

cerebral injection of the Lansing strain of virus. Control animals inoculated at the same time with the same amount of virus were allowed to rest in their cages. In all 7 experiments, the incidence of the disease as measured both by paralysis and by death was greater in the exercised animals than in the resting controls.

Valuable technical assistance in this work has been rendered by Esther Parker and Alice Hamlin.

1. Russell, W. R., *Brit. M. J.*, 1947, v2, 1023.
2. Hargreaves, E. R., *Brit. M. J.*, 1948, v2, 1021.
3. Russell, W. R., *Brit. M. J.*, 1949, v1, 465.
4. Horstmann, D. M., *J. Am. Med. Assn.*, 1950, v142, 236.
5. Albrecht, R. M., and Locke, F. B., *J. Am. Med. Assn.*, 1951, v146, 769.
6. Brahdy, M. B., and Katz, S. H., *J. Am. Med. Assn.*, 1951, v146, 772.
7. Kilham, L., Levens, J., and Enders, J. F., *J. Am. Med. Assn.*, 1949, v140, 934.
8. Levinson, S. O., Milzer, A., and Lewin, P., *Am. J. Hyg.*, 1945, v42, 204.

9. Hill, A. B., *Principles of Medical Statistics*, London, The Lancet Limited, 3rd edition, 1945, 92.
10. Perla, D., and Marmorston, J., *Natural Resistance and Clinical Medicine*, Boston, Little, Brown and Co., 1941, 1137.
11. Schwartzman, G., *Proc. Soc. Exp. Biol. and Med.*, 1950, v75, 835.
12. Ainslie, J. D., Francis, T., Jr., and Brown, G. C., *J. Lab. and Clin. Med.*, 1951, v38, 344.
13. Foster, C., Sigel, M. M., Henle, W., and Stokes, J., Jr., *J. Lab. and Clin. Med.*, 1951, v38, 359.
14. Schwartzman, G., and Fisher, A., *J. Exp. Med.*, 1952, v95, 347.
15. Findlay, G. M., and Howard, E. M., *J. Pharm. and Pharmacol.*, 1952, v4, 37.
16. Mann, G., *J. Anat. and Physiol.*, 1894, v29, 100.
17. Faure, C., and Soula, C., *Compt. rend. Soc. Biol.*, 1913, v74, 350.
18. Hydén, H., *Acta Physiol. Scand.*, 1943, v6, Supp. 17.
19. Barr, M. L., and Bertram, E. G., *J. Anat.*, 1951, v85, 171.

Received June 11, 1953. P.S.E.B.M., 1953, v83.

Oral Administration of Co⁶⁰ Vit. B₁₂ in Tropical Sprue and Hepatic Cirrhosis and Diarrhea.* (20457)

LEO M. MEYER, RAMON M. SUAREZ, JR., ROBERTO BUSO, JUAN SABATER, AND
RAMON M. SUAREZ.

From the Laboratories of the Fundacion de Investigaciones Clinicas and the Hospital Mimiya, Santurce, P. R.

Smith reported that in the stools of rats fed Co⁶⁰ vit. B₁₂ the radioactivity is present in a conjugated or degraded form of the vitamin but not as ionized cobalt(1). Rosenblum and his coworkers regarded this as unlikely and concluded that vit. B₁₂ is destroyed in the feces, probably by bacterial action(2). Barbee and Johnson, by means of radioautographs of paper strip chromatograms, showed that the feces of rats contained considerable ionic

Co⁶⁰ after oral administration of the labelled vitamin, and that all the radioactivity in the feces after injection is in this form(3).

The present study was undertaken to determine fecal excretion of radioactive cobalt following oral administration of Co⁶⁰ vit. B₁₂

TABLE I. Radioactivity of Stools Following Oral Administration of 0.5 µg of Co⁶⁰ Vit. B₁₂ to 4 Normal Subjects.

Patient	Age	Total fecal excretion of Co ⁶⁰ (%)
D.	26	78
O.	30	31
R.	30	39
S.	33	50

* Radioactive vit. B₁₂ was supplied by Merck and Co., Rahway, N. J. Expenses for these studies were partially defrayed by grants from the Squibb Institute for Medical Research, New Brunswick, N. J. and the Lederle Laboratories Division, American Cyanamid Co., Pearl River, N. Y.

TABLE II. Radioactivity of Stools Following Oral Administration of 0.5 μ g of Co⁶⁰ Vit. B₁₂ and Folic Acid to 6 Patients with Tropical Sprue in Relapse and 1 Person with Cirrhosis of the Liver and Diarrhea.

Patient	Age	Free HCl	.5 μ g Co ⁶⁰ B ₁₂ (%)	.5 μ g Co ⁶⁰ B ₁₂ + 1 mg folic acid (%)	.5 μ g Co ⁶⁰ B ₁₂ + 5 mg folic acid (%)	.5 μ g Co ⁶⁰ B ₁₂ + 10 mg folic acid daily for 7 days (%)	.5 μ g Co ⁶⁰ B ₁₂ + 10 mg folic acid daily for 3 mo (%)
M.R.	25	+	46				
A.C.	60	+	32				
R.H.	62	+	34				
P.V.	25	+	19			57	
V.L.	65	—	59 66*	83	18	88	
J.S.	15	+	91 67†	56	24	3	1
C.L.	30	+	90	100	91	33	

* Repeated after patient received .5 μ g Co⁶⁰ B₁₂ and 1 mg folic acid.

† " " " " " " " " 5 mg " " " "

to 6 patients with tropical sprue in relapse and one subject with hepatic cirrhosis and diarrhea. Free HCl was present in the gastric juice in all instances except one (V.L.). All cases showed a flat glucose tolerance curve following ingestion of dextrose. The labelled vitamin had a specific activity of 0.245 μ C/ μ g. In each experiment the patient received 0.5 μ g in 250 ml of water in the morning. Breakfast was withheld until noon. During the period of observation the patients received an inadequate diet, the so-called "preliminary sprue diet" which is low in proteins and vitamins, and consists mainly of rice, beans, root and starchy vegetables, and small amounts of milk and cod-fish. Stool collections and measurements were made in the manner previously described(4). When fecal radioactivity returned to background 3 of the patients received one and 5 mg of folic acid orally with the radioactive vit. B₁₂. Four of the subjects were given 10 mg of folic acid, orally, daily, for one week and then treated with one dose of Co⁶⁰ vit. B₁₂. One patient received 10 mg of folic acid orally, daily, for 3 months and then a single dose of the labelled vitamin. Four normal young adults on regular hospital diets served as controls. No gastric extractions were performed on them.

Results. Summaries of the data are presented in Tables I and II. Patients M.R., A.C., and R.H. refused to cooperate after the preliminary survey and were lost for future study. Under the conditions of the experi-

ment the normal subjects excreted 31 to 78% activity of the orally administered dose. Patients with tropical sprue in relapse excreted 19 to 91%. Following the simultaneous ingestion of 1 mg of folic acid and 0.5 μ g of labelled vit. B₁₂ there was no change in fecal radioactivity in 2 cases and reduction of about 30% in a third (J.S.). This latter patient showed a suboptimal reticulocytosis and hematologic improvement following the single combined dose. Oral administration of a second dose of Co⁶⁰ vit. B₁₂ to this patient was followed by an excretion of 67% of ingested activity. The ingestion of 5 mg of folic acid and 0.5 μ g of radioactive vit. B₁₂ to 3 subjects resulted in high fecal activity in one (C.L.) and striking reductions in 2 (V.L. and J.S.). The oral administration of 10 mg of folic acid, orally, daily, for one week, followed by a single dose of 0.5 μ g of labelled vit. B₁₂ resulted in elevated fecal activity in 2 patients (P.V. and V.L.) and low activity in the others (J.S. and C.L.). There was an almost complete absence of stool radioactivity in the patient who was treated with 10 mg of folic acid, orally, daily, for 3 months and received 0.5 μ g of Co⁶⁰ vit. B₁₂ at the end of that period.

Summary. From the data it is apparent that no conclusion can be reached regarding interpretation of Co⁶⁰ activity in the stool following oral administration of 0.5 μ g of radioactive vit. B₁₂ because of the wide normal range which overlaps with that of patients

with tropical sprue in relapse and one subject with hepatic cirrhosis and diarrhea. No consistent pattern of change was observed when folic acid was added. The variable results do not bear any relationship to the presence or absence of free HCl in gastric juice.

1. Smith, E. L., *Brit. Med. Bull.*, 1952, v8, 203.

2. Rosenblum, C., Chow, B. F., Condon, G. P., and Yamamoto, R. S., *J. Biol. Chem.*, 1952, v198, 915.

3. Barbee, K. W., and Johnson, B. C., *PROC. SOC. EXP. BIOL. AND MED.*, 1951, v76, 720.

4. Meyer, L. M., *PROC. SOC. EXP. BIOL. AND MED.*, 1953, v82, 490.

Received June 15, 1953. P.S.E.B.M., 1953, v83.

Accentuation of Human Diabetes by "Pituitary Growth Hormone".* (20458)

LAURANCE W. KINSELL, HARRY E. BALCH, AND GEORGE D. MICHAELS.
(With the technical assistance of June Bilisoly, George Fukayama, Eleanor Kipp,
Florence Olson, and Sadie Smyrl)

*From the Institute for Metabolic Research of the Highland Alameda County Hospital,
Oakland, Calif.*

Young demonstrated that extracts of the anterior pituitary, which possessed growth-promoting effects, were also diabetogenic(1). Subsequently it has been shown that more highly purified growth hormone preparations retain the property of diabetogenicity in experimental animals(2). It appears to be well established that these diabetogenic effects are not related to ACTH contamination. In studies with "pituitary growth hormone preparations" in human subjects, under chemically controlled metabolic ward conditions extending over the period 1948 to 1953, we have failed to note any diabetogenicity of the preparations used. However, except in one subject, we have also failed to obtain growth-promoting effects(3).

The present study was carried out in a 60-year-old male patient with diabetes mellitus of at least 5 years' duration, and of some severity. It was designed to determine whether "highly purified pituitary growth hormone" would have either growth-promoting or diabetogenic effects under the experimental conditions used.

Experimental. The patient was well equilibrated on a formula diet containing 119 g of protein, 130 g of fat, and 184 g of carbohy-

drate. The formula was ingested at hourly intervals during the period 6:00 a.m. to 10:00 p.m. Urine and stool collections and chemical and other determinations were carried out as described elsewhere(4). The growth hormone was administered by slow intravenous drip in a solution containing 2 g of potassium chloride and 2 g of sodium chloride per liter. In order to make for precise constancy of conditions throughout the study, the intravenous sodium-potassium chloride solution was administered during the control as well as the treatment periods. Growth hormone (Armour, Lot No. 491132) was administered during the treatment period in a dose of 100 mg equivalents per day, in one liter of solution at a rate of 180 cc per hour. Forty units of N.P.H. insulin daily were given throughout. The assay of the growth hormone provided by Drs. Hays and Steelman and their associates of the Armour Laboratories was as follows: potency— 49.5 ± 10 mg stand./vial; T.S.H.— $.04 \pm .02$ USP u/mg; oxytocin — $<.8$ u/vials; fill—50 mg; ACTH — $<.01$ u/mg; pH—9.4.

Experimental findings. As shown in Fig. 1 and 2, the effects of "pituitary growth hormone" in this patient were as follows: 1. Blood and urine sugars were elevated during and following the administration of the hormone. The daily urinary sugar excretion

*This work was supported by grants from the Armour Laboratories and the National Institutes of Health.