82 E. VICENS-CALVET, J.M. VENDRELL, M. ALBISU, N. POTAU, L. AUDI, M. GUSIÑE. Children's Hospital Autonomous University. Barcelona. Spain.

The dosage dependency on growth and maturity in growth hormone deficiency(GHD)treated with human growth hormone(hGH).

28 GHD patients aged 3-10 yrs. were treated with hGH (Roos-Kabi) during 1-4yrs. without pubertal interference. Dosages were 2mg in D_1(N=19) and 4mg in D_2(N=9), 3 times/week.11 patients received treatment during 4 full yrs.:6 in $D_1(rD_1)$ and 5 in $D_2(rD_2)$.The mean Chronological Age(CA),Bone Age(BA),Height(Ht)SDS*and BA.SDS were comparable in both groups at the onset of treatment. 1.-The evolution of height showed that in D_2/rD_2 the increase in SDS was significantly higher than in D_1/rD_1 through the treatment.The catch-up period was 3 yrs. in D_1/rD_1 and it was still present in D_2/rD_2 in the 4th yr. 2.-In D_1/rD_1 the BA increased parallely to the CA,but in the D_2/rD_2 there was a continuous catch-up of BA with BA>CA in the 4th yr. 3.-The relationship $\Delta Ht/\Delta BA$ was : $\frac{\Delta Ht.SDSD_1}{\Delta BA.SDSD_1}=1.45$; $\frac{\Delta Ht.SDSD_2}{\Delta BA.SDSD_2}=1.12$; $\frac{\Delta Ht.SDSD_2-\Delta Ht.SDSD_1}{\Delta BA.SDSD_2-\Delta BA.SDSD_1}=0.81$. Whether this expected early bone fusion using the D_2 dosage is due to the hGH itself or to a contamination by TSH/Gonadotrophins is now being investigated.

*SDS = Standard Deviation Score

83 A. Broughton*, L. Jones*, L. Underwood**, J. Van Wyk**.

Nichols Institute, San Juan Capistrano, California*, University of North Carolina, Chapel Hill, North Carolina**.

A New Improved Method for Collecting Samples for Somatomedin C Determination.

The current specimen collection for the determination of Somatomedin C requires venipuncture, centrifugation, then serum or plasma separation followed by shipment to a laboratory performing the assay. Collection of capillary blood on specially prepared filter paper followed by air drying and mailing to the laboratory, removes all the steps of the traditional approach. Upon receipt by the laboratory, a 1/8" disc is cut in the dot and the blood eluted by a buffer. The volume of blood in the 1/8" dot is 0.15 microliters of plasma (Neonatal Screening programs). The radioimmunoassay is then performed using second antibody separation technique following a sequential immunoassay using a rabbit anti-somatomedin C antibody and 125_I somatomedin C. The technique was compared with the reference plasma assay and a correlation coefficient of 0.93 obtained. The assay was also extensively validated with samples from five hundred normal children and forty children with growth hormone deficiency.

84 D. EVAIN* and E. BINET* (Intr. by J.C. JOB) INSERM U. 188. Av. Denfert Rochereau 75014 Paris.

Secretion of calcitonin and parathyroid hormone by embryonal carcinoma cells : variations with differentiation.

Differentiation of teratocarcinoma cells in culture allows to study certain aspects of the early embryogenesis. The adenylate cyclase system of cultured F9 cells is specifically stimulated by calcitonin. Differentiation into endodermal cells by treatment with retinoic acid is followed by a loss of calcitonin responsiveness and the appearance of parathyroid hormone stimulation of the cyclase system. In addition radioimmunological and biological active forms of calcitonin are secreted by F9 cells in the culture medium. Along with differentiation with retinoic acid a progressive decrease of calcitonin secretion is observed : after 4 days of treatment no calcitonin is any longer detectable. But at this stage of differentiation a parathyroid hormone-like substance is radioimmunologically and biologically detectable. These specific changes in hormonal secretion and receptivity can be used as markers of differentiation. These results also suggest a possible role for Calcitonin and Parathyroïd hormone-like activities during the initial steps of embryogenesis.

85 L. FRYKLUND*, K. FHÖLENHAG*, B. HOLMSTRÖM*, A. SKÖTTNER-LUNDIN*, A. WICHMAN*, and H. FLODH* (Intr. by Prof. K. Hall), KabiVitrum AB, S-112 87 Stockholm, Sweden.

Biosynthetic human growth hormone produced in E. coli.

The gene for human pituitary somatotropin (hGH) has been inserted into the plasmid PBr 322 in E.coli K_{12} by recombinant DNA techniques. The recombinant bacteria have been grown in batch culture and the hGH extracted from the disintegrated cells. Conventional biochemical separation methods such as ion exchange and gel chromatography have been used for purification in a scale suitable for industrial production.

The biosynthetic hGH appears to be identical with regards to molecular weight and sequence with the exception of an N-terminal methionine. No contaminating proteins are present. Biological activity, determined by weight gain in hypophysectomized rats and sulfate incorporation into connective tissue appears to be identical to that of the pituitary hormone. Extensive toxicoligical studies suggest that the product should be safe for human use.

We conclude that the biosynthetic human growth hormone is comparable to the pituitary hormone and this product once available should alleviate the shortage of hormone for the treatment of hypopituitary dwarfism.

86 Z.GREIF; A.BENDERLI; Z.HOCHBERG; and J.LEVY* (Intr. by M. Karp). Faculty of Medicine, Technion, Haifa, Israel.

Growth response to chronic treatment by Dopa in rats.

To study the effect of chronic administration of L- Dopa on growth 10 pairs of rats, matches by sibship and sex were injected 5mg/kg Dopa, or saline s.c. twice daily, from 3 to 13 weeks of age. Pair feeding was assured. At 13 weeks, after 2 days off treatment the animal were sacrificed. Blood was collected for GH RIA and the thymus, thyroid, adrenals, uterus and gonads weighed. Female and male rats grew significantly better on L-Dopa:

	3 weeks		9 weeks		13 weeks	
	W(g)	L(cm)	W(g)	L(cm)	W(g)	L(cm)
Fem. Con.	30±2	17±.5	180±9	34±.7	206±15	37±.2
Dopa	31±2	17±.5	207±14	36±.5	242±14	39±.3
Mal. Con.	38±3	18±.2	272±6	38±1.3	305±14	41±.8
Dopa	37±3	18±.3	305±12	40±.2	342±14	43±.6

Serum GH was 8.44±1.4ng/ml in the Dopa and 4.6±0.9 in the control group. All organs weighed tended to be heavier in the Dopa group, though not significantly. In conclusion: Chronic administration of L-Dopa produce a chronic stimulation of GH secretion and enhances growth in male and in female rats.

87 M.H. HEULIN, M. ARTUR, D. MALAPRADE, J. STRACZEK, M. PIERSON, J.F. STOLTZ, F. BELLEVILLE, P. PAYSANT, P. NABET (Intr. by M. Pierson). C.H.U. Central. Lab. of Biochemistry - 54000 NANCY - FRANCE

Evidence for the presence in human serum of an ultrafiltrable factor activating somatomedins

Human serum contains an ultrafiltrable factor (350 < M.W. < 700) which stimulates sulphation activities of native, or purified somatomedin A of either small or high molecular weight. The factor is heat stable, resists protease hydrolysis but is destroyed by strong acidic hydrolysis. It is not extractible by chloroform. It restores somatomedin activities of conserved fractions and allows good conditions of bioassays of purified fractions. This factor is not a known amino-acid, a polyamine, vitamin A, zinc, T4 or T3. It stimulates somatomedin activity equally if added together with the somatomedin, or if added before (and removed) the adding of somatomedin.