223 THE PITUITARY ADRENAL RESPONSE TO HEMORRHAGIC STRESS OF LAMB FETUSES IN UTERO. A.A. Macdonald, J. Rose, M.A. Heymann & A.M. Rudolph. U. of Calif., Depts. of Ped., Physiol. and Ob-Gyn. and C.V.R.I., San Francisco.

29 ewes and their chronically catheterized fetuses (0.46-0.99 gestation) were allowed 48 hr to recover from surgery prior to study. We measured plasma ACTH and Corticosteroid (C) concentration by radioimmunoassay. Maternal plasma ACTH (54±4 pg.ml⁻¹) and C (3.0±0.2 µg.dl⁻¹) did not change. Fetal ACTH (44±4 pg.ml⁻¹) was low. Fetal C increased progressively from 1.5±0.1 µg.dl⁻¹ before 0.85 gestation to maximal concentrations of 9.4±1.2 µg.dl⁻¹ after 0.95 gestation. Lack of parallel increase in fetal ACTH and C suggested increasing fetal adrenal responsiveness to apparently constant fetal ACTH. In 7 of 8 fetuses (0.72-0.89 gestation) hemorrhage of 15% estimated fetal blood volume at 1.5 min⁻¹ caused a decrease (P<0.05) in fetal mean arterial pressure (FMAP) from 43±3 Torr to 26±4 Torr, and increase (P<0.05) in ACTH (ΔACTH=140±45 pg.ml⁻¹) and a small increase (P<0.05) in C (ΔC=0.9±0.2 µg.dl⁻¹). A much larger increase in plasma C levels (ΔC=7 µg.dl⁻¹) despite comparable FMAP and ACTH responses to hemorrhage occurred in 2 fetuses >0.95 gestation. These findings also suggest increased fetal adrenal responsiveness to endogenous ACTH towards term. Hemorrhage of 15% in 6 younger fetuses (0.55-0.67 gestation) produced no increase in plasma ACTH or C despite a drop in FMAP from 37±1 Torr to 29±2 Torr (P<0.01). This suggests system(s) subserving the plasma ACTH response to mild hemorrhage are either not yet developed or are inactive in fetuses <0.67 gestation. Fetal hemorrhage caused no change in maternal blood pressure, ACTH or C.

224 DECREASE IN HEPATIC LIPOGENESIS IN TERM RAT LIVER EXPLANTS. William M. Maniscalco, Ian Gross, Joseph B. Warshaw, Yale University School of Medicine, Depts. of Ped. and Ob/Gyn, New Haven, Conn.

Hepatic lipogenesis in the fetal rat is highly active until the time of birth when it decreases and remains low throughout the suckling period. High fat intake during suckling is thought to suppress hepatic lipogenesis. By utilizing explants of fetal rat liver we have demonstrated that the decrease in hepatic fatty acid synthesis may occur independent of nutritional influences. Explants obtained from fetal rats at 17 and 22 days gestation were incubated for 48 hours in F12 medium without added hormones or serum. Incorporation of acetate-1-¹⁴C into long chain fatty acids during a 6 hour pulse was determined at 0 time and after 48 hours in culture and is shown below. Data are expressed as % incorporation/mg protein/6 hours.

	0 time	48 hours	P
17 day	0.35±.03	0.35±.10	n.s.
22 day	0.39±.04	0.059±.003	<.025

Production of ¹⁴CO₂ from uniformly labeled glucose was examined as an index of viability. There was no significant decrease in glucose oxidation in explants from either 17 or 22 day gestation fetuses during the 48 hours in culture.

The results indicate that acetate incorporation into fatty acids in liver explants from 17 day fetuses remained constant between 0 and 48 hours in culture. Explants from 22 day fetuses, however, showed a striking decline in acetate incorporation. These data suggest that the decline in hepatic lipogenesis in the newborn rat may be independent of dietary influences.

225 AMINO ACID METABOLISM IN DYSMATURE NEWBORN RATS: POSSIBLE EXPLANATION FOR THE ANTIHYPOGLYCEMIC EFFECT OF PRENATAL GLUCOCORTICOIDS. Robert L. Manniello, Joseph D. Schulman, and Philip M. Farrell, Bethesda, MD.

Using a model of intrauterine growth retardation (IUGR), we have previously shown that 91% of dysmature rat pups develop hypoglycemia 2-4 hrs after birth and that prenatal glucocorticoid treatment significantly reduces this tendency. The present study was designed to examine the possible interrelationship between the protective effect of corticoids and the metabolism of gluconeogenic (GNG) substrate. Accordingly, plasma aminograms were determined at birth and at 2-4 hrs of age in untreated (I) and treated (II) IUGR pups. Values below are in µmoles/ml. ± S.E.

	I at birth	I at 2-4 hrs	II at birth	II at 2-4 hr
Alanine	.78 ± .10	.34 ± .10	2.3 ± .30	1.1 ± .30
Gln+Glu	.75 ± .02	.35 ± .04	.96 ± .07	.57 ± .08

Compared to control newborns, both groups of IUGR pups showed higher total plasma amino acid (aa) concentrations at birth. As shown, the group given glucocorticoid had higher concentrations than untreated pups of major GNG aa, alanine or glutamine & glutamic acid. This difference was evident both at birth (ala, p<.001; gln + glu, p<.001) and at 2-4 hrs of age (ala, p<.02; gln + glu, p<.06). Thus, the reduced tendency to develop hypoglycemia after treatment is associated with greater availability of GNG aa. Furthermore, the decrease in alanine concentration after birth is greater in group II, suggesting increased utilization of this amino acid. We therefore postulate that the hormone may act to both increase the supply of GNG substrate and stimulate enzymes essential for gluconeogenesis from alanine.

226 PYRUVATE DEHYDROGENASE IN PRETERM, TERM AND ADULT RABBIT TISSUES. Lawrence F. Mazzuckelli and James F. Soodma (Spon. by Robert V. Kotas). The William K. Warren Medical Research Center, Suite 1010, 6465 So. Yale, Tulsa, Okla. 74136.

Pyruvate dehydrogenase activity was determined in the livers (LV), kidneys (KD), hearts (H), lungs (LG) and brains (BR) of 28.5d. (preterm), 30.5d. (term) and adult rabbits as part of our investigations of neonatal oxidative metabolism.

We found that in KD, H, LG and BR the sp. act. of this enzyme (nmoles CO₂ liberated from [1-¹⁴C] pyruvate/mg mitochondrial protein per min) decreased with gestation, reaching adult levels in 30.5d. rabbits. In the liver, we found an approximate two-fold increase in the sp. act. from 28.5d. to 30.5d. rabbits (8.32 vs 14.20). In addition, the percentage of the enzyme in the active form in the 30.5d. rabbit was found to be 5 and 2.5 fold greater in the H and BR than in the H and BR of the 28.5d. rabbit.

The activity of this enzyme was also determined in whole tissue homogenates. When total activities per gram of tissue (active + inactive) were compared, it was found that the livers of the 28.5d. and 30.5d. rabbits were capable of the most rapid rates of pyruvate oxidation of the tissues studied. This is quite different from the relationship of the activities of the various tissues in the adult. The order of the maximum possible rates of pyruvate oxidation per gram was found to be: LV>H>KD>BR>LG, LV>H>BR>KD>LG and H>KD>BR>LV>LG in 28.5, 30.5 and adult rabbits, respectively.

227 THE ONTOGENESIS OF SOMATOSTATIN IN THE FETAL RAT AND SHEEP PANCREAS. N. McIntosh*, P.L. Mueller*, R.L. Pictet*, S.L. Kaplan*, and M.M. Grumbach*. Depts. of Pediatrics* and Biochemistry and Biophysics*, University of California San Francisco, San Francisco, California 94143.

The localization of somatostatin (GIF) in pancreatic D cells and in the gastrointestinal tract led to the concept that SRIF may have a physiologic role at these sites as well as in the CNS. Its role in the fetus is not known. Previously we demonstrated GIF in the human fetal hypothalamus and cerebral cortex. The present study examines the ontogeny of GIF in rat and sheep fetal pancreas using a homologous radioimmunoassay with tyrosyl 11-GIF as label and standard, with a sensitivity of 5 pg cyclic GIF. In the rat, GIF is detected at 14 days gestation in pooled extracted pancreases at .0016 ng/pancreas. GIF increases proportional to DNA until day 19, with a subsequent rapid rise to 3.8 ng/pancreas (72 pg/µg DNA) at term. Two days postnatally GIF increases to 8.3 ng/pancreas (135 pg/µg DNA). In the adult rat 71.3 ng GIF/pancreas is detected (54 pg/µg DNA). In the fetal sheep, GIF is present by 58 days at 1.6 ng/pancreas, rises to 5.3 ng at 65 days and to 1900 ng/pancreas at term. The content in the adult sheep is 7000 ng GIF/pancreas. GIF is present by mid-gestation in the fetal rat and sheep pancreas with a sharp 1000-fold increase by term. The biphasic developmental pattern of somatostatin in the fetus is similar to that of insulin but differs from that for glucagon.

228 MESSENGER RNA TRANSCRIPTION IN REGENERATING KIDNEY. Walter L. Miller and Brian J. McCarthy (Spon. by Melvin M. Grumbach) University of California, San Francisco, Departments of Biochemistry & Biophysics and of Pediatrics, San Francisco, California.

As part of a larger project studying potential reactivation of genes active in fetal organogenesis which are not expressed in adult tissue, we have examined the control of transcription in kidney regeneration, a process involving hypertrophy and hyperplasia of several cell types. Renal polyadenylated mRNA binding to oligo(dT)-cellulose was prepared from mice 2 and 4 days following unilateral nephrectomy and from controls and used as template for the synthesis of ³²P complementary DNA (cDNA). The complexity of the mRNA population was evaluated by hybridization to its homologous cDNA. Hybridization occurred over 5 log units of R t (mols nucleotide/liter x seconds) and reached 90% saturation indicating a broad frequency distribution of mRNA populations. The 4 day post-nephrectomy curve showed a twofold increase in the complexity of the most abundant class of mRNA molecules, but no significant difference in the complexity of mRNA species present in lesser abundance. Heterologous hybridizations failed to show a significant change in saturation values. We conclude that few if any new species of mRNA are required for kidney regeneration, but that some species must be produced in increased numbers. *In vitro* translation of these mRNAs substantiated these conclusions, as no new proteins unique to compensatory growth were identified, although several proteins were present in significantly different amounts compared to control.