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BIOLOGICAL ACTIVITY OF GROWTH HORMONE (GH) IN THE FIRST MONTHS OF LIFE

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The aim of our study was to evaluate GH levels using RIA and bioassay in the 1 months of life. Serum samples from 22 normal full-term newborns were collected at the 5th day and then at the 1st and 4th month of life, at the time of biological routine samplings (anti-hepatitis B immunization). In the same serum sample we evaluated both radioimmunological activity of GH and biological activity of GH using Nb2 rat lymphoma cell bioassay. High GH concentrations measured by RIA (32.72±3.95 ng/ml) and Nb2 bioassay (3.29±3.95 U/ml) were observed in neonates at the 5th day of life. At the 1st and 4th month we found a significant decrease ($p<0.001$) of radioimmunological (of 75.27% and 92.29%, respectively) and biological activity of GH (of 24% and 42.76%, respectively). A significant correlation ($p<0.01$) between GH values measured by RIA and Nb2 bioassay was observed at the 5th day, but not at the 1st and 4th month of life, since the biological activity of GH decreased less than the radioimmunological 1 during the 1 months of life. Our results indicate a good agreement between immunoactivity and bioactivity of GH in the first days of life, but not later.

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INTRAUTERINE GROWTH RETARDATION : HOW TO DEFINE IT

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Intrauterine growth retardation (IUGR) is generally defined by birthweight below the P3. However, weight can be affected in the last weeks of pregnancy without necessarily reflecting prolonged impairment in intrauterine growth. Early in pregnancy growth is affected proportionally and the term "intrauterine growth retardation" seems more appropriate. In an attempt to clarify this we assumed that by taking into account the proportions of the infant independent of weight, we could be able to define intrauterine growth better. Crown-rump length, subischial leg length and head circumference were measured and the proportion in a three dimensional way was studied in 49 infants with a birthweight below the third percentile.

	boys		girls	
number	20		29	
mean gestational age (weeks, SD)	37.5	(3.0)	38.6	(2.4)
mean postnatal age at examination (weeks, SD)	2.9	(3.0)	1.6	(1.7)
number of infants with a score outside 2 SD				
Weight	20/20	(100%)	29/29	(100%)
Ponderal index	12/20	(60%)	18/29	(62%)
Crown Rump length	3/20	(15%)	2/29	(6%)
Subischial leg length	3/20	(15%)	0/29	(0%)
Head circumference	1/20	(5%)	0/29	(0%)
P-score	7/20	(35%)	6/29	(20%)

The P-score indicates the 95% normality value for the body proportion.

There was no correlation between the Ponderal Index and the P-score of the body proportions, nor for birthweight and P-score.
These preliminary results indicate that the body proportion could be a more appropriate indication of IUGR than weight or than the relation weight to height (Ponderal index).

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GLUCONEOGENESIS FROM LACTATE IN FASTING INFANTS. N. Nurjhan, F. Rocchiccioli, J. Zeller, P.F. Bougnères, U342 INSERM, St Vincent de Paul, Paris.

Gluconeogenesis, the predominant source of glucose to the fasting infant, allows only a precarious balance to be maintened with glucose utilization, as reflected by the fasting decrease of plasma glucose. This study is the first quantification of gluconeogenesis at this age. [3-^{13}C] lactate and [6,6-$^{2}H_2$] glucose tracers were infused in 12 infants aged 1-25 mo during a brief 6-16 h fast. At substrate and isotopic steady-state, glucose and lactate averaged 4.0±0.2 mM and 1.8±0.1 mM respectively, with [3-^{13}C] lactate and [6,6-$^{2}H_2$] glucose enrichments at 1.9±0.2 and 2.5±0.2 mol%E. The appearance of glucose (28±3 µmol/k.min) and lactate (29±5 µmol/k.min) in bloodstream was 2-3 fold that in postabsorptive adults. The incorporation of ^{13}C from lactate into specific carbon positions of glucose was measured using a new gas chromatography-mass spectrometry technique, which corrects for metabolic exchange of carbons in the Krebs cycle. 32±4% of the total glucose production was due to lactate gluconeogenesis, both being correlated ($r=0.67$, $p<0.01$). Gluconeogenesis was the major route (40-90%) for lactate disposal, with a MCR of 18±2 ml/k.min).
In conclusion, lactate gluconeogenesis accounts for approximatively 1/3 of the total fasting glucose production in infants, and its rate is 2.5-4 fold higher than in adults.

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GROWTH HORMONE (GH) SECRETION AND GH RESPONSE TO GH-RELEASING PEPTIDE 1 (GHRP-1) IN PUERPERAL WOMEN.

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In end-gestational women, pituitary GH secretion and responsiveness to GH-releasing factor are dramatically decreased, possibly due to the abundant presence of placental GH in the maternal circulation (de Zegher et al, JCEM, 1990). As there are no data on postpartum secretion of pituitary GH, it is unknown when pituitary GH secretion recovers. Pituitary GH secretion was evaluated in lactating, puerperal women (n=20; 38-58 h postpartum) and in age-matched, mid-cycle women (n=10, including 3 mothers, 6 months or more after last delivery). Serum GH concentrations were measured at 20 min intervals from 20 min before until 100 min after an IV bolus of either GHRP-1 (100 microgram in saline) or saline. Saline-injected puerperal women produced uniformly flattened GH profiles characterized by lower ($p<0.01$) GH peaks (median 5.6 ng/ml; P10-P90 range : 2.5-6.9 ng/ml) than mid-cycle women (9.1 ng/ml; 8.2-16.5 ng/ml), and higher ($p<0.01$) GH troughs (2.1 ng/ml; 1.5-2.9 ng/ml) than control women (all undetectable). The GH response to GHRP-1 in mid-cycle women (88.6 ng/ml; 44-111 ng/ml) was sevenfold higher ($p<0.001$) than in puerperal women (12.9 ng/ml; 5.0-29.0 ng/ml). Basal serum prolactin concentrations were twentyfold higher in puerperal than in control women, whereas serum IGF-1 concentrations were similar. In conclusion, puerperal women appear to present a distinct pattern of GH secretion and a strikingly low GH responsiveness to GHRP-1, suggesting that the pituitary hyposomatotropism of late gestation persists at least during the first days of puerperium.

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ALTERED MONONUCLEAR CELL IMMUNE RESPONSE IN WOMEN EXPOSED TO DES IN UTERO.

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In utero diethylstilbestrol (DES) exposure results in long term reproductive consequences. Preliminary evidence suggests a link between prenatal DES exposure and long term alterations in the immune system. To further test this hypothesis, we compared the phytohemaglutinin (PHA) and concavlin A (con A) induced blastogenic response of mononuclear cell in prenatally exposed women (n=13) to age matched non DES exposed women (n=9). 15 ml. of whole blood obtained during the early follicular phase of cycling women were heparinized, diluted 1:2, layered over ficoll-paque density gradient. The mononuclear cells were washed X 3 (10% R.P.M.I. 1640). Aliquots (0.1ml) of cell suspension were added in triplicate to micro-wells (final conc. of 5 x 10^5/ml). Either PHA (7.5ug-1ug/ml) or Con-A were added to each well. After 48 hours of incubation at 37° C the cells were pulsed with 1 Cµ-thymidine(H-Td), reincubated for 18 hours, harvested, counted, and a geometric mean of 3 determinations obtained. Results: Decreasing H^3-Td proliferation responses paralleled declining mitogen concentrations both with PHA and Con-A. Con-A showed no significantly different response in cells from DES subjects compared to controls. In contrast, PHA responses were greater in DES subjects ($p<.005$ 2 way ANOVA).

PHA Concentration ug/ml	DES HT-d Inc. Ctsx10^3	Controls HT-d Inc. x10^3
7.5	220.3 ± 64.1(S.D.)	160.9 ± 27.0 (S.D.)
5.0	187.9 ± 72.8	122.7 ± 27.0
2.5	146.1 ± 84.2	74.7 ± 38.8
1.75	114.4 ± 87.8	46.8 ± 46.0
1.0	75.5 ± 76.1	2.6 ± 2.6

These data indicate long lasting effects on the immune system in DES exposed women. Such lasting effects on the immune system may be accounted for by a genomic mechanism altering the cellular responses in daughter cells throughout the reproductive years.

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SERUM IGF1 LEVELS IN NORMAL SIZED AND GROWTH RETARDED (GR) HUMAN FETUS.

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It has been shown by several authors that neonates with intrauterine growth retardation (IUGR) have a profound decrease of IGF1 levels in cord blood. According to previous animal studies this is believed to be the consequence of fetal malnutrition. This work was undertaken to study IGF1 levels in normal sized and GR fetuses. Serum IGF1 was obtained during the second and third trimester of gestation. 135 fetal blood samples taken for prenatal diagnosis were drawn from the umbilical cord in utero. Gestational age was determined from the date of the last menstrual period and was confirmed by ultrasound. Diagnosis of IUGR was made according to the ultrasound data growth curves < 10th perc. (n=35) and non IUGR fetuses > 10th perc.(n=100). IGF1 (ng/ml) was measured by RIA after acid gel filtration and results expressed as mean ±sem.

Gestational age (wks)	Normal sized fetuses	IUGR fetuses
18-29	38.4 ± 1.7 (n = 66)	34.2 ± 3.3 (n = 24)
30-40	62.3 ± 3.9 (n = 34)	41.7 ± 4.8 (n = 11)

In normal sized fetuses IGF1 levels increased gradually during gestation ($r=0.40$). On the contrary, in GR fetuses this increase did not occurred. Between 18 and 30 wks of gestation, IGF1 levels were similar in GR and normal sized fetuses. However after 30 wks of gestation a significant difference was demonstrated between these 2 groups ($p=0.008$). In conclusion : compared to normal sized fetuses, IUGR fetuses have a decreased IGF1 levels during the third trimester of gestation.These results suggest that fetal IGF1 might be regulated by nutritional factors only during the last part of gestation.