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THE EFFECT OF ACUTE EXTRACELLULAR VOLUME EXPANSION ON MYOCARDIAL GLYCOGEN IN THE NEWBORN RAT. Margery A. Heneghan and Richard Sosulski. (Spon. by Leonard I. Kleinman), SUNY at Stony Brook, Sch. of Med., Dept. of Radiology and Pediatrics, Stony Brook, NY.

Glucose and its metabolites are the principal cardiac energy substrates in the fetus and neonate. Anoxia and adrenergic stimulation have been shown to deplete myocardial glycogen stores, but the effect of extracellular volume expansion on carbohydrate metabolism has not been previously studied. The effect of acute saline loading on myocardial glycogen concentration was studied in 8 littermate pairs of newborn rats, matched for age. One member of each pair, assigned to the experimental group, received an intraperitoneal bolus injection of isotonic saline, 80 ml/kg body weight. The remaining member (control) received a multielectrolyte maintenance solution, 8.4 ml/kg, in the same manner. At 2 hours, the animals were sacrificed and the hearts excised and weighed. Myocardial glycogen was assayed using a modification of the glucose oxidase method. No significant difference in cardiac weight was noted between groups (exp=0.064±0.003 SEM gm, cont=0.057±0.011gm). The glucose concentration in mg/dl/gm wet weight tissue was 176.4±17.9 in exp group and 257.7±94.4 in the cont group (p<.05). The finding of lower myocardial glucose content in the saline loaded rats in the absence of a significant increase in water content, suggests that acute extracellular volume expansion exerts a significant effect on cardiac carbohydrate metabolism in newborns.

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ALTERED CRANIOFACIAL DEVELOPMENT AND SOMATIC GROWTH IN THE PERINATAL RAT FOLLOWING TREATMENT WITH EPIDERMAL GROWTH FACTOR (EGF). Steven B. Hoath, (Spon. by Jeffrey Whitsett), Univ. of Cincinnati, College of Medicine, Dept. of Pediatrics, Cincinnati, Ohio

Identification of molecular mechanisms regulating the timing of ontogenetic events is a major focus in developmental biology. In the rat, craniofacial development consists of a sequence of precisely timed topological "discontinuities" each associated with the acquisition of higher functions; e.g. incisor eruption (mastication), ear canal opening (hearing), eyelid unfusion (vision). We tested the ability of EGF (500 ng/gBW/d) given on postnatal days 0-3 to affect the timing of these selected events. The results are compared to littermate controls:

Topological Event	Postnatal Day (mean ± SEM)	
	Control (N=35)	EGF (N=34)
Lower incisor eruption	10.3±0.1 1st	9.1±0.2* 2nd
External ear canal opening	12.7±0.1 2nd	14.4±0.1* 3rd
Eyelid unfusion	13.5±0.1 3rd	7.9±0.2* 1st

*p<.01 (EGF versus controls)

The EGF treated pups also exhibited reductions in body weight and body length up to the 20th postnatal day (p<.01). EGF treatment (500 ng/gBW/d) on days 4-7, however, produced no significant growth retardation & only intermediate eyelid unfusion (day 10). These results identify 1) the early perinatal period as a critical time for EGF action and 2) the ability of EGF to alter the normal sequence of craniofacial development, prolonging the time for ear canal opening while shortening the time for incisor eruption and eyelid unfusion.

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THE HUMAN FETUS AND AIR TRAVEL. Renate Huch (spon. by Mary E. Avery, Boston), H. Baumann, F. Fallenstein, K.T.M. Schneider, A. Huch, Univ. Hospital, Dept. of Obstetrics, Zurich/Switzerland

At artificially maintained cabin pressure in modern aircrafts, the arterial P_{O_2} in healthy adults is close to 60 mm Hg. This relative oxygen deficiency has been discussed as a potential risk for the fetus during flight of pregnant women. In addition, there are speculations about the possible effects of acceleration and emotional stress during flight on the maternal and fetal organism. Investigations in human pregnancy have not been carried out under simulated or real flight conditions. We measured maternal respiratory and heart rate, ECG, transcutaneous blood gases, blood pressure and uterine contractions, fetal beat-to-beat heart rate and cabin pressure in 10 healthy pregnant women during 20 European continental flights. Commercially available or specially adapted instruments were used and observations were recorded on Epproms. The instrumentations were battery powered. Data were analyzed according to the various flight phases and related to the initial phase on the runway (take off, climb, maximal height, descent and landing). Maternal heart rate and blood pressure increased. P_{O_2} decreased significantly. Maternal respiration and P_{CO_2} remained unchanged. In the fetuses there was no instance of bradycardia, no decelerations or reduction in baseline heart rate variability. Mean fetal heart rate remained normal during all flight periods. Significant accelerations of fetal heart rate were observed in some cases.

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DEVELOPMENT OF ARGININE SYNTHESIZING ENZYMES IN MOUSE INTESTINE. Ruth Hurwitz and Norman Kretschmer. University of California, Berkeley, Department of Nutritional Sciences.

The function of the urea biosynthetic pathway in mammalian liver is to convert excess ammonia to urea and to maintain the ammonia concentration at non-toxic levels. Activities of the hepatic enzymes adapt to increasing or decreasing dietary protein. The pathway contributes minor amounts of intermediates such as citrulline or arginine to the circulation. Adult intestine has the first two enzymes of the pathway and is capable of synthesizing citrulline. Unlike these two enzymes in liver, their activity is not affected by changes in dietary protein. It has been shown in the rat, that intestinally-produced citrulline is carried by the blood stream to the kidney where it is converted by the next two enzymes of the pathway to arginine (Windmueller). This mechanism serves as the source of circulating arginine in the adult. We have found that, at birth, the arginine synthesizing enzymes in mouse kidney are minimally developed, while in the intestine, the citrulline synthesizing enzymes are elevated. However, argininosuccinate synthetase and lyase, usually present only in trace quantities in the adult, are markedly developed in the newborn. Arginase which converts arginine to urea, does not appear in intestinal cells until the age of 15 days. This finding would suggest that newborn mouse intestine, with a complete and functioning arginine synthesizing pathway, is the primary endogenous source of arginine in the neonatal mouse.

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REGULATION OF MOUSE RENIN EXPRESSION DURING ONTOGENY. Julie R. Ingelfinger, Richard E. Pratt, Kristin E. Ellison, and Victor J. Dzau, Harvard Medical School, Children's and Brigham and Women's Hospitals, Boston, MA

Renin is expressed in many tissues other than the kidney and may play an important role in the control of local tissue processes. The regulation of renin expression in many extrarenal tissues has not been defined. We examined the CD-1 mouse, which has two renin genes--Ren-1 (expressed predominantly in the kidney) and Ren-2 (expressed in the submandibular gland (SMG)). The latter is regulated by androgen, whereas the former is not. During ontogeny in the male mouse SMG renin increases at puberty as androgen rises, while renal renin remains unchanged throughout development. Like SMG, other extrarenal tissue renin levels, e.g. testes and adrenal, also increase markedly at puberty. In contrast, these dramatic increases in extrarenal renin levels are not observed in the female CD-1 mouse, nor in the male C57 mouse, which contains only the Ren-1 gene. The influence of androgen on CD-1 mouse SMG renin mRNA was examined by hybridization "dot blot" analysis using the renin cDNA probe ID-2. Indeed renin mRNA increases at puberty paralleling the enzyme activity. Taken together, the above data suggest that extrarenal renins are regulated by androgen, at least at the transcriptional level, and are probably products of Ren-2 gene expression. The data also imply that control of extrarenal renins may be distinct from renal renin.

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ANDROGEN REGULATES SUBMANDIBULAR GLAND (SMG) RENIN SYNTHESIS AND SECRETION AT MULTIPLE SITES. Julie R. Ingelfinger, Richard E. Pratt, Timothy P. Roth, and Victor J. Dzau, Harvard Medical School, The Children's and Brigham and Women's Hospital, Boston, MA

Mouse SMG renin expression exhibits sexual dimorphism. In the mature male, renin is synthesized under androgen influence, as prorenin which is converted intracellularly to intermediate single chain polypeptide (1-C renin) and subsequently processed to mature enzyme consisting of two polypeptide chains (2-C renin). 2-C renin is secreted from storage granules while 1-C renin is secreted predominantly via a constitutive pathway. Previous studies in this laboratory documented increases in SMG renin mRNA in male mice at puberty, as androgen rises. In this study we examined androgen effect on post-translational processing of renin during ontogeny. SMG from male CD-1 mice (ages 18-45 days) were incubated in RPMI 1640 media at 37°C for various time periods. Secretion rates as well as tissue renin levels increased with age (<1 ng AI/h/mg protein at day 18 to 5X10⁴ ng AI/h/mg protein at day 45 in media and <100 ng AI/h/mg protein at day 18 to 3X10⁶ ng AI/h/mg protein at day 45 in tissue). Western blot analysis of tissue and secreted renins from pre-pubescent mice showed that both storage and secreted forms contained 1-C:2-C renin in a 1:1 ratio. With puberty, both the storage and secreted renins were primarily of 2-C form. These data suggest that androgen influences renin transcriptional rates as well as post-translational processing and secretion.