newborn. *American Journal of Diseases of Children*, **106**, 137–146.
Nickman, S. L., Buckler, J. M., and Weiner, C. B. (1968). Further experiences with water intoxication. *Pediatrics*, **41**, 149–151.
Pickering, C. K., and Hugan, G. R. (1971). Voluntary water intoxication in a normal child. *Journal of Pediatrics*, **78**, 316–318.
Rutter, N., and Smales, C. R. (1977). Role of routine investigations in children presenting with their first febrile convulsions. *Archives of Disease in Childhood*, **52**, 188–191.
Wynn, V., and Rob, C. G. (1954). Water intoxication: differential diagnosis of the hypotonic syndromes. *Lancet*, **1**, 587–594.

Correspondence to Dr A. Etzioni, Department of Paediatrics A, Rambam University Hospital, Aba Khoushy School of Medicine, Rambam Medical Center, Haifa, Israel.

Copper deficiency in a low birthweight infant

P. YUEN, H. J. LIN, AND J. H. HUTCHISON

University Departments of Paediatrics and Pathology, Queen Mary Hospital, Hong Kong

SUMMARY Copper deficiency is reported in an infant of very low birthweight. It was characterised by extensive bone changes, severe neutropenia, and hypocupraemia. These manifestations could have been missed but for an intercurrent pneumonia which led to an *x*-ray of the chest.

Low birthweight infants go into negative nitrogen balance from birth and there may also be substantial losses of trace elements (Shaw, 1973). Absorption of nutrients may also be poor. It is surprising, therefore, that there have been so few reports of copper deficiency in low birthweight infants (Al-Rashid and Spangler, 1971; Griscom *et al.*, 1971; Ashkenazi *et al.*, 1973; Sann *et al.*, 1978) and it is possible that some cases go unrecognised.

Case report

A Chinese baby, son of a 28-year unmarried hostess at a dance hall, was born spontaneously in the hospital casualty department at 28 weeks' gestation on 24 August 1977. Birthweight 970 g; length 39 cm; head circumference 26 cm. The clinical and radiological features of idiopathic RDS rapidly developed. The infant was nursed in an incubator in 60% O_2, an umbilical artery was catheterised for blood–gas studies, and IV 10% dextrose was given at a rate of 3 ml/hour. Apnoeic attacks necessitated the use of CPAP on 25 August and IV aminophylline was given 1·5 mg six-hourly. Pao_2 varied between 47 and 115 mmHg (6·2 and 15·3 kPa). Metabolic acidosis was corrected with sodium bicarbonate. Parenteral feeding with Aminofusin, dextrose, and Intralipid was started on 26 August. CPAP was stopped on 30 August, and the ambient O_2 concentration gradually reduced. An attempt at nasogastric feeding on 31 August produced blood from the gastric aspirate and Hb fell to 10 g/dl, and then rose to 15 g/dl after a transfusion of 25 ml fresh blood. Parenteral feeding was discontinued on 20 September when the infant's full caloric requirements were being given in the form of Nan (Nestlé) by nasogastric tube. Hb was 11·5 g/dl. On 1 October proprietary ferrous sulphate and multivitamin preparations were started orally. However, on 4 October Hb was 7·6 g/dl; WBC 45·1 $\times$ 10^9/l; neutrophils 31%; lymphocytes 69%; platelets 645 $\times$ 10^9/l; reticulocytes 4·8%. Films showed 12 nucleated RBC/100 WBC. On the suspicion of vitamin E deficiency (Willoughby, 1977) IM tocopherol 100 mg daily was given for 4 days. Unfortunately, the infant developed bronchopneumonia (treated with IV gentamicin and ampicillin) and on 17 October Hb was 6·3 g/dl; reticulocytes 8·7%. A further 4-day course of tocopherol was given and on 10 November Hb was 11·3 g/dl; reticulocytes 2·6%. The infant was discharged home on 22 November on Nan 75 ml three-hourly $\times$ 8, plus iron and vitamin supplements. Weight 2·33 kg; head circumference 32·5 cm.

The baby was readmitted on 13 December extremely ill and convulsing with bronchopneumonia. Weight 3·0 kg. Respirations 60/min. Blood pH 7·03; Pao_2 73 mmHg (9·7 kPa); $Paco_2$ 94 mmHg (12·5 kPa); base excess—7·5 mmol/l. Serum Na 132 mmol/l; K 5·8 mmol/l; Ca 2·4 mmol/l (9·6 mg/100 ml); P 2·38 mmol/l (7·4 mg/100 ml); Mg 1·0 mmol/l (2·4 mg/100 ml). Hb 10·2 g/dl; WBC 20·3 $\times$ 10^9/l; neutrophils 26%; lymphocytes 67%; monocytes 7%; reticulocytes 4·6%. CSF normal. There was a good response to cephradine given IV combined with nursing in 40% O_2. However, a repeat chest *x*-ray on 21 December showed widening of the anterior rib ends, subperiosteal reaction, and fractures of the right 6th, 7th, and 8th ribs and of the left 5th, 6th, 7th, and 8th ribs.

A skeletal survey showed diaphyseal subperiosteal

new bone formation with cupping and flaring of the metaphyses and severe osteoporosis. There were fractures of the lower ends of the left radius and right ulna (Figure). Repeat blood tests showed serum Ca 2·1 mmol/l (8·4 mg/100 ml); P 2·94 mmol/l (9·1 mg/100 ml); alkaline phosphatase 610 μmol/min per litre (Chinese adults 35–115). VDRL negative. On 19 January 1978 serum Cu was 0·7 μmol/l (4·5 mg/100 ml) (normal 11–25), and serum caeruloplasmin was barely detectable (normal 62–108 μmol/min per litre). Hb was 11·9 g/dl; WBC $7·3 \times 10^9$/l; neutrophils 1%; lymphocytes 90%; monocytes 8%; eosinophils 1%; serum Fe 8 μmol/l (44·7 μg/100 ml); TIBC 51 μmol/l (285 μg/100 ml). On 25 February, when the infant had been on cereals in addition to the milk formula for 52 days, serum Cu was 2·0 μmol/l (12·7 μg/100 ml); caeruloplasmin 10 μmol/min per litre; plasma ascorbate 94·2 μmol/l (1·6 mg/100 ml); serum zinc 9·2 μmol/l (60·1 μg/100 ml) (Chinese adult range $15·7 \pm 2·75$ μmol/l). *X*-rays taken on 1 March already showed early healing of bone lesions but the infant was started on 0·6 ml of 0·5% copper sulphate solution daily. On 14 March serum Cu was 10 μmol/l (63·7 μg/100 ml); caeruloplasmin 43 μmol/min per litre. Hb was 12·4 g/dl; WBC $15·6 \times 10^9$/l; neutrophils 47%; lymphocytes 51%; monocytes 1%; eosinophils 1%; reticulocytes 2·6%; platelets 339×10^9/l. Copper supplements were stopped on 22 March when serum Cu was 22 μmol/l (140 μg/100 ml); caeruloplasmin 65 μmol/ min per litre. *X*-ray on 29 March showed almost complete healing of bone lesions apart from residual subperiosteal reaction in both femora, although bone-age was only 3 months. The infant went home on 18 May, weight 4·8 kg, on feeds of Cow and Gate Babymilk Plus and mixed feeding. He was still unable to sit unsupported or to roll over from the supine to the prone posture, but in the prone position he could lift his head and chest off the table and he made attempts to grasp objects. Unfortunately his home environment is unlikely to encourage much stimulation.

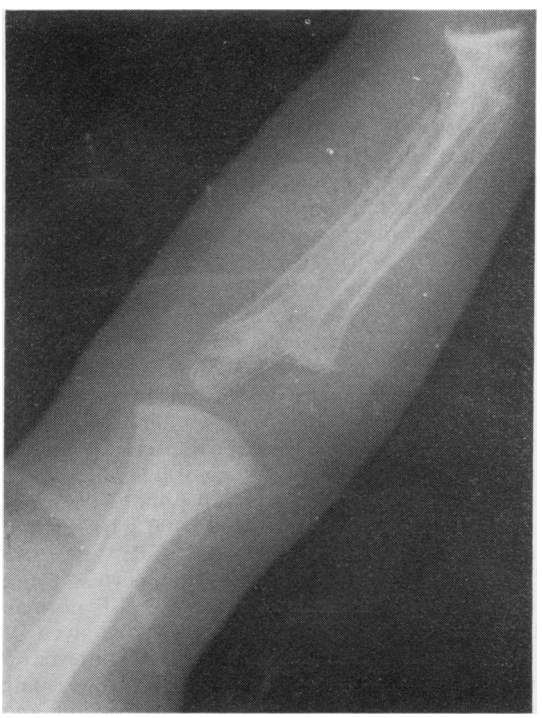

Figure *X-ray at age 4 months showing subperiosteal reaction, osteoporosis, flaring and cupping of metaphyses, and fracture of lower end of radius.*

Discussion

The diagnosis of copper deficiency in this case is based upon the characteristic bone changes, severe neutropenia, and extremely low serum copper and caeruloplasmin levels. Anaemia is common in copper deficiency but was absent in our patient. When the bone changes were first discovered our initial suspicion was rickets. Indeed, this has been reported in association with copper deficiency in a low birthweight infant (Sann *et al.*, 1978). However, the high serum phosphate level made this diagnosis unlikely, particularly as the infant had been receiving a calculated daily intake of at least 10 μg vitamin D. We have not seen such severe subperiosteal new bone formation in rickets but measurements of plasma 25-OHD_3 or iPTH were not available to us. There was no evidence of nonaccidental injury and the long bone changes were incompatible with this diagnosis. If this infant had not been readmitted to hospital with pneumonia the diagnosis would have been missed because even after finding extensive bone changes on *x*-rays there was no clinically obvious beading of the ribs or epiphyseal enlargement, and it is probable that spontaneous healing would have followed the introduction of mixed feeding. On the other hand, a neutropenia of 1% must have greatly reduced the infant's resistance to infection.

Copper deficiency has been reported in older infants after prolonged total parenteral nutrition (Karpel and Peden, 1972; Heller *et al.*, 1978) as well as in very low birthweight infants. In our patient parenteral nutrition was only total for 6 out of 26 days, and the extreme prematurity and low birthweight were likely to be more important factors leading to copper deficiency.

We thank Dr L. Y. Y. Fong for the serum zinc analysis.

References

Al-Rashid, R. A., and Spangler, J. (1971). Neonatal copper deficiency. *New England Journal of Medicine*, **285**, 841–843.
Ashkenazi, A., Levin, S., Djaldetti, M., Fishel, E., and Benvenisti, D. (1973). The syndrome of neonatal copper deficiency. *Pediatrics*, **52**, 525–533.
Griscom, N. T., Craig, J. N., and Neuhauser, E. B. D. (1971). Systemic bone disease developing in small premature infants. *Pediatrics*, **48**, 883–895.
Heller, R. M., Kirchner, S. G., O'Neill, J. A., Jr, Hough, A. J., Jr, Howard, L., Kramer, S. S., and Green, H. L. (1978). Skeletal changes of copper deficiency in infants receiving prolonged total parenteral nutrition. *Journal of Pediatrics*, **92**, 947–949.
Karpel, J. T., and Peden, V. H. (1972). Copper deficiency in long-term parenteral nutrition. *Journal of Pediatrics*, **80**, 32–36.
Sann, L., David, L., Galy, G., and Romand-Monier, M. (1978). Copper deficiency and hypocalcaemic rickets in a small-for-date infant. *Acta paediatrica Scandinavica*, **67**, 303–307.
Shaw, J. C. L. (1973). Parenteral nutrition in the management of sick low birthweight infants. *Pediatric Clinics of North America*, **20**, 333–358.
Willoughby, M. L. N. (1977). *Paediatric Haematology*, p. 149, Churchill-Livingstone: Edinburgh.

Correspondence to Professor J. H. Hutchison, Queen Mary Hospital, Department of Paediatrics, Hong Kong.

Pulmonary candidiasis in cystic fibrosis

B. M. JENNER, L. I. LANDAU, AND P. D. PHELAN

Royal Children's Hospital, Melbourne, Australia

SUMMARY A child with cystic fibrosis and asthma developed pulmonary candidiasis. Predisposing factors in this patient were prolonged antibiotic therapy, high-dose corticosteroids, and intravenous catherisation. A diagnosis was made by lung puncture and confirmed by rapid response to 5-fluorocytosine.

Pulmonary candidiasis is an invasion of viable lung tissue by *Candida* species. It has long been known that this occurs in patients with impaired host resistance—such as those with Hodgkin's disease or leukaemia, and those on cytotoxic therapy. In 1844 Bennett commented: 'it is indicative of great depression of the vital powers and impairment of the nutritive functions of the economy' (Winner and Hurley, 1966).

Candida colonisation is seen in the tracheobronchial tree of children with cystic fibrosis on long-term antibiotics. Pulmonary candidiasis, however, has not been reported in such children.

This is a report of a child with cystic fibrosis and asthma requiring corticosteroids, who developed pulmonary candidiasis and responded to treatment with 5-fluorocytosine.

Case report

A 6½-year-old girl had cystic fibrosis diagnosed in the first year of life and associated bronchial asthma. She was initially well maintained on standard antibiotic and physical therapy for cystic fibrosis lung disease, with intermittent bronchodilator treatment for the asthma.

At age 5 years she required continuous bronchodilators and, subsequently, three intermittent courses of corticosteroids to control the wheeze. At 6 years more prolonged courses of high-dose prednisolone were necessary to control quite severe airways obstruction but these were reduced to a maintenance dose of 4 mg daily. During a course of high-dose prednisolone for an acute exacerbation of airways obstruction she became increasingly lethargic, lost weight, and developed a fever which reached 39°C daily. She developed rapid shallow breathing with fine inspiratory crepitations. Chest *x*-rays showed increased reticulonodular markings (Figure).

Intravenous cloxacillin and gentamicin, and later chloramphenicol and carbenicillin, were given for nearly 4 weeks without response. On several occasions sputum cultures grew *Escherichia coli*, *Streptococcus* species, *Haemophilus influenzae*, and *Achromobacter* species, but moderate to profuse growth of *Candida* species, not *C. albicans*, was always present. Multiple blood cultures were negative. Immune function tests were normal. Tuberculosis, autoimmune disease, and sepsis elsewhere were excluded.

A lung puncture was performed with instillation of 2 ml saline into the lung and aspiration of alveolar fluid. This fluid was smeared and cultured. A pure growth of *Candida* species, not *C. albicans*, was obtained.

She was started on 5-flurocytosine orally; within