

**1665** DIAPHRAGMATIC VENTILATION, WORK, AND CHEST WALL DISTORTION IN PREMATURE INFANTS. Gregory P. Heldt, Paul D. Goodrich, and Malcolm B. McIlroy. (Spon. by William H. Tooley). Cardiovascular Research Institute, Univ. of California, San Francisco, California.

We studied diaphragmatic ventilation, work, and chest wall distortion (CWD) in 7 premature infants (wt.  $1510 \pm 176g$ , age  $11 \pm 6d$ ) who were recovering from hyaline membrane disease. Tidal volume was partitioned into the movement of the chest wall and abdomen using circumferential mercury-in-rubber strain gauges. A multiple linear regression was used to find the best fit between the weighted sum of the circumference changes and the lung volume, measured with a face mask and pneumotachograph. Changes in tidal volume could be estimated to within  $\pm 6\%$  on a breath-by-breath basis. Esophageal and gastric pressures were measured using a two-lumen feeding tube with a 3 cm esophageal balloon connected to the proximal lumen. Diaphragmatic work was calculated using the abdominal volume changes and the transdiaphragmatic pressure. The diaphragm provided 53 to 198% of the ventilation of the lungs, being greater than 100% due to CWD in four of the infants. The work done by the diaphragm, however, was 90 to 396% ( $21$  to  $121$  ml $\cdot$ cm H $_2$ O) of that performed on the lungs, increasing roughly in proportion to the square of the diaphragmatic ventilation. The chest wall was stiffer during diaphragmatic contraction than during expiration, being up to 14 times as compliant during expiration. Thus, even small amounts of CWD produce increases in diaphragmatic ventilation, and lead to dramatic increases in the diaphragmatic work. (Supported by HL-24075 and HL-07159)

**1666** USE OF INTRAVENOUS ISOPROTERANOL FOR STATUS ASTHMATICUS IN CHILDREN. James J. Herman, Zehavah Noah, Robert Moody (sponsored by Henry L. Nadler) Northwestern University Medical School, Children's Memorial Hospital, Department of Pediatrics, Chicago, Illinois.

The use of intravenous isoproterenol (ISO) administered in a continuous drip was studied to determine its efficacy and indications. The indications were asthma score of 6 or greater indicating a pCO $_2$  of 60mmHg or higher or a pCO $_2$  of 55mmHg or greater without response to therapeutic levels of aminophylline, corticosteroids, and inhaled isothrane as well as oxygen therapy. Twenty-four patients (6 months to 16 years) monitored in the ICU received intravenous ISO for these indications, mean pCO $_2$ , 58.4, and score  $\geq 6$ . The initial starting dose of ISO was 0.005mcg/Kg/min; if there was no response in pCO $_2$ , the continuous drip was increased by increments of 0.005mg/Kg/min. every 15-20 minutes. With response, the ISO was infused until the pCO $_2$  decreased to 40, then decreased by increments to 0.005mcg/Kg/min. over a interval equal to the length of time of the continuous infusion. There was a complete response in 22 patients (mean dose 0.21mcg/Kg/min; mean response time 1.4 hrs., range .25 to 3.2 hrs.). One patient had a partial response but the ISO was discontinued with reversal of an arrhythmia. A second patient had initial resolution to ISO but had rebound bronchospasm when the ISO was discontinued too rapidly. Two patients had resolution of increased pCO $_2$  but were subsequently ventilated for severe hypoxia. Thus, IV isoproterenol has been an effective means of reversing increased pCO $_2$  in status asthmaticus in children but the limitations and complications must be monitored.

**1667** DETECTION OF GASTRIC CONTENTS IN TRACHEAL FLUID OF PRETERM INFANTS. Andrew O. Hopper, Linda K. Kwong, Ronald L. Ariagno (Spon. by Philip Sunshine), Dept. of Pediatrics, Stanford Univ. Sch. of Medicine, Stanford, Calif.

Aspiration of feedings in critically ill preterm infants requiring mechanical ventilation may prolong their ventilatory course and may contribute to the development of chronic lung disease. While massive aspiration can be diagnosed radiographically, we became concerned with the problem of identifying recurrent subclinical aspiration. A more sensitive method of detection utilizes an in vitro lactase assay to measure the presence of lactose (breast milk has approx. 0.2M lactose) in the tracheal aspirates of these infants. In this assay each mole of lactose is hydrolyzed to an equimolar amount of glucose. In order to establish a baseline glucose range, we measured the tracheal glucose level from 17 preterm infants (G.A. 26-37 wks; B. wt. 670-2950 gm) during the 1st wk of life while the infants were intubated. A total of 52 samples were collected (36 samples from gavage fed/16 infants not fed). The mean tracheal glucose level was  $2.67 \pm 2.77$  mg/dl ( $15.05 \pm 15.23$  umole/dl). The range was 0.02-11.57 mg/dl (.08-64.22 umole/dl). The glucose level did not vary with gestational age, birth weight, postnatal age or feeding. We then obtained tracheal aspirates from 5 infants on ventilators who received breast milk by gavage. In 2 infants, lactose levels were 112 mg/dl (327 umole/dl) and 21.9 mg/dl (64.1 umoles/dl) respectively. Lactose was not detected in the other 3 infants. These preliminary findings suggest that the lactase assay may provide a sensitive method for detecting aspiration of gastric contents in ventilator dependent infants.

**1668** SURFACTANT ACTIVITY FOLLOWING NATURAL SURFACTANT (NS) TREATMENT OF PREMATURE LAMBS. Machiko Ikegami, Alan H. Jobe, Theodore H. Glatz, UCLA School of Medicine, Harbor-UCLA Medical Center, Department of Pediatrics, Torrance.

Six 120-day and 6 130-day gestational age lambs were delivered by C-section and supported on ventilators with 100% oxygen. With respiratory failure (pCO $_2$ = $114 \pm 11$ ) the lambs were treated with 50 mg/kg of  $^3H$  labeled NS by tracheal instillation. All the lambs responded dramatically, however the effect was gone within 3 hrs. The specific activity of the  $^3H$  labeled saturated phosphatidylcholine (SPC) in the NS used for treatment had decreased by only 30 $\pm$ 4% in the alveolar wash (AW) at sacrifice; thus the treatment dose was minimally diluted. However, IV injections of  $^{14}C$ -palmitic acid resulted in the appearance of  $^{14}C$ -SPC in sequential samples suctioned from the airways (AS) indicating endogenous synthesis and secretion. Minimum surface tension (ST) measurements (dynes/cm) made on AS fell from  $29 \pm 2$  to  $8 \pm 5$  after NS and again rose to  $32 \pm 2$  at sacrifice. AW samples taken at sacrifice and containing 1 umole phosphatidylcholine (PC) did not lower ST below  $27 \pm 4$ , while "surfactant" recovered from the AW (R-SA) containing 0.2 umoles PC lowered ST to  $<10$ . (NS containing 0.1 umoles PC will lower ST to  $<10$ ). While the phospholipid compositions were similar, the ratio umole PC/mg protein was  $0.13 \pm 0.02$  in AW,  $4 \pm 0.4$  in R-SA and  $5.7 \pm 0.6$  in NS. Following removal of the R-SA from the AW samples by centrifugation, the supernatant, when mixed with NS, raised ST from 0 to  $>30$ . We demonstrated 1) NS remains in the airways following treatment, and 2) the ability of NS to lower ST is reversibly inhibited.

**1669** ALTERATIONS IN PLASMA AMINO ACIDS IN CHILDHOOD ASTHMA. Laura S. Inselman, Farida Khan and Hugh E. Evans, Jewish Hospital and Medical Center of Brooklyn, Department of Pediatrics, Brooklyn, New York.

Abnormalities in plasma amino acids (AAs), particularly those related to catecholamine (CTA) or glucose synthesis, may have etiologic or pathogenetic significance in asthma. Plasma AAs and cortisol and urinary CTAs were measured at 8AM and 4PM in randomly selected children with status asthmaticus (n=9; group A), moderately-severe chronic asthma (n=9; group B), mild chronic asthma (n=9; group C) and controls without lung disease (n=7; group D). Group assignment was based on severity of wheezing and medication requirements. All had PaO $_2$   $>65$ mmHg. Several conditions believed to alter plasma AAs such as infection and recent corticosteroid use were excluded. AAs were determined chromatographically using an autoanalyzer. Cortisol was measured by competitive protein-binding inhibition, and CTAs were analyzed by spectrophotofluorimetry. Of the 24 AAs analyzed, 11 including tyrosine, proline and alanine were decreased at 8AM or 4PM in group A compared with the other groups (P $<0.05$ ). Plasma cortisol was elevated in group A (P $<0.05$ ), and urinary CTAs remained unchanged. Normal diurnal variations of AAs and cortisol were preserved. Sequential daily determinations in 5 children in group A showed progressive increases in total AA levels as symptoms subsided. Thus certain AAs which are gluconeogenic (proline) or CTA precursors (tyrosine) are decreased in status asthmaticus. Tyrosine deficiency may lead to altered CTA synthesis and play a role in the pathogenesis of asthma. If these findings are confirmed, tyrosine administration may be helpful in therapy of asthma.

**1670** NATURAL SURFACTANT THERAPY (NST): CLINICAL AND BIO-PHYSICAL CORRELATES IN PREMATURE LAMBS. Harris C. Jacobs, Machiko Ikegami, Alan H. Jobe, Sally Jones, Theodore H. Glatz, Luciano Barajas, UCLA School of Medicine, Harbor-UCLA Medical Center, Department of Pediatrics, Torrance.

31 lambs were delivered by C-section at 120 days gestational age and divided randomly into 6 groups (G1-6) of 4-7 lambs. G1 lambs were killed before the first breath. G2-6 were supported with 100% O $_2$  at 30 breaths/min and 30/2 cm H $_2$ O on infant ventilators. Frequent blood gases and tidal volumes (TV) were measured. All lambs were in respiratory failure by 28.6 min (pH= $6.93 \pm 0.1$ ; pO $_2$ ,  $30.6 \pm 1.8$ ; pCO $_2$ ,  $108 \pm 3$ ). G2 lambs were killed before NST and G3-6 lambs were treated with 50 mg/kg NS by tracheal instillation. G3-6 lambs were killed 10 min, 40 min, 1.5 hr and 3 hr post NST, respectively. All lambs responded dramatically to NST; mean maximal responses were: pH,  $7.29 \pm 0.2$  at 1.25 hr; pO $_2$ ,  $196 \pm 20$  at 5.6 min; and pCO $_2$ ,  $39 \pm 4$  at 58 min post NST. Responses of lambs in different groups were uniform. Pressure-volume curves (P-V) were measured using the left lung, an alveolar wash (AW) was recovered from the right upper lobe (RUL), and the RLL was fixed by perfusion at constant pressure for histology. P-V curves improved following NST. Surface tension (ST) measurements of AW samples were  $31 \pm 1$  dynes/cm before NST and fell to  $6.3 \pm 2.8$  at 10 min post NST, before rising to  $21.7 \pm 4.6$  by 3 hr post NST. ST correlated with pO $_2$  (p $<0.001$ ) but not pCO $_2$  or TV at sacrifice. A grid count of % distal air space (%) in tissue sections showed dramatic improvement in aeration with NST; %A correlated with pCO $_2$  and TV at sacrifice (p $<0.05$ ).