Letters to the Editor

More on the Beckwith-Wiedemann syndrome

Sir,

We read with interest the article on Beckwith-Wiedemann syndrome: a quantitative, immunohistochemical study of pancreatic islet cell populations by Stefan et al. [1].

The authors suggest that the Beckwith-Wiedemann (BW) syndrome is a separate entity of neonatal hyperinsulinaemic hypoglycaemia characterized by a massive increase in insulin and glucagon cells together with a defect in glucagon and PP-cell segregation to distinct pancreatic regions.

We recently delivered a baby with the BW syndrome, already prenatally suspected by a combination of polyhydramnios, omphalocele and pronounced oedema of the placenta.

In order to obtain information on lung maturity, an amniocentesis was performed at 34 weeks of gestation. C-peptide was 0.25 pmol/ml and insulin 5 μ U/ml of amniotic fluid, both values being low. The mother went into spontaneous labour at 35 weeks of gestation. Polyhydramnios of more than 3 l was present. The birthweight was 3,500 g. The baby, a boy, survived and had the typical aspect of the BW syndrome. During the first day of life, blood Dextrostix values were around 1.8 mmol/l under a continuous glucose infusion of about 4 mg $\cdot$ kg⁻¹ $\cdot$ min⁻¹. Plasma insulin was 8 μ U per ml and C-peptide 0.47 pmol per ml.

Although our patient had the typical aspect of the BW syndrome with marked macrosomia, amniotic and plasma insulin and C-peptide

levels were not excessive during fetal and neonatal life respectively. There was also no hypoglycaemia under administration of glucose in usual dosages [1].

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Vitamin D deficiency and the endocrine pancreas

Sir,

Gedik and Akalin [1] have demonstrated that insulin release following glucose challenge is impaired in patients with vitamin-D deficiency, and that it is restored to normal following vitamin-D treatment. This phenomenon is well established [2], but it is not established that vitamin D deficiency has no effect on glucagon release.

There are a few unusual features about the patients studied by Gedik and Akalin [1] which should be highlighted. All of their vitamin-D deficient patients had plasma calcium concentrations in the normal range. This can occur in vitamin-D deficiency, but is usually associated with secondary hyperparathyroidism. Parathyroid hormone (PTH) concentrations in sera of these patients were not elevated. This is particularly surprising since the patients had severe vitamin-D deficiency according to clinical and radiological criteria. Furthermore, PTH concentrations did not alter following treatment; this is most unusual. We have previously described the persistence of PTH hypersecretion following vitamin D therapy in osteomalacia, but even in this select group of patients there was some fall in PTH [1]. We have recently demonstrated a significant inverse correlation between 1,25 dihydroxyvitamin D [1,25(OH)₂D] and PTH concentrations (Fig. 1) in patients with vitamin D deficiency [4]. It is surprising, therefore, not to find elevated PTH concentrations in association with the low concentrations of 1,25(OH)₂D described. It is also relevant to mention that we have shown a significant inverse relationship between bone density and PTH concentrations in patients with vita-

Fig. 1. Geriatric study

min D deficiency [5]. Since all four patients included in the series by Gedik and Akalin [1] had marked demineralisation, it would be appropriate to expect an elevated PTH. The only explanation that we can offer for the difference between our observations and theirs is that we have used either an N-terminal [6] or a mid-molecule PTH radioimmunoassay [7], whereas they have used a C-terminal assay. The other mechanism which would account for a normal PTH in osteomalacic patients would be low plasma magnesium [8]; however, all patients included in the present series had normal magnesium levels.

Finally, it is tempting to speculate on the clinical significance of diminished insulinogenesis in vitamin D-deficient patients. Asian immigrants in the U.K. have been shown to have a higher prevalence of diabetes and ischaemic heart disease [9, 10]. They are also known to have frequent vitamin D deficiency [3]. Whether their vitamin D deficiency contributes to the pathogenesis of their diabetes is an area ripe for investigation.

Yours faithfully,

P. Dandona, V. Fonseca and R. K. Menon

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Response from the authors

Dear Sir,

It is a well-known fact that there is parathyroid hormone (PTH) hypersecretion during vitamin D deficiency. Serum calcium levels may be borderline low or normal, and these normal levels are maintained at the expense of PTH hypersecretion [1]. Our vitamin D deficient patients had normal or subnormal calcium levels along with serum PTH levels above the normal range during their first admission to the hospital. As clearly indicated in the study protocol, all patients were admitted to our metabolic ward and were given a diet supplemented with calcium gluconate until serum calcium and PTH levels were normalized in order to eliminate the effects of high serum PTH and subnormal serum calcium on insulin release and glucose tolerance. In spite of vitamin D deficiency, supplemental calcium treatment lowered PTH levels into the normal range; these were given as “pretreatment” values. As shown by Schobach et al. [2], with appropriate calcium replacement sufficient ionized calcium enters cells and normalizes high PTH levels. This has also happened in our vitamin D deficient patients.

As demonstrated by Joffe et al. [3], vitamin D replacement therapy normalizes PTH levels in a short period of time in patients with nutritional vitamin D deficiency. Dandona et al. [4] have found similar results in two of their five patients with florid osteomalacia despite using a different PTH assay. Therefore, it is not possible to accept the explanation that different PTH assays affected the results.

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The actual role that vitamin D deficiency plays in the pathogenesis of diabetes mellitus may only be understood after further research in large groups of patients.

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