283 **POST-OPERATIVE APNEA AND BRADYCARDIA IN FORMER PREMATURE INFANTS.** D. Kurth, A.R. Spitzer, M. Broennle, W.W. Fox. Univ. of PA. Sch. of Med., Dept. of Pediatrics & Anethesia, Children's Hosp. of Phila., Phila., PA.

Apnea in the immediate post-operative period is often observed in young former premature infants. In order to characterize post-operative apnea in this population, 30 infants were evaluated prospectively with pre-operative and recovery room pneumocardiograms for a minimum of two hours. Episodes of apnea and bradycardia were also recorded by nuring staff. Mean birthweight ± SEM was 1900 ± 142 g and mean G.A. ± SEM was 32 ± 0.6 wks. Apnea was defined as cessation of breathing of 15 seconds or longer, or less than 15 seconds accompanied by bradycardia (> 40 bpm below resting heart rate). Fourteen of 30 (46.7%) infants had post-operative apnea not diagnosed prior to surgery. Two infants (6.6%) had apnea with no discerable change pre- and post-operatively. The remaining 14 (46.7%) had no post-operative apnea. Factors placing these infants at greatest risk were post-conceptional age 32-55 weeks ($p < .05$) and postnatal age of 4-25 weeks ($p < .05$). The apnea was central in origin in all cases. The last post-operative apneic episode occurred in 11 (78.5%) infants within 24 hours of surgery, while 2 (14.3%) infants had apneic episodes more than 24 hours after surgery. One patient (7.2%) required continuous intubation and ventilatory support following surgery. These data suggest former premature infants undergoing surgery should be carefully monitored during the post-operative period, and the use of day surgery in these infants may place them at high risk for significant apnea-related complications.

● **284** **REGULATION OF PROENKEPHALIN mRNA AND LEUCINE-ENKEPHALIN IN EXPLANTED RAT ADRENAL MEDULLAE.** La Gamma, EF, White, JD, Adler, JE, Krause, JE, McKelvy, JF, & Black, IB. Cornell Medical Ctr. and Stony Brook Univ., New York. (Spon: PAM Auld).

Impulse activity differentially regulates enkephalinergic and catecholaminergic (CA) transmitter phenotypic characteristics in rat adrenal medullae in vivo and in vitro (LaGamma, et al, Science 224:1102, 1984). Adult male rat adrenal medullae, grown as explants for 4 days, show a 50-fold rise in leu-enkephalin-like immunoreactivity (LEU) following a 2 day plateau period. To further characterize cellular mechanisms governing the rise in LEU, 2 1/2 day cultured medullae were treated with inhibitors of protein, RNA, and DNA synthesis. Cycloheximide completely prevented the rise in LEU, while Actinomycin-D prevented 50% of the increase. Cytosine arabinoside had no effect. To begin characterizing the molecular level of regulation, proenkephalin mRNA was measured in this culture system using a 918 base pair cDNA probe. Proenkephalin mRNA levels in 2 and 4 day explants revealed a striking increase in proenkephalin mRNA which preceded the rise in LEU and could be prevented by depolarization. These data suggest tht ongoing synthesis of both mRNA and protein is required to increase LEU. This culture system may permit characterization of the genomic processes involved in transsynaptic regulation of CA and LEU in explanted adrenal medullary cells. (Supported by NIH Grants HL00756, NS10259 and HD12108).

285 **INHIBITION OF THROMBIN MEDIATED PLATELET AGGREGATION BY UTEROGLOBIN.** Sondra W. Levin, Ramanathapuram Manjunath, Ryojiro Fujita, Kuzhiyilethu K. Kumaroo, Jean DeB. Butler, Jerome A. Donlon and Anil B. Mukherjee. (Spon. by James B. Sidbury). Human Genetics Branch, NICHD, The Clinical Center, NIH and Naval Medical Research Institute, Bethesda, MD.

One of the putative functions of pregnancy-specific proteins is the inhibition of platelet aggregation. This function may facilitate the free flow of blood through the uterine microvasculature during pregnancy. Uteroglobin (UG) is a small molecular weight (15K) protein first discovered in the rabbit uterus during early pregnancy. The present investigation was undertaken to determine the effect of UG on platelet aggregation. Gel-filtered platelets (GFP) or platelet-rich plasma (PRP) from human volunteers and/or from rabbits were tested in an aggregometer with various inducers of aggregation including thrombin, ADP, collagen and arachidonic acid. Similar aggregation trials were carried out after preincubating GFP or PRP with various concentrations of UG.

Aggregating agents	UG Concentration	Aggregation Inhibition (%)
Thrombin (0.2U/ml)	8 µM	33
Thrombin (0.2U/ml)	24 µM	100
ADP (6 µM)	8 µM	0
Collagen (0.3 µgm)	8 µM	0
Arachidonic acid (0.1mM)	8 µM	0

These results suggest that uteroglobin specifically prevents thrombin mediated platelet aggregation in both rabbits and humans. This effect may be due to phospholipase A_2 inhibition.

† **286** **DETECTION OF RABBIT UTEROGLOBIN-LIKE PROTEIN IN THE NEONATAL HUMAN LUNG.** Ramasubbareddy Dhanireddy, Ryojiro Fujita, Uwe Schumacher and Anil B. Mukherjee. (Spon. by James B. Sidbury). Human Genetics Branch, NICHD, NIH and Dept. of Pediatrics, Georgetown Univ. Med. Sch., Wash. D.C.

Uteroglobin (UG) is a hormone dependent small molecular weight (15K) protein found in the rabbit uterus, prostate, seminal vesicle and the lung. UG has been suggested to prevent maternal immunological assult on the allogenic fetus and also to mask immunogenicity of male gametes in the female genital tract. Additionally, UG is known to inhibit chemotaxis of both rabbit and human neutrophils and monocytes and it is a potent inhibitor of thrombin mediated platelet aggregation. Preliminary evidence suggests that this may be due to the inhibition of phospholipase A_2. However, conclusive evidence is lacking for the presence of UG-like protein in species other than the rabbit and the rat. To delineate the presence of UG-like protein in the humans, we have investigated the tracheal aspirates and sera from four neonates who were on the respirator for aspiration syndromes. Using a radioimmunoassay specific for UG, SDS-PAGE and immuno-blot techniques, a protein with a molecular weight of 15K and UG-like immunoreactivity has been detected in the tracheal aspirates but not in the sera of these neonates. The amount of UG-like immunoreactivity in the tracheal aspirate varied from 50-114 ng/mg protein. This is the first time a protein similar to UG has been detected in the human lung. We speculate that this protein may modulate the immunoreactivity of airborne antigens in the tracheobronchial tree through phospholipase A_2 inhibition.

287 **POTENTIAL ROLE OF INTERCELLULAR COMMUNICATION IN MORPHOGENESIS OF HYDRA REAGGREGATES.** Rita Loch-Caruso and James E. Trosko (Spon. by Michael L. Netzloff), Michigan State University, Department of Pediatrics and Human Development, East Lansing, MI.

An association between teratogenesis and carcinogenesis is suggested by clinical and experimental observations. Accumulating evidence supports a role for direct, junction-mediated intercellular communication in the coordination of cell proliferation and differentiation. Interruption of this intercellular communication may be a common mechanism of teratogenesis and carcinogenesis. We are testing this hypothesis using hydra reaggregation as a developmental model. Hydra reaggregates were exposed to structurally related phorbol compounds. Some of these compounds are tumor promoters, inhibit junctional communication and are embryotoxic to amphibian and mammalian systems. We found that the ability of these compounds to interrupt hydra reaggregation correlated with their ability to promote tumor formation in mouse skin and inhibit junctional communication in an in vitro cell system. The strong tumor promoters, 12-0-tetradecanoyl-phorbol-13-acetate (TPA) and phorbol-12,13-didecanoate, were much more potent (>100-fold) in their ability to disrupt hydra reaggregation compared to the weakly promoting compounds, phorbol-12,13-diacetate and 4-0-methyl-TPA. This correlation supports the hypothesis that the phorbol compounds may induce tumor formation and abnormal development by similar mechanisms. We are currently exploring whether the phorbol compounds inhibit junctional communication in the actual reaggregating hydra, and whether the morphological characteristics of the junctions are altered.

288 **EFFECT OF HYPOVOLEMIC HYPOTENSION (HVH) ON CEREBRAL METABOLISM IN NEWBORN PIGLETS.** Hiroo Matsuda, Haruo Maeta, Margaret Go, Yvette Roberson, Mark Anderson, Evangelia Zikos, Tonse Raju, Dharmapuri Vidyasagar. University of Illinois Hospital, Department of Pediatrics, Chicago, Illinois.

We studied the effects of HVH on systemic and cerebral metabolism of glucose (gl.mmol/L), lactate (lac.mmol/L) and O_2 content ($C'O_2$ vol.%) in eight, 1-4 days old piglets under anesthesia during assisted ventilation. HVH was induced by exsanguination dropping the mean BP to 40 mmHg (50% of baseline) for 60'. Arterial (art.) venous from saggital sinus (v), lac. gl. and $C'O_2$ and CSF lac. were measured sequentially. Cerebral blood flow (CBF) was measured with radioactive microspheres. Results: ($\bar{x}$±SE: p values for significant difference as compared to baseline: *<0.05, **<0.01).

	Before HVH	After 30 min.	45 min.	60 min.
Art.lac.	2.35±0.40	7.37±0.89**	9.21±0.94**	10.27±0.93**
Δ lac.	-0.09±0.04	0.44±0.22*	0.86±0.12**	0.60±0.14**
CSF lac.	2.75±0.24	2.73±0.39		4.78±0.73**
Art.gl.	7.93±0.75	15.81±3.34*	15.25±3.30*	15.29±2.96*
Δ gl.	1.13±0.23	1.29±0.41	1.35±0.45	1.72±0.81
$C'aO_2$	10.8±0.8	9.8±0.9	9.6±1.0	9.6±0.8
Δ CO_2	6.7±0.5	8.0±0.7	7.7±0.8	7.6±0.6

During HVH, CSF lac., art. lac., gl. and Δ art.-v for lac. increased. The product of CBF and Δ art.-v $C'O_2$ was constant, indicating brain oxygenation remained stable during HVH. We therefore conclude: 1) Increased art.-v lac. and CSF lac. are due to systemic increase in lac. production; 2) Therefore, increase in CSF lac. by itself does not reflect brain compromise during HVH; and 3) By changing flow and O_2 extraction rates, brain maintains its oxygenation under a wide range of adverse situations.