- 23** J.L. CHAUSAIN, D. GENDREL*, M. ROGER, J.C. JOB
Hôpital Saint-Vincent-de Paul, Paris, France.
Pituitary-gonadal function in normal boys and in male pseudohermaphrodites (MPH) during early infancy. Testosterone (T) and LH were measured in the plasma of 39 full-term males aged 7 to 180 days, and in 44 plasmas from 10 infants with MPH (XY karyotype and 2 palpable testes) in the same age range. Patients with enzyme defects on the T pathway were excluded. A LHRH test (0.1 mg/m²) was performed in MPH only. In both groups, plasma T rose progressively to peak around 2 months of age, before to decrease. The mean $\pm$ SEM peak levels of T were identical in normals ($3.6 \pm .2$ ng/ml) and MPH ($3.4 \pm .1$ ng/ml). Plasma LH underwent parallel changes, with mean peak values identical in normals (3.02 ± 0.41 mIU/ml) and MPH ($2.92 \pm .32$ mIU/ml). T and LH values were highly significantly correlated in normals ($r = 0.73$, $p < 0.001$) and MPH ($r = 0.59$, $p < 0.001$). In MPH, post-LHRH peak values of LH and FSH seemed also to peak at 2 months of age, and were significantly correlated with basal levels: $r = 0.76$, $p < 0.02$ for LH, $r = 0.86$, $p < 0.005$ for FSH. The data establish that 1/ the postnatal rise of T in male infants is secondary to an activation of the hypothalamopituitary gonadal axis; 2/ the negative feedback mechanism is normal during this period of life in MPH presumably secondary to a lack of receptivity to androgens.

- 24** M. DAVID*, P. BRAUN*, M.G. FOREST and P. MOLLARD*, Pediatric and surgical departements, INSERM U34, Hôp. Debrousse 69322-LYON Cedex 1 FRANCE.

Comparative study of persistent müllerian structures in 5 boys with ambiguous genitalia and in 2 true hermaphrodites (TH): implication for sex orientation.

The 7 subjects, considered male at birth, were studied at 3-17 yrs. Blood karyotypes were 46 XY/47 XXY (n=1), 45XO/46XY (n=2), 45XO/46 XY (n=3) in the 3 cases of mixed gonadal dysgenesis, 46XX (n=4), 47XXY/46XY/46XX (n=5) in the 2TH, 45XO/45Xt (Y-16) in n=6, 46XY in n=7, the latter two presenting with so-called "simple hypospadias". A vagina of variable dimensions (up to 10 cm) was shown by genitography or during micturition at cystography in all cases. Neither its size nor the radiological appearance could help to predict the presence of an uterus, which was found in nos 1-5. Endocrine studies ruled out any enzyme defect. An inadequate, although substantial, rise in plasma testosterone (T) after HCG did not discriminate the groups. In n=3 the T response to a 2nd HCG test was lower 6 yrs later and the apparently normal pubertal development in n=6 did not progress further than stage 3 despite high plasma LH and FSH, suggesting perhaps that testicular dysgenesis might be an evolving process. All cases but the 2TH were kept in the male gender, previous testing having suggested normal androgen sensitivity. However plastic surgery was difficult and the results poor, mostly because of small size of the phallus. In contrast, surgical and psychological results were satisfactory in the 2 TH subsequently raised as girls. We thus feel that the presence of a vagina is an important factor to consider when a decision of sex orientation has to be taken.

- 25** M. KNIP*, P. LAUTALA*, J. LEPPÄLUOTO* and H.K. ÅKER-BLOM, Departments of Pediatrics and Physiology, University of Oulu, Oulu, Finland.

Insulin-releasing activity in serum fractions of m. wt. 1,000-5,000 from obese and non-obese children.

Obese children have in a serum fraction of m. wt. 1,000-5,000 an insulin-releasing activity (IRA) occurring also in some normal-weight children, particularly in infants (Lautala, P.: Acta Univ. Oul D 32 Med. Interna Paediatr. 3:1978). The aim of the present study was to further characterize the IRA. The serum fractions of m. wt. 1,000-5,000 were prepared by urea treatment and filtration of the sera through four Amicon[®]-membranes of different pore sizes. Eight serum fractions containing IRA from four obese and four non-obese children were subfractionated with reversed-phase high pressure liquid chromatography into four subfractions (SF). IRA of the fractions and their SFs was measured by perfusion of isolated rat islets. The first SF did not in any case contain IRA. The second SF was positive in all eight children. The third SF contained IRA in six children, while the fourth SF was positive in four children. IRA did not show a relationship to the radioimmunologically measured concentrations of pancreatic glucagon, gut GLI or GIP in the serum fractions. These results indicate that serum fractions of m. wt. 1,000-5,000 from obese and some non-obese children contain at least one insulin-releasing substance, which is obviously not identical with glucagon or GIP.

- 26** M. GOURMELEN, F. GIRARD and M. BINOUX
Laboratoire d'Explorations Fonctionnelles
INSERM U 142, Hôpital Trousseau, Paris, France.
IGF (Insulin-like growth factors) levels in cases of total GH deficiency caused by a tumour.

A study has been made of 36 cases (24 children and 12 adults) in whom the total GH deficiency could be attributed to the presence of a tumour: craniopharyngioma (n = 20), chiasmatic glioma (n = 7), medulloblastoma, pinealoma, chromophobe adenoma (n = 9). Serum IGF were assayed by means of a radioligand assay using purified NSILA-S (gift from Dr Zapf, Zurich) and a specific binding protein produced by rat liver in culture. Results are expressed in relation to a standard pool of serum from normal adult males arbitrarily assigned a value of 1 U/ml IGF. The mean IGF level for these cases was 0.55 ± 0.06 (SEM) U/ml, which is significantly lower than that for normal adults (1.09 ± 0.03 U/ml, n = 21) ($p < 0.001$) but significantly higher than that for patients with non-tumoral GH deficiency (0.18 ± 0.03 U/ml, n = 16) ($p < 0.001$). Ten of the patients under study had normal or slightly increased IGF levels (0.75 - 1.6 U/ml). Among the cases of non-tumoral GH deficiency, IGF levels were constantly lower than 0.5 U/ml. Neither age nor association of the condition with obesity or a disorder of the secretion of any other pituitary hormone could account for the differences in IGF level between the two groups. These data bring to mind our findings on the production of IGF by rat brain explants in culture. A tumoral etiology, which is systematically investigated in cases of total GH deficiency, is therefore more especially to be suspected if the IGF levels are normal.

- 27** L. AKSNES* and D. AARSKOG, Department of Pediatrics, University of Bergen, Bergen, Norway.

Vitamin D metabolites in serum from hypoparathyroid patients treated with vitamin D₂ and 1 α -hydroxy vitamin D₃.

After separation on HPLC vitamin D₂ and D₃ and their metabolites 25OHD₂, 24,25(OH)₂D₂, 25,26(OH)₂D₂ and 1,25(OH)₂D₃ were measured in sera from two hypoparathyroid patients on high doses of vitamin D₂.

After change of treatment from vitamin D₂ to 1 α -hydroxy vitamin D₃ there was an initial relatively rapid fall of vitamin D₂ and its metabolites followed by a more slow decline. High levels of vitamin D₃ metabolites were still present after 13 months. Taken into account the marked preponderance of 25OHD₂ to 25OHD₃ the relative concentration of dihydroxyvitamin D₃ metabolites were higher than expected, which might indicate a preferential 25OHD₃-hydroxylation, or alternatively, a more rapid degradation of vitamin D₂ metabolites in these patients.

The high and sustained release of vitamin D₂, presumably from fat stores, more than a year after vitamin D₂ ingestion was stopped should be considered in the long term follow-up of patients shifted from the traditional high doses of vitamin D to the newly synthesized 1 α OHD₃ or 1,25(OH)₂D₃.

- 28** H.J. DEGENHART, G.J. ALSEMA and H.K.A. VISSER
Dept. Pediatrics Erasmus Univ. Rotterdam.

Effects of cholestenone feeding in rats.

In several conditions (e.g. congenital lipid adrenal hyperplasia; disorders of bile acid synthesis), sterol metabolism is disturbed and formation of abnormal sterols can be expected. In a pilot study we investigated the effects of cholestenone, a cholesterol metabolite which occurs normally in low concentrations only. Cholestenone, fed for 3½ months, (1% w/w in the standard laboratory chow) was found to cause significant growth retardation in male Wistar rats (mean weight 270 g (n=3) vs. 380 g (n=3) of controls). The adrenals were grossly enlarged (mean weight 44.4 mg vs. 19.1 mg in controls). Growth retardation also occurred in female rats fed cholestenone. Their ovaria as well as adrenals were hyperplastic and pale yellow. Isolated adrenal cells of test animals showed complete loss of sensitivity for ACTH at a concentration of 100 µU/ml. They were unable to synthesize corticosterone from exogenous 25-OH-cholesterol. Corticosterone production from exogenous pregnenolone dropped to 20% of control values. In the blood and other tissues cholesterol, both free and esterified, was partly replaced by cholestanol and its esters. Resistance of the erythrocytes to osmotic shock was significantly decreased.