560 EFFECT OF RICINUS COMMUNIS TOXIN (RICIN) ON RABBIT INTESTINAL EPITHELIUM: A MODEL OF PROTEIN-INDUCED MUCOSAL DAMAGE. J.E. Grunow, A. Larrosa, T. Pysher, J.R. Alvarez, R. Torres-Pinedo. Univ. of Okla. College of Medicine, Departments of Pediatrics and Pathology, Oklahoma City.

Ricin inhibits protein synthesis in eukaryotic cells following binding to galactose membrane receptors and cytoplasmic internalization of its A subunit. Similar but less well defined mechanisms are probably involved in small bowel toxicity by certain food and bacterial proteins. We have therefore used ricin to develop an in vitro model of protein-induced small bowel epithelial damage using organ culture methodology. Rabbit jejunal mucosal explants were exposed (30 min, 25°) to varying doses of ricin (0.1-50 µg) and then cultured in ricin-free medium for 2 to 24 hours at 37°. Inhibition of protein synthesis (^{14}C-leucine incorporation) occurred as a function of ricin dose and culture time. A t_{50} plot ($1/\sqrt{[ricin]}/t_{50}$) revealed a lag time of about 30 minutes for infinite ricin dose. Light and electron microscopy showed a progression of damage in epithelium which correlated to ricin dose and level of inhibition of protein synthesis. The effect of ricin was blocked by lactose and lactulose (100 mM) added during the ricin exposure period. The dose and time relationships of the effect of ricin on intestinal epithelium in culture suggest membrane responses and down regulation processes identical to those of endocytotic cells. This approach is therefore useful for investigations of the membrane and cellular mechanisms associated with protein-induced enterocyte toxicity.

561 NECROTIZING ENTEROCOLITIS (NEC) IN THE VLBW: AN ENCOURAGING FOLLOW-UP REPORT. M.Hack, D.Gordon, P.Jones, A.Fanaroff, Dept Ped, CWRU, Cleveland

To evaluate the long term growth and development of VLBW(<1.5 Kg)infants with NEC, we prospectively followed all those surviving NEC from 1975 to 1978. Out of 551 VLBW admissions, 48(5.5%) developed NEC confirmed radiologically or at surgery. 23(48%)survived. 2 were lost to follow-up and 1 died after discharge. The remaining 20 infants(mean BW 1.2Kg,range.8-1.4Kg,GA 30 wks, range 27-32wks)were followed to a mean of 28 mos and compared to 330 surviving infants without NEC(non-NEC) of similar birth wt.

The course of NEC included perforation requiring surgery in 20, of whom 11 required an ileostomy. Only 4/20 were SGA(<3%) at birth but by discharge 17/20(85%)weighed less than the 3% for age. During infancy 16/20 were rehospitalized. 12 for reasons related to NEC. 6 infants had failure to thrive due to short bowel syndrome or secretory diarrhea which resolved with parenteral nutrition and ileostomy closure.

		Follow-up Growth and Development						
		DQ or IQ*	Neur. Abn.		Wt.<3%	H.C.<3%	
	n	(mean DS)	n	(%)	(%)	(%)	
NEC	20	90.3 ± 15	1	(5%)*	(20%)*	(20%)*	
Non-NEC	330	93.7 ± 17	35	(11%)*	(11%)*	(10%)*	*NS

*Bayley or Stanford Binet

Despite the high mortality and severe morbidity during infancy, most survivors of NEC subsequently progress well and function at the same level as infants without NEC.

562 EVOLUTION OF ANORECTAL PHYSIOLOGY IN PATIENTS TREATED FOR FECAL SOILING (FS). Roxanne Hecht, Benny Kerzner, H. Juhling McClung, Thomas Frye. Ohio St. Univ. Coll. of Med., Cols. Children's Hosp., Dept. Peds., Cols., OH.

Physiological explanations for recurrent FS were sought in a longitudinal study of rectal contour, elasticity (E), sensation, and internal anal sphincter (IAS) action in 26 patients with chronic FS. Manometric tracings from the IAS and rectal ampulla were recorded prior to treatment, after initial rectal evacuation, and after 6 months on a standard treatment regimen which included oral mineral oil, enemas and positive reinforcement of bowel habit. Data were compared to those of 10 age-matched controls. Barium enemas were obtained before and after the study. 9 patients became totally asymptomatic, 13 improved substantially, and 4 who were non-compliant remained symptomatic. The magnitude and duration of reflex IAS relaxation were normal but decreased transiently (p<.05), after initial evacuation. The volume eliciting IAS relaxation decreased from 18±2 to 13±3 (p<.04) over 6 months. Megacolon was apparent in 11 and resolved in 9. E was consistently low, improved with treatment (p<.05), but never reached control values. A striking deficit in the appreciation of rectal volumes (25±3 vs. 9±2 p<.01) and tolerance for distending volumes (180±15 vs. 85±13 p<.001) persisted for 6 months in the FS patients including the 9 asymptomatic and the 15 with normal colon size. Conclusion: After 6 months of treatment, despite improvements in symptoms and E, failure to perceive rectal distention at rectal volumes that induce IAS relaxation leaves FS patients vulnerable to recurrence of symptoms. This is true even in the absence of acquired megacolon.

563 ROLE OF MILK-BORNE FACTORS IN INTESTINAL DEVELOPMENT. Susan J. Henning, University of Houston, Department of Biology, Houston, Tx.

In recent years, milk from both humans and experimental animals has been shown to contain a variety of hormones and growth factors. The aim of this study was to determine whether these appear in the milk at a particular stage of lactation and cause developmental changes in the intestine. The approach was to take litters of rat pups born one week apart and exchange their dams when the older pups were at postnatal day 13 and the younger ones were at day 6. Thus, 13 day-old pups were given to dams that were 6 days postpartum (13→6) and vice versa (6→13). The rationale was that if a factor appears in the milk at the end of the second week postpartum and acts as a cue for the enzymic changes in the small intestine that are known to occur in the third postnatal week, then such changes should be delayed in "13→6" pups and accelerated in "6→13" pups. Using jejunal sucrase as a marker enzyme there was no difference between the two experimental groups at ages 17 and 19 days. However, by 21 days of age, sucrase activities of "6→13" pups were significantly higher than those of "13→6" pups. Analysis of stomach contents showed that weaning was complete by day 21 in the "6→13" pups but not in the "13→6" pups. It is concluded that the lactational stage of the dam plays no role in the initiation of sucrase development and affects the later activity of the enzyme only as a result of changes in the timing of weaning. Thus, the possibility that milk-borne factors cue ontogenic changes in the intestine has not been substantiated. (This work was supported by NIH grant number HD 14094.)

564 DISORDERED UPPER GASTROINTESTINAL MOTILITY IN INFANTS WITH GASTROESOPHAGEAL REFLUX (GER). C.Hillemeier, J. Gryboski, B.Grill, R.McCallum, R.Lange. Yale Univ., Yale-New Haven Hospital, Dept. of Pediatrics, New Haven, CT.

Thirty four infants were evaluated for their symptoms of GER with esophageal manometrics, prolonged pH probe studies and gastric emptying. Manometrics examined the lower esophageal sphincter and the body of the esophagus had a minimum of 10 peristaltic sequences examined. The pH probe studies were most valuable in the 2 hours after ingestion of 4 oz of apple juice. Gastric emptying was performed with a gamma counter and computer imaging after ingestion of 4 oz of ^{99m}Tc labeled cow's milk formula. Group A consists of 15 infants with RT's of <30% in the 2 hours post prandial and Group B consists of 19 infants with RT's of >30% in this period. (RT=reflux time with esophageal pH <4).

Group	No.	% RT 1 hr	%RT 2 hr	$\bar{x}$ longest reflux	#with FTT	#with pulm dx	$\bar{x}$GE at 1 hr
A	15	21.8	11.7	5.2 min	1	0	41.9%
B	19	53.5	36.5	16.5 min	11	7	20.1%

Group	Amplitude of waves Distal 1/3	Mid 1/3	#pts >70% nl peristalsis	% nl peristaltic waves	LESP mmHg
A	50.2 mmHg	60.6 mmHg	2/15	85.4%	22.8
B	28.7 mmHg	49.3 mmHg	13/19	54%	19.2

Infants with severe reflux as defined by pH probe criteria have disordered esophageal peristalsis,↓ amplitude of peristalsis in the distal esophagus and delayed gastric emptying of a cow's milk formula. We conclude that infants with severe GER have a diffuse disorder of upper gastrointestinal motility.

565 CONTRACTILITY OF THE DEVELOPING LOWER ESOPHAGEAL SPHINCTER IN THE KITTEN. C.Hillemeier, J.Gryboski, R. McCallum, P.Biancani. Yale Univ. School of Med. New Haven,CT., Dept. of Pediatrics.

The lower esophageal sphincters (LES) of kittens aged 3 days, 1 week, 3 weeks, and 6 weeks were identified by a probe with a perfused side opening adjacent to a metal plug, and basal LESP was measured. A suture was placed under fluoroscopy at the LES. 1.75 mm wide rings were cut transversely from the LES region and studied in vitro. Force/length curves were obtained in standard tyrode solution, in tyrode with 140 mM KCL, and in calcium-free tyrode with 5 mM EDTA to determine basal, total and passive forces respectively. Active force was obtained as the difference between total and passive force. Circular smooth muscle thickness was determined in such age group from frozen sections. The forces generated were then normalized for the amount of muscle able to generate them to give stress or contractility of the muscle.

age	LESP mm Hg	MAF gm	t mm	MAS gm/cm^2
3 days	9.5	2.84	0.277	290
1 week	12.5	3.5	0.296	520
3 weeks	14.0	5.37	0.347	653
6 weeks	21.5	8.33	0.472	294

LESP=in vivo LES pressure
MAF=maximum active force
t=circular muscle thickness
MAS=maximum active stress

In the kitten, in vivo LESP, forces generated by LES rings in vitro, and thickness of the smooth muscle all increase throughout life. Contractility of the LES rises to a peak at 3 weeks and then declines. This increased contractility may be important in determining sphincter competence during infancy.