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Growth, Genetics, and Hormones

Although there were no presentations devoted specifically to growth in children with diabetes, there were several presentations on growth hormone (GH) pulsatility, insulin-like growth factor I (IGF-I), insulin resistance, and the relationship between GH and proliferative diabetic retinopathy that should be of interest to readers of this publication.

Cohen and Frohman (Cincinnati) characterized GH pulsatility in type I diabetic men. Utilizing both DETECT and PULSAR computer programming and 20-minute sampling for 24 hours before and after 10-14 days of improved glycemic control, they demonstrated an increased number of GH pulses (compared with controls) that did not change over the short term with improved glucose control. The diurnal rhythm of GH secretion was markedly abnormal in poorly controlled diabetics, with $44 \pm 6\%$ of the pulses occurring between 8:00 A.M. and 8:00 P.M. After improved glucose

control, only $26 \pm 4\%$ of pulses occurred during these hours.

The authors postulated that the time available for target tissues to recover from prior GH exposure is reduced in diabetics, particularly in those with poor glycemic control. They also postulated that these changes in GH secretory patterns may alter the nature of time-dependent GH metabolic effects in persons with diabetes.

Moxley et al (Rochester, New York) evaluated the effects of IGF-I infusions in adult rats using 2-hour euglycemic infusions. Measurements of 2-deoxyglucose uptake and hepatic glucose production were also performed. With infusion of low-dose IGF-I (21 U/kg/min), or high dose IGF-I (83 U/kg/min), whole body glucose disposal was similar to that seen when low and high doses of insulin were infused (2 mU/kg/min and 40 mU/kg/min, respectively). However, glucose disposal during the first hour of IGF-I infusion was significantly lower than that associated with insulin at each dose. At the low-dose infusion, IGF-I was less effective than insulin in suppressing hepatic glucose output. The authors con-

clude that IGF-I has insulin-like activity in vivo that results in part from crossover effects on the insulin receptor. They also demonstrated that IGF-I produces a fall in serum insulin. The physiologic significance of these findings is not clear.

Lager et al (Sweden) infused a tritiated glucose accompanied by either a placebo, propranolol, or somatostatin to evaluate glucose turnover following hypoglycemia. Hypoglycemia was shown to produce a prolonged insulin resistance (up to 7 hours). Propranolol did not prevent the insulin resistance, but somatostatin, which completely abolished GH release, significantly reduced this insulin resistance. The authors conclude that the late insulin resistance seen after hypoglycemia is not, like early-phase insulin resistance, due to β -adrenergic stimulation and that GH significantly contributes to this observation.

Two teams of investigators evaluated IGF-I and stimulated GH release in adults with proliferative diabetic retinopathy. Dills et al (Madison, Wisconsin) determined IGF-I levels in a large group of

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patients with diabetes. IGF-I levels were negatively correlated with age, duration of diabetes, and glycosylated hemoglobin, but were positively correlated with proteinuria. Using logistic regression analysis and controlling for duration of disease, glycosylated hemoglobin, blood pressure, and proteinuria, the authors demonstrated that higher levels of IGF-I

were significantly associated with an increased risk of proliferative diabetic retinopathy.

Janka et al (Boston) prospectively evaluated GH release to arginine in 91 insulin-dependent patients who had diabetes for more than 15 years and who had minimal background retinopathy. After 4 years of follow-up, those individuals who exhibited severe proliferative and preproliferative retinopathy had significantly higher postarginine GH responses. These differences remained after adjustments were made for hemo-

globin A_{1c}, insulin dose, and creatinine. The study demonstrated, for the first time in a prospective manner, that individuals responding to arginine with high GH levels might be at risk for developing severe eye lesions.

The findings described by Dills et al and Janka et al differ from previous reports since it has been previously shown that high GH levels in persons with diabetes are usually associated with lower IGF-I levels. It should be noted, however, that Dills et al did not determine GH levels in their patients.