11 S.C.VAN BUUL-OFFERS*, L.DUMOLEIJN*, M.FEYLBRIEF*, C.HOOGERBRUGGE*, P.VAN DE KLUNDE* and J.L.VAN DEN BRANDE. Dept. of Pediatrics, Univ. of Utrecht, the Netherlands.

The effect of hGH, thyroxine and semipurified somatomedin (SM) on cellular growth of some organs of the Snell dwarf mouse.

Growth of the hypopituitary Snell mouse is partially restored by administration of hGH, thyroxine and SM. In order to investigate whether these preparations induce cell division and/or hypertrophy DNA and protein of liver, kidney and spleen were measured after treatment and contrasted with normal and dwarfed controls. Results of the latter are as follows:

	liver(mg)*			kidney(mg)*			spleen(mg)*		
	W	D	P/D	W	D	P/D	W	D	P/D
control	367	0.97	47.3	72.5	0.70	12.4	9	0.23	5.3
hGH	503	1.38	51.6	89.7	0.81	14.9	17.6	0.49	5.2
T4	572	1.95	45.9	167.9	0.99	22.4	48.6	1.24	5.8
control	421	1.05	58.1	76.6	0.70	14.7	12.8	0.35	5.2
SM-P1	453	1.18	71.0(?)	102.1	0.76	17.8	21.9	0.50	6.4
control	319	1.21	35.5						
SM-P4	464	1.50	39.3						

*SEM <10%; W=weight; D=DNA; P=protein

SM induces cell division but only little cell enlargement in the liver and the spleen, as do hGH and T4. Cell division of the kidney is barely affected by SM and hGH, but markedly by T4, whereas all preparations induce hypertrophy of this organ.

12 E.Heinze, Ch. Nguyen Thi⁺, R.D. Fussganger⁺, Center of Pediatrics and Internal Medicine, University of Ulm/Donau, F.R.G.

SERUM SOMATOMEDIN (SM) IN FETAL RATS. EFFECT OF GLIBENCLAMIDE AND GLUCOSE.

In adult rats insulin increases the serum SM concentration. This effect is unknown in the fetus. In the present experiments the influence of glibenclamide on serum SM was studied in normal, glibenclamide treated (1mg/kg/day for 5 days) and in continuously glucose-infused (20g glucose/day/rat mother for 2 days) 21 days old fetal rats. After an overnight fast of 12-14 hours SM was measured with the porcine bioassay. In addition, the effect of glibenclamide on fetal insulin (IRI) secretion was determined:

Results: Glibenclamide decreased the fetal blood glucose (0 min: 76±8 mg/dl⁺; 20 min: 48±12 mg/dl⁺; n=9; p<0.05) and increased fetal IRI (0 min: 97±7 µU/ml⁺; 20 min: 155±17 µU/ml⁺; n=9; p<0.0025). Fetal SM: normal 0.42±0.06 U/ml⁺; n = 9; glibenclamide: 1.08±0.19 U/ml⁺; n = 7, vs normal p<0.02; glucose infused: 0.98±0.12 U/m, n = 5; vs normal p<0.001.

Conclusion: Insulin seems to influence fetal serum SM activity. This fact complicates the suggestion that insulin as a fetal "growth hormone" may stimulate growth directly and/or via the generation of SM. M ± SEM⁺

13 R.M. SCHIMPF*, and G.THERIOT-PREVOST* (Intr. by J.C. Job). Hôp. St-Vincent, Paris, France.

An hormonally controlled serum factor stimulates thymidine incorporation into lectin-activated lymphocytes.

The in vitro stimulation of 3H-thymidine (T) incorporation into lectin-activated human lymphocytes was studied in presence of various sera and compared to a normal reference serum (1 U/ml activity). The mean precision of the assay was 5%. The inter-assay variability was 0.06 U/ml (95% confidence). Compared to 19 normal adults (mean ± SEM : 1.04 ± 0.06 U/ml), serum T activity was increased in 3 acromegalics (2.63 ± 0.48, p<0.001) and decreased in 17 hypopituitary dwarfs (0.37 ± 0.04, p<0.001), T activity being significantly less in them than in 17 constitutional dwarfs in the same age range (1.51 ± 0.13, p<0.001). In hypopituitary, a single IM hGH injection increased the T activity (p<0.001) after 24 to 48 h. Only high supraphysiological doses of hGH, insulin and T3 were slightly effective. Purified Somatomedin A diluted at physiological levels increased the T incorporation and its effects were enhanced in the presence of serum. These data demonstrate that 3H-T incorporation into activated lymphocytes is stimulated by a GH-dependent serum factor. They suggest to use this technique for a rapid, accurate and sensitive evaluation of serum somatomedin activity.

14 M.A. PREECE*, L. GRECO*, M.O. SAVAGE, N. CAMERON* and J.M. TANNER. Department of Growth and Development, Institute of Child Health.

The Auxology of Growth Delay.

Growth delay is the commonest cause of short stature, especially in boys, accounting for 26% of patients seen in the Growth Clinic of the Hospital for Sick Children. Despite the good prognosis the disorder causes much unhappiness and concern.

Growth and pubertal development were studied in detail in 315 boys in the age range 2 to 21 years. Mixed longitudinal analysis showed a concordant delay of body measurements and skeletal maturity, apparent from the earliest ages. Pubertal development was comparably delayed. Forty boys were followed until mature height was reached (less than 1 cm gained over the last year). In these, mature height averaged 164.0 cm (-1.7 SDS) with 10th and 90th centiles at 155 and 168 cm. Mean height prediction (TW2-RUS) made at first clinic visit (mean age 13.7; SD 2.9 years) was 161.7 and was therefore unduly pessimistic. The mean height of fathers (mostly reported) was 172.7 cm, (-0.3 SDS) and of mothers 160.5 cm, (-0.3 SDS). We suppose that selection for attendance at the clinic accounts for most or all of the discrepancy between heights of sons and parents; their small sons attend; their tall ones do not. Correlation of the patients' mature heights with fathers' heights was 0.55; with mothers' 0.22; neither were significantly different from the theoretical 0.5.

15 R.ILLIG, T.TORRESANI, H.BUCHER and A.PRADER Dept. of Pediatrics, University of Zürich, Switzerland Transient rise of normal LH and FSH secretion during puberty in 85 healthy girls with tall stature.

In 85 healthy tall girls (age 10-16, bone age 10-14), LHRH tests (25 µg/m2 i.v.) were carried out before treatment with high dose steroid hormones in order to exclude risk factors. Results (mean and SEM) grouped according to breast stages in girls before and after menarche show significant rises of hormone levels, particularly of peak LH values, with increasing breast development in premenarcheal girls, and a remarkable fall after menarche.

Breast stages	n	LH ng/ml (LER 907)		FSH ng/ml (LER 907)	
		basal	peak	basal	peak
pre menarche B 1	9	12.6 (1.1)	32 (5.0)	80 (12.3)	227 (1.8)
B 2	6	20.2 (5.1)	67 (13.3)	199 (38.6)	278 (27.2)
B 3	30	23.4 (2.0)	114 (12.7)	180 (9.5)	301 (14.7)
B 4/5	20	30.8 (3.9)	169 (16.4)	150 (17.5)	294 (20.8)
post men. B 3/4/5	19*	19.5 (2.0)	68 (7.1)	152 (14.5)	268 (18.9)

*tested during first half of menstrual cycle

One could speculate that a transient rise of gonadotropin secretion during puberty is essential to switch the regulation of the hypothalamo-pituitary-gonadal axis from the infantile to the adult type.

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16 S.KORTH-SCHUTZ, A. GROTERS*, B. WEBER, and H. HELGE Kinderklinik der Freien Universität, Berlin, FRG

Increased PRL-reserve in hypogonadal patients during puberty. - Evidence for negative feed-back regulation during puberty?

Hypophyseal hormones' secretion was stimulated by a test procedure using simultaneously TRH, LH-RH, and insulin in 3 hypo- and 9 agonal patients aged 8-16 ys, with bone ages ranging from 8-14 ys. The results were compared to those of 10 normal prepubertal and 6 pubertal subjects. PRL, TSH, LH, FSH, and hGH were measured by RIA, for PRL the Serono Kit was used. In normal children (C) and adolescents (A) PRL increased to maxima from 15 -50 (♀) or 18-44 (♂) ng/ml after 15-60 min. No difference was observed between C and A or between ♀ and ♂. 5 out of 8 girls with Turner's syndrome showed exaggerated PRL-responses at 60min (26-84 ng/ml), 3 of them also at 15-30 min (64-85 ng/ml). Similar results were observed in 1 agonal boy and 2 boys with Klinefelter's syndrome. The 60min value, in particular, was greatly elevated compared to results in normal boys (33-78 vs 8-25 ng/ml). This difference could not be attributed to variations of the hypoglycaemic responses. The peak PRL concentrations were positively correlated to the basal LH and FSH concentrations (r=0.80, n=10) in the hypogonadal patients, but not in the normal children. From these results it is concluded that in patients with diminished gonadal function the lack of gonadal steroids during puberty may lead to an increased PRL reserve of the pituitary gland. The significance of this finding remains to be determined.