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Structural Similarity of Human and Bovine Somatomedin Receptors and Human Insulin Receptor: Analysis by Affinity Labeling.

The growth promoting and insulin-like actions of somatomedin-C (Sm-C) are thought to be mediated respectively by interactions with the Sm-C and insulin (In) receptors. Since Sm-C and In are structurally homologous, we compared the size and subunit structure of their respective radiolabeled receptors in human placental membranes (hPM) and bovine chondrocytes (bC) by crosslinking with disuccinimidyl suberate (DSS). The labeled hormone-receptor complexes (RCs) were analyzed by SDS polyacrylamide gel electrophoresis (PAGE) and autoradiography. Specificity of the respective RCs was demonstrated by competitive inhibition studies. Both hPM RCs had apparent molecular weights of > 250,000 daltons. Reduction with 2-mercaptoethanol yielded subunits of ~ 140,000 daltons. Limited proteolysis with trypsin, chymotrypsin and staphylococcal V-8 protease of the labeled RCs gave similar products. The Sm-C RC in bC isolated from calf epiphyseal plates also contained a 140,000 dalton binding subunit indistinguishable from the HPM receptor. Conclusions: 1) the hPM receptor for Sm-C has a 140,000 MW binding subunit linked by disulfide bonds. 2) By this technique, the hPM Sm-C receptor is structurally indistinguishable from either the Sm-C receptor in bC or the In receptor in hPMs, 3) The sizes of In and Sm-C receptors and their subunits differ from that reported for MSA and certain other hormones.

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The Effect of Amino-Acid-Infusions in Pregnant Rats on some Fetal Growth Parameters.

The hormonal and metabolic factors which contribute to fetal growth are poorly understood. In the present experiments pregnant rats were continously infused from day 18 to 20 post conception with saline (S) or amino acids (AA: 2.5g/kg/day). After an overnight fast of 14 hours fetal body weight, fetal serum somatomedin (SM, porcine cartilage bioassay) and the "endogenous" fetal cartilage bioactivity were determined (=incorporation of $^{35}SO_4$ into the fetal costal cartilage in response to 0, 5 or 10 per cent normal rat serum). Results: AA-compared to S-infusions increased fetal body weight (S:4.0± 0.5*g, n=9; AA: 4.9±0.3*g, n=6; p<0.01), fetal SM (S:0.42±0.17 U/ml, n=9; AA:0.85±0.22 U/ml, n=6; p<0.001) and the fetal "endogenous" cartilage bioactivity (S:629±507 cpm/mg, n=33; AA:956±684 cpm/mg, n=21; p<0.01 = sum of the cpms in the presence of the various serum concentrations). Conclusions: As reported previously an increased serum somatomedin concentration, as in fetal hyperglycemic rats, may not be associated with an augmented fetal growth rate, while the results of the present study suggest that at least amino acids plus somatomedin are appropriate growth factors for the rat fetus.
*M ± SD

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Characterization of somatostatin (S), binding to solubilized placental cell membranes.

Membranes were prepared from homogenates of human placenta by differential centrifugation and treatment of the final pellet with Triton-X100 to solubilize the receptors. On incubation in 0.5 ml (0.05 M TRIS, 0.025 M EDTA, 0.5% BSA, pH 8.5, 0.0005 M PMSF), 125-I-tyr S specific binding to placental membrane protein (10-25 µg) was 14.4±3% and non-specific binding was 10.3±8% (±S.D.) at 4°C, with equilibrium by 18 hrs. Equivalent binding occurred at 37°C with equilibrium by 2.5 hrs. The dissociation constant (Kd) for cyclic S was 130 nM at 4° and 230 nM at 37°. At 4° displacement of the label required 0.16 µg cyclic S (cS) and a similar 0.22 µg Ala^5S and 0.14 µg Ala^{11}S, but more linear S (0.465 µg), Ala^8S (0.36 µg) and 28-aminoacid S (0.65 µg). No displacement of binding was shown with 10 µg growth hormone, 10 µg insulin, or 50 µg naloxone, but gastric inhibitory polypeptide produced a dose-response parallel to cS requiring 3.5 µg for 50% displacement. 20 µg of both CCK_{33} (cholecystokinin) and CCK_{10-20} also displaced the labelled S. The cross-reactivities of these gut hormones, especially of CCK_{10-20}, are not readily explained by sequence homology to S. Nevertheless, the levels of S are high in amniotic fluid and with these data on a putative receptor in the placenta, one could postulate a role of S in modulating nutrient transport across the placenta, as has been demonstrated across the gut.

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Plasma and urinary melatonin in male infants during the first 12 months of life.

Testosterone (T) and LH secretions during the first 3 months of life are well documented. In view to investigate possible changes of melatonin (MEL) secretion during this period, 26 normal male infants aged 15 days to 12 months were studied. MEL was measured by radioimmunoassay in blood samples taken at 5.a.m and in 24 hours urine samples collected during the same day. Additionally, plasma T and urinary T and LH were measured. Plasma MEL was undetectable or low up to 3 months of age, and increased later with individual values ranging from 0.4 to 6.5 nmol/l. The trend of variation of T and LH was opposite to that of melatonin. During these two periods, urinary native melatonin mean concentrations were 0.13 and 0.08 nmol/kg/24 hours respectively, without significant difference. These data demonstrate that plasma MEL is low at the time of post natal T and LH rise in male infants and increases later when testicular activity falls.

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Effects of Medium-Chain Triglycerides (M.C.T)in the starved newborn rat.

Newborn rats,starved from birth develop between 12 and 16h a profound hypoglycemia due to a deficient gluconeogenesis.The lack of lipid stores results in a low rate of hepatic fatty acid oxidation which has been proposed as the rate limiting factor in gluconeogenesis.When 13h old starved rats are fed with M.C.T,blood glucose increases,in 3h,from 1.30 ± 0.09mM to 4.23 ± 0.23mM.This results from a stimulation of glucose production (6^3H glucose) from 3.9 ± 0.5mg/min/kg to 11.1 ± 0.6mg/min/kg due to a 5-fold increased gluconeogenesis.Despite their utilization for glucose synthesis, blood levels of lactate,alanine and pyruvate are increased 2 to 3-fold after M.C.T feeding. When M.C.T feeding is given in association with dichloroacetate (an activator of pyruvate dehydrogenase-(P-D.H)) there is no increase in blood lactate,alanine and pyruvate levels and the increase in glycemia is prevented.This suggests that hyperketonemia due to M.C.T feeding could decrease the oxidation of 3 carbons glucose precursors in peripheral tissues secondary to an inhibition of P.D.H and thus enhances their release in blood. These studies demonstrate that M.C.T feeding stimulates glucose production in the newborn rat,both,by increasing the availability of gluconeogenic precursors and by a direct effect on hepatic gluconeogenesis.

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Longitudinal study of 8 plasma mineralocorticoids(MC), glucocorticoids(GC) and progestins in premature infants (PI) at birth and during the neonatal period.

To evaluate fetoplacental and adrenocortical functions of the PI at birth and during postnatal adaptation, plasma aldosterone(Aldo), corticosterone(B), 11-deoxycorticosterone(DOC), progesterone(P), 17-hydroxyprogesterone(17OHP), 11-deoxycortisol(S), cortisol(F) and cortisone(E) were simultaneously followed in 8 PI of 33-36 weeks gest. age. Multi-steroid analysis was done by specific RIAs after extraction and automated LH-20 gel chromatography of a 250 µl sample obtained from umbilical vein(UV) and artery(UA), and at 2,6,12,24,48 h and 4,7,10 and 14 d after birth. In comparison with 12 term infants (TI), mean Aldo was 2-5 times lower in PI than in TI ($P<0.01$) from UV until 7d, but also showed the marked postnatal rise from 0.54 ng/ml in UA to 1.10 ng/ml at 12h. Similarly, the 2nd MC, DOC, dropping by over 200-fold from 9.8 (UV) to 0.05 (14d) ng/ml, showed lower mean levels in PI than in TI from 2h ($P<0.001$) until day 7. The active GCs B and F were at birth (UV,UA,2h) slightly lower, but later on higher (6h: $P<0.01$) in PI, whereas the inactive GCs S and E showed less variation with levels still elevated after 24 h. In comparison with TI, P levels in UV were higher ($P<0.01$) and after birth lower, while mean 17OHP (6h→7d) was signif. higher in the PI group. The data suggest a higher fetoplacental and fetocortical activity and possibly a less stressful delivery but more stressful postnatal adaptation in PI than in TI.