by inclusion within the National Health Service. The Faculty fellows, members, and medical associates are all registered medical practitioners, who obtain a diploma of MFHOM or FFHOM as a postgraduate degree. Any other homoeopathic qualification in the UK is not a medical qualification, and anyone who advertises as a homoeopath is a lay practitioner.

We are aware that there is still a great deal of antipathy and opposition to homoeopathy in this country in certain medical quarters, but I would appeal to those who hold this view to support those of us who sincerely believe in the value of homoeopathy, used with judgment and skill together with a sound knowledge of clinical medicine and therapeutics. Failure to do so will not cause homoeopathy to wither away—it will only encourage more lay practice, to which patients will turn if there are not enough qualified doctors practising homoeopathy.

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24,25-Dihydroxycholecalciferol and calcium absorption in uraemia

SIR,—We were interested to read of the apparent lack of effect of 24,25-dihydroxy-vitamin D₃ (24,25(OH)₂D₃) on calcium absorption in uraemic patients reported by Drs J Szymendera and K Galus (25 November, p 1465), which contrasts with our own previously reported findings.¹

This contrast may reflect differences in the type of patient studied (our patients were anephric); in the dose and duration of treatment with 24,25(OH)₂D₃; or, as they suggest, in the method used to measure calcium absorption. Although the differences between tests for calcium absorption were clearly not critical in demonstrating effects of 1,25(OH)₂D₃ or 1 α -hydroxycholecalciferol, we have additional evidence that the effects of 24,25(OH)₂D₃ on calcium absorption differ from those of 1,25(OH)₂D₃. Using a low dose of carrier calcium (20 mg) for the ⁴⁵Ca tracer dose, we have noted little change in plasma ⁴⁵Ca curves in anephric patients given 24,25(OH)₂D₃, whereas large changes were seen after 1,25(OH)₂D₃ (Cochran *et al*, unpublished). From our inability to demonstrate effects of 24,25(OH)₂D₃ in this way, and the apparent increases in calcium absorption noted using the whole body counter,¹ we deduce that 24,25(OH)₂D₃ either increases intestinal calcium transport at distal sites in the gastrointestinal tract or affects its metabolism following absorption, but has little if any effect on duodenal calcium transport.

It seems possible that Drs Szymendera and Galus have additional information which might be helpful. In an earlier paper² Szymendera, using his double isotope technique, demonstrated that maximal rates of absorption occurred only 16 minutes after ingestion of the tracer dose. It seems reasonable to assume that the kinetics of calcium absorption at the time of its peak rate are particularly indicative of its absorption in the proximal gut. We would be interested to know if they have been able to calculate maximal rates of absorption from the data obtained in their series of uraemic patients,

and, if so, whether these rates changed as little as the fractional absorption in response to 24,25(OH)₂D₃. We have previously shown that the maximal rate of absorption changed more markedly in response to therapy than the fractional absorption,³ so the former variable should have the twin advantages of increased specificity and increased sensitivity in determining whether 24,25(OH)₂D₃ has any measurable effect on calcium absorption in the upper small intestine of uraemic patients.

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¹ Kanis, J A, *et al*, *British Medical Journal*, 1978, **1**, 1382.

² Szymendera, J, Heaney, R P, and Saville, P D, *Journal of Laboratory Clinical Medicine*, 1972, **79**, 570.

³ Reeve, J, Hesp, R, and Veall, N, *British Medical Journal*, 1974, **3**, 310.

* * * We sent a copy of this letter to the authors, whose reply is printed below.—Ed, *BMJ*.

SIR,—We appreciate Dr Kanis and others' comments. But we feel that the data presented in our report do not contrast with those they reported.¹ Our data simply provide evidence that 24,25-dihydroxycholecalciferol (24,25(OH)₂D₃) does not influence active calcium transport in the proximal jejunum. This is also their contention—they state in their letter that this agent has little if any effect on calcium absorption in the duodenum. It may be deduced from the apparent difference between the increased absorption shown by whole-body counter and the unchanged absorption shown by our double-isotope technique that 24,25(OH)₂D₃ increases intestinal calcium absorption at distal sites. But this contention needs straightforward evidence. The second possibility is that 24,25(OH)₂D₃ affects calcium accretion only; this effect might explain the increased retention of calcium tracer as well. The latter contention is in agreement with a recent report by Ornoy *et al*,² which presents evidence that 24,25(OH)₂D₃ is intimately associated with bone formation and mineralisation.

Concerning the relation of total and maximal absorption of calcium in the intestine, the data presented in the accompanying table show that maximal rates of absorption tended to increase with the increased total absorption, and vice versa. However, the changes were of about the same size, which is contrary to expectation. If the changes in the maximal rate of absorption were affected by treatment with 24,25(OH)₂D₃, one would expect that they would be many times greater than the increase in total absorption.³

In conclusion, we contend that differences in both the peak rate of absorption and the

percentage absorption represent natural variability and do not seem to be influenced by the treatment.

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¹ Kanis, J A, *et al*, *British Medical Journal*, 1978, **1**, 1382.

² Ornoy, A, *et al*, *Nature*, 1978, **276**, 517.

³ Reeve, J, Hesp, R, and Veall, N, *British Medical Journal*, 1974, **3**, 310.

1-alpha-hydroxy vitamin D₃ in primary hyperparathyroidism

SIR,—We have read with interest the paper from Dr D A Heath's group on the value of 1 α -hydroxy vitamin D₃ (1 α HCC) in the treatment of primary hyperparathyroidism before parathyroidectomy (17 February, p 450). While we agree on the need for careful monitoring of the serum calcium we would like to record our conclusion that the Birmingham experience may relate to patients with less severe bone problems than the group previously described by ourselves.¹

It is difficult to grade the severity of skeletal disease in primary hyperparathyroidism; but, in addition to the serum alkaline phosphatase concentration and the results of routine radiology, we believe that quantitative bone histology, serum 25-hydroxy vitamin D₃ concentration, radiocalcium absorption, ^{99m}Tc-diphosphonate retention, and even symptoms relating to musculoskeletal involvement, may be relevant indices, which also relate to the probability of severe postparathyroidectomy hypocalcaemia and related complications. Each of Dr Heath's bone disease groups of six patients contains at least one patient with a normal serum alkaline phosphatase concentration, and the highest concentration in the group not receiving 1 α HCC was only about three times normal; whereas six patients with primary hyperparathyroidism initially described by ourselves as having been treated by 1 α HCC had levels ranging from three to 12 times normal. In our experience the combination of severe osteitis fibrosa and a normal alkaline phosphatase concentration occurs only in the presence of marked magnesium deficiency. It is a pity that, with the exception of the serum calcium concentrations, the data for the Birmingham patients have been averaged as there must be real doubt about the true comparability of the two groups with bone disease.

It was not possible to judge the variation in the serum calcium from day to day before the administration of 1 α HCC in the Birmingham patients, but, from the experience of ourselves and others,² the fluctuations in five of the six patients after starting 1 α HCC could be accounted for by the spontaneous changes in the serum calcium which occur in this disease. The sixth patient, whose serum calcium concentration rose by 1.5 mmol/l (6 mg/100 ml) after starting on 2 μ g of 1 α HCC daily, is the first such report we have encountered—and we ourselves have experience of some 15 patients with primary hyperparathyroidism and bone disease managed in this fashion. It would have been of great value to have had further details of this particular case.

Calcium absorption in uraemic patients treated with 24,25-dihydroxycholecalciferol

Case No	Total absorption (% oral dose)		Maximal rate of absorption					
			Time (min)		% dose/min		μ mol Ca/min	
	Before	After	Before	After	Before	After	Before	After
1	8.25	8.24	22	22	0.0603	0.0726	3.00	3.50
2	23.07	24.28	13	16	0.2574	0.1681	12.75	8.25
3	12.34	7.55	36	86	0.1120	0.0410	5.50	2.00
4	5.72	14.34	155	74	0.0203	0.0573	1.00	2.75
5	14.06	3.80	46	175	0.1243	0.0142	6.25	0.75
6	9.76	28.19	23	15	0.0734	0.4990	3.75	24.50

Conversion: SI to traditional units—Calcium: 1 μ mol/min = 40 μ g/min.

We believe that the most dramatic effect of preoperative and postoperative 1 α HCC in primary hyperparathyroidism is in the management of those few patients with really severe bone disease whose postoperative management in previous times remained stormy over several months. We have been accustomed to seeing about one such patient per year at Glasgow Royal Infirmary and believe that at least five of our 15 patients mentioned above would have fallen in this category (all had serum alkaline phosphatase and parathyroid hormone levels (where measured) some 10 times higher than the upper limits of normal). Such patients may not be encountered in Birmingham but still unfortunately turn up in Glasgow.

A body of evidence now exists³⁻⁵ to suggest that vitamin D deficiency may play a role in the genesis of the bone disease in these severe cases. On the one hand the vitamin D deficiency may cause an increase in parathyroid hormone secretion, while on the other hand the primary hyperparathyroidism may cause an increased requirement for vitamin D, possibly through the increased renal turnover of 25-hydroxy vitamin D₃. On this basis one might anticipate some amelioration of the clinical problem by giving 1 α HCC before operation, and in a few cases we have indeed demonstrated some reduction in the serum parathyroid hormone level. In addition, the prophylaxis of paraesthesiae and tetany, even in the less severe cases, seems preferable to awaiting their postoperative appearance, and preoperative administration of 1 α HCC for three or four days, in addition to continuing it postoperatively for a similar period, usually achieves this aim as well as probably contributing to bone healing.

Our present treatment schedule for 1 α HCC administration in primary hyperparathyroidism varies with the severity of the bone disease—1 or 2 μ g daily for five to 10 days preoperatively followed by 1 or 2 μ g daily for five to 50 days postoperatively.

As Dr Heath's series demonstrates, one must monitor serum calcium daily to identify any idiosyncratic sensitivity to 1 α HCC. It would be a great pity if the occurrence of hypercalcaemia in the one patient were to deprive the group with severe bone disease of the potential benefits of this therapy.

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- ¹ Boyle, I T, *et al*, *Clinical Endocrinology*, 1977, 7, 215S.
- ² Nordin, B E C, *Metabolic Bone and Stone Disease*, p105, Edinburgh, Churchill Livingstone, 1973.
- ³ Woodhouse, N J Y, *et al*, *Lancet*, 1971, 11, 283.
- ⁴ Stanbury, S W, *Clinical Endocrinology and Metabolism*, 1972, 1, 239.
- ⁵ Mawer, E B, *et al*, *Clinical Science and Molecular Medicine*, 1975, 48, 349.

Diet, sunlight, and 25-hydroxy vitamin D

SIR,—We read with interest the article by Dr E M E Poskitt and others (27 January, p 221) in which they discuss possible mechanisms for physiological control of circulating 25-hydroxy vitamin D (25-OHD). Bhattacharya and De Luca¹ showed evidence of suppression of hepatic D₃-25-hydroxylase in the rat liver and Haddad *et al*² proposed the same mechanism in humans.

We have reported previously on the use of vitamin D supplements and ultraviolet light in old age.³⁻⁴ In 15 subjects on supplements there was, after one month of treatment, a strong negative correlation between the initial plasma 25-OHD levels and the change in this ($r = -0.484$). In 12 subjects treated with ultraviolet light for one month there was a

similar association between the two variables ($r = -0.589$).

We would suggest that this provides further evidence of product inhibition in the control of hepatic D₃-25-hydroxylase in humans. It should be noted that the regulatory system appears to operate only for physiological amounts of vitamin D. The toxic effects from large doses of vitamin D are well recognised.

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- ¹ Bhattacharya, M H, and De Luca, H F, *Journal of Biological Chemistry*, 1973, 248, 2969.
- ² Haddad, J F, and Stamp, T C B, *American Journal of Medicine*, 1974, 57, 57.
- ³ MacLennan, W J, and Hamilton, J C, *British Medical Journal*, 1977, 2, 859.
- ⁴ Snell, A P, MacLennan, W J, and Hamilton, J C, *Age and Ageing*, 1978, 7, 225.

Registers for the prevention of genetic disease

SIR,—We read your leading article (27 January, p 215) with interest, and share your concern about confidentiality of genetic registers and the apprehension about "authoritarian intervention in this area." You very aptly stressed the great importance of support for affected families to whom we are the harbingers of bad tidings, saying that our "Genetic counselling should be a humane and cost-effective way of preventing intractable disease."

In the area of Huntington's disease, we wish to point out that although no preventive measures are currently available a register of affected families should be maintained for both research and a service commitment. In our seven years' experience of conducting a Huntington's disease clinic we have found in the register an invaluable clinical tool in the diagnosis and management of this disorder. Your argument that "some heterozygotes may take no notice of genetic counselling: they tend to be defiant towards the disorder, often refusing to let it interfere with their lives or their procreation" takes no real account of the empathetic process of genetic counselling and belies your advocacy of support for these families, as well as being contrary to the principle of families' affliction with severe genetic disorders. There has been a growth of public and family concern in this field. The concept of cost-effectiveness should be viewed in terms of alleviation of human suffering and assisting families to cope constructively, rather than just reducing the prevalence of the disorder in the future.

A properly maintained register, we have found, not only assists in the diagnosis of the disease by clinicians: it also provides valuable data in the planning of management now and in the future. It has provided us with a view of the family network system, from which we can begin to plan to make full use of family resources by support for the ill members of the family. The marshalling of supportive resources in the nuclear and extended family network is an integral part of counselling services for Huntington's disease families.¹

We therefore support the establishment of genetic registers for Huntington's disease by specialised units, with built-in, stringent safe-

guards in confidentiality and accountability, for both research and service commitments.

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- ¹ Chiu, E, and Teltscher, B, *Medical Journal of Australia*, 1978, 2, 394.

Management of refractory oedema

SIR,—Dr J McCormack writes on the trick of combining a thiazide diuretic with a loop diuretic (10 February, p 412). I have also found this combination very useful (and effective in producing hypokalaemia).

Trials with combinations of diuretics made by Olesen and Sigurd have demonstrated the very impressive natriuresis and diuresis achieved when a small dose of bendrofluzide is added to frusemide and spironolactone, or bumetanide.^{1,2} For example, in patients with congestive heart failure given 3 g sodium chloride in their diet and a fluid intake of 1500 ml, bumetanide, 4 mg, and spironolactone, 100 mg, gave a natriuresis of 81 ± 13 mmol(mEq)/24 hours and a diuresis of 1628 ± 131 ml.² Doubling the dose of bumetanide did not increase diuresis. In contrast, combining bendrofluzide, 5 mg, increased natriuresis and diuresis significantly to 209 ± 50 mmol and 2533 ± 437 ml/24 h.

This effect is ascribed to loop diuretics supplying ample sodium at the distal sites of the nephron, inducing an accelerated reabsorption at these sites—which is effectively depressed by a thiazide.

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- ¹ Olesen, K H, and Sigurd, B, *Acta Medica Scandinavica*, 1971, 190, 233.
- ² Sigurd, B, *et al*, *American Heart Journal*, 1975, 89, 163.

Tuberculin testing

SIR,—Dr H G Calwell's observation (3 February, p 345) on the use of Heaf testing as an alternative to tine and Mantoux tests is noted with interest.

After 36 years' experience of a variety of tuberculin tests in chest clinics and hospital staff health departments (approximately 700 a year) I agree that the multiple puncture (Heaf test) is the method of choice. It is quick, painless, and easily administered even in struggling babies. If accurately used it is consistently reliable in its interpretation, differentiating clearly between non-specific (grade 1), post-BCG-positive, acquired immunity (grade 2), and possible occult infection.

The article by Drs J A Lunn and A J Johnson (3 June 1978, p 1451) and subsequent letters have indicated that the tine test produces false-negative results but have not clarified the reasons for this. In my experience the tines are often blunted at the tips and are not always at right angles to the base. Very firm pressure is therefore necessary to obtain adequate skin puncture. In a small series of 35 routine tuberculin tests on hospital staff, I used Heaf and tine tests on opposite arms. The comparative results were identical in every case. In some tests I purposely induced excessive bleeding from the tine punctures to exclude "washing out" the purified protein