

IA2-Ab POSITIVITY AT DM 1 MANIFESTATION IS PEAKING IN SEPTEMBER IN SLOVAK CHILDREN

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Background & Aims: Separate year seasons are connected with changing exo- and endogenous conditions, as viral infections or hormonal annual cycles. Similar cycling in pathogenetic parameters of DM 1 could help in revealing its pathogenesis. Question is posed: Is positivity rate for IA2-Ab autoantibody, determined at manifestation of DM in children, related to year season?

Material & Methods. There were 150 Slovak children, born 1981-2000 and manifesting DM1 1989-2001 aged 1-17 years, taken into investigation. Autoantibody to pancreatic protein tyrosin phosphatase (IA2-Ab) was investigated in blood plasma by RIA not later than one month after diagnosis. Results were evaluated as score 0 for negativity and score 1 for positivity. Cut-off-point value was 0.75 U/ml. Positivity score values were plotted versus days of year and processed by Halberg's cosinor to test significant ($\alpha=0.05$) presence of annual, semiannual and quarterly rhythm.

Results. Mean positivity score was 0.71: in 150 patients with newly diagnosed DM1 there were 71% IA2-Ab-positive. Annual rhythm for this positivity ($P<0.02$) peaked in November with double amplitude of 0.29 score, the semiannual one ($P<0.05$) in February and August with double amplitude of 0.22 score, and quarterly rhythm ($P<0.02$) in March, June, September and December with double amplitude of 0.31 score. Total range of estimated fluctuation was over 1.0 of score unit. Maximal proportion of children positive on IA2-Ab – with the mean estimated value of 1.0 of the score unit – was encountered in subjects manifesting DM 1 in September, a minimal one – with lower 95% confidence bound near to zero score value – in early May.

Conclusion. September maximum of IA2-Ab positivity, determined at the time of the manifestation of diabetes type 1 in Slovak children, has been found. It could correspond with late-summer peaking of coxsackie infections in Slovak children's population. No significant seasonality was detected for autoantibodies to glutamic acid decarboxylase nor to insulin.

INSULIN GENE POLYMORPHISM IN CHILDHOOD DM1: ITS RISK PATTERN RELATED TO YEAR SEASON OF BIRTH?

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Background & Aims. Recent studies find seasonal fluctuation in various parameters connected with pathogenetic and clinical features of childhood DM 1. Question was posed: does the proportion of children with the risk pattern, based on insulin gene polymorphism, cycle according their calendar date of birth?

Material & Methods. There were 98 Slovak children, born 1983-1999 and manifesting DM1 1992-2001 aged 1-16 years, taken into study. Two insulin single nucleotid polymorphisms of the insulin gene (-23 Hph I; 1127 Pst I) were typed by PCR-RFLP (courtesy of Dr. Peter Minárik, Novo Nordisk, Bratislava). Results for 1127 Pst I were expressed as score between the maximal (0) and minimal (2) risk. Seasonality of proportion of genetic risk in births was tested using daily arranged birth-risk score data for one fictive calendar year. Moving averages of risk score values, from 3 observations each, were plotted versus the days of year and processed by Halberg's cosinor procedure (programme by Kubáček & Valach) to test significance ($\alpha=0.05$) of annual, semiannual and quarterly rhythm.

Results. The mean risk score, based on insulin gene polymorphism, was 0.21. The only significant ($P<0.001$) periodicity was the semiannual one. Maximal risk proportion from insulin gene polymorphism is estimated for children born in March and September. The double amplitude, and thus the maximal range of the fluctuation is low – around 0.29 (0.12-0.44) of the score unit.

Conclusion. Significant cycling of insulin gene risk was found with the peaks in early spring and autumn.

**CLINICAL AND EPIDEMIOLOGIC FEATURES
CORRELATED WITH DIABETES MELLITUS IN CYSTIC
FIBROSIS (CFRD).**

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Background: Factors affecting CFRD development are not entirely clear.

Aim: To evaluate exocrine pancreatic insufficiency degree (as lipase/Kg /die intake), nutritional status (as BMI) and lung function (as FEV1% predicted) one year before CFRD onset and the association of CFRD with gender, family history for Diabetes Mellitus (DM), CF diagnosis reason (family history, screening, meconium ileum, symptoms) and preexisting severe hepatopathy (considered as esophageal varices presence).

Methods: The study population consisted of a group of 61 CFRD patients (males: 31; mean age of CF diagnosis: 5 yrs; mean age of DM diagnosis: 19 yrs). CFRD with fasting hyperglycemia (FH) was diagnosed in 36 patients and CFRD without FH in 25 patients. CFRD group was compared with a control group of 61 CF pts matched for year of birth and presence of pancreatic insufficiency.

Results: No significant differences were found between the two groups for all the examined parameters, except for the presence of preexisting hepatopathy (11/61 in the CFRD pts and 1/61 in the control group: $p < 0.004$), and FEV1 % predicted one year before CFRD onset (mean FEV1 predicted 57,71% in the 61 CFRD and 67,22% in the control group: $p < 0.04$)

Conclusion: Our study showed that patients with preexisting hepatopathy are more exposed to the risk of CFRD development. Gender, DM family history and all the investigated reasons for CF diagnosis do not have any prognostic value. A more compromised lung function was found in the year before CFRD onset in all CFRD patients, with or without FH.

**SCREENING FOR TYPE 1 DIABETES GENETIC RISK IN
NEWBORNS OF CONTINENTAL ITALY. PRIMARY
PREVENTION (PREVEFIN STUDY)**

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Background: Genetic patterns (HLA class II) and autoimmune response to various β -cell antigens have been demonstrated to play a very important role in T1DM pathogenesis. Early exposure to β -casein, - a cow-milk antigen - has been proposed as a possible trigger for the immune response. Vitamin D deficiency seems to play a crucial role in the development of β -cell autoimmunity, as vitamin D seems to act as an immunosuppressive agent.

Aim: To validate short-term efficacy of primary prevention strategies for T1DM in high genetic risk subjects (defined as HLA DRB1 03/DRB1 04, DQB1 0302, in absence of the protection allele DRB1 0403).

Methods: In this interventional study the enrolled subjects, at one month of age, are randomly assigned to one of the two groups of the trial (group A: Vitamin D supplementation and diet without β -casein for the first 12 months of life; group B: Vitamin D supplementation and free diet for the first 12 months of life).

Results: Up to now, after informed consent, we sampled cord blood from 5059 Caucasian newborns who were born in 10 Centers of Continental Italy and screened them for type 1 associated HLA class II markers. The enrollment started in February 2001; 31 newborns (0.6%) were found to be "high risk" for T1DM. This prevalence is lower than that reported in the literature (1.5-2%). 26 babies are now in long- term follow up, each randomized into one of the two groups of treatment. β -cell antibodies (GADA and IA-2A) are monitored every three months, as well as growth rate and other clinical data. If the child should have one of these antibodies, metabolic studies to assess insulin secretion (i.e. glucagon test) will be performed. None of the children has become positive for either GADA or IA-2A.

**THE INFLUENCE OF METABOLIC DISTURBANCES IN
DIABETES TYPE 1 AND THE ANTRAL-MODULLAR
REFLEX IN CHILDREN AND YOUNG ADULTS.**

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Background: Diabetic neuropathy is characterised by different disturbances of the somatic and autonomic nervous system and has an important influence on the prognosis and course of diabetes.

Aim: of the presented report is the evaluation of the state of static and dynamic balance through the appreciation of the atrial-medullar-reflexes in children and young adults with diabetes type 1.

Material: included 95 children and young adults, aged 6 to 28 years with diabetes type 1. The control group included 44 healthy individuals matched properly in sex and age, without otolaryngological diseases. In all the patients after anamnesis, clinical and biochemical examinations performed were ORL, stato-posturografical investigations with the posturograph PE6Z Model 04. Performed were statical sensorical and posturography. Ascertained were balance disturbances, head turbulences in 6 patients. In patients with diabetes in comparison with the control group observed higher parameters of the stabilogramms, statistical significant in the group of younger children. Shown were a significant increase of the disturbances in children with decompensated diabetes.

Conclusions: 1. Diabetes without complications or with only complications at a minor degree don't influence the atrial-medullar reflexes and the balance in the patients. 2. Observed were in children and adolescents with type 1 diabetes subclinical disturbances in the balance system. 3. Necessary may be a monitoring of the observed disturbances in the course of the disease.

TARGETED PEDAGOGICAL DEVICES MAY CONTRIBUTE TO PREVENTION OF SEVERE HYPOGLYCAEMIA

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Background and Aims: Severe hypoglycaemia is common also with modern insulin treatment. In spite of all health service efforts, learning is not always as effective as it needs to be. We have studied diabetes education by video and self-study leaflets at home and the costs for this type of intervention.

Materials and Methods: 332 type 1 diabetes patients aged 2-18 years were randomised to receive by mail one of the following:

- Two videotapes (17+18 min) and a leaflet where interviewed patients, parents and medical expertise reviewed important skills for self-control and treatment, aiming to prevent severe hypoglycaemia (*intervention n=111*).
- A videotape (13 min) and leaflet with general diabetes info (*controls n=111*).
- Only traditional treatment (*traditionals n=110*).

Assessment at start of the study and by mailed retrospective patient/parent questionnaires after 12 months and 24 months respectively.

Results: Intervention (and control) videos had been used after 12 months in the families median 2 times, range 1-10 (2, 1-20), and 49% (53%) had shown the videos to other people important for the diabetic child.

Attitudes in both groups were predominantly positive, within wide ranges.

Intervention patients at a higher extent indicated having learnt something useful from video ($p=0.0075$) and brochure ($p=0.0049$). Severe hypoglycaemia decreased in the intervention group, but treatment and HbA1c did not differ between groups.

SH any last 12 mo	At baseline %	After 12 mo %	After 24 mo %
Intervention	42	27 ($p=0.0394$)	24
Controls	34	37	40
Traditionals	37	31	35

SH= Severe hypoglycaemia self-reported as needing help by others, mo=months

The cost for reproducing the intervention videos to 100 patients was <EURO 500, lower than the cost for three visits at the diabetes polyclinic.

Conclusions: Mass-distributed self-study materials such as high quality video programs and leaflets for home use may be a complement to regular visits to a diabetes team and to other types of education. This method may contribute to the prevention of severe hypoglycaemia.

CONTINUOUS QUALITY DEVELOPMENT OF DIABETES MANAGEMENT IN DENMARK

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Background: In Denmark 170-180 children under 18 years of age are diagnosed with type 1 diabetes mellitus every year corresponding to an incidence of 18 per 100,000. International studies have shown that intensive diabetes management may delay the onset and slow the progression of late complications.

Aims: To describe and compare the management of children and adolescents with type 1 diabetes at the different centres in Denmark. As a part of the quality assessment process quality indicators for childhood diabetes have been chosen.

Methods: The results are based on data from the nation-wide Danish Registry for Childhood Diabetes. These data have been supplemented with data collected from two questionnaires and a centralised HbA_{1c} determination on all children. One questionnaire addressing the children's treatment and their opinion on the diabetes outpatient clinic was sent to all children under 18 years of age with diabetes (n=1335). Another questionnaire was sent to the health professionals at the 19 centres in Denmark managing these children. This questionnaire addresses the differences in the structure and process of care at the outpatient clinics.

Results: Preliminary results show a grand mean HbA_{1c} of 8.8% (normal range 4.3-5.8, mean 5.1%) with significant variation (p<0.001) among the centres (HbA_{1c} 8.2-9.7%). This difference remained after adjustment for the confounders age, sex, diabetes duration, and ethnical background. Further analyses aim to uncover if this difference persists during time. The rate of severe hypoglycaemic events varied significantly across centres (p<0.0001) but without any association with the HbA_{1c}-level. Suggested treatment target for HbA_{1c} was less than 9% for 0-6-years old and less than 8% for children above 7 years of age. Only 36% of the children reached these goals.

Conclusion: Significant outcome differences remain across centres after adjustment for case-mix. Only approximately 1/3 of the children reaches the suggested target levels for HbA_{1c}. Continuous quality development with intervention is needed to improve the quality of care of childhood diabetes in Denmark.

CHILDREN'S AND ADOLESCENTS' PERCEPTIONS OF THE FIRST DAYS OF HOSPITALIZATION ON DIABETES UNIT

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Background: The first stay in the hospital is always stressful and anxious experience for a child. It happens especially when hospitalization is sudden and connected with diagnosis of chronic illness – diabetes DM.

Purpose: The purpose of this study was to answer the questions: 1) What are children's and adolescents' the most frequent experiences connected with the first days on diabetology unit? 2) What are the differences between children's and adolescents'/girls' and boys' perceptions of their first days of hospitalization? 3) What kind of theme/elements are repeated on the pictures?

Patients and Methods: 98 patients (duration of DM ?1 year; age ?7) wrote short description of their first days on diabetology unit and 15 already diagnosed patients (age ?4) drew a picture showing their first day in hospital and told a few words about it. All patients were divided into 4 groups according to: 1) age: group I; children (7-12 yrs old; n=54), group II; adolescents (13-18 yrs old; n=54); 2) gender: group III, girls (n=52), group IV, boys (n=56). All contents of descriptions were categorized (8) after analyzing all oral and written descriptions.

Results: 52,8% of all participants considered invasion procedures (i.v catherization for infusion, pricking fingers for measuring blood glucose) as the most impressed experiences connected with the first days on diabetology unit. 44,7% of all patients pay attention to own emotional reactions (anxiety, suspense, astonishment) during the first day in hospital. Adolescents more often describe their emotions and physical symptoms than children ($p<0,05$). Children more often describe the role of other hospitalized children's support and more often suffer from reduction of physical activity connected with staying in bed ($p<0,05$). Girls more often describe their own and their families' emotions. 9 from 15 pictures show a person laying in a bed, attached to intravenous infusion.

Conclusions: The most stressful experience connected with the first hospitalization on diabetology unit is often repeated: invasion procedures. Contact with other children is very important for the youngest patients. Children and adolescents, especially during the first stay on diabetology unit connected with diagnosis of diabetes, should have possibility to express their emotions.

FOOT STATUS IN YOUNG TYPE 1 DIABETIC PATIENTS¹B.S. Olsen*, ²K. Larsen, ²B.Storm, ¹I.K. Larsen & ¹K.Dyrløv¹*Glostrup University Hospital and* ²*Steno Diabetes Center, Gentofte DK*

Background: Foot pathology is a major cause of morbidity and mortality in adults with diabetes. Good foot-care can prevent later serious problems.

Aim: To investigate the current foot status and foot-care behaviour in young patient with type 1 diabetes and estimate the significance of regular childhood foot-care and education.

Methods: 58 type 1 diabetic patients, 24 males, mean age 24.8 (\pm 3.4) years and mean diabetes duration 15.5 (\pm 3.6) years were evaluated at a normal visit in the out-patient clinic by the same chiropodist. The feet and footwear were examined and the patients filled in a questionnaire focusing on symptoms and foot care behaviour in childhood and at present. Mean HbA_{1c} was 8.1 (\pm 1.2) %. 77.6 % of the patients had normoalbuminuria (AER < 20 mg/min), 19 % microalbuminuria (AER \geq 20 and < 150 mg/min) and 3.4 % macroalbuminuria (AER \geq 150 mg/min). 57 % of the patients had diabetic retinopathy (level 1 to 3), and one patient had elevated VPT (> 19 V).

Results: Paresthesia occurred in 3 patients. 2 of these patients had absent Achilles and Patella reflexes and all of them had level 2-3 retinopathy. 19 % complained of intermittent pain in the feet, related only to current HbA_{1c} ($p=0.04$). 71 % of the patients had inappropriate footwear, 76 % had foot deformities including 22 % with LJM, and 24 % influencing the gait. 31 % had stiff-hand syndrome, 23 % hyperhidrosis, 26 % nail problems and 24 % callosities. Four patients had absent sensation for light touch, related to VPT ($p<0.0001$) and 3 of the 4 patients had level 2-3 retinopathy. 7 patients had absent Patella reflex and 3 of these had absent Achilles reflex as well. One patient had foot ulcer and abnormal sensation for light touch. One patient had lacking foot pulses. 16 % had skin pathologies including necrobiosis lipoidica (4), dermopathia diab. (5), and anhidrosis (1). At present 60 % of the patients did not visit a chiropodist, and as confirmed by other studies education did not result in better foot compliance in adulthood.

Conclusion: Even young patients with type 1 diabetes have a high incidence of minor foot problems and poor compliance to foot-care. To prevent foot complications, education and chiropody should be initiated early after diagnosis and the education repeated by the yearly foot-examination.

**CONTINUOUS SUBCUTANEOUS INSULIN THERAPY
IMPROVE AND STABILISE METABOLIC CONTROL IN
CHILDREN AND ADOLESCENTS WITH TYPE 1
DIABETES. 1-YEAR CLINICAL OBSERVATION.**

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Background: Good metabolic control in children and adolescents patients is strongly related to the individual possibility in realising the diabetes regimens like discipline in diet, regular self-monitoring and insulin injections. The method of continuous subcutaneous insulin infusion (CSII) in closely imitates natural delivery of insulin and in this method it is possible to increase the flexibility in diet and day-time. **Objective:** To evaluate the results received in group treated by CSII compared to the group treated by multiply daily injection (MDI) in the 1-year period. **Material and method:** we followed 88 patients (42M, 46F) treated by CSII (MinMed 507C, 508 -60 patients, Disetronic H-TRON V100 – 28p.). Av. age was 13.8 y <1,5y – 25y>, duration of diabetes 5,42 y. <0,5 – 13,8y>, the metabolic control av. HbA1c was 8,87 stD 1,43 <6,7-12,3>, the group treated by MDI (n=88 p.) was matched regarding the age, diabetes-duration and metabolic control. CSII method was proposed for youth diabetes patients as an alternative intensive insulin therapy. Psychosocial data were collected in the second part of the study. **Results:** The significantly improving in metabolic control was observed only in group treated by CSII HbA1c decreased Mean(-1,13) (p=0,0001), and in 1-year of follow-up was in similar levels: HbA1c-7,8 stD 1,21. In MDI group no significant difference was observed in HbA1c (8,91 stD 1,53, stEr0,16 → 8,97 stD 1,61; stEr0,17). Patients treated by CSII at the end of study significantly increasing BMI (Mean +0,45; p=0,015), but dose of insulin was lower-0,80j/kg/d (Mean-0,05, stD 0,15, p=0,0024). This trend wasn't in MDI group. The number of patients in poor metabolic control decreased from 36,4% to 11,1%. Adverse events: ketoacidosis was higher in CSII group 5,6/100/y in MDI-3,4/100/y. Severe hypoglycaemia 2,2/100/y in both groups, skin problems in CSII-2,2/100/y. Parents of patients using CSII have significantly higher feeling of satisfaction with treatment (t=4.418, df=41, p<0.05) and life (t=2.20, df=45, p<0.05). **Conclusions:** The pump therapy is more efficiency than pen therapy for diabetes children. It is the chosen method for poor controlled adolescents patients.

CHARACTERISTICS OF DIABETES AT PRESENTATION IN YOUTH WITH DIABETES

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Background: The incidence of diabetes (both type 1 and type 2) in young people is increasing across the globe. In the United States, the increase in type 2 diabetes in youth is more dramatic, a trend attributed to the increasing prevalence of obesity and sedentary lifestyle in children. Recently it has become apparent that diabetes classification requires added attention.

Objective: To determine the relationship between clinical characteristics at presentation with measures related to disease process, we examined the presence of diabetes autoantibodies (DAA), fasting and stimulated C-peptide levels, and insulin-like growth factor binding protein 1 (IGFBP-1) levels in an ethnically diverse group of youth presenting with diabetes.

Methods: The subjects were recruited shortly after diagnosis; age 8-17 years, 40 Caucasian, 11 Asian/Pacific Islander, 8 Hispanic, 3 African American, 1 Native American. A scoring system of objective clinical measures at diagnosis was used to divide subjects into clinical groups. Autoantibodies [glutamic acid decarboxylase-65 (GAD), insulinoma associated protein-2 (IA-2), islet cell antibodies (ICA), and insulin antibodies (IAA)] were obtained within two weeks of diagnosis. Fasting and stimulated C-peptide (standardized beverage mixed meal) and fasting IGFBP-1 were obtained within 6 weeks of diagnosis.

Results: Both fasting and stimulated C-peptide, as well as fasting IGFBP-1, correlated well with clinical classification, with C-peptide being highest in type 2 subjects (mean fasting 1.26 nmol/l, stimulated 2.15 nmol/l), lowest in type 1 subjects (0.19 nmol/l fasting, 0.43 nmol/l stimulated), and intermediate in the indeterminate subjects (0.36 nmol/l fasting, 0.83 nmol/l stimulated). DAA were present in the majority of subjects, in 19/28 type 2, 14/15 indeterminate, and 20/20 type 1 subjects.

Conclusions: Although measures of insulin secretion correlated with clinical features at diagnosis, there was a high frequency of positive DAA in all groups, including those with a clinical picture consistent with type 2 or atypical diabetes. Further studies of genetic risk/HLA and clinical course of diabetes in this heterogenous population are in progress.

**TRANSIENT FOCAL NEUROLOGIC DEFICITS (TFND)
ASSOCIATED WITH HYPOGLYCEMIA IN A CHILD
WITH TYPE 1 DIABETES MELLITUS**

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Transient focal neurologic deficits (TFND) associated with hypoglycemia and possibly due to cerebral vascular disease have been well described in adults, but only a few cases have been described in diabetic children. The exact etiology for TFND remains unclear. We present a Hispanic girl with type 1 diabetes who had multiple episodes of TFND associated with mild hypoglycemia.

She was diagnosed at age 2.5 years, and was followed by the authors while at New York Hospital-Cornell. At age 5.3 years she had the first episode of right hemiparesis with facial and body weakness. Serum glucose was 57 mg/dl, without other overt symptoms of hypoglycemia. Although hemiparesis resolved within five minutes, weakness persisted for two hours. Eventually she regained normal function of her right side. She had normal neurological exam with a normal head CT scan. MRI of the head and MRA study of the neck vessels and circle of Willis done within one month were unremarkable. She had normal EEG sleep study. She had no history of migraine headaches or seizures. Family history was negative for strokes, migraines or sickle cell disease. Follow up brain MRI and EEG 3 years later were unremarkable. At 8.6 years old she had normal nocturnal dipping of her blood pressures on 24 hour ambulatory monitoring, and no evidence of autonomic neuropathy per E/I heart rate variability at 6 breath/min. At age 8.7 years she had a second episode of right hemiparesis and dysarthria that lasted 45 minutes. Blood glucose was 56 mg/dl. Neurological exam, EEG study and brain MRI were normal. At age 9.6 years she had a third episode of hemiparesis lasting few minutes. Blood glucose was 54 mg/dl. No imaging studies were done. HbA1c at time of the 3 episodes was 9%, 8.2%, and 8.2%[4.5-6.5%], respectively, thus not a tight glycemic control. The mechanisms underlying hypoglycemia-induced TFND and how to prevent them remain unclear, and further research is indicated. Hypotheses include cerebral vasospasm, impaired cerebral autoregulation, selective neuronal vulnerability and underlying cerebrovascular disease. It is unclear whether such recurrent episodes of TFND in children have any long term consequences.

EVALUATION OF BLOOD KETONE BODIES AT DIAGNOSIS OF TYPE 1 DIABETES IN ITALY: A MULTICENTER STUDY

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Background: The recent introduction of a method for measuring 3B-hydroxybutyrate (3HB)- the most predominant ketone body in the blood - in capillary blood allows a simple and quantitative analysis of metabolic decompensation in patients with recent onset Type 1 diabetes

Patients & Methods : 53 consecutive patients (35 M and 18 F, aged 8.3 ± 4.2 yrs, range 1.3-17.2) at the diagnosis of Type 1 diabetes were studied. Patients were diagnosed in four Italian cities (Genoa, Florence, Rome and Naples) as part of a multicenter project aimed to define the clinical and metabolic features of patients with recent onset Type 1 diabetes. In addition to the usual chemical parameters required in such cases including evaluation of urine ketone bodies 3HB was measured every hour since admission until disappearance from blood was reached. The Optium (Abbott Medisense) device which employs a drop of venous blood for measurement of 3HB was employed.

Results: On admission mean blood 3HB was 3.66 ± 1.9 mmol/l. Blood 3HB appeared to be correlated with venous pH ($p < 0.0001$). Significantly ($p < 0.001$) lower values were found in patients with venous pH > 7.25 (n.28 , 2.85 ± 1.85 mmol/l) than in patients with pH < 7.25 (n.25 , 4.57 ± 1.49 mmol/l). Required time to obtain normal blood 3HB (< 0.6 mmol/l) was 11.4 ± 7.1 h (range 1-31) and correlated with blood 3HB on admission ($p < 0.01$). Urine ketone bodies disappeared later than blood 3HB (21 ± 13.3 h, range 1-60) and were not correlated with blood 3HB on admission

Discussion: This is the first study which measures 3HB in a consecutive series of patients with recent onset Type 1 diabetes. Evaluation of 3HB offered a useful, rapid and economical mean to evaluate the effect of intensive insulin therapy for the optimisation of metabolic control. Compared to persistence of ketone bodies in the urines, the measurement of 3HB in blood represents a better indicator of the actual degree of metabolic control, thus allowing implementation and especially monitoring of a correct insulin therapy

**INFLUENCE OF DIABETES MELLITUS ON THE
CONCENTRATION OF LONG CHAIN POLYUNSATURATED
FATTY ACIDS (LCPUFA) IN HUMAN MILK**

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In human milk there are many important compounds among which we can find LC PUFA. They constitute one of the most important components of the cell-membranes, and they are present, among others in the central nervous system. The most important are: arachidonic acid C20:4 (n-6) and docosahexaenoic acid C22:6 (n-3), generated from linoleic acid C18:2 (n-6) and linolenic acid C18:3 (n-3). In metabolism of fatty acids, an extremely important role is attributed to the desaturase delta 6, from which the transformation cycle begins. The cycle in question is activated, among others, by insulin. According to our observations, an impaired psychophysical development is noted, more frequently, among the offspring of diabetic mothers than in the general population. The aim of this study was to determine the composition of fatty acids (FA) in breast milk and, in particular, to determine the metabolic ratios for the LC PUFA.

Methods: 30 lactating women in the 22-25th week after delivery: 10 women suffering from type1 diabetes (DM); 10 women with gestational diabetes and a correct carbohydrate management during the lactation (GDM); 10 healthy women, which represented a control group. All subjects were on standard diet and fed their infants with breast milk only. The FA composition of breast milk was determined by using the gas chromatography technique.

Results: There were no significant differences in the supply of energy and nourishing ingredients and BMI among studied groups. HbA_{1c} in DM group were within the ranges 5-7%. The FA composition of human milk from mothers with type1 diabetes was different from GDM and N groups. The observed differences related, in particular, to the metabolites of FA families n-3 and n-6. The FA ratios, obtained for the LC PUFA from n-6 family, were 0,06±0,01 in DM group, whereas in healthy mothers these ratios were 0,09±0,02 (p<0,05). Similarly, the decreased FA n-3 concentration in breast milk collected from mothers with type1 diabetes; at the same time, the metabolic ratio of the FA n-3 family was 0,34±0,09, whereas for control mothers 0,65±0,18. Conclusion: Metabolic ratios for the LC PUFA families n-3 and n-6 in mothers with type1 diabetes differ significantly from the analogous ratios ascertained within the control group. No such differences were found with respect to the group of women with gestational diabetes. Analogous tests, as well as lipid and carbohydrate metabolism tests, should be conducted in a larger group of mothers with the type1 diabetes in different metabolic status.

TYPE 2 DIABETES IN ADOLESCENCE

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Introduction: Age older than 40 years old has always been considered as a typical diagnostic criterium for type 2 diabetes (T2DM); in the last years, however, a significant increasing frequency of T2DM has been reported in young people mainly from certain ethnic groups (Afro-americans).

Aim of the study: to evaluate the clinical features, at the onset and during the follow-up, of children and adolescents diagnosed as type 2 diabetic patients by the Centre of Childhood Diabetes of Turin University, during the period 1997-2000.

Results: in the period of the study 149 children and adolescents (age 1-14ys) have been admitted to our Centre for diabetes mellitus at onset: among them, 143 patients (32% in diabetic ketoacidosis, and 68% in hyperglycemia) were diagnosed as Type 1 Diabetes.

The remaining 6 patients (all females, mean age 12 ± 1 ys, puberal stadium P3-4) showed history of T2DM in at least one 1st grade relative, no specific autoimmunity for T1DM, mild loss of weight and long-lasting poliuria and polydipsia (>3-4 months), BMI 30.4 ± 2 , nigricans achantosis in one female patient, dislipidaemia and hepatic steatosis in two patients, mean HbA1c $9.5 \pm 1\%$, mean glycaemia at the admission 290 ± 40 mg/dl, definetly pathological OGTT, high basal and after stimuli plasma insulin and C-peptide levels (respectively of 22.8 ± 7 μ U/ml and 3 ± 0.2 ng/ml) suggestive for insulin-resistence. These findings led to diagnosis of T2DM, and therefore the 6 patients were subjected to diet therapy with restriction of total calories, fast absorbed sugars and saturated fatty acids intake. After six months follow-up, all patients showed a significant decrease of BMI (26 ± 2), HbA1c ($6.5 \pm 2\%$) and fasting and after meal blood glucose levels.

Conclusions: in according with previous reports, our data suggest that T2DM is increasing in adolescence. Obesity, familial history for T2DM, female gender and puberty are risk factors for the development of the disease. Diet therapy may ameliorate the metabolic control.

CONTINUOUS SUBCUTANEOUS INSULIN INFUSION IN YOUNG CHILDREN

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Background: The incidence of Type 1 diabetes mellitus (T1DM) in the age group < 5yr is increasing steadily and treatment of these young children is especially difficult. Recent technologies have provided new therapeutic options. So far only few data exist about continuous subcutaneous insulin infusion (CSII) therapy in this young age group.

Aim: The purpose of this study was to determine the feasibility of CSII therapy in young children (younger than 3 yr of age at time of manifestation).

Methods: Since the beginning of 2000 we have started all newly diagnosed children with T1DM below 3 yr of age on CSII (with Lispro insulin). We compared this group retrospectively to children previously started on conventional insulin therapy (CT) with 2-3 daily injections (longacting insulin 1-2 x and shortacting insulin 1-3 x daily). The observation period was 2 yr. Hb_{A1c}, SDS for height and weight, daily dose of insulin, frequency of severe hypoglycemia and frequency of hospitalisation were documented.

Results: 6 children on CSII (m=4, f=2) versus 6 children on CT (m=4, f=2) were included in the study. The mean age of manifestation of T1DM was 15,3 ± 7,9 mo in the CSII-group vs. 20,5 ± 7,5 mo in the CT-group. The Hb_{A1c} -values after 3 mo of treatment were: CSII: 7,15 ± 0,97 vs. CT: 7,7 ± 1,09 rel.%, after 6 mo.: 7,16 ± 0,57 vs. 7,32 ± 1,19 rel. % and after 12 mo.: 7,16 ± 0,65 vs. 7,45 ± 1,62 rel. %. Daily dose of insulin was similar in both groups. For patients on CSII less severe hypoglycemias were reported than for patients in the CT-group (0 vs. 0,25/patient years) during the 2yr-observational period. The frequency of hospitalisation was 0,33 vs. 0,17/ patient years retrospectively (gastroenteritis, stomatitis or bone-fractures were reported, but no DKA or severe hypoglycemias in both groups).

Conclusion: In our small cohort CSII proved to be a feasible and safe alternative to the common conventional therapy in very young children with diabetes. We observed less severe hypoglycemias in children with CSII treatment.

SILENT COELIAC DISEASE IN CHILDREN AND ADULTS WITH TYPE I DIABETES

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Background: The association between type I diabetes and coeliac disease has been recognised for some years. The prevalence of coeliac disease among patients with type I diabetes is higher than suspected, with rates of 2 to 8%. Most cases with associated coeliac disease do not present with gastro intestinal symptoms and these cases would be missed without screening.

Aim: The aim of this study was to determine the frequency of coeliac disease in our patients, to detect silent forms and to prevent coeliac-associated disorders.

Methods: We studied 236 patients (age 2-41 years, mean 17,7) 101 female and 135 male. Duration of diabetes ranged from 1 to 36 years (mean 17,7 years). Coeliac disease-specific antibodies: endomysium and antigliadin antibodies were analysed in annual screening programme in our patients. All those subjects who tested positive for both endomysium and antigliadin antibodies underwent intestinal biopsy.

Results: 7 patients (2,9 %) (6 female, 1 male, age 9-24, mean 15,4, duration of diabetes ranged from 2-16 years, mean 8,6 years) were positive for endomysium and antigliadin antibodies. In 1 patient coeliac disease was diagnosed before manifestation of diabetes. In 6 patients a intestinal biopsy was performed.

5 patients showed a total villous atrophy, 1 a partial villous atrophy.

None of the patients presented with gastro-intestinal symptoms.

1 of this patients were also suffering from Hashimoto thyroiditis.

Conclusion: This report provides further confirmation of the high prevalence of undiagnosed coeliac disease among diabetic patients. It also confirms the increased presence of other autoimmune disorders in these patients. Autoimmune disorders were more frequent in females than in males.

We would recommend that all patients with type I diabetes, even those asymptomatic, should be screened yearly for CD using the specific antibodies EMA and AGA and also for other autoimmune disorders.

PRESENTATION OF TYPE 1 DIABETES

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Background: The clinical onset of type 1 diabetes in children and adolescents is generally abrupt, occurring over a 2-3 week period in the majority. The most commonly described presenting symptoms are the classical triad of polyuria, polydipsia and weight loss. The frequency of presentation in the life-threatening condition of diabetic ketoacidosis (DKA) varies amongst different populations.

Aims: To identify in an Irish population, the presenting features of type 1 diabetes in an incident cohort aged under 15 years, to ascertain the proportion presenting in DKA, and occurrence of a family history.

Methods: A prospective national study of paediatricians was undertaken to identify all incident cases of type 1 diabetes presenting over a 2 year period using an active monthly reporting card system. Those who reported cases were sent a questionnaire to complete on each patient. Paediatricians who did not report cases were also contacted. In addition a national survey of adult physicians and endocrinologists, was undertaken.

Results: 283 incident cases were identified and completed responses were available on 211/283 (75%) relating to symptom duration. The median duration of symptoms was 10days, range 0-180 days. There was a significant difference in the duration of symptoms when analysed by age category (KS χ^2 8.1;p=0.02). The main presenting symptoms were: polyuria and polydipsia (96%); weight loss (46%); enuresis (18%); nocturia (9.3%); and lethargy (21%). Enuresis was reported in 19% of those under 5 (with nocturia in 2%) and in 31% of those aged 5-9.99 (nocturia in 10%). 25% of respondents presented in moderate/severe DKA, 67% were not in DKA and 6% were treated as DKA (pH 7.2-3). There was no significant association between age category and presentation in DKA (p=0.4). 10.2% had a family history of type 1 diabetes in a first degree relative.

Conclusions: This study confirms the short history and classical symptoms of type 1 diabetes. The duration of symptoms is shortest in the youngest patients. Enuresis is an important symptom in the younger child. The majority of cases have no family history and do not present in DKA, regardless of age category.

CHARACTERISTICS OF IDDM AT DIAGNOSIS MONTENEGRO EPIDEMIOLOGIC FOLLOW-UP STUDY

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The incidence of Type 1 diabetes mellitus is increasing worldwide. Some perinatal factors, like older maternal age, maternal preeclampsia, neonatal respiratory disease, blood group incompatibility, birth weight, are significant risk factors for Type 1 diabetes. Also, an initial low levels of c-peptide is strong risk factor for decrease in β -cell function, and conversely, high c-peptide levels is protective.

Aims: To determine the incidence of Type 1 diabetes in Montenegrin children aged below 14 years; to analyze familial aggregation, clinical and hormonal characteristics of the children with IDDM at the time diagnosis.

Design and methods : Prospective epidemiological study. We have studied a children with diagnosis of IDDM during period 1980-2001y.

Results : Incidence of IDDM in Montenegro in last 10-year period (1992- 200 y.) in age group 1-14 y. were 9,4/100 000 in relation to 1980-91 y., when were 5,8/100 000. We found strong evidence for familial occurrence of Type 1 diabetes (28% our patients have first-degree, second-degree or third-degree relatives with IDDM). The youngest age group had more severe metabolic decompensation at clinical onset, and their serum C-peptide levels, compared with those of older children, were lower (in age group 0-5 y. 0.12 ± 0.06 ; 6-15 y. 0.19 ± 0.16 and >15 y. 0.24 ± 0.18 nmol/L). Birth weight in children aged 0-5 y. were 3850 ± 640 ; 6-15 y. 3580 ± 585 , >15 y. 3360 ± 520 g for boys, and aged 0- y. 3320 ± 450 ; 6-15 y. 3600 ± 480 and >15 y. 3250 ± 670 g. for girls.

Conclusions: The incidence of Type 1 diabetes in age group 0-14 y. in Montenegro is increasing, especially last 10 years. We found strong evidence for familial occurrence of IDDM. The clinical presentation of Type 1 diabetes at very young age is associated with severe metabolic decompensation, and poorly preserved residual β -cell function. Birth weight were significantly higher in the younger boys with IDDM.

**METFORMIN IMPROVES GLYCAEMIC CONTROL IN
ADOLESCENTS WITH TYPE 1 DIABETES**

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Background: Metabolic control often deteriorates and weight is gained during puberty in children with Type 1 diabetes. Alternative therapeutic strategies are needed when optimized insulin regimen fails to regulate the metabolic control.

Aim: The aim of the present study was to investigate whether addition of metformin for three months improves metabolic control and insulin sensitivity in poorly controlled adolescents with Type 1 diabetes.

Methods: Twenty-six adolescents with Type 1 diabetes (18 females, 8 males) were included in a double-blind placebo controlled trial. The mean age was 16.9 ± 1.6 years, mean HbA_{1c} was 9.5 ± 1.1 % and the daily dosage of insulin was 1.2 ± 0.3 U/kg. The primary endpoint, glycated haemoglobin (HbA_{1c}), was measured every 4 weeks with a HPLC method (upper reference limit 5.3 %). An euglycaemic hyperinsulinaemic clamp was performed at baseline and at the end of the trial after 3 months to measure peripheral insulin sensitivity. Hepatic insulin sensitivity was estimated with IGF-I and IGFBP-1 measurements.

Results: We found a significant reduction in HbA_{1c} from baseline to the end of the study in the group treated with metformin (9.6 vs 8.7%; $p < 0.05$). The HbA_{1c} was unchanged in the placebo group (9.5 vs 9.2 %; ns). We found no change in body-mass index, insulin dose, IGF-I concentrations, blood lipid levels or peripheral insulin sensitivity in neither of the groups. IGFBP-1 concentrations were reduced in the metformin group, although not statistically significant (123 µg/l vs 57 µg/l). Side effects were mild, no case of diabetic ketoacidosis or severe hypoglycaemia occurred during the study period.

Conclusion: In this double-blind placebo controlled study we found that metformin improves metabolic control in adolescents with Type 1 diabetes. Our data suggest that the effect might be mediated by increased hepatic insulin sensitivity. Further larger studies are needed to confirm these results.

MISMANAGEMENT IN ADOLESCENT WITH TYPE 1 (INSULIN DEPENDENT) DIABETES

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Background: Many physical, psychological, social and cognitive changes take place in adolescence. Emerging personal values and beliefs, an acute awareness of body image and a desire for peer conformity and increasing independence can make the transition to adulthood troublesome. For teenagers with insulin-dependent diabetes (IDDM), usual adolescent needs and concerns are complicated by the demands of a complex treatment regimen. This can result in non-adherence to the recommended programme of care and, consequently, poor glycaemic control.

Aim: To document the existence and prevalence of mismanagement in adolescents with IDDM.

Methods: Twenty-eight adolescents (10-18 years) with IDDM (1-15 years) completed the confidential questionnaire developed for this study. Glycohemoglobin was also obtained for each individual.

Results: Many adolescents admitted to engaging in various mismanagement behaviours, with 49.5% admitting having done it for some time. Parents tend to underestimate adolescent mismanagement. Mismanagement was significantly related to poor control ($p < 0.01$).

Conclusions: IDDM is a heavy burden for adolescent patients. First of all, an adolescent does not wish to be diabetic and the doctor keeps reminding him that he is diabetic. Facing this inadequacy, the adolescent is reluctant to develop a confident relationship with his doctor and compels us to question our practice. Adolescence is a period of life when the boy (or girl) tend to conquest his (her) independence. On the contrary, the treatment of diabetes increases passiveness and dependency and crystallises the conflicts of adolescence. Some adolescents try to accommodate this relation of dependency by adopting either an opposing behaviour or other mental defences like splitting or denying. They are (in some way) led to mismanage their diabetes. This is a way of keeping their illness at a distance, of putting it aside. In conclusion, this study shows the importance of recognising the existence and prevalence of mismanagement among adolescents.

**PROSPECTIVE MEASUREMENT OF INSULIN
LEAKBACK IN CHILDREN WITH TYPE 1 DIABETES
MELLITUS**

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Background: Following administration of subcutaneous insulin in children with type 1 diabetes mellitus, a small amount of clear fluid sometimes leaks back. Little data exist as to how frequently such leakback occurs. Since insulin doses in children are sometimes titrated in fractions of units, even a small amount of leakback of insulin may be significant.

Aims: To assess the frequency and amount of insulin leakback in a subset of children with type 1 diabetes mellitus.

Methods: A technique using capillary tubes to accurately measure the volume of fluid on skin was devised. The measurement technique involved drawing up fluid by capillary action from the skin into a glass tube with fixed inner diameter and measuring the length of the fluid within the tube. We then questioned 37 consecutive children and their families coming to our diabetes clinic as to the frequency of leakback. We instructed fifteen patients (14±2 years) who reported intermittent leakback in the capillary technique and asked them to prospectively measure leakback over one week.

Results: Forty-three percent of the children reported at least one episode of leakback in the previous 7 days. The average number of leakback events in this group of children was 3±1 over 1 week. Assuming the clear fluid was insulin, leakback ranged from 0.1 to 2.3 units with an average of 0.7 units. Leakback was independent of insulin dose. Leakback occurred ($p<0.05$) most frequently in the buttocks and legs (compared to arms and stomach), when 8 mm needles were used (compared to 12 mm needles) and with needles that had 30 gauge width (compared to 29 gauge width). Larger volumes of leakback ($p<0.05$) occurred in the legs, compared to the arms, buttocks and abdomen. No significant differences were found between frequency of leakback and age.

Conclusion: We conclude that insulin leakback can be an important factor that must be considered when trying to optimize diabetic control in children with type 1 diabetes mellitus. Longer, wider needles with injections given in the arms and stomach seem to be preferable.