325 DEVELOPMENT OF INTESTINAL SUCRASE ACTIVITY: INTERACTION OF THYROID AND ADRENAL HORMONES. Yvonne E. Vaucher, Judy A. Grimes, Otakar Koldovsky. (Spon. by T. Allen Merritt). UCSD Medical Center, School of Medicine, Department of Pediatrics, San Diego. University of Arizona, College of Medicine, Department of Pediatrics and Physiology, Tucson, AZ.

Administration of exogenous thyroid hormones precociously increase intestinal sucrase activity (SA) in suckling rats. To differentiate the effects of thyroid and adrenal hormones on SA, intact suckling Sprague-Dawley rats were given TSH (0.5U) bid or water subcutaneously from day 14 until sacrifice on day 18. Results are shown below (X+SEM). Serum T4 and corticosterone (CS) as well as SA in the jejunum (J), mid-jejunum (MJ) and ileum (I) were all significantly increased in intact TSH treated rats.

	N	CS	T4	SA-J	SA-MJ	SA-I	ΔBody Wgt.(g)
H_2O	4	1.4±.5	5.5±.1	.16±.04	.31±.07	.10±.01	7.9±.2
TSH	5	17.5±1.0	8.8±.1	.69±.13	1.3±.17	.25±.04	6.3±.2
	p	<.001	<.001	<.01	<.001	<.05	<.001

Sucklings were then adrenalectomized (ADX) on day 14 and given TSH (0.5 or 1.0U) bid or water subcutaneously until sacrifice on day 18. No significant differences in SA were found between ADX sucklings given TSH(1 or 2U/day) and ADX controls given water only.

	N	CS	SA-J	SA-MJ	ΔBody Wgt.(g)
ADX-H_2O	4	.25±.07	.20±.03	.14±.02	3.3±1.8
ADX-TSH	10	.19±.08	.23±.02	.19±.02	4.9±.9
		NS	NS	NS	NS

In the absence of the adrenal glands, physiologic elevation of endogenous thyroid hormones by TSH does not alter the maturational time course of intestinal sucrase activity.

● 326 LIPOMODULIN ANTIBODY PREVENTS THE GLUCOCORTICOID-INDUCED INCREASE ON PULMONARY β-ADRENERGIC RECEPTORS (β-AR). I. Vermes-Kunos, G. Kunos, F. Hirata. (Spon. by A. Papageorgiou). McGill Univ.- Dept. of Pharmacology, The SMD Jewish General Hospital - Dept. of Neonatology, Montreal, Que., Canada, and NIMH, Laboratory of Cell Biol., Bethesda, Md.

Glucocorticoids produce most of their effects by inducing the synthesis of endogenous, phospholipase A_2 inhibitory proteins, such as lipomodulin (J Biol Chem 256:7730). Glucocorticoids also increase the cellular numbers of β-AR in the lung (Bioch Biophys Res Commun 94:390), which may be the mechanism of the synergism between glucocorticoids and β-adrenergic agonists for increasing surfactant production, and of the sensitization of the lung to β-adrenergic bronchodilation. We studied the mechanism of the increase in β-AR by glucocorticoids in a human lung adenocarcinoma cell line (A549) frequently used as a model of alveolar type II cells. Cells were cultured to confluency in RPMI 164 medium containing 10% fetal calf serum. Cells were then incubated for a further 24 hours in serum-free Dulbecco MEM with or without 10 μM corticosterone, in the presence of 5 μl/ml of saline (S), a monoclonal antibody of lipomodulin (AB), or control ascites fluid (ASC). Cells detached in calcium-free medium were freeze-thawed, and β-AR binding was assayed using ^{125}I-cyanopindolol. CORT increased β-AR/cell from 680 to 1460 in S and from 240 to 1650 in ASC ($P < 0.05$ for both), but CORT was ineffective in the presence of AB (450 vs 480 β-AR/cell). These findings suggest that glucocorticoids do not directly induce the synthesis of lung β-AR, but increase their numbers indirectly through the induction of the phospholipase inhibitory protein, lipomodulin.

† 327 HORMONAL REGULATION OF CHOLINE PHOSPHATE CYTIDYLTRANSFERASE (CYT) IN FETAL RAT ALVEOLAR TYPE II CELLS. Rose M. Viscardi, Richard H. Simon, Paul Weinhold. Depts. of Pediatrics, Internal Medicine, and Biological Chemistry, Univ. of Mich., Ann Arbor. (Spon. by SM Donn).

CYT is the rate limiting enzyme in the CDP choline pathway, the major pathway of phosphatidylcholine synthesis. Fetal rat CYT activity increases during the last 2 days of gestation (G). Most fetal CYT is present in cytosol and requires added lipid for activity while adult CYT is present in microsomes and cytosol and does not require added lipid. We examined the possible involvement of the hormones T_3 and Dexamethasone (Dex) and fibroblast pneumocyte factor (FPF) in the regulation of the developmental changes of CYT activity in late G. Alveolar type II cells from 19 and 21 day G fetal rats were grown to confluence in media containing 10% carbon-stripped FCS and incubated for 48h in varying concentrations of T_3 or Dex with and without fibroblast conditioned media (source of FPF). Enzyme activity was assayed by the incorporation of ^{14}C-Me-phosphocholine into CDP choline. CYT activity from 19D cells increases from 30-130% with 0.55-5.5 nM T_3 and 300% with 5.5 nM Dex. Fibroblast conditioned media (FCM) alone increased activity 190% and combined with T_3 5.5 nM increased activity 270%. Enzyme from 21D cells was only minimally responsive to T_3 alone and increased 30-45% with 0.55-5.5 nM Dex. In control 19D cells 65% activity was located in cytosol and 35% in microsomes. This ratio was unchanged with T_3 simulation alone. FCM and Dex preferentially increased cytosol activity (80-86% total). Dex and FPF stimulate CYT activity and T_3 acts synergistically with FPF. These interactions may be responsible for changes in CYT during late G.

= 328 ALPHA ADRENERGIC RECEPTOR SUBTYPES IN THE CEREBRAL CIRCULATION OF NEWBORN PIGLETS. L. Craig Wagerle and Maria Delivoria-Papadopoulos. Univ. of PA. School of Medicine, Dept. of Physiology, Phila., PA

Previous studies show sympathetic nerve stimulation decreases cerebral blood flow (CBF) in newborn piglets. Effects of α_1-antagonist (prazosin) and α_2-antagonist (yohimbine) on cerebral sympathetic vasoconstriction were studied. In 21 newborn piglets ventilated ($PaCO_2$=35 mmHg) with 30% N_2O, both cervical sympathetic trunks were isolated and CBF was measured (microspheres) during (1) baseline (no stimulation), and (2) electrical stimulation of the right sympathetic trunk (15 Hz, 15 v, and 3 msec). A third CBF measurement was made during sympathetic stimulation following either 0.5 mg/kg, I.V. prazosin (n=11), or yohimbine, 0.5 (n=6) or 1.0 (n=4) mg/kg I.V. Sympathetic nerve stimulation decreased blood flow to ipsilateral cerebrum by -15 ± 2% in comparison to unstimulated side (58 ± 4 and 69 ± 5 ml/min/100g, respectively). Flow to the hippocampus, choroid plexus, and masseter muscle was decreased by -10 ± 2, -51 ± 5, and -94 ± 5%, respectively. Prazosin inhibited sympathetic vasoconstriction by ∿ 50%, where flow to the ipsilateral cerebrum, hippocampus, choroid plexus, and masseter muscle was decreased by -8 ± 2, -4 ± 3, -7 ± 7, and -53 ± 8%, respectively. Yohimbine had no effect on sympathetic vasoconstriction at 0.5 mg/kg; however, at 1.0 mg/kg, CBF increased from 85 ± 5 to 184 ± 44 ml/min/100g. Sympathetic stimulation decreased flow by -23 ± 7, -18 ± 4, -47 ± 9, and -93 ± 3% in the respective regions. The data indicate that sympathetic nerves reduce CBF via α_1-adrenoceptor vasoconstriction. In contrast to adult pigs, where α_1-adrenergic receptors in cerebral arteries have not been demonstrated, it appears that, in the newborn, α-$_1$ receptors mediate cerebrovascular vasoconstriction.

= 329 CHRONIC HYPERGLYCEMIA AND HYPERINSULINEMIA REDUCE cAMP DEPENDENT PROTEIN KINASE ACTIVITY IN FETAL LAMB LUNG. David Warburton. Univ. of Southern California, Childrens Hospital of Los Angeles, Neonatal and Pulmonary Division, Dept. of Pediatrics, Los Angeles.

Chronic hyperglycemia and hyperinsulinemia have recently been shown to increase glycogen and decrease alveolar surfactant in fetal lamb lung. Since cAMP regulates lung energy metabolism and surfactant release, we postulated that chronic hyperglycemia and hyperinsulinemia would alter cAMP metabolism of fetal lamb lung. Infusion of glucose into 6 chronically catheterised fetal lambs between 112 and 143d. gestation increased serum glucose 2 fold and serum insulin 3 fold compared to twin controls. Adenylate cyclase activity increased 105% in the glucose treated v. controls, 6.71±0.16 v. 3.27±0.18 pmoles cAMP/min/mg lung, ($P < 0.001$) and lung cAMP content increased 111% in the glucose-treated v. controls, 0.76±0.19 v. 0.36±0.02 pmole/mg lung, ($P < 0.001$). However, lung cAMP dependent protein kinase (PK) activity decreased 40% in the glucose-treated v. controls, 135.5±5.6 v. 225.5±4.1 pmole/min/mg supernatant protein ($P < 0.001$), while the ratio of non-cAMP PK to cAMP PK was similar ($P > 0.05$) in both groups (0.34±0.02 v. 0.38±0.02). These data show that chronic hyperglycemia and hyperinsulinemia influence energy metabolism in fetal lamb lung. Accumulation of cAMP may be attributed to increased cAMP production by adenylate cyclase. But decreased cAMP PK activity may be an important control point in the inhibition of fetal lung maturation by chronic hyperglycemia and hyperinsulinemia.

† 330 EGF DECREASES LUNG GLYCOGEN AND STIMULATES LUNG PHOSPHATIDYLCHOLINE SYNTHESIS IN FETAL RAT. Joseph B. Warshaw, Thomas S. Jamison and Janice F. Sissom. The University of Texas Health Science Center at Dallas, Department of Pediatrics, Dallas, TX.

We previously demonstrated a relationship between the decrease in the glycogen content of developing rat lung and the appearance of surfactant phospholipids. In the present study we utilize a fetal injection technique to examine the influence of EGF on lung maturation. Our laboratory and others have shown specific binding of EGF to membranes prepared from developing lung. Pregnant rats of 17 to 19 day gestation had uteri exposed by a small lateral suprapubic incision. EGF (10-100 ng) was injected through the uterine wall directly into the amniotic sac of the exposed fetuses. PBS injected fetuses on the contralateral side of the cervex served as controls. Fetal lungs were removed 48 hours later for measurement of glycogen content of lung and for determination of ^{3}H-choline incorporation into phosphatidylcholine. EGF stimulated the incorporation of ^{3}H-choline into phosphatidylcholine by lung slices prepared from fetal rats exposed to intraamniotic EGF from day 17 through 21. A maximal stimulation of 118% was observed in fetuses injected on day 18 and sacrificed on day 20. Lung glycogen content was reduced by 54% in the EGF group. These data provide further support for a relationship between carbohydrate and phospholipid synthesis during lung maturation and provide direct evidence for an EGF influence on fetal lung maturation.