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SOMATOSTATIN (SRIH) INCREASES GLOMERULAR PG E_2 PRODUCTION IN DIABETIC AND NORMAL RATS. D A Nickels and M Poth, Department of Pediatrics, Walter Reed Army Medical Center, Washington, DC 20307 and Uniformed Services University of The Health Sciences, Bethesda, MD 20814, USA

SRIH has recently been shown to be effective in reversing many of the changes observed in early diabetic nephropathy (DN), including kidney hypertrophy and increased urinary albumin excretion. Although GH is elevated in IDDM, it is unknown whether SRIH exerts its protective renal effects via its ability to suppress GH or via other unspecified direct renal effects. We hypothesized that the beneficial effects of SRIH on DN may be secondary to its ability to alter local PG E_2 synthesis. SRIH has been shown to increase PG E_2 in other tissues, however no such data exists on the glomerulus. We therefore sought to determine if SRIH altered glomerular PG E_2 production in the rat. Whole glomeruli were isolated from both STZ-diabetic rats and from normals. Glomeruli were incubated briefly with either saline, captopril 10^{-4}M, or SRIH in varying concentrations, and PG E_2 in the supernatant was determined by standard RIA.

CONDITION	PG E_2 (% of control±SEM) NON-DIABETIC	DIABETIC	n= 6-15 depending on condition
SALINE	100±4%	95±12%	
SRIH 10^{-10}M	95±9%	164±14%*	
SRIH 10^{-8}M	106±17%	155±13%*	*p<0.05 vs respective saline control group
SRIH 10^{-7}M	146±13%*	156±10%*	
SRIH 10^{-6}M	140±12%*	146±4%*	
CAPTOPRIL 10^{-4}M	141±13%*	150±19%*	

CONCLUSIONS: Both SRIH and captopril increase glomerular PG E_2 production, and diabetic glomeruli were more sensitive to SRIH at the lower concentrations tested compared to normal glomeruli (p=0.001 at 10^{-10}M). Since SRIH appears to have similar clinical effects on DN as captopril, the above data provide preliminary evidence supporting the hypothesis that SRIH may be acting via its ability to alter glomerular PG E_2 rather than by lowering GH levels as previously thought.

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LIPID PEROXIDATION IN THE DIABETIC RAT MODEL-A COMPARISON OF TWO METHODS. M. Curley, M. Payne, J. Betz and M Poth. Department of Pediatrics, Uniformed Services University of the Health Sciences, Bethesda, MD 20814;Department of Clinical Investigation,Walter Reed Army Medical Center, Washington, DC 20307, USA.

As the initial step in a study to investigate the interactions of gonadal steroids and free radicals on diabetic complications we compared methods for the measurement of MDA in plasma of control and diabetic rats. We compared the method of HPLC with fluorimetric detection(Annals Clinical Biochemistry 28:504,1991)with fluorimetric determination of malondialdehyde using diethylthiobarbituric acid (DETBA)(Clinical Chemistry 37:1273, 1991).This method has been reported as being more sensitive and specific than previous MDA assays and less cumbersome that HPLC techniques. Five week old previously castrated Sprague Dawley rats were made diabetic with streptozotocin. At 30 days tail vein bleeds were done for HBA1C and plasma MDA(measured by HPLC and DETBA methods). The results are as follows (mean±SD,*p<.005,**p<0.03, ***p<0.001):

	N	HBA1C (%)	DETBA(uMol/L)	HPLC(uMol/L)
DIABETIC	14	14.03±2.818*	0.021±0.009**	4.877±2.039***
CONTROL	7	5.83±0.899	0.013±0.004	2.568±0.497

The DETBA method detected less MDA than the HPLC method.Previous studies reported problems with interfering substances in plasma resulting in decreased recovery of MDA, using other variations of the fluorimetric method. It appears that contrary to the report of authors who developed this modified method, it is not appropriate for use with plasma and it is necessary to use HPLC for accurate results.

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HLA-DR ANTIGENS IN GREEK CYPRIOT PATIENTS WITH IDDM

It has been well established that Insulin Dependent Diabetes (IDDM) is associated with the HLA-DR antigens. HLA-DR3 and DR4 are strongly associated with IDDM which DR2 and DR5 are protective against the disease. We have studied 37 children with IDDM with HLA typing and compared them with 50 healthy controls. Statistical analysis was made with X^2 test. The frequency of the HLA-DR antigens is as shown below.

HLA	IDDM	Controls	P value
DR4	75.6	28	<0.0001
DR3	48.6	20	0.01
DR5	2.7	40	<0.0001
DR2	35.1	32	0.76

The most frequent allelic combination was that of HLA-DR3/DR4 which was observed in 27% of the IDDM patients followed by HLA-DR2/DR4 21.1% and DR2/DR3 10.5%. We conclude that IDDM in Greek Cypriot patients who developed the disease before the age of 20 years is strongly associated with the "diabetogenic" alleles HLA-DR4 and DR3. It is of particular interest that while the HLA-DR5 is protective against the disease the DR2 antigen does not offer any protection.

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INCIDENCE OF CHILDHOOD IDDM IN AUSTRIA 1979-1991 - TEMPORAL TREND.

The incidence of IDDM in childhood has been increasing at least in some parts of Europe during the last decades. To provide information on the incidence trend of IDDM in Austria, the nation-wide age adjusted incidence rates from Jan.1st,1979 till Dec.31st, 1991 were analysed. Data were collected retrospectively for 1979-1987 and prospectively since 1988. Primary case ascertainment was done by a hospital reporting system. Valididation by an independent source revealed a degree of ascertainment of 93% and 95% respectively. An average annual incidence rate of 7.51/100.000 (95% C.I. 6.98-8.04) was observed during the study period. The annual incidence varied markedly over time, it was lowest in 1981 (6.1/100.000) and highest in 1984 (8.9/100.000). By Poisson regression modelling age was found to be the strongest predictor of the risk (p<0.01). A significant increase in incidence could be demonstrated over time for both sexes (p<0.01), but there was no evidence for differences in the increase in incidence by age. An interaction between monthly temperature (p<0.05) and monthly precipitation (p<0.01) was observed reflecting the typical seasonal variation. Seasonal variation was found to be age dependent (p<0.01). Our study shows a rise of IDDM incidence in Austria over the last decade. This indicates an increase of IDDM manifestations even in a European country with low risk for IDDM.

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GROWTH, DEVELOPMENT AND CARBOHYDRATE TOLERANCE OF FORMERLY SMALL FOR GESTATIONAL AGE INFANTS WITH AND WITHOUT GLUCOSE INFUSION THERAPY.

Up to 1983, placental insufficieny used to be treated by glucose infusions to the mother. We performed a clinical investigation and an oral glucose tolerance test (OGTT) in 20 children, aged 4.9 to 10.5 years, whose mothers underwent a minimum of 8 i.v. infusions with 2000 ml of 10 % glucose during pregnancy because of suspected placental insufficiency (GT-group). 20 of formerly small for gestational age children without a history of glucose infusions were counterparted as matched pairs (NON-GT group). The children of the NON-GT-group were significantly smaller, lighter, showed a lower head circumference and a marked retardation of bone age. The OGTT showed unexpected results: a disturbed glucose tolerance was found in 14 (70 %) patients of the GT-group and in (45 %) patients of the NON-GT-group. The insulin response was normal in only 2 (10 %) of the GT-group and in 5 (25 %) patients of the NON-GT-group. These results could support recent findings that reduced growth in early life is strongly linked with impaired glucose tolerance and appearance of diabetes mellitus.

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ELEVATED ANTI-BOVINE SERUM ALBUMIN (BSA) ANTIBODIES PREDICT DEVELOPMENT OF TYPE 1 DIABETES IN SIBLINGS OF DIABETIC CHILDREN. J. Karjalainen*, M. Knip*, H.-K. Åkerblom[#], H.-M. Dosch[O] and the Study Group of Childhood Diabetes in Finland. Department of Pediatrics, University of Oulu * and the Children's Hospital, II Department of Pediatrics, University of Helsinki, Helsinki [#], Finland, and Department of Immunology & Cancer [O], the Hospital for Sick Children, Toronto, Canada.

Based on our recent observation that IgG anti-BSA antibodies as determined by a fluoroimmunoassay are highly elevated at diagnosis of Type 1 diabetes in children, we studied the predictive value of these antibodies in 101 ICA and/or IAA-positive and 101 ICA/IAA-negative siblings of children with Type 1 diabetes. The mean age of the siblings was 9.3±4.3 and 9.6±4.5 years, respectively. The first blood sample was drawn right after diagnosis of diabetes in the proband and every 6 months thereafter. Altogether 4.4 samples were collected /person over a mean observation period of 47 months (range 0.5-70 months). BSA antibody level exceeding the 90th percentile in continuously ICA-negative siblings was considered as elevated. Results: Elevated anti-BSA antibodies were detected in 46 siblings in the very initial sample and 7 turned positive later on. During the observation period 81 siblings were at least once positive for conventional (IF-ICA) ICA, 58 for complement fixing (CF-ICA) ICA, and 37 for IAA, of whom 46 (56.7%), 27 (46.5%), and 11 (29.7%) were positive for IgG-anti-BSA antibodies. IgG-anti-BSA antibodies were associated with both types of ICA (p<0.001) but not with IAA. Initial levels of anti-BSA antibodies also correlated with the levels of IF-ICA (r_s= 0.37, p<0.001) and CF ICA (r_s= 0.44, p<0.001). Nineteen siblings (19/730, 2.6%) have so far presented with diabetes over a mean observation period of 47 months. Of those 90% (N=17) were IF-ICA-positive, 84% (N=16) CF-ICA-positive, and 84% (N=16) IgG-anti-BSA antibody positive in their initial sample compared to 1.7%, 2.1%, and 1.9% of the siblings remaining non-affected (p<0.001). Only 3 (15%) IAA-positive siblings developed diabetes. During the prediabetic phase out of those 3 cases remaining continuously IgG-anti BSA antibody negative, 1 was negative for all antibodies and 2 were positive for both ICA. One ICA-negative child had elevated IgG-anti-BSA during the prediabetic period. Conclusion: The results suggest that anti BSA antibodies are predictive for diabetes almost equally to ICA in high risk siblings and are consistent with the hypothesis of BSA as a trigger of the disease.