

Special Report

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Growth, Genetics, and Hormones

Several of the presentations at this meeting may be of interest to readers of *Growth, Genetics, and Hormones*. Geneticists, in particular, will be interested in the symposium on "New Developments in Immunology and Genetics of Insulin-Dependent Diabetes Mellitus [IDDM]," which included a talk by John I. Bell (Oxford, England) entitled, "Genetics of Insulin-Dependent Diabetes Mellitus—Has a Susceptibility Gene Been Found?" Dr. Bell described the epidemiologic and laboratory studies that have led to the identification of the association between the amino acid at position 57 of the human leukocyte antigen-DQ (HLA-DQ) beta chain and IDDM susceptibility in whites. The hypothesis is that aspartic acid (Asp) at position 57 protects against IDDM.

Dorman and Trucco (*Diabetes* 1989;38[2]:34A) reported on the contribution of the HLA-DQ phenotype to the incidence of IDDM in Allegheny County, Pennsylvania. Their previous studies demonstrated that the relative risk of developing IDDM for individuals homozygous for lack of Asp at position 57 of the DQ beta chain, compared to those with at least one DQ gene with Asp, was 107. The incidence of IDDM for non-Asp homozygotes was calculated to be 74 per 100,000, and for those with at least one Asp allele it was 0.69 per 100,000. The annual incidence attributable to the phenotype was thus 73.3 per 100,000. They then calculated the population attributable fraction to be 95%. The non-Asp/non-Asp phenotype is therefore a major determinant of the incidence of IDDM in Allegheny County, Pennsylvania. Trucco et al (*Diabetes* 1989;38[2]:19A) described a relatively simple and quick test that within 24 hours

can detect the presence or absence of Asp-57 without using either allele-specific oligonucleotide probes or radioactive probes. Ikegami et al (*Diabetes* 1989;38[2]:19A) analyzed HLA-DQ beta chain sequences in Japanese patients and determined that the DQ beta characteristics in Japanese IDDM patients are different from those in white populations, and that the DQ-alpha and/or DR sequence also may affect susceptibility.

Presentations regarding the relationship of growth hormone and diabetic retinopathy also were of interest. Rymaszewski et al (*Diabetes* 1989;38[2]:30A) studied the response of retinal capillary endothelial cells of humans in vitro to human growth hormone (hGH) stimulation. They determined, using long-term cultures of retinal endothelial cells from normal, postmortem human eyes, that exposure to hGH (200 ng/mL x 4 days) after the second passage in the presence of 10% horse serum, resulted in a $55 \pm 9\%$ greater cell number versus controls. Tritiated thymidine incorporation was stimulated at hGH concentrations as low as 1.2 ng/mL. Thus, physiologic concentrations of hGH stimulated mitotic activity of highly purified human retinal capillary endothelial cells. These studies suggest a direct responsiveness of the retinal endothelium to hGH. Dills et al (*Diabetes* 1989;38[2]:5A) measured insulin-like growth factor I (IGF-I) serum levels in 876 subjects with diabetes diagnosed at 30 years of age or older. Proliferative retinopathy was found in 15.6% of the insulin-taking population (N = 488). After controlling for duration of diabetes, glycosylated hemoglobin, blood pressure, proteinuria, and age at diagnosis, higher levels of IGF-I were associated with an increased risk of proliferative retinopathy in those subjects taking insulin. The authors suggest that

high IGF-I levels may be a factor for the development of proliferative retinopathy. Grant et al (*Diabetes* 1989;38[2]:56A) measured vitreous concentrations of IGF-I and -II by radioimmunoassay in 40 subjects with retinopathy and 18 nondiabetic subjects. Seventy-two percent of the diabetic subjects had vitreous concentrations of IGF-I capable of inducing increases in chemotaxis of human retinal endothelial cells (>5.0 ng/mL). IGF-II concentrations in the vitreous exhibited a distribution similar to IGF-I levels, and the concentrations of both correlated moderately with their serum concentrations.

Horber and Haymond (*Diabetes* 1989;38[2]:56A) studied the insulin resistance induced by hGH and prednisone in nondiabetic subjects. Glucose and leucine oxidation after an 18-hour fast, and during gut infusion of glucose and amino acids, was measured. Subjects were studied after 7 days of placebo, hGH 0.1 mg/kg/day, prednisone 0.8 mg/kg/day, or hGH plus prednisone. Fasting glucose was similar during the placebo and hGH administration, but was elevated during prednisone administration and during the combination of hGH and prednisone. Leucine oxidation was increased by prednisone but decreased by hGH administration and unchanged during combined treatment. By indirect calorimetry, glucose oxidation was similar in all groups. Insulin levels were higher during combined therapy than during placebo, hGH, or prednisone treatment. In summary, the insulin resistance of hGH and prednisone was demonstrated to be additive. The authors concluded that the insulin resistance of hGH and of prednisone may be caused by independent mechanisms. Prednisone decreased fat oxidation and increased leucine oxidation, whereas hGH treatment did the opposite. hGH and prednisone may reciprocally regulate oxidation of protein and fat, while decreasing the efficiency of glucose disposal.