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CYTOTOXIC ANTIBODIES FOR HUMAN PANCREATIC ISLETS IN PATIENTS WITH IDDM. M.Pocecco^,O.Radillo^,C. Betterle+, A.Nocera+,S. Perissutti^ and F.Tedesco*.^IRCCS, Burlo Garofolo, and *Istituto di Patologia Generale, Università di Trieste,Trieste,Italy;+Istituto di Semeiotica Medica,Università di Padova,Padova,Italy; +Cattedra di Immunologia,Università di Genova, Genova,Italy

Complement (C) fixing islet cell antibodies (CF-ICA) are regarded as a marker of active disease in IDDM patients, but their role in the pathogenesis of the disease has yet to be defined. We have evaluated the ability of CF-ICA to promote the assembly of the terminal C complex (TCC) and to be cytotoxic for human pancreatic islet cells. Sera were screened for ICA and CF-ICA on frozen sections of human pancreas by standard immunofluorescence (IF) and a mAb to C9 neoantigen was used to reveal bound TCC. CF-ICA were also tested by IF on islets purified from human pancreas by collagenase treatment and their cytotoxic activity was assayed on a cell suspension obtained from the islets by further trypsin digestion. The results were as follows: 1) Of 300 ICA+ sera examined, 34 were found to be CF-ICA+ and 17 of these were TCC+;2) Double IF staining showed presence of TCC only on insulin-producing cells;3) Purified viable islets could bind TCC when treated with TCC+ sera and human C and,as a result of this, islet cells were killed. We conclude that some CF-ICA may be responsible for the ß cell damage.

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LONG-TERM TREATMENT WITH RECOMBINANT HUMAN INSULIN-LIKE GROWTH FACTOR-I (rhIGF)FOR PATIENTS WITH EXTREME INSULIN RESISTANT DIABETES. Nobuo Matsuura, Pediatric Clinic, Tonan General Hospital, Sapporo, 060 Japan

IGF-I has similar chemical structure to insulin and can exert its biological action through specific IGF receptor and/or insulin receptor. Insulin resistant diabetes exhibit elevated plasma glucose and markedly increased insulin levels. Insulin administration even high dose has little or no effects on blood glucose levels.rhIGF-I was given to three patients with insulin resistant diabetes to find out whether hyperglycemia was improved with this treatment.

MATERIALS AND METHODS: Three patients with insulin-resistant diabetes(lipoatrophic diabetes, type-A insulin-resistant diabetes and leprechaunism) were subjects of this study. 0.4mg/Kg, twice a day of rhIGF-I (Fujisawa Pharm. Comp. Osaka) was given subcutaneously for 2-6 months. In one patient with lepechaunism whose plasma IGF-I level was extremely low was given by CSII. Blood glucose, plasma insulin, IGF-I , HbA1 were determined.

RESULTS AND CONCLUSIONS: HbA1 and fructosamine levels were decreased with IGF-I treatment. Plasma insulin levels were correlated with blood glucose. Plasma IGF-I levels were not correlated with glucose, insulin nor insulin/glucose ratio. These results suggested that IGF-I has no direct effects on insulin secretion but will lower the insulin levels by lowering blood glucose.

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TRANSIENT HYPOPARATHYROIDISM DURING DIABETIC KETO-ACIDOSIS.

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Phosphorus depletion which is a well known phenomenon occuring during diabetic keto-acidosis led to assess parathyroid hormone (PTH) secretion.

32 children (mean age 9) admitted with diabetic keto-acidosis were studied. They required IV insulin 0.1 U/kg/day, IV rehydration (Cl Na 9 ‰) and IV bicarbonates 14 ‰. Only 3 needed a phosphorus supplement.

Sequential serum native 1-84 PTH determinations (normal values 15-85 ng/ml) were done at day 1, 2, 8 and in outpatient clinic at day 30, as compared to all glucose and calcium metabolism serum parameters.

An obvious hypoparathyroidism exists at day 1 (mean 11 ng/ml range 1-30), especially as regards to subnormal serum calcium and magnesium levels, and remains on day 2 despite of hyperglycemia and acidosis resolution.

No statistical correlation was found with any glucose (serum glucose, bicarbonates...) or calcium (serum calcium, phosphorus, magnesium, $1,25(OH)_2D$...).

Serum PTH levels normalization was obtained at day 8 or more later at day 30.

So a transient hypoparathyroïdism occurs in keto-acidosis, but its pathophysiology remains unclear.

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EFFECTS OF ARGININ-INSULIN TOLERANCE TEST ON GLUCOSE AND GLYCEROL LEVELS IN PLASMA AND IN MICRODIALYSATE FROM THE SUBCUTANEOUS ADIPOSE TISSUE. C. Marcus, V. Margery, A. Kamel, B. Persson, M. Brönnegård, U. Ungerstedt. Departments of Pediatrics Pharmacology, Karolinska Institute, Stockholm, Sweden.

We have compared the changes in glucose concentration in dialysate and plasma and studied the effects on lipolysis in the subcutaneous adipose tissue with microdialysis during first the insulin and glucagon surge induced by arginin and thereafter under the insulin infusion in 6 children. Before the test, the mean plasma and dialysate glucose levels were identical. During the arginin infusion, plasma glucose levels increased whereas the dialysate levels decreased. After insulin, the dialysate and plasma glucose decreased similarily; there was no delay in the dialysate. The stress induced a rapid increase in blood glucose levels but the increase in the dialysate was significantly delayed. The dialysate glycerol decreased during the arginin infusion. After insulin, no further decerease was found. Instead, all subjects showed an increased lipolysis. In conclusion, differences between interstitial and plasma glucose levels were due to a local insulin effect combined with a slow diffusion rate between blood and interstitium. The catecholamine surge induced by the hypoglycemia partly overcomes the antilipolytic effect of insulin.

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THE PREVENTION OF FETAL DISTRESS IN DIABETIC PREGNANCIES

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Seventy-one diabetic pregnancies and one hundred healthy pregnancies were monitored, on two occasions between the 27th-32nd and 33rd-36th week of gestation, by standard biometric echography, behavioural state analysis (quiet state percentages (S1F) and activity state (S2F)) and umbilical artery Doppler velocimetry (UA) (Resistance Index or RI). Our purpose was to determine if behavioural state and Doppler velocimetry:

1) are different in normal and diabetic cases
2) are correlated,in diabetic cases, with maternal glycemia;
3) are predictors of some perinatal outcomes selected: emergency cesarean section (CS); Apgar score < 7 at 1st and 5th min.; Respiratory Distress Syndrome (RDS); Neonatal Hypoglycemia (NH); Neurological Injury (NI) (evaluated at the birth and at the IV month of life).

Our findings suggest:

* there are significant behavioural state and Doppler velocimetry differences between normal and diabetic cases;
* abnormal glycemia values are correlated with abnormal behavioural state and UA Doppler velocimetry values;
* S1F and S2F are negative predictive factors of fetal sufference, abnormal glycemia values and non balanced insulin therapy, unsatisfactory perinatal outcome and neonatal short-term follow-up;
* UA RI is an important factor in fetal sufference detection and negative perinatal predictor only if combined with abnormal behavioural state percentages.

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ABDOMINAL CIRCUMFERENCE INDEX; A NOVEL ANTHROPOMETRIC MEASURE PREDICTING METABOLIC COMPLICATIONS IN OBESE CHILDREN. K. Asayama, H. Hayashibe, K. Dobashi, N. Uchida, K. Kato and S. Nakazawa, Department of Pediatrics, Yamanashi Medical College, Tamaho, 409-38, Japan

To determine the best index of body fat distribution for prediction of metabolic complications, four skinfolds (biceps, triceps, subscapular and iliac) and three circumferences (abdominal, hip and thigh) were measured in obese children. Abdominal circumference (AC) index (ACI) was defined as AC^2/height. We calculated AC to hip ratio (AHR) and AC to thigh ratio (ATR), and explored the relation between these anthropometric variables and chemicals (immunoreactive insulin; IRI, triglyceride; TG, total cholesterol; TC, alanine aminotransferase; ALT, and apolipoproteins A_1, A_2, B) in fasting blood specimens. Sixty-six obese children (>120 % of standard body weight, SBW, for the height), 44 boys and 22 girls, ages ranging from 6 to 15 years, were studied. The IRI, TG, atherogenic index, apo A_2 and B correlated with % SBW in boys, but not in girls. On the other hand, TG and TC correlated with AHR and also with ATR in girls, but not in boys. ACI correlated with IRI, ALT and TG in both boys and girls. In stepwise multiple regression analysis assigning ACI as the dependent variable, explanatory variables selected were IRI, ALT and apo B in boys (R^2=0.539); ALT and apo B in girls (R^2=0.492). Trunk:arm skinfold ratio and % body fat calculated from skinfolds correlated with few blood chemicals. Thus, for the prediction of complications in both sexes, ACI was a better anthropometric index than either %SBW, AHR, ATR or skinfolds. These results suggest the involvement of visceral fat accumulation in progress of disease process in child obesity, as is the case in adult obesity.