Editorial

*Vitamin B_{12} Absorption**

VITAMIN B_{12} is the only known nutrient for which there is required a specific gastric secretion to promote its absorption. It is not known whether the intrinsic factor is absorbed with vitamin B_{12}. The predominant site of absorption in man is believed to be the ileum. Without this gastric secretion persons will become deficient in vitamin B_{12} in spite of a "normal" dietary intake. Vitamin B_{12} which has been biosynthesized with radioactive cobalt as an integral part of the molecule has greatly facilitated the study of vitamin B_{12} absorption in health and in a variety of diseases.

Absorption may be estimated from radioactivity in the feces, urine, plasma, or over the liver. The percentage of the oral dose which is absorbed decreases rapidly as the oral dose is increased above one or two micrograms. To have any meaning, the figure "percentage of the oral dose absorbed (or excreted)" must be stated in reference to the quantity of vitamin B_{12} in the oral dose, and the range of normal will vary depending upon this quantity. To illustrate the importance of the quantity of vitamin B_{12} ingested, one should compare the average percentage of orally administered radioactivity which appears in the urine after a 0.5 μg dose with that appearing after a 2.0 μg dose: 26 per cent vs. 11 per cent. It should be evident that the physiologic significance revolves around the quantity of the vitamin absorbed, *not* the quantity of radioactivity.

Vitamin B_{12} which is bound to intrinsic factor appears to be absorbed preferentially over the unbound vitamin given at the same time. Therefore, one must be certain that the intrinsic factor preparation being tested by radioactive-B_{12} technics is free of nonradioactive vitamin B_{12}. Because of the variability of patients with pernicious anemia, one must be wary of the comparison of intrinsic factor preparation A in patient A with intrinsic factor preparation B in patient B. It is better to compare preparations A and B in the same patient.

Recent publications have described the finding that several hog intrinsic factor preparations, which were known to be active as sources of intrinsic factor in patients with pernicious anemia, inhibited the absorption of a single dose of vitamin B_{12} by some normal persons. There is insufficient evidence to conclude that intrinsic factor preparations should be administered to persons who have normal gastric function. The available data demonstrate that this "inhibition" of vitamin B_{12} absorption in normals is probably due to hog or partially denatured intrinsic factor.

Published data have demonstrated that hog intrinsic factor preparations given daily with vitamin B_{12} over a period of months will raise the serum vitamin B_{12} levels of "normal" or elderly recipients. Of interest are the several reports of treatment of pernicious anemia with oral intrinsic factor-vitamin B_{12} combinations over a period of many months. The hematologic relapse rate has been unexpectedly great and the serum vitamin B_{12} levels have not risen to normal. It would appear that pernicious anemia and other forms of vitamin B_{12}-deficiency due to malabsorption of the vitamin should be treated by injections of the vitamin.

* This editorial has been prepared at the request of the Editorial Board.

After the oral ingestion of "physiologic" (i.e., 1–2 μg) doses of radioactive vitamin B_{12}, there is a delay of three to four hours before radioactivity appears in the plasma, and the maximum is reached at about eight to twelve hours. If a much larger oral dose of vitamin B_{12} is given, radioactivity will appear in the plasma much sooner. This second mechanism for absorbing at higher oral doses appears to be intact in patients with pernicious anemia.

Sorbitol (D-sorbose) has been shown to enhance plasma vitamin B_{12} levels in normal subjects given oral doses of the vitamin. It is possible that this action is due to a stimulation of gastric secretion of intrinsic factor. Data showing the effects of D-sorbose on vitamin B_{12} absorption in patients unable to produce intrinsic factor will be helpful in understanding the mechanism of action of this compound in normals.

The above comments demonstrate a well-known truism in biology: the answers to yesterday's questions provide the framework for today's problems.[6]

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Letter to the Editor

ON ENHANCEMENT OF VITAMIN B_{12} ABSORPTION

Dear Sir:

The demonstration by Chow, Meier, and Free[1] of facilitation of enteral vitamin B_{12} absorption by admixture with D-sorbitol is of extreme interest, but this may not have been "the first substance other than intrinsic factor" shown to effect such absorption. Some time previously I reported in another connection[2] that on administration by mouth of crude, streptomyces-derived vitamin B_{12} concentrates emulsified in vegetable oil with sorbitan monooleate polyoxyethylene derivative (Tween 80) there appeared to be marked vitamin B_{12} assimilation as evidenced by the same pinkish "skin-flush" and copious diuresis which had been noticed in an occasional patient receiving large parenteral doses of cobalamine. Since the patients in the particular series reported were not those with Addisonian anemia (and therefore may have had absorption conditioned by intrinsic factor) another study was conducted with three patients with relapsant pernicious anemia.

It had been determined previously that hydroxycobalamine, cyanocobalamine, nitrocobalamine, and carbimidocobalamine were all soluble in oleic acid-glycerol trioleate mixtures and that such solutions immediately dispersed to less than 0.5 micron droplet size in aqueous menstruums when 2 to 20 per cent of Tween 80 was incorporated. A single, one ml dose of such Tween-oil-oleic acid solutions containing 500 μg of hydroxycobalamine was given orally to each of three patients with pernicious anemia in relapse.

However, because high oral dosing with ordinary vitamin B_{12} preparations was already known to be followed by remission of classic pernicious anemia, this eventuation in all three patients was not used as a criterion for absorption. Instead, total 24-hour urine outputs, both immediately before and after the test dosings were given to Dr. Roger Kersey of Chas. Pfizer and Company for vitamin B_{12} assay. These assays on the post-dosing specimens were rendered difficult because of unanticipated *high* vitamin B_{12} content which necessitated repeated dilutions to get within the range of the assay procedure.

It was finally determined that each patient excreted from 50 to 150 μg of vitamin B_{12} (activity) during the 24 hours following the 500 μg dose, an order of magnitude, which while not approaching that which would have followed