the difference between and results in the so-called "wiring with electrolysis" and the non-electrolytic methods commonly employed in the treatment of aneurysms.

Ten different wires were used; namely, aluminum, bronze, copper, dental alloy, German silver, gold, piano wire, silver, pliable steel, and zinc. A small piece of each of these wires was inserted in the aorta of a cat and allowed to remain for 7 days. The animal was then killed and examined.

Zinc containing less than 0.1% lead, 0.01% iron, and 0.002% cadmium always produced clotting and was found to be the best metal for this purpose. Copper and its alloys produced clotting but to a much less degree, and steel and silver appeared to exert the least influence. Gold, aluminum, and platinum would seem to produce practically no clotting.

It was seen that the Moore-Corradi method as practiced surgically with a current of 50 ma. is apparently detrimental in both its immediate and its later effects to the strength of the vessel wall. Evidence points to the fact that such a procedure tends to weaken rather than to strengthen the vessel wall. The low current (10 to 12 ma. for 60 minutes) also causes some burning of the vessel wall. The amount of clotting produced by a low current of the strength commonly used in human surgery (10 to 12 ma. for 1 hour) is no greater than that produced by a similar wire placed without current in the freely running blood stream. The dangers of embolus formation are great.

All in all, however, it would seem that the wiring of aneurysms, although at all times a dangerous procedure, may be developed into a useful therapeutic measure.

5225

Effect of Histamine on the Secretion of Gastric Pepsin.

ALFRED GILMAN AND GEORGE R. COWGILL.

From the Laboratory of Physiological Chemistry, Yale University.

Histamine is known generally as a gastric secretogogue, and the results of many investigations have shown that the secretion of the normal stomach, in response to this stimulus, is rich in free acid; the response of the peptic glands, however, has received but slight attention. In a series of experiments upon human subjects, Polland

and Bloomfield[1] have observed that with an increased volume of gastric secretion in response to a histamine stimulation there is a progressive decrease in pepsin concentration, although the total amount of pepsin secreted is actually greater.

A new micro technique for estimating peptic activity was recently developed in this laboratory.[2] Utilizing this method in a series of experiments upon dogs possessing either Pavlov or Heidenhain pouches the authors find that:

(a) With increased volume of secretion produced by histamine stimulation there is a progressive decrease in the concentration of pepsin in the gastric juice.

(b) The pepsin concentration of the fasting juice is invariably greater than that of any subsequent sample.

(c) In the first sample of juice obtained following histamine stimulation the concentration of pepsin is diminished, but due to the increased volume of flow, the total amount of pepsin apparently secreted per unit of time is greatly increased.

(d) In subsequent samples the concentration of pepsin and the total amount of enzyme secreted per unit of time is rapidly diminished.

(e) Examination of samples collected subsequent to 45 minutes after the injection of histamine shows with few exceptions, that the total pepsin secreted per unit of time is less than is the case before the administration of histamine. The concentration of pepsin in these samples may be as low as 1/40 the concentration found in the fasting juice.

(f) The content of pepsin in the sample is roughly parallel to the content of neutral chloride.

The authors therefore conclude that histamine acts exclusively upon the acid secreting glands, merely filling the stomach with an acid fluid. The sudden rise in total pepsin immediately subsequent to the administration of histamine is in all probability due to a flushing of the lumen of the glands and the mucosa of the stomach with the acid secretion produced and in this way increasing the peptic content of the sample in a purely mechanical fashion. In support of this assertion the authors find that a second injection of histamine, made after the volume of the juice secreted in response to the first stimulation has begun to diminish, will not again bring about a sharp rise in total pepsin, the explanation being that the stomach has already been washed free of residual enzyme.

[1] Polland, W. S., and Bloomfield, A. L., *J. Clin. Invest.*, 1929, **7**, 57.

[2] Gilman, A., and Cowgill, G. R., *J. Biol. Chem.*, 1930, **88**, 743.

These experiments were conducted upon 4 dogs having gastric pouches of the Pavlov type, and one having the Heidenhain pouch.

5226

The Toxicity and Balantidicidal Action of "Di-Hydranol" in Guinea Pigs.*

NORMAN A. DAVID AND CHAUNCEY D. LEAKE.

From the Pharmacological Laboratory of the University of California Medical School, San Francisco.

The frequent natural infestation of guinea pigs with such an easily observed intestinal parasite as *Balantidium coli* offers an excellent opportunity for a carefully controlled study of the parasiticidal action *in vivo* of new drugs of possible use in this regard. With proper toxicity studies of the same drugs in healthy uninfected guinea pigs, one may thus obtain quantitative data of considerable value in estimating the relative chemotherapeutic indices of a series of compounds, and thus the more readily estimate their worth for clinical trial in humans. Sweeney[1] has already nicely demonstrated the possibilities of this technique. We determined to use this method as an adjunct to our general investigation of the chemotherapy of amebiasis, especially to assist in determining whether or not a compound is worth the time and expense of study in natural or induced amebic infestation in monkeys or other animals.

Such studies of toxicity and experimental activity, together with quantitative data on the rate of secretion, we consider absolutely necessary before one may be justified in attempting the clinical evaluation of a new drug in human therapy.[2] New drugs are continually being offered for clinical evaluation in amebiasis and we are amazed that so many come to clinical trial without reference to quantitative data either on toxicity and therapeutic activity in experimental

* This note is part of an extended cooperative study of the chemotherapy of amebiasis conducted by the Pacific Institute of Tropical Medicine of the Hooper Foundation for Medical Research and the Pharmacological Laboratory of the University of California Medical School, San Francisco, and supported in part by Eli Lilly and Co., Indianapolis, and the Ciba Co., Inc., New York City.

[1] Sweeney, M. A., *Am. J. Hyg.*, 1929, **9**, 544. We desire to express our thanks for advice from Dr. E. L. Walker and Miss M. A. Sweeney in connection with this study, and to Miss Dorothy A. Koch for aid in stool examinations.

[2] Leake, C. D., *J. Am. Med. Assn.*, 1929, **90**, 1632.