tion, the PH test should be positive. The PH test was performed in 20 patients age 7 weeks to 7 months with documented obstructive liver disease. Eighteen of these patients came to surgery. All of the biliary atresia (BA) patients, regardless of age, had a positive PH test. One patient with BA had a positive PH test prior to corrective surgery. The PH test became normal when bile flow was restored. In contrast, the PH test was variable in neonatal hepatitis. Some patients with complete obstruction demonstrated by Rose Bengal excretion the obstruction ceased. Others were normal at the outset.

We conclude that the PH test is a simple and useful adjunct in evaluation of jaundiced infants. If normal, BA has been ruled out. If initially abnormal, but corrected with oral vitamin E, BA has also been ruled out. Thus the PH test rapidly provides as much diagnostic information as Rose Bengal excretion. It is not associated with sampling difficulties or radiation exposures and should be used as a diagnostic test for complete biliary obstruction in neonatal liver disease.

162 *Dipeptide Transport Across the Intestinal Brush Border.* ARMIDO RUBINO, MICHAEL FIELD and HARRY SHWACHMAN, Depts. of Ped. and Med., Harvard Med. Sch., The Children's Hosp. Med. Center and Beth Israel Hosp., Boston, Mass.

Recent observations suggest that some oligopeptides are hydrolyzed within the mucosal cells and not in the lumen. The possibility that there are specific transport processes for dipeptides in the brush border was explored in rabbit ileum. The unidirectional influx across the brush border of 14C-glycyl-L-proline (GlyPro), 3H-glycine (Gly) or 3H-proline (Pro) was determined by measuring tissue radioactivity following 30–60 sec exposure of the mucosal surface to a solution containing the substrate [SCHULTZ *et al.*, J. gen. Physiol. *50:* 1241, ...]. GlyPro influx, measured over the concentration range 0.1 to 32 mM, displays an easily saturated component with $K_m = 1.0$ mM and $V_{max} = 0.7$ μmoles/cm^2 h and a difficult to saturate component which may represent simple diffusion. Influx of 0.5 mM GlyPro was 40% $\pm$5.1 (1 SE) less in Na-free, choline Ringer than in Na-Ringer ($n = 4$). Percent inhibition ($\pm$1 SE) of the influx of 0.5 mM GlyPro was determined in the presence of 20 mM concentrations of the following amino acids and peptides: Gly (4 ± 0.5 $p > 0.5$), Pro (10.5 ± 3.5 $p < 0.05$), L-leucine (23 ± 4.2 $p < 0.01$), glycylglycine (52 ± 2.8 $p < 0.01$), L-leucil-L-leucine (85 ± 2.5 $p < 0.01$) and L-phenylalanylglycine (63 ± 2.9 $p < 0.01$). 20 mM GlyPro did not inhibit the influx of 2 mM Gly ($n = 8$) or 2 mM Pro ($n = 8$).

It is concluded that (1) GlyPro is transported across the brush border of rabbit ileum by a Na-stimulated, saturable process which is shared by other dipeptides and for which amino acids have a low affinity, and (2) GlyPro has no measurable affinity for the Gly and Pro transport processes.

163 *Neutral Amino Acid Absorption in Diabetic Rats.* M. KABIR YOUNOSZAI and HAROLD P. SCHEDL, Univ. of Iowa Coll. of Med., Univ. Hosps., Depts. of Ped. and Med., Iowa City, Iowa (introduced by Samuel J. Fomon).

Small intestinal function is altered in diabetes: hexose absorption is increased in diabetic rats, and glucose absorption is elevated in human juvenile diabetes. Because the transport mechanisms for hexoses and amino acids are inter-related, it is important to characterize effects of the diabetic state on amino acid transport. To dissociate metabolic from transport effects of diabetes, we used the non-metabolized neutral amino acid, α-aminoisobutyric acid (AIB). We perfused *in situ* the mid 30 cm segment of the small intestine of control (C) and diabetic (D) rats. We have previously shown this to be the site of maximal AIB transport [Amer. J. Physiol. *216:* 1131, 1969]. AIB absorption rate was significantly greater ($p < 0.05$) in the diabetic animals: μmoles/0.5 h/cm; C, 0.44; D, 0.56; μmoles/0.5 h/g wet weight; C, 6.56; D, 7.88. The intestinal tissue concentrations of AIB (μmoles/g tissue water) were significantly greater ($p < 0.001$) in the diabetic rats in both mucosa (C, 1.74; D, 3.15) and underlying tissues remaining after scraping off the mucosa (C, 1.42; D, 2.89). These tissue concentrations suggest that the primary step in transport stimulation is at the brush border of the mucosal cell. In normal rats, we have already shown that the segment absorbing most rapidly (mid-intestine) has the lowest tissue AIB concentration. In the present study, however, transport enhancement by diabetes was associated with increased intestinal tissue AIB concentration. Thus, there appear to be two mechanisms for increasing intestinal transport: (1) at the brush border in diabetes and (2) at the basal-lateral cell membrane for the normal longitudinal gradient.

164 *Studies on Infant Diarrhea. V. Mechanisms of the Impaired Jejunal Absorption.* CARMEN LUGO-DE-RIVERA, HELEN RODRIGUEZ-DE-CURET and RAMÓN TORRES-PINEDO, Gen. Clin. Res. Center and Dept. of Ped., Sch. of Med. of the Univ. of Puerto Rico, San Juan, Puerto Rico (introduced by Antonio Ortiz).

Studies on infants with diarrhea and in recovery have shown that there is impaired jejunal absorption of carbohydrates. It is not known whether this malabsorption is due to interference with normal active transport processes or to alterations in the permeability characteristics of the intestinal mucosa. To clarify this, the following experiments were undertaken. A series of perfusion studies with amino acids and hexoses were performed on 12 infants with acute diarrhea and on 18 infants who were either normal or in the process of recovery. Absorption velocities were lower in diarrhea and the response to increasing concentrations tended to follow a saturation pattern. In recovery, the response to increasing concentrations was linear and K_m and V_{max} values could not be calculated. These results suggest that *in vivo*, the rapid removal of substrate from the mucosal cell by the circulation is a factor which markedly modifies the kinetics of absorption. A probable explanation of the impaired jejunal absorption in diarrhea is a derangement in the permeability characteristics of the mucosa which results in intracellular accumulation of the absorbed substrate.

165 *Clinical Emphysema with Hereditary Alpha$_1$-antitrypsin and Antielastase Deficiency in Childhood.* RICHARD C. TALAMO, HENRY LEVISON, MATTHEW J. LYNCH, ALBERT HERCZ and HARRY W. BRAIN, Dept. of Ped., Harvard Med. Sch., Boston, Mass., and Dept. of Ped., Univ. of Toronto, and Res. Inst. Hosp. for Sick Children, Toronto.

Hereditary deficiency of serum alpha$_1$-antitrypsin and anti-elastase is associated with clinical familial emphysema with onset usually in the third or fourth

decade. In other families alpha$_1$-antitrypsin deficiency has been accompanied by cirrhosis in infancy or childhood, without clinical pulmonary disease. A 13-year-old girl has recently been studied, who has had recurrent pulmonary infections and progressive dyspnea since age 18 months. Chest x-rays show bullous emphysema and pulmonary function tests reveal severe airway obstructive disease with a low diffusing capacity. Lung biopsy done 5 years ago show emphysema and smooth muscle hypertrophy of the small bronchioles. Immunoglobulins, sweat electrolytes and liver function studies have been normal. Biochemical and electroimmunodiffusion studies of serum reveal a deficient level of alpha$_1$-antitrypsin and biochemical studies show a deficiency of inhibition of elastase. Family studies indicate that the deficiency is inherited in an autosomal recessive manner. The emphysema associated with hereditary alpha$_1$-antitrypsin deficiency may become symptomatic in early childhood and should be considered in the diagnosis of obstructive pulmonary disease in infants and children.

166 *Abnormal Erythrocyte Sodium Transport in Cystic Fibrosis (CF).* ALLEN LAPEY and JERRY D. GARDNER, NIH, Bethesda, MD (introduced by Paul A. di Sant'Agnese).

To further explore the recently reported erythrocyte cation transport defect in cystic fibrosis (CF) patients and their parents [BALFE *et al.*, Science, *00:* . . ., 1968], we have measured sodium (Na) content and the major components of Na outflux in erythrocytes from 21 normal young adults, 22 CF patients (ages 7–27), and 20 obligate heterozygotes.

Na content of red cells from patients and heterozygotes was normal. Of the various components of Na outflux measured, there was no difference between heterozygotes and their normal male or female counterparts.

Of the major components of Na outflux, that portion sensitive to ouabain (0+) was normal in all CF groups. Abnormalities of Na outflux in CF were primarily due to that portion which was insensitive to ouabain and sensitive to ethacrynic acid (0–/E+). 0–/E+ fractional outflux was decreased in CF males of all ages (0.027±0.02/h) relative to male controls (0.051±0.02). 0–/E+ was decreased in 7 CF females over the age of 16 (0.012±0.005) compared to female controls (0.023±0.01). However, in the 4 CF females under 16, 0–/E+ outflux (0.057±0.003) was greater than that of older CF females.

The normal data from heterozygotes indicate that erythrocyte Na outflux cannot be used as a 'genetic marker' for CF. These data document altered cation transport in non-exocrine tissue from males and older females with CF. Furthermore, this abnormality does not simply reflect a general alteration of erythrocyte cation transport, but is localized to a single specific component of Na outflux, which has a characteristic requirement for metabolic substrates as well as distinctive kinetic parameters. Studies of this transport system in other tissue from patients with CF may permit a characterization of the disease at the molecular level.

167 *The Distribution of Fluid Intake from Mist Tent Therapy.* NORMAN ASPIN, SAMUEL K. BAU, HENRY LEVISON and DONALD E. WOOD, Dept. of Paed., Hosp. for Sick Children, and Div. of Nucl. Med., Toronto Gen. Hosp., Toronto (introduced by Andrew Sass-Kortsak).

Mist tent therapy is widely used in the treatment of cystic fibrosis to increase deposition of fluid in the lower airways of the lung. To measure the time course and extent of this fluid uptake we have introduced a solution of radioactive ^{99m}Tc into the fluid reservoir of an ultrasonic nebulizer. Subjects breathed in the mist tent for periods up to 5 h following which the distribution of inhaled radioactivity was measured with a whole body counter and a rectilinear scanner. The results show that less than 5% of the radioactive aerosol entering the tent is inhaled by the subject. Of the inhaled aerosol 90% is initially trapped by the nasopharynx and later much of this radioactivity appears in the stomach. It is difficult to detect radioactivity in the lung. Similar results have been obtained in ten subjects using three different ultrasonic nebulizers. This work indicates that very little fluid from a mist tent reaches the terminal airways of the lung. (Supported by Canadian Cystic Fibrosis Foundation.)

168 *Re-evaluation of Mist Therapy in Children with Cystic Fibrosis Using Maximum Expiratory Flow-volume Curves.* ETSURO K. MOTOYAMA, LEWIS E. GIBSON, CHARLENE J. ZIGAS and CHARLES D. COOK, Yale Univ. Sch. of Med., Depts. of Ped. and Anesth., New Haven, Conn.

The measurement of maximum expiratory flow rates (Vmax) on MEFV curves is a simple yet sensitive method for detecting peripheral airway obstruction. In order to re-examine the efficacy of mist therapy (MT) in cystic fibrosis, MEFV curves as well as vital capacity (VC) and timed vital capacity ($FEV_{1.0}$) were measured in 16 patients every two weeks for a period of 4 to 5 months. In half of the patients, all of whom had been in mist tents at night for at least 6 months, the studies were done during an initial 8 to 12 week period out of mist and then a similar period in mist; in the other half the test conditions were reversed. The results were expressed as percent of predicted values.

	$\dot{V}$max (25% VC)	$\dot{V}$max (50% VC)
In mist (% pred. ±S.E.)	43.3±6.2	60.3±6.9
Out of mist	45.9±6.7	63.9±6.4
Significance	n.s.	n.s.
	VC	$FEV_{1.0}$
In mist (% pred. ±S.E.)	86.6±4.5	71.0±4.5
Out of mist	89.9±5.3	74.5±4.7
Significance	n.s.	$p < 0.025$

During the period without MT, 4 patients improved and 2 worsened as indicated by changes in all 4 parameters studied. As a group, $FEV_{1.0}$ was significantly ($p < 0.025$) better when they were without MT. VC and Vmax at 25% VC and 50% VC were also closer to normal without MT but the difference was not significant. Thus, these studies failed to show any beneficial effect of mist therapy in cystic fibrosis. (Supported by PHS HD00989, NCFRF and the State of Conn.)

169 *Physiological Mechanisms Underlying Periodic Breathing in Low Birth Weight Infants.* HENRIQUE RIGATTO, JUNE BRADY, WARREN TICKNOR and FE DUMPIT, Dept. of Ped. and Cardiovascular Res. Inst., Univ. of California, San Francisco, CA.

Twenty babies (b.w. 1–2 kg) were studied 106 times in the first 34 days of life. In 11 babies breathing periodically and 9 breathing regularly, we compared minute