

## 1294

LUNG WATER IN VENTILATED, IMMATURE FETAL LAMBS. Edmund A. Egan, SUNYAB & Children's Hospital, Depts. Physiol. & Pediatrics, Buffalo, NY 14222.

The rate and mechanism of fetal alveolar liquid clearance and the change in extra-alveolar lung water was studied during the initial 4 hours of positive pressure ventilation in 15 exteriorized fetal lambs, 125-135 days gestation, with negative lung liquid bubble stability tests, and intact umbilical circulation. Alveolar liquid volume was calculated from dilution of  $^{57}\text{Co}$ -cyanocobalamin mixed with alveolar after periods of ventilation. Extra-alveolar lung water was determined from wet/dry weights, corrected for residual alveolar liquid, at sacrifice. Alveolar liquid was rapidly absorbed, 71+6% in 15 minutes, > 90% in 1 hour. Large tracer solutes,  $^{131}\text{I}$ -albumin and  $^{125}\text{I}$ -cytochrome C, were not retained in the alveolar space by lung epithelial sieving, but absorbed at the same rate of water. Rapid absorption of alveolar liquid was not associated with its retention in the lung. Wet/dry ratio was 4.3+0.3 at 1 hour and 4.5+0.3 after 2 hours. At 4 hours it was significantly greater, 5.5+0.4. Positive pressure ventilation of immature lambs produces a much more rapid initial absorption of fetal alveolar liquid than previously measured in spontaneously breathing mature lambs, > 90% in the 1st hour vs 25%. Molecular sieving of alveolar liquid solutes typical of term fetuses was absent. The expected accumulation of excess lung water in immature lungs occurred only after completion of clearance of fetal alveolar liquid from the lungs. The edema of immature lungs is not retention of fetal alveolar liquid in the lung but a later phenomenon and of different origin. (Supported by Grant HL22552).

## 1295

EFFECTIVENESS OF VITAMIN E (E) ADMINISTRATION DURING RESPIRATORY DISTRESS SYNDROME (RDS) IN PREVENTING RETROLENTAL FIBROPLASIA (RLF). Richard A. Ehrenkranz,

James E. Puklin and Joseph B. Warshaw, Yale Univ. Sch. of Med., Depts. of Pediatrics and Ophthalmology, New Haven, Connecticut.

71 infants with RDS who participated in a randomized double-blind study to evaluate whether E administration could prevent bronchopulmonary dysplasia have been evaluated with indirect ophthalmoscopy and fluorescein angiography of the fundus without knowledge of treatment. Infants received E or the carrier vehicle (P) (0.4 ml/kg, Hoffmann-LaRoche, Inc.) IM at admission to the study and 24, 48 and 168 hrs later; more doses were given twice/week while the infant needed  $\text{O}_2$ . E- and P-treated infants were not significantly different in wt., gest. age, Apgar scores, age at treatment and initial severity of RDS. Mean serum E levels were 0.43 mg% pretreatment and averaged 0.64 mg% and 3.90 mg% in the P-treated and E-treated infants, respectively, during the next 7 days. RLF developed in 16 infants; 3 P-treated and 1 E-treated had Stage II changes, the other 12 only Stage I (Reese classification). None developed severe cicatricial changes and most findings have regressed. Although the sample size is small, E administration during the acute phase of RDS does not appear to prevent the development of the active changes of RLF ( $\chi^2 = 0.58$ ; df = 1; p = 0.45).

	No.	Survivor >10 d	Total Examined	RLF
E-treated	45	36	34	9
P-treated	51	41	37	7

## 1296

STUDIES OF RENAL FUNCTION IN NEONATES WITH HYPERBILIRUBINEMIA. William D. Engle and Billy S. Arant, Jr. University of Texas Southwestern Medical School, Department of Pediatrics (Dallas).

Recent studies have suggested that neonates with hyperbilirubinemia have impaired renal function. In order to study this problem, timed-urine collections and blood samples were obtained initially (I) from 22 neonates with hyperbilirubinemia (mean = 15.1 mg/dl, range = 11.5-19). Follow-up studies (II) were performed (n=18) within 1-12 days, when serum bilirubin was < 10 mg/dl. Study infants (S) were grouped by gestational age (GA) (33-36 or 37-42 wks) and postnatal age (PN) and results were compared between sequential studies in the same infant and with those obtained in age-matched controls (C), (n=29). There were no significant differences between S and C infants for fractional urine flow rate (V/GFR), fluid intake, or changes in body weight. Results of creatinine clearance ( $C_{CR}$ ) and fractional reabsorption of sodium ( $T_{Na}$ ) and  $\beta_2\text{M}$  ( $T_{\beta_2\text{M}}$ ) were:

Study	GA	PNA	n(S/C)	$C_{CR}$ ml/min		$T_{Na}\%$		$T_{\beta_2\text{M}}\%$	
				S	C	S	C	S	C
I.	37-42	≤4d	12/10	3.8	5.0	99.8	99.5	92.9	95.2
I.	37-42	>4d	5/6	6.8	4.9	99.8	99.8	95.6	94.4
I.	33-36	≤4d	5/3	1.9	2.7	98.7	99.2	85.7	93.0
II.	37-42	4-7d	11/4	5.5	5.0	99.6	99.7	94.2	97.8
II.	37-42	>7d	2/2	5.7	4.6	99.7	99.9	98.7	87.8
II.	33-36	>4d	5/4	2.5	2.2	99.4	99.1	84.4	85.3

There were no significant differences between S and C infants or in paired studies for individual infants. No evidence of bilirubin nephrotoxicity as assessed by  $C_{CR}$ ,  $T_{Na}$ , and  $T_{\beta_2\text{M}}$  was observed in these infants.

## 1297

A NARROW SPECTRUM LIGHT SOURCE FOR PHOTOTHERAPY.

John F. Ennever, Manoel DeCarvalho, Maxim F. Mutzhas and William T. Speck, Case Western Reserve University, Rainbow Babies and Childrens Hospital, Department of Pediatrics, Cleveland, Ohio

The increasing use of phototherapy for the treatment of neonatal jaundice has generated some concern in view of the potential long-term genetic consequences of this therapeutic modality. Our laboratory has determined that light at wavelengths  $\leq 450$  nm is the portion of the visible spectrum responsible for the *in vitro* and *in vivo* DNA-modifying activity of phototherapy. In view of this and subsequent work which has shown that light at wavelengths > 460 nm generate water-soluble bilirubin photoisomers, we have developed a new, portable phototherapy unit in which more than 95% of the spectral emission falls between 460 and 480 nm. The light source is a 5 kilowatt mercury arc lamp which has been doped with metal halides. The light is then passed through a series of three filters which remove all undesired radiation, including infrared. The resulting irradiance is 20 watts/M<sup>2</sup> over an area 60 x 45 cm, or 10 times the 460-480 nm spectral output of a standard phototherapy unit (Duro Test, Vita Lite). Using UV-difference spectroscopy to compare the generation of bilirubin photoproducts by these two light sources, we found enhanced photooxidation of bilirubin with the standard phototherapy unit, while the narrow spectrum unit proved more effective in bilirubin photoisomerization. These results demonstrate the feasibility of developing a phototherapy unit devoid of wavelengths with a potential for long-term genetic sequelae yet effective in bilirubin isomerization.

## 1298

THE DNA-MODIFYING ACTIVITY OF PHOTOTHERAPY AND RIBOFLAVIN. John F. Ennever and William T. Speck, Case Western Reserve University, Rainbow Babies and

Childrens Hospital, Department of Pediatrics, Cleveland, Ohio

Previous studies from our laboratory demonstrating the intracellular DNA-modifying activity of phototherapy with and without physiologic photosensitizing agents (e.g. vitamins, amino acids) have generated concern since many carcinogens and/or teratogens derive their activity from a similar ability to modify DNA. The present study extends these observations and characterizes the DNA-modifying activity of light-activated riboflavin, a coenzyme ubiquitous to living cells. More specifically, we have demonstrated that among the four naturally occurring deoxyribonucleotides, light-activated riboflavin induces a photochemical change only in deoxyguanosine. Utilizing scavengers and promoters of singlet oxygen ( $^1\text{O}_2$ ) we have determined that this reaction, although oxygen dependent, does not involve  $^1\text{O}_2$ . In addition, experiments with purified DNA have identified a second, oxygen-independent, photochemical reaction which results in the formation of a covalent adduct between riboflavin and the biopolymer. Moreover, when synthetic copolymers [poly (dA\*dT); poly (dG\*dC)] are substituted for DNA, covalent binding is observed only with the poly (dA\*dT). Therefore, this latter photochemical reaction is independent of deoxyguanosine. The relevance of these two distinct *in vitro* photochemical reactions to the jaundiced infant receiving phototherapy is under investigation. Our results suggest that phototherapy is a complex process with an inherent potential for serious long-term sequelae.

## 1299

SOMATOMEDIN-C (SM-C) IN THE NEONATE. Casey G. Falterman, Richard W. Furlanetto, C. Joan Richardson, M. Cassandra Matustik. (Spon. by Walter J. Meyer III).

University of Texas Medical Branch Hospitals, Department of Pediatrics, Galveston.

The somatomedins (SM) are a group of peptide hormones which are believed to mediate at least some of growth hormone's anabolic effects. While the role of SM in postnatal growth is well established, its function in prenatal and early postnatal growth is not clear and studies on SM levels in the neonatal period have given conflicting results. Part of the confusion is due to the fact that the assays employed are relatively non-specific for the different SMs. We have used a highly specific immunoassay to measure SM-C levels in 18 healthy full term neonates (birth weight 2750-3825 gm). SM-C was measured on cord blood (CB) and on samples obtained on days 1, 2, 3, 4, 5 and 14. Relative to normal adult serum (1  $\mu\text{M}$ ) the CB levels were low (0.27 ± .21) and fell to almost undetectable levels within the first day (< 0.1). SM-C levels remained low through day 4 but began to rise on the 5th day (.19 ± .09). By day 14 the levels were above those seen in cord serum (0.47 ± .28). The low SM-C levels observed in early postnatal life, a period when growth hormone levels are elevated, suggests a relative insensitivity of the neonate to the somatogenic effects of growth hormone.