35 M.V.L. DU CAJU, R. ROOMAN*, M. DE SCHUTTER* and M. VINCKX*. Department of Pediatrics, University of Antwerp, Antwerp, Belgium.

In vitro biological effects of a low molecular weight somatomedin inhibitory fraction extracted from normal serum.

Gel chromatography of normal human serum exhibits a low molecular weight fraction, which significantly inhibits the action of somatomedin on porcine rib cartilage segments. This somatomedin inhibitory fraction (SmIF) has a molecular weight of about 1250 daltons, an iso-electric point between 5 to 5.5 and shows several characteristics of a peptide nature (Ped. Res. 18:101,1984). This SmIF strongly reduces both ^{35}S-sulphate and ^{3}H-Thymidine incorporation into costal cartilage of young pigs and rabbits and ^{35}S-sulphate uptake by embryonic chick cartilage. This effect is dose-dependent, both in basal and in serum stimulated conditions, and is reversible. To a similar extent, SmIF decreases the conversion of ^{14}C-glucose into $^{14}CO_2$ in epididymal fat pads of young rats, with or without addition of normal serum, insulin or triiodothyronine. In conclusion, this low molecular weight SmIF does not only inhibit specifically the in vitro action of somatomedin on cartilage of several animal species, but also counteracts the insulin-like activity of normal serum and the effect of insulin and triiodothyronine on glucose metabolism of rat adipose tissue.

36 A. GRUETERS*. J.ALM, J. LAKSHMANAN, and D.A.FISHER, Free University Berlin, FRG* (intr.by H.Helge) and Harbor UCLA Medical Center, Torrance, USA.

Nerve growth factor (NGF) and epidermal growth factor (EGF) are present in mouse milk during early lactation

NGF is important for the differentiation and maintenance of the sympathetic nervous system and EGF promotes eyelid opening, tooth eruption and maturation of the intestine in newborn mice. Both growth factors are present in high concentrations in mouse submandibular gland (SMG) and distributed in lesser amounts in many mouse and human body fluids and tissues. The present study was conducted to prove the biological activity of milk-NGF and to characterize the ontogeny of NGF and EGF and molecular profile of EGF in early lactation in normal and sialoadenoectomized mice to determine whether the SMG contributes significantly to milk growth factors. Concentrations of NGF, determined by RIA, did not change from day 1 to day 9 of lactation (600 pg/mg protein) and were not different in sialoadenoectomized mice. Biological activity was proven by PC-12 bioassay after partial purification. EGF showed only one component, similar to SMG-EGF (MW 6045), in gel exclusion chromatography, but removal of the SMG did not change the concentration which peaked around day 6 of lactation (10 ng/mg protein).
Conclusion: Growth factors are present in significant concentrations in mouse milk and the SMG is not their origin.

37 J.L. CHAUSSAIN, M. COLLE, P.F. BOUGNERES, J.E. TOUBLANC. Hôpital Saint Vincent de Paul, Paris, France.

Fasting blood glucose (BG) concentration long before the onset of insulin-dependent diabetes melitus (IDDM) in children.

Among several hundred children with IDDM, 22 had a fasting BG fortituously measured 5 years to 6 months prior to the clinical onset of the disease, because of intercurrent illness or minor surgery. Fasting BG averaged 107 ± 27 mg/dl (SD) VS 79 ± 09 mg/dl in controls studied in similar conditions ($p < 0.001$), with a wide range of values from 53 to 152 mg/dl in patients. Among them 16 (77%) had fasting BG over 106 mg/dl, with a delay to the diagnosis of IDDM ranging from 5 years to 6 months. All of them were asymptomatic and had no familial history of IDDM. Abnormal BG (> 200 mg/dl) and insulin (< 30 µg/ml) responses were documented in 4 of them during an OGTT. These data, rarely available in children with IDDM, indicate that the clinical onset of the disease may be preceeded by a long period of minor hyperglycemia and hypoinsulinism. At the time when the efficiency of immunosuppressive therapies at the very onset of IDDM is under investigation, a systematic screening of BG in children may proove useful.

38 C.LEVY-MARCHAL[1],M.C.QUINIOU[2],M.DEBRAY-SACHS[2] and P.CZERNICHOW[1]. [1]Unité d'Endocrinologie Pédiatrique et [2]INSERM U.25, Hôpital Enfants-Malades, PARIS FRANCE.

Longitudinal study of cytotoxic antibodies and inhibitory lymphocytes in 7 diabetic children during the first year of their disease.

To investigate the possible role of autoimmune phenomenons during the remission period in type I diabetes, we have studied the time-course of two immunological markers in 7 diabetic children (age:1.5-7 y). During 12 months following diagnosis, we determined: 1)cytotoxic islet cells antibodies(CICA) by the release of ^{51}CR from mice islet cells after complement fixation;2)inhibitory lymphocytes(IL)tested by the inhibition of mice islet cells insulin secretion after patients lymphocytes addition. All the children have been treated by highly purified pork insulin. 5/7 children underwent a remission period (insulin requirements<0.5 U/kg/d) within the first weeks of treatment. CICA were found positive in 85% of the children at the time of diagnosis, and were decreasing after 6 months of disease(10% of positive sera at 12 months).CICA titration was not stable in a same patient. IL were found in 85% of the children at the onset and remained elevated,(80% at 12 months)despite a slight decrease after 6 months of disease. No correlation was found between insulin requirements and immunological parameters. In conclusion :-CICA were present in diabetic children with a high frequency early after diagnosis, which was decreasing after 6 months. -IL were present as well early after diagnosis. They appeared to be more stable during the first year of disease.

39 E.SCHOBER,+ H.FRISCH, G.SCHERNTHANER,+ M.BORKENSTEIN.+ Ped.Dept., 2.Med.Dept., LBI Ped. Endocrinology, Univ.Vienna, Ped.Dept.Univ. Graz, Austria. INCREASED ENDOGENOUS INSULIN PRODUCTION AND DECREASED DAILY INSULIN REQUIREMENT IN DIABETIC CHILDREN WITHOUT ANTIBODY FORMATION AFTER HUMAN INSULIN.

51 diabetic children (mean age 15,5±2,0 years) were exclusively treated with semisynthetic human insulin (HI) since manifestation of the disease. Insulin-antibodies (Iab), HbA_1 and stimulated C-peptide levels (120min. after standard breakfast) were determined before and 2-12 months after HI-treatment. After 12 months therapy 32 patients were Iab negative (group A) while 19 patients developed low Iab titres (group B). There was no difference in the HbA_1 values between the two groups. Stimulated C-peptide secretion was significantly higher in group A (0,18±0,02 vs 0,12±0,02pmol/ml, $p < 0,025$). Daily insulin requirement was significantly lower in group A (0,39±0,05 vs 0,61±0,11 IU/kg b.w., $p < 0,025$) after one year treatment. This finding indicates that the Iab negative condition is associated with preservation of endogenous B-cell secretion and lower exogenous insulin requirement.

40 S.M. HERBER* Intro. by Professor A.Aynsley-Green. Department of Paediatrics, University of Sheffield. Children's Hospital, Sheffield S10 2TH.

Growth hormone therapy following intracranial neoplasia: the final outcome

The final height of 27 children who developed growth hormone (GH) deficiency following treatment of an intracranial neoplasm (excluding craniopharyngioma) was studied. Eighteen children had tumours of the hypothalamo-pituitary tract, all but one of these had additional trophic hormone deficiencies. Nine children had other intracranial tumours, seven of these had isolated GH deficiency. Twelve patients finished with a height above the third centile for the population, but none fulfilled their genetic potential for stature. Sitting height was disproportionately reduced in all patients, this being even more pronounced in those with GH and gonadotrophin (Gn) deficiency. Patients with hypothalamo-pituitary tumours or those with GH and Gn deficiency showed significantly greater rise in height standard deviation score following therapy ($p<0.005$) than those with other cranial tumours or those who underwent spontaneous puberty. This was due largely to improved spinal growth. Sex of the patients and spinal irradiation were not significant factors in the overall response to therapy. It is postulated that cranial irradiation sufficient to cause GH deficiency may induce partial Gn deficiency in which sexual maturation occurs but the full effect of the pubertal spinal growth is not experienced