THE RELATIONSHIP OF FEEDING TO NECROTIZING ENTEROCOLITIS. Richard W. Krouskop, Edwin G. Brown, Avron Y. Sweet. Case Western Reserve Univ. at Cleveland Metropolitan Gen. Hosp., Dept. of Ped., Cleveland.

The records of all newborns with necrotizing enterocolitis (N-E) were reviewed for the years 1968-73. Of the 24 cases, 19 died & N-E was confirmed in all 18 autopsies. The previously reported associations with low birth weight, PROM or amnionitis, asphyxia, & RDS were found. Also, a relationship with feeding was seen--the infants forming 3 groups: Group I-18 infants begun on formula feedings between 4 hrs. to 8 days of life. They developed G.I. signs an average of 31 hrs. later (S.E.=5.6). Formula intake by the 2nd day of feeding averaged 72 cc/kg/day, 133% of the usual daily formula intake in this nursery for infants without overt illness. All 5 who lived (of which none perforated or had surgery) were in this group. Group II-3 infants developed the onset of G.I. signs 15, 20 and 28 days following initiation of feeding, but had other intercurrent problems. Group III-3 infants never fed formula. These had no x-ray or autopsy evidence of pneumatosis. In these 24 patients with N-E, 75% developed the disease related to the onset of feeding. The remainder appeared to develop their disease in relationship to other problems. Formula feeding in this series is very closely associated with the development of N-E, particularly over-aggressive feeding. Feeding is not the sole cause of N-E but is closely enough related to its development to warrant delayed and cautious feeding of infants at risk of N-E.

CRITICAL AGE OF LACTASE DEFICIENCY IN CAUCASIANS. Emanuel Lebenthal, Irena Antonowicz and Harry Shwachman. Harvard Med. Sch.,The Children's Hosp. Med. Ctr. Dept. of Medicine, Boston.

Small intestinal lactase activity in the healthy adult is either the same as in early infancy or may drop to very low levels. The incidence varies with the ethnic group studied but very little information is available as to the age lactase decreases. We selected 150 specimens with normal histologic appearance out of 1047 mucosal biopsies. They were derived from a heterogenous white ethnic group with failure to thrive, healthy siblings and parents, ranging in age from 6 weeks to 50 years. Mucosal lactase activity and sucrase/lactase ratios in these 150 subjects were plotted against their age. In the first 3 years of life lactase activity averaged 32.1 ± 10.1 μmoles/gP/min. and sucrase/lactase ratio was 1.7 ± 0.5. There was no significant difference in mean or S.D. from year to year in the first three years. After the age of 5, two separate groups emerged. One group with low lactase activity and the other with the same mean value as in the first three years. The group with low lactase included children and adults with clinical lactose intolerance and some (8) upon testing, had a flat lactose tolerance test. They consumed relatively small amounts of milk. The other group with high lactase activity consumed an average of one quart of milk a day, and some (3) on testing, had a normal lactose tolerance test. This study implies that healthy Caucasian children up to age of 5 can safely consume milk without fear of lactose intolerance.

ENTEROKINASE AND INTRALUMINAL TRYPSIN ACTIVITY: DISTURBED RELATIONSHIP IN CHRONIC DIARRHEA IN CHILDREN. Emanuel Lebenthal, Irena Antonowicz and Harry Shwachman. Harvard Med. Sch.,The Children's Hosp. Med. Ctr. Dept. of Medicine,Boston.

Enterokinase initates digestion of protein by conversion of trypsinogen into trypsin. The possible failure of this function and the interactions between the two enzymes were investigated in two groups of infants with chronic diarrhea. The first group, included six infants (age 1 to 3 months) with intractable diarrhea of infancy, revealed reduced mucosal enterokinase activity (9.5±6.5 μM/gP/min) and low intraluminal trypsin and enterokinase activities. After treatment with I.V. alimentation the activities of enzymes returned toward normal (enterokinase values = 49.6±17.5 μM/gP/min; normal values 91.0±43.2 μM/gP/min.). The mucosal morphology of all the pretreatment biopsies showed Grade III atrophy which improved to Grade I and II after treatment. The second group consisted of eight children (age 6 months to 4 years) with chronic nonspecific diarrhea. Their intestinal mucosa demonstrated normal morphology and disaccharidase activities but decreased activity of enterokinase (10.4±3.8 μM/gP/min.) and intraluminal trypsin. These findings suggest that enterokinase deficiency and reduced trypsin in intractable diarrhea in infancy may be a contributing factor to the protein malabsorption and consequent malnutrition. The enterokinase deficiency in chronic nonspecific diarrhea has not been reported previously and may represent a new entity.

INTESTINAL DISACCHARIDASES IN EXPERIMENTAL OSMOTIC DIARRHEA. Fima Lifshitz, Robert Pergolizzi and Raul A. Wapnir. North Shore Univ. Hosp., Dept. of Ped., Manhasset, N. Y. and Cornell Univ. Med. Col., Dept. of Ped., New York, N. Y.

The effects of osmotic diarrhea on jejunal disaccharidases were studied. Wistar male rats, 60-80 g, were daily forced fed 5 ml/100 g body weight of 20% (w/v) mannitol (Mtl) for 2 to 14 days. Water and a diet containing 69% of either glucose (Glc), sucrose (Suc) or starch (Sta) plus 18% protein, 8% fat, vitamins and minerals were given ad libitum. Pair fed control rats received saline instead of Mtl. Another group was forced fed twice daily 5 ml/100 g of a 50% suspension of the basal diet, but with 45% lactose (Lac) and 24% Glc or 45% Sta and 24% Glc. All rats given Mtl or Lac developed diarrhea within the first 24 hr and this condition persisted throughout the experimental period. In rats on a Sta diet, Mtl induced lactase (L) and sucrase (S) deficiencies after 7 and 14 days of diarrhea (means, in IU/mg protein), L: .0390 vs .0135 ($p<.05$); S: .1592 vs .1030 ($p<.05$); maltase (M): 1.1563 vs 1.1539 (N.S.). Similarly, rats on Suc showed a drop in L and M, but not in S. In contrast, Lac induced an increase in all disaccharidases after 4 days which was sustained only for L up to 14 days, but not for S and M; L: .0996 vs .2037 ($p<.01$); S: .3867 vs .3687 (N.S.); M: 1.0290 vs 1.8790 (N.S.). The results indicated that changes in jejunal disaccharidases after osmotic diarrhea were directly related to intake of the corresponding carbohydrate. (Supported in part by a grant of Ross Labs.)

PARENTERAL NUTRITION IN ACUTE TUBULAR NECROSIS AND ANOREXIA NERVOSA. Rebecca Ma and James C M Chan. George Washington Univ Children's Hosp Nat Med Ctr, Dept of Nephrology; Univ of Southern Calif, Dept of Peds, Children's Hosp of Los Angeles, Calif. (Intr by Wellington Hung).

A sixteen year old girl sustained a 35% weight loss (52 to 34 kg) secondary to anorexia nervosa over a 5 month period. Acute renal failure occurred after two consecutive episodes of hypovolemic and hypoglycemic shock. Acute tubular necrosis was confirmed by kidney biopsy. Parenteral feeding with 50% dextrose and 2.1% synthetic amino acid solution at 300 ml per m^2 per day plus replacement of urine output was instituted. Intravenous feeding was maintained for 15 days. Diuresis began on the 22nd day and she went on to complete recovery.

To investigate the endogenous acid production under the dual impact of starvation and total intravenous feeding, the technique of estimating endogenous acid production by Relman et al (JCI 40: 1921,1961) was applied. Mean values for the patient and controls (in brackets) are presented in uEq/min/$1.73m^2$: sulfuric acid production, 7.8 ± 0.8 (25.9 ± 3.5); hydrogen ion production incident to organic anion excreation, 7.8 ± 0.8 (25.9 ± 3.5); urinary sulfur, 1.3 ± 0.1 (7.6 ± 3.8) and the infusate sulfur 2.5 ± 0.5 (7.9 ± 0.1). The data indicate retention by the patient of 50% of the sulfur infused; this suggests that the sulfur was utilized in new tissue formation for this severely malnourished patient.

MATERNAL LEUKOCYTE METABOLISM & FETAL GROWTH Jack Metcoff, Mostafa Nameesh, Gail Jacobson, Warren Crosby, Paul Costiloe, Univ. Oklahoma Health Sci. Ctr. Depts. Ped., Biochem., OB, Biostatistics. Okla. City

Fetal Malnutrition (FM) may compromise more than 130,000 pregnancies/year in the USA. Postnatal treatment of FM does not increase the reduced number of cells; antenatal treatments might, but require prenatal identification of FM. We hypothesize that metabolic changes in rapidly replicating maternal leukocytes (ML) will indicate FM. In the first 67 women of a prospectively studied series, ML Protein/DNA, pyruvate kinase (PK), glucose-6-phosphate dehydrogenase (G6PD) & energy ((ATP+½ADP/ATP+ADP+AMP)xPK/AK) increased from 24 weeks to term. Protein & RNA synthesis (^3H incorp) by ML were unchanged. Of 36 single births to date, 10 had ponderal indices (PI=100xWt ÷ L^3)<3 percentile, suggesting FM. Pregnancy changes of phosphofructokinase (PFK), ADP & energy in the ML & diet protein & calorie intakes correlated with the babies' PI. ML trends for ATP, energy, & PFK differed in mothers of FM vs normal babies. Kinetic studies of PK in FM term ML showed reduced Vmax for substrates (PEP & ADP), suggesting inhibitory or allosteric effects on the enzyme. Further, ML PK is allo-sterically modulated by L-alanine & fructosediphosphate. Thus, some metabolic aspects of the ML seem correlated with fetal growth & may be modulated by nutrient factors. (Supported by HD 06915)