

Absorption of Nitrite After the Oral Ingestion of Bismuth Subnitrate.

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Stieglitz¹ advocated the use of bismuth subnitrate in the treatment of hypertension. He suggested that the nitrate was partially reduced in the intestine and that the absorbed nitrite was responsible for the desired therapeutic action. In the majority of cases, nitrite was found in the urine. Ayman² recently reported that the drug had no demonstrable effect on the blood pressure. Several cases of nitrite poisoning following ingestion of bismuth subnitrate have been reported.^{3, 4} In most cases, large quantities had been given for x-ray examination to patients with open intestinal lesions or hypersensitive mucosae.

If bismuth subnitrate is partially decomposed with absorption of nitrite, the absorption of some bismuth might be expected. The metal has been reported in the tissues and urine following ingestion of the subcarbonate.⁵

It was planned to study the urinary excretion of bismuth, nitrate and nitrite in normal individuals receiving the amount of the subnitrate recommended by Stieglitz. The diet was not rigidly controlled, although variation from day to day was not great. Corned meats and large amounts of vegetables were avoided. 0.5 gm. of the drug was taken 3 times a day for a month. At the end of the period a purge of magnesium citrate cleared the intestinal tract as quickly and thoroughly as possible, and a short after-period was run. Bismuth determinations were made by the method of Leonard,⁶ nitrates after Whalen,⁷ and qualitative nitrite tests by the Gries (as modified by Hyman and Mann⁸) and Fearon⁹ procedures.

Within 2 days of the start of the bismuth subnitrate ingestion, the urinary nitrate nitrogen increased from 4.9 mg. to 57.8 mg. in

¹ Stieglitz, E. J., *J. Am. Med. Assn.*, 1930, **95**, 842; *Arterial Hypertension*, New York, Paul B. Hoeber, Inc., 1930.

² Ayman, D., *J. Am. Med. Assn.*, 1932, **98**, 545.

³ Beck, E. G., *J. Am. Med. Assn.*, 1909, **52**, 14.

⁴ Frick, A., *J. Am. Med. Assn.*, 1924, **82**, 595.

⁵ Müller, H., and Kärthy, L., *Biochem. Z.*, 1924, **149**, 239.

⁶ Leonard, C. S., *J. Pharmacol. and Exp. Therap.*, 1926, **28**, 81.

⁷ Whelan, M., *J. Biol. Chem.*, 1930, **86**, 189.

⁸ Hyman, A., and Mann, L. T., *J. Urol.*, 1929, **22**, 521.

⁹ Fearon, W. A., *Dublin J. Med. Science*, March, 1920, Fourth Series, No. 1. Abstracted in *J. Am. Med. Assn.*, 1920, **74**, 1128.

24 hours, or over 1000%, and remained at about 800% of the normal during the drug period. Two days after the purge, the nitrate excretion was back to normal.

Bismuth was never detected although the method used measures 0.01 mg. in 100 cc. of urine. All of the samples gave negative nitrite tests with the Gries method, which gives a positive test with less than 0.0001% of nitrite nitrogen. The Fearon test, however, was positive throughout the period of drug ingestion. This was due to the fact that the test is not specific for nitrite. Nitrates, in concentrations such as were found in the urine during the experimental period, will give a green color which more or less resembles the test for nitrites.

A repetition of this experiment with another individual gave similar results. Blood pressure readings on 2 dogs given 2 gm. each of bismuth subnitrate per day over a period of some weeks showed no significant change.

This study neither supports nor opposes the Stieglitz theory. It indicates that the bismuth subnitrate is partially broken down in the intestinal tract, that little, if any, bismuth is absorbed but that the anion is absorbed in appreciable amounts in some form. If the absorption is as nitrite as Stieglitz believes, the ion must be fully oxidized before excretion. The opposite finding of Stieglitz might be explained either as the result of an infection of the urinary tract which would cause a reduction of the nitrate by bacteria in the bladder^{8, 10} or from the use of a non-specific test such as we found the Fearon test to be. Stieglitz did not mention the test used by him.

6170

Time of Appearance and Duration of Pregnancy Cell Types in Hypophysis of the Rat.*

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Numerous observers have reported the presence of peculiar cell types ('pregnancy cells') in the pars anterior of the hypophysis during pregnancy. Despite their rather distinctive appearance little is

¹⁰ Salén, E. B., *Acta med. Scandinav.*, 1926, **68**, 369.

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