283 PROSTACYCLIN (PGI_2) AND HYDROCORTISONE (HC) MEDIATES BRUSH BORDER PROTEIN (BBMP) SYNTHESIS. Josef Neu and Wendell Crin (Spon. by C.L.Kien) Medical College of Wisconsin, Department of Pediatrics, Milwaukee Children's Hospital, Milwaukee, WI.

Glucocorticoids are known mediators of small intestinal maturation. In this study, the effects of exogenously administered HC and PGI_2 on BBMP and DNA synthesis along with other indices of maturation were evaluated. Suckling rats were administered PGI_2, HC or saline between days 10 to 13 of life and sacrificed on day 14. DNA and BBMP synthesis were analyzed using in vivo ^{3}H-thymidine and ^{3}H-leucine incorporation into DNA and BBMP in separate groups of animals. DNA synthesis was not significantly altered by PGI_2 or HC. The ratio of ^{3}H-leucine incorporation into BBMP to total intestinal homogenate protein was elevated in both PGI_2 and HC administered animals as follows:

Control	PGI_2	HC
1.67 ± 0.13	2.41 ± 0.76*	2.08 ± .028*
$\bar{x}$ ± S.D.	*p<0.025	n = 6

RNA and RNA to DNA ratios were elevated in animals administered PGI_2 or HC. Intestinal lactase was elevated in PGI_2 administered animals, whereas, sucrase, maltase and enterocyte turnover time was considerably less in PGI_2 than in HC administered littermates. These data suggests a preferential stimulation of brush border to total intestinal protein synthesis. A specific effect of PGI_2 on lactase and HC on sucrase is also suggested.

284 INSULIN RECEPTOR (IR) DEVELOPMENT IN NORMAL (N) AND DIABETIC (D) PREGNANCIES: DOES INSULIN (I) UP REGULATE THE RECEPTOR? Naomi D Neufeld, L Corbo, S Brunnerman, Cedars-Sinai Medical Center-UCLA School of Medicine, Department of Pediatrics, Los Angeles, California.

Offspring of D pregnancies have increased concentrations of IR on plasma membranes associated with differences in membrane lipid composition and physical structure. We have previously suggested that increased [I] occurring in human and animal offspring of D pregnancies caused up-regulation of IR. Since ambient [I] is the difference between its secretion by the pancreas and its degradation, we have studied these factors in rat fetuses from both N and D pregnancies. Twenty nine pregnant rats of timed gestation received either saline (N, n=13) or streptozotocin 60 mg/kg (D, n=16) on d 7 of pregnancy, and were sacrificed on d 21. Pooled fetal serum I levels were comparable (47 ± 8 vs. 34 ± 2μ U/ml), whereas blood glucose levels were markedly elevated in offspring of D, (39 ± 13 vs. 321 ± 63 mg/dl, p < 0.001). Tracer I binding was also elevated on liver plasma membranes from D (5.3 ± 1.0 vs. 2.1 ± 0.3%/100μg protein, p <0.02) due to increased high and low affinity receptors. I content of fetal pancreatic islets, quantitated by immunoperoxidase staining, was significantly lower in D offspring. I degradation was significantly higher in fetal liver homogenates from D offspring compared to N, (34 ± 1.7 vs. 26 ± 1.2% degradated/30 min/100μg protein, p<0.001).

Conclusions: Elevation in IR concentrations on fetal liver membranes in D pregnancies appears to occur independently of I presented to the liver. The data support the concept that I degradation and IR regulation occur by separate pathways. A causal relationship between fetal hyperglycemia and/or hyperlipidemia and alterations of membrane structure increasing IR exposure cannot be excluded.

285 ENDOTOXIN BINDING TO EPITHELIAL CELLS OF THE SMALL INTESTINE. Anna P. Newman, Kam Y. Pang, John N. Udall, Marvin L. Dixon, W. Allan Walker, Harvard Medical School, MGH/CHMC Dept. of Pediatrics, Boston, MA.

Previous studies have suggested that immaturity of the gastrointestinal barrier of young animals may lead to increased uptake of potentially toxic macromolecules. To further extend these observations, we have studied the binding of endotoxin (E. Coli 026: B6) to immature (crypt) and mature (villus) small intestinal epithelial cells of 2 week old and adult rats. Endotoxin was radiolabeled with ^{51}Cr, and its concentration measured using a hexose assay. Cells were obtained from the small intestine in a gradient from villus to crypt using the modified method of Weiser. Binding was studied by incubating endotoxin with the cells. The endotoxin binding was found to be concentration-dependent and saturable, suggesting receptor, not non-specific, binding. Endotoxin was incubated with immature crypt cells and mature villus cells of 2 week old rats at concentrations ranging from 5-100 μg of endotoxin/ml and at a cell protein concentration of .2 mg/ml. Approximately two times as much endotoxin bound to crypt as to villus cells. Preliminary binding experiments with epithelial cells from adult rats also show differences in endotoxin binding to crypt versus villus cells. These studies suggest that the surface of the immature cell has different binding properties for this potential toxin. The increased binding may place the immature host at a greater risk for enteric infection.

286 LAMELLAR BODY CONTENT OF FETAL RABBIT LUNG-EVIDENCE OF A SEX DIFFERENCE IN FETAL SURFACTANT SYNTHESIS. Heber C. Nielsen, Cynthia Gebhardt, (spon. by Joseph B. Warshaw), Southwestern Med. Sch., Dept. Peds., Dallas, Tx.

It is unknown if the sex difference in fetal lung surfactant is due to synthesis or secretion. To address this we studied the lamellar body(LB) content of fetal rabbit lung at 27-30d of gestation. LBs were isolated from sex-specific lung homogenates by centrifugation on discontinuous sucrose density gradients (Longmuir et al, Arch Biochem Biophys 212:491,1981). Phosphatidylcholine(PC), saturated PC(SPC), sphingomyelin, phosphatidyl-glycerol,-inositol,-serine, and -ethanolamine were separated by one- and two-dimension thin layer chromotography and measured by phosphorus assay. Marked increases with gestation were noted, reflecting accumulation of LBs with development. At 27 and 28 days females had more total LB phospholipid/gm lung wgt and 10-25% more of each component, for example (nanomoles/gm lung wgt, mean±SE):

	PC		SPC	
	female	male	female	male
27 day	68.7±9.0	59.9±6.9	28.7±5.9	22.9±2.5
28 day	291.1±31.8	190.7±25.6	79.6±11.3	69.8±8.9

Interassay variability in LB recovery affected statistical comparison of means, but the likelihood of a female advantage in all phospholipids at 27 and 28 days was significant (p=.015, binomial sign test). At days 29 and 30 no trend in sex difference was manifest. We conclude that sex differences in fetal lung surfactant are due at least in part to differences in surfactant synthesis.

† **287** POSTNATAL MATURATION OF α-ADRENERGIC MECHANISM IN THE NEWBORN RAT LIVER A. Noguchi, P. Jett, J. Bendeck, (Spons. Wm. J. Keenan), Dept. of Pediatrics, Saint Louis University, School of Medicine.

Epinephrine (Epi) stimulated liver glycogenolysis is mediated by cAMP independent α-mechanism in the adult rat as opposed to cAMP dependent β-mechanism in perinatal rat. However the mechanism and timing of β→α switchover is unclear. Alpha receptor stimulation increases plasma membrane phosphatidylinositol (PI) turnover which subsequently leads to glycogen phosphorylase (GP) stimulation. We examined ontogeny of adrenergic stimulated cAMP, PI phosphorylation and GP in newborn hepatocytes. Epi stimulated cAMP was 7 times higher (P<0.01) but PI phosphorylation was 54% lower (P<0.01) at 5 day than adult. GP stimulation by α and β mechanisms in Control and PTU treated (17d gestation on) rats were:

		5d	15d	28d	Adult
Control	Epi + phe (β)	206±11	181±13	172±12	109±10 §
	Epi + Alp (α)	93± 4	95± 9	160± 9*	181± 9Δ
PTU	Epi + Phe (β)	238±50	195±10	160± 7	-------
	Epi + Alp (α)	101±10	99± 6	121± 9	-------

GP expressed as hormone stimulation/basal (M±SE%). n=6-8 each. Phe:phentolamine, Alp; alprenolol. *:Control>PTU P<0.03. §:Adult <5, 15, 28 day P<0.01. Δ:Adult>5, 15 d P<0.01. We conclude that Epi stimulated glycogenolysis is totally mediated by cAMP-β mechanism before 15 days, 2) ontogeny of α but not β mechanism is regulated by thyroid hormone during postnatal period. We speculate that the low but present PI phosphorylation despite total lack of α-mediated GP before 15 days indicates receptor as well as post-PI site are involved in the maturational process of α-adrenergic mechanism in the rat liver.

●**288** AUTOIMMUNE SYMPATHECTOMY IN FETAL RABBITS. J.F. Padbury, D.H. Polk, J.P. Newnham, R.W. Lam, Depts. of Pediatrics and Obstetrics & Gynecology, Harbor-UCLA Medical Center, UCLA School of Medicine, Torrance, CA

We previously reported that 27 day (d) rabbit fetuses born to does immunized against nerve growth factor (NGF) demonstrate extensive depletion of tissue catecholamines (CAT). Here we report results of studies with this model at 31 d gestation (term) and the effects of autoimmune sympathectomy on beta adrenergic receptor development. Virgin 12 wk old female rabbits were immunized with 100 μg 2.5S NGF and boosted monthly for 12 wks. Serum anti-NGF titers were determined by radioimmunoassay. Animals were then date bred and sacrificed at 31 d. Tissue CAT were determined by a sensitive, specific radioenzymatic assay. BAR were determined in pooled lungs from control or immunized litters by radioligand binding assay using dihydroalprenolol (DHA). Lung, heart, adrenal, paraaortic gland and brown adipose tissue CAT all were extensively decreased in animals with high anti-NGF titers (p<.001). Lower titers, which cause denervation at 27 d were not effective at 31 d. Lung BAR increased from 108 to 140 fmole bound DHA/mg protein following successful denervation (p<.05). Organ weight, carcass weight, survival and duration of gestation were unaffected by the immunization. Conclusions: 1) Organ sympathetic innervation in the fetal rabbit is dependent on NGF; 2) the extent of denervation in the autoimmune sympathectomy model is dependent upon NGF antibody titer; 3) fetal rabbit lung BAR are increased following denervation. Speculation: With advancing developmental age, the role of NGF in sympathetic innervation becomes less critical.