

then supplemented by 0.15 unit of progestin weekly in 3 injections for periods up to 110 days. Total doses of from 1.75 to 2.4 units of progestin were given. The mammary rudiments of all the mice had developed into moderately extensive duct systems.

Fourteen male mice were given Proluton§ in daily doses of 0.05 to 0.1 i.u. for periods of from 15 to 26 days. A definite growth of the mammary ducts was observed in 8 non-castrate and in 1 castrate animal. The rudimentary mammary glands of three mature mice receiving 0.05 i.u. and of 2 receiving 0.1 i.u. had failed to grow. Two non-castrate males and one castrated male were given 5 r.u. of theelin and 0.1 i.u. of Proluton daily. All of these animals showed definite growth of the mammary gland.

Two of the above preparations were assayed for the presence of estrogenic hormone. Two-tenths of a unit failed to give vaginal cornification or mucification in castrated female mice. [The minimum amount of estrogenic hormone in oil solution which will give mammary growth has not been determined, but 1 r.u. of theelin in aqueous solution daily, when given in sufficient dilution in two injections, is sufficient. It has also been indicated that old male mice require larger amounts of estrogenic hormone to induce the growth of the mammary glands than younger mice. This might account for the failure of response in 5 of the animals receiving Proluton.

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Does Magnesium Sulphate Cause Catharsis by Being Absorbed and then Excreted into the Colon?

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There are numerous reports in the literature dealing with the mode of action of the saline purgatives. Invariably, 2 main theories are advanced. The first, favored by Meltzer and Auer,¹ Auer,^{2, 3} Frankl,⁴ Mendel and Benedict,⁵ and Cohen,⁶ suggests that the action

¹ Meltzer, S. J., and Auer, J., *Am. J. Physiol.*, 1905, **14**, 366.

² Auer, J., *Am. J. Physiol.*, 1906-7, **17**, 15.

³ Auer, J., *J. Biol. Chem.*, 1908, **4**, 197.

⁴ Frankl, T., *Arch. f. exper. Path. u. Pharmacol.*, 1907, **57**, 386.

⁵ Mendel, L. B., and Benedict, S. R., *Am. J. Physiol.*, 1908-09, **23** (Proc. 18).

⁶ Cohen, H., *Quart. J. Med.*, 1925-26, **19**, 249.

is from the lumen of the intestine. The saline purgative when administered by mouth increases the fluidity and bulk of the feces by causing retention of liquid with some extraction of fluid from the blood; thus catharsis is produced. The salt which is absorbed is incidental and is excreted largely by the kidney, except in cases of nephritis in which the magnesium content of the blood may be increased to dangerous levels.^{7, 8} The second theory, on the contrary, which is supported by the work of MacCallum,⁹ Bancroft,¹⁰ Hertz, Cook and Schlesinger,¹¹ and Robin and Sourdél¹² intimates that the saline purgatives act only after being absorbed and not from the lumen of the intestine. This theory is well stated by MacCallum,⁹ who investigated the problem on the suggestion of Loeb, that, "the presence of the salt in the lumen of the intestine is not necessary for its cathartic action—the salt must be absorbed into the blood before it can act on the intestine."

To determine whether magnesium sulphate was absorbed and excreted in quantity into the colon, we anesthetized several dogs (13 in all) using barbital, nembutal, or morphine and ether. The small intestine was isolated by tying it off at the stomach and the ileocecal valve; the large intestine was washed free from magnesium with warm isotonic sodium chloride solution—care being taken not to damage the intestinal mucosa. A solution of magnesium sulphate (10-15 gm. of the salt, according to the weight of the dog) at approximately 37.6°C. was injected into the small intestine, the abdomen closed and the temperature of the animal kept as nearly normal as possible. At the conclusion of the experiment, which lasted from ½ to 9 hours, the colon was washed out with distilled water and the magnesium of the washings determined following the method of McCrudden.^{13, 14} The amount of magnesium excreted into the colon was found to be insignificant—invariably, less than ½ of 1% of the amount of magnesium injected into the intestine.

An ileostomy was performed aseptically on each of 3 dogs and on the third day after the operation the isolated colon and rectum were washed out with warm isotonic sodium chloride solution. The

⁷ Hirschfelder, A. D., *J. Am. Med. Assn.*, 1934, **102**, 1138.

⁸ Hirschfelder, A. D., *J. Biol. Chem.*, 1934, **104**, 647.

⁹ MacCallum, J. B., *Am. J. Physiol.*, 1903-04, **10**, 101.

¹⁰ Bancroft, F. W., *J. Biol. Chem.*, 1907, **3**, 191.

¹¹ Hertz, A. F., Cook, F., and Schlesinger, E. G., *Proc. Roy. Soc. Med. Lond.*, 1908-9, **2**, Part 3 (Therap. and Pharmacol. Sect.), 21.

¹² Robin, A., and Sourdél, M., *Bull. d. l. Soc. Méd. d. Hopt. d. Paris*, 1912, **38**, 881.

¹³ McCrudden, F. H., *J. Biol. Chem.*, 1909-10, **7**, 83.

¹⁴ McCrudden, F. H., *J. Biol. Chem.*, 1911-12, **10**, 187.

magnesium in the washings was determined. Magnesium sulphate was then given by stomach tube and the colon washed out at the end of 24 hours; the dog having not evacuated within that period. The magnesium was determined from the washings. In all, 5 sets of determinations were made before and after the administration of magnesium sulphate but the salt did not appear to be excreted into the colon to any extent.

Seven normal dogs were kept in separate stalls on a uniform diet. During the first period of 6 days the feces were discarded; during the second period of 6 days an attempt was made to obtain a normal pattern for a particular dog by collecting the feces as soon as possible after they had been excreted and noting the form, markings and other criteria of laxation. The water content was determined later. The feces of a particular dog appeared to be fairly uniform during this period. Then, magnesium sulphate was injected subcutaneously in some cases and intramuscularly or intravenously in others. In the event of a second injection several days were allowed to elapse between the injections. The injection of magnesium sulphate did not appear to influence significantly the water content, form, time, weight or other criteria of laxation as outlined by Cowgill and his coworkers.^{15, 16} In some instances at a later date the dogs were given by stomach tube the same quantity of magnesium sulphate which they had been given intramuscularly and within 24 hours the stools indicated a laxative effect of the salt.

A dog was kept on a uniform diet for 17 days. During this period the dog was injected subcutaneously with 25% $\text{MgSO}_4 \cdot 7\text{H}_2\text{O}$, 2 cc. per kg. bodyweight, and 2 days later was given a dose of magnesium sulphate by stomach tube. The comparative osmotic pressure which the dried material of each stool would exert was determined by the freezing point method. There was no significant change after the injection of the salt but after the administration by stomach tube there was evidence of increased osmotic pressure.

Conclusion. (1) Magnesium sulphate in the dog does not cause laxation or catharsis by being absorbed into the blood and then excreted into the colon. (2) The parenteral administration of magnesium sulphate does not augment the excretion of magnesium by the colonic mucosa to an appreciable extent.*

¹⁵ Cowgill, G. R., and Anderson, W. E., *J. Am. Med. Assn.*, 1932, **98**, 1866.

¹⁶ Cowgill, G. R., Anderson, W. E., and Sullivan, A. J., *J. Am. Med. Assn.*, 1933, **101**, 273.

* This work was aided in part by a grant from the Carnegie Corporation of New York.