So far as we are aware there are no reports on the poliovirus immunity of immigrants in the United Kingdom. Our results show that the children of immigrants in the Glasgow area do not constitute a health hazard with regard to poliomyelitis. This contrasts with reports from several other countries that children of immigrants predominate among the few residual cases of poliomyelitis, presumably because their parents may be less aware of the importance of immunisation than parents indigenous to the recipient, developed country.⁸⁻¹¹

The present poliovirus activity in the United Kingdom—12 cases so far during 1977¹²—underlines the danger of complacency, which is becoming widespread owing to the dramatic reduction in the incidence of paralytic poliomyelitis since the introduction of polio vaccination programmes. This and the fact that children commonly accompany their parents on inter-continental journeys increase the chance of non-immune travellers mixing with people from countries where poliomyelitis is still endemic; conversely, emigrants from such areas are flocking to countries of high industrial development.

Antibody surveys are a more reliable method of assessing immunity than either statistics of vaccine uptake or waiting for sporadic cases or outbreaks of paralytic poliomyelitis to signal a dangerous decline of immunity due to complacent under-vaccination or to technical flaws in the vaccination procedure. Our investigations again emphasise the continued need for polio vaccination in the first year of life and the importance of revaccination, irrespective of ethnic group, at school entry and leaving age, when children can be "administratively captured."

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Osteomalacic dialysis osteodystrophy: a trial of phosphate-enriched dialysis fluid

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Summary and conclusions

To assess whether phosphate depletion is an aetiological factor in osteomalacic dialysis osteodystrophy we undertook a prospective trial of phosphate-enriched dialysis fluid, in association with oral 1 α -hydroxycholecalciferol, for this condition. Thirty patients started the trial; of the 27 who completed more than 6 months' treatment, 14 had iliac crest bone biopsies at the beginning and end of the treatment period. Side effects included pruritus, stiffness, and increase in corneal and vascular calcification. Only one patient showed histological improvement of osteomalacia, and eight deteriorated; in seven the osteitis fibrosa worsened. Myopathy showed some improvement in four patients, but became worse in four.

This treatment does not seem to have a place in the routine management of non-hypophosphataemic patients on dialysis.

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Introduction

In Newcastle upon Tyne and several other centres an appreciable proportion of patients on regular haemodialysis develop an incapacitating type of bone disease characterised by bone pain and numerous fractures accompanied by proximal myopathy.^{1,2} Histological examination shows osteomalacia, with few active osteoblasts and little or no osteitis fibrosa. Serum concentrations of alkaline phosphatase and parathyroid hormone are often raised only slightly or not at all. This syndrome has failed to respond to treatment with calcium carbonate and phosphate binders,³ vitamin D₂ or dihydrotachysterol,³ 1 α -hydroxycholecalciferol,^{4,5} or 1-25-dihydroxycholecalciferol,⁶ or the withdrawal of hepatic-enzyme-inducing drugs. A similar syndrome is sometimes seen in hypophosphataemic osteomalacia.⁷⁻⁹ Some patients with hypophosphataemia and osteomalacia being treated with dialysis have responded to phosphate therapy,^{10,11} and it has been suggested that phosphate depletion may contribute to renal osteodystrophy.¹² We carried out a prospective trial of phosphate-enriched dialysis fluid in 30 patients for 6-12 months to see whether we could treat or prevent osteomalacia by improving phosphate balance.

Patients and methods

Thirty patients were entered in the trial, 15 men and 15 women, aged between 18 and 60 (mean 41) years. All had been on regular haemodialysis for more than 6 months, using Meltec Multipoint 1 m² dialysers and Lucas Mark II proportionating units, and dialysing 5-7 hours three times a week against a dialysate calcium of 1.6 mmol/l.

One patient received a renal transplant before completing the trial; 13 refused follow-up bone biopsy, or were considered unsuitable for this because of previous bleeding or anticoagulation treatment; two could not tolerate the treatment. The analysis refers to the 14 patients from whom full details were obtained.

No patient had had hypophosphataemia, either before or after dialysis, in the three months before the trial, though some had had it previously. Six patients had been taking aluminium hydroxide within six months of starting phosphate treatment; this had been withdrawn before the trial. At the beginning of the trial five patients were already taking 1 α -hydroxy vitamin D₃ (1 α -OHD₃); the remaining patients were given 1 α -OHD₃ within 6 weeks of starting phosphate. The dose was adjusted to avoid hypercalcaemia and ranged from 1 μ g daily to 1 μ g twice a week.

Phosphate was given by dripping a 0.21 molar solution of phosphate buffer containing Na₂HPO₄ and KH₂PO₄, pH 7.4, into the mixing chamber after the standard concentrate had been diluted. There were no problems of calcium phosphate precipitation. At first the dose was 30 drops a minute during dialysis, giving dialysate phosphate concentrations of 0.8–1.0 mmol/l. Owing to a high incidence of pruritus, this dose had to be reduced to 20–30 drops a minute, giving dialysis phosphate concentrations of 0.5–0.8 mmol/l.

Iliac crest bone biopsies and radiological skeletal surveys were carried out at the beginning and end of the trial where possible. We regularly monitored clinical progress, predialysis and postdialysis serum calcium and phosphate, and predialysis serum alkaline phosphatase, magnesium and parathyroid hormone. Detailed records of the degree of myopathy included the patient's assessment of himself and results of formal clinical testing; inability to rise unaided from the squatting position three times in rapid succession was the most sensitive formal test of myopathy. Complaints of bone pain and degree of disability arising from it were also noted. Pain in the feet during exercise was a frequent early symptom. Histological osteitis fibrosa was assessed on a scale of 0–5 according to the extent of marrow fibrosis, active osteoclasts, and woven bone formation; and osteomalacia was assessed on the amount of osteoid, the number of osteoid lamellae, and the calcification front.¹³

Results

The results of biochemical, clinical, radiological, and histological assessment are shown in the table.

Biochemical—At the start of the trial all patients had a raised serum phosphate concentration before dialysis and nine of them after it. During treatment the predialysis concentration rose in 10 of the 14 patients, five of whom had an appreciable rise (and one other a transient rise) in the postdialysis concentration also.

Seven patients showed a rise (and two others a transient rise) in serum alkaline phosphatase concentration, though the phosphate concentrations did not increase in all of them. In four of these seven patients, serum parathyroid hormone concentration rose appreciably, having initially been normal or only slightly raised in the 10 who had it measured.

Clinical—Myopathy was present in 13 patients at the start of the trial. Two (patients 1 and 5) improved dramatically and two others moderately, and four became worse.

Radiological—Skeletal surveys at the start of the trial showed unhealed fractures or Looser zones in seven patients. After the phosphate treatment one (patient 5) showed unequivocal healing; two (patients 1 and 10) showed some healing of rib fractures but developed new pelvic Looser zones; two developed new fractures; and two were unchanged. One patient had fractures that were already healing before the trial started, and continued to heal. Three of the six patients who had no fractures at the beginning developed them for the first time during the trial. Moreover, one (patient 1) developed striking radiological changes of osteitis fibrosa, and two (patients 2 and 3) appreciably increased vascular calcification. All 30 patients who had received phosphate-enriched dialysis fluid were found to show similar trends.

Histological—Osteitis fibrosa, which was absent or mild in all patients at the start of the trial, showed appreciable deterioration in six cases, becoming very severe in patient 10 (table). Histological osteomalacia was present at the start in 12 patients, of whom one (patient 4) showed improvement with phosphate, four were unchanged, and seven deteriorated. One of the two patients who had no osteomalacia at the start developed it during the trial (patient 13).

Discussion

Patients on regular haemodialysis often have diets restricted in phosphate and take phosphate-binding drugs, and they are likely to be in negative phosphate balance when dialysed with phosphate-free dialysate, though they may not be hypophosphataemic.¹² This has been suggested as a contributory factor in dialysis osteodystrophy.^{12–16} An average dialysis against phosphate-free dialysate with a calcium concentration of 1.6 mmol/l removes 1 g of phosphorus,^{12–15} about half of which has been calculated to come from the intracellular pool.¹⁵ We undertook this study to see whether reversing this negative phosphate balance would improve the osteomalacic syndrome.

Our preliminary results, based largely on patients' reports of improvement in muscle power and lessening of bone pain, gave grounds for optimism.¹⁷ We therefore started treatment in 30 patients, and continued where possible for at least six months before repeating radiological skeletal surveys and bone biopsies. Analysis of these results has not supported our initial optimism.

In 10 of our 14 patients we know that enough phosphate was administered to increase predialysis or postdialysis phosphate concentrations. We do not know whether there was a positive phosphate balance, but it would not have been possible to give more phosphate as pruritus and stiffness became intolerable at high doses.

Effects of phosphate-enriched dialysis fluid in 14 patients with osteomalacic dialysis osteodystrophy (B=before trial, A=at end of trial)

Patient No	Months on phosphate	Serum phosphate (mmol/l)				Serum alkaline phosphatase (U/l)		Serum parathyroid hormone (U/l)		Changes in myopathy	Radiology—fractures		Histology			
		Predialysis		Postdialysis		B	A	B	A		B	A	B	A	B	A
1	12	B	A	B	A	B	A	B	A	Improved	B	A	B	A	B	A
2	7	3.05	3.85	1.65	3.4	160	96	0.7	1.6		No change	Numerous	†	12	20	0
3	12	2.55	3.00	1.10	1.90	23	30	—	0.9	No change	Numerous	Healed	8	8	1	0
4	6										healing	None	Numerous	6	10	0
5	6	2.42	3.41	1.2	1.58	97	87‡	1.8	1.0‡	Mild improvement	Never present		8	6	1	3
6	12	2.3	3.0	1.45	2.5	121	130	2.4	6.6	Improved	Few	Healed	7	11	1.5	3
7	6	2.78	3.47	0.95	2.50	130	182	2.7	5.1	Worse	Numerous	Worse	11	22	0	0
8	9	2.55	3.3	1.95	1.9	123	150	1.4	1.4	Worse	None	Numerous	5	6	0	1.5
9	6	2.45	3.00	1.7	1.75	57	78	2.5	3.2	No change	Never present		6	5	0	1
10	8	1.75	3.00	1.15	1.9	43	60	0.5	0.8	Worse	Few	Little change	6	20	0	0
11	9	2.9	3.05	1.45	1.55	86	130	2.1	3.8	Mild improvement	Few	†	6	5	1	4
12	11	2.15	2.25	1.35	1.40	80	167	1.5	8.0	No change	Numerous	Numerous	24	30	1	2
13	9	2.98	3.34	2.06	1.94	286	153‡	—	—	Worse	Numerous	Worse	9	17	0	0
14	6	3.05	2.00	2.4	1.5	104	136	0.3	0	No change	None	Numerous	2	6	1.5	1
		2.55	2.4	1.5	1.5	46	79	—	1.9	Not present	Never present		3	3	1	1
		2.0	1.75	1.25	0.97	47	37	—	—							

*Normal 4 or less: more indicates osteomalacia.

†Some fractures healed slowly, but patient developed new Looser zones.

‡Initial rise, then fall.

Conversion: SI to traditional units—Serum phosphate: 1 mmol/l $\approx$ 3.1 mg/100 ml.

The meaning of the slow radiological healing of fractures or Looser zones in three of the seven patients in whom they were present is uncertain, as partially mineralised osteoid, which is radio-opaque, may appear around the fractures without there being any true remodelling and healing of trabecular bone. There was no improvement in histological osteomalacia in these cases.

Histologically, osteomalacia became worse in eight patients, three of whom showed an appreciable increase in osteitis fibrosa, and improved in only one. There is thus no evidence that phosphate treatment—or induction of osteitis fibrosa—promotes healing of osteomalacia.

The effect of phosphate treatment on myopathy and on bone pain, which was present in those with severe myopathy, is more difficult to assess. Assessment of myopathy is affected by the patient's motivation, which may have a large role in patients selected for special treatment. Nevertheless, two patients showed unequivocal improvement of myopathy, though not of bone histology; one was wheelchair-bound at the start of therapy through weakness and pain, was walking within three months, and is now clinically normal. The cause of these changes may be questioned, however, as 1α -OHD₃, which she started at the same time as phosphate treatment, may sometimes help myopathy in renal osteodystrophy,¹⁸ and she has indeed continued to improve since stopping phosphate treatment. But the other patient who improved appreciably had been taking 1α -OHD₃ for two years without improvement before starting phosphate. Four patients became progressively weaker and suffered increasing pain during the course of treatment. Review of all 30 patients we have treated shows similar results; of 22 who had initial symptoms, two showed appreciable improvement, six subjective improvement, one an apparent transient improvement, and six no change; while four could not be assessed and five deteriorated. We could not predict which patients were the potential responders from the initial clinical, biochemical, radiological, or histological findings, or from changes during treatment.

The most frequent clinical complications of phosphate treatment—pruritus and stiffness of joints and muscles—could be controlled by reducing the dose in all except two patients, who stopped treatment after two months. There is a great theoretical risk of inducing ectopic calcification in a group of patients with high serum phosphate concentrations whose calcium concentration level is maintained with vitamin D derivatives. The incidence or importance of this cannot easily be assessed

over a six-to-12-month period, especially as many patients already had corneal or arterial calcification at the start of the trial. Nevertheless, three of the 30 patients showed a definite increase in arterial calcification, and three new corneal calcification.

Our patients on dialysis with osteomalacia have similar serum phosphate concentrations to those without osteomalacia. Phosphate depletion without hypophosphataemia has not been recorded as causing osteomalacia in other circumstances. Our results suggest similarly that in patients on dialysis who are not hypophosphataemic phosphate depletion is not a cause of osteomalacia. Our policy now is to use phosphate therapy only in patients with persistent predialysis or severe postdialysis hypophosphataemia.

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SIDE EFFECTS OF DRUGS

Erosive gastritis and duodenitis during continuous cimetidine treatment

Cimetidine accelerates the healing of duodenal ulcers, and symptomatic improvement is usually accompanied by endoscopic evidence of healing.^{1 2} We report an unusual mucosal appearance that developed in a patient receiving continuous cimetidine treatment.

Case report

A 43-year-old man presented with a typical history of peptic-ulcer disease of 14 years' duration. Barium-meal examination in January 1976 showed a shallow ulcer 5 mm in diameter on the anterior wall of the duodenal bulb with associated duodenal scarring and deformity. The gastric mucosa was normal apart from a mild antral gastritis. The patient agreed to participate in a six-month pharmacokinetic study of cimetidine, and treatment was started at 800 mg/day. Compliance with treatment was checked by tablet counts at monthly intervals. Symptomatic relief was complete within a few days and

continued throughout the study period, during which no other drugs were given.

Three months after starting treatment repeat endoscopy showed complete healing of the ulcer. Widespread punctate erosive gastritis was noted, however, with altered blood at some erosion sites; there was also a florid duodenitis, with several areas of punctate erosion. Three months later endoscopy showed an almost identical appearance. On each occasion the patient had no symptoms and said that he had taken neither aspirin nor alcohol. Blood urea and electrolyte concentrations, liver function values, and routine haematological tests assessed at monthly intervals remained normal throughout. At six months a blood sample taken six hours before endoscopy showed no trace of either salicylate or alcohol. Four months after stopping treatment the patient was still asymptomatic and endoscopy showed no evidence of erosive gastritis, although duodenitis was still present. A pentagastrin test showed a basal acid output of 10.8 mmol(mEq)/h and a stimulated acid output of 58.9 mmol(mEq)/h.

Comment

These endoscopy appearances usually occur in patients who have recently taken either aspirin or alcohol or both. We were satisfied that our patient had taken neither. During our study over 40 endoscopic examinations were carried out on patients receiving continuous