cause insulin release in vitro (Milner, Ashworth, and Barson, 1971). Infants with transient diabetes may have β-cells which are unresponsive to all stimuli or which, as in the fetus, are unresponsive to glucose alone. In the former case, the cell might be morphologically immature but in the latter case morphological normality would be expected.

**Summary**

An infant, whose two elder brothers had suffered from transient neonatal diabetes mellitus, developed the same condition. An intravenous glucose tolerance test at the age of 24 hours was diabetic and caused no rise in plasma insulin levels. Urinary insulin excretion during the first three days of life, before insulin therapy began, was within or below the low normal range. These findings support the view that transient neonatal diabetes is due to a delay in β-cell maturation.

**REFERENCES**


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**Transient Metastatic Calcification Complicating Renal Failure in an Infant**

Ectopic calcification is a well-recognized complication of chronic renal insufficiency in adults (Black, 1967), whereas in infancy it is rare. The purpose of this report is to document the occurrence of transient generalized soft tissue calcification in association with chronic renal insufficiency in a 2-month-old child.

**Case History**

Male infant, 3.55 kg, born to healthy parents after a normal pregnancy. He was fed on full-cream dried milk. At 2 weeks he was admitted to the local hospital with a history of weight loss and vomiting. *Esch. coli* was isolated from culture of blood and urine. At this time a random serum calcium was 12.0 mg/100 ml. Treatment with kanamycin and cloxacillin was started and his clinical condition improved. An intravenous pyelogram failed to opacify the renal tract when the blood urea was 284 mg/100 ml. No ectopic soft tissue calcification was visible. By the age of 5 weeks he had gained weight, though urine was still infected with *Esch. coli* and the blood urea was 184 mg/100 ml. Treatment was continued at home with nalidixic acid. When 8 weeks old, he was readmitted with a short history of vomiting and twitching and was transferred to this hospital. On admission he was a normal looking infant and his developmental age was in keeping with his chronological age. His weight was below 3rd centile. Systolic blood pressure was 100 mmHg. The genitalia were normal and he had a good urinary stream. A hard intracutaneous nodule was palpable over the anterior aspect of the left tibia (0.5 cm in diameter) and several similar nodules were palpable in the occipital region.

Fig. 1 shows the concentration of blood urea, serum calcium, and serum alkaline phosphatase at the ages of 2 and 6 months.

![Fig. 1](http://adc.bmj.com/726)
calcium, and phosphorus from the age of 2 to 9 months. The plasma electrolytes were normal. The initially high blood urea fell rapidly when the protein intake was reduced by changing the feed to a 'humanized' dried milk. An intravenous pyelogram showed bilateral hydronephrosis. A micturating cystogram confirmed the presence of gross hydronephrosis and hydrourerter, with no evidence of urethral obstruction. The urine was infected with klebsiella and treatment was continued with trimethoprin-sulphafurazole.

A left ureterostomy and right pyelostomy were performed (Mr. D. Innes Williams). Renal biopsies taken at that time showed no evidence of renal dysplasia or nephrocalcinosis. The urinary tract drained satisfactorily, the urine became sterile, and the blood urea stabilized at 50 mg/100 ml.

![Image](https://example.com/image.png)

**Fig. 2.—An x-ray showing calcification in the buttocks and around the left femur.**

At age 2 weeks a random serum calcium had been noted to be 12·0 mg/100 ml and Fig. 1 shows that the serum calcium was still raised at 2 months. Phosphate retention was marked but fell to normal after operation. Histological examination of a biopsy of the nodule on the left leg showed soft tissue calcification, and the x-rays showed ectopic calcification in the buttocks, around the left femur, and over the lumbar spine (Fig. 2). The serum calcium levels fell when aluminium hydroxide (B.P.), 10 ml, with each feed was given in addition to the low calcium diet. This treatment was discontinued at 4 months, when clinical and radiological examination showed no evidence of soft tissue calcification and a rise in serum alkaline phosphatase. He continued on a reduced calcium diet in the form of 'humanized' milk together with cereals. The calculated vitamin D intake was 380 IU/day.

At the age of 8 months he was well; the blood urea was marginally raised while the creatinine clearance was severely impaired at 3 ml/min.

**Discussion**

The serum calcium concentration is usually low or normal in chronic renal failure, while phosphate retention is marked. If the serum (Ca) × (P) product exceeds 75, then deposition of calcium salts occurs (Stanbury and Lumb, 1966). In adults ectopic calcification has been described in the conjunctiva (Berlyne, 1968), blood vessels (Black, 1967), skin, and kidney (Herbert, Miller, and Richardson, 1941). The infant described in this report had phosphate retention and hypercalcaemia and therefore the presence of ectopic calcification was not surprising. However, there has been only one previous report of ectopic calcification complicating renal failure in infancy (Lugo et al., 1969) describing the necropsy findings of arterial calcification in 2 infants dying of acute renal failure.

The present case report is of interest since it demonstrates, firstly, that in renal failure ectopic calcification can occur when the product of serum calcium and phosphorus is raised, even in the first months of life. Secondly, these changes are rapidly reversible provided that the intake and absorption of calcium and phosphorus are reduced.

Why the infant described had an initial period of hypercalcaemia in the presence of a high blood urea is far from clear. There was no radiological evidence of hyperparathyroidism or other bone disease and the intake of vitamin D was never excessive.

**Summary**

A male infant aged 2 months developed soft tissue calcification in association with chronic renal failure. The calcification disappeared after the renal failure was improved, and a lower intake of calcium and phosphorus given.

**References**


Familial Haemophagocytic Reticulosis in First Cousins*

Familial haemophagocytic reticulosis is a lethal reticulendotheliosis with a familial proclivity and characteristic histological manifestations (Varadi, Gordon, and Abbott, 1964). The disease has been described in a number of families (Farquhar, MacGregor, and Richmond, 1958; MacMahon, Bedizel, and Ellis, 1963; Marrian, and Sanerkin, 1963; Miller, 1966; Nelson et al., 1961; Goodall, Guthrie, and Buist, 1965; Neff and Senhauser, 1967; and Bell et al., 1968), but has not been reported in relatives other than sibs. This report documents the occurrence of the disease in two first cousins.

Case Reports

Case 1. This was the second child born to a 20-year-old Caucasian after a normal pregnancy. Her mother and the mother of Case 2 were full sisters. After four months, she developed diarrhoea, vomiting, fever, anaemia, and hepatosplenomegaly which were unresponsive to antibiotics.

The abnormal laboratory studies were: WBC 2500–4150/mm³ (20–30% neutrophils, 6–15% bands, 20–37% lymphocytes, 7–15% monocytes, 20–45% disrupted 'smear' cells), reticulocytes 0·5–8·6%, platelets 60,000–120,000/mm³, Hb 5·0–8·0 g/100 ml, the red cells showed marked anisocytosis and poikilocytosis; serum albumin 2·8 g/100 ml, globulin 1·8 g/100 ml. Bone marrow aspirates showed only very active erythropoiesis and no abnormal cells. Heterophil antibodies, typhoid antibodies, Kahn, PPD, and fungal tests were negative. The chest x-ray and skeletal survey were normal.

During the ten-week admission, there were recurrent pyrexial episodes during which the haematocrit, white cell, and platelet counts fell and the 'smear' cell count rose. She was treated with blood transfusions and several antibiotics without effect. Splenectomy and liver biopsy were performed but the child died of pneumonia and subdural haematoma consequent to thrombocytopenia two weeks later.

Pathology. Microscopically, the spleen showed hypoplastic lymphoid follicles, and infiltration of the splenic cords and sinusoids by large histiocytes. These cells had oval, band-shaped nuclei and mildly acidophilic, vesicular cytoplasm (Fig.). Some of them showed haemophagocytosis, particularly of lymphocytes. The hepatic sinusoids and portal tracts showed similar infiltrates with many of the histiocytes and several Kupffer cells showing active haemophagocytosis. Similar infiltrates were present in the lungs and meninges.

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