Intestinal Malabsorption in Malnourished Children Before and During Recovery

Relation Between Severity of Protein Deficiency and the Malabsorption Process

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Thirty-two protein-calorie malnourished (PCM) children were studied on admission to hospital and throughout recovery. Absorption studies included nitrogen, fat, purified ^{131}I-labeled triolein and oleic acid, vitamin A palmitate, glucose, D-xylose, and vitamin B_{12}. Protein depletion was measured by the creatinine/height index (CHI). Severe malabsorption of all substances was present in all severely malnourished children (CHI < 0.55). As children became less protein-depleted with nutritional recovery, malabsorption decreased, in the following sequences: absorption of nitrogen, D-xylose, and vitamin A palmitate recovered soon after initiation of therapeutic diets; absorption of fat, purified ^{131}I-triolein and -oleic acid, and vitamin B_{12} recovered slowly and in a highly correlated fashion. Results with both purified ^{131}I substrates were identical throughout. The findings of this investigation are compatible with the concept that malabsorption in protein-calorie malnourished children affects mucosal function throughout the gut as a consequence of protein depletion per se.

Intestinal malabsorption has been amply documented in protein-calorie malnourished (PCM) children (1, 2). The physiopathologic basis for the malabsorption, however, still remains unclear, although decreased pancreatic function (3), lactase deficiency (4), intestinal mucosal abnormalities and dysfunction (2, 5), and abnormal distribution and composition of the autochthonous intestinal flora (6) have been documented.

Recently we have shown that fat malabsorption is severe in PCM children; that it involves, in the same proportion, the absorption of purified ^{131}I-triolein and ^{131}I-oleic acid; and that a prolonged period of dietary therapy is needed for regaining normal fat absorption (2). The role of pancreatic lipase deficiency in producing the malabsorption, therefore, seems doubtful. Also doubtful in our cases is the role of lactase deficiency, since the same pattern of malabsorption has been found in children receiving lactose-free diets, and the addition of 40 g of lactose per day to these diets has not produced significant gastrointestinal alterations (7, 8).

The purpose of this investigation was to explore the intestinal absorptive function of PCM children before and during recovery in relation to the severity of protein deficiency, estimated by the creatinine/height index (CHI) (9).

A battery of tests designed to investigate the functional capacity of various parts of the gas-

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trointestinal tract and the handling of various substrates were done in children on admission to hospital and during recovery. The tests included absorption of D-xylose, glucose, nitrogen, fat, purified ^{131}I-triolein and -oleic acid, vitamin A palmitate, and ^{57}Co-vitamin B_{12}. Fat, glucose, and vitamin B_{12} absorption improved slowly and in a highly correlated fashion with protein repletion, while D-xylose, nitrogen, and vitamin A palmitate absorption appeared to recover quickly after initiation of therapeutic diets, before any significant degree of body protein repletion had taken place.

MATERIALS AND METHODS

A total of 32 severely PCM children with edema were studied. Of these, 22 were included in absorption studies other than ^{57}Co-vitamin B_{12}; the absorption of this vitamin was studied in 10 children. The children were studied again at different stages of recovery and also when they were fully recovered (judged by clinical appearance, weight for height greater than 95% of the 50th percentile of weight for their height according to Stuart and Stevenson's tables [10], and CHI greater than 0.85) (9). The CHI index, which estimates the severity of protein deficit of malnourished children in relation to normal children of the same height, is calculated as follows:

$$\frac{\text{72-hour urinary creatinine of the malnourished child}}{\text{72-hour urinary creatinine of a well-nourished child of the same height}}$$

This measurement yields the same results as total body potassium (11). The pertinent characteristics of the children are shown in Table 1.

Table 1. Characteristics of the Children Studied

	Admission	During recovery	Recovered
No. of subjects	32	27	22
Age (months)	28* (14–73)	33 (15–72)	34 (24–60)
Weight for height (%)	74† (60–96)	87 (62–102)	106 (95–120)
Total serum proteins (g/100 ml)	3.47 (2.66–5.40)	5.38 (4.76–7.60)	7.15 (7.01–7.60)
Serum albumin (g/100 ml)	1.92 (0.87–2.84)	3.35 (3.17–4.60)	4.05 (3.60–4.60)
Creatinine height index	0.55 (0.36–0.77)	0.78 (0.51–1.01)	0.94 (0.85–1.09)

*Mean and range
†Mean minimal edema-free weight and range

On admission 27 of the 32 children (84%) had nonspecific diarrhea, ranging from mild to severe; assessment was based on the number of bowel movements per day, the stool weight/24 hours, and the characteristics of the feces.

A smaller number of the children had diarrhea in the recovery phase (33%) and when fully recovered (23%).

Stool cultures revealed *Shigella flexneri* in 5 children on admission and in 2 during recovery. No enteropathogens were isolated in the rest of the children. Moderate degrees of infection with helminths and protozoa were present in the majority of children. *Ascaris lumbricoides*, *Necator americanus*, and *Trichuris trichiura* in single or combined infections were present in 60% of the children. *Entamoeba histolytica* was identified in 3 (none of which had dysenteric syndrome), and *Giardia lamblia* infection was diagnosed in 4 children. No specific treatment was administered for these infections until after the study. Fifty percent of the children presented helminth infections during recovery and when fully recovered. *Entamoeba histolytica* and *Giardia lamblia* were identified in 4 children during recovery and when fully recovered. There was no association between diarrhea and parasites or enteropathogens throughout the study.

Treatment was divided into two phases (12). During the first week of hospitalization, treatment for respiratory infections and water and electrolyte imbalances was administered. At this time the children were receiving milk or casein-based diets which provided 7 g of protein/kg/day and 70 calories/kg/day, 20 to 30% of which were derived from cottonseed oil. Carbohydrate sources were corn starch, sucrose, and dextrin-maltoses. After this period, the concentration of the diet was increased so as to produce an intake level of 2 to 4 g protein and 120 to 180/kg/day calories. Throughout the study the children received a vitamin–mineral mixture (including $FeSO_4$) to provide the recommended allowances of these nutrients.

The tests used to measure fat absorption have been described in detail (2); they included fat balances and purified ^{131}I-triolein and -oleic acid absorption. Vitamin A absorption was explored by Mendeloff's procedure (13). D-xylose absorption was measured both by 5-hour urinary excretion and by blood levels obtained in 0.2 ml of blood at 30, 60, 90, 120, and 180 minutes. The dose of D-xylose was 5 g/150 ml water. One hour after this dose, 100 ml extra water was given. D-xylose was determined by the Somogyi-Nelson method (14) against appropriate D-xylose standards; the

samples were preincubated with glucose oxidase.* The variation coefficient of this method was 1.5% and the residual reducing power of D-xylose-free samples after glucose oxidase treatment was less than 2 mg/100 ml. D-glucose absorption was measured by the sequential determination of oral glucose tolerance and intravenous glucose disappearance. These tests were done 1 day apart, alternating their sequence in different children. Results did not vary with the sequence used. The oral glucose dose varied between 2.5 and 1.75 g/kg, depending on the weight of the child (15); the intravenous dose was 0.5 g/kg. Capillary blood (0.2 ml) was obtained a) on fasting, b) after the glucose dose at 15-minute intervals for 1 hour, c) at 30-minute intervals up to 4 hours during the oral glucose tolerance test, and d) every 5 minutes for 40 minutes during the intravenous glucose disappearance test.

The rate of glucose absorption was estimated mathematically by increasing the blood glucose levels obtained during the oral test by the amount of glucose which would have disappeared as expected from the blood glucose levels obtained at different times after the oral dose, based on the glucose disappearance rate obtained in the intravenous test. This correction would yield theoretic blood glucose values in time after the oral dose, as if no glucose were disappearing from the blood. Glucose was determined by the glucose oxidase method (16).

Nitrogen (N) absorption was determined by accurately measuring N intake and fecal N between two carbon markers during a 3- to 4-day period. Nitrogen was determined by the Kjeldahl method (17). Measurement of ^{57}Co-vitamin B_{12} absorption was done by a modified Schilling test, administering the ^{57}Co-B_{12} in solution. The amount of ^{57}Co given was 0.05 μCi (specific activity 750 μCi/mg B_{12}) † and was followed by an intramuscular injection of 1000 μg vitamin B_{12} 2 hours later. On admission, the test was performed with and without intrinsic factor (1/3 the adult dose) one preceding the other in an alternate fashion. Urine was collected in 24-hour periods for 3 days.

RESULTS

To investigate the role of the severity of protein deficiency in the absorptive processes, the children were cataloged according to CHI on admission as follows: those with CHI below 0.55 (Group I, N = 12) and those with CHI above 0.55 (Group II, N = 20). Group I was the most severely protein-depleted. These groups did not differ in their minimal edema-free weight for height (Group I = mean 0.76, range 0.60–0.96; Group II = mean 0.73, range 0.67–0.89). Serum albumin levels were lower in Group I (mean 1.84, range 0.87–2.46) than in Group II (mean 1.98, range 1.34–2.84). The differences were not statistically significant. The recovering children were also divided into two groups based on their CHI. Group III consisted of the children whose CHI was still below 0.85, and Group IV contained those whose CHI was above 0.85. This last group differed from the fully recovered children (Group V) in that they did not fulfill one of the three criteria previously indicated for full recovery.

Fat Absorption

The results of the fat absorption studies are presented in Table 2. On admission fat malabsorption was severe, particularly in the children with greater protein deficit, indicated by a CHI below 0.55. These children, besides showing very low values in the fat balance studies, were unable to absorb vitamin A palmitate. The malnourished children belonging to Group II, however, had less severe fat malabsorption, some showing only minor fat malabsorption on the three tests in this study. As recovery took place, fat malabsorption soon reached normal levels, based on fat balances and in vitamin A absorption tests. However, the ^{131}I fat absorption was still abnormally low. The results of purified ^{131}I-triolein and ^{131}I-oleic acid are presented together since, as was shown previously (2), there were no differences between the absorption of these two substrates in any of the groups studied.

The regressions between CHI and apparent fat absorption determined by fecal fat and ^{131}I fat absorption are shown in Figures 1 and 2, respectively. In both cases, the correlation coefficient is highly significant; however, the scattergram of CHI and ^{131}I fats discloses a more progressive trend for improved absorption as CHI increases than is observed with fat balance. In this case a rapid increase in fat absorption seems to occur up to a CHI of around 0.70, and to remain essentially constant at higher

* Worthington Biochemical Co, Freehold, NJ
† Abbot Radiopharmaceuticals

Table 2. Fat Absorption of PCM Children. Test Results for Fat Balance, Purified ^{131}I-Triolein and -Oleic Acid, and Vitamin A Palmitate Absorption

	Admission		During recovery		Recovered
	Group I	Group II	Group III	Group IV	Group V
Creatinine height index (range)	<0.55 (0.36–0.53)	≥0.55 (0.55–0.77)	<0.85 (0.60–0.83)	≥0.85 (0.85–1.01)	0.94 ± 0.08 (0.85–1.09)
Percent of fat absorption ($\bar{X}$ ± SD)	55.3±18.8 (9)*	78.5±16.5 (7)	92.4±4.6 (6)	84.1±8.7 (9)	92.4±8.7 (11)
Percent of ^{131}I fat absorption ($\bar{X}$ ± SD)	25.6±10.1 (7)	54.3±25.5 (6)	70.1±17.7 (5)	74.5±11.6 (4)	89.5±4.5 (11)
No. of children who absorbed vitamin A palmitate	0 (9)	5 (7)	4 (4)	4 (4)	12 (12)

*Numbers in parentheses are numbers of children studied.

Significance levels among groups for fat absorption were: I: all others, $P < 0.01$; II: V, $P < 0.05$; for ^{131}I fat absorption levels were: I:II, $P < 0.02$; I:III & V, $P < 0.01$; II & IV:V, $P < 0.01$; III:V, $P < 0.02$.

CHI values. In Figure 2 the results obtained in a malnourished child who also had celiac disease are indicated. This child, in spite of having recovered nutritionally, still presented fat malabsorption, based on ^{131}I-triolein and -oleic acid absorption values.

Correlations between serum albumin levels or weight for height, and absorption of ^{131}I fat were less satisfactory than with CHI: $r = 0.572$ and $r = 0.489$, respectively.

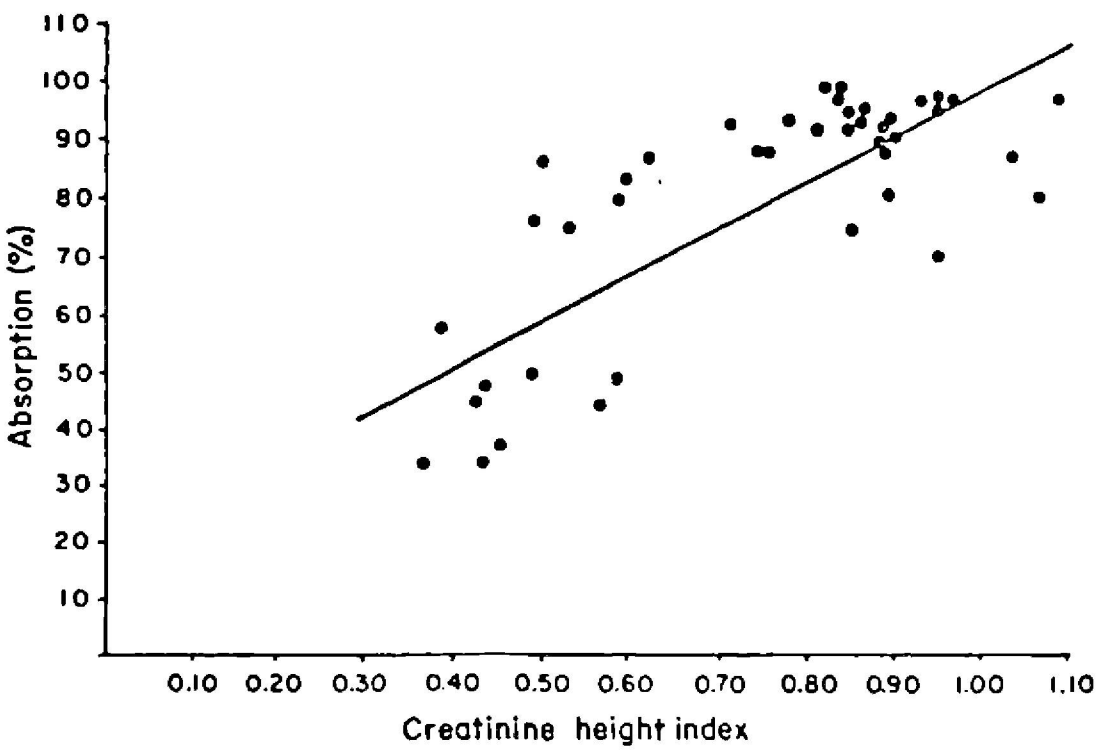

Fig 1. Scattergram of fat absorption vs creatinine height index (CHI) in malnourished children and during recovery. Correlation between CHI and apparent total fat absorption as percent of intake. Fat absorption was measured by fat determinations of intake and feces on 3 days. $Y = 19.7 + 77X$; $r = +0.79$

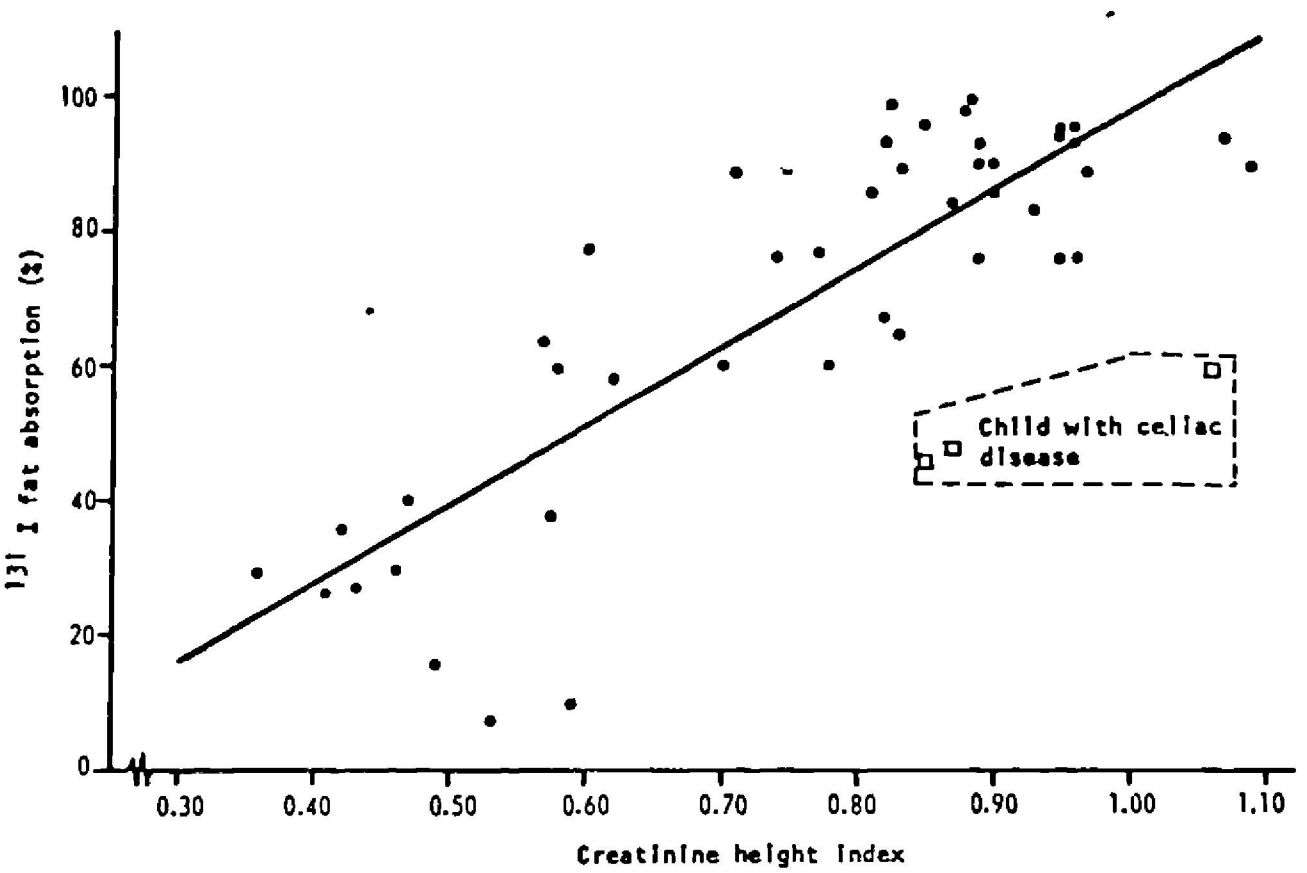

Fig 2. Scattergram of ^{131}I purified triolein and oleic acid absorption vs CHI in malnourished children and during recovery. Y = -18.93 + 1.16X; $r = 0.85$

D-Xylose Urinary Excretion and Glucose Absorption Rate

Five-hour urinary D-xylose excretion was significantly lower in children on admission (Table 3) but reached normal levels early in recovery, independent of the degree of protein repletion. Studies conducted in 6 children showed that as early as 10 days after initiation of therapeutic diets, D-xylose excretion increased significantly, reaching values near normal levels (mean 28.6 ± 9.8). D-xylose blood levels were higher in the children who excreted

Table 3. D-Xylose Urinary Excretion and Rate of Glucose Absorption

	Admission		During recovery		Recovered
	Group I	Group II	Group III	Group IV	Group V
Creatinine height index	<0.55	≥0.55	<0.85	≥0.85	0.94 ± 0.08
Percent of D-xylose excretion (X ± SD)	15.4 ± 3.1 (9)*	17.7 ± 1.8 (7)	34.0 ± 11.7 (6)	31.8 ± 10.7 (9)	34.0 ± 7.6 (11)
Rate of glucose absorption† ($\bar{X}$ ± SD)	68.7 ± 37.4 (9)	124.0 ± 71.3 (6)	145.8 ± 38.7 (6)	226.6 ± 79.4 (11)	298.2 ± 130.5 (11)

*Numbers in parentheses are numbers of children studied.

†Theoretic rise of blood glucose (mg/100 ml/60 min)

Significance levels among groups for D-xylose excretion were: I & II:III,IV,V, $P < 0.01$; for glucose absorption rate levels were: I:III,IV,V, $P < 0.01$; II:V, $P < 0.01$; III:IV, $P < 0.02$; III:V, $P < 0.01$.

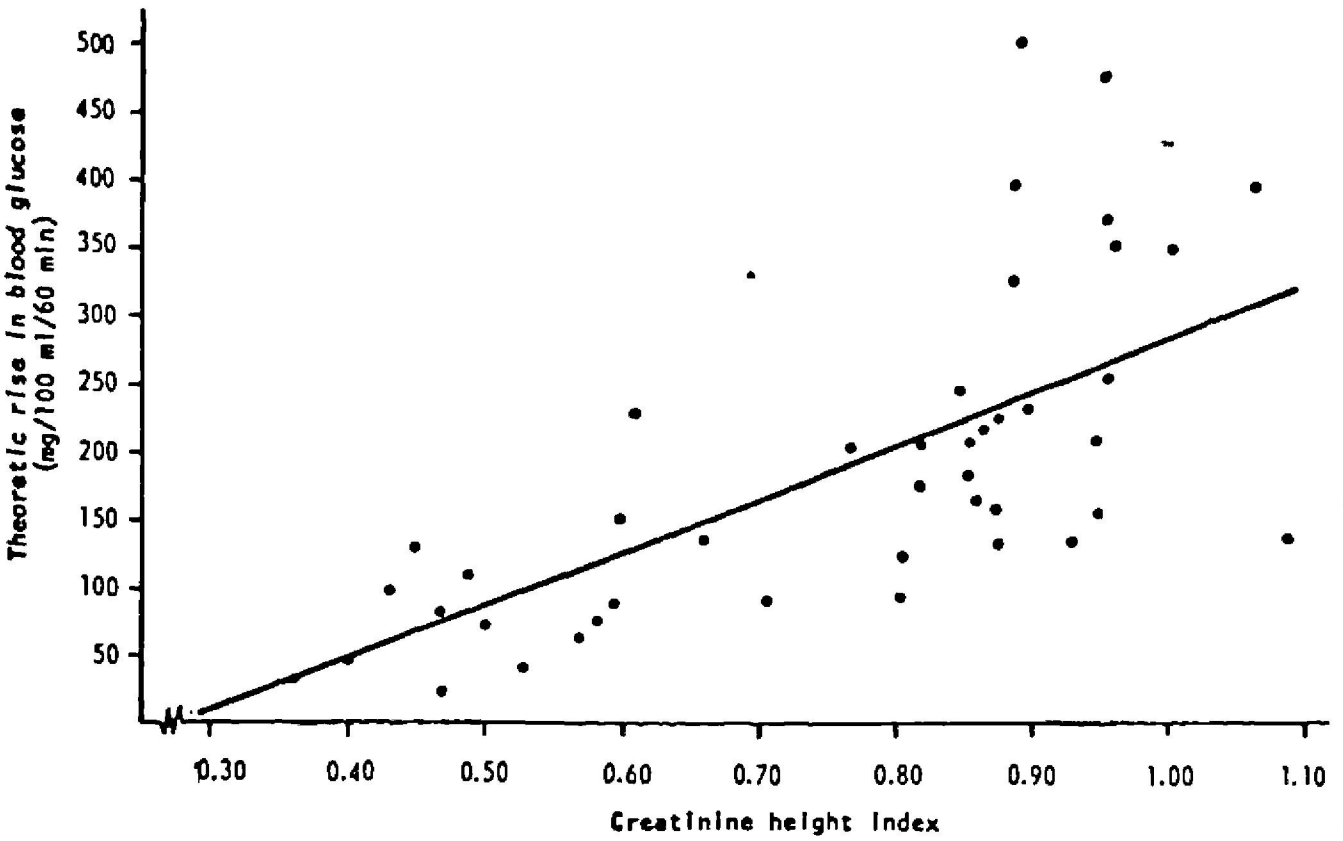

Fig 3. Scattergram of theoretic blood glucose rise in 60 min vs creatinine height index in malnourished children and during recovery. $Y = -114 + 4.07X$; $r = 0.695$

Table 4. Characteristics of Blood Glucose Metabolism

	Admission		During recovery		Recovered
	Group I	Group II	Group III	Group IV	Group V
Creatinine height index	0.55	0.55	0.85	0.85	0.94 ± 0.08
No. children studied	9	7	6	9	11
Fasting blood glucose (mg/100 ml)	62.4 ± 12.6	68.2 ± 6.8	70.2 ± 8.0	74.3 ± 5.0	76.6 ± 10.3
Blood glucose levels at time 0 in IV test (mg/100 ml)	301.4 ± 96.6	264.0 ± 12.0	252.6 ± 35.1	247.1 ± 51.2	245.8 ± 55.1
Glucose disappearance rate constant (K) (%)	2.03 ± 0.66	3.63 ± 0.36	3.66 ± 0.21	2.98 ± 0.54	3.00 ± 0.25
Peak blood glucose in oral test (mg/100 ml)	107.5 ± 9.7	104.3 ± 5.3	127.6 ± 6.4	134.0 ± 16.3	132.4 ± 10.1

Significance levels were: for fasting blood glucose: I:IV&V, $P < 0.02$; for glucose disappearance rate constant (K):I:all others, $P < 0.01$; II:IV, $P < 0.02$; II:V, $P < 0.01$; for peak blood glucose in oral test: I&II:all others, $P < 0.01$.

more urinary xylose. In no case was there a reverse situation, indicating that the low urinary excretion was not due to a decreased renal excretion of absorbed D-xylose. On the other hand, in 7 of the 16 children belonging to Groups I and II the highest D-xylose concentration in blood occurred in the 90-minute sample, while in the rest of the children the blood levels peaked in the 60-minute sample.

The rate of glucose absorption for the 5 groups of children, expressed as the theoretic rise in blood glucose (mg/100 ml) in 60 minutes, as if no glucose disappeared from the blood, is also shown in Table 3. A progressive rise is observed as the CHI increases. The scattergram of the values obtained, as well as the linear regression and correlation coefficient between CHI and theoretic rise in blood glucose in 60 minutes, are shown in Figure 3. The correlation coefficient ($r = 0.695$) is highly significant. As occurred with fat absorption, the correlations between rate of glucose absorption and weight for height or serum albumin levels were much lower ($r = 0.477$ and $r = 0.436$, respectively).

The fasting blood glucose levels in the 5 groups of children, their extrapolated blood glucose values at time 0 in the intravenous glucose disappearance test, the blood glucose disappearance rate constant (K), and the peak blood glucose levels obtained in the oral glucose tolerance test are shown in Table 4. In all of the variables listed, except for the extrapolated blood glucose levels at time 0 in the intravenous glucose disappearance test, children belonging to Group I had significantly lower values. Children belonging to Group II on admission did not differ from those in Group III, except in the peak values in the oral glucose test, but were significantly different from those in Groups IV and V in the glucose disappearance rate constant (K), as well as in the peak values in the oral glucose test. The highest blood glucose concentration in the oral glucose tolerance test was delayed in only 1 child belonging to Group I, whose blood glucose peaked in 90 minutes. In Group I, 5 of 9 children and in Group II, 3 of 6 children had the highest blood glucose levels in the 60-minute sample. In Groups III, IV, and V, 47% of children had the highest blood glucose concentration in the 60-minute sample. The 240-minute blood glucose concentration in the oral test was the same for all groups (total mean, 74.7 mg/100 ml), although in the children belonging to Group I the mean was slightly higher (79.4 mg/100 ml).

Apparent Nitrogen Absorption

On admission, in the malnourished children who were receiving 112 mg N/kg/day, N absorption (as % of intake) was significantly lower ($P < 0.02$) in Group I (mean ± SD = 52.6 ± 16.4) when compared to Group II (mean ± SD = 69.7 ± 7.3). However, when N intake was raised to 320 mg/kg/day (2 g of protein/kg/day), apparent N absorption as % of intake did not differ in any group, the means and corresponding standard deviations ranging from 78.6 ± 5.4 to 84.7 ± 5.2.

Vitamin B_{12} Absorption

To investigate the absorptive capacity of this vitamin, 10 PCM children were studied on admission, 9 during early recovery (12 days of therapeutic diet) and 10 when fully recovered or in advanced recovery. The results of these stud-

Table 5. Urinary ^{57}Co-Vitamin B_{12} Excretion

	Admission	Early recovery	Recovered
Creatinine height index	0.58 ± 0.10*	0.64±0.09	0.87±0.02
^{57}Co Urinary excretion in 24 hr (% of dose)	9.4 ±8.5	17.0±10.1	31.4±9.7
Number of tests	20	9	10

*Mean ± SD

Significance levels; recovered vs. admission, $P<0.01$; recovered vs. early recovered, $P<0.02$

ies are presented in Table 5. The children were not separated on the basis of their CHI on admission, since there was no significant difference in those with CHI above or below 0.55. Also, since intrinsic factor administration had no effect (18) the 20 tests are presented together. Over 90% of the urinary radioactivity appeared during the first 24-hour collection in all cases. Recovered children excreted significantly greater amounts of ^{57}Co than children on admission or during early recovery. There was a significant correlation ($P < 0.01$) between CHI and ^{57}Co urinary excretion ($r = 0.493$).

DISCUSSION

Severely PCM children were tested for substrates requiring different processes of digestion and absorption and also utilizing both upper and lower small intestinal function; these children appeared to have marked malabsorption of all the substrates tested. Furthermore, the degree of protein depletion on admission and of protein repletion during recovery were highly correlated with the absorptive capacity for fat, nitrogen, and vitamin B_{12}, as well as with the calculated rate of glucose absorption. Clearly lower correlations were found between these absorption tests and serum albumin levels or weight for height of the children on admission and during recovery.

Vitamin A palmitate absorption and D-xylose urinary excretion did not follow this pattern. We believe that this is due more to the nature of the tests than to the recovery of specific gastrointestinal functions. Nevertheless, they are of value in the final interpretation of results.

Vitamin A palmitate absorption is abnormal only when the malabsorption is severe. This is probably because of the massive dose administered (75,000 units of vitamin A, IV) and because the indicator of its absorption is the peak of vitamin A blood level (13). This peak is subject to various influences such as the space of distribution of vitamin A and liver and tissue uptakes of this vitamin, which make the magnitude of the peak unreliable to measure different degrees of vitamin A absorption. Vitamin A blood levels do not reach 90 to 100 $\mu g/100$ ml of serum (positive absorption) only when vitamin A palmitate is essentially unabsorbed. However, taking this test in conjunction with the results of fat balances, and particularly with the results of the ^{131}I-labeled fats, two facts become apparent: first, that lipolysis, which is an essential intraluminal step for vitamin A palmitate absorption (19), is not a primary factor in the malabsorption of fat in PCM, except possibly in the children who are most severely protein depleted. Furthermore, from this work and from previous results (20), it can be seen that vitamin A palmitate absorption recovers very quickly (in less than a week on adequate therapy), while fat malabsorption persists for longer periods of time. This is in agreement with the fact that lipase activity, even when clearly deficient in severe cases on admission, recovers very early in the process of protein repletion as has been shown in studies in Africa (3) and also in our laboratories (21). Second, lipid transport from the gut and from the liver may be impeded in severe PCM and thus may limit fat absorption (22). However, available evidence (23) also indicates that the lipoprotein systems recover early during nutritional rehabilitation. Blood radioactivity patterns after a dose of purified ^{131}I-labeled fats (2) also do not favor defects in intestinal re-esterification of fatty acids or defects in postintestinal transport of fat.

Urinary excretion of D-xylose may be affected by other variables besides malabsorption per se. Low urinary excretions in 5 hours have been reported in the presence of edema (24); also, the possible metabolism of D-xylose in the intestine by abnormal bacterial flora in the upper gastrointestinal tract may decrease its apparent absorption (25). Protein–calorie malnourished children have increased bacterial flora in the duodenum (6). Because of the coincidence of high D-xylose blood levels with high urinary excretion of this pentose we believe that the renal

phase of this test is not impaired. This belief is also favored by the results of renal function studies in PCM children (9, 26).

The rate of glucose absorption, measured as was done in these children, deserves discussion in light of the data in Table 4. First, in spite of lower fasting blood glucose values in the PCM children on admission, no signs or symptoms of hypoglycemia were observed. Second, the extrapolated blood glucose levels at 0 time in the IV glucose test were similar in all groups, indicating similar spaces of glucose distribution on a per kilo body-weight basis. However, the blood glucose disappearance constant was significantly slower in children in Groups I, II, and III in comparison to Groups IV and V. The reason for this fact is not clear, but PCM children have elevated growth hormone levels (27), and insulin output secondary to glucose stimulation is poor (28, 29). The decreased blood glucose disappearance rate on admission and during early recovery validates further the use of the theoretic blood glucose rise obtained by correcting the glycemia obtained from the oral test, by its disappearance calculated from the IV test. The rate of decline in blood glucose after the maximal rise in the oral glucose test was variable, but the blood glucose concentration in the samples obtained from 150 minutes after the dose was similar in all groups. Figure 4 shows the usefulness of the calculations of the rate of glucose absorption, giving results in the same child when malnourished and when fully recovered. Glycemia throughout the oral absorption test was similar in both instances; however, the rate of glucose disappearance was significantly slower when the child was malnourished. As a consequence, the rate of glucose absorption (theoretic rise in blood glucose in 60 minutes) when the child was recovered was significantly greater than on admission.

With regard to N absorption, we do not know if the malnourished children in this study had some degree of protein-losing-enteropathy, as has been described in severe PCM (30). This possibility would easily explain the lower apparent N absorption observed in children of Groups I and II, and the fact that the decreased N absorption was evident only when the children were receiving 7 g protein/kg body weight/day.

The defect in vitamin B_{12} absorption in PCM children on admission and during early recovery, which is not corrected by giving intrinsic

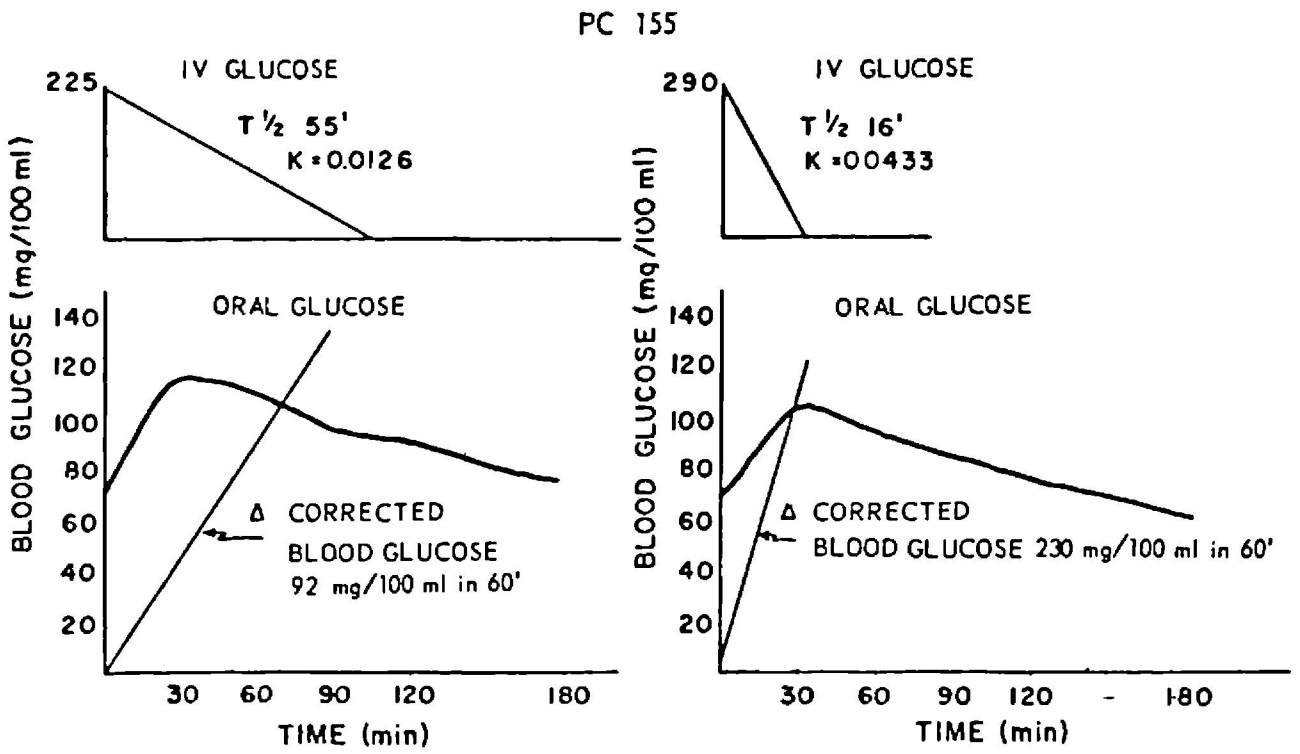

Fig 4. Theory for correction of blood glucose values after an oral dose, by the blood glucose disappearance rate. Results from 1 child studied when severely malnourished (**left**). Results from same child when fully recovered (**right**).

factor, indicates that the terminal ileum of these children is also affected in severe PCM and that its function also recovers slowly, being partly related to the degree of protein repletion. Other factors besides protein depletion, such as bacterial contamination, may be playing an added role in ileal dysfunction in PCM (6, 31, 32). Bacterial overgrowth may also be metabolizing vitamin B_{12} in the intestine (33).

The total integration of the results obtained in this and other studies from our laboratories point to a generalized decrease in the intestinal mucosal function in PCM, which affects the absorption of substances which pass the mucosa through various mechanisms and at different preferential intestinal sites. Neither lactase nor pancreatic lipase deficiencies appeared to be major factors since: a) a similar evolution of the malabsorption in PCM children is observed with lactose-free therapeutic diets (8), and b) lipase levels increase in a matter of days after fat administration even when protein intake is inadequate for protein repletion, the malabsorptive process remaining essentially unchanged (21). Alterations of the intraluminal milieu as a consequence of abnormal proliferation of autochthonous flora (6) and bacterial metabolism of various substrates may play a concomitant role with protein deficiency by altering the physiology of the mucosa (31, 32). However, the high correlations between relative body protein mass as estimated by the CHI and fat, vitamin B_{12}, and rate of glucose absorptions suggest that protein depletion per se is an important factor in the malabsorptive process present in protein deficiency.

It is concluded that the malabsorption in PCM is primarily due to mucosal malfunction or alterations in intestinal milieu which impede mucosal function. The high correlation observed between the degree of protein depletion and repletion and the severity of malabsorption in these children is compatible with the concept that protein deficiency per se is primarily responsible for the malabsorption through still unclear mechanisms.

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