Oral Administration of Co^{60} Vitamin B_{12} in Pernicious Anemia.* (20155)

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Welch *et al.*(1) reported the fecal excretion of 70-95% of radioactive cobalt after an orally administered dose of 0.5 μg of Co^{60} vit. B_{12} in pernicious anemia in remission. The addition of normal gastric juice or concentrated hog stomach reduced the excretion to 5-30%. One subject excreted 70, 95, and 95% activity of 3 administered doses. When 10.0 mg of hog stomach concentrate were ingested, the stools contained only 25% of this activity. One hundred mg of this extract did not affect the amount excreted. Smith(2) demonstrated in the rat that orally administered Co^{60} vit. B_{12} is found in the stool largely in a conjugated or degraded form but not as ionized cobalt(2).

The present study was undertaken to determine the effect of various agents on the excretion of radioactive cobalt after oral administration of Co^{60} vit. B_{12} to 4 patients with pernicious anemia. All were in satisfactory clinical and hematologic remission. One of the persons was receiving 30 μg of vit. B_{12} intramuscularly twice weekly, another 30 μg parenterally every 2 weeks. The 2 remaining cases had not been treated for 6-9 months because of failure to attend the clinic. The subjects were in the lower economic group but apparently consumed adequate nutritional diets. No effort was made to limit the diet in any respect during the period of the experiment. The radioactive vit. B_{12} used in these studies had a specific activity of about 245 μc per mg. A standard was prepared consisting of 1.0 μg diluted in 280 cc of water and set up in a paraffin lined sealed waxed cardboard container. Measurements were made by placing the container directly on a well shielded scintillation counter. The dose administered to the patients (1.0 μg) was adjusted to equal the activity of this standard. It was given in the morning in 280 cc of water. Breakfast was withheld until noon. Each person was instructed to defecate into a waxed container identical in size with the standard. These were identified by name, date, and time of evacuation. Specimens of stools were diluted with water to 280 cc and stirred until a homogenous mixture was obtained. Calculations of excretion were based on a comparison with the known standard. Two to 3 stools were collected and measured for radioactivity after background values were attained. No urine excretion studies were made in pernicious anemia cases. After base line fecal excretions were determined the patients received in addition to 1.0 μg of Co^{60} vit. B_{12} 2.0 mg of folic acid, 15.0 mg of a known potent intrinsic factor prepared from hog duodenal mucosa, 50.0 g of ventriculin,† a "primary period" of 10.0 mg of folic acid orally, daily, for one week prior to administration of the radioactive vit. B_{12}, 150 cc of neutralized normal gastric juice (3 cases) and 2.0 g of aureomycin daily for 6 days (3 cases). Five healthy normal persons and 2 patients in mild cardiac decompensation served as controls. Urine from this latter group was examined for radioactivity.

TABLE I. Radioactivity of Stools Following Oral Administration of 1.0 μg of Co^{60} Vit. B_{12} to 7 Normal Subjects.

Patient	Age	Total fecal excretion of Co^{60}, %	Days to reach max. excretion
H.N.	53	12	5
N.N.	48	21	5
N.A.	30	39	3
N.R.	30	30	3
F.A.	24	36	9
L.M.	47	47	4
S.M.	28	59	3

Results. Summaries of the data are pre-

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† Manufactured by Parke, Davis and Co., Detroit, Mich. (Two different batches used.)

TABLE II. Radioactivity of Stools Following Oral Administration of 1 μg of Co^{60} Vit. B_{12} and Various Agents to 4 Patients with Pernicious Anemia in Remission.

Patient	Age	Co^{60} B_{12}, %	Co^{60} B_{12} + intrinsic factor, %	Co^{60} B_{12} + 50 g ventriculin, %	Co^{60} B_{12} + 2 mg folic acid, %	Co^{60} B_{12} preceded by 1 wk of 10 mg folic acid daily, %	Co^{60} B_{12} + 150 cc gastric juice, %	Co^{60} B_{12} + aureomycin, %
M.S.	50	98	80	90* 91†	99	94	70	96
L.F.	65	93 89	51	75*	55	91	73	93
J.M.	68	99	85	99†	95	96	—	—
L.G.	52	97	98	98†	99	92	67	97

* Ventriculin A. † Ventriculin B.

sented in Tables I and II. It is evident that under the conditions of this experiment the normal subject excreted between 12 and 59% activity of the orally administered dose of Co^{60} vit. B_{12} in 3 to 9 days. Unfortunately, the supply of material did not permit repeated studies in the same subjects to determine if the amount excreted is constant for the individual. Such investigations are now being pursued with a radioactive compound having a lower specific activity. The 2 persons (L.M. and S.M.) showing 47% and 59% excretion, respectively, had adequate free HCl in the gastric juice. Urine specimens from cases H.N. and N.N. failed to disclose any radioactivity for periods up to 8 days after ingestion of vit. B_{12}.

The patients with pernicious anemia showed an excretion of radioactivity varying from 89-99% of the administered dose. Addition of 2 mg of folic acid had no effect in 3 subjects but significantly reduced the excretion about 39% in patient L.F. Oral administration of 10 mg of folic acid for one week prior to ingestion of Co^{60} vit. B_{12} produced no change from the "pernicious anemia pattern" in any of the cases. With the use of a known potent intrinsic factor patient L.F. showed a reduction in excretion of about 45% but no significant change was observed in the other 3 patients. She also had a decrease in excretion when the dose of Co^{60} vit. B_{12} was given with 50 g of ventriculin, whereas the other patients maintained a high excretion rate. The 3 subjects given 150 cc of neutralized normal gastric juice showed a reduction of about 30% in excretion. Aureomycin, 2.0 g daily for one week, had no effect.

In a series as small as the present one it is difficult to reconcile these results with those of Welch and his coworkers(1). The latter administered 0.5 μg of Co^{60} vit. B_{12} (0.03 μc), whereas in the present study each patient received 1.0 μg with a specific activity of 0.245 μc. More patients with pernicious anemia, both in relapse and in remission, are being investigated, using a compound having a specific activity of 0.03 μc/μg.

Conclusions. Following oral administration of 1.0 μg of Co^{60} vit. B_{12}: 1. Seven normal persons excreted 12-59% of radioactive cobalt in the stool in 3-9 days. 2. No activity could be found in the urine of 2 normal subjects up to 8 days after ingestion of the vitamin. 3. Four patients with pernicious anemia in remission excreted 89-99% of the dose in the stool. 4. In 3 of these cases 2 mg of folic acid, 10 mg of folic acid for one week, 50 g of ventriculin, and 15 mg of intrinsic factor had no appreciable effect on the amount excreted. 5. In one case 2 mg of folic acid and 15 mg of intrinsic factor reduced the excretion of Co^{60} about 40%, and 50 g of ventriculin cut the fecal activity about 25%. 6. In 3 patients 2 g of aureomycin for one week had no effect and 150 cc of neutralized normal gastric juice reduced the fecal activity about 30%.

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1. Welch, A. D., Scharf, V., Heinle, R. W., and Meachum, G. C., *Fed. Proc.*, 1952, v11, 308.
2. Smith, E. L., *Brit. Med. Bull.*, 1952, v8, 203.

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