

fecting antigen uptake are largely unknown. Studies relating molecular size to the clearance of macromolecules from intestinal loops suggest a diffusion phenomenon. However, the uptake of horseradish peroxidase and fluorescent-labelled gamma globulin by epithelial cells is affected by metabolic inhibitors suggesting an energy-dependent process. To clarify mechanisms of antigen absorption the uptake of horseradish peroxidase (HRP) (M.W. 40,000) and two C<sup>14</sup>-dextrans (M.W. 15,000 and 60,000) were studied in rat everted gut sac preparations. Electron micrographs showed that HRP progressed from membrane-bound structures within epithelial cells into the intercellular space and finally into the lamina propria. Absorption of HRP was five times greater in the jejunum than in the ileum and jejunal uptake was inhibited by S-13, an uncoupling agent. Large weight dextran was absorbed at three times the rate of small weight dextran at equivalent concentrations. Experiments performed at 0° or under nitrogen reduced the absorption of the large weight dextran to that seen with smaller weight dextrans. These studies suggest that the uptake of some antigens occurs by an energy-dependent pinocytotic mechanism. The uptake appears to be greater in the jejunum than the ileum and the jejunal absorption shows a more marked energy-dependency. The energy dependent uptake of the larger dextran suggests a mechanism for absorption of macromolecules other than diffusion. (Work supported by grants from The John A. Hartford Foundation, Inc.)

#### Role of bile acids in fat absorption in low birth weight infants.

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Low birth weight (L.B.W.) infants absorb fats with greater difficulty than normal term infants. The possible role played by intestinal bile acid concentrations (B.A.C.) in this defect was studied. Seventeen L.B.W. infants aged 10 to 34 days weighing 1540-2300 Gm. (mean-1790) were intubated and duodenal contents were aspirated for a period of one hour starting between 2-3 hours after feedings of unsaturated fat formula. Aspirates were kept on ice and were subsequently assayed for lipase activity and total B.A.C. (Method of Iwata). Concurrent 48 hr. stool collections were analyzed for fat. Lipase activity was normal in all infants (6.5-16 I.U./ml). In infants with duodenal B.A.C. below 2mM/L (critical micellar concentration) coefficients of fat absorption were 48%-77% (normal 80%). In 7 of 8 infants with levels greater than 2mM/L, fat absorption was above 80%. Attempts to correlate ages or weights of the infants with levels of fat absorption did not yield consistent relationships. However, when age of the infants was related to total B.A.C., 10-19 day old infants (12) showed a mean value of  $2.07 \pm 1.3$  mM/L, compared to 20-34 day old infants (7) with a mean of  $5.8 \pm 2.7$  mM/L. Control babies of three weeks to 8 mos. of age (8) had a mean B.A.C. of  $6.8 \pm 2.7$ . Four younger L.B.W. infants were restudied after 2-3 weeks and showed a three-fold rise in B.A.C. Conclusions from these preliminary studies indicate that L.B.W. infants display lower levels of duodenal B.A.C. than do older and larger infants. There is a good inverse correlation between B.A.C. and steatorrhea.

Enhanced calcium and magnesium absorption in premature infants by feeding formulas containing medium chain triglyceride (MCT). PHIENVIT TANTIBHEDHYANGKUL and SAMI A. HASHIM

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Thirty-four premature infants were divided into three groups of comparable weight and fed three formulas differing only in fat composition. Group 1 (control) corn oil, oleo, and coconut oil (39:41:20); Group 2: MCT, corn oil, and coconut oil (40:40:20); Group 3: MCT and corn oil (80:20). Formula feeding was begun within 1 week after birth and continued throughout hospital stay. In all groups two 5-day stool collections were made early and late during the study and analyzed for fat, Ca and Mg. Mean absorption values  $\pm$  SE for the three groups of infants are:

Group	Ca Absorption: % of dietary Ca		Mg Absorption: % of dietary Mg	
	early period	late period	early period	late period
Control	29.5 $\pm$ 3.7	39.1 $\pm$ 4.1	56.1 $\pm$ 4.2	58.4 $\pm$ 4.5
40% MCT	60.1 $\pm$ 4.0	64.3 $\pm$ 3.3	66.0 $\pm$ 4.6	64.6 $\pm$ 2.7
80% MCT	75.0 $\pm$ 2.9	81.2 $\pm$ 3.0	83.6 $\pm$ 2.2	87.5 $\pm$ 2.7

In the MCT groups Ca absorption was significantly increased when compared with control ( $p < .001$ ). The 80% MCT group absorbed more Ca than the 40% MCT group ( $p < .01$ ). When the 80% MCT group was compared with the 40% MCT and control groups, significantly higher Mg absorption was observed ( $p < .005$ ). There was a positive correlation between improvement in fat absorption and both Ca and Mg absorption. The results indicate that calcium and magnesium absorption can be improved in premature infants by administration of MCT-containing formulas.

Congenital defect in folic acid absorption. PEDRO J. SANTIAGO-BORRERO, RAFAEL SANTINI, ENRIQUE PÉREZ-SANTIAGO and NORMAN MALDONADO (Intr. by Antonio Ortiz). *University Hospital, Univ. of Puerto Rico Sch. of Med., San Juan, Puerto Rico.*

A caucasian girl was noted to have persistent diarrhea and progressive pallor since age of two months. Hematologic evaluation at 3 months revealed anemia of 6.0 gm/100 ml and severe megaloblastic erythropoiesis. She failed to respond to oral treatment with folic acid, but she had a prompt hematologic and gastrointestinal response with folic acid I.M. She remained free of anemia and diarrhea and kept growing and developing adequately while receiving parenteral therapy with folic acid. Anorexia and severe stomatitis and glossitis developed regularly three to four weeks after the administration of 15 mg of folic acid I.M. Evaluation at age 11 yrs., 3 weeks after the last dose of folic acid I.M., revealed a normal girl except for moderate stomatitis and glossitis and some hypersegmented PMN leukocytes. Her serum and whole blood folates were 2.0 and 60 ng/ml, respectively, and the serum B-12 was 500 pg/ml. Intestinal absorption tests were normal. Gastric and jejunal biopsies revealed normal mucosa. Folic acid and citrovorum factor absorption tests with 5 mg doses showed flat curves. Forty mg. of folic acid orally also failed to produce an increase in serum folate or to control the early signs and symptoms of folic acid deficiency. The clearance of folate after the administration of 5 mg. of folic acid intravenously was normal, but the urinary excretion of folate was unusually low (100  $\mu$ gm) in 8 hours. Studies for the presence of a folate inhibitor in the plasma were negative. These studies demonstrate an alteration in the

normal mechanism of absorption of both physiologic and pharmacologic doses of folate compounds and suggest also a defective metabolism of folate in the tissues.

Studies on the dietary regulation of jejunal pyruvate kinase and sucrase activities. REUBEN S. DUBOIS, RONALD W. GOTLIN, and DENIS O. RODGERSON (Intr. by Donough O'Brien). *Univ. of Colorado, Denver, Colo.*

The dietary regulation of jejunal glycolytic and disaccharidase enzyme activities is well documented, however failure of adaptation has been described (*Gastroenterology* 58:990 1970). The mechanism of these adaptive changes is not known. This report describes 2 females aged 9 and 11 years with exogenous obesity. Both had 5 hour oral glucose tolerance tests (OGTT) with serial measurement of blood glucose, insulin and serum inorganic phosphorus (SIP). There was an inappropriate insulin-glucose ratio (I/G), mean 1.4, range 0.6 to 1.8 (normal controls, mean 0.4, range 0.2 to 0.7) and a lack of fall in SIP during the OGTT, suggesting that the insulin was biologically abnormal (*Clin. Res.* 19:201 1971). Jejunal biopsies were performed after 48 hours of fasting and again after 96 hours of a high carbohydrate (CHO) diet. The activities of jejunal pyruvate kinase (PK) lactase and sucrase(S) were assayed. The PK activities (U/g wet wt.) and the sucrase-lactase ratio (S/L) with fasting were 34.6 and 1.81 in one and 39.6 and 2.54 in the other subject, while with feeding were 36.2, 1.63, 40.4 and 2.38 respectively. Both patients were re-studied 2 months after the institution of a low simple CHO diet. At this time I/G and SIP fall during the OGTT were normal. The PK activities with fasting and feeding were 27.2 and 51.8 in one and 42.2 and 53.1 in the other, while the S/L with fasting and feeding were 1.73, 2.79, and 1.88, 2.41 respectively. These data suggest that the dietary regulation of PK and S is mediated through insulin and the lack of adaptation in obesity may be due to the presence of biologically abnormal insulin.

Carbohydrate dependent protein synthesis and enzyme activity in the jejunum. RICHARD J. GRAND. *Children's Hosp. Med. Ctr., Boston, Mass.* (Intr. by Park S. Gerald).

The mechanism by which dietary carbohydrate (CH) regulates jejunal disaccharidase activity has not been elucidated. Studies were undertaken to determine whether adaptive changes in disaccharidase levels were accompanied by variations in protein synthesis; and if so, whether they were related to cell migration and RNA synthesis. 200 g rats were fed a CH-free diet (with isocaloric protein replacement) for 7 days and then fed a diet rich in either sucrose (68% cal) or starch (51% cal). Incorporation of  $^{14}\text{C}$  amino acids into total mucosal and brush border (BB) proteins (TCA insoluble) was measured. Both sucrose and starch stimulated an increase of 30% in the labeling of total mucosal proteins and greater than 100% rise in that of BB proteins. Simultaneously, there was 100% rise in sucrase and lactase activity and a 60% increase in maltase activity in crude jejunal homogenate and BB. When actinomycin-D was injected IP 6 hrs prior to feeding sucrose, RNA synthesis measured 24 hrs later was reduced 50%, and cell migration was arrested. Although neither basal rates of total mucosal protein synthesis nor the increases stimulated by CH feeding were inhibited,  $^{14}\text{C}$  labeling of the BB was reduced. Sucrase, lactase and maltase levels in the crude homogenates rose 75-100%, but these activities in the BB did not increase in actinomycin-D treated animals. The data suggest that dietary CH controls

disaccharidase activity by changes in protein synthesis independent of RNA synthesis and cell migration, and support the concept that there is an RNA-dependent step required for the transfer of newly formed disaccharidases from sites of synthesis to the BB.

Nutritional adaptation: Effect of dietary carbohydrate on intestinal disaccharidase activity in the infant rat. E. LEBENTHAL, N. KRETCHMER and P. SUNSHINE. *Stanford Univ., Stanford, Calif.*

The activities of intestinal sucrase and isomaltase are not detectable in rats prior to 15-16 days of age, but corticosteroids as well as feeding heterologous protein precociously induce the activities of the  $\alpha$ -glucosidases. We studied the ability of the intestine of infant rats to adapt to alteration in the carbohydrate content of their diets by evaluating changes in activity of disaccharidases and in histological maturation of intestinal mucosa. Ten day old rats were removed from their mothers, warmed in an incubator, and fed by constant infusion through gastrostomies. The basic diet was a soya preparation to which various sugars were added. When the diet contained 2% sucrose, diarrhea ensued for 48 hours, but subsided when intestinal sucrase and isomaltase appeared precociously. In animals fed sucrose, the activities of sucrase and isomaltase were markedly increased as compared to animals on carbohydrate free diets. (Sucrase  $2.41 \pm .23$  vs  $0.6 \pm .13$ , isomaltase  $3.43 \pm .42$  vs  $0.78 \pm .18$ ). Maltase activity was doubled, while lactase was unaltered. The mitotic index of crypt cells, and depth of crypts, and incorporation of  $^3\text{H}$ -thymidine into DNA were increased. In adrenalectomized rats, activities of sucrose and isomaltase were not detected nor induced by sucrose. These animals had continuous diarrhea. Steroids given to adrenalectomized rats caused appearance of the enzymes; but if cortisone and sucrose were given together, there was synergism evidenced by a marked increase in activities. In contrast to observations in adult animals, the effect of sucrose on  $\alpha$ -glucosidases in developing animals demands the participation of the adrenal gland.

Absorption of lactose by various Nigerian ethnic groups. OLIKOYE RANSOME-KUTI, NORMAN KRETCHMER, RUTH HURWITZ, CLAIRBOURNE DUNGY, and WOLE ALAKIJA. *Univ. of Lagos, Lagos, Nigeria, and Stanford Univ., Palo Alto, Calif.*

Reports have emanated from a number of regions in the world indicating that various ethnic groups are intolerant to lactose in milk. We accomplished lactose tolerance tests on four major tribal groups in Nigeria: Yoruba, Ibo, Fulani, and Hausa. The Yoruba and Ibo live in an area where there never was cattle-raising and, until recently, no milk was taken after weaning. The Hausa and Fulani live in the north of Nigeria where cattle-raising and ingestion of milk and milk-products are traditional. The data indicate that 99% of the Yoruba and 96% of the Ibo after the age of 1½ to 3 years malabsorb lactose, whereas only 64% of the Hausa and Fulani show malabsorption. But nomadic Fulani, who are migratory cattlemen, show only 20% malabsorption. We also found that when white Semites were compared with Anglo-Saxons, the Semites were incapable of absorbing lactose in contrast to the Anglo-Saxons. Individuals with lactose malabsorption showed no difficulty in their ability to hydrolyze sucrose. Since no other mammal, so far examined, is able to hydrolyze lactose efficiently after weaning, we contend that malabsorption of lactose after two years of age is genetically normal in man and that the individuals who are capable of