*Letters to the Editor***Insulin Antibodies in an Infant with Hyperinsulinism and Persistent Hypoglycaemia Treated with Glucagon**

Dear Sir,

The occurrence of anti-insulin antibodies in patients who have not received exogenous insulin, although a rare event, has been reported in adult patients [1, 2] and also in newborn infants [3]. The antibodies have been considered to be causally related to hypoglycaemic episodes, by occasional dissociation of the insulin-antibody complex and subsequently raised free plasma insulin concentration.

We here wish to report the occurrence of anti-insulin antibodies in a female infant with nesidioblastosis, hyperinsulinism and persistent hypoglycaemia. On the third postnatal day treatment was started with zinc-protamine glucagon (Novo, Copenhagen) with a dose of $0.2 \text{ mg} \cdot \text{kg}^{-1} \cdot 24 \text{ h}^{-1}$. Since hypoglycaemic episodes could not be prevented, a subtotal pancreatectomy (four-fifths) was performed at the age of 2 months. Postoperatively the hypoglycaemia recurred, and the glucagon treatment was continued. Plasma obtained when the patient was $11\frac{1}{2}$ months old showed the presence of insulin-binding IgG. Analysis of three samples showed 0.429, 0.275, and 0.287 mU/ml (Lise G. Heding, Novo Research Institute, Copenhagen). Plasma from the mother (non-diabetic) contained only traces of insulin antibodies (0.01 mU/ml). A transplacental transfer [3] was therefore unlikely. Another possibility was the occurrence of insulin autoantibodies [1, 2]. Since the patient died at 13 months of age, this possibility could not be further explored. A remaining possibility is the development of insulin-binding IgG in response to glucagon with insulin impurities. Commercial glucagon (Novo) contains about

0.02% insulin. It is noteworthy, however, that a glucagon preparation with somewhat higher insulin content did not give rise to insulin antibodies in rabbits.

Doubtless the cause of hypoglycaemia in the present case was hyperinsulinism, with rapid regeneration of the endocrine pancreas after the operation. In our opinion insulin antibodies in the measured concentrations had no importance in this context.

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Plasma Beta-Thromboglobulin in Diabetics with and without Microangiopathic Complications

Dear Sir,

Abnormalities of platelet function may be of considerable importance in the pathogenesis of diabetic microangiopathic complications. The determination of beta-thromboglobulin (β TG), a platelet specific protein released during platelet aggregation, offers a potential useful measure of platelet activation in vivo. Elevated β TG values have been reported in several disease states. Borsley et al. [1] found significantly higher levels of β TG in diabetic patients, as compared with normal subjects. However, there was no difference between patients with and without microangiopathic complications. In contrast with these findings, Preston et al. [2] and Burrows et al. [3] found the highest levels of β TG in diabetics with signs of established tissue damage. In all these studies, however, the patients with and without complications were not matched for degree of metabolic control and duration of the disease.

To resolve these contradictory observations we have measured platelet activation in vivo in a carefully selected group of nine diabetic patients with microangiopathic complications and nine diabetics without complications, matched for age, duration of diabetes and for diabetic control as measured by HbA_{1c}-level (reference $\leq 5.4\%$). Patients with manifest macrovascular complications were excluded. Patients with complications were chosen because

of retinopathy early in the course of their disease and a good degree of metabolic control (mean HbA_{1c} in an outpatient population $8.2 \pm 2.0\%$). Plasma levels of β TG (Radiochemical Centre, Amersham, UK, reference range 25–51 ng/ml) and platelet factor 4 (PF 4, Abbott, Chicago, USA, reference range 0.8–8.4 ng/ml) were measured as indicators of platelet activation in vivo. We measured the plasma level of PF 4 in addition to β TG because both factors are indicators of the same physiological phenomenon [4, 5]. Blood was taken in the non-fasting state. The biochemical parameters are shown in Table 1.

In diabetic patients with microangiopathic complications significantly higher levels of β TG and PF 4 were found ($p < 0.05$), while no significant difference was demonstrated between the control group and the reference group. In our study, β TG and PF 4 correlated significantly ($r = 0.84$; $p < 0.001$). In cases of advanced renal failure, plasma levels of β TG are elevated but those of PF 4 are normal [6]. In our study the mean creatinine clearance was slightly diminished due to concomitant diabetic nephropathy in three patients.

In conclusion, diabetics with microangiopathic complications had significant higher levels of β TG and PF 4 as compared with diabetics matched for age, duration of diabetes and degree of met-