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LRA by ELISA/ACT[®]

CLINICAL PEARLS UPDATE#6

Diabetes

October 6, 2003

Dear Colleague:

Insulin resistance (Syndrome X), type 1 diabetes, and type 2 diabetes affect 15-75 million Americans according to the American Diabetes Association. Successful comprehensive management using LRA by ELISA/ACT[®] tests and treatment plans are illustrated in the attached abstract reports.

Functional, *ex vivo* lymphocyte response assays (LRA by ELISA/ACT) offer the most advanced tests available for determination of the individual's responses to the widest available range of substances tested by any lab in the world.

We are grateful for the opportunities to be of service to you and your patients.

Sincerely,



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Lab Director

Vaarala O. The gut immune system and type 1 diabetes. *Ann N Y Acad Sci* 2002;958:39-46.

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Accumulating data suggest that the gut immune system plays a role in the development of autoimmune diabetes: (1) Diet modifies the incidence of autoimmune diabetes and the phenotype of the islet-infiltrating T cells in the animal models of human type 1 diabetes; (2) gut-associated homing receptor beta7-integrin is found on the islet-infiltrating T cells in both human type 1 diabetes and in the animal models of autoimmune diabetes; (3) mesenterial lymphocytes from young NOD mice are able to transfer diabetes to healthy recipients; (4) autoantigen feeding modifies the disease development in the animal models (prevents or accelerates autoimmune diabetes). In humans, a link between the gut immune system and type 1 diabetes has also been suggested. Early introduction of cow milk formulas in infancy may increase the risk of type 1 diabetes. We have demonstrated that primary immunization to a beta cell-specific autoantigen, insulin, occurs in the gut by exposure to cow milk formulas, which contain immunogenic bovine insulin. **The induced antibody and T cell responses to bovine insulin cross-react with human insulin.** In children at genetic risk who developed beta cell autoimmunity, bovine insulin-binding antibodies increased during follow-up in contrast to autoantibody-negative children. This suggests that insulin-specific immune response induced by dietary insulin may not be controlled in children prone to beta cell autoimmunity. The gut immune system has a key role in controlling insulin-specific immunity induced by dietary insulin. Indeed, indications for aberrant function of the gut immune system have been reported in type 1 diabetes, such as intestinal immune activation and increased intestinal permeability. Research on the gut immune system in human type 1 diabetes is needed to reveal the role of oral immunity in this disease.

Orchard TJ, Olson JC, Erbey JR, Williams K, Forrest KY, Smithline Kinder L, Ellis D, Becker DJ. Insulin resistance-related factors, but not glycemia, predict coronary artery disease in type 1 diabetes: 10-year follow-up data from the Pittsburgh Epidemiology of Diabetes Complications Study. *Diabetes Care* 2003;26(5):1374-1379.

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OBJECTIVE: To determine the independent risk factors for coronary artery disease (CAD) in type 1 diabetes by type of CAD at first presentation.

RESEARCH DESIGN AND METHODS: This is a historical prospective cohort study of 603 patients with type 1 diabetes diagnosed before 18 years of age between 1950 and 1980. The mean age and duration of diabetes at baseline were 28 (range 8-47) and 19 years (7-37), respectively, and patients were followed for 10 years. Patients with prevalent CAD were excluded from the study. Electrocardiogram (ECG) ischemia was defined by Minnesota Code (MC) 1.3, 4.1-3, 5.1-3, or 7.1; angina was determined by Pittsburgh Epidemiology of Diabetes Complications (EDC) study physician diagnosis; and hard CAD was determined by angiographic stenosis $>$ or $=50\%$, revascularization procedure, Q waves (MC 1.1-1.2), nonfatal myocardial infarction (MI), or CAD death.



RESULTS: A total of 108 incident CAD events occurred during the 10-year follow-up: 17 cases of ECG ischemia, 49 cases of angina, and 42 cases of hard CAD (5 CAD deaths, 25 nonfatal MI or major Q waves, and 12 revascularization or $>$ or $=$ 50% stenosis). Blood pressure, lipid levels, inflammatory markers, renal disease, and peripheral vascular disease showed a positive gradient across the groups of no CAD, angina, and hard CAD ($P < 0.01$, trend analysis, all variables), although estimated glucose disposal rate (eGDR) and physical activity showed inverse associations ($P < 0.01$, trend analysis, both variables). In addition, depressive symptomatology predicted angina ($P = 0.016$), whereas HbA(1) showed no association with subsequent CAD.

CONCLUSIONS: These data suggest that although the standard CAD risk factors are still operative in type 1 diabetes, greater glycemia does not seem to predict future CAD events. In addition, depressive symptomatology predicts angina and insulin resistance (eGDR) predicts hard CAD end points.

Note: We believe the comprehensive repair treatment guide, available as an option with LRA by ELISA/ACT tests, if requested, provides the best current therapy for sustained remissions in insulin resistance, as well as type 1 (insulin dependent) and type 1 (non-insulin dependent) diabetes.

