331 HIGH CONCENTRATIONS OF NERVE GROWTH FACTOR (NGF) AND EPIDERMAL GROWTH FACTOR (EGF) IN SYNAPTOSOMAL FRACTIONS OF MOUSE CEREBRAL CORTEX. M.E. Weichsel, Jr., J. Lakshmanan, H. Kim and D.A. Fisher, UCLA School of Medicine, Harbor-UCLA Medical Center, Dept. of Pediatrics, Torrance, CA.

We examined NGF and EGF concentrations in synaptosomal fractions from mouse cerebral cortex during weaning. Pooled cortex tissues were homogenized in ice-cold 0.32 M sucrose with a glass-teflon homogenizer. The synaptosome enriched fraction was then prepared by differential centrifugation followed by a discontinuous sucrose density gradient. The purity of the preparation was confirmed by electron microscopy. Synaptosomal pellets were homogenized in phosphate buffered saline pH 7.4 and centrifuged to obtain 115,000 xg supernatant referred to as "synaptosomal extract (SE)". βNGF and EGF concentrations were quantified by respective radioimmunoassay (RIA). The mean (± SEM) NGF and EGF concentration in whole brain (B), cerebral cortex (C) and SE were as follows:

Growth factors	B	C	SE
NGF (pg/mg protein)	61±2	59±2	279±13†
EGF (pg/mg protein)	101±25	24±6	713±130†

†p <0.01 vs B and C.

Intraventricular injections of NGF and EGF 15 minutes prior to sacrifice did not significantly alter either NGF or EGF concentrations in SE. Summary and conclusion: a) NGF and EGF are present in cerebral cortical synaptosomal fractions in high concentrations, b) their presence and differential distribution in brain suggest that both peptides may have physiological functions specific to synaptic regions.

● **332** IN VITRO SYNTHESIS AND SECRETION OF A NERVE GROWTH FACTOR (NGF) BY NEONATAL MOUSE ASTROCYTES. M.E. Weichsel, Jr., R.H. Tarris and D.A. Fisher, Perinatology Laboratories, Dept. of Pediatrics, Harbor-UCLA Medical Center, UCLA School of Medicine, Torrance, CA.

We have grown neonatal mouse astrocytes (2 days old) in cell culture for nine days followed by mechanical removal of the contaminating oligodendrocytes. Astrocytes are continued in culture in serum-free medium for an additional 5 days. Assays for both glutamine synthetase and glial fibrillary acidic protein revealed the cultures to contain predominantly astrocytes. Cell pellet lysates and the glial conditioned medium (GCM) from these cultures were assayed for βNGF synthesis and secretion by radioimmunoassay (RIA) using βNGF purified from male mouse submaxillary gland as standard. Biosynthetic labeling with S^{35}-cystine labelled at 24 hour intervals for 120 hours demonstrated cellular synthesis of NGF between 72 and 96 hours with secretion of labelled NGF into the GCM between 96 and 120 hours. Immunoprecipitates from cell homogenate supernatants and GCM on polyacrylamide gel electrophoresis (PAGE) showed bands in the same molecular weight range as purified βNGF. Partial purification of the NGF-like material in the GCM with Sephadex G-100 gel filtration showed both immunoreactivity and bioactivity; bioactivity was blocked by anti-NGF antiserum. Results and conclusions: 1) An NGF-like factor (NGF-LF) is synthesized and secreted by neonatal mouse astrocytes in culture, 2) NGF-LF is similar, if not identical to βNGF synthesized in the mouse submaxillary gland, 3) NGF-LF is produced locally in normal brain tissue, 4) NGF-LF may be important in the developing CNS.

333 EFFECT OF CAPTOPRIL ON POTASSIUM INDUCED ALDOSTERONE SECRETION IN NEWBORN LAMBS. Douglas N. Weismann, William V. Page, Fred G. Smith, Jr., and Jean E. Robillard. University of Iowa College of Medicine, Dept of Pediatrics and Cardiovascular Center, Iowa City, IA.

The role of endogenous angiotensin-II (A-II) production in modulation of potassium (K+) induced increase in serum aldosterone concentration (Aldo) was studied in chronically-catheterized newborn lambs 10-14 days of age. Captopril (5 ug/kg/min) was given to one group of lambs (Exp) to block the conversion of angiotensin-I (A-I) to A-II, whereas the control group (C) received only 5% dextrose in water (0.1 ml/min). All lambs received dexamethasone phosphate (0.1 mg/kg/dose) 12 hours and 2 hours prior to potassium infusion (KCl) to suppress adrenocorticotropin (ACTH) secretion. Data are expressed as mean ± SD. Blockade of A-II formation by captopril was documented by 1) at least 90% inhibition of vasopressor response (from 25±8 mmHg pre- to 2±2 mmHg post-captopril) to a bolus of A-I (1 ug/kg) without altering vasopressor response (26±8 mmHg) to A-II (0.5 ug/kg); 2) decrease in baseline serum A-II (from 68.1±41.2 to 46.2±18.5 pg/ml); and 3) increase in baseline plasma renin activity (from 13.7±4.4 to 157±138 ng/ml/hr). KCl (1.80±0.09 mEq/kg) in C increased serum K+ (from 3.8±0.1 to 5.5±0.4 mEq/L, p<0.001) and Aldo (from 22.6±11.8 to 97.3±46.6 pg/ml, p<0.001). KCl (1.77±0.03 mEq/kg) in Exp increased serum K+ (from 3.9±0.4 to 5.7±0.6 mEq/L, p<0.001) in a similar fashion to C, but the increment in Aldo (from 22.7±19.3 to 55.2±61.6 pg/ml, p<0.05) was suppressed relative to C. These data suggest that endogenous A-II is a modulater of K+-induced aldosterone secretion in ACTH suppressed newborn lambs.

† **334** POTASSIUM MODULATES FETAL AND NEWBORN ALDOSTERONE SECRETION. Douglas N. Weismann, William V. Page, Fred G. Smith, Jr., and Jean E. Robillard, Univ of Iowa, Dept Pediatrics and Cardiovascular Center, Iowa City, IA.

The role of serum potassium (K+) in modulation of serum aldosterone concentration (Aldo) during development was studied in chronically-catheterized fetal (134-144 days gestation) and newborn (10-14 days of age) lambs. Dexamethasone phosphate was given to fetuses (0.1 mg/kg/dose) and ewes (5 mg) or newborn lambs (0.1 mg/kg/dose) at 12 hours and 2 hours prior to potassium infusion (KCL) to suppress adrenocorticotropin (ACTH) secretion. Data are expressed as mean ± SD. KCl (1.2±0.4 mEq/kg) in fetuses increased K+ from 4.0±0.5 to 5.4±0.6 mEq/L (p<0.001) and was associated with a small increase in Aldo (from 13.5±9.7 to 27.9±13.7 pg/ml, p<0.05). Plasma renin activity (PRA) and angiotensin-II concentration (A-II) did not change significantly (p>0.05). Maternal K+ and Aldo also did not change significantly. Similar KCl infusion (1.8±0.1 mEq/kg) in newborns increased K+ in similar fashion (from 3.8±0.1 to 5.5±0.4 mEq/L, p<0.001) but induced a greater increase in Aldo (from 22.6±11.8 to 97.3±46.6 pg/ml, p<0.01). PRA and A-II did not change significantly. If fetuses were given higher dosages of KCl (3.8±0.3 mEq/kg) to increase K+ further (up to 8.2±1.3 mEq/L), Aldo increased proportionately (up to 101±33 pg/ml). Newborns given high dose KCl (4.3±0.3 mEq/kg) increased K+ (to 10.3±2.6 mEq/L) with only slight increment in Aldo (to 125.0±87.8 ng/ml) suggesting near-maximal stimulation. These results suggest that after ACTH suppression, KCl induces increase in Aldo in both fetuses and newborns, but the fetal adrenal is less sensitive to such stimulation.

335 CARDIAC DEVELOPMENT IN THE PERINATAL PERIOD. Victor Whitman, H. Gregg Schuler, Raymond R. Fripp. Penn. State Univ. Coll. of Med., M. S. Hershey Medical Center, Department of Pediatrics, Hershey, PA

In early extrauterine life the heart undergoes rapid anatomic development. The underlying biochemical events responsible for this change are poorly understood. We investigated the mechanism of myocardial growth in fetal and neonatal animals. Piglet hearts from 0.9 gestation(0.9G), one day(1 DPP), 5 day(5 DPP) and 10 day(10 DPP) old animals were divided into left ventricular free wall(LVFW), right ventricular free wall(RVFW) and intraventricular septum(IVS). Between 0.9G and 10 DPP total heart weight increased from 3.63 ± 0.23 to 13.63 ± 0.47g. During this period, LVFW weight increased 5-fold (1.34 ± 0.11: 6.70 ± .18g) and IVS increased almost 4-fold (0.93 ± 0.06: 3.71 ± 0.16g). RVFW demonstrated an approximate 2.5-fold increment in growth (1.31 ± 0.08: 3.22 ± .17g). Total protein content parallels total RNA content of each myocardial structure at every age studied. Nuclear hyperplasia was greater in the LVFW and IVS than in the RV (DNA levels (μg):RVFW 313 ± 34 VS 554 ± 44; LVFW 342 ± 25 VS 1036 ± 53; IVS 255 ± 11 VS 630 ± 26). Cellular hypertrophy was likewise greater in LV and IVS than in RV as indicated by changes in protein/DNA content (LV .46 ± .02 VS .93 ± .05 IVS: .45 ± .01 VS .86 ± .04: RV .51 ± .03 VS 0.80 ± .06) however hypertrophy did not occur in RV beyond 1 DPP. These data indicate the importance of hypertrophy as well as hyperplasia in early neonatal cardiac development and that changes in protein synthesis of each myocardial structure are due to changes in RNA levels at this age.

336 RELATIONSHIP OF UMBILICAL VENOUS PO_2 TO UMBILICAL BLOOD FLOW. Randall B. Wilkening and Giacomo Meschia (Spon. by Frederick C. Battaglia), Departments of Pediatrics, OB/GYN and Physiology, University of Colorado School of Medicine, Denver, Colorado 80262.

Experiments to reduce umbilical blood flow have demonstrated varying PO_2 results in the umbilical vein ranging from no significant change to increases in umbilical vein PO_2. A clarification of these observations is important in order to understand the respiratory function of the placenta. Eleven paired experiments in 5 sheep were performed with an occluder around the fetal abdominal aorta (Group I). Eight paired experiments in 4 sheep were performed with an occluder around one umbilical artery (Group II). PO_2 and O_2 content were measured across the umbilical and uterine circulations. Umbilical and uterine blood flow were determined by application of the Fick Principle. Umbilical blood flow was reduced up to 30% of normal. Fetal O_2 consumption decreased up to 60% of normal. In Group I, when fetal O_2 consumption was unchanged by occlusion, PO_2 in the umbilical vein remained constant. When fetal O_2 consumption decreased, umbilical vein PO_2 increased. In Group II, there was a consistent decrease in umbilical vein PO_2 (ΔPO_2 = -5.4 ± 1.2 torr). These data demonstrate that the magnitude and direction of changes in umbilical venous PO_2 depends upon several factors, i.e., whether the reduction in umbilical blood flow occurs evenly (Group I) or unevenly (Group II) and whether fetal O_2 consumption remains constant or decreases.