1846 PNEUMOGRAMS AND VENTILATORY RESPONSE TO CO2 IN INFANTILE APNEA

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We studied 16 ventilatory response to CO2 and (12 hour) pneumograms (PPG) in 14 infants who had apnea or cyanotic spell at home or in the hospital in order to evaluate the comparative results of these tests in infantile apnea. Pneumograms were classified as normal, borderline or abnormal after studying the following factors-(Apnea density (A6/D), Prolonged apnea, Periodic breathing, Disorganized breathing and Bradycardia). Ventilatory responses to 2% and 4% CO2 in 21% O2 were studied the day after the pneumogram. A mean slope of the CO2 response curve of <25 ml/kg/mmHg. PACo2 was considered abnormal; 25-30 borderline and >30 normal.

	PPG		CO2		PPG+Co2	
	n	%	n	%	n	%
Normal:	10	(62.5)	9	(56.25)	7	(43.75)
Abnormal:	4	(25)	6	(37.5)	8	(50)
Borderline:	2	(12.5)	1	(6.25)	1	(6.25)

Our results indicate that combining both tests identified more abnormalities than by PPG or CO2 response test alone. 30% of the normal PPG had abnormal CO2 response and 22% of normal CO2 response had abnormal PPG. We recommend a CO2 response test in infants with normal PPG with clinical history of apnea. Combining both tests increases the sensitivity of either test alone.

1847 SURFACTANT AEROSOL: ADMINISTRATION BY HAND-HELD GENERATOR AND EFFECTS ON EXCISED LUNGS.

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Dipalmitoyl phosphatidylcholine (DPPC) and cholesteryl palmitate (CP, a spreading agent), 200:1 w/w, were suspended in fluorocarbon propellents and delivered directly to the lungs from Valois metering valve, 5.36±0.16 mg DPPC per actuation. Aerosol deposited in vitro (22°C) as crystalline structures, 100 Å thick, and on normal saline solution (NSS)(37°C, humidified atmosphere) as an amorphous film, which spread rapidly and also formed stable bubbles (γ ~ zero). Compression of the film produced γ <1.0 dyne/cm. We assessed delivery of DPPC (5 actuations) into excised adult rabbit lungs at 22°C and 37°C. Volume-pressure (VP) curves before and after either DPPC:CP or placebo (propellent) were not different, except for end-deflation volume of the DPPC:CP group, which was larger than the others ($p<0.05$). Excised lungs were also lavaged with NSS to mobilize and remove natural surfactants prior to aerosolization of either DPPC:CP or placebo. VP diagrams of lavaged and placebo-treated lungs were essentially the same. In contrast, control and DPPC:CP-treated lungs contained larger volumes ($p<0.05$) throughout deflation. DPPC recovered from the lungs (^{14}C-DPPC marker) was 74.6% of the amount aerosolized. DPPC:CP to normal lungs produced no morphologic changes as assessed by light microscopy. We conclude that rapidly spreading DPPC:CP can be administered efficiently to the lungs by convenient hand-held nebulizer; it sustains VP function of normal lungs and returns function to normal after surfactant-depletion.

†1848 CIRCADIAN VARIATION OF THEOPHYLLINE (T) PHARMACOKINETICS IN ASTHMATIC CHILDREN.

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Most previous T pharmacokinetic studies have been conducted during the day. We examined nocturnal pharmacokinetics in five asthmatic patients (aged 7 to 11 y) who received equivalent doses of either TheoDur® tablets (TD) or Somophyllin-CRT® capsules (S), given every 12 h, during 1 week and the alternate preparation during the next. Patients remained on TD and S for six days, after which blood was obtained at 1 min pre-dose and at 1, 2, 3, 6, 9 and 12 h post-dose for two consecutive dosing intervals. Sera were analyzed in duplicate for T by an enzyme immunoassay method.

	STCmax-min(mg/l)		AUC(mg·h/l)		Tmax(h post-dose)	
	Day	Night	Day	Night	Day	Night
S	14.8±6.9	10.2±4.2	190±43	164±35	2.6±0.5 **	6.6±1.3
TD	8.2±2.5	6.9±3.2	160±30 *	134±25†	3.8±2.0 *	10.8±1.6††

Day/Night: *P<0.02; **P<0.005 S/TD: †P<0.05; ††P<0.005

Differences of maximum and minimum serum T concentrations (STCmax-min); areas under concentration/time curves (AUC); and times to maximum concentrations (Tmax) were determined for TD and S during each dosing interval. Although in all patients TD provided for less STC fluctuation at night, S is better absorbed than TD during the night. Tmax for TD occurs very late in the night dosing interval. These preliminary results indicate that a circadian variation of T pharmacokinetics exists and that the characteristics of this variation are different for S and TD.

1849 PROSPECTIVE ANALYSIS OF HEART RATE AND BREATHING PATTERNS IN INFANTS SUCCUMBING TO SIDS AND IN CONTROLS.

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In studies of babies at high risk for SIDS (near-SIDS and siblings), we have identified among some who died excess periodic breathing (PB) excess variability (var) of respiratory frequency (f) and increased oscillation of heart rate (HR), at 4-7 cycles per min., (low frequency peak-LFP). The present study was planned to test the hypothesis that in an unselected prospectively studied population, these same variables might discriminate SIDS from controls. From 6914 term infants, we selected 24 hour pneumograms performed at 6 weeks on 11 SIDS and 101 random controls. One SIDS had one near-SIDS spell. Casettes were coded for blind analysis. From data recorded between 12MN and 6AM we transcribed ECG and respiratory signals onto hard copy for visual inspection and we transferred these signals during all 5 min epochs of quiet breathing (Q) onto FM tape for spectral analysis. We inspected hard copies for PB and apnea ≥10s. Spectral analysis identified f and var, HR and var and power at f (resp. sinus arrhythmia) and at the LFP. We rank ordered results to test hypothesis 1) that PB and 2) that abnormal spectral var were markers for SIDS. We performed cluster analysis on each data set. The code was then broken; neither hypothesis was correct. These results neither support nor negate the apnea hypothesis of SIDS.

†1850 TYPE II PNEUMOCYTE MEMBRANE PHOSPHOLIPID METHYLATION IS NECESSARY FOR SURFACTANT SECRETION,

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Membrane phospholipid methylation has been implicated in membrane receptor signal transmission and cell secretion. In the type II pneumocyte, beta-adrenergic cell membrane receptors are important in initiating secretion of pulmonary surfactant. We studied membrane methyltransferase activity in type II pneumocytes. Type II pneumocytes were purified to near homogeneity from adult rabbit lung and cultured at a density of 3×10^6 cells per culture well. Cells were grown in Eagle MEM with 10% FCS. ^{3}H-l-methionine was utilized as the methyl donor. Phospholipid methylation was stimulated by terbutaline and isuprel, both potent beta-adrenergic agonists, and inhibited by the beta-adrenergic agent propanolol. Methylation was also inhibited by 3-deazoadenosine, a potent methyltransferase inhibitor. For evaluation of surfactant secretion, ^{3}H-choline Cl was added to cultures. Surfactant secretion was stimulated by terbutaline. 3-deazoadenosine inhibited surfactant secretion in response to a beta-adrenergic stimulus. Thus, membrane phospholipid methylation plays a necessary role in surfactant secretion in the type II pneumocyte.

1851 A COMPARISON OF DIFFERENT METHODS TO ISOLATE GOBLET CELLS.

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Three different methods of enzymatic treatment were compared to determine the optimum method to isolate goblet cells. For each method, tracheas were excised from adult mongrel cats, trimmed of excess tissue and cut into segments. Thermolysin Method (TH): Tracheal rings were agitated in a solution of 60 u/ml Thermolysin in PBS. After each of 5 agitation periods, the cell suspension was centrifuged into a 10^{-6} M EDTA solution. The cell pellet was washed, pipetted x 10, and separated on a 45% Percoll gradient formed at 20,000 xg for 25 min. Pronase Method (PR): Tracheal segments were incubated in .5% Pronase (Type B:45,000 PUK/gm) and .1% BSA in media 1-9 for 55 min. The surface epithelium was removed by pipette and gentle scraping. The cell pellet was washed and separated as described above. Elastase Method (EL): Tracheal segments were incubated in 20 mM EDTA in Ca, Mg free EBSS for 1½ hours after which the surface epithelium was removed. The epithelium was incubated in Elastase 40 u/ml in EBSS for 30 min. The cell pellet was then incubated in DNAase 20,000 u/ml for 1 hour and then separated on the Percoll gradient. TH yielded no goblet cells which excluded trypan blue or appeared intact by electron microscopy. PR yielded 2×10^6 cells per trachea of which 10% were goblet cells with excellent viability and intact ultrastructure. EL yielded 3.3×10^5 healthy appearing goblet cells/trachea with virtually no contamination by other tracheal cell types. EL appears to be superior to PR or TH as a method to isolate cat tracheal goblet cells.