

## 275 DEVELOPMENT OF SMALL BOWEL MOTILITY IN BEAGLE PUPPIES.

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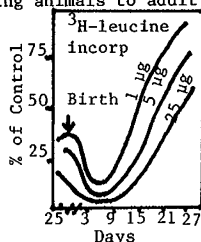
To investigate the neonatal development of upper small bowel (SB) peristalsis and the effect of pentagastrin (PG) on motility, we monitored duodenal intraluminal pressure manometrically in 11 beagle puppies from birth until weaning at 5 wk. The response rate of the system employed was 150 mm Hg/sec. Electrodes were implanted on the SB serosal surface for subsequent monitoring of myoelectric activity during the first 2 mo. in 3 add'l puppies. During the first 3 wk there was an increase in duodenal contraction rate immediately after a liquid meal from  $11 \pm 0.4/\text{min}$  to  $16 \pm 1/\text{min}$  ( $p < 0.001$ ) followed by a slight decrease during weaning. Peak duodenal pressure increased from 17 to 38 mm Hg ( $p < 0.002$ ), and subsequently decreased to 25 mm Hg with weaning. The duration of each contraction shortened during the first 3 wk from 3.4 to 2.4 sec ( $p < 0.001$ ). Myoelectric monitoring revealed a gradual increase in slow wave activity from 14 to 20 cycles/min in both fasting and fed states, corresponding with the increased contractions observed in the manometric studies. These developmental changes are similar to those which occur in the beagle lower esophageal sphincter (LES) and stomach during suckling and weaning. However, in contrast to the lack of sensitivity to PG by the beagle LES and stomach during the first week, SB contractions were inhibited on day 1 with  $0.03\text{--}8 \text{ ug/kg PG s.c.}$  We speculate that the differential PG sensitivity of LES, stomach, and SB during the first week of life in the beagle is due to differential gastrin receptor number and/or affinity.

## 276 POSSIBLE MECHANISM FOR NON-REJECTION OF THE DEVELOPING MAMMALIAN EMBRYO: THE ROLES OF UTEROGLOBULIN AND TRANSGLUTAMINASE.

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The suppression of embryonic immunogenicity by the interaction of rabbit blastocysts with uteroglobin (UG) (a pregnancy specific protein) and transglutaminase (TG) (Factor XIIIa) has been investigated *in vitro*. When incubated with maternal lymphocytes, washed, mitomycin-C inactivated blastomeres stimulated lymphocyte  $^3\text{H}$ -thymidine incorporation ( $1.23 \times 10^5 \text{ cpm} / 2 \times 10^6 \text{ lymphocytes}$ ), suggesting recognition of embryonic antigens. When these blastomeres are pretreated with pregnant uterine flushings (PUF),  $^3\text{H}$ -thymidine incorporation was dramatically reduced ( $1.0 \times 10^4 \text{ cpm} / 2 \times 10^6 \text{ lymphocytes}$ ). Pretreatment of blastomeres with UG alone, isolated to homogeneity from PUF, or in combination with TG caused significant dose dependent suppression of thymidine incorporation by the lymphocytes. Suppression to  $< 100 \text{ cpm} / 2 \times 10^6 \text{ cells}$  was achieved by 250  $\text{ug/ml}$  of UG alone; with added TG ( $3 \text{ u/ml}$ ) only  $1.0 \text{ ug/ml}$  of UG caused total suppression. Suppression was blocked by incubation of UG with its antiserum, or with TG plus anti-TG, prior to blastomere pretreatment. Inhibition of exogenous transglutaminase by neopentyl chloroethyl nitrosourea also greatly reduced the inhibition of thymidine incorporation by UG. The data clearly indicate that UG and TG suppress blastomere immunogenicity, perhaps by a cross-linking mechanism between UG and blastomere antigens. We suggest that uteroglobin in conjunction with transglutaminase may inhibit immunorejection of embryos at about the time of implantation.

## 277 CHANGES IN SENSITIVITY TO RICINUS COMMUNIS TOXIN (RICIN) OF RABBIT JEJUNUM DURING THE SUCKLING PERIOD.

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Pinocytosis is the predominant route of penetration of macromolecules across the small bowel epithelium of newborn animals. We have developed a model system to study this process on jejunal mucosal explants using ricin. Ricin is a potent toxin which inhibits protein synthesis by a mechanism involving binding to galactose surface residues, internalization of its enzymatic component and inactivation of the 60 S ribosomal subunit. Protein synthesis ( $^3\text{H}$ -leucine incorporation) in jejunal explants from fetal, suckling and adult rabbits was measured in organ culture following an initial exposure (30 min,  $25^\circ$ ) to ricin ( $1\text{--}25 \text{ ug}$ ). The rate of inhibition of protein synthesis was age dependent (Fig). High in the fetus, it increased further to a maximum at day 6 postnatally, then decreased rapidly in suckling animals to adult levels at weaning. The high sensitivity to ricin during the colostral period may be related to the following factors currently under study: 1) colostral-milk components stimulating a high rate of endocytosis, 2) transitional maturation changes in membrane properties and 3) changes in sensitivity at the target ribosomal site. The model presented is useful to study modifiers and events influencing mucosal permeability in the developing small intestine.



## 278 THE MATERNAL AND FETAL CATECHOLAMINE (CAT) RESPONSE TO HYPOXIA IN SHEEP.

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The plasma CAT responses to hypoxia were investigated in six pregnant ewes at 133-140 days gestation. Hypoxia was induced by exposure of the ewe to 6-9%  $\text{O}_2$  -3%  $\text{CO}_2/\text{nitrogen}$  for 30 min. Maternal and fetal arterial blood samples were obtained at 5 min intervals before and during the hypoxic stress for measurement of epinephrine (E), norepinephrine (NE) and blood gases. Analyses of maternal CAT responses revealed a significant elevation of mean NE from 191 to 685  $\text{pg/ml}$  ( $p < 0.05$ ) and E from 129 to 311  $\text{pg/ml}$  ( $p < 0.05$ ). The levels of plasma NE correlated with duration of hypoxia ( $r=0.93$ ,  $p < 0.05$ ) based on mean NE values at 10, 20 and 30 min). Fetal CAT responses correlated ( $r=0.54$ ,  $p < 0.05$ ) with severity of maternal hypoxia as follows:

| %Mat $\text{paO}_2$ | Fet. E  | Fet. NE |
|---------------------|---------|---------|
| 100 (C)             | 26      | 179     |
| >51                 | 43      | 265     |
| 40-50               | 7,332*  | 2,101*  |
| 30-40               | 30,333* | 33,190* |

% Mat  $\text{paO}_2$  =  $\text{paO}_2$  during hypoxia/ $\text{paO}_2$  control X 100.

Conclusions: 1) Significant maternal E and NE secretion occurs with hypoxia. 2) The levels of maternal NE correlate linearly with time of hypoxic exposure. 3) Fetal E and NE secretion increase with maternal hypoxia. 4) There is a direct correlation between fetal E or NE levels and severity of maternal hypoxia.

## 279 SYMPATHO-ADRENAL RESPONSE TO UMBILICAL CORD CUTTING (UCC).

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Catecholamine (CAT) release has been observed in near term fetal sheep in response to a variety of stimuli including hypoxia, maternal hypovolemia or exercise and parturition. In earlier studies of fetal sympatho-adrenal activity in response to parturition it has not been possible to differentiate the effects of labor, intrapartum asphyxia, delivery and UCC on CAT release. We have used the acutely exteriorized near term fetal lamb to study the effects of delivery and UCC on CAT release. Results show that delivery alone evokes an elevation of newborn plasma CAT which is brief and followed by return to basal values by 30 min. Subsequent UCC evokes a marked release of norepinephrine (NE) and epinephrine (E) (peak plasma levels 32,000  $\text{pg/ml}$  and 35,000  $\text{pg/ml}$ ), maximal at 5 min. and persisting over the 4 hour study period. There is a concomitant rise in plasma free fatty acids (FFA) and reversal of post-delivery hypothermia. The magnitude of the CAT surge is inversely proportional to the degree of acidosis; a blunted FFA response and slower correction of hypothermia were observed in more acidotic animals despite higher CAT levels. Conclusions: 1) UCC is an important stimulus for fetal CAT release. 2) UCC stimulated neurosympathetic activity is of sufficient magnitude to influence many metabolic and cardiovascular functions. 3) Acidosis stimulates CAT release in the near term ovine fetus. 4) Acidosis obviates neonatal chemical thermogenesis.

## 280 THE EFFECTS OF POSTNATAL AGE ON THE WHOLE BODY PROTEIN METABOLISM AND SKELETAL MUSCLE PROTEIN BREAKDOWN OF PREMATURE INFANTS.

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Rates of whole body nitrogen flux (Q), protein synthesis (S), and breakdown (C), and skeletal muscle protein breakdown were measured in 24 growing premature infants. The infants were each studied twice. The first study (A) was conducted once the infants were clinically stable and ingesting an oral intake of at least 120 kcal/kg/d. The second study (B) was started 2 weeks later.

There was a marked increase in rates of skeletal muscle protein breakdown, from  $0.93 \pm 0.21 \text{ g}$  to  $2.9 \pm 0.26 \text{ g/kg/d}$  ( $p < 0.01$ ). During Study A, very low birth weight ( $< 1500 \text{ g}$ ) infants had significantly higher rates than larger infants ( $1.19$  cf  $0.66 \text{ g/kg/d}$ ); however, these differences were no longer present during Study B; both groups showing a marked increase in muscle breakdown rates ( $2.95$  cf  $3.03 \text{ g/kg/d}$ ). There were no differences in Q, S or C with increasing postnatal age. It appears that skeletal muscle protein metabolism increases postnatally from about 8% to 24% of whole body protein turnover with a concomitant decrease in other tissues. Skeletal muscle has been estimated to constitute about 22% of total body protein in infants. Thus, these changes may reflect an increase in skeletal muscle protein turnover from a low rate to one that is in proportion to skeletal muscle's contribution to whole body protein.