Table *Clinical and laboratory details of the 3 preterm infants who developed rickets*

Case no.	*Sex*	*Gestation (w)*	*Birthweight (g)*	*Age at diagnosis (w)*	*Feeding*	*Laboratory investigations*			
						Ca (mmol/l)	*Po_4 (mmol/l)*	*Alkaline phosphatase (IU/l)**	*25 (OHD_3) (ng/ml)*
1	M	31	1300	10	EBM for one month then Cow & Gate Premium	2·44	1·88	1265	—
2	F	29	950	19	Own mother's milk from birth	2·52	0·95	3620	23
3	M	28	1225	22	Own mother's milk from birth	2·49	1·40	1765	12·2

*Normal paediatric level 56–190 IU/l (Forfar and Arneil, 1973).

Conversion: SI to traditional units—Calcium: 1 mmol/l ≈4 mg/100 ml. Po_4: 1 mmol/l≈ 3 mg/100ml.

Thomas suggest that vitamin D deficiency causes softening and fracturing of the ribs and weakening of respiratory muscles which leads through impaired respiratory movements to respiratory distress. If this is really the sequence of events perhaps it is surprising that the severe osteodystrophy in our infants was not associated with any respiratory problem. Admittedly the thoracic cage was not *x*-rayed so that we do not know for certain that the ribs were affected but since rickets is a generalised disturbance of bone growth it would be surprising if the ribs were spared. We wonder therefore whether some other factor is responsible for 'rachitic respiratory distress'.

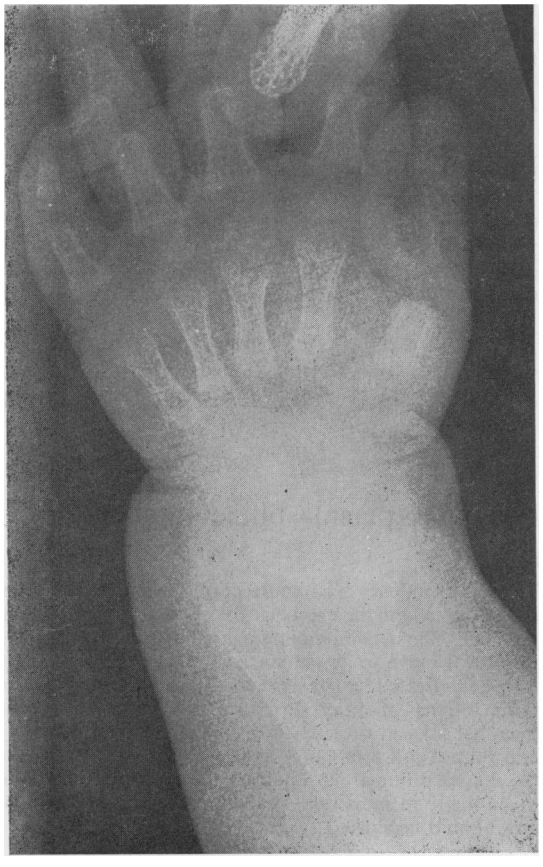

Fig. *Case 2. X-ray of right wrist showing severe bone rarefaction with marked cupping of distal radial and ulnar metaphyses.*

Glasgow and Thomas draw attention to the association of copper deficiency and bone disease. Copper deficiency in preterm infants has been reported to cause enlargement of the costochondral cartilages, cupping and flaring of the long bone metaphyses, and spontaneous fractures of ribs, apnoeic episodes, and muscle hypotonia (Hambidge, 1976). The liver plays an important role in copper metabolism through the production of caeruloplasmin which is the main means of copper transport and in liver diseases plasma levels of copper are low (Alexander, 1974). In view of the disordered liver function in the Belfast infants we wonder therefore whether the syndrome of subacute respiratory distress with severe metabolic bone disease might be due at least in part to an abnormality of copper metabolism.

Finally Glasgow and Thomas postulate that their infants developed rickets because of malabsorption of vitamin D or impaired 25-hydroxylation of cholecalciferol in the liver. Plasma 25-hydroxycholecalciferol was measured in 2 of our infants and in both instances the levels were well within the normal range. It is unlikely therefore that malabsorption or impaired hepatic conversion was responsible for rickets. Instead it is tempting to speculate that transient interference of renal production of 1,25-dihydroxycholecalciferol or target organ unresponsiveness to this active hormone was responsible.

D. P. Davies, C. A. Hughes, and J. R. Moore
Department of Child Health,
Leicester Royal Infirmary,
Leicester LE1 5WW.

Dr J. F. T. Glasgow comments:

We are grateful to Dr Davies and colleagues for their interest in and helpful comments on our report. The

infants they describe are similar, but not identical, to ours, particularly with respect to presence of symptoms, age at diagnosis, and type of nutrient used. Their *x*-ray shows rachitic changes and it is unlikely that marked rib abnormality was present in the absence of respiratory difficulty. We too have found that the serum levels of 25-hydroxyvitamin D (25-OHD_3) were normal in all infants in whom it was measured; the value for Case 3 was 19·5 ng/ml. 3 of 7 other patients with bone disease, but without respiratory distress, also had normal concentrations (range 16·5–34·5 ng/ml).* These findings do not of themselves exclude the possibility of an abnormality in vitamin D metabolism, but do suggest that treatment with 25-OHD_3 is unlikely to be beneficial.

We are confronted by a difficulty however, since radiological changes in Cases 1, 2, and 4 were definitely those found in classical nutritional rickets. Another infant with similar bone disease but no respiratory distress had biochemical changes consistent with rickets, including reactive hyperparathyroidism, which returned to normal after therapy with 1α-hydroxyvitamin D (Glasgow and Reid, 1977). Curiously this child also had a normal level of 25-OHD_3.

Deficiency of trace elements may also be an important aetiological factor. Several authors have described infants with copper deficiency and noted a variety of features, namely costochondral beading, demineralisation, rib fractures, expanded metaphyses, muscular hypotonia, and apnoeic episodes (Al-Rashid and Spangler, 1971; Griscom *et al.*, 1971; Ashkenazi *et al.*, 1973). In addition, however, anaemia was a prominent finding in each of these reports; it was usually of some severity, resistant to iron treatment (sideroblastic anaemia), and associated with erythroid and myeloid hypoplasia. Hypoalbuminaemia also was sometimes present. Any anaemia in our infants was mild with features such as leucocytosis and reticulocytosis which are not consistent with copper deficiency. Plasma proteins were always normal.

The questions which none the less remain to be answered are first, whether the infants we describe with a potentially fatal respiratory disorder have a deficiency of, say, 1,25-dihydroxyvitamin D; and second, is this compounded in some of the lightest and sickest infants by deficiency of trace elements such as copper, manganese, or silicon? Further prospective study of affected babies, careful review of existing histological material, and measurements of trace elements in existing serum samples are required.

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*Kindly carried out by Dr Angela Fairney, St Mary's Hospital, London.

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J. F. T. Glasgow and P. S. Thomas
Nuffield Department of Child Health, The Queen's University of Belfast, Institute of Clinical Science, Grosvenor Road, Belfast BT12 6BJ, and Royal Belfast Hospital for Sick Children, Northern Ireland.

Neonatal records and the computer

Sir,

Readers will no doubt have noticed an error in my paper (*Archives*, 1977, **52**, 452). Owing to a faulty provisional print out from which the data on jaundice were derived, the 1975 entries for 'absent' and 'mild' jaundice and their percentages and ranges were transposed in Tables 3 and 4. The accompanying text should read 'In 1975 as many as 26% (range 17–39%) of 21 030 babies had bilirubin levels between 86 and 204 μmol/l (5 and 12 mg/100 ml). . . .' This change, however, does not alter the significance ($P<0·001$) of the increase in jaundice between 1974 and 1975 as reported. I apologise for this oversight on my part, and trust it has not caused confusion among your readers.

Colin H. M. Walker
Department of Child Health, Ninewells Hospital and Medical School, Dundee DD1 9SY.

Neonatal plasma bilirubin chart

Sir,

There is a tendency for phototherapy to be used too often or for too long in the management of babies with neonatal jaundice. The accompanying chart has been constructed in order to give some guidance as to when phototherapy may be indicated. It has been found useful in practice. In term infants plasma bilirubin levels lying below the diagonal line on the chart are unlikely to cause anxiety and do not call for phototherapy. Bilirubin levels above the diagonal line are an indication for a careful decision to be made in individual cases as to what treatment, if any, should be started.

Harry V. L. Finlay and Sam M. Tucker
Paediatric Unit, Hillingdon Hospital, Uxbridge, Middlesex UB8 3NN.