Treatment of hereditary hypophosphataemic rickets

Sir,

We read with interest the article by Stamp and Baker (*Archives*, 1976, **51**, 360). While the conclusions of the authors with respect to genetics are of much importance, equally so are the therapeutics of this disorder, and here we should like to give our experience with phosphate supplements.

Our results with Phosphate-Sandoz (Sandoz Products, London) compare very favourably with earlier results, both in our own and in other institutions. This phosphate preparation (one tablet contains sodium acid phosphate 68.1%, sodium bicarbonate 9.5%, and potassium bicarbonate 8.5%; providing, in addition to phosphorus 500 mg, sodium 481 mg=20.9 mEq and potassium 123 mg=3.1 mEq) is given in a dose usually of 4-6 tablets per day. This basic medication, usually given for life, is supplemented by vitamin D. The dosage of vitamin D can be kept remarkably low (usually 20 000-60 000 IU/day) thus avoiding the hazards of intoxication. Indeed the sequelae of vitamin D intoxication could have been the cause of some of the clinical findings of the patients described by the authors.

This therapeutic regimen for hereditary hypophosphataemic rickets has proved successful in both biochemical (serum phosphate, alkaline phosphatase, and calcium; urinary calcium) and clinical terms; side effects of the phosphate supplementation such as diarrhoea are only rarely observed.

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Dr. T. C. B. Stamp comments:

Many workers have reported satisfactory long-term control of hypophosphataemic rickets with combinations of vitamin D and a phosphate supplement (West *et al.*, 1964; Stickler, Hayles, and Rosevear, 1965; Wilson *et al.*, 1965; Glorieux *et al.*, 1972; McEnery, Silverman, and West, 1972). The convenient commercial preparation advocated by Dr. Koepf was used by us in one of our cases.

In our experience optimum long-term control of X-linked rickets can be achieved without extra phosphorus (Dent, Round and Stamp, 1973), in contrast to the situation in adult-presenting hypophosphataemic osteomalacia where supplementation seems necessary (Dent and Stamp, 1971). Additional phosphate may also benefit the severe homozygous disease described in our paper, since supplementation in one patient produced an alkaline phosphatase 'flare'.

One of the major problems of therapy in all these diseases is that the only generally available preparations of vitamin D, 'strong calciferol' (BP and USP), contains 50 000 IU in each tablet, a quantity far too large to permit accurate dosage (Dent *et al.*, 1973). These tablets may even contain up to 30% more vitamin D than is

stated (so-called 'overage') in order to allow for slow deterioration on storage. For this reason alone we can look forward to alternative therapy such as 25-hydroxycholecalciferol.

Phosphate supplementation in X-linked rickets can certainly reduce the danger of intoxication that is present with such high doses of vitamin D and may also lower the requirement. Its disadvantages are firstly the need to 'juggle' two lots of pills instead of one, secondly the still-present danger of vitamin D intoxication if a patient should stop the supplement for any reason, and finally the increased secondary hyperparathyroidism which phosphate produces (Arnaud, Glorieux, and Scriver, 1971) and to which these patients may be particularly liable.

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REFERENCES

- Arnaud, C. D., Glorieux, F. H., and Scriver, C. R. (1971). Serum parathyroid hormone in X-linked hypophosphatemia. *Science*, **173**, 845.
- Dent, C. E., and Stamp, T. C. B. (1971). Hypophosphataemic osteomalacia presenting in adults. *Quarterly Journal of Medicine*, **64**, 303.
- Dent, C. E., Round, J. M., and Stamp, T. C. B. (1973). Treatment of sex-linked hypophosphataemic rickets (SLHR). *Clinical Aspects of Metabolic Bone Disease*, p. 427. Ed. by B. Frame, A. M. Parfitt, and H. Duncan. International Congress Series No. 270. Excerpta Medica, Amsterdam.
- Glorieux, F. H., Scriver, C. R., Reade, T. M., Goldman, H., and Roseborough, A. (1972). Use of phosphate and vitamin D to prevent dwarfism and rickets in X-linked hypophosphatemia. *New England Journal of Medicine*, **287**, 481.
- McEnery, P. T., Silverman, F. N., and West, C. E. (1972). Acceleration of growth with combined vitamin D-phosphate therapy of hypophosphatemic resistant rickets. *Journal of Pediatrics*, **80**, 763.
- Stickler, G. B., Hayles, A. B., and Rosevear, J. W. (1965). Familial hypophosphatemic vitamin D resistant rickets. *American Journal of Diseases of Children*, **110**, 664.
- West, C. D., Blanton, J. C., Silverman, F. N., and Holland, N. H. (1964). Use of phosphate salts as an adjunct to vitamin D in the treatment of hypophosphatemic vitamin D refractory rickets. *Journal of Pediatrics*, **64**, 469.
- Wilson, D. R., York, S. E., Jaworski, J. F., and Yendt, E. R. (1965). Studies in hypophosphatemic vitamin D-refractory osteomalacia in adults. *Medicine*, **44**, 99.

Genetic aspects of nutritional rickets

Sir,

In their study Doxiadis *et al.* (*Archives*, 1976, **51**, 83) conclude that '... in at least some cases of nutritional rickets there is a genetic element which may manifest itself only under adverse environmental conditions'. This explains why only some children with nutritional deficiency may develop rickets, and why only some children treated with phenobarbitone may also develop rickets. 162 children on long-term treatment with phenobarbitone (5 mg/kg per day) have been observed as outpatients. In 30% of those aged 0-13 years (average duration of treatment 20 months) and in 60% of patients aged under 2 (average duration of treatment