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Microalbuminuria in adolescents with type 1 diabetes

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Ninety-three adolescent patients with type 1 diabetes (45 male) and 81 healthy control subjects (36 male) took part in a cross-sectional study, where the incidence of microalbuminuria in adolescence (urine albumin excretion rate AER 20–200 μg/min) was assessed by timed night-time urine samples. Pubertal development was evaluated by Tanner staging.

Persistent microalbuminuria (AER 20–200 μg/min in three consecutive timed urine samples) was detected in five diabetic patients (7%), and their mean AER was 62.4 μg/min (range 24.0–159.0 μg/min). All patients with microalbuminuria were girls, one patient was prepubertal, one in late puberty (Tanner stage IV), and the remaining three postpubertal. The mean AER was 4.7 μg/min (range 0.2–14.0) in the normoalbuminuric diabetic patients and 3.7 μg/min (range 1.0–14.0) in healthy controls. Among the controls there were two boys who had AER values of 44 and 75 μg/min in their first sample, but the microalbuminuria was transient when re-assessed.

The mean GHbA1c value was significantly higher in the patients with microalbuminuria than in those with normoalbuminuria [10.8 (1.6)% vs. 8.4 (1.6)%, $p < 0.001$]. The mean age of the patients with microalbuminuria was 14.6 years (range 10.8–17.6 years), diabetes duration 7.9 years (range 3.9–15.6 years), systolic blood pressure (BP) 114 (10) mmHg and diastolic BP 65 (10) mmHg, and these characteristics were not significantly different from those seen in the patients with no microalbuminuria. Neither was there any difference in the prevalence of type 1 diabetes or hypertension in first degree relatives between the patients with microalbuminuria and those without.

We conclude that microalbuminuria may sometimes be detected already in prepuberty, and that poor metabolic control and female gender predispose to the development of microalbuminuria in adolescents with type 1 diabetes. Our results indicate that diabetes duration and familial predisposition to systemic hypertension seem not to play a major role in the development of the first signs of microalbuminuria in adolescence.

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Hepatomegaly in children with IDDM (3 case reports)

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Issue: Liver damage in patients with IDDM may result of abnormal glycogen storage in the liver due to prolonged hyperglycemia or of steatosis as a consequence of adipositas and insulin resistance. Accumulation of glycogen in the liver is reported to be fully reversible, whereas steatosis occasionally leads to cirrhosis with organ failure. Both disorders are not surely distinguishable by ultrasound imaging and require different treatment. Other causes of hepatopathy have to be excluded. If they are additionally present, liver damage might aggravated.

Case report: We report 3 adolescents out of a population of 174 juvenile diabetic patients presenting hepatomegaly and transient elevation of liver enzymes. These patients had been suffering from IDDM 3, 4 resp. 10 years before liver disturbance became evident.Needle biopsy revealed primary glycogen storage in patient 1 and 2 and steatotis in patient 3. Additional hepatic stressors such as heterocygote alpha1-antitrypsine-deficiency (M2S) and a history of hepatitis B in pat. 1 was noted. In pat.1 and 3 hyperlipoidaemia (complicated by pancreatitis in case 3) was found. There were laboratory findings compatible with a disturbance of mitochondrial intermediary metabolism in patient 1 and 2.

After one year of follow up, duplex ultrasound showed an abnormal flow of the hepatic veines of pat. 2, indicative of beginning portal hypertension.

The course of hepatopathy will be discussed with regard to the HbA1c.

Conclusion: In children with IDDM it is important to follow up liver size and its function tests regulary. When hepatic disturbance is observed, histologic examination should be executed.

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Acute pancreatitis due to uncontrolled diabetes mellitus in a 14 year-old Moroccan girl

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Although pancreatitis is well known, this is not the case for acute pancreatitis resulting from bad gylcemic control, especially in the absence of ketoacidosis.

We report the case of a 14 year-old Moroccan girl, diagnosed of type 1 diabetes mellitus since the age of 10. Her HLA-DQ genotype was A1B1.AZH/A4B2. During the first three years after diagnosis, she had good glycemic control. In October 1996 the control get bad and HbA1c became higher than 12%, due to lack of compliance. The insulin regimen was changed from 2 to 4 daily injections, but the glycemic control was still worsening with a HbA1c at 13.3%. In January 1997, she came to the emergency unit of our hospital with abdominal complaints and vomiting. Blood pH was 7.38, glycemia 247 mg/dl and the urine contained a large amount of glucose without ketone bodies. Serum lipase was very high at 571 IU/l ($N < 60$) and amylase at 114 IU/l ($N < 82$). Further investigations couldn't demonstrate any metabolic, infectious or immunologic origin for the pancreatitis. After 10 days of good glycemic control, pancreatic enzymes returned to normal. About three months later the patient came again to the emergency unit with stomach pain but without vomiting. Blood pH was 7.30, glycemia 756 mg/dl and there was important ketonuria. Serum lipase and amylase activities were elevated at 1158 and 380 IU/l, respectively. HbA1c was at 10.5%. After 2 weeks, serum amylase returned to normal but serum lipase stayed elevated at 145 IU/l. An abdominal CT Scanner showed an oedema of the pancreas. Endoscopic retrograde cholangiopancreatography was normal. Viral serology was negative. In May 1997, HbA1c was at the upper nomal range (6,1%) and serum lipase was normalized.

In summary, this 14 year-old patient presented two successive episodes of acute pancreatitis as a consequence of bad glycemic control. Ketoacidosis was absent during one of the two episodes. The mechanism responsible for acute pancreatitis after bad glycemic control with(out) ketoacidosis warrants further explanations.

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Ambulatory 24 hrs blood pressure monitoring in diabetic children and adolescents: A pilot study

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Background: Prevention and early treatment of hypertension in diabetic patients is one of the major targets. A recent article reports in a group of adult normoalbuminuric subjects affected by IDDM that normal circadian variation of blood pressure is disturbed (Wester P. et al., J. Chromatogr. 415:261–288, 1994). The aim of our study was to examine the 24 hrs ambulatory blood pressure profile in well-controlled normoalbuminuric, normotensive (assessed by classic method) diabetic children and adolescents in order to show ''incipient hypertension'' and to find out a possible correlation between blood pressure and duration of diabetes, metabolic control, iatrogenic hyperinsulinism, insulin-resistance and sympathetic nervous system activity.

Patients and methods: We have studied 15 diabetic patients (age range 5.8–27.8 years; 9 M and 6 F) divided into three groups according to the duration of the disease: Group A less than 5 years (4 M and 1 F; aged 12.9 ± 4.5 years), group B from 5 to 10 years (3 boys and 2 girls; aged 15.2 ± 5.4 years) and group C more than 10 years (2 boys and 3 girls; aged 22.2 ± 4.3 years). The sample size was calculated in order to achieve a power of 0.90 in detecting at least 15 mmHg variation (estimated SD 8 mmHg). We studied also 8 healthy controls (6 M and 2 F; aged 13.9 ± 5.2 years) comparable with the patients for age and BMI. We have examined in all subjects the following parameters: 24-h oscillometric ambulatory blood pressure and heart rate (every 15' during the day and 30' during the night) (TM2421, And and D Co. Ltd, Tokyo, Japan), anthropometric examination, body composition by skinfolds and BIA.We measured also catecholamines level (adrenaline, noradrenaline, epinephrine, norepinephrine, dopamine) in a 24hrs urine collection and in plasma (in diabetic group only) in basal conditions. Data are given as mean $\pm$ SD. Anova, multiple regression analysis and simple regression were used for statistical analysis.

RESULTS: Mean systolic and diastolic blood pressure, adjusted for height and heart rate, studied both in the 24hrs period, and separately for day-time (from 7a.m. to 10 p.m.) and night-time (from 10 p.m. to 7 a.m), and urinary cotecholamines were similar in diabetic and control group and within the three diabetic subgroups. The normal circadian variation of blood pressure in diabetic subjects was conserved. Plasmatic catecholamines were similar also in the three diabetic subgroups. Mean systolic and diastolic BP of all subjects studied was below 75th centile (Soergel et al., J. Pediatr.130:178–84,1997) except in 4 diabetic subjects of group C (3 of them had night-time systolic BP $>$ 95th centile and 2 of them night-time diastolic BP $>$ 95th centile). We found a statistical significant direct correlation between nocturnal diastolic BP and HbA1c ($r = 0.64$;$p < 0.05$) while we didn't found any correlation between BP and AER or Insulin requirement. Moreover diurnal diastolic BP resulted significantly correlated to plasmatic adrenaline and dopamine ($p < 0.05$).

Conclusion: Although these preliminary results have to be confirmed by larger studies, they suggest that ambulatory blood pressure monitoring may detect early increase in blood pressure something which is not clinically apparent yet.

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Utilising the partial remission phase for a multicentre audit of glycaemic control in the first year after diagnosis

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There is increasing evidence that tight metabolic control in the first year after diagnosis is associated with continuing better control, prolongation of the partial remission phase (PRP) and better preservation of β-cell function. At least 30–40% of children should exhibit a PRP with near-normalisation of glycated haemoglobin (GHb) levels.

Aims: To review GHb levels in 10–20 children diagnosed sequentially in 1997 in 19 different paediatric centres (mainly within one geographical UK region) and followed for one year (a) to measure the proportion achieving a GHb within each centre's reference range (WRR) (b) to compare the proportion of children in each centre achieving a GHb WRR.

Results: 27% of 239 children achieved a GHb WRR in the first year independent of the age of the child. GHb WRR in different clinics ranged from 0% to 74% (in 9/19 clinics 30% or more children achieved GHb WRR). The average number of GHb estimations in different clinics ranged from 1.1 to 5.7 per child per year.

Conclusions: (a) Many clinics in the UK perform too few GHb measurements to adequately audit metabolic control in the first year (b) More attention should be paid to the assessment of good control soon after diagnosis (c) A yearly audit of GHb in the first year after diagnosis might provide a useful QUALITY STANDARD for childhood diabetes.

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Diabetic renal disease in children with newly diagnosed type 1 diabetes mellitus

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The aim of the study was to estimate the kidney volume and function in children with newly diagnosed type 1 diabetes mellitus.

56 patients (36 male, 20 female) at the age 6–16 years ($11{,}4 \pm 2{,}8$ years) participated in the study. In the first week of

disease kidney size was estimated by ultrasound method. After 3 months the examination was repeated and renal clereance examination (GFR, ERPF — radioisotopic method) were performed. At the same time urinary albumin excretion rate and C-peptide level was estimated by radioimmunological methods. During clereance examination glicaemia and blood pressure were monitoring. The patients were divided into two groups according to GFR values. 23 children were included into normofiltrating group (GFR < 131 ml/min/1,73m^2) and 33 to hiperfiltrating group. There were no differences in the age of patients, level of HbA1c and C-peptide between groups, but dose of insulin was higher in hiperfiltrating patients (0,49 v. 0,34 UI/kg/day; $p < 0{,}05$). ERPF (666 v. 551ml/min/1,73m^2, $p < 0.01$) and kidney volume (156 v. 128 cm^3/1,73m^2) was greater in hipefitrating group. At 3 month the decreasing of kidney volume was observed in both groups. The positive correlation was found for GFR with UAE ($r = 0{,}4$; $p < 0{,}01$) and GFR with kidney volume ($r = 0{,}4$; $p < 0{,}005$) and for FF with systolic blood pressure ($r = -0{,}3$; $p < 0{,}05$). In the hiperfiltrating patients the relationship was noted for GFR and SBP($r = 0{,}4$; $p < 0{,}05$) and for FF with blood pressure (SBP $r = 0{,}52$; $p < 0{,}02$ and DBP $r = 0{,}5$; $p < 0{,}05$). It was not observed the correlation for GFR and ERPR with actual glicaemia. We concluded that kidney hiperfunction and hipertrophy not depending of actual metabolic control was observed in 60% children with newly diagnosed type 1 diabetes mellitus.

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Prevalence of microalbuminuria in prepubertal children with insulin dependent diabetes mellitus

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There is little information on the prevalence of microalbuminuria in childhood diabetes particularly in prepubertal age.

We evaluated a population of 346 prepubertal diabetic children recruited from 12 Italian Departments of Pediatrics. These patients must comprise at least 80% of the eligible patients in each clinic. Persistent microalbuminuria was defined using classic definition (AER ≥ 20 μg/min/1.73m^2 in at least 2 of 3 timed overnight urine samples). The inter-laboratory coefficient of variation in albumin urine concentration was evaluated by an external quality control programme: it was 18.9% around 2.9 mg/dl, but less than 10% (at the concentration in the microalbuminuric range (29.6 mg/dl). Glycated haemoglobin was measured locally and data were then individually readjusted to the local mean and SD of normal and expressed in number of SD above the mean of normal. Clinical data of entire population were: Age: 7.8 ± 2.7 yrs; Duration of disease: 2.7 ± 2.4 yrs; HbA1c (SD above normal): $+2.84 \pm 2.7$ SD; AER: 15.04 ± 29.75 μg/min/1.73m^2.

Among prepubertal patients 4.5% had persistent microalbuminuria. In multiple stepwise regression analysis only HbA1c ($p < 0.0001$) and age ($p < 0.01$) were significantly associated with AER.

Our data support the hypothesis that metabolic directly affects AER, even in prepubertal children.

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No indications for delayed chylomicron clearance in adolescents with diabetes mellitus type 1

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Background: A delayed clearance of chylomicrons (CM) has been identified as a risk factor for atherosclerosis. In adults with type 1 diabetes (DM1), a delayed clearance of CM has been found. It is not known, if CM clearance is already delayed in adolescents with DM1 and herewith could contribute to their risk for atherosclerosis. CM clearance is classically quantified by a vitamin A test, by determination of plasma disappearance of retinyl palmitate (vitamin A). Theoretically, CM clearance can also be investigated by stable isotopically labeled oleic acid. For the disappearance from plasma of ^{13}C-oleic acid and the appearance of $^{13}CO_2$ in breath is related to chylomicron metabolism. In the present study the vitamin A and stable isotope test were compared.

Patients and methods: We determined in adolescents with DM1, whether CM clearance was delayed ($n = 9$), compared to controls ($n = 4$), and whether CM clearance was correlated with their glycemic control (HbA1c > 9.5%, $n = 4$; HbA1c < 8.7%, $n = 5$; age 17–21 years). After an overnight fast, all individuals ingested a standardized fat-rich meal, together with vitamin A (50.000 U/m^2) and ^{13}C-oleic acid (5mg/kg). Before and for 6 h after ingestion, breath and plasma samples were obtained to quantitate breath $^{13}CO_2$, and plasma concentrations of retinyl palmitate, triglycerides, cholesterol, ^{13}C-oleic acid, glucose and FFA.

Results: Fasting plasma cholesterol concentration was significantly higher in DM1 patients with HbA_{1c} > 9.5%, compared to the other 2 groups ($p < 0.05$), and appeared significantly correlated with glycemic control (HbA_{1c}, $R = 0.80$, $p < 0.01$). Postprandially, the percentual changes in plasma triglyceride concentration were not significantly different between the 3 groups. After reaching a maximum value at 2 h after administration of vitamin A, postprandial retinyl palmitate concentrations decreased, in each group at a similar rate ($p = 0.89$). For 6 h after ^{13}C-oleic acid administration, both plasma ^{13}C-oleic acid concentrations and breath $^{13}CO_2$ expiration rates were virtually identical in the 3 groups. Yet, whereas retinyl palmitate showed a peak value at 2 h after administration, ^{13}C-oleic acid and $^{13}CO_2$ showed a continuous increase during the 6 h time period. This observation indicates that the ^{13}C-oleic acid test provides different information on the fate of absorbed lipids compared to the vitamin A test.

Conclusions: Present data indicate that in adolescents with DM1, a delayed CM clearance does not contribute to the increased risk of atherosclerosis. In contrast to fasting plasma

cholesterol concentrations, chylomicron clearance appeared not correlated with level of glycemic control.

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Study of complement in children with type 1 diabetes

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Low levels of C_4 and C_3 have been found in adult type 1 diabetic patients and to be associated with a high risk of microvascular complications. We analyzed C_3 and C_4 changes in children with type 1 diabetes and looked for a possible influence of metabolic control and autoantibodies and an association with renal function studies after a disease duruation of 5 years. 58 diabetic children between 1.3 and 15 years we studied at diagnosis and in 17 of them yearly measurements during the first 5 years were performed. All patients received biosynthetic regular and NPH insulins and were without signs of infection at evaluation. C3 and C4 were determined by nephelometry.

Compared to the mean results in age matched healthy control group, both mean C_3 (99 ± 21 vs 118 ± 21 mg/dl) and C_4 (16 ± 6 vs 21 ± 8 mg/dl) were significantly lower at diagnosis. Initial C_4 levels were below normal range in 13 patients. At diagnosis C_4 levels were unrelated to age, pubertal stage, glycated haemoglobin, the titer of circulating pancreatic autoantibodies and the HLADQ genotype. No significant changes in C_4 conc. were observed in the following 5 years. In all but to of the 7 patients with initials C_4 levels followed in longitudinally C_4 remained below normal range. No relationship was found between the C_4 levels at diagnosis and level of microalbuminuria and glomerular filtration after 5 years of disease.

In conclusion, low C_4 were found in 22% of type 1 diabetic children and were not associated with an increased antibody response, worse metabolic control or a higher succeptibiligy of early renal complications.

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Visual evoked potentials in newly diagnosed diabetic children

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Electrophysiological tests reveal an abnormal function of the visual system in patients with insulin-dependent diabetes mellitus (IDDM) but there are no data about visual function in newly diagnosed diabetic subjects. The aim of our paper was to assess whether electrophysiological abnormalities in visual functions exist in newly-diagnosed diabetic patients free of any fluorangiographic signs of retinopathy.

Fourteen IDDM patients (7 male and 7 female) with mean $\pm$SD age 19.1 ± 3.9 years and with HbA_{1C} $9.8 \pm 1.9\%$ and without clinical and laboratorial signs of diabetic ketoacidosis and/or hypoglycemia, and twenty control subjects (10 male and 10 female) with mean age $\pm$ SD 19.7 ± 4.7 years were evaluated. Visual evoked potentials (VEP) were recorded basally and after photostress when blood glucose levels ranged between 90 mg/dl and 125 mg/dl in all patients. This study showed that P100 latency was significantly higher in diabetic patients compared to control subjects (100.2 ± 6.2 ms vs 92.1 ± 3.9; $p < 0.01$), while N75–P100 amplitude was similar in both groups (9.1 ± 0.9 μV vs 9.0 ± 0.9; ns). The recovery time of VEP after photostress was equivalent in diabetic patients and control subjects. In fact, after photostress, a significant ($p < 0.01$) increase in P100 latency was observed in diabetic patients (after 20 sec: 105.7 ± 3.1 ms; after 40 sec: 100.1 ± 3.0; after 60 sec: 99.1 ± 2.9) and in control subjects (after 20 sec: 116.9 ± 2.9 ms; after 40 sec: 113.2 ± 2.6; after 60 sec: 110.1 ± 3.6). The mean increments in P100 latency found at 20, 40 and 60 sec after photostress were similar and the difference between controls and diabetics continued to be significant ($p < 0.01$) at every time. Moreover, the mean percentage decrements of N75–P100 amplitude found at 20, 40 and 60 sec after photostress were significantly higher in diabetics than in control subjects (26.9 ± 3.1 vs 15.09 ± 1.9; $p < 0.01$).

These data suggest that early functional abnormalities of the optic nerve can be detected also at the onset of the diabetes. It is probable that at this stage of disease no pathological change of the optic nerve fibers is present and these abnormalities can be reversible after the achievement of a tight metabolic control.

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Serum leptin levels in children and young adults with insulin dependent diabetes mellitus

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Leptin, a hormone secreted by adipocytes, is elevated in serum of obese subjects and decreases after weight reduction. It is unknown whether the concentration is affected by insulin-dependent diabetes mellitus (IDDM) and if there is a difference in serum leptin levels before and after the puberty. The aim of our work was to evaluate serum leptin levels in children and young adults (obese and non obese) with type 1 diabetes mellitus.

Serum leptin levels were measured in three groups of diabetics (prepubertal, pubertal and young adults, divided in obese (defined as BMI > 35) and non obese. Three groups of sex, age and body mass index (BMI) matched healthy subjects served as controls.

In patients with type 1 diabetes serum leptin levels were similar to those of control subjects in all the three groups (prepubertal non obese diabetics vs controls: 6.5 ± 1.1 vs 6.1 ± 1.2 ng/ml; prepubertals obese diabetics: 28.7 ± 2.9 vs 27.1 ± 2.0 ng/ml; pubertal non obese diabetics: 8.7 ± 1.5 vs 8.1 ± 1.2 ng/ml; pubertal obese diabetics: 36.1 ± 3.9 vs 37.5 ± 3.5; young adult non obese diabetics: 9.9 ± 1.7 vs 9.7 ± 1.9; young adult obese diabetics: 37.8 ± 9.1 vs 38.1 ± 10.1.

A significant difference in serum leptin levels ($p < 0.001$) was found between obese and non obese subjects both in diabetics and controls. A weak but not significant increase of leptin values was found from three groups of prepubertals to young adults in both diabetics (non obese: 6.5 ± 1.1 vs 9.9 ± 1.7 ng/ml; obese: 28.7 ± 2.9 vs 37.8 (9.1.) and controls (non obese: 6.1 (1.2 vs 9.7 ± 1.9; obese: 27.1 ± 2.0 vs 38.1 ± 10.1). A

significant relationship of serum leptin levels with BMI ($p < 0.001$), female sex ($p < 0.001$) and age in both diabetics and control group was present.

These data suggest that IDDM does not modify serum leptin concentrations. Moreover, the association between obesity and leptin concentration was similar in diabetic and non-diabetic subjects.

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Serum concentration of insulin-like growth factor-I (IGF-1) in a diabetic child with retinopathy

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The aim of this study was to investigate the possible role of insulin-like growth factor-I (IGF-1) in the pathogenesis of diabetic retinopathy and severity of retinal damage. Serum IGF 1 levels were assayed using radiometric assays. There were 38 boys and 28 girls at age (CA) ranged from 8,3 to 19,1 years (mean ± SD, 13,7 ± 2,1 years). The duration of disease was 0,7 to 13 years (mean ± SD, 7,8 ± 2,9 years), their glycozylated haemoglobin HbA1 ranged from 6,5% to 14,2% (mean ± SD, 10,4 ± 1,7%). Retinopathy was evaluated by definition of visual acuity, ophtalmoscopy, retinal photography and video recording with laser scan camera (CLSO, Zeiss). We divided our patients into four groups according to their ophtalmological status: group A (n = 23, 34,8% without retinopathy), group B (n = 36, 54,5% with nonproliferative retinopathy), group C (n = 3, 4,5% with proliferative retinopathy) and group D (n = 6, 9% with cataract). No significant difference was found between groups in CA, sex, IDDM duration, BMI, HbA1c, doses of insulin. SDS of serum IGF-1 level in group A was −0,83 ± 0,04, in group B was −1,1 ± 0,03, in group C it was −0,16 ± 0,5 and in group D −0,7 ± 0,16, respectively. We did not observed differences between serum IGF-I and the severity of diabetic retinopathy among the groups included in the study. In conclusion, the above data suggest that serum levels of IGF-I are not related with presence and the degree of diabetic retinopathy.

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Benchmarking of diabetes-care in the southwestern part of the Netherlands: First steps of a quality improvement program

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Diabetes care needs improvement as stated by both St. Vincent and Cos declarations and supported by studies such as the DCCT. However, feasibility and goals for children and adolescents are not well defined. It is obvious from recent studies that improvement of care is required in these patients regarding the early start of microvasular disease. To define which aspects of care need improvement and how to achieved this, the existing care needs to be evaluated. Similar to the Hvidore study we asked pediatricians in the South-western part of the Netherlands (approx. 5 million inhabitants) to participate in a cross-sectional bench-mark study. Centers completed a questionnaire on their diabetes care and sent 1 sample of each patient for HbA1c determination to 1 (central) lab. In addition, patient data (age, duration, weight, length, insulin scheme, and severe hypoglycemia's as well as socio-demographic parameters) were collected. This interim analysis includes 14 of 21 participating centers (24 in the region) and 504 children (6 mo −20 years, M:F = 0,9). Mean HbA1c (central lab) was 8.7% ± 1.3. Male and female HbA1c's did not differ in average, but females had higher levels from 8 year to 14 years old and needed more insulin. Our data show relative high values of HbA1c in schoolchildren (7−10) and in particular young boys (< 7 yrs) tended to have high HbA1c levels. Sixty-two percent were on 2 injections, 3 injections in 8% and 28% were on 4 injections. Eleven kids used CSII. Sixty-seven percent of those on two injections had a 30/70 premixed insulin at breakfast and of those 75% had the same insulin at dinner. All on 2 injections were on premixes and only 24% of these had a different insulin at dinner. No significant center differences were found in the questionnaire and HbA1c differed between 8.2 and 9.0% (av.). Children and adolescents do not tend to 'shop' for other clinics as only 3% had another diabetes team than the one that diagnosed the disease.

Conclusion: HbA1c levels in the Netherlands are, even with rather 'stringent' insulin schemes with a majority on premixed insulins, comparable to other countries. Improvement could come from more flexible use of insulins, a more frequent use of more frequent insulin injections and from the study of center differences.

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Health monitoring in Moscow's children with onset of type 1 diabetes in 1994. Follow-up study

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Since 1994, the cohort of 124 newly diagnosed patients aged from 2 to 16 yrs. are enrolled in this study. The age distribution of cases was as follows: 0−4 yrs. — 16,94%, 5−9 yrs. — 40,32%, 10−14 yrs. — 42,74%. Diabetic coma was present in 17,7% of newly diagnosis' patients. 71,7% of the patients had ketoacidosis at the time of diagnosis. A viral infections preceded manifestation of diabetes in 58,7% of the cases. Few parents of the patients have been believed that diabetes is bound up with severe postvaccination reactions (7,25%) or psychological stress (5,64%). 10,5% of the patients had never been breast-feeding. 39,5% of the children with diabetes have affected relatives.

The patients were divided into three groups. Group A comprised of 64 patients who were educated and performed daily self-control for 4 yrs. Group B comprised of 28 patients who were educated but rarely performed self-control. Group C comprised of 32 patients who were not educated. The subjects in group A had a better glycaemic control (mean HbA1- 10,0 ± 2,1%, HbA1c- 8,4 ± 1,8%). Subjects in group C

had a poorer glycaemic control (mean HbA1- 14,8 ± 2,1%, HbA1c- 11,1%1,9%).

The height expressed as SDS in total group was 1,36 ± 0,2 (from −3,72 to 4,48) in 1994 and SDS was 0,07 ± 0,1 (from −2,91 to 3,02) in 1998 ($p < 0,05$). Reduction of heigth SDS was observed in both boys and girls. The patients in Group A had higher SDS 0,16 ± 0,13. Correlation was found between SDS and glycaeted haemoglobin level ($p < 0,05$). In 1998 the prevalence of complications was 19,3% for illegibility of a disk area, venous dilatation and isolated cases of microaneurism, 1,6% for background retinopathy, 1,6% for cataracta (mean age 11yrs.), 8,06% for microalbuminuria (mean age 12,5 yrs.), 5,64% for delayed puberty (age 13–15 yrs.).

In conclusion: These results indicate that quality of metabolic control was associated with self-monitoring. Height SDS was higher in the educated patients who daily performed self-control. Diabetes complications were found in the pre-pubertal children.

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Improving glycaemic control in adolescents by using appropriate meters and focused support

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Glycaemic control in adolescents with Type 1 diabets is ofter poor and controversy surrounds home blood glucose monitoring (HBGM). Diaries can be unreliable and misleading. Some adolescents do not test, do not record results, falsify results or fail to present results at clinic. We suspected that the frequency of HBGM and presentation of results in our adolescent population increased following the introduction of Profile meters. These meters can be downloaded and patients are given printouts of their results. We therefore evaluated the information which we had available from 40 of adolescents (22M) who had received the same package of care. Their HbA1c (reference range 5.0–6.5%) was measured at clinic and they were given a Profile meter. They were then visited at home, by a diabetes nurse specialist for adolescents (DNSA) twice between clinic visits. Their results were downloaded, discussed, and appropriate action on results was agreed between the patient and the DNSA. They returned to clinic after using the meters for 4 months when HbA1c was measured again. The median (range) number of tests in the first month of using the meters was 43 (4–135) and 35 (4–123) in the fourth month of using the meters. Mean HbA1c fell from 10.4 ± 1.8% prior to use of the meters to 9.5 ± 1.5% after using the meters for 4 months ($p = 0.004$). The total number of tests performed did not correlate with changes in HbA1c. We conclude that despite a fall in the median frequency of HBGM, HbA1c improved significantly following the introduction of the Profile meters in conjunction with intensive personal support from the DNSA. This package empowered patients to take action on their results and improve their gylcaemic control significantly.

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An audit of glucagon use in youth with type 1 diabetes

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Glucagon is a potent hormone that rapidly reverses severe hypoglycemia (hypo) in Type 1 diabetes (DM). We teach all families about Glucagon and encourage its availability. Our objectives were to assess: i) families' knowledge about Glucagon and indications for its use; and ii) the frequency of sever hypo and use of Glucagon in 1997. We devised a Glucagon Evaluation Questionnaire (GEQ) and administered it to families of 189 (63%) of 298 children and adolescents who attended our Diabetes Clinic over a 6 week period. Nonresponders did not differ from the participants in mean age or HbA1c. Subjects included 91M, 98F; mean ± SD age 11.6 ± 4.0 yr; DM duration 5.0 ± 3.9 yr; HbA1c 8.6 ± 1.4%; with 89 on ≥ 3 daily insulin injections. Of the 189 subjects, 143 (76%) reported no severe hypo in 1997; 17 (9%). Moderate hypo requiring assistance but not Glucagon; and 29 (15%). Severe hypo in which Glucagon should have been used. GEQ scores were higher in the Moderate group (7.3 ± 1.7 out of 10) than in the No or Severe groups (6.9 ± 1.9 & 7.1 ± 1.9 respectively, $p = 0.002$). The age of the Severe group (10.6 ± 4.4 yr.) was lower than the No or Moderate groups (11.9 ± 3.8 & 11.4 ± 4.0 yr., respectively, $p = 0.03$). Glucagon was used in only 15 of 29 subjects experiencing severe hypo (52%), even though 86% had it at home. Reasons for not using Glucagon included expiration of the Glucagon Vial; hypo away from home; panic during the episode; forgetting how to use Glucagon. Thus, while most families have a good understanding of what Glucagon is and when it should be used, they actually use it in only about half the episodes of severe hypo. This suggests that families require routine reminders about indications for using Glucagon and regular review of how to give it.

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Multidimensional, international quality of life questionnaires for children / adolescents with IDDM, and their families.

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Metabolic control and Quality of Life (QOL) are closely associated, and QOL assessment is fundamental in evaluating medical outcome. QOL of child and family was assessed using self-rating questionnaires on 2,103 adolescents from 17 countries in Europe, Japan and North America. Adolescents used the Diabetes Quality of Life Questionnaire (DQOL) and multidimensional self-rating QOL questionnaires were constructed for parents and health professionals. The questionnaires were translated into 14 languages, focus group and lay panel tested, back translated and validated for each country.

1979 (92%) adolescents, median age 14 (range 10–18) yrs, completed the questionnaire. Item completion rates were high

(85% adolescents; 85% parents, 93% health professionals) indicating good face validity. High Cronbach's α co-efficient levels (0.91 adolescent; 0.80 parent; and 0.87 health professional) showed internal consistency. The overall DQOL score for adolescents was 101.5 (SD 22.9). The statistical relationships of QOL between adolescents, parents and health professionals were low (range r = 0.12–0.36). These DQOL, parent and professional questionnaires have also been used to assess the relationships between Quality of Life, the perceived burden of diabetes and the measured level of metabolic control.

The psychometric adequacy and acceptability of these instruments indicates their value as QOL assessment tools which are brief, easy to administer and score in a busy clinical setting. They also enable comparisons across countries and languages and the development of international health outcome parameters. The inclusion of parent and health professional perspectives completes a comprehensive assessment in this quality assurance approach.

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Ketoacidosis remains the main diagnostic circumstance for IDDM in children

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The analysis of 129 IDDM patients with onset before the age of 15 years, consecutively registered in the Bucharest Diabetes Centre in the years 1993–1997 showed the following clinical characteristics: 1. A slight male predominance (67M/62F); 2. Mean age ($\pm$SD) 10.2 $\pm$ 3.1 years; 3. Family history for IDDM in the first degree relatives in 3.1% of cases; 4. Prediagnostic period (the delay between the onset of the first symptoms and diagnosis) of 17.1 $\pm$ 8.2 days; 5. The majority of cases (129, i.e. 82.9%) were diagnosed in ketoacidosis and in 67 cases (51.9%) the ketoacidosis was severe (pH $\geq$ 7.20 and or total-$CO_2 \geq$ 10 mEq /l); 6. In 88 cases (60.8%) the triggering factor for metabolic decompensation was a viral or microbial infection; 7. The number of consultations in the symptomatic prediagnostic period in which the diagnosis of diabetes was missed was 1.7 $\pm$ 0.8% suggesting that the main direction of education action must be towards general practitioners.

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Initial clinical approach of childhood type 1 diabetes mellitus in the Netherlands

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Aim: To analyze the clinical approach (i.v. infusion therapy and/ or admission to hospital) and the clinical parameters influencing these decisions at diagnosis.

Methods: Nation-wide study using questionnaires to attending paediatricians of 0–14 year olds, who were reported as type 1 diabetes mellitus to the Dutch Paediatric Surveillance Unit.

Results: 671 patients with first insulin injection between 1/1/93 and 31/12/94 were included. Ascertainment was 91.2%. Diabetic ketoacidosis (DKA) i.e. p H < 7.30 was present in 26% of the cases. Admission to hospital was significantly related to pH (r = −013), hydration status (r = 0.09) and blood glucose level (r = 0.10). After exclusion of cases with clinical reasons for admission, 251 children in good clinical condition at diagnosis remained. 193 of these 251 cases in good condition were admitted to hospital. 154 cases were admitted to hospital due to DKA (pH < 7.30, 171 cases) or impaired consciousness and/or hydration status (154 cases). 52 patients were admitted for psychosocial reasons and 43 cases for other clinical reasons.

I.v. infusion was more closely related to pH (r = 0.28), hydration status (r = 0.17) and blood glucose (r = 0.13) in logistic regression (p < 0.00001). Patients were assigned to three groups, according to the facilities of the hospital: Group 1: No diabetes nurse practitioner (DNP) available for paediatric patients (68 cases); Group 2: DNP services available inside the hospital (521 cases); Group 3: DNP services available, including home visits (82 cases). The groups did not differ in age, duration of symptoms, glucose level and blood pH. The percentage of cases in DKA (pH < 7.30) was not different between the groups. Outpatient treatment was started in 11% of the cases, but varied significantly between the groups: Group 1: 10.3%, Group 2: 5.4%, Group 3: 45.1% (χ^2 p < 0.00001). The distribution of the 193 patients admitted to hospital in good clinical conditon in the three groups was: Group 1: 27 cases (40% of the group), Group 2: 165 cases (32%) and Group 3: 1 case (1%).

Conclusions: Assessment of the clinical condition of the patient was a the main basis for the decision to admit a child to hospital at clinical onset of type 1 diabetes mellitus. However, correlation coefficients are low since 193 children (29% of all cases) were admitted to hospital despite good clinical condition. The availability of services of diabetes nurse practitioners only influenced the number of admissions if home visits were included as a standard procedure.

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Diabetes-manifestation in children (0–14 years) in Berlin before and after German reunification: incidence, clinical presentation and initial therapeutic management

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Aim: To compare the diabetes incidence, clinical presentation and therapeutic management during the initial hospitalization of children with type 1 diabetes before (1988) and after German reunification (1996–1997).

Methods: Data of all children aged 0–14 years that were diagnosed in the respective years in the 8 Berlin Children's Hospitals with manifestation of type 1 diabetes was analyzed

(capture-mark-recapture-method; sources: 1) admission records, 2) independent regional patient organization).

Results: A total of 173 children living in Berlin were identified. The incidence (r/10.000/a) increased from 6,93 (95%-CI 4,86–9,60) in 1988 to 14,13 (11,05–17,79) (1996) and 13,16 (10,16–16,78) (1997), respectively. The proportion of children manifesting with severe ketoacidosis (pH < 7,20) remained high: age < 4 years: 30%, 5–9 years: 14%, 10–14 years: 22%. In all three years half of the children were admitted to the hospital by their pediatrician. The proportion of children admitted by private practitioners with a non-pediatric specialty rose from 2,8% (1988) to 13,8% (1997). The proportion of children diagnosed upon admission in the emergency room was approximately 20% at all three time points. The average duration of the initial hospital stay varied largely between the different hospitals ranged from 12 to 33 days. It remained unchanged over time (median: 17 days). Furthermore, significant differences between hospitals were apparent with respect to the initial therapeutic management: the average insulin dose on the second day of admission varied between 0,4-1,1 IU/kg.

Conclusions: The Berlin Data confirms reports on the increase in the incidence of childhood diabetes in the past years in Germany. No differences in the initial clinical presentation were apparent despite significant changes in the general delivery of care. Significant differences in the initial therapeutic management between hospitals are present with unknown consequences for the long-term prognosis and quality of care.

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Quality of diabetes care: developing a patient care database for continuous monitoring individual patients and the centre performance

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Paper based databases (ordinary medical records) are not the proper tool to monitor longitudinal data as will be obtained in patients with chronic diseases like diabetes mellitus. Moreover, as many will have experienced, the relatively absence of firm checks on completeness of data or even the inconsistency of data lead to possible false conclusion in individual patients. It is also time consuming to produce a simple centre profile and is especially troublesome to detect possible complex relationships between different parameters of the disease.

With further improvements in software packages making it easier to build your own database, seems easy but often fail due to lack of knowledge to built a robust programming code or the programmers misinterpretation of the clinicians needs. Lack of standardisation of the field definitions and underlying table structure makes the database vulnerable for possible loss of data when moving to another improved database. Standardisation of field definitions is an important issue to fulfil, not only to prevent future loss on investments but also to make it possible to merge and compare data from different clinics and countries.

Nevertheless trial and error in designing a database are the necessary steps to rethink the needs and requirements of a database standard as well as the needs for the front end. The data standard is under current consideration of ISPAD.

We have developed a system accessible from different locations in the hospital where the clinicians and diabetes nurses record patient's data. This presentation will show the disease independent core (160 data items) which is linked to several disease specific tables (diabetes outpatient clinic, data on the diagnosis, insulin type and dosage) and tables consisting of specific measurements (growth, laboratory results). Most questions have formalised answers making data analysis easier. Laboratory data are inserted electronically from elsewhere. Output per patient will be shown in text and graphs. Listings are produced of patients who have not been seen or contacted in the last 3 months. Moreover, those who did not comply with our care or have a possible inappropriate insulin dose per Kg bodyweight for their age etc are shown. The database records every change in the data made and puts the old and new values in a report table together with the timestamp and the user thus providing ultimate safety.

In conclusion, it is our firm believe that the use of patient care database systems will undoubtedly improve the quality of care in centres and allow comparing of data between centres. Agreement upon a data standard should be one of the prime goals to achieve.

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Special outpatient diabetes department for young adult diabetics in Bratislava

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According to the law of the Slovak Republic for every patient after the time he reached 18 years of age is obligatory to change his pediatric doctor for the specialist dealing with adult people.

To decrease this great change we have established the special outpatient diabetes department for young adult people in the year 1986, which is situated at the Outpatient Department for Youngsters and Young Adult People in Bratislava. The practising diabetologist is pediatrician and member of the Children Diabetes Center of the Slovak Republic, who makes this job two times a week in the afternoon hours from 2 to 7 p.m.

Nowadays 255 patients are in evidence this department, 223 with type 1 diabetes, 13 with type 2 diabetes, 7 with impaired glucose tolerance, 11 with renal glycosuria and 1 with hypoglycemias. Majority of them are former patients of the Children Diabetes Center, part of them are university students, or young workers who are teporarily in Bratislava.

The whole patient cohort with diabetes (236) is in the age group 19–49 years. According to duration of diabetes 29 have duration 5 and less years, 67 patients 6–10 years, 112 patients

11–20 years, 28 patients 21–30 years. Diabetic retinopathy have 78 patients, 2 of them in prolipherative form and 7 are treated with lasercoagulation. Every patient without any pathologic finding is examined once a year, with pathologic finding two to four times a year. 10 patients have diagnosed diabetic neurpathy. Every patient with duration of diabetes 9 and more years is once a year examined in Diabetes Foot Center in Bratislava. 18 patients have hypertension and 10 hyperlipoproteinemia.

We have good experience with such special outpatient department for young adult diabetics and we advice to establish such units also in other bigger towns in Slovakia.

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Congenital anomalies in newborns of mothers with diabetes type 1 and gestational diabetes

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Aim of the study: 1) the incidence of congenital anomalies in children of diabetic mothers, 2) what factors of the mother influence the development of an anomaly or perinatal disturbances in the newborn. The investigations included 95 newborns of mothers with diabetes type 1 and gestational diabetes born in the years 1985–1995. 47 were offsprings of mothers with type 1 diabetes, 48 of mothers with gestational diabetes. All the children were examined twice after birth and at age 12 years. Performed were physical examinationsm, USG of the heart, abdomen, eeg, ekg. The parameters of mothers and children were analysed on the basis of a performed questionnaire. A statistical analysis was made. Analysed was the metabolic control of the mother during pregnancy. Calculated were hyper- and hypoglycemia during the I, II, III trimester, HbA_{1c}, edema, hypertension, glycosury, acetonury, proteinury. Planning of the gravidity, drug or alcohol abuse, diabetes in the family. Ascertained were congenital anomalies in 16% children of mothers with diabetes type 1 and in 12% in children of mothers with gestational diabetes. Most frequent were in both anomalies of the heart, urinary tract and bones.

Conclusion: 1) mothers diabetes type 1 and gestational diabetes are risk factors for congenital anomalies in the offspring, 2) intensive insulintherapy, planning of pregnancy reduces the risk of congenital anomalies in the child.

PU1

Diagnostics of the autonomic disorders in diabetic children

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PU2

Some factors for compensation insulin-dependent diabetes mellitus in children

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PU3

Subclinical hypothyroidism in children with diabetes mellitus type 1

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PU4

The influence of IDDM on intellectual development and CNS disorders in younger school age children

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PU5

Coxsackie types in acute infection at the childhood IDDM onset in Slovakia

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PU6

Some immunological findings in the childhood IDDM

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PU7

The average time delay between the birth and IDDM manifestation in Slovak children 1968–98

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PU8

Is motivation the major determinant of metabolic control in diabetic adolescent?

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PU9

Association between microabluminuria and retinopathy in children and adolescents with type-1 diabetes mellitus

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PU10

Insulin analog humalog ($LYS_{B28}PRO_{B29}$) in the therapy of two infants

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