

neuronal degeneration, but the aetiology was not established.

Twenty nine children (41%) aged 3 months to 2½ years (mean 9 months) had infantile spasms. Of these, only 7 (24%) had normal scans, 14 (48%) had generalised cerebral atrophy, 3 including 2 with Aicardi's syndrome had agenesis of the corpus callosum, and 2 had tuberous sclerosis. In 3 cases communicating hydrocephalus was found, but ventriculoperitoneal shunting was not indicated.

Discussion

The CT scan was normal in all children with petit mal and myoclonic seizures and is not considered to be indicated in these cases. In grand mal plus retardation the CT scans showed possible aetiological features in 3 children: 1 with porencephalic cyst, 1 with agenesis of the corpus callosum and 1 with cerebral degeneration, but failed to show a treatable pathology or influence treatment. We found that in children with infantile spasms plain CT scans were worth while. Again lesions requiring specific treatment are uncommon, but genetic counselling is required if tuberous sclerosis is shown. In no case in our series did contrast enhancement give additional

information and it is rarely indicated unless an unexpected pathology is shown on plain CT scan.

Conclusion

When infantile spasms occur with non-specific mental retardation CT scanning will show an abnormality in about 75% of cases. Specific abnormalities occur in under one third of these children, few will require definitive treatment, but genetic counselling may be initiated. Some 60% of retarded children with other forms of non-focal epilepsy have normal CT scans and uncommonly show specific, treatable, or genetically transmitted abnormalities.

We thank Drs J Wilson and E M Brett for allowing us to study these patients who were admitted under their care and Dr J Wilson for his helpful criticism.

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Hypophosphataemic rickets in the preterm infant; hypocalcaemia after calcium and phosphorus supplementation

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SUMMARY A preterm infant with hypophosphataemic rickets became hypocalcaemic when given milk specially formulated for preterm infants that contained increased phosphorus and calcium. The rickets resolved spontaneously. Routine calcium and phosphorus supplementation for preterm neonates should be investigated further.

Rickets and poor bone mineralisation in the preterm infant is common and of uncertain aetiology.¹ Human milk, as the sole source of nutrition for these infants, may not provide adequate mineral substrate and supplementary calcium and phosphorus have been advocated.² We report on an infant with rickets of prematurity secondary to phosphorus depletion. Symptomatic hypocalcaemia developed when phosphorus supplementation was

given, while the rickets resolved spontaneously on an un-supplemented diet.

Case report

A baby girl, the second of twins, was born at 30 weeks' gestation, after an unbooked delivery with no antenatal care. She weighed 1420 g. Her sibling was stillborn. The neonatal period was complicated by mild hyaline membrane disease and hyperbilirubinaemia. Feeding from the first week was with mother's expressed breast milk supplemented daily from week 3 with 400 IU of calciferol (BP).

Plasma alkaline phosphatase activity, measured at 4 weeks of age to screen for rickets,³ was 2600 U/l (childhood reference range (CRR), 170-850 U/l). Radiographic examination of the long bones showed no evidence of active rickets, although a

skull radiograph suggested some demineralisation of the skull table. The plasma calcium was 2.40 mmol/l (9.6 mg/100 ml) (CRR=2.20–2.67 mmol/l (8.8–10.68 mg/100 ml)), inorganic phosphorus was 0.90 mmol/l (2.7 mg/100 ml) (CRR=1.02–1.96 mmol/l (3.06–5.88 mg/100 ml)), and 25-hydroxycholecalciferol was 53 nmol/l (22 ng/ml) (adult reference range = 25–43 nmol/l (10.4–17.9 ng/ml)). Serial biochemical values are shown in the Figure. At 7 weeks the plasma alkaline phosphatase had increased to 3500 U/l and was of bone origin, while the plasma inorganic phosphorus had fallen to 0.74 mmol/l (2.22 mg/100 ml). Urinary inorganic phosphorus was undetectable and urinary calcium was 2.55 mmol/l (102 mg/100 ml). The mother's breast milk had a low measurable phosphorus content (1.02 mmol/l (3.091 mg/100 ml)) and a calcium to phosphorus ratio of 5:1 but this was not followed serially. The mother's plasma biochemical values were all normal.

A provisional diagnosis of hypophosphataemic rickets was made and a trial of phosphorus supplementation was given. A specially formulated milk (Nenatal) for preterm infants, containing 16.6 mmol/l (50.3 mg/100 ml) of phosphorus and 25 mmol/l (100 mg/100 ml) of calcium with a molar calcium to phosphorus ratio of 1.5:1 was given and calcium and phosphorus intake per kg bodyweight are shown in the Figure. Despite an increase in absolute calcium intake, plasma and urinary calcium values fell, possibly suggesting increased calcium utilisation in bone. Urinary inorganic phosphorus remained undetectable. The infant became lethargic, fed poorly, and the clinical diagnosis of hypocalcaemia was made. Her plasma calcium value was 1.75 mmol/l (7.0 mg/100 ml). The formula milk was stopped and the baby was fed mother's expressed breast milk and calcium supplements. Although the total calcium content of the expressed breast milk and added calcium was less than had previously been given, the baby's plasma and urinary calcium concentrations increased.

In retrospect, out-patient radiographs taken at 10 weeks of age did suggest rickets. At 12 weeks the mother (without advice) began feeding with a standard formula (Cow & Gate Premium) mixed with expressed breast milk. By 14 weeks there was clear radiological evidence of healing rickets and the biochemical values had returned to normal. The infant's progress continued to be observed. At 18 weeks radiographs were normal, growth and development were satisfactory, biochemical values remained normal, and inorganic phosphorus, when checked at 28 weeks, was present in the urine.

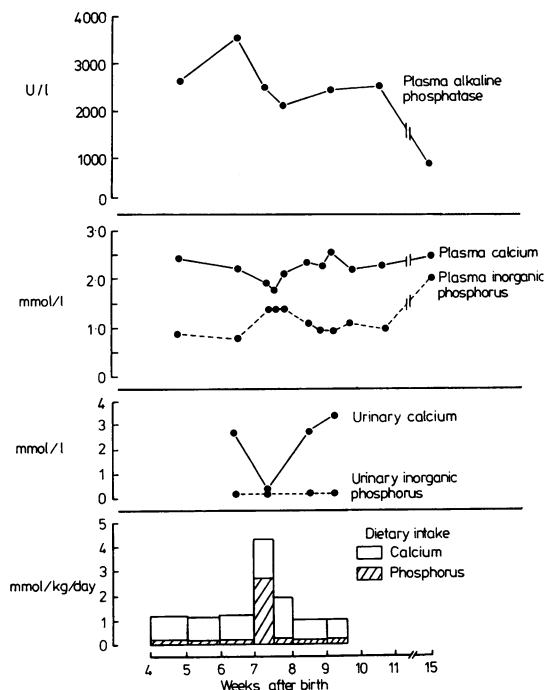


Figure Serial biochemical values in relation to time and calcium and phosphorus intake.

Conversion: SI to traditional units—plasma calcium 1 mmol \approx 4 mg/100 ml; plasma inorganic phosphorus 1 mmol/l \approx 3 mg/100 ml.

Discussion

A phase of rachitic bone growth may be a normal phenomenon in the breast fed preterm infant.⁴ This infant's rickets resolved without active treatment as neither calciferol nor vitamin D analogues were given. It is possible that the short term supplementation with calcium and phosphorus at 7 weeks and the addition of standard formula from 12 weeks contributed to healing, but the time scale makes this unlikely. The most likely cause of the rickets was phosphorus substrate deficiency of the mother's breast milk.

Treatment with calcium and phosphorus for infants with this clinical picture has been suggested,⁵ and routine prophylactic supplementation of breast milk fed to preterm infants has been advocated.² It has been argued that where there is sufficient vitamin D intake an inadequate intake of calcium and phosphorus is a major factor in causing rickets of prematurity,⁶ and because of this several new proprietary formula milks for preterm infants, containing additional calcium and phosphorus, have

been introduced. Many neonatal units use these formulas to complement breast milk fed to infants but our findings illustrate a potential hazard in this approach. Despite an increase in absolute calcium intake, the additional phosphorus to correct the low plasma inorganic phosphorus and presumed total body phosphorus depletion caused symptomatic hypocalcaemia.

The molar calcium to phosphorus ratio may be as important as the absolute concentration of these minerals in the correction of any deficiency. There may, however, be a delay in maturation of 1α hydroxylase enzyme in the low birthweight baby.⁷ Further data are needed before preterm infants can be safely given routine calcium and phosphorus supplements.

We thank Professor D Barltrop for advice.

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Neonatal paracetamol poisoning: treatment by exchange transfusion

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SUMMARY The metabolism and excretion of paracetamol was studied in an infant of 29 weeks' gestation who was exposed to the drug when his mother ingested 32.5 g 16 hours before delivery. We have confirmed that sulphation is the major pathway and that the mixed function oxidase system is sufficiently active at this gestational age to produce hepatotoxic metabolic products. As most of the recognised drug treatments for paracetamol poisoning seemed unsuitable in this case, the infant was treated with exchange transfusions.

We report a case of paracetamol poisoning in an infant of 29 weeks' gestation whose mother ingested paracetamol before delivery. Studies have shown that the human neonate can conjugate paracetamol predominantly by sulphation and also by glucuronidation.^{1,2} Human fetal liver cells can also oxidise paracetamol by the mixed function oxidase system to the reactive arylating intermediate and unless this latter substance is conjugated with glutathione, liver necrosis is likely. Although there are no data concerning the human fetus after 23 weeks' gestation,³ oxidation is slower than in the adult liver and increases with gestational age. Paracetamol poisoning in a premature infant in vivo has never been described

and thus there are no guidelines for treatment. In this infant we performed exchange transfusion of whole blood because of the risk of severe hepatic necrosis.

Case report

A 22 year old Caucasian mother had a normal third pregnancy until 29 weeks' gestation when she took a drug overdose because of acute depression. She ingested 50 tablets of Anadin (aspirin 325 mg, caffeine 15 mg, and quinine sulphate 1.0 mg) 33 hours before delivery and 65 Hedex (paracetamol 500 mg) 16 hours before delivery. Severe vomiting occurred and premature labour began 10 hours after she had taken the paracetamol. Six hours before delivery salicylate concentrations were reported to be in the non-toxic range but her paracetamol value was 1056 $\mu\text{mol/l}$ (15.95 mg/100 ml), indicating severe poisoning and she was therefore given 1 dose of methionine, 2.5 g orally.⁴ She had no clinical signs of liver damage after delivery, but 50 hours after the ingestion of paracetamol (Table 1) her aspartate transaminase activity rose to a maximum of 4300 IU/l, bilirubin to 30 $\mu\text{mol/l}$ (1.75 mg/100 ml) and prothrombin time to 22 seconds (control 13). Her liver function had returned to normal by 126 hours and there were no sequelae.