3054

On the influence of gastric section on gastric secretion.

W. H. BARBER.

[*From the Department of Experimental Surgery, University and Bellevue Hospital Medical College, New York City.*]

Resection of the pyloric end of the stomach is followed by a diminution in the hydrochloric secretion of the stomach. Circumscising the stomach in the pyloro-fundic region through the serous, muscular, and submucus coats of the gastric wall, or the excision of an annular segment from the wall of the stomach in this region, does not appear to be followed by a persistent fall in the gastric acidity, but by such relative decrease in acidity as can be demonstrated after other intra-abdominal operations. When these two procedures are combined, by dividing the pyloric end from the fundic portion of the stomach, and the pyloric part is left in the abdomen (See preceding paper) it appears that the pyloric pouch, thus created, continues to secrete acid.

From these observations, it appears (a) that the pyloric portion is active in secretion (as it is generally agreed to be in motility); (b) that this secretory function continues after the section of vagal or vago-sympathetic nerves incorporated within or running upon the stomach wall (as does also the motor function of the pyloric portion after section of these same nerve fibres).

3055

The toxicity and urinary elimination of various bismuth preparations.

CLIFFORD S. LEONARD.* (Introduced by Lafayette B. Mendel).

[*From the Department of Pharmacology and Toxicology, Yale University, School of Medicine, New Haven, Conn.*]

A method has been devised for the rapid accurate determination of small quantities of bismuth in body-fluids and tissues.

* National Research Fellow in Medicine.

This depends upon the wet combustion of the organic matter followed by colorimetric determination of bismuth as the iodide.

This new method was used for quantitative studies of the urinary elimination and tissue distribution of bismuth after injection of various bismuth preparations. At the same time the toxicity, M.T.D. and kidney pathology were studied. The bismuth preparations used included the soluble sodium potassium bismuth tartrate, sodium bismuth citrate, sodium bismuth thiosulfate, insoluble bismuth oleate, and the insoluble suspension of precipitated bismuth. All bismuth preparations studied exert a toxic action upon the kidney of the rabbit producing necrosis of the tubules.

Twenty-four rabbits were used in the determinations upon which the results here reported are based. The daily urinary bismuth excretion was followed in some cases for three weeks. Dosages were checked when possible upon at least three animals. The intramuscular M.T.D. in the rabbit of the soluble sodium potassium bismuth tartrate is close to 100 mg. per kilo (40 mg. Bi). Twice this dose kills in from 1½ to 5 days. The intramuscular M.T.D. of sodium bismuth thiosulfate is about 150 mg. per kilo (50 mg. Bi). Its effect upon the kidneys is nearly as great as the tartrate, even though here the acidic ion is not nephrotoxic, as is tartrate. Twice the above dose of the thiosulfate kills in from 5 to 6 days. Soluble sodium bismuth citrate is much less toxic. Intramuscular doses of 300 mg. per kilo (200 mg. Bi) of the citrate are just nephropathic, while doses of 125 mg. per kilo (85 mg. Bi) are practically non-toxic. In the case of the insoluble preparations the intramuscular M.T.D. of bismuth oleate is close to 200 mg. Bi per kilo. This heavily necroses of the kidney. 100 mg. Bi per kilo in the form of oleate is tolerated but is still quite nephropathic. An intramuscular dose of 535 mg. per kilo of precipitated bismuth is lethal. 400 mg. per kilo are tolerated, though heavily nephropathic, 85 mg. per kilo are still partially nephropathic. Evidence has been adduced for an additive effect of bismuth and tartrate in producing the toxicity of tartrobismuthates.

The soluble tartrate displays the greatest initial rate of urinary excretion followed by a diminishing rate to death in lethal doses, while sublethal but nephropathic doses show a series of such changes of rate and stoppage of excretion of bismuth. The thiosulfate displays a slightly lower initial rate but, in lethal doses a

similar diminishing rate to death. In sub-lethal dose variation but no sharp stoppage of excretion is shown. The citrate displays a bismuth excretion lower in rate than the tartrate, for the same dose of bismuth, variable, but without sharp stoppage of excretion. The excretion rate of the insoluble bismuth oleate resembles the citrate. The urinary excretion of metallic bismuth is very regular, with the smallest dose of 85 mg. per kilo averaging 1.60 mg. per day. For this dose of bismuth, this is a rate the lowest of all the bismuth preparations studied. All the preparations display a lower rate of urinary excretion and lessened total excretion the larger the dose, and this agrees with the extent of the kidney damage.

In view of the widespread use of thiosulfate as a detoxicant of heavy metal poisoning, the findings with regard to the toxicity and elimination of bismuth after injection of sodium bismuth thiosulfate are of particular interest. Thiosulfate is not a detoxicant of the acute toxicity of bismuth in the rabbit. The rate of excretion of sodium bismuth thiosulfate, while not as great as the soluble tartrate or citrate for the same dose of bismuth, is greater than that of the various insoluble bismuth preparations. Its toxicity is nearly as high as that of soluble sodium potassium bismuth tartrate and far higher than the soluble citrate. On many grounds, it is proposed that the so-called detoxicant action of thiosulfates upon heavy metals may be explained as a mobilization or solvation of insoluble depots which are producing a local pathology in the skin or mucus membranes. The metal when thus mobilized is actually rendered more toxic in its acute effects, such as kidney toxicity, but human therapeutic doses rarely reach a kidney excretion concentration dangerous to normal kidneys even when thus mobilized. The findings as to distribution of bismuth in the tissues will be published later.

(This work will appear in a forthcoming issue of the *Journal of Pharmacology and Experimental Therapeutics.*)