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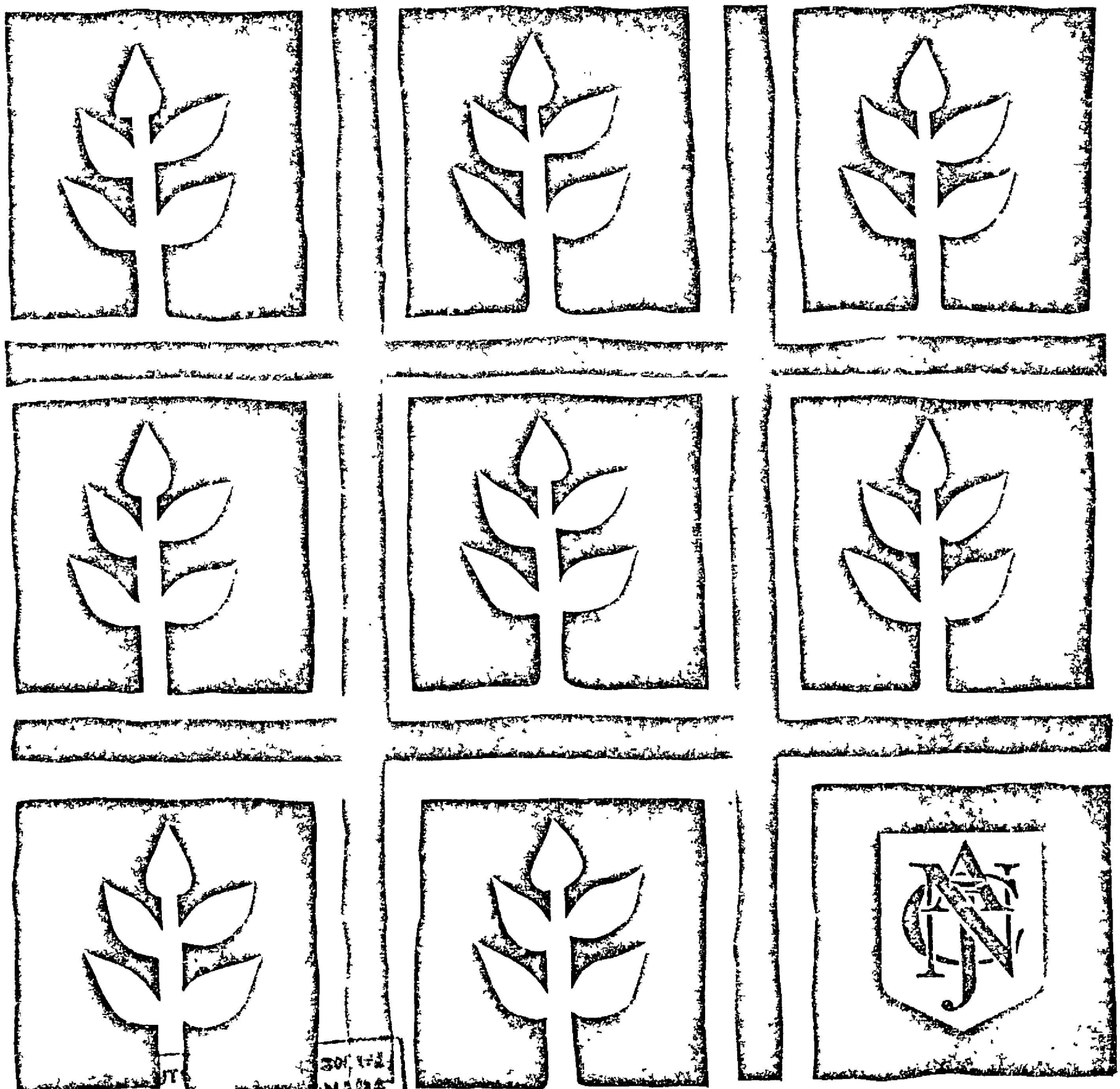

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Vitamin B_{12} absorption in protein–calorie malnourished children and during recovery: influence of protein depletion and of diarrhea[1, 2, 3]

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Information on the absorption of vitamin B_{12} in children is scarce; the only data available pertains to children with infantile pernicious anemia, in whom absorption becomes normal upon the administration of intrinsic factor (1).

A malabsorptive process that appears to be proportional to the severity of protein deficiency and that affects a variety of substrates has been demonstrated in children with severe protein–calorie malnutrition (PCM) (2). Deficiency of intrinsic factor has been suggested in PCM children because free hydrochloric acid had been found to be either low or absent; however, serum levels of vitamin B_{12} are generally high in these children (3).

In protein-deficient rhesus monkeys, a decreased urinary excretion of ^{58}Co-labeled vitamin B_{12} has been documented by the standard Schilling test (4). In these animals, the administration of gastric juice from normal monkeys increased the urinary excretion of ^{58}Co to near normal levels.

Recently, Schneider and Viteri (5) have found decreased conjugated bile salts and increased unconjugated bile salts in duodenal aspirates from PCM children, particularly when diarrhea is present. Alterations in the flora of the small intestine have also been documented in these children (6).

The study of vitamin B_{12} absorption in PCM children and during recovery seems important because it explores a functional aspect to the terminal ileum (where most of the conjugated bile salts are absorbed) and it can provide valuable information for the understanding of bile salt metabolism in PCM and diarrhea. This study demonstrates that vitamin B_{12} absorption is depressed in PCM, particularly when diarrhea is present, and that vitamin B_{12} malabsorption in PCM is not secondary to deficiency of intrinsic factor.

Materials and methods

Twenty-five children with severe PCM were studied. Of these, 15 were investigated within 48 hr after admission to the General Hospital of Guatemala and 10 were studied on the 4th day after admission to the Clinical Center of INCAP.

During the first 8 days of hospitalization, the children studied at INCAP received a casein + 0.2% methionine diet, providing 0.7 g protein and 70 kcal/kg body wt per day, 30% of which were provided by vegetable oil (stabilization diet). Vitamins and minerals, including folic acid and iron, but excluding vitamin B_{12} were given as described before (7). After this period, the same diet at progressively higher concentrations was administered to provide 4 g protein and 120 to 150 kcal/kg per day from day 11 of hospitalization until full recovery was attained. The amount of water given was that necessary to obtain adequate urinary output (more than 200 ml/24 hr). Diarrhea was considered present when at least two of the following criteria were fulfilled: total 24-hr stool weight of 150 g or more, four or more stools per day, and 50% of the stools with abnormal characteristics (8). The children at INCAP were studied again on day 7 after admission while they were receiving a stabilization diet (5, 7), and after 12 days on a high protein diet. Alternate children at the Clinical Center received intrinsic factor during the test on day 4 or on day 7 after admission. All the studies were performed on day 12 after a therapeutic diet that

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included intrinsic factor. Ten children in whom complete nutritional recovery was achieved were also studied at INCAP (control subjects). The main clinical characteristics of the children at the different clinical stages are shown in Table 1.

Vitamin B_{12} absorption was evaluated as follows: a dose of 0.067 μg containing 0.05 μCi ^{57}Co B_{12} (S.A. 750 μCi/mg B_{12}, Abbott Radiopharmaceutical Division, Chicago, Illinois) was administered in a fasting state through a tube placed in the stomach. The tube was rinsed with 60 ml water before withdrawal. Two hours later, 1,000 μg vitamin B_{12} were administered intramuscularly. Three separate 24-hr urine collections were obtained thereafter, and aliquots were counted in a 3-inch NaI well counter. The counting efficiency was adequate, and there was no need for sample concentration. Above 90% of the urinary radioactivity was excreted in the first 24 hr. When intrinsic factor was administered, the dose given was one-third the adult dose. This was given also by stomach tube, simultaneously with the labeled vitamin B_{12}.

TABLE 1
Clinical characteristics of the children

Clinical stage	Admission	Early recovery	Recovered
No. of children	25	9	10
Age, months	25 (14–83)	33 (17–84)	30 (21–44)
Weight-for-height, % of normal	82 (54–109)[a]	82 (55–98)	100 (92–111)
Creatinine height index	0.58[b] (0.38–0.73)	0.64 (0.45–0.78)	0.88 (0.75–0.95)

The nine children studied during early recovery had also been studied upon admission to the Clinical Center. Six of these are also included in the fully recovered group.

[a] Weight with edema. [b] n = 10.

Results

The 24-hr urinary excretion of ^{57}Co-vitamin B_{12} was found to be low in both groups of children with severe PCM studied (Table 2). The simultaneous administration of intrinsic factor produced no improvement in ^{57}Co-B_{12} urinary excretion, some children excreting slightly less or slightly more with intrinsic factor than without. The 24-hr urinary radioactivity rose with nutritional repletion; the children studied 12 days after consuming the therapeutic diet already had significantly higher urinary excretion of ^{57}Co-B_{12} than the same children upon admission ($P < 0.05$). A further rise ($P < 0.01$) was seen in the fully recovered children. The values obtained in the recovered children are similar to those found in children with pernicious anemia to whom intrinsic factor was also administered (1).

Because diarrhea is common in severe PCM and during early recovery, its influence on vitamin B_{12} absorption was also investigated; the children in this study were divided into those with and without diarrhea, accord-

TABLE 2
^{57}Co-vitamin B_{12} urinary excretion in 24 hr in PCM children and during recovery

Clinical stage	Admission		Early recovery	Recovered
Clinical Center				
Creatinine height index	0.58 ± 0.10[a]		0.64 ± 0.09	0.87 ± 0.02
No. of children	10		9	10
Intrinsic factor administration	+	−	+	−
Urinary ^{57}Co-vitamin B_{12} excretion in 24 hr, % of dose	9.4 ± 7.3	10.5 ± 9.6	17.0 ± 10.1	31.4 ± 9.7
General Hospital				
No. of children	15			
Intrinsic factor administration	−			
Urinary ^{57}Co-vitamin B_{12} excretion in 24 hr, % of dose	13.5 ± 9.4		−	−

Recovered children $P < 0.01$ with others. Recovering children $P < 0.05$ with children upon admission in Clinical Center series.

The nine children studied during early recovery had also been studied upon admission to the Clinical Center. Six of these are also included in the fully recovered group.

[a] Mean ± SD.

ing to the criteria previously mentioned (Table 3). The ^{57}Co 24-hr urinary excretion obtained in the PCM and recovering children with diarrhea was lower than that in children without diarrhea. In children without diarrhea, the values obtained during early recovery were similar to those in children with severe PCM but were significantly less than in fully recovered ones.

Finally, Fig. 1 shows the correlation between ^{57}Co-vitamin B_{12} urinary excretion and the degree of protein depletion judged by means of the creatinine height index (CHI) (9).

TABLE 3

^{57}Co-vitamin B_{12} urinary excretion in 24 hr in PCM children and during recovery; influence of diarrhea

Clinical stage	Admission	Early recovery	Recovered
Children with diarrhea	7.9 ± 6.3[a] (22)	4.0 and 0.3[b] (2)	
Children without diarrhea	16.8 ± 9.2 (13)	21.2 ± 6.2 (7)	31.4 ± 9.7 (10)

Number in parentheses refers to number of children.

Significance of differences: upon admission, children with diarrhea versus those without diarrhea, $P < 0.02$. Children without diarrhea, recovered versus admission, $P < 0.01$; versus early recovery, $P < 0.02$.

[a] Mean ± SD. [b] Individual observations.

Discussion

This study indicates that PCM children have decreased urinary excretion of the radioactive vitamin B_{12} administered intragastrically when compared with that excreted by recovered children. As adequate urine output was insured and Viteri and Alvarado (9) have shown unimpaired glomerular filtration rate in PCM children with adequate diuresis, this can be translated into abnormally low vitamin B_{12} absorption. The presence of diarrhea reduced it further not only in children at admission but also after 2 weeks of adequate dietary therapy. Unfortunately, we do not have studies on fully recovered children with diarrhea to observe if vitamin B_{12} absorption is equally reduced when diarrhea is present, but we suspect this may be the case.

With the simultaneous administration of intrinsic factor to severely malnourished children failing to improve the absorption of vitamin B_{12}, it can be concluded that this factor is not responsible for the observed vitamin B_{12} malabsorption; therefore, the cause must lie at the level of the ileum. This situation may be similar to adults with tropical sprue (10) in whom diarrhea is accompanied by ileal malfunction associated with

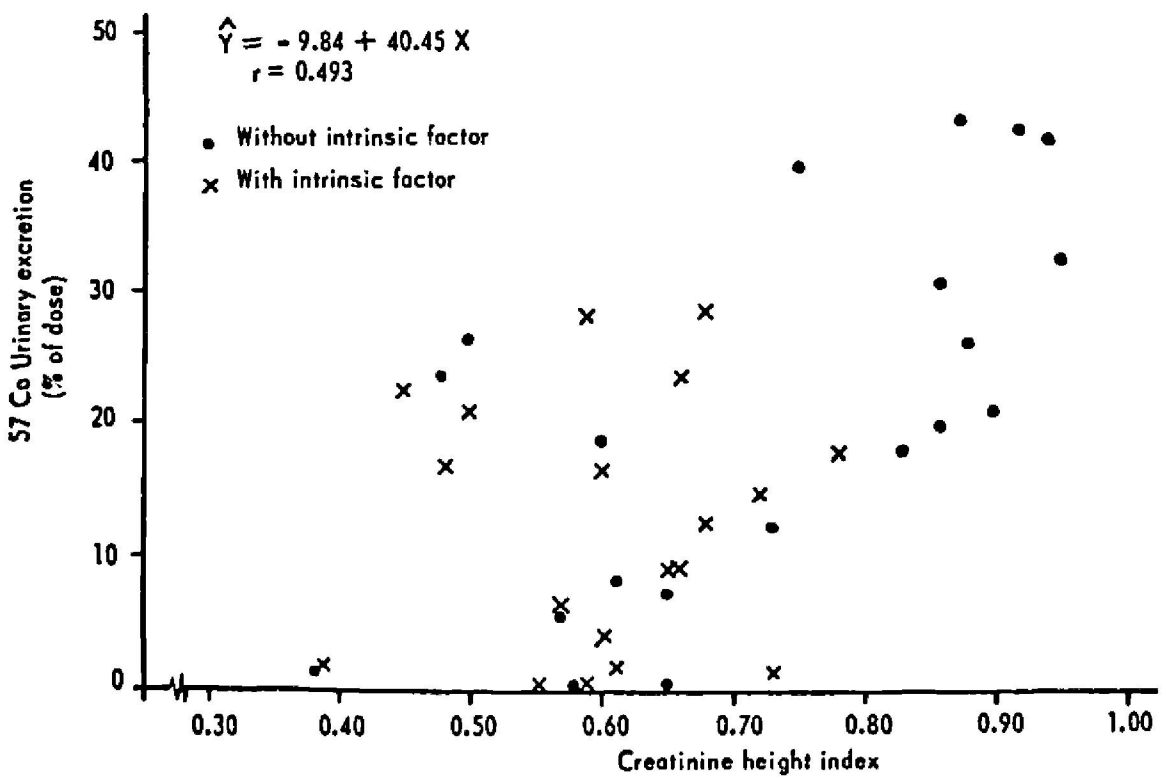

FIG. 1. Vitamin B_{12} absorption in PCM children and during recovery. Correlation between creatinine height index and ^{57}Co-vitamin B_{12} urinary excretion in 24 hr.

bacterial overgrowth and morphological changes in the mucosa; bacterial overgrowth and mucosal morphological alterations have also been observed in PCM children with and without diarrhea (6, 11, 12).

These studies provide information that may be important in explaining the decreased concentration of conjugated bile salts in PCM and diarrhea and the relative increase in unconjugated bile salts. We can speculate that in PCM, decreased ileal function allows a greater proportion of conjugated bile salts to reach the colon (13) and be subjected to bacterial deconjugation and dehydroxylation. Diarrheal episodes could have the same effect, particularly if repeated. These results can also be interpreted as indicative of reduced ileal reserve in PCM that could make these children diarrhea-prone.

Summary

The absorption of ^{57}Co-vitamin B_{12} was studied by means of the Schilling test in 25 severely protein–calorie malnourished children upon admission to the hospital. In 10 of these, the effect of simultaneous intrinsic factor was evaluated, and absorption studies were repeated after 12 days of therapeutic diet. Ten fully recovered children served as controls.

Results indicate that in severe PCM, vitamin B_{12} absorption is low and does not improve with intrinsic factor administration (the mean ± SD urinary excretion of ^{57}Co-B_{12} as percent of dose without intrinsic factor was 12.3 ± 9.5; with intrinsic factor, it was 8.4 ± 7.3). During early recovery, the percent urinary excretion of ^{57}Co rose to 17.0 ± 10.1. These tests were done with the administration of intrinsic factor. The values obtained in fully recovered children were 31.4 ± 9.7; these are similar to those obtained in children with pernicious anemia to whom intrinsic factor is given.

In severely malnourished children and during their early recovery, diarrhea produces a marked drop in vitamin B_{12} absorption, but children without diarrhea in the same clinical stages will absorb subnormal amounts of vitamin B_{12}. Vitamin B_{12} absorption correlates with the creatinine height index (r = 0.493), suggesting that the degree of protein depletion influences vitamin B_{12} absorption. These results are discussed in the light of the possible role the terminal ileum might have in the altered bile salt metabolism described in PCM children and in the presence of diarrhea.

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