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MYOCARDIAL ENERGY IMBALANCE IN NEWBORN CARDIO MYOPATHIC TURKEYS. Ting Wang, John E. Foker, Cathleen Marquardt, George Noren, Nancy Staley, Stanley Einzig,

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 Turkey (TK) inbred for congestive cardiomyopathy (CCM) have reduced hatchability and a mortality approaching 30% by 10 days of age; cardiac dilation begins at this time. We examined the possibility that an imbalance in cardiac high energy phosphate (HEP) compounds may contribute to these abnormalities. Ventricular ATP, ADP, AMP and CP were compared in control (Con) and CCM TK, 1-31 days old. There was no significant age-related difference in myocardial HEP compounds or in the energy charge $[EC = (ATP + 0.5 ADP) / (ATP + ADP + AMP)]$ in Con TK (Table). In contrast, ATP and EC in CCM hearts at 1-2 days were reduced compared to 19-31 day TK, and ATP content in CCM hearts at 1-2 days was lower compared to age-matched Con tissue. When cardiac dilation was present in CCM TK (ie 10-31 days), ATP and EC were similar in Con and CCM hearts. CP content in Con and CCM TK hearts was similar at all ages indicating adequate energy formation.

	a (1-2 days)		b (8-10 days)		c (19-31 days)	
	CCM(n=5)	Con(n=7)	CCM(n=4)	Con(n=4)	CCM(n=6)	Con(n=10)
ATP*	2.60±0.26	3.31±0.16*	3.40±0.22	3.29±0.30	3.54±0.24	3.91±0.30
EC	0.69±0.01	0.74±0.02	0.74±0.02	0.73±0.02	0.77±0.01	0.79±0.01

*nmole/mg wet wt; $\bar{x} \pm SE$; n=# of TK; * $p < .05$, CCM vs Con; + $p < .05$, CCM a vs c
 These results suggest that energy imbalance in hearts of newborn CCM TK may, in part, contribute to the reduced hatchability or high early mortality; dilation of myopathic hearts is not associated with HEP imbalance.

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ONTOGENESIS OF GAMMA-GLUTAMYL TRANSEPTIDASE (GGTP) IN RAT TISSUES. Raul A. Wapnir, Lori A. Goldstein and Vincent J. Mancusi. (Spon. F. Lifshitz). Cornell U.

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One of the mechanisms for amino acid active transport into the cell is GGTP. In order to map its developmental patterns this enzyme was studied in Wistar rat tissues before and after birth. Glycylglycine was the acceptor and L- γ -glutamyl-p-nitroanilide the donor in the assays. Placental GGTP activity (as nmol/min x mg protein) decreased from 2.06 ± 0.15 to 0.69 ± 0.07 between the 14th and 21st day of gestation. Fetal kidney GGTP had the highest mean sp. act. than any other tissue at every stage of development. It doubled from the 20th day of gestation to birth (200 to 409), and then increased to 1,452 at 21 d. of age. GGTP in the small intestinal mucosa reached a peak by the middle of the lactation period (106 at 12 d. of age), returning to lower, fetal levels (22) at three weeks of age. Brain GGTP was minimal in utero (2.8 at the 20th day of gestation), and fell to zero at birth, increasing again during lactation and adulthood. Liver GGTP was measurable only in the gestational period, but after birth it became almost negligible. These data suggest that GGTP may play a role in amino acid transport into cells of various tissues in the later part of gestation. After birth, the only organ with significant GGTP activity is the kidney, where its physiologic role has been well studied (Supported in part by USPHS NIH grant S08 RR-09128-02).

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PRIMARY HYPERINSULINEMIA REDUCES SURFACE ACTIVE MATERIAL FLUX IN TRACHEAL FLUID OF FETAL LAMBS. David Warburton, Cheryl D. Lew and Arnold C. G. Platzker

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We induced chronic hyperinsulinemia by continuous intravenous infusion of insulin (0.24 ± 0.4 U/Kg/hr, M $\pm$ SE) into 5 chronically catheterized fetal lambs from 112 through 137 days gestation. Serum insulin levels in these fetuses (95 ± 10 μ U/ml) were greater than in 5 untreated chronically catheterized control fetuses of the same gestational age (10 ± 1 μ U/ml, $p < 0.001$) and in the mothers (38 ± 6 μ U/ml, $p < 0.001$). Serum glucose levels were lower in the insulin treated fetuses (10 ± 1 mg/dl) than in the control fetuses (19 ± 1 mg/dl, $p < 0.01$) and in the mothers (60 ± 3 mg/dl, $p < 0.001$). Surface active material (SAM), assayed on a surface balance, began to appear in tracheal fluid of control fetuses at 119 days and was present in all 5 controls at 125 day gestation. SAM did not appear in the tracheal fluid of insulin treated fetuses until 127 days, and did not appear at all in 3 of them. SAM flux was significantly reduced in the tracheal fluid of insulin treated fetuses (1 ± 0 μ g/Kg/hr) in comparison with control fetuses (18 ± 3 μ g/Kg/hr, $p < 0.01$).

We conclude that chronic hyperinsulinemia reduces SAM flux in tracheal fluid of fetal lambs. We speculate that this effect may be partially mediated by a reduced substrate (glucose) availability for SAM phospholipid synthesis and/or secretion.

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EPIDERMAL GROWTH FACTOR BINDS TO EMBRYONIC TISSUES AND STIMULATES THYMIDINE INCORPORATION INTO DNA.

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The binding of epidermal growth factor (EGF) and its effects on 3 H-thymidine (3 H-T) incorporation into DNA were examined in mouse embryos. With isolated tissues from 11 to 15 day embryos, specific EGF binding was most active in amnion, lung, trophoblast and visceral yolk sac. 3 H-T incorporation into amnion, limb bud and lung increased with EGF concentration to a maximum at 1-5 ng/ml EGF. Above 10 ng/ml EGF there was reduced incorporation which may indicate down regulation of EGF receptors. To assess the significance of these data, EGF binding and 3 H-T incorporation were studied *in vivo*. Two hours after injection of EGF through the uterine wall into the yolk sac specific binding was found in amnion and visceral yolk sac with binding also seen in lung, placenta, heart, brain and liver in decreasing order. These data were similar to *in vitro* binding of EGF to embryonic tissues and crude membrane fractions. Sixteen hours after EGF injection (5-100 ng/ml), incorporation of 3 H-T was reduced in amnion, visceral yolk sac and placenta and to a lesser degree in lung, brain, limb, liver and heart suggesting down regulation of EGF receptors. These studies demonstrate specific EGF binding to a variety of embryonic tissues and provide evidence for biological activity of EGF in mouse embryos.

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EFFECTS OF HYDROCORTISONE AND CHOLECYSTOKININ-OP ON MATURATION OF RAT PANCREAS. Steven L. Werlin, Medical

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Development of pancreas and pancreatic secretory function was studied in the rat. Neonatal rat pancreas failed to respond to carbachol with increased secretion of amylase at 8, 12, or 17 hours of age but responded at age 24 hours. Pancreas from enterally fasted neonatal rats failed to respond to carbachol at 24 hours of age, however, fasted newborn rats parenterally treated with hydrocortisone (HC) (10mg/kg) or cholecystokinin octapeptide (CCK-OP) (5ug/kg) shortly after birth responded to carbachol at age 24 hours. HC or CCK-OP was injected into pregnant rats on days 16-19 of gestation. Term fetal pancreas from mothers treated with HC or CCK-OP responded to carbachol with increased secretion of amylase. At 24 hours of age, HC treated pancreas responded to carbachol but CCK-OP treated pancreas did not. In fetal pancreas, HC and CCK-OP significantly increased pancreatic weight, DNA, protein and lipase but not amylase or chymotrypsinogen. In HC and CCK-OP treated 24 hour old pancreas, DNA was increased but secretory proteins were decreased.

Conclusions: 1) The ability of the rat pancreas to respond to secretagogues develops between 17 and 24 hours of age. 2) Enteral feeding is necessary for normal development of secretory function. 3) HC and CCK-OP mimic the effects of first feeding on secretory function. 4) HC and CCK-OP induce hyperplasia and precocious maturation of function. Speculation: The actions of these exogenous agents may mimic endogenous release stimulated by first feeding.

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THE RELATIONSHIP OF PLACENTAL OXYGEN UPTAKE AND TRANSFER TO UTERINE BLOOD FLOW. Randall B. Wilkening, Giacomo Meschia, and Frederick C. Battaglia, Depts.

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Although several theoretical models have been proposed to explain the relationship of placental oxygen uptake and transfer to uterine blood flow, there is no supportive experimental data in a chronic, non-stressed animal preparation. To provide this evidence, uterine blood flow was decreased by mechanical arterial occlusion in 5 ewes. Each ewe was studied at her normal uterine blood flow and at 3 to 7 different uterine blood flow levels. Uterine and umbilical blood flows were measured with antipyrine by application of the Fick Principle. Oxygen tension (PO_2) and oxygen content were measured in the uterine artery and vein and in the umbilical artery and vein. In each animal, we found that fetal and placental oxygen uptake remained constant to at least a 50% reduction in uterine blood flow before decreasing. The PO_2 's decreased in the uterine vein and in the umbilical vessels as uterine blood flow decreased, but the PO_2 difference between uterine and umbilical venous blood remained constant. We conclude that (1) variability in uterine blood flow has no effect on fetal and placental oxygen uptake over a wide range, and (2) the placenta does not become a more efficient respiratory organ as uterine blood flow decreases.