5 **HISTAMINE RELEASE OF INTACT AND IgE-DEPRIVED BASOPHIL LEUCOCYTES IN CHILDREN WITH HYPERSENSITIVITY REACTIONS TO TENIPOSIDE (VM-26)**

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Since 1980, Rigshospitalet's Paediatric Department has used teniposide (VM-26) primarily in the treatment of children with neuroblastoma and high-risk lymphoblastic leukaemia. A review of the files showed 11 cases of hypersensitivity up to the end of 1986. All the reactions, apart from one, occurred early into the infusion (<1 to 15 min), and after a varying number of previous courses. All the children recovered, but in 3 cases the acute course was critical. In order to elucidate the mechanism and to identify a possible allergen, in vitro investigations of histamine liberation of the basophil leucocytes were carried out by use of a glass microfibre method. Blood samples from 5 of the 11 cases, 6 children exposed to VM-26 without reactions, and 12 healthy children without exposure at all, were tested. The results indicated, that VM-26 itself, and not its vehicle (Cremaphor), is a potent histamine liberator due to a toxic, dose-dependent reaction, and not to a type I (IgE-mediated) allergy.

8 **CARDIOMYOPATHY IN CHILDHOOD TYPE I DIABETES MELLITUS**

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We evaluated systolic and diastolic left ventricular function using computer-assisted analyses of M-mode echocardiograms in 36 young diabetics without clinical evidence of cardiovascular disease. In the older diabetics with longer duration of the disease diastolic function was impaired; isovolumic relaxation and the time between minimum dimension and mitral valve opening were prolonged ($p<.05$; $p<.005$). Rapid diastolic filling and change of dimension between minimum dimension and mitral valve opening were normal. A significant correlation between the mean HbA_1 averaged over the last two years and the isovolumic relaxation period ($p<.003$) and the time between minimum dimension ant mitral valve opening ($p<.001$) could be shown. Fractional shortening as parameter of systolic function showed an inverse relation to the mean HbA1 ($p<.0008$), thus systolic and diastolic dysfunction occurs depending on the quality of metabolic control.

6 PROSPECTIVE STUDY OF VASCULAR FUNCTION IN CHILDHOOD IDDM. Ewald U, Kobbah M, Tuvemo T. Dept of Pediatrics, Univ. Hospital, S-751 85 Uppsala, Sweden.

A diminished vascular response to hypoxia has been demonstrated in type 1 diabetes (IDDM). This functional abnormality might be a phenomenon preceding the late structural vascular disease. In order to evaluate the prognostic value of this vascular dysfunction a prospective study has been started.
Vascular reactivity of skin vessels was evaluated as changes in transcutaneous Po_2 at 37° C during postocclusive hyperemia (Clin Physiol 1984;4:413). All children in our county, acquiring IDDM 1983-4 (n=38) comprised the study group. Vascular reactivity was evaluated at admission before insulin therapy and then at 1, 6, 12 and 24 months after diagnosis. Vascular reactivity at admission (3.0±0.2 kPa, M±SEM) was impaired ($p<0.001$) but improved at one month (3.9±0.2) into the range of the control children (n=58) (3.9±0.1). Thereafter a deterioration was noted and at 24 months the vascular response to hypoxia (3.0±0.2) was as low as at admission. Age, sex or puberty was not correlated to the vascular response. Carbohydrate control, C-peptide, trace elements and lipids in serum were only weakly correlated to the degree of vascular dysfunction. The changes in vascular reactivity and carbohydrate control during the first years occurred in parallel but were not correlated. Other factors must be considered to explain the deterioration in vascular response to hypoxia after the initial normalization in childhood IDDM.

9 URINARY EXCRETION OF α_1-MICROGLOBULIN IN CHILDREN WITH TYPE 1 (INSULIN-DEPENDENT) DIABETES MELLITUS

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α_1-microglobulin (α_1-M) is a low-molecular-weight protein easily filtered by the glomerulus and almost completely reabsorbed and then catabolized in the proximal tubular cells. Urinary excretion of α_1-M was determined in 48 diabetic children (28 females), aged 3-20 y (mean 12.1), duration of disease 1 week to 13 y (mean 6.1) and in 39 healthy controls (22 females), aged 4-19 y (mean 11.7). Urine was collected at high diuresis and the pH adjusted with 0.1 % sodium azide to about 7.0; urine samples were stored at - 20° C for two weeks. α_1-M urinary concentrations were measured by an Enzyme-Immuno-Assay (Fujirebio Inc., Japan). Urinary excretion of α_1-M was significantly higher in diabetics than in healthy children (1.19 ± 0.24 vs 0.99 ± 0.21 ng/min; $p<0.01$); urinary excretion was greater in poor-controlled diabetics (stable HbA_1c more than 10 %) than in well-controlled ones (HbA_1c less than 10 %) (1.30 ± 0.26 vs 1.11 ± 0.18 ng/min; $p<0.05$).
Urinary excretion of α_1-M is a suitable method to detect tubular dysfuntion in type 1 diabetic children and adolescents.

7 Detection of surface antibodies against pancreatic B cells in insulin-dependent diabetes.

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Islet cell surface antibodies (ICSA) have been detected in insulin-dependent diabetes (IDD). Current techniques for the detection of ICSA often suffer from a lack of standardization and from a poorly defined specificity. We have developed a standardized method to quantify binding of circulating IgM and IgG fractions with the surface of purified rat pancreatic B cells; parallel experiments on islet non-B cells serve as control for islet cell specificity. Using this procedure no abnormalities were detected in the binding of circulating IgM from 30 recent onset IDD to islet B or non-B cells, comparison being made with 30 healthy age-matched controls. On the other hand, the IgG fraction from IDD patients was found to bind selectively to islet B cells (p 0.01) while no binding was observed with IgG from the normal controls. It is concluded that the developed procedure allows the recognition, quantification and specification of autoimmune reactions against surface components of islet cells.

10 **TREATMENT WITH HIGH DOSES OF ESTROGENS AND ANDROGENS INDUCES MARKED CHANGES NOT ONLY ON GONADAL AND ADRENAL STEROIDS AND THEIR BINDING GLOBULINS BUT ALSO ON THE THYROID HORMONES AND ON THYROXIN BINDING GLOBULIN**

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Little is known about the influence of high doses of sexual steroids on other hormones and their binding globulins. We studied 28 children treated for tall stature: 14 boys treated with 500 mg testosterone oenanthate every two weeks; 14 girls treated with 0.5 mg ethinyestradiol from day 1 to 25 and 15 mg norethisterone day 20 to 25. Results boys: TBG reduced (19.03 ± 0.9 (SE) mg/l), T4 and T4/TBG-ratio markedly reduced (51.4 ± 6.4 (SE) ug/l and 2.65 ± 0.25 (SE)). T3 variable, basal TSH levels and TSH-rise in TRH-test normal. Cortisol normal, CBG slightly reduced and C/CBG-ratio slightly increased. SHBG levels markedly reduced and T/SHBG-ratio extensively increased. Results girls: TBG markedly increased (36.6 ± 2.3 (SE) mg/l) but T4 only slightly elevated (94.9 ± 7.4 (SE)), reduction of the T4/TBG-ratio (2.55 ± 0.17 (SE)). T3 variable, TSH in TRH-test normal. Cortisol and CBG increased, but C/CBG-ratio unchanged. T increased slightly, SHBG increased markedly, T/SHBG decreased distinctly. We conclude that high doses of sexual steroids induce profound changes in hormone levels which are either compensated or aggravated by simultaneous changes of their binding globulins.