non-rachitic infants, 14 (54%) showed an increase–peak–decrease pattern of bone origin alkaline phosphatase activity with increasing postconceptional age. There was no significant change in plasma calcium or inorganic phosphorus.

Because of the difference in techniques of estimation it is not possible to compare directly our published results with those of Glass *et al.* Their recommendation of 500 U/l as an upper limit of normal cannot be directly related to our laboratory, or to any which used different methodology.

It is also difficult to define age based reference intervals for plasma alkaline phosphatase activity in preterm infants because of the non-Gaussian distribution of data. Moreover, because infants of identical postnatal age, but differing postconceptional ages, are not equivalent, it is not appropriate to use postnatal age as a basis for establishing normal values. We have noticed that alkaline phosphatase activity when measured serially in an infant will invariably exceed, at some stage, a gestational age related range (I Kovar *et al.*, unpublished data).

To avoid these problems we suggest that alkaline phosphatase activity in an individual neonate and infant should be expressed in relation to a fixed range, rather than as a gestation related mean and standard deviation; use of a percentage of an upper limit of an adult reference range permits comparison between laboratories. This then allows recommendations to be made for intervention in a given case when a fixed multiple is recorded. We agree, however, that serial plasma alkaline phosphatase activity estimation is a useful means of screening for rickets in this susceptible population.

References

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Skeletal changes in preterm infants

Sir,

We were interested to read the paper by Koo *et al.*[1] in which they mention that none of the infants fed exclusively on breast milk had abnormal skeletal *x*-rays.

We undertook a similar study of the possible effect of breast milk or humanised formula on infants' blood 25-hydroxycholecalciferol and parathyroid hormone concentrations.[2] It was found that parathyroid hormone concentrations at age 8 weeks (measured by radioimmunoassay which predominantly detects the C-terminal end) were normal in infants fed exclusively on breast milk, but were appreciably higher in infants receiving a formula milk in addition to breast milk. This difference was not explained by the plasma 25-hydroxycholecalciferol concentrations, which were normal and similar in both groups. We wonder whether the serum biochemical findings (calcium, phosphate, alkaline phosphatase, immunoreactive parathyroid hormone) and radiological findings in the 7 infants fed exclusively on breast milk were different from those of the 7 infants fed with the formula in the study of Koo *et al.*

References

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2 Sann L, Rigal D, David L, Frederich A, Lahet C. Late evolution of serum immunoreactive parathyroid hormone, calcitonin, and plasma 25-hydroxycholecalciferol concentrations in very low birthweight infants. *Acta Paediatr Scand* 1981; **70**: 479–84.

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Dr Koo and co-workers comment;

We have reviewed the data from our study[1] and those published by Sann *et al.*[2] It appears there are a number of aspects which make direct comparison of the results difficult. The patients in our study who developed radiological skeletal abnormalities have more severe illnesses and have significantly lower birthweights than those with normal skeletal *x*-rays. In addition, 9 infants in our study received human milk for 2 to 37 (median 18) days—a period far shorter than the formula supplemented group of infants in the study of Sann *et al.*[2] Furthermore, the dose of vitamin D_2 supplement used in our study was 800 IU/day from age 14 days compared with the dose of 2400 IU/day from age 10 days in the study of Sann *et al.*[2]

However, we analysed our data further, using one way analysis of variance and Newman Keuls' multiple comparison procedure to determine if there were any differences between the infants with radiological skeletal abnormalities (group 1) and the infants with normal skeletal radiographs but who were fed human milk only (group 2) and those who were fed some or no human milk (group 3).

The results showed that infants in group 2 were significantly larger (birthweight 1183 ± 76 g, mean $\pm$ 1 SD) and had greater gestational ages ($30 \pm 2{\cdot}9$ weeks, mean $\pm$ 1 SD) at birth than group 1 infants ($P < 0{\cdot}05$). They also tolerated a predetermined volume of feeds (>160 ml/kg per day) significantly sooner ($7{\cdot}3 \pm 1{\cdot}9$ days of age, mean ± 1 SD) than group 1 infants ($P < 0{\cdot}05$). There were no significant differences in these parameters between groups 2 and 3 or between groups 1 and 3.

There were no important intergroup differences in serum calcium, phosphorus, alkaline phosphatase, total protein, 25 hydroxyvitamin D (25-OHD), and immunoreactive parathyroid hormone in the cord blood, at 5 weeks and 10 weeks postnatal age. In group 2 infants,