surprising that Gustavsson *et al* have found that omeprazole in doses of 20-60 mg a day is highly effective in healing duodenal ulcers.¹

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¹ Gustavsson S, Adami H, Loof L, Nybers A, Nyren O. Rapid healing of duodenal ulcers with omeprazole: double-blind dose-comparative trial. *Lancet* 1983; ii:124-5.

Parathyroid hormone and 25-hydroxyvitamin D concentrations in the elderly

SIR,—The conclusions drawn by Ms M M Petersen and others (20 August, p 521) are invalid, principally because the authors did not adequately define the renal function of their patients other than in a simplistic manner.

In the elderly, who often have a reduced muscle mass, plasma creatinine concentrations may be normal or minimally raised in the presence of a major reduction in glomerular filtration rate. It is unfortunately necessary, when dealing with any age group, but particularly the elderly, to measure creatinine clearance so as to avoid this well recognised pitfall, and this was done in one study.¹ Thus, in the elderly the skeletal muscle mass may be reduced to one quarter of normal, so the plasma creatinine concentration will be disproportionately low and may even be in the normal range despite the presence of advanced renal failure. Also, many workers have shown that in the elderly there is an age dependent reduction in glomerular filtration rate, and it is thus imperative not to assume that renal function is normal because of normal serum creatinine concentrations. Even in the so called normal elderly group (mean age 75.1 years) of Ms Petersen and her colleagues parathyroid hormone concentrations were lower than in either of the much older groups of patients (mean ages 80.9 and 83.3 years), perhaps supporting my contentions.

I would recommend therefore that Ms Petersen and colleagues repeat their study with 24 hour urine creatine clearances, and then perhaps more meaningful results will be obtained. Perhaps they will even agree with my observations.

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¹ Berlyne GM, Ben Ari J, Kushelovsky A. The aetiology of senile osteoporosis; secondary hyperparathyroidism due to renal failure. *Q J Med* 1975;44: 505-21.

* * We sent a copy of this letter to the authors, who reply below.—ED, *BMJ*.

SIR,—Those of us who spend our lives working with the elderly are well aware of the pitfalls in defining renal function in terms of serum creatinine concentrations.¹ As we explained in our paper, that is why "impaired renal

function" was defined primarily by a raised blood urea concentration. In elderly patients such as we studied, blood urea values are highly correlated with glomerular filtration rate measured by a radioactive chromium labelled edetic acid technique.² Estimates of renal function which rely on urine collections are most unsatisfactory in elderly subjects; this is presumably the reason why Dr Berlyne and others could measure creatinine clearance in only nine of the 16 old people whom they studied.³

The correlation between circulating immunoreactive parathyroid concentrations and age which they reported was very strong ($r=0.92$), though based on only 26 subjects. We found a rather weak correlation of immunoreactive parathyroid hormone with age in our study of 119 subjects; as we state, circulating immunoreactive parathyroid hormone concentrations in our normal old subjects were lower than in normal young adults and were raised only in elderly inpatients (with or without "impaired renal function"). These contradictions cannot be explained away on the basis of age-related changes in body composition or renal function.

Our study showed what it was designed to detect—namely, an interrelation between circulating immunoreactive parathyroid hormone and 25-hydroxyvitamin D concentrations in sick and normal elderly people. Had we wished to test the hypothesis that age-related decline in renal function leads to increasing secretion of immunoreactive parathyroid hormone, we would have measured biologically active parathyroid hormone (not a portion of the molecule cleared by glomerular filtration) and glomerular filtration rate (using radiolabelled edetic acid, not urine collections) in an adequate number of normal subjects right across the adult age range. The study by Dr Berlyne and others³ fulfils none of these criteria.

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¹ Petersen MM, Hall MRP, Briggs RS. Blood urea, serum creatinine and anthropometry in the elderly. *Clin Sci* 1983;65:13P.

² Denham MJ, Hodgkinson HM, Fisher M. Glomerular filtration rate in sick elderly inpatients. *Age Ageing* 1975;4:32-6.

³ Berlyne GM, Ben Ari J, Kushelovsky A. The aetiology of senile osteoporosis: secondary hyperparathyroidism due to renal failure. *Q J Med* 1975; 44:505-21.

Standardisation of oral anticoagulant treatment

SIR,—In his valuable and timely review (8 October, p 1000) Dr N K Shinton indicates that changing from the established British ratios to the international normalised ratios would present little disturbance as the values are so close.

The data on the international normalised ratios corresponding to British ratios provided by Dr Shinton were based on a preliminary calibration performed in this laboratory. Results with the international reference preparation were correlated with those of Manchester comparative reagent, the routine reagent in over 90% of British hospitals. The complete data from this calibration show that the agreement between Manchester reagent

and the international reference preparation is in fact even closer, as the accompanying table shows. Within the therapeutic range of 2.0 to

Comparison of British ratios and international normalised ratios

Clotting time (s)	British ratio	International normalised ratio
24.0	2.0	2.0
25.0	2.1	2.1
26.0	2.2	2.2
27.0	2.2	2.2
28.0	2.3	2.3
29.0	2.4	2.4
30.0	2.5	2.5
31.0	2.6	2.6
32.0	2.7	2.7
33.0	2.8	2.8
34.5	2.9	2.9
36.0	3.0	3.0
38.0	3.2	3.2
40.0	3.3	3.3
44.0	3.7	3.7
47.0	4.0	3.95
50-60	4.2-5.0	4.15-4.9

*Recommendation of British Anticoagulant Panel.³

4.0 ratio advocated by the British system for anticoagulant control, these values and international normalised ratios are interchangeable. Clinicians at home and abroad may therefore apply international normalised ratio to their patients stabilised on oral anticoagulants with the confidence in safety and effectiveness of this range derived from cumulative clinical experience and therapeutic trials.^{1,2}

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¹ Taberner DA, Pollar L, Burslem RW, Jones JB. Oral anticoagulants controlled by the British comparative thromboplastin versus low dose heparin prophylaxis of deep vein thrombosis. *Br Med J* 1978;i:272-4.

² Hull R, Hirsh J, Jay R, *et al*. Different intensities of oral anticoagulation therapy in the treatment of proximal vein thrombosis. *N Engl J Med* 1982;307: 1676-81.

³ Blackburn EK. Long term anticoagulation therapy. *Prescriber's Journal* 1977;17:73-4.

Substitution of Maloprim for dapsone

SIR,—We have recently seen two patients undergoing treatment for dermatitis herpetiformis in whom Maloprim was inappropriately substituted for dapsone. The antimalarial preparation Maloprim contains 12.5 mg of pyrimethamine as well as 100 mg of dapsone and is normally prescribed in a dose of one tablet a week. Pyrimethamine is a diaminopyrimidine with a half life of about four days. As the dose of dapsone required to control dermatitis herpetiformis may be up to 400 mg a day considerable overdoses of pyrimethamine may be given with the risk of severe megaloblastic anaemia.

There appear to be two reasons for the substitution taking place in our patients. Firstly, Maloprim appears in *Monthly Index of Medical Specialties* but dapsone does not because there are no proprietary brands of the pure drug. Secondly, the entry under dapsone in the *British National Formulary* relates only to the treatment of leprosy and makes no mention of dermatitis herpetiformis. Attention was drawn to the problem of substitution two years ago,¹ and one of our patients had been warned of this possibility as a result. We hope that further difficulties may be avoided by appropriate changes in the *British National*