1659 SUPRA-ADDITIVE EFFECTS OF HORMONES ON PHOSPHOLIPID SYNTHESIS BY FETAL LUNG IN ORGAN CULTURE. Ian Gross and Christine M. Wilson. Department of Pediatrics, Yale University School of Medicine, New Haven, Connecticut.

Dexamethasone (Dex), theophylline (Th) and triiodothyronine (T_3) act directly on fetal lung to enhance phosphatidylcholine (PC) synthesis. We have investigated the effects of combinations of these agents on PC synthesis in organ culture in order to determine whether there is a biologic basis for hormone interactions in the developing lung. Explants of 18 day fetal rat lung were exposed to optimal doses of these agents, alone or in combination, for 48 hours. The effects on the rate of choline incorporation into PC were:

	Dex	Th	T_3	Dex + Th	Dex + T_3
% stimulation:	101 ± 9	116 ± 13	38 ± 5	363 ± 26	197 ± 10

These effects are supra-additive. Similar results were obtained when Dex was combined with cyclic AMP, but the changes were less striking with caffeine. The disaturated PC content of the explants was increased 89 ± 4% by Dex, 79 ± 5% by Th and 143 ± 10% by Dex + Th. These data imply that the agents act via different mechanisms and provide a rationale for in vivo animal studies of combined hormone administration. The findings also suggest that the general hormonal milieu of the fetus must be considered in studies of the induction of fetal lung maturation. (Supported by USPHS grant HL 19752.)

1660 MATURATIONAL RESPIRATORY RESPONSE TO ENDOGENOUS OPIATES IN NEWBORN RABBITS. Michael M. Grunstein, and Judith S. Grunstein (Spon. by Richard B. Johnston, Jr.) Univ. of Colo. School of Med. and Nat. Jewish Hosp., Dept. of Pediatrics. Denver, Colorado.

Significant changes in respiratory control occur in the human neonate during the early post-natal period. These changes may be related to the action of endorphins, which have been isolated from amniotic fluid and cord blood, and are known to affect respiration. To determine the maturational effects of these agents on respiration, we measured ventilation ($\dot{V}_E$), tidal volume (V_T) and respiratory frequency (f) in 18 rabbit pups (age range: 1 to 19 days) before and after systemic administration of D-Ala^2,D-Leu^{5}enkephalin (ENK). Tracheostomy and carotid artery catheterization were performed under light ether anesthesia. After anesthetic recovery the pups were placed in a body plethysmograph. Saline infusion had no effect. Twenty minutes after infusion of 0.5 ug/g ENK, however, $\dot{V}_E$ was significantly reduced in all pups, ranging from 25 to 80% below control. The $\dot{V}_E$ changes were secondary to decreases in f, although V_T increased (+15 to +65%) due to prolongation of inspiratory duration. The degree of $\dot{V}_E$ depression varied inversely with age, being most marked in pups< 4 days old. Indeed, in 4 of 7 pups < 4 days old, ENK produced periodic breathing with apnea. All effects of ENK were abruptly reversed with infusion of naloxone (0.8ug/g), an opiate antagonist. These data provide evidence that: a) opiate-like peptides depress ventilation but their effect diminishes with age; b) early in post-natal life these agents may cause periodic breathing with apnea.

1661 ACIDIC SURFACTANT PHOSPHOLIPIDS IN RDS AND IN ADULT RDS (ARDS): ROLE OF MYOINOSITOL (INO) IN REGULATION. M. Hallman, Ola D. Saugstad, Benita L. Epstein, and Louis Gluck. University of California, San Diego, Department of Pediatrics, La Jolla, California.

Present evidence indicates that phosphatidylglycerol (PG), phosphatidylinositol (PI), and phosphatidylserine (PS), in decreasing order, activate surfactant lecithin synthesis and maintain surface activity. Animal studies indicate that INO suppresses surfactant PG synthesis. We have studied serum INO levels in newborns with RDS and in adults with ARDS. The INO levels have been correlated with phospholipid (PL) levels from tracheal aspirates (newborns) or alveolar lavage (adults). During 1st neonatal day INO levels were significantly higher in RDS (n=7) than in no RDS (n=12) [mean 1004 (530-2830), vs 179(58-345)μM, p<0.005]. As studied in 4 cases, INO decreased before PG appeared [1st day: 1738 (530-2830), vs 3rd day:510(280-1380) μM, p<0.05]. In 6 ARDS cases PL's were different from 11 cases without ARDS:

	PG(% of PL)	PI	PS	serum INO (μM)
ARDS	0.4(0.0- 0.8)	7.6(1-15)	23.5(15-25)	174(24-470)
Non-ARDS	14.3(4.2-20.0)	11.7(6-20)	5.6(1-12)	30(15- 57)
P<	0.001	0.1	0.001	0.025

The two ARDS cases with highest INO (395 and 470 μM) had renal failure. Absence of PG in RDS may be mainly due to high INO and in ARDS mainly to deficient PG+PI synthesis. We propose that INO is synthesized at the expense of surfactant PL. Thus serum INO may be helpful in monitoring the course of RDS.

1662 INDOMETHACIN, IMMATURE FETAL PULMONARY VASCULAR RESISTANCE (PVR), AND LUNG INFLATION. Cathy A. Hammerman and Emile M. Scarpelli. Pediatric Pulmonary Division, Albert Einstein College of Medicine, Bronx, N.Y.

Indomethacin (I) was studied in the isolated, perfused immature (27 days' gestation) fetal rabbit lung. Lungs contained normal volume of fetal pulmonary fluid (FPF) during pulmonary vascular perfusion with either balanced, buffered electrolyte solution (BES), 3% O_2 (C, control, n=5) or BES, 3% O_2, plus .50 μg/ml I (n=5). Within 5 min of start of perfusion, the ductus was ligated and after 1.5-2 h, the lungs were inflated to maximal volume, then deflated to atmospheric pressure, the first air volume-pressure (VP) diagram. PVR was the same in both groups at the start and immediately after ductal ligation when PVR increased. However, after 1.5-2 h C PVR had returned to pre-ligation level, whereas I PVR remained elevated. When the lungs were inflated, PVR decreased in C, but increased in I. With deflation C PVR did not change and I PVR decreased to pre-inflation level. Comparison of VP diagrams with age-matched, but unperfused fetal lungs showed larger volumes and greater air retention in C, but no difference from I. These studies indicate that (1) "resting" prostaglandin (PG) activity is minimal in the isolated, perfused immature fetal lung; (2) normal accommodation to volume load produced by ductal closure may be mediated by PG and is blocked by I; (3) pulmonary vascular perfusion itself may induce surfactant release (which is blocked indirectly by I) into FPF; and (4) PVR decrease during inflation is related, in part, to PG activity and/or surfactant release. (Supported by NIH HL 07060).

1663 ESSENTIAL FATTY ACID DEFICIENCY (EFAD) IN THE RABBIT AS A MODEL OF NUTRITIONAL IMPAIRMENT IN CYSTIC FIBROSIS (CF): EFFECTS ON ALVEOLAR MACROPHAGES. T.B. Harper, H.P. Chase, J.E. Henson, and P.M. Henson. National Jewish Hospital and Univ of Colo Med Sch, Dept of Peds, Denver, Colo.

EFAD is a frequent finding in patients with CF and has been associated in animal studies with an impaired ability to clear lung bacteria. To determine the specific deleterious effects of EFAD on lung defense mechanisms, a rabbit animal model for EFAD has been developed, and aspects of alveolar macrophage morphology, activation, and response to bacterial stimuli were studied. Results demonstrate that alveolar macrophages from EFAD animals have (1) normal light and ultrastructural morphology, (2) normal stimulated and background production of superoxide anion and the granular enzyme, β-glucosaminidase, and (3) normal phagocytosis of S. aureus (bacteria per macrophage after 1 hr incubation - control 6.7, EFAD 7.9), and a non-mucoid strain of Ps. aeruginosa (bacteria per macrophage after 1 hr incubation - control 4.6, EFAD 4.3). However, impairment of macrophage lysozyme production, both zymosan-stimulated (EFAD 72% of control) and background (EFAD 70% of control) was noted. Likewise, impaired intracellular killing of S. aureus (percent of initial intracellular organisms viable after 3 hrs - control 34%, EFAD 54%) and Ps. aeruginosa (control 18%, EFAD 32%) was observed. Thus, EFAD was associated with decreased alveolar macrophage lysozyme production and impaired macrophage bactericidal activity. These results may implicate essential fatty acid deficiency as contributing to impairment of antibacterial lung defense mechanisms in cystic fibrosis.

1664 EFFECT OF NALOXONE ON THE VENTILATORY RESPONSE TO CARBON DIOXIDE IN YOUNG RABBITS. T. Hazinski and M. Schlueter (Spon. by W.H. Tooley). Dept. of Pediatrics and Cardiovasc. Res. Inst., Univ. of California, San Francisco; and Dept. of Pediatrics, Northwestern Univ. School of Medicine, Chicago, Illinois.

We have shown that naloxone (NLX) produces respiratory stimulation in rabbits ≤4 d old but has no effect in pups 5-15 d of age (J Appl Physiol, in press). To determine if NLX effects CO_2 sensitivity in this latter group, we measured ventilation ($\dot{V}E$) by plethysmography in 10 rabbit pups aged 6-14 d while they breathed room air, 2% CO_2 in 30% O_2, and 4% CO_2 in 30% O_2. We inserted a tracheostomy tube and carotid artery catheter under light ether anesthesia. After a 40 min recovery period, each gas mixture was breathed for 8 min; $\dot{V}E$ was measured and an arterial blood sample was obtained during the eighth min. After 4 μg/g NLX IV, the protocol was repeated. For each pup, $\dot{V}E$ and $PaCO_2$ were compared by linear regression. Results: (Data expressed as mean ± SD)

	BEFORE NLX		AFTER NLX	
	$\dot{V}E$(ml/min/g)	$PaCO_2$(torr)	$\dot{V}E$(ml/min/g)	$PaCO_2$(torr)
Room Air	.544±.148	43.8±4.3	.573±.137	40.7±2.6
2% CO_2	.712±.177	48.0±4.6	.819±.238	43.0±3.4
4% CO_2	.920±.192	49.5±3.1	1.002±.289	45.5±3.6
Slope:	0.0589±.0132		Slope:	0.0618±.0308
x-intercept:	28.8±5.3 torr		x-intercept:	33.3±5.4 torr

Comparison of these and other measured variables before and after NLX showed no significant differences (p=.78-.90). We conclude that NLX has no effect on the ventilatory response to CO_2 in rabbits over 6 d of age.