† 241 LIPID CLEARING IN PREMATURE INFANTS. RESPONSE TO INCREASING DOSES OF INTRALIPID(IL): I-CIRCULATING LIPOPROTEIN LIPASE(LPL) AND HEPATIC LIPASE(HL).

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Plasma levels of lipase (LPL, HL) and free fatty acids (FFA) were measured in 21 infants (gest. age 26-35 wks) aged 1-8 days, maintained on total parenteral nutrition with heparin (1 U/ml) and given 1, 2 and 3 g IL/kg/day (over 15 h) on day 1, 2 and 3, respectively. Blood samples were drawn before and at the end of IL administration.

		RESPONDERS (R)			NONRESPONDERS (NR)	
Lipase	Day	Before		After	Before	After
Activity	1	1.69 ± .40	+	3.60 ± .55	1.29 ± .29	1.62 ± .19**
(LPL + HL)	2	1.88 ± .61	*	4.78 ± .89	1.88 ± .35	1.70 ± .50**
	3	3.60 ± .88	+	6.67 ± 1.01	1.94 ± .68	1.67 ± .40**

Lipase activity(U) = μmol FFA/ml/h (mean ± SEM).
R = Lipase > 3.0 U (N = 14). NR = Lipase < 3.0 U (N = 7).
+ = $p<.05$, * = $p<.01$ Before vs. After; ** = $p<.001$ R(After) vs. NR (After).

HL, determined with anti-human HL antibody was 50% and 27% of total activity in R and NR, respectively, both before and after IL infusion. There were no differences in BW or gest. age between R and NR. In all infants there was a significant correlation between FFA and LPL activity ($r = .749$, $p < .001$). The increase in HL and LPL activity in infants given increasing doses of IL with continuous heparin may be due to stabilization of enzyme activity and/or to enhancement of the effect of heparin on enzyme release. The resulting high levels of FFA (>2.0 mmol/l) warrant caution in the use of large amounts of IL in association with continuous low level heparin. (Supported by NIH grants HD-15631 and RR-00240).

244 CHARACTERISTICS OF HUMAN FETAL HEPATIC RECEPTORS FOR INSULIN (INS) AND SOMATOMEDIN-C (SM-C)

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The roles of Ins and Sm-C as stimulators of cellular metabolism and growth in the human fetus remain controversial. Since the effects of these hormones are initiated by their interaction with specific cell surface receptors, the binding and structural characteristics of the Ins and Sm-C receptors were examined in second trimester fetal hepatic membranes (FHM). A membrane-rich homogenate was prepared from frozen human fetal livers provided by the National Diabetes Research Interchange. Hormone binding was assessed by incubating the FHM for 14h at 4C with either ^{125}I-Ins or ^{125}I-Sm-C (generously provided by J VanWyk, Chapel Hill, NC) with and without native hormone. Specific binding by FHM at 12,16, and 20 weeks gestation was 10-11% for ^{125}I-Ins and 5-7% for ^{125}I-Sm-C. Dose response curves for the Ins receptor generated curvilinear Scatchard plots with 50% of the ^{125}I-Ins displaced by $0.75\text{-}1.2 \times 10^{-9}$ M native Ins. When FHM were affinity labeled using the crosslinking agent, disuccinimidyl suberate and analyzed by SDS-polyacrylamide gel electrophoresis followed by autoradiography, the receptors for both Sm-C and Ins had apparent MWs > 250K. After disulfide bond reduction a 135K radioactive band predominated. The results of binding studies and affinity-labeling were similar at all three gestational ages. Conclusions: 1) Second trimester human FHM possess specific Ins receptors with subunit structures similar to that described in adult tissues. 2) There is no change in Ins receptor binding or subunit structure over 12-20 weeks gestation. 3) Sm-C receptors structurally similar to the Ins receptor are also present on human HFM.

† 242 FETAL AUDITORY RESPONSES.

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The eyelids, midface, and mouth are monitored ultrasonically during transuterine vibroacoustic stimulation. The test sequence is an "orienting", .5 second noise burst (150-1600 Hz, 100 dB), followed after 30 seconds with 10 bursts spaced one second apart.

We have shown previously that motor responses begun abruptly at 24½ weeks gestational and are elicited invariably by 28 weeks in normal fetuses. Head aversion, eyelid, and mouth movements are dissociated initially. By 28 weeks these startle components are linked. We now report decremental response after 32 weeks for head aversion (but not eyeblink), which is exponential with gestational age. The effect may represent discriminatory response threshold, progressive cerebral modification of a midbrain response mechanism, or a type of prestimulus inhibition.

Deafness is diagnosed by absence of any response in the presence of normal eye and diaphragm movements (or other indicator of wellbeing). Declining fetal condition is associated with irritability, reversal of startle decrement, and finally, loss of responsiveness. Delayed response patterns were seen in individual cases of fetal alcohol and marijuana sydromes, triplody, trisomy 18, and 3 cases of hydrocephalus, but not in one case of Down's syndrome.

† 245 DEVELOPMENT OF SYMPATHETIC REGULATION OF PHOSPHOLIPID SECRETION IN FETAL RABBIT LUNG.

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42 litters of newborn rabbits were killed and a tracheostomy tube inserted. All pups had 8 saline lavages, but alternate pups had 10^{-3} molar propranolol added. Samples were analysed for phospholipid (mg/g dry lung wt) as a reflection of lavage -induced secretion. Some litters then had 6 lavages after 3 or 15 minutes, followed by a further 6 lavages after total interval of 18 minutes. The phospholipid yield after 15 minutes was used to calculate the basal secretion index (SI). Other litters had constant air inflation and were again lavaged to calculate post-inflation secretion. Results expressed as mean ± standard error; C = saline controls; P = propranolol treated.

	27.5d gestation			29.5d gestation			2.5d post-term		
	basal SI	post-lavage	post-infl	basal SI	post-lavage	post-infl	basal SI	post-lavage	post-infl
C	0.12± 0.02	1.38± 0.25	0.97± 0.19	0.35± 0.05	3.54± 0.25	3.15± 0.38	1.68± 0.29	27.7± 1.9	5.30± 0.30
P	0.11± 0.01	1.05± 0.11	0.95 0.10	0.23± 0.03	1.74± 0.11	2.72± 0.32	1.05± 0.18	24.1± 2.1	4.07± 0.44
	NS	NS	NS	<0.01	<0.01	<0.05	<0.01	<0.05	<0.01

At 29.5 d, but not at 27.5 d, propranolol inhibited basal, lavage -induced and inflation-stimulated secretion. At 2.5 d post-term secretion was greatly increased, but propranolol inhibition was still detected. Present data suggest that sympathetic regulation develops near term in the rabbit and persists after birth.

243 INTRAAMNIOTIC ADMINISTRATION OF NUTRIENTS.

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The effects of intraamniotic administration of nutrients on fetal metabolism was investigated. Four fetal lambs with carotid(CA), femoral artery(FA) and amniotic fluid(AF) catheters were used. 13 studies were performed 5-21days post-surgery, at 122-138days gestation. At study, 20g of either glucose(n=6) or L-amino acids(n=7) were injected into the AF. Changes in fetal metabolism were followed for 4hrs. Fetal levels of the injected nutrient rose quickly:

CA Conc.	-15	0	15	30	60	120	180	240,min
Glucose, mg/dl	24.1 ±4.1	23.4 ±4.1	42.7 ±4.6*	49.2 ±7.2†	48.7 ±7.0§	49.7 ±6.5¶	48.8 ±7.5†	41.7 ±6.3§
αAmino N, mg/dl	8.0 ±0.3	8.1 ±0.4	11.9 ±0.8†	13.5 ±1.3†	16.5 ±1.7§	19.3 ±2.5§	21.3 ±3.2†	22.3 ±3.1§

Values are mean±SEM. Versus time 0: *p<0.05; †p<0.02; §p<0.01; ¶p<0.005
After glucose injection: CA O_2 sat. decreased(-5.7±1.4%, p<0.02); lactate increased(+8.1±1.4mg/dl, p<0.01); and pH decreased(-0.04± 0.01, p<0.02). These changes were maximal at 3hrs. Hgb showed a trend to increase and O_2 content was stable. The CA-FA glucose concentration difference widened(from 0.7to2.7mg/dl, n=3, p<0.10), as glucose levels rose. After amino acid injection: urea increased(+3.6±0.6mg/dl, p<0.002); ammonia rose(+123±28ug/dl, p<0.05); O_2 sat. decreased (-8.4±1.9%, p<0.005); O_2 content decreased(-1.2±0.2ml/dl, p<0.01); pH fell(-0.05±0.01, p<0.005) and Hgb rose(1.0±0.3gm/dl, p<0.05). These changes plateaued by 3-4hrs. AF injection of nutrients had more noxious effects on the fetus than has been seen with intestinal supplementation. However, the quantity of nutrients administered via AF was greater, as was the change in fetal nutrient levels.

246 EFFECT OF THE CONCEPTUS ON THE GLUCOSE PRODUCTION RATE IN THE SECOND TRIMESTER OF PREGNANCY.

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The conceptus is dependent on his mother for glucose availability in utero. There is an increase in the absolute glucose production rate (GPR) during the third trimester to facilitate that transfer. To determine if the effect of the conceptus on maternal glucose kinetics occurs earlier in gestation, the GPR of 6 normal second trimester women (P-2T) (G:23±1 wk) (presumed fetal-placental weight 650 gms) was compared to similar measurements in 6 normal third trimester women (P-3T)(G:37±0.3 wks)(presumed fetal-placental weight 3425 gms). Kinetic analyses were performed with a prime constant infusion of D[U-^{13}C] tracer glucose.

M±SEM Group	N	Pl.Glu. mg/dl	Pl.Ins. μU/ml	GPR $mg \cdot kg^{-1} \cdot min^{-1}$	Absolute GPR $mg \cdot min^{-1}$
P-2T	6	76±2	20±3	1.4±0.2	86.8±12.2*
P-3T	6	76±2	16±2	2.0±0.3	141.7±15.5
	unpaired t-test				*p<.02

The pl. glucose and pl. insulin concentrations, and the GPR of the two groups were similar. Both P-2T and P-3T had increases in the absolute GPR, but the P-2T was less ($p<.02$). Based on the known GPR in the neonate of 3.2 $mg \cdot kg^{-1} \cdot min^{-1}$, the calculated absolute GPR accountable by the increase in fetal weight was 8.9 $mg \cdot min^{-1}$. Maternal glucose kinetics during the second and third trimesters are influenced primarily by non-fetal factors.