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185 DETERMINATION OF RISK FACTORS PREDICTIVE OF HYPOGLYCEMIA IN INFANTS OF DIABETIC MOTHERS (IDM) : AN EFFICIENT METHOD, THE QUICK INSULIN RADIOIMMUNOASSAY (RIA).

Post natal hypoglycemia related to hyperinsulinism of diabetic women fetuses is presently the major complication of IDM. The aim of this study was to determine hyperinsulinism degree to lead to an appropriate metabolic management. Circulating immunoreactive C peptide provides a means of studying B cell function of IDM because insulin-antibodies cross the placenta ; but its RIA requires some delay and so is not usefull in practice. So, other criteria were successively investigated, and were compared to blood C peptide nmol/l / glucose mmol/l ratio (0.12 ± 0.01 sem in control group). No significant correlation with maternal HbA_1c % determined on prenatal period is found. There is no significant difference in serum glucosamine levels between IDM and controls. A statistical correlation (r_s 0.62 $p < 0.05$) with macrosomia index is found for an index > 1.2. It appeared a negative correlation (r 0.56 $p < 0.001$ n 35) with serum levels of branch chain aminoacids which is thought to be an indirect index of hyperinsulinism ; results were obtained in relative short time (24 h) : hyperinsulinism is found to a sum level < 200 mcmol/l. There is a close correlation with serum insulin determined by classical or recent quick RIA (r 0.98 $p < 0.001$ n 33). Results can be obtained within very short time (4 hours). So, actually, 3 repeated routine quick insulin RIA compared to relative blood glucose, offer a direct and rapid way to evaluate IDM hyperinsulinism and hypoglycemic risk, making possible an appropriate management.

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186 RELATION BETWEEN INSULIN AUTOANTIBODIES (IAA), ISLET CELL ANTIBODIES (ICA) AND COXSACKIE-B4- AND MUMPS-VIRUS SPECIFIC ANTIBODIES AT DIAGNOSIS OF INSULIN-DEPENDENT DIABETES MELLITUS (IDDM)

The study comprised 194 children and adolescents with newly diagnosed insulin-dependent diabetes mellitus (IDDM). Blood sample for IAA, both conventional (IF-ICA)- and complement fixing (CF-ICA) islet-cell antibodies was drawn before the first insulin injection and the data were analysed together with some clinical parameters. Coxsackie-B4- and mumps-virus specific antibodies (IgG, IgM and IgA) were measured at diagnosis and 2 months after. Definition for a recent viral infection was based on high IgM, IgG and IgA antibodies or fourfold increase in paired serum samples.
Sixty-one children (31.4%) had an insulin-binding exceeding that (2.8%) of 68 matched controls and 45 (73.8%) of them were positive for IF-ICA ($p<0.01$) and 32 for CF-ICA. Subjects with IAA were younger than IAA-negative patients (7.1 ± 0.5 vs.9.3 ± 0.3(±SEM);$p< 0.001$). IAA did not show any significant association to other endocrine disorders or to a positive family history of IDDM, the duration of symptoms before diagnosis, preceding infections and the degree of metabolic derangement at diagnosis nor did ICA. Patients positive for IF-ICA had higher titers of IAA (5.5 ± 0.9 vs. 2.5 ± 0.3 (±SEM);$p<0.01$) at diagnosis. Coxsackie-B4- or mumps-virus specific IgG-, IgM- or IgA-antibodies had no association to IAA and/or ICA at diagnosis. However, subjects with recent mumps infection (n=13) had higher IAA levels compared to the 181 subjects without($p<0.02$).
In conclusion this study substantiates on one hand the association between IAA and IF-ICA and dissociation between autoantibodies (IAA and ICA) and Coxsackie-B4- and mumps-virus specific antibodies on the other. However, the relationship between recent infection and autoantibodies remains to be confirmed.

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187 THE EFFECT OF GROWTH AT ADOLESCENCE ON INCREASED INSULIN REQUIREMENTS OF DIABETICS.

Accelerated growth at adolescence maybe partly responsible for the increased insulin requirements often seen in diabetic children at this time. We have studied growth velocity (ΔHt) in diabetic girls (diagnosed >2 years) who were either pre-adolescent (PA), intrapubertal (IP) (Tanner Stage II or more) and pre-menarcheal or post-Menarcheal (PM) and related this to insulin dose and diabetic control. Overall, there was an inverse relationship between glycated haemoglobin A_1 (HbA_1) and insulin dose (ID) (u/kg/d) (r -0.38 = p 0.01) and the slope of this regression allowed calculation of an index of insulin resistance (IIR) for each patient. (Relative theoretical insulin dose required to achieve HbA_1 = 10%.)

	ID (u/kg/d)	HbA_1 (%)	ΔHt (cm/yr)	IIR
PA	.99±.25	12.41±2.29	6.02±1.09	.79±.23
IP	1.34±.19	13.15±4.26	6.55±2.79	1.05±.42
PM	1.13±.28	14.26±5.76	1.49± .93	1.13±.45

Diabetic control worsened as puberty progressed and IIR increased despite the expected slowing of growth in late puberty. There was no significant relationship between ΔHt and IIR. These results suggest that accelerated growth plays a relatively small part in determining increased insulin requirements at adolescence and longitudinal studies in individual children are required to determine it more precisely.

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188 RAISED RENAL THRESHOLD FOR GLUCOSE IN THALASSEMIC PATIENTS WITH DIABETES MELLITUS

Diabetes is a common complication in older children and adults with thalassemia major. During insulin therapy we often observe discrepancies between blood and urine glucose levels. In order to assess the renal threshold for glucose, the relation of blood glucose to urinary was studied in 15 insulin and in 9 glibenclamide treated diabetic patients with thalassemia. Mean age 16.4 years, M/F ratio 9/15, frequently transfused, serum ferritin (500-12.800ng/ml). None had consumed ascorbic or salicylic acid prior to testing. Blood area and creatinine normal. Blood and urine glucose were tested simultaneously on several occasions in each diabetic and in ten during O.G.T.T. Blood glucose was estimated by glucose oxidase method and urine glucose by Clinistix and Benedict's method. In 3/24 renal threshold for glucose was <10mmol/L. In 21/24 although blood glucose were 11.6-20.1mmol/L, glycosuria did not occur. These patients showed glycosuria with blood glucose levels (13.8-22.6mmol/L). We have no obvious explanation for this phenomenon. It is concluded that thalassemic patients with diabetes have raised renal threshol for glucose. Metabolic control should be assessed by frequent blood glucose estimations.

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189 ANTIGLIADIN ANTIBODIES (AGA) IN THE SCREENING OF CELIAC DISEASE (CD) in IDDM.

To select the children with CD, the AGA serum determination has been recommended. Using this screening test we have tried to establish the prevalence of CD in 103 IDDM patients. We studied 53 F and 50 M, 3.4 to 24.7 years old, diabetic from 3 to 156 months. None of them had symptoms of malabsorption. In 102 patients the height curves were normal; in the remaining patient short stature and delayed puberty (not related to metabolic control) were present. AGA (immunofluorescence) was found in 9 of 103 (6.7%) patients. Eight had IgG class only and one both IgG and IgA-AGA. Seven of positive patients for IgG or IgA underwent small bowel biopsy. As expected, flat intestinal mucosa was found only in the patient positive for IgA-AGA and with growth disorders. At the present, the prevalence of CD in our patients is 0.97%. The IgA-AGA determination is particularly recommended in the diabetic children with growth disorders unrelated to metabolic control, because a CD symptom less may be detected.

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190 EARLY ALTERATIONS OF GLUCOSE METABOLISM IN PREPUBERTAL OBESITY (pPOb).

The liver, muscles and adipose mass of adults with long-lasting obesity are insulin resistant. This explains why, despite chronic hyperinsulinism, they produce and utilize glucose at a similar rate than normal adults. We studied (d_2-glucose tracing, iv somatostatin, euglycemic clamp) 7 children (13 ± 0.5 yrs), obese (176 ± 9% ideal BW) for 5 ± 0.5 yrs, gaining 13.5 ± 1.4 kg kg/yr. Normoglycemic (82 ± 4 mg/dl) and hyperinsulinemic (22 ± 4 μU/ml) in the fasting state, they produce 2.5 times more glucose (295 ± 18 mg/min) than age-matched controls (C) and than obese adults. The similar increase of glucose utilization suggests a large glucose uptake by the adipose tissue of pPOb. Normalized to BW, the glucose uptake of pPOb (3.6 ± 0.2 mg/kg.min) equalled that of C (3.7 ± 0.2). This indicates that the main component of BW in pPOb, adipose tissue, takes up a similar relative amount of glucose than the main component of BW in C, lean body mass (as opposed to obese adults). Suppression of insulin by somatostatin reduced glucose utilization by 110 ± 19 mg/min in pPOb (C: 41 ± 14), as expected from an insulin-sensitive enlarged adipose mass. But hyperinsulinic clamp increased glucose uptake in pPOb (250 ± 20 mg/M^2.min, insulin 402 μU/ml) much less than in C (366 ± 31, insulin 366 μU/ml), as expected from insulin-resistant muscles.
Glucose overproduction by the liver, overutilization by adipose tissue contrasting with muscle insulin resistance characterize recent obesity in prepubertal children.