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 gesta-
tional age related range (IKovar et al., unpublished data).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 laboritories. 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
1 Glass E J, Hume R, Hendry G M A, Strange R C,
Forfar J O. Plasma alkaline phosphatase activity in

2 Kovar I, Mayne P, Barltrop D. Plasma alkaline phos-
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Skeletal changes in preterm infants

Sir,

We were interested to read the paper by Koo et al. 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 radio-
immunoassay 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, phosphatase, 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
1 Koo W W K, Gupta J M, Nayyar V V, Wilkinson M,
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2 Sann L, Rigal D, David L, Frederick A, Lahet C. Late
evolution of serum immunoreactive parathyroid hormone,
calcitonin, and plasma 25-hydroxycholecalciferol con-
centrations in 500 non-Gaussian distribution of data.

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Dr Koo and co-workers comment;

We have reviewed the data from our study1 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 supple-
mented group of infants in the study of Sann et al.2
Furthermore, the dose of vitamin D3 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±1 SD)
and had greater gestational ages (30±2.9 weeks, mean±1
SD) at birth than group 1 infants (P<0.05). They also
tolerated a predetermined volume of feeds (>160 ml/kg
per day) significantly sooner (7-3±1.9 days of age,
mean±1 SD) than group 1 infants (P<0.05). 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 immuno-
reactive parathyroid hormone in the cord blood, at
5 weeks and 10 weeks postnatal age. In group 2 infants,