Details of 40 Arabs and Summary of Results

Group	No. Studied			Mean Age in Years (Range)	Mean Body Weight in kg (Range)	Estimated Daily Milk Intake (ml)			No. with Symptoms after Milk	Mean Fasting Blood Glucose in mmol/l (Range)	Mean Maximum Rise in Blood Glucose in mmol/l (Range)	No. (%) of Patients with Maximum Blood Glucose Rise >1.1 mmol/l
	M.	F.	Total			0	<250	250-500				
Bedouin	9	5	14	34 (18-60)	54 (44-73)	3		10	3	4.5 (3.7-5.6)	3.2 (0.2-9.7)	12 (85.7)
Urban Saudi	5	3	8	40 (17-65)	51 (39-64)	2		6	3	4.2 (3.4-4.7)	2.4 (0.8-4.7)	7 (87.5)
Khadiiry	4	5	9	33 (14-60)	51 (35-74)	1		8	2	4.6 (3.6-6.8)	1.2 (0.1-4.2)	2 (22.2)
Yemeni	8		8	31 (16-40)	51 (43-64)	1	1	6	4	4.3 (3.9-5.0)	2.2 (0.2-4.7)	6 (75.0)
Syrian	1		1	48	53			1	1	4.5	0.6	

Conversion: SI to Traditional Units—Glucose: 1 mmol/l $\approx$ 18 mg/100 ml.

Four Bedouin, two urban Saudis, seven *Khadiiry*, and three Yemenis had symptoms (colic or diarrhoea or both) after lactose; 11 out of 13 with a rise in glucose of less than 1.1 mmol/l had symptoms.

Discussion

An increase in blood glucose after 50 g lactose by mouth gives a good indication of intestinal lactase activity.¹ Adult Arabs on the Arabian peninsula⁶ constitute the third major group to be shown to have high lactase activity; they seem, therefore, to be ethnically distinct from eastern Mediterranean populations. It seems likely that high lactase in most northern Europeans and the Hamitic people of Africa originated there.

The selective advantage of lactase in adult life in evolution is unknown. Bedouin have for thousands of years lived as nomads in the deserts of Arabia, and for long periods calorie and fluid intake have been largely derived from camels' milk. Adults with a high lactase concentration are likely, therefore, to have had an increased survival rate. In severe gastrointestinal infections active absorption of monosaccharides is coupled with water absorption⁷; thus it seems possible that adults with high lactase concentrations who lived largely on milk could have survived epidemics such as cholera. That the selective advantage of lactase has been associated with increased calcium absorption in groups not exposed to strong sunlight⁸ is untenable.

Childhood malnutrition, especially marasmus, is common in many areas where adult hypolactasia is prevalent and high lactase concentrations fall soon after birth.¹ Though marasmus is common in Arab children in eastern Mediterranean countries, where adult hypolactasia is prevalent, it seems to be uncommon in Riyadh.

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Osteomalacia Presenting as Chorea

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British Medical Journal, 1975, **3**, 136-138

Summary

A 16-year-old epileptic developed chorea. He had osteomalacia, hypocalcaemia, and hyperphosphataemia, which were due not to hypoparathyroidism but to vitamin D deficiency—itsself secondary to longstanding dietary deficiency and anticonvulsant drug administration.

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Introduction

Choreiform movements are a rare but well described feature of hypocalcaemia^{1,2} though in all reported cases the hypocalcaemia was due to hypoparathyroidism. We report here a case of osteomalacia accompanied by hypocalcaemia and hyperphosphataemia which presented with severe generalized choreiform movements. Several factors, including anticonvulsant drugs, were probably implicated in the causation of the underlying osteomalacia and hypocalcaemia.

Case Report

EARLY HISTORY

The patient was born on 7 July 1957. Delivery was normal and he weighed 6 lbs (2.7 kg). Between the ages of 2 and 5 years he had several febrile convulsions. When he was 11 he was investigated for abdominal pain and constipation. Physical examination showed nothing abnormal, but an iron deficiency anaemia (9.6 g/dl) and a low serum albumin

level (27 g/l) were found. Serum calcium was not measured but serum alkaline phosphatase was normal (42 IU/100 ml). Barium studies showed dilated small bowel loops but no evidence of a malabsorption pattern. His diet was poor. Treatment with laxatives and oral iron corrected his anaemia but caused little improvement in his abdominal symptoms.

In 1969 he developed grand mal convulsions and eventually required phenytoin sodium 200 mg and phenobarbitone 90 mg to control his fits. An electroencephalogram (E.E.G.) in June 1971 was within physiological limits. In September 1972 his abdominal symptoms recurred. Investigations showed low serum folate (1.3 µg/l) and normal faecal fat excretion (2.7 g/24 h). Since his initial admission he had failed to gain any height and had only increased in weight by 5½ lb (2.5 kg) (fig. 1). A gluten-free diet was tried but after six months there was no improvement in height, weight, or abdominal symptoms.

FIG. 1—Changes in height and weight before and after treatment with vitamin D in relation to Tanner and Whitehouse percentile scale.

ADMISSION

He was admitted to the General Hospital, Nottingham, in August 1973 when aged 16 after a two months' history of involuntary movements lasting between two and six hours each. Two days before admission he had become irrational and occasionally lapsed into a semi-comatose state. On examination the chorea was generalized but more severe on the right, where he had multiple contusions and abrasions over his fingers and toes. He was fully conscious and there were no other neurological signs apart from generalized hypotonia. His height was 56 inches (1.4 m)—below the third percentile (fig. 1); body proportions were normal; and he showed early pubertal change. There were no cataracts and none of the developmental abnormalities found in pseudohypoparathyroidism³; Chvostek's and Trousseau's signs were not present. He was otherwise physically normal apart from slight gingival hyperplasia.

Initial investigations showed: serum calcium 1.1 mmol/l (4.2 mg/100 ml), phosphorus 2.3 mmol/l (7.0 mg/100 ml), and alkaline phosphatase 392 IU/100 ml. Chest and skull x-ray films were normal. Radiographs of the wrists, hands, knees, ankles, and pelvis showed florid changes of rickets. Subperiosteal erosions were seen in the femoral necks. Iliac crest bone biopsy showed osteomalacia with evidence of secondary hyperparathyroidism. Dietary history by recall suggested an intake of vitamin D of 30 IU/day and calcium of 625 mg/day.

An iron deficiency anaemia of 9.5 g/dl responded rapidly to iron treatment. The serum folate was low at 2.6 µg/l but there was no other evidence of malabsorption (faecal fat excretion 4.8 g/24 h; xylose absorption, radiological appearances of the small bowel, and jejunal biopsy were normal). Other biochemical tests and relevant renal function studies gave normal results. An E.E.G. showed evidence of a metabolic encephalopathy.

TREATMENT

The chorea was initially treated with chlorpromazine 25 mg and tetrabenazine 50 mg by mouth with little effect. Within 24 hours of admission he became semi-comatose with severe chorea and laryngeal stridor; 20 ml of 10% calcium gluconate was given intravenously as a

single injection and the chorea and laryngeal stridor immediately stopped and the conscious level improved. Calcium gluconate (to provide 900 mg of calcium) was infused over the next 48 hours. Generalized choreiform movements and irritability recurred once when the serum calcium fell to 1.6 mmol/l (6.3 mg/100 ml). Relatively normal serum calcium levels were quickly established with oral dihydrotachysterol (fig. 2) and subsequently maintained by calciferol 1.25 mg/day. In January 1974 the pharmacological doses of vitamin D were replaced by smaller amounts (0.05 mg) without recurrence of hypocalcaemia. There was clear radiological evidence of healing of osteomalacia and subperiosteal erosions after three months' treatment. The growth spurt which was initiated with pharmacological doses of vitamin D was maintained subsequently by physiological replacement doses (fig. 1). Anticonvulsant drugs were withdrawn but after a further grand mal seizure phenobarbitone was restarted and the dose subsequently stabilized at 30 mg three times daily.

FIG. 2—Changes in calcium phosphate and alkaline phosphatase in relation to treatment.

Discussion

McKinney¹ drew attention to chorea as a presenting symptom in nine cases of hypoparathyroidism. Only four of the nine cases showed evidence of basal ganglia calcification; there is a poor correlation between this feature and the presence of neurological symptoms⁴ and the ganglia dysfunction probably reflected the metabolic consequences of hypocalcaemia.¹ In our patient chorea seemed to be related to the degree of hypocalcaemia in that abnormal movements were seen only when the serum calcium fell below 1.6 mmol/l (6.3 mg/100 ml).

The cause of the hypocalcaemia in our patient was vitamin D deficiency rather than hypoparathyroidism. The low serum calcium (1.1 mmol/l (4.2 mg/100 ml)) in the presence of hyperphosphataemia (2.3 mmol/l (7.0 mg/100 ml)) was typical of the biochemical features of hypoparathyroidism, but the severe rickets, raised serum alkaline phosphatase, and normal circulating parathyroid hormone levels (0.8 µg/l when serum calcium was 2.1 mmol/l (8.5 mg/100 ml)) due to vitamin D treatment mitigated against the diagnosis of hypoparathyroidism.

Evidence of parathyroid overactivity in the presence of the biochemical features of hypoparathyroidism (hypohyperparathyroidism) may be found in some cases of pseudohypoparathyroidism.^{5, 6} Though this diagnosis would explain many of the clinical features of our case there were none of the morphological features of pseudohypoparathyroidism³ and the presence of osteomalacia could not be explained in terms of a single diagnosis. The maintenance of normocalcaemia and continuing evidence of healing of osteomalacia by physiological as opposed to pharmacological doses of vitamin D is also strong evidence against the diagnosis of pseudohypoparathyroidism.

Vitamin D deficiency as the primary condition seems to provide a more complete explanation of the features of this case. There was hypocalcaemia with raised serum alkaline phosphatase in the presence of typical radiological and histological changes of osteomalacia. Secondary hyperparathyroidism is often found under these circumstances⁷ and growth retardation is often found in osteomalacia, though it was not a feature of the case of hypohyperparathyroidism reported by Costello and Dent.⁶ The growth spurt which occurred with vitamin D is strong supportive evidence for a diagnosis of osteomalacia.

Hyperphosphataemia in osteomalacia is unusual, but a mechanism for phosphate homeostasis which depends not on parathyroid hormone secretion but on serum calcium levels was shown by Eisenberg.⁸ In the presence of severe hypocalcaemia the renal tubular reabsorption of phosphate is increased and contributes to hyperphosphataemia. Thus, all the clinical features of this case may be explained on the basis of vitamin D deficiency with failure of the calcium homeostatic mechanism leading to profound hypocalcaemia and hyperphosphataemia.

The severe degree of hypocalcaemia in this patient probably arose from a combination of longstanding dietary deficiency of vitamin D and increased requirements due to anticonvulsant drug administration. The maintenance of normocalcaemia and continued evidence of healing of the bone lesion on physiological doses of vitamin D support a nutritional aetiology for the osteomalacia.

It remains uncertain whether this boy's epilepsy was initially

due to hypocalcaemia, but the existence of a normal serum alkaline phosphatase three months before his first fit makes osteomalacia with significant hypocalcaemia unlikely at this time. His case illustrates that osteomalacia as well as hypoparathyroidism may present with chorea as a manifestation of hypocalcaemia, though basically the failure of the calcium homeostatic mechanism in these two conditions may be similar.

We thank Dr. Graham Joplin for his help and advice, Dr. Phillip Bordier for his bone biopsy report, Dr. B. J. Preston for x-ray reports, Drs. G. H. Walker and B. Foote for biochemical help, and Dr. J. L. H. O'Riordan for the estimation of parathormone.

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SHORT REPORTS

Infectious Mononucleosis with Jaundice, Anaemia, and Encephalopathy

Infectious mononucleosis is usually a benign illness. We report on two children with similar and uncommon complications of the condition—namely, hypoplastic anaemia, deep jaundice, and non-hepatic encephalopathy. The children lived within 8 miles (13 km) of each other in Essex but had no known mutual contact. One died.

Case 1

In March 1974 a previously healthy 7-year-old boy developed fever, sore throat, and generalized lymphadenopathy. Infectious mononucleosis with a positive Monospot test was diagnosed. He continued unwell and a month later became drowsy, irritable, and confused, with neck stiffness, ankle clonus, and extensor plantar reflexes but no papilloedema. He also had jaundice, fever, and pallor, with hepatomegaly but no splenomegaly. Haematological investigation showed a hypoplastic anaemia and granulopenia (table), iliac crest bone marrow biopsy showing greatly reduced erythropoiesis, granulopoiesis, and platelet production. Serum bilirubin was 169 $\mu\text{mol/l}$ (9.9 mg/100 ml), 154 $\mu\text{mol/l}$ (9.0 mg/100 ml) conjugated, and aspartate transaminase was 22 (normal 4–15) IU/l. Percutaneous liver biopsy showed mononuclear cell infiltration of portal tracts and sinusoids and minimal fatty change of centrilobular distribution. Lumbar puncture produced normal cerebrospinal fluid (C.S.F.), and electroencephalography showed the pattern of encephalitis with focal elements. There were no signs of liver failure. Management was conservative, and spontaneous bone marrow regeneration occurred with coincidental and complete recovery of all features of the illness.

Case 2

In April 1974 a girl of 11 years had a sore throat. After six weeks of continuous fever she developed hepatomegaly, splenomegaly, and generalized lymphadenopathy. Glandular fever with positive Monospot and Paul-Bunnell tests was diagnosed and a week later she became jaundiced, drowsy, delirious, and anaemic and had extensor plantar reflexes but no papilloedema. Investigations (table) showed a hypoplastic anaemia. Serum bilirubin was 246 $\mu\text{mol/l}$

Results of Haematological Tests

	Case 1	Case 2
Hb (g/dl)	6.5	7.5
Reticulocytes (%)	0	2.0
W.B.C.:		
Total ($\times 10^9/\text{l}$)	0.47	1.1
Neutrophils	10%	54%
Lymphocytes	76% + 4% atypical lymphocytes	46%, many atypical
Monocytes	10%	0
Eosinophils	0	0
Basophils	0	0
Platelets ($\times 10^9/\text{l}$)	50	80
Direct Coombs test result	Negative	Negative
Bone marrow	Hypoplastic	Peripheral blood aspirated
Monospot test result	Positive	Positive
Paul-Bunnell test result	Negative	Positive 1 in 40 absorbed by ox, but not by guinea-pig cells
E.B.-virus-specific IgG antibody titre	1 in 128	1 in 64
E.B.-virus-specific IgM antibodies	Negative	Negative

(14.4 mg/100 ml), and aspartate transaminase 650 IU/l. Electroencephalography showed symmetrical fast activity with no features of hepatic encephalopathy, and lumbar puncture produced uniformly blood-stained C.S.F. She developed a klebsiella septicaemia and died three days after admission despite intravenous lincomycin, gentamicin, penicillin, and methylprednisolone. Necropsy showed small subdural haemorrhage and pulmonary oedema. Histologically the liver showed centrilobular collapse with degeneration and necrosis of hepatocytes and atypical mononuclear cell infiltration of portal tracts and parenchyma. There was no fatty change. Lumbar vertebral marrow showed predominantly fat with some blast cells of both series and atypical mononuclear cells. Brain histology showed perivascular aggregation of monocytes only.

Discussion

Neurological complications, including meningitis, encephalitis, meningoencephalitis, and polyneuropathy, are seen in fewer than 1% of cases of infectious mononucleosis, with complete recovery in 85%.¹ Only nine deaths from encephalitis have been reported,^{2,3} necropsy