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GENETIC INHERITANCE OF TYPE 1 DIABETES

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Background: We have carried out interrogation among the parents of the patients of children with type 1 diabetes (DM1). Were studied 50 patients. Mean age was $12,1 \pm 0,35$ yrs, mean DM1 duration $1,57 \pm 0,17$.

Aims: The aim of our investigation was to studying of inheritance DM1. Definition of frequency of DM1 at boys and girls, at brothers and sisters of patients, definition of frequency of inheritance DM1 children, at children who have been given birth in related marriages, at children which relatives have endocrinology pathology.

Methods: It was carried out on a questionnaire which included the following items: age of the child, sex of the patient, whether are available close and long related marriages for parents of the patient, the child from not a related marriage, presence of a diabetes of 1 and 2 type diabetes at close and distant relatives of the patient, presence of others endocrinological pathologies at close and distant relatives of patients.

Results: Frequency DM1 at boys and girls- $58 \pm 7,5\%$ and $42 \pm 7,5\%$ accordingly ($p > 0,05$), at brothers and sisters of patients – $10 \pm 4,3\%$ and $4 \pm 2,8\%$ accordingly ($p > 0,05$), at children who have been given birth from closely related marriages concerning children from long-related marriages - $70 \pm 6,5\%$ and $30 \pm 6,5\%$ accordingly ($p < 0,01$), frequency of pathologies of a thyroid gland at relatives of patients concerning others endocrinology diseases - $70 \pm 6,5\%$ and $30 \pm 6,5\%$ accordingly ($p < 0,01$).

The conclusion: Frequency of DM1 appeared authentically above at children from closely related marriages, frequency of pathologies of a thyroid gland at relatives of patients appeared authentically more than others endocrinology diseases.

**SERUM INTERCELLULER ADHESION MOLECULE
(sICAM-1) LEVELS IN TYPE 1 DIABETES AND IN THE
HEALTHY SIBLINGS OF THE PATIENTS**

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Background: Type 1 Diabetes Mellitus (D.M.) is the most common chronic disease of the childhood. Therefore, it is too important to diagnose and treat the disease early.

Aim:

1. To search biochemical parameters and autoantibody levels of nondiabetic healthy siblings who are considered to be under the risk of type of 1 Diabetes Mellitus.
2. To investigate the predictive value of sICAM-1 levels in diabetes.

Methods:

For this study, 28 diabetic patients, 30 nondiabetic healthy siblings and 29 healthy children (as control group) are evaluated with physical examination, blood pressure, body mass index, family history and previous diseases, blood count, total cholesterol, HDL, LDL, VLDL, triglyceride, urea, AST, ALT, sICAM-1 levels, microalbuminuria, retinopathy and pubertal stage. Then, 3 groups are compared statistically.

Results: Total cholesterol, HDL and LDL levels of the diabetic patients and the siblings were higher than the control group, but there were no difference in sICAM-1 levels of the three group. When the whole cases were evaluated totally, number of platelets and HDL levels were found to be correlated with sICAM-1 levels. Besides, leukocyte count of group 2, was separately correlated with sICAM-1. There were no correlation between the autoantibody positivity and sICAM-1 levels.

Conclusion: We think that, sICAM-1 molecule, does not have a high predictive value for diabetes and its complications, but nondiabetic healthy siblings which are considered to be under the risk of diabetes, needs detailed investigation for lipid profiles.

EDUCATION FOR CHILDREN AND ADOLESCENT DIABETES IN BANGLADESH

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Background and Aims: Education is acknowledged to be the cornerstone of diabetes care as demonstrated by the Diabetes Care and Complications Trial. Sadly, in developing countries this aspect of management is neglected, more so in the case of children and adolescents. Although there are no prevalence/incidence data on children and adolescents with Diabetes Mellitus, the magnitude of the problem can somewhat be perceived by the numbers of the under-18 age group (20-30/month) reporting to BIRDEM. Education has always been an integral part of the management of patients but had catered for the majority of patients ie adults with Type 2 DM. That children and adolescents have special needs and that education of their caregivers is equally important was not given due consideration. **Design:** It was felt that a tailor made education programme for children and their caregivers was a priority. Our task was made more challenging by the fact that target groups were of different literacy levels and socio-economic backgrounds (mainly rural) and from varying distances from the centre. The components of the programme are: a) a video using puppets, actors, and staff b) a colourfully illustrated guidebook for children, c) a handbook for parents , and d) interactive group sessions. The programme started in November 2000 and has become very popular with children and caregivers **Result:** The impact of the old and new programmes was compared using a questionnaire; analysis on 50 patients shows a significant improvement in knowledge after the introduction of the new programme. Studies using HbA1c are in progress. **Conclusion:** Our experience impresses the importance of need-based programmes.

INTERNATIONAL DIABETES COMPLICATION STUDY

„DIACOMP“ – OUR RESULTS.

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The target of the International Diabetes Complication Study „DIACOMP“ with more than 30 participating countries all over the world, is to map the occurrence of the diabetes chronic complications among children youngsters and young adults with type 1 diabetes (T1D), who had duration of the disease 5-15 years in the year 1997. In this trial amount of complications is correlated with compensation status and with glycated hemoglobin levels.

Subjects and Methods: In the trial is evaluated the situation among 68 patients with type 1 diabetes, who are treated in Children Diabetes Centre of the Slovak Republic and in the Diabetes Outpatient Department of the Policlinics for Youngsters in Bratislava by the same diabetologist. Values of glycated hemoglobin were from the onset of diabetes to the end of the year 2001. Eye, neurological and angiological examinations were concluded by the common criterias, for the pathological status after the nephrological examination sufficed only one microalbuminuria value above 20 ug/min.

Results: From 68 T1D patients have 32 (47%) at least one chronic complication. All three complications occurred in 3 patients (4,4%). Two complications (retinopathy and neuropathy) are in 8 (11,8%) patients, resp. (retinopathy and nephropathy) in 9 (13,3%) patients. 12 patients have only diabetic retinopathy, 4 patients have diabetic nephropathy, no one has only diabetic neuropathy. The whole cohort is divided according occurrence of diabetic complications with relation to the values of glycated hemoglobin.

Conclusions: In comparison this cohort with very similar one, but before some years, is clear, that contemporary results are markedly better, but this trend we can see in majority of the participating countries.

CONVENTIONAL VS MULTIPLE INSULIN REGIMENS IN TYPE 1 DIABETES MELLITUS IN CHILDHOOD

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Background: The Diabetes Control and Complications Trial results suggest that better glycemic control is achieved by intensive insulin regimens. However, this trial study did not include children under 13 years of age.

Aim: To compare the effects of multiple versus conventional insulin regimens on glycemic control in childhood and adolescence.

Patients and Methods: Fifty eight children who were younger than 10 years (Group 1) and 46 children older than 10 yrs. (Group 2) were included in the study. Eighteen children in Group 1 (Group 1A, mean age 4.5 ± 2.1 yrs) received conventional 2- dose insulin and 40 (Group 1B, mean age 5.4 ± 2.4 yrs) received a multiple dose regimen. Seven children in Group 2 (Group 2A, mean age 11.5 ± 1.6 yrs) received 2 doses and 39 children (Group 2B, mean age 12.7 ± 2.2 yrs) were given multiple doses. All children were assessed every 3 months for a period of 3 years. Mann-Whitney U test and Friedman's variance analysis were used in the assessments.

Results: In Group 1A, mean HbA_{1c} value at the end of the first year of follow-up was $8.2 \pm 2.1\%$. This value was $8.3 \pm 1.4\%$, $7.5 \pm 1.2\%$, $8.2 \pm 2.7\%$ for groups 1B, 2A and 2B respectively. No significant differences were found between the conventional and multiple dose regimen patients at any age group. Similarly, no differences were found at subsequent follow-ups. Daily insulin requirements showed no significant increases over time and ranged between 0.6 U/kg and 0.9 U/kg for Groups 1A and 1B; and between 0.8 U/kg and 1.2 U/kg for Groups 2A and 2B. BMI SDS values remained unchanged in both Groups 1A and 2A, but showed statistically insignificant increases in Groups 1B and 2B.

Conclusions: No significant differences in glycemic control were found between children receiving one of the two insulin regimens over a follow-up period of three years. In all groups there were some children who were not able to attain a satisfactory HbA_{1c} level. These results implicate that while institution of a satisfactory treatment schedule is important, it is difficult to attain a good glycemic control in all diabetic children.

**THE EFFECT OF NITRATE-CONTAMINATION OF THE
SOIL AND WATER ON THE PATHOGENESIS OF CHILD'S
DIABETES MELLITUS**

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This paper is based on the pathogenic role of nitrosamins on the child's diabetes mellitus, and on the fact that nitrates, which contaminates the soil and the water, transforming metabolically into nitrosamins, may have the same role.

The nitrate-contamination of the soil and the water is important in the district of Satu Mare, because there are many contaminated regions, and even regions with a high contamination.

In our study we will assess comparatively the levels of the nitrate-contaminations in different regions of the district, and the epidemiology of the child's diabetes mellitus in the same regions. We will made a mapping of the district, first for the nitrate-contamination of the soil and of the water, and after it for the incidence and prevalence of the diabetes mellitus in childhood. Comparing the two maps, we'll try to establish some conclusions about the possible role of the nitrate-contamination of the soil and of the water in the pathogenesis of child's diabetes mellitus.

The possible (and probably) positive associations could alarm us about the importance of profilactic measures in this public health area.

SEASONAL CYCLING OF HLA GENETIC RISK IN BIRTHS OF CHILDREN WITH LATER DM 1?

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Background & Aims. Seasonal cycling in frequency of births of future diabetic children and in incidence of DM1 stimulates the question: Does the proportion of subjects with genetic risk seasonally fluctuate according to the year time of birth of future diabetic children?

Patients & Methods. There were 123 Slovak children, born 1981-2000 and manifesting DM1 1989-2001 in the age of 1-14 years, scrutinized. Seasonality of the proportion of genetic risk in births of this children's sample was tested on daily arranged birth data for one ideal calendar year. The HLA class II alleles' pattern, typed by PCR-SSP, was summed up to score values between 0 (maximal risk) to 3 (minimal risk). Moving averages of these values, from 3 observations each, were plotted versus days of year and processed by Halberg's cosinor regression to test a significant ($\alpha=0.05$) presence of the annual, semiannual and quarterly periodicity.

Results. The overall mean risk score was 1.16. The leading rhythm ($P<0.001$) was that with period of 3 months. Its double amplitude was 0.51 (0.23-0.80, 95% confidence interval) of the score unit. Maximal risk proportion in the births was found around middle of January, April, July and October. Another significant ($P<0.01$) cycling was that with the period of one year, with the maximal risk pattern in early August. Its double amplitude was 0.41 (0.13-0.69). Accordingly, the total range of the seasonal fluctuation is almost one score unit, with the actual estimated maximum of the genetic risk in summer.

Conclusion. These results, obtained from a relatively low sample size, need to be verified from other sources. If confirmed, a comparative study with other seasonally cycling variables will be necessary to search for the responsible factors modifying the proportion of genetic risk-positive and -negative births in various times of year.

EVALUATION OF THE PLACENTA IN DIABETIC MOTHERS - INFLUENCE ON THE NEWBORN.

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Aim of the study: Macroscopic and histopathological analysis of the placenta from mothers with gestational diabetes (GDMG1, GDMG2), with diabetes type 1 and healthy mothers. Determination of the correlation between the pathological changes in the placenta and the time of delivery and the state of the newborn at the moment at birth.

Material: examined were 122 placentas in following mothers: 37 with GDMG1, 35 with GDMGF2, 30 with diabetes type 1. The control group consisted of 20 placentas from healthy mothers without diabetes in the family. Investigated were also 123 newborns (one couple twins). Macroscopic and microscopic examinations of the placenta were performed in the Department of Anatomopathology. A correlation of the changes in the placenta and the body mass and health state of the newborn was evaluated. Analysed was also the correlation between inflammative infections in the newborn and the changes in the placenta.

Results: In the placenta of mothers with intrauterine infections found were also markers for the inflammative process. The placenta of mothers with type 1 diabetes was more heavy than the placenta of mothers from the remaining groups and the differences were statistical significant. The microscopic examinations shows a more frequent occurrence of pathologic changes in the placental villi and basal lamella in the placenta of mothers with type 1 diabetes (hemorrhagia, lymphocytic infiltration, calcipexy, fibrinoid, mole changes). The changes in the placenta don't correlate with the Apgar scale and the body mass of the newborn but there was a negative correlation with the time of delivery ($p < 0,02$).

Conclusions: 1. The inflammatory markers may be responsible for the acceleration of the delivery. 2. The cause of an intrauterine infection in newborns may be an inflammatory process of the placenta. 3. In the placenta of mothers with type 1 diabetes observed was an increase of the mass and frequently pathologic changes.

ANALYSIS OF BACTERIAL AND MYCOTIC FLORA IN CHILDREN WITH DIABETES

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Background: Children with poorly controlled diabetes are exposed to infections often caused by endogenous flora.

Aim: To estimate incidence of pathogenic and opportunistic bacteria and fungi of *Candida* species, with their susceptibility for antibiotics in children with diabetes.

Material and methods: Smears from the oral cavity, the pharynx, the urethra, and the vestibule of vagina, as well as urine were examined in 130 diabetic children (53 newly diagnosed; 77 poorly controlled diabetes; 68 girls, 62 boys, aged 1-17 yrs). 29 children with short stature were as a control group. Culture and identification of microorganisms were performed according to the methods used in microbiological diagnosis. Drug susceptibility was estimated with the NCCLS standards and FUNGITEST Sanofi Pasteur test.

Results: Infections, mostly vulvitis and urethritis were observed in 40 (31%) children. *Staphylococcus aureus* (42 cases/32%), *Streptococcus* group B (totally: 29 cases/22%; from vagina 17cases/25%), less often *Streptococcus* group C and G, *Streptococcus pneumoniae*, *Enterococcus* spp., *Candida* species (58 cases/45%; *Candida albicans* 48 cases) were isolated. MRSA were isolated from the pharynx (3 cases), MRSE from urine (1 case). Among *Candida* spp. strains with lower sensitivity and resistant to Amfotericine B and rarely to Azoles were observed. In 17 diabetics (13%) and 3 children from the control group (10%) significant bacteriuria were present. Mostly Gram-positive bacteria were isolated: *Streptococcus* group B, staphylococci and enterococci, less frequently Gram-negative *bacilli*. In 13 diabetics (10%) *Candida* spp. were found in urine.

Conclusions: Microbial analysis of vagina should be routinely performed in diabetic adolescents.

Urine of diabetics should be examined towards fungi.

**THE ASSESSMENT OF PSYCHO-MOTOR DEVELOPMENT OF
INFANTS BORN TO DIABETIC MOTHERS**

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Aim: The aim of study is the prospective evaluation of psychomotor development of 103 infants born to diabetic mothers during 1 years observation.

Material: The children were divided into 3 groups acc. to class of maternal diabetes (acc. to White classification). Consequently, the following groups were established: 41 infants of mothers with gestational diabetes, 44 infants of mothers with class B,C, and the group of 18 children of mothers with severe diabetes class D-F.

Methods: The psychomotor development was classified in Brunet- Lezine scale. The examination was done at age of 3, 6 months and 12 months of age by psychologist and separate domains (physical, cognitive, social-emotional) were calculated for each child. If necessary the rehabilitation was performed.

Results: To sum up 8.73 % (9 cases) all children had disturbances in psychomotor development during one year of life, mainly those were children of GDM (12.1%) and class D-F (11.1%) mother's diabetes. In 5 children with psychomotor disturbances congenital defects were detected.

Conclusions:

The children of diabetic mothers revealed disturbances in psychomotor development.

Congenital defects were the main cause of stated complication.

There is still the need to improve the diabetological and obstetric care for women with diabetes during pregnancy.

A STUDY OF GROWTH IN CHINESE LOW BIRTH-WEIGHT CHILDREN DURING PERIPUBERTY AND PUBERTY

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Background: Low birth-weight children (LBW) have a higher risk of short stature than normal birth-weight children (NBW). It is recognized that growth retardation of LBW children before puberty is related to abnormal function status of insulin-like growth factor I (IGF-I) axis.

Aims: to characterize the growth and development of LBW children during peripuberty and puberty, and evaluate the relation between serum IGF-I level and growth and development of LBW children in this period.

Methods: Height, weight, HtSDS, WtSDS and serum IGF-I levels were compared between 56 Chinese LBW children and 100 NBW controls in different ages and different pubertal stages. Serum IGF-I levels were determined by methods of radioimmunoassay.

Results: (1) The average height, weight, HtSDS and WtSDS of LBW children in different pubertal stages was similar with those of NBW children. 16.1% of LBW children had their HtSDS between $-2\sim-1$, 17.9% had their WtSDS between $-2\sim-1$, whereas in controls they were 5.7% and 6.1% respectively ($P<0.01$). (2) With ages, the serum IGF-I concentration of two groups increased gradually, and the serum IGF-I levels were significantly lower in LBW children of different ages compared with those of controls. Serum IGF-I level was positively correlated with age, height, weights and birth weight in two groups. (3) With the pubertal development, IGF-I concentration of two groups increased steadily, the IGF-I levels of two groups in different pubertal stages still showed significant difference.

Conclusions: Height and weight of part of LBW children at 7-14 years was still at lower levels, and IGF-I levels were reduced at this period. Lower IGF-I level might be one of the mechanisms to lead to the growth retardation of LBW children during peripuberty and puberty.