

A.Cicognani, L.Mazzanti*, O.Parisini*, A.Pellacani*, O.Tassinari*, V.Venturoli*, S.Sandri*, A.Forabosco*, E.Cacciari.
2nd Pediatric Clinic, University of Bologna and Chair of Hystology and Embryology, University of Modena, Italy.
DIFFERENCES IN GLUCOSE TOLERANCE IN TURNER'S SYNDROME DEPENDING ON AGE.

Carbohydrate homeostasis was evaluated in 41 Turner-syndrome (mean age 11.5±2.7, range 5-16yrs) and in 25 short normal girls (mean age 10.8±2.7, range 6-16 yrs) by means of OGTT. Impaired glucose tolerance was present in 31.7% of patients and in 8% of controls ($p < 0.025$). Mean glucose at 60' ($p < 0.05$), 90' ($p < 0.01$), 120' ($p < 0.05$), glucose peak ($p < 0.005$), and the integrated curve ($p < 0.005$) were significantly higher in the patients. Mean insulin levels were lower than in controls and the difference was significant at 30' ($p < 0.05$) and for the mean peak ($p < 0.05$). The insulinogenic index was lower in the patients ($p < 0.005$). Subdividing all the subjects into 2 groups (older or younger than 12 yrs) we found that while in the 17 patients < 12yrs mean glucose level was higher than in the 18 controls of the same age with significant difference at 60' ($p < 0.025$), 90' ($p < 0.005$), 120' ($p < 0.05$) and for the peak ($p < 0.05$) and the integrated curve ($p < 0.01$), no differences were present in the 24 patients > 12yrs whose glucose profile was similar to that of the controls. Both the Turner groups however had mean insulin values lower (the difference was significant at 120' for the first group and at 60', 120', 160', peak and area for the 2nd group) and an insulinogenic index in the 1st group ($p < 0.005$) significantly lower than the controls. In the older Turners, insulin release, although lower than in the controls, shows better metabolic efficiency and this could be due to the low or absent estrogen levels of these patients.

S.Salardi*, E.Cacciari, U.Volta*, G.Biasco*, S.Partesotti*, A.Reggiani*, A.M.Baldoni*, A.Balsamo*, A.Cassio*, S.Zucchini*
2nd Pediatric Clinic, 2nd and 3rd Clinical Medicine, University of Bologna, Italy.
PREVALENCE OF COELIAC DISEASE IN TYPE I DIABETES MELLITUS: A STUDY PERFORMED VIA TESTS FOR ANTIGLIADIN ANTIBODIES.

The association between diabetes mellitus and coeliac disease has been described a number of times. By using tests for antireticulin antibodies, Maki et al. found a greater prevalence of the disease in diabetic subjects. In our opinion, this method is not wholly reliable, which led us to study the problem using the test for antigliadin antibodies (AGA) by immunofluorescence (IFL-AGA) or microenzyme-linked immunosorbent assay (ELISA-AGA). This technique appeared to be more specific and more sensitive (Cacciari et al.) in identifying children with coeliac disease. We examined 132 subjects with type I diabetes (66 m, 66 f) with age ranging from 2 3/12 to 22 7/12 years. Antigliadin antibodies were assayed from 0 to 17 2/12 years after diagnosis of diabetes. 8 subjects were seen to be positive with either one technique or the other: all subjects for IgG, 7 out of 8 for IgA. These subjects underwent duodenal biopsy (4th portion). In 1 case crypt hyperplasia with total villous atrophy was observed, while 3 patients had a crypt hyperplasia with severe partial villous atrophy. These 4 patients were diagnosed as probably suffering from coeliac disease since other causes of alteration to the mucosa similar to those observed are practically unknown in children. All subjects were positive for IFL-AGA belonging to class IgG. No positive patients had shown signs of malabsorption or diarrhoea. Prevalence was 1 : 33. It is probable that genetics might shed light on the relationship between these two diseases, both diseases being associated with HLA B8 and DR3 antigens.

JM.Saudubray*, F.Brunelles*, A.Lombes*, P.Czernichow, W.Gepts* and C.Nihoul-Fekete*.
Hôpital des Enfants Malades, Paris, France, and Vrije University, Bruxelles, Belgium.
HYPERINSULINISM IN INFANCY: TOPOGRAPHICAL LOCALISATION OF A PANCREATIC FOCAL LESION BY TRANSHEPATIC PORTAL CATHETERISM, SELECTIVE BLOOD SAMPLING AND INSULIN MEASUREMENT.

Severe hypoglycemia was documented in a 3 months old child and hyperinsulinism was ascertained by glucose-insulin measurement in several blood samples. To further understand the cause of this hyperinsulinism, retrograde splenic vein catheterism was performed by transhepatic puncture of the portal vein. Blood samples (n=14) were taken in the splenic vein from the tail to the isthmus and in the outcoming vein from the head. In one sample high insulin (140 μ u/ml) other samples ranging from 10 to 40.5) was documented suggesting a secreting lesion localised in the isthmus of the pancreas according to the localisation of the tip of the catheter. During surgery a 3mm lesion was found by lens examination of the pancreas at the exact place indicated by selective catheterism and insulin assay. Hypoglycemia resumed immediately after partial pancreatectomy and the child remained normoglycemic at 3 months follow up. Histological analysis of the removed pancreas confirms the presence of a single focal lesion with normal size nuclei in the β -cells of the remaining part of the gland.

In conclusion: As reported in adults selective portal catheterism is of value in the localisation of a secreting lesion of the pancreas in infantile hyperinsulinism. This introduces a rational approach in the discussion of the extent of the pancreatectomy.

P.Amendt*, K.-D.Kohnert* (Introd. by R.Illig)
Childrens Hospital, Humboldt University, Berlin and Central Institute of Diabetes, Karlsburg, German Democratic Republic.
THE HYPERINSULINEMIC HYPOGLYCEMIA IN INFANTS AND CHILDREN. A STUDY ON 9 CASES.

Circulating levels of blood glucose, immunoreactive insulin (IRI) and C-peptide immunoreactivity (CPR) were measured in 6 infants (4 had islet cell adenoma and 2 had nesidioblastosis) and 3 children (all had islet cell adenoma) with hyperinsulinemic hypoglycemia. The ratio blood glucose : insulin on several days had high value for diagnosis of hyperinsulinemic hypoglycemia. The oral glucose load gave variable results, and the arginine infusion was without abnormality of hormone secretion. After intravenous administration of somatostatin, the suppression of CPR was more prominent than the inhibition of IRI. Hormone secretion after diazoxide infusion ranging from paradoxical stimulation to transient decrease of IRI or CPR. Intravenous injection of actrapid results in suppression of CPR secretion in most cases. In two patients we could diagnosed the pancreatic distribution, by measuring IRI in the portal blood, preoperatively.

It is suggested, that the various stimulation or suppression tests do not differentiate hyperinsulinism caused by an islet cell adenoma, from that, caused by nesidioblastosis of the pancreas.

P.F. Bougnères, L. Castano*, J.L. Chaussain, M. Roger
Service d'Endocrinologie Pédiatrique, Hôpital Saint Vincent de Paul, Paris, et Fondation de Recherche en Hormonologie, Fresnes, France.
INSULIN AUTOANTIBODIES (IAA) PREDICT OVERT DIABETES MELLITUS (DM) IN CHILDREN.

We have measured IAA titers in 113 children: 36 had newly diagnosed but untreated type I DM (group I), 53 were first-degree relatives of type I DM (group II), 24 had mild fasting hyperglycemia (110-135 mg/dl) and no familial history of DM (group III).

After dextran-charcoal extraction of endogenous insulin, the binding of mono 125 I-human insulin (200 μ Ci/mg) was determined in serum by PEG precipitation. Insulin binding (IB) averaged $1.02 \pm 0.16\%$ (SD) in 35 healthy normoglycemic children (range 0.68 - 1.35). 14/36 of group I (39%) had IB higher than 5 SD ranging from 1.9 to 57% (average 11%).

1 patient in group II, aged 4 years had 14% IB, with high islet-cell antibody (ICA) titers (1/16) and decreased insulin response to IVGTT: $1' + 3' < 30 \mu$ U/ml. He became diabetic the following weeks. Similarly 1 child of group III had 3.7% IB, elevated ICA (+1/10), and almost no insulin response to IVGTT. The child became insulin-dependent DM 2 months later. No other children of any group had IB higher than 1.4%.

The present prospective data confirm the significance and specificity of increased titers of IAA for prediction of type I diabetes mellitus.

P.Betts* T.J. Wilkin*, M. Armitage*, E.McCaughy*
L.Scott-Morgan*, D.Lee* (Introd. by S.A. Greené)
Southampton General Hospital, Southampton, England
AUTOANTIBODY MARKERS FOR INSULINITIS IN THE FAMILIES OF INSULIN DEPENDENT DIABETICS

If specific markers for juvenile diabetes could be identified then future susceptible individuals could be recognised. Auto-antibodies to Islet Cells (ICA) and to insulin (IAA) were sought in 81 healthy, and insulin-naïve siblings (38 boys, 43 girls) of childhood Type 1 diabetics by immunofluorescence on cryocut human group 0 pancreas and by enzyme linked immunosorbent assay respectively. ICA were found in 9 (11.1%) siblings (age range 5 - 22 years) and IAA in 6 (7.4%) (age range 3 - 13 years). None of the ICA positive siblings were IAA positive. IAA binding was clearly high (mean $21.8\% \pm$ SD 6.8%: Normals $3.2 \pm 2.0\%$). IAA positive siblings were significantly younger than those who were negative and showed a female preponderance (5F : 1M). These pilot data suggest that either IAA and ICA are markers for subtypes of autoimmune insulinitis or (as we have previously proposed) IAA are markers for genetic susceptibility while ICA indicate active insulinitis.