10 R. COLLU, A.M. MARCHISIO* and D. ELJARMAK*. Pediatric Research Center, Hôpital Ste-Justine and Université de Montréal, Montréal, Canada.

Role of ions in Prolactin release.

To study the role of ions in the release of Prolactin (PRL), several experiments were performed utilizing dispersed pituitary cells obtained from adult, female Sprague-Dawley rats. All tests were done after a culture period of 5 days in multiwell Petri plates at 3 x 10^5 cells per well. Culture medium was Dulbecco's modified Eagle's medium (DMEM) supplemented with 10% horse serum, 2.5% fetal calf serum, non-essential amino-acids and antibiotics. PRL secretion was measured by specific RIA after 4 h of test incubation in various media at 37° in a CO_2/air incubator. Basal PRL secretion in DMEM (154±12 ng/ml) was drastically reduced in a hypoosmolar, sodium deprived medium (48±4 ng/ml), remained low when NaCl was replaced by isoosmolar concentrations of glucose (33±2 ng/ml), and was restored by the addition of either sodium or choline 110 mM. When DA 10^{-11}M was added to the medium with sodium, an 83% increment of PRL secretion was observed, while the neurotransmitter was completely inactive in absence of NaCl. DA 5 x 10^{-6}M strongly inhibited PRL release in the presence of sodium but was inactive either in the absence of the ion or when the ion channel was blocked by tetrodotoxin (TTX). Baseline and DA-stimulated PRL release were also strongly inhibited by the addition to the medium of either Co^{++} (a calcium channel blocker) or TTX. These results indicate that a normal ionic charge in the medium is essential for baseline PRL secretion, while both sodium and calcium ions are necessary for DA control of hormone release.

11 D.M. STYNE, J.B. TYRELL*, F.A. CONTE, S.L. KAPLAN, C.B. WILSON*, and M.M. GRUMBACH. Depts. of Pediatrics & Neurosurgery, Univ. California San Francisco, CA.

Treatment of Cushing's disease (C.D.) by transphenoidal microadenectomy (Tr.M.) in childhood and adolescence.

The efficacy of Tr.M. in the treatment of C.D. in children and adolescents has not been assessed. We treated 8 patients (7-6/12-18-9/12 yrs old) with C.D. by Tr.M. (followup 8-72 months postoperatively). Growth failure and weight gain were the first signs of C.D.; pubertal delay, virilization and fatigability were variable features. Preoperative evaluation showed elevated urinary free cortisol and no diurnal variation in plasma cortisol or ACTH values; high dose dexamethasone therapy suppressed excretion of urinary free cortisol. Two of 8 patients lacked definite radiographic evidence of a pituitary adenoma. Transphenoidal exploration revealed 1-4 mm adenomas in 7 of 8 patients; no definite adenoma was noted in the 8th patient in spite of CT scan evidence of adenoma. Postoperative complications were limited to transient diabetes insipidus. The 7 treated patients had low cortisol and ACTH secretion postoperatively and required replacement glucocorticoid therapy for 6-12 months. Weight loss, growth and pubertal progression without recurrence of C.D. were noted in 6 patients with long term followup. Our experience indicates that ACTH secreting microadenomas are the principal cause of C.D. in childhood and adolescence and suggests that transphenoidal microadenectomy is the initial treatment of choice for Cushing's disease in young patients.

12 K.R. LYEN and D.B. GRANT. The Hospital for Sick Children, London, UK.

Morbidity after surgery for craniopharyngioma.

Between 1953 and 1980 71 cases (M43:F28) of craniopharyngioma were treated either by cyst aspiration with DXT or tumour resection ± DXT. Of the 13 cases treated by aspiration, only one had diabetes insipidus and 2 required thyroxine treatment. However, at least 5 cases are known to have died, 4 as a result of tumour recurrence. There was a much higher incidence of pituitary deficits in the 58 cases treated by tumour resection. 46/58 had DI, 33/42 GH deficiency, 23/35 ACTH deficiency, 16/18 gonadotrophin deficiency, and 14/19 TSH deficiency. While only one patient died from tumour recurrence, at least 13 died because of endocrine deficits: 6 because of disturbed post-operative fluid balance and 7 following relatively minor intercurrent illness. In addition, 11 cases required emergency admission to hospital because of hypoglycaemia (8 cases), circulatory failure (1 case) or water overload (2 cases).

13 R. POMAREDE*, P. CZERNICHOW and R. RAPPAPORT. Hôpital des Enfants-Malades, Paris, France.

Idiopathic diabetes insipidus (DI) with transient or permanent anterior pituitary dysfunction.

Idiopathic DI is associated, by definition, with no obvious organic lesion. Despite negative clinical and neuroradiological investigations, the question remains of the tumoral origin of the disease, mainly if anterior pituitary dysfunction is demonstrated. The purpose of this study was to evaluate the course and significance of this association.

26 patients (6 familial) were investigated, with a follow-up of 4-20 yrs (x= 12.5 yrs) after onset of polyuria. Pneumoencephalography (n= 27) and/or CT scan (n= 11) were normal.

GH deficiency was present in 10/26 cases. Recovery, not related to puberty in all cases, was observed in 5 patients. TSH response to TRF (n= 17) was deficient (n= 3) or of the hypothalamic type (n= 4). Puberty was normal in 17 cases, and abnormal in 2 cases (respectively precocious and slowly progressing). GH deficiency was isolated in 5 cases or associated with ACTH +TSH (n= 1), TSH (n= 1), ACTH (n= 3) abnormalities.

In conclusion : long term observation is necessary to ascertain the diagnosis of idiopathic DI. Anterior pituitary deficiency may be associated, without any evidence of tumor. GH deficiency may be transient. These findings suggest that hypothalamic disturbances leading to idiopathic DI involve more that the hypothalamic posterior pituitary system itself.

14 J.SANDAHL CHRISTIANSEN*, K.W.KASTRUP, H.ØRSKOV*, and C.BINDER*.Steno Memorial Hospital,Gentofte and Childrens Hospital Fuglebakken,Copenhagen, Denmark.

Absorption of human growth hormone injected subcutaneously and intramuscularly in growth deficient dwarfs.

Human growth hormone (HGH) is commonly administrated by i.m. injections. The high purity of the present HGH preparations makes s.c. administration an attractive alternative enabling self-administration. In this study time courses of plasma HGH after s.c and i.m.injections of highly purified HGH (Nanormon$^{R)}$ are described and compared to the diurnal plasma HGH profile in eight normal children (11-14 years). Seven patients suffering from idiopathic HGH-deficient dwarfism (age 10-19 years) received i.m. and s.c. injection of HGH in the morning (4IU/m^2) in random order with an interval of one week. I.m. injections lead to a peak HGH concentration at 2 hours (mean 204,range 135-475 ng/ml) with a return to baseline 8-10 hours after injection.Correspondingly HGH concentration peaked at 4 hrs (mean 38,range 15-68 ng/ml)after s.c. injection and returned to baseline about 18 hours after injection. In a subsequent study on similar patients (n=7,age 10-19 years) HGH (2IU/m^2) was injected s.c. in the evening.HGH concentration peaked at 5 hours (mean 17,range 7-28 ng/ml) and returned to baseline 14 hours after injection.The results indicate that absorption from an i.m. depot is far too short to give a physiological diurnal profile of HGH in plasma - even by daily administration. However, daily s.c. injection will,if given in the evening,imitate normal nocturnal HGH profile.

15 RUTH ILLIG, M. ZACHMANN and A. PRADER Dept. of Pediatrics, University of Zurich, Switzerland

"A-type" isolated growth hormone deficiency (IGHD).

In 1970, we presented the "A-type" of autosomal recessive IGHD characterized by early and severe growth retardation, typical face with vaulted forehead, a strong metabolic and growth response to exogenous hGH, and a tendency to form high GH antibodies which abolish this effect.

Recent events prompt us to report on these patients again:

1) Philipps et al (abstr.Ped.Res. 1981) carried out restriction endonuclease studies in our original family A, yielding abnormal DNA patterns of the GH genes. In other families with IGHD, they found a normal pattern.

2) One of our female patients of the same family (26 years, 118 cm) gave birth to a healthy girl (GA 40 weeks, 2370 g, 43 cm). GH antibodies were found not only in the mother (12 years after the end of hGH R_x) but also in the newborn. Five months later, no more antibodies were detectable.

3) In another family we succeeded for the first time to treat a 5 year-old boy with hGH over a period of 1.5 years without the appearance of HG antibodies so far. This is in contrast to his 10 year-old brother previously treated with a different hGH preparation who developped high titre, growth-inhibiting GH antibodies. It appears that certain hGH preparations are tolerated by these patients who presumably suffer from a prenatal GH deficiency which may cause a lack of immunotolerance for hGH.

Supported by the Swiss National Science Foundation Grant No. 3.901.077