Correspondence

Phosphate deficiency and rickets

Sir,

Oppenheimer and Snodgrass\(^1\) concluded that phosphate deficiency might be an aetiological factor in neonatal rickets. We agree, and we think also that in some cases of vitamin D deficiency rickets the leaking of phosphate rather than of calcium may be responsible for the bone lesions.

Hurwitz \(\text{et al.}\)\(^2\) observed that rats fed a normal calcium diet without vitamin D developed hypocalcaemia and had a slight decrease in bone ash but had no evidence of rickets, whereas when they were given a low phosphate diet with vitamin D, hypophosphataemia and severe bone lesions developed. These findings led us to investigate the severity of the rachitic process (as shown by the level of serum alkaline phosphatase) and the radiological picture of the bones in relation to the serum calcium and phosphate levels.\(^3\) We studied 100 infants who were thought to have vitamin D deficiency and who had been treated with vitamin D between 1962 and 1974 at Aghia Sophia Children’s Hospital in Athens. The diagnosis was based on raised levels of serum alkaline phosphate (>20 KA units), or serum calcium levels <8 mg/100 ml (<2 mmol/l), or serum phosphate levels <4 mg/100 ml (<1·3 mmol/l). A close inverse relationship was found between serum phosphate and serum alkaline phosphatase and the presence of radiological signs of rickets. There was no correlation between serum calcium and the severity of bone lesions.

As hypophosphataemia and rickets can be produced experimentally by phosphate deficiency alone\(^4\) and as the level of plasma phosphate reflects the intake of phosphate, hypophosphataemia in infants with nutritional rickets must either be the result of a low phosphate intake or, as seems more likely, of a discrepancy between phosphate intake and the increased requirements of the growing infant. As vitamin D has been shown to act on both calcium and phosphate transport,\(^4\) it is not surprising that both groups (infants with true vitamin D deficiency and infants with phosphate deficiency) responded to treatment with vitamin D. Moreover in 4 infants with hypophosphataemia and rachitic bone lesions healing took place when increased intakes of phosphate were given without additional vitamin D. It seems that lack of phosphate in some cases is the main aetiological factor responsible for the development of rickets.

References


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Sucrase-isomaltase deficiency: difficulties in diagnosis

Sir,

We report an infant who presented with severe diarrhoea in the neonatal period, and in whom the apparent detection of large amounts of glucose in the stool while on Maxijul led to a delay in diagnosis.

The patient, a girl, had been born at 38 weeks’ gestation and had weighed 2·95 kg; pregnancy and delivery had been normal. She was fed Otermilk complete formula but soon developed persistent diarrhoea. At age 2 weeks her weight was 2·84 kg, and stool chromatography showed large amounts of lactose. Because primary alacatias was suspected her feed was changed to a low-lactose formula, Galactomin 17, but diarrhoea continued with 1% reducing substances. Stool chromatography showed small amounts of lactose, glucose, and maltose. Milk protein intolerance was considered and at 4 weeks she was changed to Prosobee (powder based formula) but there was no improvement. Stool chromatography showed no lactose or glucose, and small amounts of maltose. A further change to Albumaid and Maxijul led to torrential diarrhoea, stools became strongly positive for reducing substances, and stool glucose was 64·4 mmol/l (1·16 g/100 ml) (Beckman glucose analyser). Glucose-galactose malabsorption seemed possible, and so she was changed to a fructose-based formula, Galactomin 19, on which she thrived.

Reinvestigation at age 5 months, when her weight was 6·38 kg, led to a diagnosis of sucrase-isomaltase deficiency. Histology of jejunal mucosa was normal as was the mucosal lactase concentration (5·6 units μmol disaccharide hydrolysed/g tissue per minute; normal >2-5), but maltase was very low (0·57 units; normal >10·0) and sucrase undetectable (normal ≥6·0). Glucose, galactose, and lactose tolerance tests were normal in that no diarrhoea was precipitated by the test and there was an appreciable rise in monosaccharide in the blood whether
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glucose or galactose. Sucrose challenge led to profuse diarrhoea with identifiable sucrose in the stool thus confirming the diagnosis.

All four foods given before the fructose-based formula contained large amounts of maltose or malto-dextrins which need maltase for complete digestion; there was no sucrose in them and none was added at any stage. Ostermilk complete formula contains more maltose than lactose and presumably the lactose was swept through the bowel with the osmotic diarrhoea caused by maltose. Since then we have tested Maxijul 10 g/100 ml in water using several methods considered to be specific for glucose. The Beckman glucose analyser (glucose oxidase), gave a glucose concentration of 310 mmol/l. The other three glucose analysers (Instrumentation Laboratories IL 919: glucose oxidase, Yellow Springs Instruments 23 AM: glucose oxidase, and Union Carbide Centrifichem 400: hexokinase) gave glucose concentrations of 6-5, 6-6, and 6-6 mmol/l respectively.

Chromatography has shown that Maxijul contains free glucose, maltose, and maltotriose in addition to other glucose polymers. The high faecal glucose level with the Beckman analyser was not the result of crossreaction with maltose, as maltose at a concentration of 10 mmol/l gave very low glucose readings with all four analysers. We think that free glucose in Maxijul is greatly overestimated if the Beckman analyser is used; this problem would not arise with blood glucose which the instrument is designed to measure.

Maltose or malto-dextrins of higher molecular weight needing maltase for complete digestion are present in many specialised infant foods, and small quantities of maltose identified chromatographically in stools may be significant.

We thank Dr T A H MacDonald and Professor F Cockburn for permission to report this case, and Mr W Borland for help with the biochemical investigations.

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Circadian patterns of plasma steroids in congenital adrenal hyperplasia

Sir,
The data reported by Frisch et al. are extremely interesting. It was known that the great sensitivity of plasma 17-hydroxyprogesterone (17-OHP) concentrations to circadian rhythms, and the effect of divided glucocorticoid doses make it difficult to interpret single plasma values when monitoring treatment. It was also known that there is a close correlation between simultaneous plasma determinations of 17-OHP and testosterone in treated and untreated patients with congenital adrenal hyperplasia (CAH), except in pubertal males. Frisch et al. did not analyse their results in this way. Certainly Cases 3, 8, 9, and 10 showed obvious parallel changes in plasma 17-OHP and testosterone concentrations after various types of treatment. If strict attention is paid to sampling in relation to the time of day and time of previous glucocorticoid dose, serial measurements of plasma 17-OHP and testosterone are a useful index of control. Such data collected longitudinally over a 3-year period in 19 treated CAH patients showed a good correlation (r = 0.79) between plasma 17-OHP and testosterone concentrations (personal observation).

Frisch et al. did not say what biochemical measurements they would recommend as reliable and practical indexes of therapeutic control in CAH. It is important to remember that any therapeutic decision in CAH patients should be taken in the context of clinical parameters of control (growth, skeletal age, signs of puberty or hypercortisolism, regularity of menses, etc.) and levels of plasma renin activity as an index of mineralocorticoid replacement, in addition to the results of plasma or urinary concentrations of adrenal precursor steroids.

References


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Dr Frisch comments:

In our cross-sectional study we merely described the pronounced fluctuations of 17-OHP, testosterone, and cortisol levels in CAH patients. It was not the aim of the study, nor was it possible, to draw conclusions about the usefulness of such measurements in the long-term therapeutic control, particularly as so far as we are aware, there is no agreement on the extent to which 17-OHP, testosterone, or even urinary pregnantriol should be suppressed in order to obtain optimal growth and development throughout childhood. We think that the finding of perfectly normal levels of these parameters indicates overdosage of corticoid treatment (Cases 2 and 6).