14079

Oral Glucose Tolerance Tests in Dogs with Intestinal Resections.

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The oral glucose tolerance test depends not only on the state of the liver and pancreas but also on the absorption of the glucose from the gastro-intestinal tract. It is of interest, therefore, to know how resections of various parts of the gastro-intestinal tract influence the shape of the normal glucose tolerance curve.

Material. We had in our laboratory 6 dogs which had been operated upon more than 10 months ago and which were in good nutritional state and were kept on high caloric food rich in carbohydrate. Three of these dogs had undergone total gastrectomy; in 2 of these 3 dogs the major part of the jejunum or the ileum, respectively, had been removed in a second operation. In one dog jejunectomy and in 2 dogs ileectomy had been performed.

Test Procedure. The dogs, after a 12-15 hours' fast, were given the test meal through the stomach tube and the sugar content of the venous blood was estimated at fasting and 30', 60', 120' and 180' after ingestion of a 20% glucose solution. 1.5 g glucose was given per kg of body weight. The Miller-Van Slyke Mikromethod for blood sugar estimation was used. Three tests at intervals of one week were performed in each dog. As control, intravenous tolerance tests with 10 cc of a 50% glucose solution were performed which in all instances showed normal curves.

Results. Fig. 1 and Table 1 represent the various types of curves obtained. In the figure, the sketch at the left of each curve indicates the resection which had been performed. The curves and values represent the average value of the 3 tests. It can be seen that in all instances where a gastrectomy (alone or together with another resection) had been performed, the curves show a very high peak but return to the fasting level with little or no delay. The high peak and the return appear to be delayed after jejunecton The blood sugar curve is normal after il ectomy.

Comment. These experiments show th importance of a normal function of the stom ach for the normal oral glucose tolerance test. Under physiological conditions a hypertonic glucose solution, like the test meal, is diluted in the stomach and released into the duodenum and upper jejunum where it is absorbed almost completely.[1–4] The stomach and the ileum absorb only very little. In contrast to earlier observations,[5] it has been found that the rate of absorption from duodenum and jejunum depends on the concentration of the glucose

TABLE I.

Dog	Avg venous blood sugar				
		After ingestion of glucose meal			
	Fasting	½ hr	1 hr	2 hr	3 hr
Normal	88	110	132	100	82
Gastrectomy	84	205	189	80	76
Gastrectomy and jejunectomy	83	259	240	106	112
Gastrectomy and ileectomy	93	251	263	132	110
Jejunectomy	82	134	207	227	180
Ileectomy	86	100	124	102	85

[1] Magee, H. E., and Reid, E., *J. Physiol.*, 1931, **73**, 163.

[2] Groen, J., *J. Clin. Invest.*, 1937, **16**, 245.

[3] Shay, H., Gershon-Cohen, F., Fels, S., and Munroe, F. L., *Am. J. Digest. Dis.*, 1940, **7**, 456.

[4] Karr, W. G., Abbott, W. O., Hoffmann, O. D., and Miller, T. S., *Am. J. Med. Sc.*, 1940, **200**, 524.

[5] Cori, F. C., *J. Biol. Chem.*, 1925, **66**, 691.

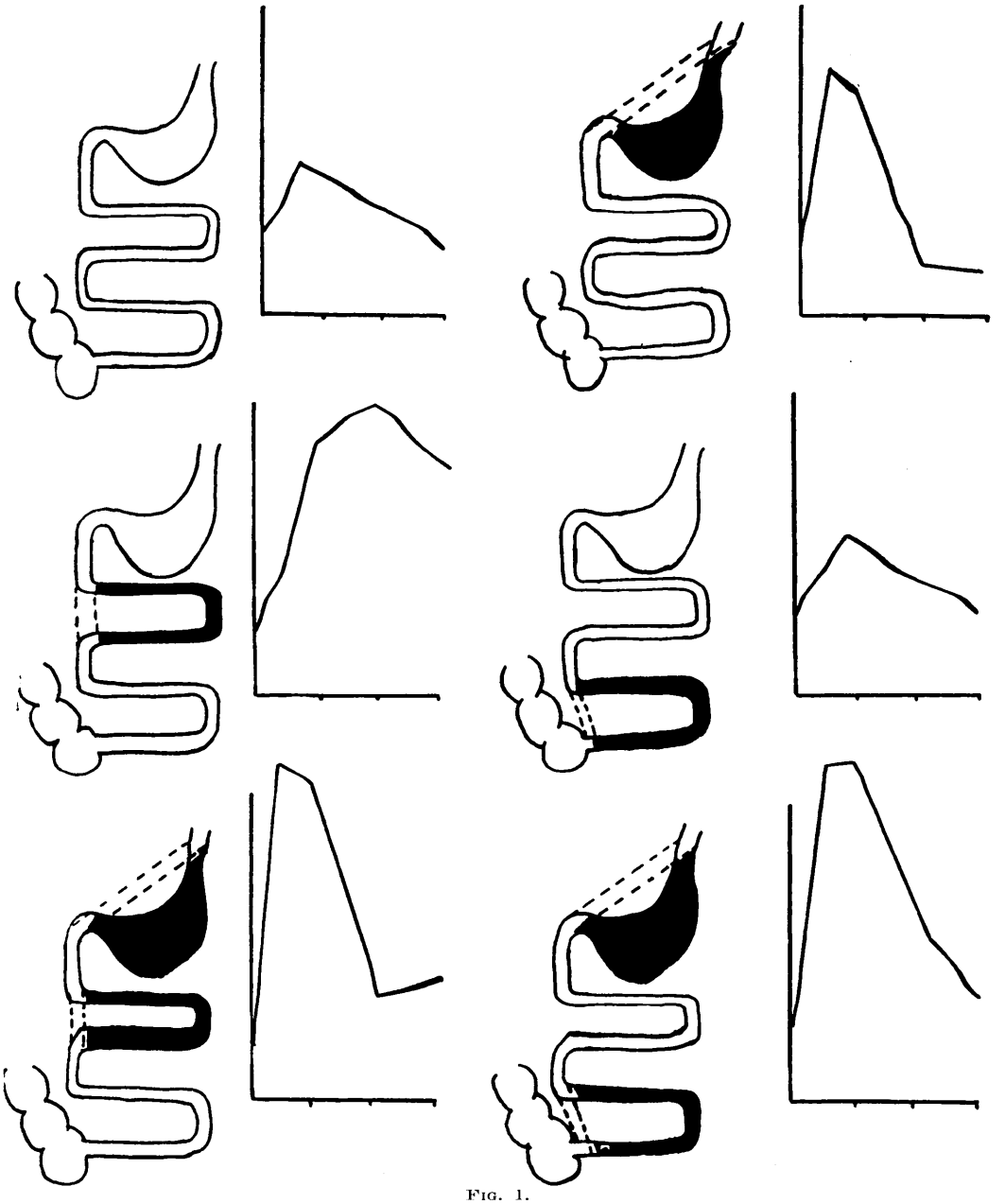

FIG. 1.

solution.[6–8] If in the case of gastrectomy the hypertonic solution enters the duodenum undiluted, glucose is absorbed at a higher speed. A higher blood sugar level is reached before the auto-regulation of the blood sugar begins. Since the ileum takes only little part in glucose absorption, ileectomy does not affect the normal oral glucose tolerance curve. The high and delayed curve after jejunectomy seems best explained by the assumption of interference with gastric and intestinal motility.

Abnormal oral glucose tolerance curves are

[6] Abbott, W. O., Karr, W. S., Glenn, P. M., and Warren, R., *Am. J. Med. Sc.*, 1940, **200**, 532.

[7] Warren, R., Karr, W. G., Hoffmann, O. D., and Abbott, O. W., *Am. J. Med. Sc.*, 1940, **200**, 639.

[8] MacKay, E. M., and Clark, W. G., *Am. J. Physiol.*, 1941, **135**, 187.

obtained not infrequently in patients with organic or functional gastro-intestinal disorders.[9] Our experiments demonstrate that in such instances the disturbed gastro-intestinal absorption and motility plays an important role in determining the shape of the blood sugar curve.

Summary. After resection of the stomach or jejunum the oral glucose tolerance test in dogs shows a high and sometimes delayed curve; the curve is not altered after ileectomy.

[9] Christlieb, W., *Dt. Arch. f. Klin. Med.*, 1937, **181**, 394.

14080

Detoxication of a Substituted Phenyl Stibonate in the Rat by Administration of *p*-Aminobenzoic Acid.

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The writer has reported[1] experiments that demonstrated the highly protective powers of *p*-aminobenzoic acid when administered in substantial but well tolerated quantities to rats that simultaneously had received high lethal doses of Carbarsone, "Tryparsamide," arsanilic acid, and Acetarsone. Further experiments, to be published *in extenso* elsewhere, have shown that *p*-aminobenzoic acid provides equally high protection against other pentavalent arsenicals including phenyl arsonic acid and also against at least one of the trivalent arsenical antisyphilis drugs.

In view of the therapeutic value placed upon some of the less toxic antimony compounds in the treatment of such important tropical diseases as kala-azar and schistosomiasis, it seems desirable to record the capacity of *p*-aminobenzoic acid to protect rats against acute fatal doses of the German proprietary drug, "Stibosan" (sodium *m*-chloro *p*-acetyl amino phenyl stibonate), the only pentavalent antimony compound which was presently available for test purposes in our laboratory.

The test animals were albino rats, weighing approximately 100 g but otherwise unselected as to breed, sex, or age. Treated and control animals were maintained on a balanced diet in large communal cages. *p*-Aminobenzoic acid in the form of its water-soluble sodium salt was administered either by mouth or parenterally at the same time as the antimonial drug was introduced into the saphenous vein of the rat.

In the early stages of these studies, we administered a so-called sustaining dose of *p*-aminobenzoic acid for the following 2 or 3 days. Experiments already completed have indicated that the quantity of *p*-aminobenzoic acid administered has usually been more than was necessary to achieve the desired effect. A typical experiment is summarized in Table I.

Discussion. As tested in our laboratory against *Trypanosoma equiperdum* in rats, "Stibosan" has proved to have a very definite but relatively low therapeutic index. The quantity of drug necessary to effect a permanent cure of rats infected with *T. equiperdum* approaches the maximum dose that the majority of rats can tolerate. Since *p*-aminobenzoic acid interferes with the bacteriostatic action of sulfanilamide and its derivatives, it is of particular interest here to mention that *p*-aminobenzoic acid does not show any evidence of interfering with the trypanocidal potency of "Stibosan." This is shown by the disappearance of trypanosomes from the peripheral blood of rats that receive "Stibosan" plus large quantities of *p*-aminobenzoic acid. Owing to the already mentioned low trypanocidal efficacy of this antimonial com-

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[1] Sandground, J. H., *Science*, 1943, **97**, 73.