increase we would need 20 million patients with 20 million controls.¹ Again this ignores all the additional practical problems of post-marketing surveillance.³

The salutary lesson with postmarketing surveillance is that 10 000 patients are too few to detect rare adverse reactions. Professor Rawlins, like many others, chose the number arbitrarily. That postmarketing studies "are likely to be worthwhile only if they enrol 10 times the number of patients in premarketing trials" is no argument. "The Grand Old Duke of York, he had 10 000 men" and he found, like we will in postmarketing surveillance, that they do not achieve what is expected of them.

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¹ Lewis JA. Post-marketing surveillance: how many patients? *Trends in Pharmacological Sciences* 1981; 2:93-4.

² Sachett DL, Haynes RB, Gent M, Taylor DW. Compliance. In: Inman WW, ed. *Monitoring for drug safety*. Lancaster: MTP Press Ltd, 1980: 427-38.

³ Castle WM, Nicholls JT, Downie CC. Problems of post-marketing surveillance. *Br J Clin Pharmacol* 1983;16:581-5.

Development of pituitary adenoma in women with hyperprolactinaemia

SIR,—Dr Antonio E Pontiroli and Dr Leopoldo Falsetti suggest that many women with hyperprolactinaemia may have pituitary microadenomas that may become radiologically apparent over a short period of time. We find it difficult to concur fully with their conclusions because only 69% of the patients had serial sector computed tomograms from the outset. The remaining patients had sellar tomography, with its well known limitations,¹ which were even apparent in the current study.

The concept of "radiological normality" persisted throughout the paper, often not clarifying which technique was being referred to; and in computed tomograms the characteristics of an important lesion were not defined^{2,3}—nor were the characteristics of the de novo lesions objectively described. Seeking out those patients who progressed from a normal to an abnormal computed tomogram during the study was difficult because of the presentation of the data but they appear to constitute only six patients or 9% of the total.

In addition we also think that Dr Pontiroli and Dr Falsetti have overstated the value of stimulatory and suppressive testing. We think that these are probably not adequate for predicting which patients with hyperprolactinaemia have a pituitary adenoma. This was apparent from their own data as more than half of the patients deemed to have a normal sella were non-responders in terms of the various tests used, and discrepancies were noted in six of 19 patients tested with more than one agent. Interpretation of the group with "normal sellas" was made even more difficult by the inclusion of seven patients with drug induced hyperprolactinaemia and an unquantified number of patients with polycystic ovaries. While we agree with evaluating the natural history of the hyperprolactinaemia in these latter two groups, we think that they should be categorised separately and not included with patients with idiopathic hyperprolactinaemia of presumptive hypothalamic pituitary origin for fear of distorting the data.

In conclusion, we think that the only valid method of monitoring the natural history of idiopathic hyperprolactinaemia is serial high resolution contrast enhanced fourth generation sector computed tomograms complementing serial prolactin measurements—and this is the approach we are adopting in our prospective study.

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¹ Burrow GN, Wortzman G, Newcastle NB. Microadenomas of the pituitary and abnormal sella tomograms in an unselected autopsy series. *N Engl J Med* 1981;304:156-8.

² Chames EF, Turski PA, LaMasters D. Regions of low density in the contrast enhanced pituitary gland: normal and pathological processes. *Radiology* 1982;144:109-13.

³ Valenta LJ, Sostrin RD, Eisenberg H. Diagnosis of pituitary tumors by hormone assays and computerized tomography. *Am J Med* 1982;72:861-73.

* * Dr Pontiroli and Dr Falsetti reply below.—
Ed, *BMJ*.

SIR,—The natural history of hyperprolactinaemia is not known¹: idiopathic hyperprolactinaemia and hyperprolactinaemia due to tumours might be two different entities or two consecutive steps of the same disease. Unfortunately, the value of both radiological tools² and provocative tests for prolactin release³ is disputed so we planned a prospective study in which women with hyperprolactinaemia were followed up for three years and were classified according to the radiological appearance at the end of the period.

After the letter by Dr Sheehan and Mr Sisam we have eliminated from our calculations women with polycystic ovaries (three cases) and with iatrogenic hyperprolactinaemia (seven cases), although at least one out of seven patients with allegedly iatrogenic hyperprolactinaemia turned out to have a tumour, which is noteworthy. Under basal conditions 26 patients had radiological evidence of tumour, and after three years 40 did (plus two cases with an empty sella). Only 16 had a normal sella after three years. The clinical and endocrine characteristics of women progressing to radiological evidence of tumour were different from those of women with a persistently normal sella. In all women with a tumour tests for prolactin release were abnormal from the beginning, and they were abnormal in about half of women with a normal sella.

Thus our conservative suggestion is that if a woman shows a normal prolactin response to provocative stimuli she is unlikely to have a pituitary prolactin secreting tumour. If she has an abnormal response to the stimuli she has to be followed up since she might develop a tumour within three years or even later. That we found so many new tumours may be due to the extensive and combined use of sellar tomography and computed tomograms.

We agree with Dr Sheehan and Mr Sisam that the best approach would include serial computed tomograms, serial prolactin measurements, and serial evaluation of the prolactin response to tests, and this we are doing. We were concerned about the reliability of sellar tomography, but we did not disregard this technique and we considered that changes in repeated examinations might be more useful than occasional examinations. This turned out to be the case, and when we compared the results obtained by sellar tomo-

graphy and by computed tomography we found good agreement. Only occasionally did computed tomography produce a result before sellar tomography.

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¹ Anonymous. Hyperprolactinaemia: pituitary tumour or not? *Lancet* 1980;i:517-9.

² Burrow GN, Wortzman G, Newcastle NB, Holgate RC, Kovacs K. Microadenomas of the pituitary and abnormal sella tomograms in an unselected autopsy series. *N Engl J Med* 1981;304:156-8.

³ Peters JR, Foord SM, Dieguez C, Rodriguez-Armas MD, Hall R, Scanlon MF. Microprolactinoma and functional hyperprolactinemia: two clinical entities or two phases of the same disease? In: Molinatti GM, ed. *A clinical problem: microprolactinoma*. Amsterdam: Excerpta Medica, 1982:21-34.

Hepatitis B and dialysis

SIR,—I am disturbed that Dr S Challah and others found that in the United Kingdom 87% of nephrologists and 85% of consultant physicians would deny dialysis to a 29 year old man who is hepatitis B positive (14 April, p 1119).

Epidemics of hepatitis B occurred when dialysis was new. Since then the technology of dialysis and understanding of the virology of hepatitis B have both improved. Today hepatitis carriers are easy to identify, and vaccination may provide some protection. The use of disposable dialysers and closed dialysis circuits greatly reduces the risk of cross infection. Dialysis may be confined to designated areas where only antigen or antibody positive patients (and perhaps staff) are admitted. Here all specimens may be labelled "high risk." In one unit of which I have experience, these precautions prevented the spread of hepatitis despite the continued dialysis of potentially infectious patients.¹

Associated factors such as drug addiction may render a patient unsuitable for dialysis, but should the combination of hepatitis B antigenaemia and chronic renal failure be a death sentence?

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¹ Ostrower VS, Litschitz MD, Craven PC, Williams DM. Successful control of hepatitis B surface antigenaemia in a dialysis unit without geographic or machine isolation. *Infect Control* 1981;2:101-4.

Staining of the bath by dithranol

SIR,—Minerva's comments on staining of the bath by dithranol (24 March, p 940) prompt us to share our experience.

Dithranol ointments are washed off the skin using soap but they retain their greasy characteristics. They are deposited on the bath surround, where the dithranol oxidises to produce anthraquinone dyes that stain the surface. Dithranol creams are made as a water miscible oil in water emulsion which is homogeneously distributed in the bath water and washed away as the bath is drained. We have had no cases of staining of the bath by dithranol cream up to a concentration of 0.5%. A 1% cream caused staining of the bath in half of our patients given 30 minute short contact treatment. Staining is less likely if the bath is cleaned immediately after use.

The only suitable method of removing dithranol stains is to gradually bleach out the