155

T.M.Strom*, J. Weil* and F. Bidlingmaier
University Children's Hospital, Munich and University of Bonn, Institute of Clinical Biochemistry, Bonn, West Germany

CHARACTERIZATION OF SPEZIFIC RECEPTORS FOR ATRIAL NATRIURETIC PEPTIDE ON HUMAN PLATELETS

The aim of our study was to characterize the receptor binding of human α-atrial natriuretic peptide (ANP) to easily available human cells. Blood cells possess receptors for peptide hormones as for instance platelets for vasopressin. We therefore, investigated the presence of receptors for ANP on human peripheral blood cells from adult volunteers. Whereas no receptors were detected on red cells, mononuclear cells and granulocytes, we found ANP-receptors on human platelets. The binding studies were performed by incubating 40 $x10^6$ platelets with ^{125}J-ANP(10^3 -10^6cpm) and the competing ligand, when used, in a total incubation volume of 1 ml. Centrifugation was used to separate bound from free hormone. Specific binding of ^{125}J-ANP was rapid, saturable and reversible. A steady state was achieved whithin 90 minutes. Scatchard analysis of saturation and competition experiments demonstrated the existence of one class of high affinity binding sites for ANP with a K_d of 8-16 pM and 10-26 receptors per cell. The K_d obtained in our binding studies was in the range of physiological ANP concentrations in human plasma (8-20 pM). Although characterization of platelet ANP receptors has the inherent disadvantage that they are few, they could be a useful model to investigate ANP receptor-status under different physiological and pathological conditions in man.

156

H.Radeke*[1], C.Kraus*[1], H.J.Balks*[2], A.Schafmayer*[3], P.Heidemann[1] Dpts. of Pediatrics[1], Internal Medicine[2] and Surgery[3], University of Göttingen, FRG

TREATMENT OF METASTATIC MEDULLARY THYROID CARCINOMA (MTC) WITH SOMATOSTATIN ANALOG (SMS 201 - 995) RESULTING IN REMISSION OF DIARRHEA AND DECREASE OF VIP AND GRP CONCENTRATIONS

A 15 year old boy was admitted to our department because of intractable diarrhea, flushes and pulmonary restriction over the last 4 years. Final diagnosis was Multiple Endocrine Neoplasia Type IIb (mucosal neuromas, MTC, marfan-like habitus) with pulmonary and lymphatic metastases of MTC secreting excessive amounts of calcitonin (CT: 150 ng/ml, normal: <0.3 ng/ml), vasoactive intestinal peptide (VIP: 484 - 91 pM, normal: <25 pM), gastric releasing peptide (GRP: >300 pg/ml, normal: undetectable) and carcino-embryonic antigen (CEA: 150 - 223 ng/ml, normal: <10 ng/ml). In adults, the long-acting somatostatin analog has been shown to suppress hormonal hypersecretion in many endocrine tumors including carcinoid syndromes and vipomas. Since no effective therapy of metastatic MTC is available so far, we used SMS 201 - 995 in an attempt to control diarrhea and tumor growth. During therapy with s.c. injections the boy experienced clinical improvement by decrease of stool frequency from 4 - 9 to 2 - 4 daily. VIP and GRP fell toward the normal range (9.94 pM and 15 pg/ml, respectively). However, CT and CEA did not change at all. Endocrine side effects were an inhibition of insulin and HGH secretion. SMS 201 - 995 appears to be a promising agent in the symptomatic therapy of intractable diarrhea. The decrease of VIP and GRP might indicate a partial inhibition of tumor activity and growth.

157

P.Ahonen*, E.v.Willebrand*, J.Perheentupa (Introd. by S.Leisti) Children's Hospital and Transplantation Laboratory, University of Helsinki, Helsinki, Finland

LYMPHOCYTE SUBSETS AND AUTOANTIBODIES IN PATIENTS WITH AUTOIMMUNE POLYENDOCRINOPATHY - CANDIDOSIS ECTODERMAL DYSTROPHY (APECED).

The basic derangement leading to immune destruction of endocrine glands in APECED is unknown. We studied lymphocyte subsets in 42 patients with APECED and in 21 healthy controls. Lymphocytes were treated with monoclonal antibodies detecting pan-T (OKT3), T-helper (OKT4), T-suppressor/killer (OKT8), E-rosetting (OKT11) T-lymphocytes, and surface immunoglobulin (SIG)-positive B-lymphocytes, and analyzed by fluorescence activated cell sorter (FACS IV). The patients had higher lymphocyte counts than controls (2.71+1.20 vs 2.10+0.52 $x10^9$/l; mean+SD; p=0.006). For all T-lymphocyte subsets studied, the dispersion of counts was wider for the patients than the controls. The mean counts were significantly different only for SIG-positive B-lymphocytes (0.50+0.28 vs 0.28+0.11 $x10^9$/l; p=0.0001). The OKT4-OKT8-ratio was subnormal (>1.0) in 5 and supranormal (<3.1) in 5 patients. The deviations observed did not correlate with any indicator of the severity of APECED or presence of any component of it. Presence of circulating ovarian, testicular or placental antibodies in contrast to adrenal antibodies was associated with supranormal counts of SIG-positive cells (p=0.031, p=0.02, p=0.004, p=0.35; respectively). Presence of circulating thyroid microsomal or thyroglobulin antibodies, or parietal cell or islet cell antibodies did not correlate with any lymphocyte subset pattern. No single feature was characteristic of APECED. Presumably the lymphocyte subset deviations are secondary manifestations of APECED.

158

S.Greene*, L.Rees*, P.Adlard*, J.Jones*, C.Chantler*, M.Preece
University Department of Paediatrics, Guy's Hospital and Department of Growth and Endocrinology, Institute of Child Health, London, UK.

ABNORMAL OVERNIGHT HORMONE PROFILES IN ADOLESCENTS WITH RENAL DISEASE RECEIVING LONG TERM STEROID THERAPY

We have investigated children following renal transplantation (PTX) and with steroid sensitive nephrotic syndrome (SSNS), both groups receiving long term alternate day steroid therapy; in children with SSNS frequent relapses necessitated periodic dose increases. Height SDS was below the population mean; PTX (n=10) -1.4(1.3), $p < 0.05$; SSNS (n=29) -0.82(0.22), $p < 0.001$. In children with SSNS Ht SDS correlated with duration of therapy ($r = -0.63$, $p < 0.005$), but not with relapse rate. We measured overnight endocrine function in 5 severely growth affected subjects (2 PTX age 14.4 and 17.6 yr; 3 SSNS age 14.1, 15.1 and 17.1 yr). Blood samples for GH, prolactin, FSH, LH, testosterone and cortisol were obtained every 15-20 min from 20.00 hr until 07.00 hr. Sleep state was monitored by continuous portable EEG. Abnormal profiles were seen in all 5 subjects. In the PTX adolescents there was no rise in GH or prolactin and no pulsatility of gonadotrophins. In the SSNS adolescents the patterns were consistent with pubertal delay (low amplitude and frequency pulses of GH and LH). These preliminary results indicate two different mechanisms of endocrine dysfunction which may account for growth failure and maturation delay in children with renal disease treated by long term steroids.

159

A.Chatziljami*, Ch.Mengreli*, M.Anapliotou*, S.Papadakou-Lagoyanni*, S.Pantelakis*(introd.by C.Dakou-Voutetaki).
Paediatric Unit of Aghia Sophia Children's Hospital and Institute of Child Health, Athens, Greece.

ENDOCRINE ASSESSMENT OF MULTI-TRANSFUSED PATIENTS WITH HOMOZYGOUS β-THALASSEMIA 16-24 YEARS OLD.

Clinical and laboratory examination of 41 multi-transfused β-thalassemic patients aged 16-24 years (18 boys and 23 girls) showed that 27 had entered puberty. The remaining 14 patients were at a prepubertal stage clinically with very low values of LH and FSH after LHRH test and with a ratio FSH/LH > 1. Daily administration of clomiphen citrate for 5 days showed no response of LH, FSH oestradiol and progesterone in females or LH, FSH and testosterone in males. Basal levels of testosterone and oestradiol were below normal values for puberty and there was no increase of testosterone release after HCG administration. The above results demonstrate that the hypogonadisme observed in one third of the patients aged 16-24 years is not perhaps exclusively secondary but that a primary damage of the target organ may also be present. Serum GH after insulin induced hypoglycemia, sleep or L-Dopa administration was ranging within normal levels. The study of T3, T4 and basal TSH in the 14 prepubertal patients showed normal levels in 5. A TRH test revealed normal TSH response only in 8 out of 14 prepubertal patients, the remaining 6 showed an increased response suggesting sub-clinical hypothyroidism. Our study shows that one third of the homozygous β-thalassemic patients aged more than 16 years were at a prepubertal stage and that at this age a more generalized endocrine dysfunction is present.

160

BP Leheup*, P Bordigoni*, B Dousset*, D Olive*, M Pierson. Departments of Pediatrics and Biochemistry, Hopital d'Enfants, 54500 Vandoeuvre les Nancy, France

GONADAL AND SOMATROPIC FUNCTIONS OF 13 CHILDREN AFTER BONE-MARROW TRANSPLANTATION

The long term efficiency of bone-marrow transplantation in children has to be judged both on the survival rate and on the importance of potential side effects. Alteration of growth pattern and of the gonadal and thyroid functions has been reported. 13 patients, 7 M and 6 F, aged 4y9m to 21y8m (mean = 11y2m) have been examined 9m to 3y5m (mean = 1y4m) after bone-marrow transplantation (9 allo, 4 auto) for the treatment of ALL in 6, lymphoma in 2, AML in 2, aplastic anaemia in 2 and Chediak-Higashi in 1. Growth velocity was found below the 5th percentile in 9 with height below the 3th percentile in 4. It was a trend to find lower growth velocity among patients with allotransplantation and TBI. Evidences of gonadal dysfunction were found in 5 cases. The 8 other patients were too youg to allow conclusion. The somatropin (GH) secretion judged on the pharmacological responses was fully normal in 6, deficient in 3 and border line in 4 patients. 9 of the 10 patients with decreased responses were explored for the nocturnal GH secretion pattern. Only 2 have a normal secretion, 4 have a decreased peak and 3 decreased peak and integrated secretion. The patients given total body irradiation tend to have a lower GH secretion. Such changes require a mandatory endocrinological follow-up for early diagnosis and treatment if necessary to allow a normal subsequent physical development.