41 M.B.RANKE[+],P.HILDEBRAND[+],C.RUDOLPH[+],E.HEINZE[+], R.BREITNER[+], and D.GUPTA.Dept.of Diagnostic Endocrinology,University Children's Hospital, D-74 Tübingen, FRG.

A longitudinal study of the effects of SRIF on growth and peripheral hormones in the male rat during pubertal development.

Although many aspects of the biological activities of SRIF or somatostatin had been studied previously, its effects on body growth in relation to various blood hormones related to growth during pubertal development has not been clarified. In the current study SRIF (protamin-Zn) was administered S.C.(1mg/kg b.w.) to male Wistar rats daily over a period of 20-90 days of life, and body growth together with serum concentrations of GH,insulin,LH,FHS,T,DHA,SM(porc.cart.) and sugar were examined longitudinally. In parallel experiments effects of withdrawal of SRIF at various phases of development were also studied. Somatostatin inhibited secretion GH,insulin,and SM and had severe adverse effects on body growth and its velocity. Withdrawal of SRIF at various stages of life led to catch-up growth and normalization of GH and insulin levels. SM,however, remained low and DHA peaked in all animals. These multiple effects of SRIF leads to conclude that this hormone permanently blocks SM; and catch-up growth is perhaps SMindependent but GH and insulin dependent. Further, adrenarche is also present in the rat.

42 M.D.C. DONALDSON[*], M.G. FOREST and J.M. SAEZ. INSERM U 34 and U 162, Hôpital Debrousse, 29 Rue Soeur Bouvier, 69322 Lyon Cedex 1, France.

Effects of oestradiol benzoate (E2B), tamoxifen (tamox.) and 1,4,6-androstatriene-3,17-dione (ATD) on rat testicular function.

The effects of 2 anti-oestrogens - ATD, an aromatase inhibitor, and tamoxifen - as well as E2B itself were studied in adult male rats. E2B and tamox were both given in a single I.M. dose of 100 µg either 12, 24 or 36 hrs before sacrifice while ATD 10 mg was given I.M. 12 hrly for 12, 24 or 36 hrs. Half the animals in each group received 500 IU hCG I.M. 2 hrs before sacrifice while half received none. Plasma levels and testicular content of testosterone (T), 17OH-progesterone (OHP) and progesterone (Pro), as well as plasma LH and FSH were measured by specific RIAs. E2B treated rats showed a significant decrease in plasma T, OHP, LH and FSH, but not Pro, under basal conditions. T and OHP responses to hCG were significantly lower than in controls, while plasma Pro increased but not significantly. The effect of E2B on testicular steroidogenesis under basal conditions could thus be linked with an inhibition in LH secretion, but the impaired testicular response to hCG demonstrated a direct effect on testicular steroidogenesis. Animals treated with ATD and tamox under basal conditions showed a significant rise in plasma T and LH levels, maximal at 24 hours for ATD and at 36 hours for tamox. Thus in the doses given, both drugs appeared to have an anti-oestrogen effect, associated with enhanced LH secretion. However, the T responses to hCG were significantly diminished in both ATD and tamox-treated rats. This paradoxical response might reflect a degree of steroidogenic refractoriness of the testis to hCG, caused by the drug-induced increases in endogenous LH.

43 J.R.DUCHARME, R.HAMEL*, C.POLYCHRONAKOS*, M.FOREST, F.HAOUR, G.CHARPENET*, W.GIBB* and R.COLLU. Centre de Recherche Pédiatrique, Hôpital Ste-Justine, Mtl, Que. H3T 1C5 and INSERM U 34/162, Hôpital Debrousse, 69322 Lyon.

Testicular response to hCG in the immature lamb.

Previous studies have shown of an early postnatal activation of the hypothalamic-pituitary-gonadal axis (HPGA) in the male lamb, suggesting its usefulness in the study of this phenomenon in man. To define the time sequence in the appearance of this activity, the "in vivo" and "in vitro" testicular responsiveness to hCG of the immature lamb as compared to the adult ram was studied. One, 3,7,14, 21 and 28 day old lambs and 1 year old rams were hemicastrated and the second testis removed 2h after hCG (500 IU/kg). Plasma testosterone (T) was low from 1 to 28 days (<.3ng/ml), the highest levels being found at 28 days. Plasma T increment (Δ) after hCG rose progressively from 1 to 14 days (0.26±0.01 to 0.95±0.16ng/ml), decreased at 21 days (0.64± 0.06) to rise again at 28 days (0.84±0.11ng/ml). The Δ T post hCG in adult rams was 8.3±0.66ng/ml. In general maximal Δ T levels were reached within 1h post hCG. Δ of T, 17-OH-progesterone, dehydroepiandrosterone and Δ_4-androstenedione increased from 1 to 14 days. Testicular 17-20 lyase activity rose with age without influence of hCG. T production by isolated interstitial cells in basal and stimulated conditions (hCG, db cAMP, cholera-toxin) was higher at 3 and 7 days. These data suggest that the lamb testis has the capacity to respond to hCG "in vivo" and to various stimuli "in vitro" from the first day of life.

44 P.SAENGER*, E.FORSTER*, J.KREAM* (Intr. by E.Sobel), Albert Einstein Coll.Med., Montefiore Hosp. Med. Ctr. Dept. Ped. and Clin. Res. Center, Bronx, N.Y.

6β-Hydroxycortisol: A non-invasive indicator of enzym induction.

We describe here a non-invasive, in-vivo tool to evaluate hepatic enzyme induction. We applied a specific RIA measuring the excretion of 6β-hydroxycortisol (6βOHF). 6βOHF is a polar, unconjugated metabolite of cortisol. 6βOHF is formed by the mixed function oxidase system in the liver and excreted by the kidney. Normal excretion of 6βOHF children is 0.21±.03 mg/m^2/24hr., thus comprising approx. 10% of the 17-hydroxycorticoid (17OH) excretion. Under baseline conditions there is a good correlation with 17OH excretion (r=0.7, p<.01) and an even better correlation with free cortisol (FF) excretion (r=0.9, p<.001). 6βOHF/17OH and 6βOHF/FF ratios were calculated to correct for fluctuations in cortisol production. Mean values corrected for surface area (±SD) after treatment with known inducers (Phenobarbital, Diphenylhydantoin (DPH) are:

	n	6βOHF	6βOHF/17OH	6βOHF/FF
Normal Children	(40)	0.21	0.1 ±.042	6.4±1.9
Phenobarbital	(14)	1.14	0.37±.27	20.1±4.5
DPH	(15)	1.22	0.41±.24	18.4±5.9
Phenobarbital + DPH	(9)	1.3	0.57±.32	24.5±6.5

These data show that these drugs, singly or in combination, significantly induce 6β-hydroxylase, a microsomal enzyme (p<.001).
Conclusions: 6βOHF measurements provide a sensitive and convenient probe in the non-invasive evaluation of drug effects in children.

45 S.BERNASCONI,N.REALI*,F.BACCIOTTINI*,G.ORLANDINI*,M.BARIOGLIO,G.GIOVANNELLI,A.CASTI* Dept.of Paediat.and Dept.of Biochemestry* University of Parma, Italy.

Blood polyamine changes in newborns.

A role of polyamines in the growth process and in the hormonal activity has been recently suggested.In the present study blood polyamine levels were evaluated in 53 full-term newborns within the first 5 days of life by thin layer chromatography.In an additional 4 cases polyamine concentration was determined at 24 hrs interval until the 10th day after birth.

The results demonstrated that the mean blood polyamine concentrations are higher than found in the subjects of more advanced age we had previously investigated. Furthermore,a progressive significant decrease of both spermidine and spermine was observed,during the first 10 days of life, more evident after the 5th. The significance of these changes in the polyamine concentration is still uncertain.However,the observation that,early after birth, the pattern of polyamines in blood parallels that of many hormones is likely not to be casual.

46 Z.Hochberg*,RA Richman* (Intr. by R.Kauli). New York State Univ. Upstate Med.Ctr., Syracuse. N.Y.

Instable osmoreceptors and deficient thirst in hypothalamic hypopituitarism.

A unique abnormality of osmoreceptors is reported in a child with hypothalamic hypopituitarism. Anterior pituitary testing revealed deficiency of GH, TSH and ACTH. The clinical course was characterized by fluctuation between dehydration of diabetes insipidus and coma of water intoxication. Plasma/Urine osmolality ranged from 263/110 mOsm/kg to 325/187 mOsm/kg. Osmotic threshold (OT) was determined by isovolemic infusion of hypertonic saline. An abrupt decrease of 30% or more of free water clearance defined the OT. During a hyponatremic episode the OT was detected at 263mOsm/kg. While hypernatremic OT was found at 300 mOsm/kg. These values are significantly different from the 286.6± 0.9 (M±SD) mOsm/kg found in 6 healthy volunteers. The presence of endogenous vasopressin, and the normally functioning volume receptors was demonstrated by the normal urine concentration when dehydrated. With plasma osmolality as high as 307mOsm/kg the child denied any feeling of thirst. The data indicate an instability of the osmoreceptors and a deficiency of thirst mechanism with intact volume receptors.