

# Effect of D-Sorbitol on Absorption of Vitamin B<sub>12</sub> by Human Subjects Able To Produce Intrinsic Factor

VICTOR HERBERT, M.D.,\* MARTIN BIERFASS, M.D.,† LOUIS R. WASSERMAN, M.D.,‡  
SOLOMON ESTREN, M.D.,§ AND EUGENE BRODY, M.D.¶

IT HAS BEEN REPORTED that D-sorbitol will enhance the absorption of vitamin B<sub>12</sub> by healthy young and old subjects when the quantity of vitamin B<sub>12</sub> administered is *supraphysiologic*.<sup>1-3</sup> The present report provides some slight support for the prior findings, but indicates that D-sorbitol does *not* regularly markedly enhance absorption of *physiologic* amounts of vitamin B<sub>12</sub>. It has already been demonstrated that in pernicious-anemia patients D-sorbitol does not enhance absorption of either *physiologic*<sup>1,4</sup> or *supraphysiologic*<sup>4</sup> amounts of vitamin B<sub>12</sub>.

By "physiologic amounts," we mean amounts of vitamin B<sub>12</sub>, such as are found in the usual well-balanced diet, the absorption of which is mediated by intrinsic factor. By "supraphysiologic amounts" we mean quantities of vitamin B<sub>12</sub> much greater than found in the ordinary diet. An aliquot of such large doses is absorbed even in the absence of intrinsic factor, probably by direct diffusion.<sup>8</sup>

---

From the Department of Hematology, The Mount Sinai Hospital, New York, New York.

\* Senior Research Fellow, New York Heart Association and Heart Fund, Inc. † Resident in Hematology; ‡ Director, Department of Hematology; § Assistant Attending Hematologist; Mount Sinai Hospital, New York. ¶ Anna Ruth Lowenberg Fellow in Hematology.

This work was aided by grants and material supplies from the New York Heart Association; the Institute of Arthritis and Metabolic Diseases of the United States Public Health Service; the Lederle Laboratories Research Division, American Cyanamid Company; and the Albert A. List and Frederick Machlin Research Funds.

## METHOD

The procedure, as in a prior study,<sup>4</sup> consisted of oral administration to the fasting subject of either 2 or 30  $\mu$ g of vitamin B<sub>12</sub>-Co<sup>58</sup>, with or without 15 ml of a 70 per cent w/w solution of D-sorbitol in water,<sup>8</sup> concurrent administration of 1 mg of unlabeled vitamin B<sub>12</sub> intramuscularly, collection of all urine for 24 hours, a second 1 mg intramuscular vitamin B<sub>12</sub> injection, and a second 24-hour urine collection. The entire procedure was then repeated, deleting D-sorbitol if it had been used in the first test period or adding it if it had not been used in the first test period. Each oral dose was made up to 100 ml volume prior to administration. The amount of vitamin B<sub>12</sub> excreted in the urine was determined as previously reported.<sup>4</sup>

The validity of repeated Schilling-type tests without a "rest period" between tests has been demonstrated,<sup>5</sup> and the validity of Schilling-type tests with supraphysiologic doses of vitamin B<sub>12</sub> (despite the low percentage of urinary radioactivity) has been suggested.<sup>1</sup>

## RESULTS AND DISCUSSION

Table I demonstrates that D-sorbitol may enhance the absorption of supraphysiologic (30  $\mu$ g) oral doses of vitamin B<sub>12</sub>, as previously reported (using 50  $\mu$ g doses).<sup>1,2</sup> In view of the wide possible variability in sequential Schilling-type tests with supraphysiologic doses, however, four cases provide only suggestive and not

---

<sup>8</sup> Kindly provided by E. B. Clay, Smith Kline & French Laboratories, Philadelphia, Pennsylvania.

TABLE I  
Effect of D-Sorbitol on the Absorption of 30  $\mu\text{g}$  of  
Vitamin B<sub>12</sub>-Co<sup>58</sup> by Healthy Young Adult Males  
 *$\mu\text{g}$  Vitamin B<sub>12</sub>-Co<sup>58</sup> excreted in urine*

Subject	Vitamin B <sub>12</sub> alone			Vitamin B <sub>12</sub> + D-sorbitol		
	Day 1	Day 2	Total	Day 1	Day 2	Total
1	0.38	0.28	0.66	1.00	0.41	1.41
2	0.56	0.44	1.00	1.11	0.51	1.62
3	0.24	0.15	0.39	0.57	0.20	0.77
4 <sup>a</sup>	0.38	0.07	0.45	0.27	0.25	0.52
<sup>a</sup> Average	0.39	0.24	0.63	0.74	0.34	1.08

<sup>a</sup> Excretion with added D-sorbitol measured prior to excretion without added D-sorbitol.

definitive evidence for such enhancement as a generally occurring phenomenon.

Table II records the effect of D-sorbitol on the absorption of physiologic (2  $\mu\text{g}$ ) oral doses of vitamin B<sub>12</sub> by randomly selected hospitalized adults with normal baseline ability to absorb vitamin B<sub>12</sub>. In the 12 subjects studied, D-sorbitol was associated with enhanced absorption in 8, no effect in 1, and decreased absorption in 3. While some enhancement by D-sorbitol is suggested in the majority of the subjects, statistical evaluation of the results

does not indicate a definite general enhancing effect of D-sorbitol on absorption of physiologic doses of vitamin B<sub>12</sub>.

The mechanism of action of D-sorbitol with relation to vitamin B<sub>12</sub> absorption has not yet been elucidated. The available facts suggest that its action in enhancing vitamin B<sub>12</sub> absorption (when it does so) is by stimulation of the gastric secretion of intrinsic factor,<sup>6</sup> as with carbamylcholine.<sup>7</sup> Just as carbamylcholine injection has raised the vitamin B<sub>12</sub> absorption of "low absorbers" to normal,<sup>7</sup> so, in one case studied by our group, oral administration of D-sorbitol raised a low (5.8 per cent radioactive vitamin B<sub>12</sub> in the urine in 48 hours) absorber of vitamin B<sub>12</sub> to normal (13 per cent in the urine in 48 hours). Study of other "low absorbers," using D-sorbitol to "enhance gastric secretion of intrinsic factor," is necessary before any conclusions may be drawn, however.

It is possible that D-sorbitol may prove to be a useful agent therapeutically in the limited number of individuals whose baseline secretion of intrinsic factor is inadequate but whose gastric mucosa can be stimulated to produce normal amounts of this substance. Whether

TABLE II  
Effect of D-Sorbitol on the Absorption of 2  $\mu\text{g}$  of Vitamin B<sub>12</sub>-Co<sup>58</sup> by Adults with Various Illnesses but with Normal Baseline Vitamin B<sub>12</sub> Absorption  
*% of Oral dose excreted in urine*

Age	Sex	Diagnosis	Vitamin B <sub>12</sub> alone			Vitamin B <sub>12</sub> + D-sorbitol			D sorbitol effect
			Day 1	Day 2	Total	Day 1	Day 2	Total	
63	F	Treated iron deficiency	8.4	3.6	12.0	16.4	7.5	23.9	+
34	F	Syphilitic aortitis	13.7	3.8	17.5	18.8	6.4	25.2	+
51	M	Myocardial infarction	7.5	2.8	10.3	11.1	5.7	16.8	+
58	M	Polycythemia rubra vera	7.3	3.7	11.0 <sup>a</sup>	12.4	3.9	16.3 <sup>a</sup>	+
34	F	Boeck's sarcoid	9.6	3.3	12.9 <sup>a</sup>	13.4	4.0	17.4 <sup>a</sup>	+
47	F	Subendocardial infarct	14.6	5.4	20.0	13.8	8.2	22.0	+
49	F	Diabetes mellitus	14.7	8.5	23.2	16.8	8.4	25.2	+
28	F	Cholecystitis	12.6	5.2	17.8	11.0 <sup>b</sup>	8.0	19.0 <sup>b</sup>	+
38	F	Lupus erythematosus	6.5	4.7	11.2	6.6	4.6	11.2	0
72	M	Arteriosclerotic heart dis.	7.9	4.1	12.0 <sup>a</sup>	7.9	2.3	10.2 <sup>a</sup>	-
65	F	Pleural effusion	11.4	3.7	15.1	9.1	3.7	12.8	-
35	M	Aspiration lung abscess	10.4	7.2	17.6	8.6	5.0	13.6	-
AVERAGE URINARY EXCRETION			10.4	4.7	15.1	12.2	5.6	17.8	—

<sup>a</sup> Excretion without added D-sorbitol measured prior to excretion with added D-sorbitol.

<sup>b</sup> Part of this 24-hour urine collection lost; hence enhancement by D-sorbitol actually greater than amount recorded.

it serves any useful purpose in terms of vitamin B<sub>12</sub> absorption in individuals whose baseline intrinsic factor secretion is either zero or normal is questionable.

#### SUMMARY

D-sorbitol may enhance the absorption of supraphysiologic (30  $\mu$ g) and in some cases physiologic (2  $\mu$ g) oral doses of vitamin B<sub>12</sub> in individuals whose ability to secrete intrinsic factor is normal. Any therapeutic utility of this agent in terms of enhancing vitamin B<sub>12</sub> absorption remains questionable.

#### ADDENDUM

Since submission of this paper, Chalmers and Shinton (*Nature, London* 183: 118, 1959) found that D-sorbitol, in individual doses smaller than we used, had no enhancing effect on the absorption of supraphysiologic doses of vitamin B<sub>12</sub> by normal subjects, as measured by serum vitamin B<sub>12</sub> levels. Additionally, Heinrich, Skibbe, and Staak (*Ztschr. f. Naturforsch.* 14b: 42, 1959) reported that D-sorbitol had a measurable but therapeutically insignificant enhancing effect on vitamin B<sub>12</sub> absorption by two patients with pernicious anemia, and no effect on vitamin B<sub>12</sub> absorption by two normal subjects.

#### REFERENCES

1. CHOW, B. F., HORONICK, A., and OKUDA, K.: Effect of an elixir on the absorption of vitamin B<sub>12</sub> by healthy young and old subjects. *AM. J. CLIN. NUTRITION* 4: 434, 1956.
2. CHOW, B. F., MEIER, P., and FREE, S. M.: Absorption of vitamin B<sub>12</sub> enhanced by D-sorbitol. *AM. J. CLIN. NUTRITION* 6: 30, 1958.
3. CORNMAN, H.: Elevation of plasma B<sub>12</sub> levels after oral administration of vitamin B<sub>12</sub> and a "non-intrinsic factor" additive to humans. Presented at Third Vitamin B<sub>12</sub> Symposium, New York, February, 1958.
4. ELLENBOGEN, L., HERBERT, V., and WILLIAMS, W. L.: Effect of D-sorbitol on absorption of vitamin B<sub>12</sub> by pernicious anemia patients. *Proc. Soc. Exper. Biol. & Med.* 99: 257, 1958.
5. ELLENBOGEN, L., WILLIAMS, W. L., RABINER, S. F., and LICHTMAN, H. C.: An improved urinary excretion test as an assay for intrinsic factor. *Proc. Soc. Exper. Biol. & Med.* 89: 357, 1955.
6. HERBERT, V.: Sorbitol and vitamin B<sub>12</sub> absorption (Letter to the editor). *AM. J. CLIN. NUTRITION* 6: 547, 1958.
7. MOLLIN, D. L., BOOTH, C. C., and BAKER, S. J.: The absorption of vitamin B<sub>12</sub> in control subjects, in Addisonian pernicious anaemia and in the mal-absorption syndrome. *Brit. J. Haemat.* 3: 412, 1957.
8. DOSCHERHOLMEN, A. and HAGEN, P. S.: A dual mechanism of vitamin B<sub>12</sub> plasma absorption. *J. Clin. Invest.* 36: 1551, 1957.

