increased to 80