**† 624** MECONIUM FROM INFANTS WITH CYSTIC FIBROSIS (CF) CONTAINS IMMUNOREATIVE TRYPSINOGEN. Monica C. Hsieh, Helen K. Berry (Spon. by Clark D. West). Children's Hospital Medical Center, Cincinnati, Ohio.

To understand the defect that leads to accumulation of proteins in CF meconium we measured immunoreative trypsinogen (IRT) by radioimmunoassay and trypsin catalytic activity (CA) by fluorimetric method. IRT concentration was normal in CF meconium based on total protein content, but was elevated based on wet weight, as was total protein and albumin. Trypsin CA was reduced in CF meconium compared to normal meconium:

| | CF n = 22 | Normal n = 26 | Probability |
|---|---|---|---|
| IRT[a] | 7.1 ± 4.2 | 3.1 ± 2.7 | <.001 |
| IRT[b] | 38 ± 24 | 54 ± 44 | n.s. |
| Total prot.[c] | 205 ± 81 | 57 ± 12 | <.001 |
| Albumin[d] | 72 ± 40 | <10 | Not tested |
| Trypsin CA[e] | .25 ± .27 | 1.03 ± .99 | <.001 |
| Trypsin CA | 42 ± 48 | 357 ± 196 | <.001 |

[a] µg/g meconium (wet weight); [b] µg/g protein; [c] mg/g meconium; [d] µmol substrate hydrolyzed/g meconium; [e] µmole/mg IRT

Trypsin inhibitory activity. measured by incubating porcine trypsin with meconium was: CF, 33 ± 27; normal, 1 ± 3 µg porcine trypsin inactivated/g meconium. Trypsinogen, an inactive precursor of trypsin, is synthesized by pancreatic acinar cells and secreted into intestinal lumen. The results show this process is normal in infants with CF. Presence of trypsin inhibitor(s) rather than absence of IRT accounts for accumulation of proteins in CF meconium.

**● 627** NEONATAL CHOLESTASIS: IDENTIFICATION OF A METABOLIC ERROR IN BILE ACID SYNTHESIS Norman B. Javitt, Engeline Kok, Marcel Gut, Indra Rajagopalan and Kornelia Budai (Spon. by Joseph Dancis), Dept. of Pediatrics, NYU School of Medicine, NY and Worcester Found. for Experimental Biology, Shrewsbury, MA

The metabolism of 3β-hydroxy-chol-5-en-24-oic acid, (3β-chol) a naturally occurring monohydroxy bile acid known to induce cholestasis, was studied in a 6 yr old female with cholestasis since birth. Initial evaluation revealed a total serum bile acid of 229 µmole/l of which 10% was 3β-chol. Administration of 1.1µCi of (16,17,22,23)-$^{3}$H-3β-chol intravenously was followed by recovery of 50% in the urine within 72 hrs. Urinary bile acids were fractionated as their methyl esters by glycophase column chromatography following solvolysis and alkaline and enzymatic (β-glucuronidase) hydrolysis. In contrast to previous findings in the hamster and normal humans, less than 3% metabolism to chenodeoxycholic acid could be detected. The results indicate absence of a P-450 microsomal 7α-hydroxylase that normally produces 3β,7α-dihydroxy-chol-5-en-24-oic acid, an intermediate in the "Yamasaki" pathway for chenodeoxycholic acid synthesis (Kulkharni & Javitt, Steroids, 40:581, 1982). We postulate that accumulation of 3β-chol and ita monohydroxy derivatives is pathogenetic in inducing cholestasis.

**† 625** INTRAVENOUS AMINO ACIDS STIMULATE GASTRIC ACID SECRETION IN INFANTS. Paul E. Hyman, Susan L. Everett, (Spon. by Rosemary D. Leake) UCLA School of Medicine, Harbor-UCLA Medical Center, Department of Pediatrics, Torrance.

To determine the effect of an intravenous amino acid infusion on gastric acid secretion we measured acid secretion in 7 enterally fed chronically ill infants (age 3-7 mo, weight 2-6 kg) requiring intravenous supplements. Amino acids were omitted from intravenous solutions for 8 hr, and enteral feedings were omitted for 6 hr prior to studies on 2 consecutive days. On day 1 basal acid output (BAO) was 28±5 µmoles/kg·hr, and post-pentagastrin (6 µg/kg, s.c.) maximal acid output (MAO) was 99±20 µmoles/kg·hr. On day 2 BAO was determined and then acid output was measured for 4 hr following addition of amino acids (Aminosyn, Abbott) to the intravenous solution. The rate of amino acid infusion was 0.15 gm/kg·hr. Serum gastrin was measured by radioimmunoassay before and after amino acid infusion. All results were expressed as mean ± SEM.

| | Basal | 1hr | 2hr | 3hr | 4hr |
|---|---|---|---|---|---|
| Acid Output(µmoles/kg·hr) | 26±4 | 49±10 | 51±12 | 52±8* | 54±7** |
| Serum Gastrin (pg/ml) | 63±16 | --- | --- | --- | 93±21 |

*p<.025 **p<0.01 compared to BAO, using the paired t-test

Amino acid-stimulated acid output was significantly higher than BAO in the final 2 hr. The infusion of intravenous amino acids resulted in 1) an immediate and sustained increase in acid secretion 2) a 2-fold increase in acid secretion to 50% MAO, and 3) no significant change in serum gastrin concentration. We conclude that amino acids infused at a rate typical for parenteral nutrition stimulate gastric acid secretion in infants.

**628** RED BLOOD CELL MALONDIALDEHYDE (RBC-MDA) & PLASMA VITAMIN E (E) LEVELS IN LOW BIRTH WEIGHT (LBW) INFANTS L. Johnson, J.Cennamo, C. Dalin, F. Bowen. Univ. of Penn. Sch. of Med., Penna. Hosp.Depts. OB-GYN & Peds., Phila. Pa.

The RBC-MDA assay is an indirect estimate of antioxidant protection at the membrane level. Weekly E and RBC-MDA levels were run on 85 LBW infants (See table below). Infants received 25 to 50 IU of E qd when oral feeds were begun. Non-iron enriched formulas were used until retinal vasculature was mature. Multivitamins were added when parenteral alimentation (Vit E, 5 IU/500 ml)was stopped. Though 74% of those in the larger BW group had E levels ≥1mg/dl by age 2 weeks, 84% had excessively high RBC-MDA levels (>2 SD above the adult mean of 102 ± SD 35 nM/gHgb). Only 40% of the smaller infants had E levels ≥1mg/dl. Their spuriously lower % of abnormal RBC-MDA levels reflects a greater admixture of transfused adult RBC, not a state of improved E nutrition. We conclude that many LBW infants on oral E at the recommended dosage will remain E deficient, as defined by peroxidizability of membrane lipids.

| | At Age 0 - 1 Day | | | At Age 2 Weeks | | |
|---|---|---|---|---|---|---|
| | 1000g or less | 1001-1250g | 1251-1500g | 1000g or less | 1001-1250g | 1251-1500g |
| Vit E mg/dl | | | | | | |
| 0.9 | 100% | 93% | 100% | 60% | 54% | 21% |
| 1.0-2.0 | 0% | 7% | 0% | 40% | 38% | 74% |
| 2.1-3.0 | 0% | 0% | 0% | 0% | 8% | 5% |
| RBC-MDA | | | | | | |
| >172 nM/gHgb | 96% | 93% | 94% | 56% | 71% | 84% |
| # of Babies | 25 | 29 | 31 | 25 | 24 | 19 |

**626** INDICES OF PROTEIN METABOLISM IN TERM INFANTS FED HUMAN MILK, WHEY PREDOMINANT FORMULA, OR COW MILK FORMULA. Lynn M. Janas, Mary F. Picciano, and Terry F. Hatch (Spon. by Samuel J. Fomon). University of Illinois, Department of Foods and Nutrition, Urbana, IL.

Infants (n=37) received either human milk (HM), whey predominant formula (WF), or cow milk formula (CF) as the sole nutritional source for 2 mos. At age 2, 4, and 8 wks, 2 hr fasting blood was analyzed for plasma amino acids (AA) and serum urea nitrogen (SUN). From 3-day dietary records and direct analyses of milks, intakes of AA and total nitrogen (TN) were calculated. Compared to HM feeding, elevated plasma valine (VAL), phenylalanine (PHE), methionine (MET), and SUN concentrations were observed with WF and CF feeding. Feeding WF resulted in elevations of 4 additional AA [threonine (THR), lysine, leucine (LEU), and isoleucine (ILE)]. Intakes of TN were positively correlated with plasma concentrations of VAL, LEU, ILE, tyrosine (TYR), histidine (HIS), and SUN (r=0.38-0.64, p<0.05-0.001), and negatively correlated with plasma arginine concentrations (r=-0.41, p<0.05). Intakes of the essential amino acids THR, VAL, LEU, ILE, PHE, HIS, TYR, and MET were correlated with their respective plasma concentrations (r=0.38-0.74, p<0.05-0.001). Data indicate that feeding WF does not result in indices of protein metabolism more similar to those obtained with HM feeding than does feeding CF, and that such indices will not be achieved unless TN content of formula is reduced, regardless of relative whey to casein ratios. (Supported in part by the Illinois Agricultural Experiment Station and Ross Laboratories.)

**● 629** **A CELL MODEL TO ASSESS PROTEIN SYNTHESIS AND AMINO ACID POOLS IN NEONATES** Carolyn Johnson, James Gable, Judith Haithcoat and Jack Metcoff, University of Oklahoma Health Sciences Center, Depts. of Pediatrics, Biochemistry and Molecular Biology, Oklahoma City, OK 73190.

The relation of protein synthesis (PS) to extracellular (EC) and intracellular (IC) amino acid (AA) pools, birthweight, gestational age and postnatal weight change in human neonates is unknown. Viable neutrophils isolated from 1-2 ml venous blood were used as a cell model to evaluate these relationships in 35 infants with complete data at 33 to 44 weeks postconceptual age (2d-14 weeks postnatal age), PS ($^{3}$H-leucine incorp, p moles/hr/mg DNA) and 19 cell AA (n moles/mg DNA) were quantified in the leukocytes and 19 AAs in the same plasma (n moles/ml) (Dionex high pressure AA analyzer, fluorometric detection). No significant (p <.05) correlations were detected between PS and individual plasma AAs. PS was correlated with 11 of 19 IC AAs and with sets of both essential (ESSAA) and nonessential (NESSAA) IC AAs. PS also was inversely (-) correlated with birthwt., gest.age, postconceptual age and weight at time of study. When studied in a stepwise multiple regression of PS on the age-weight variables, weight at study was the only variable selected by the model and accounted for 20% ($R^2$=.205, p=0.006) of the variance in PS. Of the AAs, the IC ESSAAs were the only set explaining a significant proportion of the variance in PS ($R^2$=0.274, p=0.001). Thus it appears that the smaller and more preterm the infant, the greater the rate of protein synthesis; which, in turn, is more closely related to levels of IC ESSAAs than to plasma concentrations of the AAs. Measures of protein synthesis and IC AAs are feasible, even in neonates, and should contribute significantly to formulation and evaluation of therapies designed to improve these modalities.