

## Comparison of Two Types of Permanent External Bile-fistula Dogs for Studying Liver Function.

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Studies of hepatic physiology involving the use of dogs with the usual types of permanent external bile fistula are open to criticism because of the great difficulty of maintaining normal liver function in such animals except for short intervals. This is emphasized by the recent report by Drill<sup>1</sup> and is borne out by our experience during the course of previous studies of the excretion of bromsulfalein in bile.<sup>2,3,4</sup> Only 6 of 22 bile-fistula dogs prepared for this purpose proved to be satisfactory for the establishment of criteria for normal excretion of the dye. The purpose of the present communication is to indicate the usefulness of another type of fistula dog for such studies.

*Materials and Methods.* The two types of permanent biliary fistula employed were the standard type (Rous-McMaster<sup>5</sup>) as modified by Beerman *et al.*<sup>6</sup> and the type in which a Thomas intestinal fistula is placed opposite the papilla of Vater.<sup>7,8</sup> In the former, following cholecystectomy, a rubber tube was placed in the cystic duct with the common duct tied, or in the common duct with the cystic duct tied, and brought out through a stab wound in the abdominal wall. Bile drained into an

attached rubber bag and was reintroduced into the duodenum through a small indwelling duodenal catheter. These dogs recovered slowly after operation, required a special diet and daily care. Because they were prone to develop biliary obstruction they usually survived for only a few weeks or months. As a rule the obstructive phenomena were not pronounced and were unrecognized until the excretion of bromsulfalein in the bile was tested or jaundice developed.

The Thomas intestinal fistula was prepared following cholecystectomy by placing a permanent metal cannula in the duodenum opposite the papilla of Vater. With the cannula open a special glass catheter<sup>9,10</sup> (modified by Thomas from those originally devised by Scott), was introduced when desired into the ampulla of Vater for the drainage of bile. Upon termination of the experimental period the catheter was withdrawn and the cannula closed, which prevented further loss of intestinal contents. These dogs recovered promptly from the operation, did not require special diet or care and survived for long periods, some for over 2 years, without developing biliary obstruction.

Studies were made on 7 dogs with standard type fistulas (11 tests) and on 3 dogs with Thomas type fistulas (19 tests). All of these dogs were given intravenous injections of 2 mg bromsulfalein per kilo of body weight. Four additional Thomas-type fistula dogs were studied by comparing the excretion of bromsulfalein injected in quantities of 2 mg and 5 mg per kilo of body weight.

Bile was collected in 15-minute periods for 2 hours subsequently. Determinations were

<sup>1</sup> Drill, V. A., Annegers, J. A., Snapp, E. F., and Ivy, A. C., *J. Clin. Invest.*, 1945, **24**, 97.

<sup>2</sup> Cantarow, A., and Wirts, C. W., Jr., *Proc. Soc. Exp. Biol. and Med.*, 1941, **47**, 252.

<sup>3</sup> Wirts, C. W., Jr., and Cantarow, A., *Am. J. Dig. Dis.*, 1942, **9**, 101.

<sup>4</sup> Cantarow, A., and Wirts, C. W., Jr., *Am. J. Dig. Dis.*, 1943, **10**, 261.

<sup>5</sup> Rous, P., and McMaster, P. D., *J. Exp. Med.*, 1923, **37**, 11.

<sup>6</sup> Berman, A. L., Snapp, E., Ivy, A. C., Atkinson, A. J., and Hough, V. S., *Am. J. Dig. Dis.*, 1940, **7**, 333.

<sup>7</sup> Thomas, J. E., *Proc. Soc. Exp. Biol. and Med.*, 1941, **46**, 260.

<sup>8</sup> Snape, W. J., and Thomas, J. E., *Fed. Proc.*, 1945, **4**, 66.

<sup>9</sup> Hart, W. M., and Thomas, J. E., *Gastroenterol.*, 1945, **4**, 409.

<sup>10</sup> Scott, V. B., Collingnon, U. J., Bugel, H. J., and Johnson, G. C., *Am. J. Physiol.*, 1941, **134**, 208.

TABLE I.  
Excretion of Bromsulfalein in the Two Types of Fistula-dogs Using 2 mg of Dye per Kilo of Body Weight.

	Standard fistula dogs		Thomas-type fistula dogs
	Unselected	Selected	
Range of conc. (mg dye per 100 cc bile)	1 to 476	1 to 532	6 to 540
Avg % excreted			
1 hr	5.9	43.6	45.7
2 hr	18.1	65.0	75.0
Vol. of bile (cc) per hour	7.4	—	7.7

Excretion of Bromsulfalein in Thomas-type Fistula Dogs Using 2 mg and 5 mg of Dye per Kilo of Body Weight.

	5 mg dosage	2 mg dosage
Range of conc. (mg dye per 100 cc bile)	5 to 1430	6 to 540
% excreted		
1 hr	51.2	45.7
2 hr	64.1	75.0

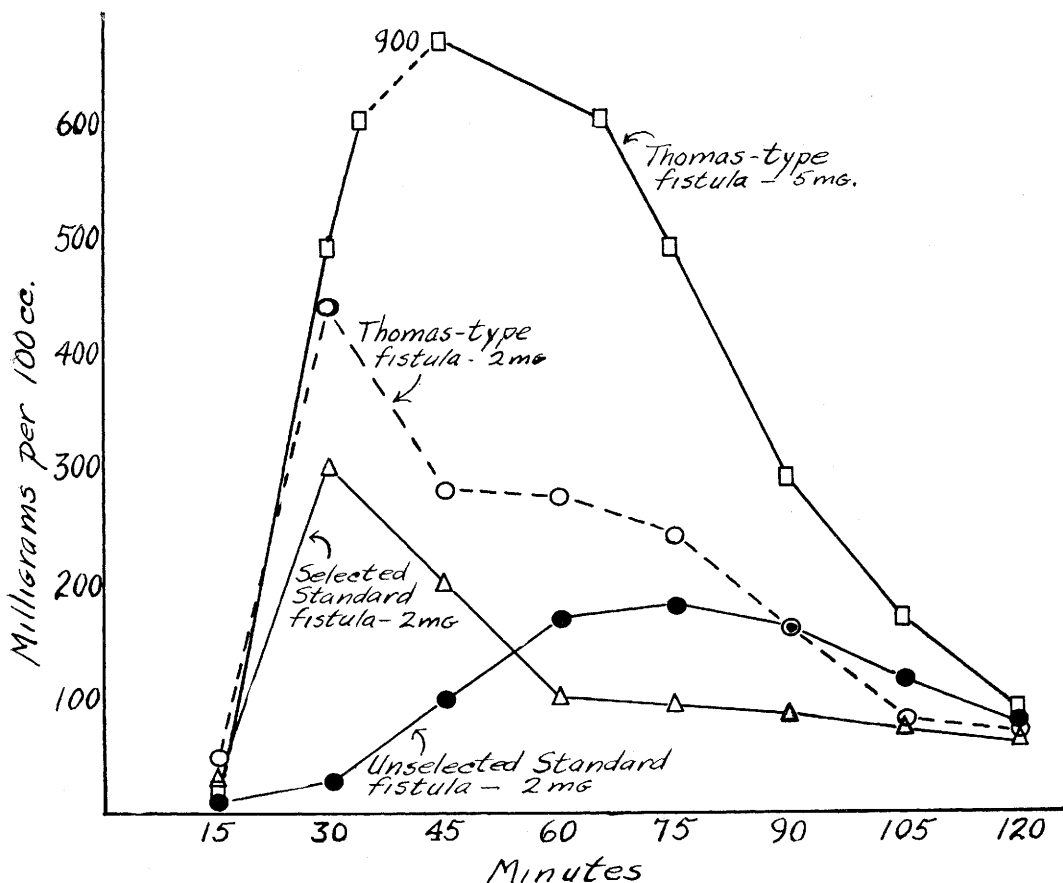


FIG. 1.  
Curves of concentration of bromsulfalein in the bile of bile-fistula dogs, after injection of 2 mg and 5 mg per kilo of body weight.

made of the concentration and amount of bromsulphalein in each sample. The following criteria were used as a basis of comparison of the two groups of animals: (1) completeness of removal of dye from the blood; (2) rate of entrance of dye into the bile; (3) time of attainment of maximum concentration of dye in the bile; (4) curve of excretion of dye in the bile; (5) range of concentration of dye in the bile and (6) total dye excretion in the bile within one- and 2-hour periods following injection.

Prior to initiating a series of liver function studies the two types of permanent biliary fistula dogs were compared for suitability by observing their prompt convalescence from operation, maintenance of good general physical condition and liver function. The liver function was tested by estimating the quantity and rate of excretion in the bile of intravenously injected bromsulphalein and, in some animals, estimating the quantity of dye retained in the blood according to a method previously described.<sup>2</sup>

*Results.* The pertinent data are summar-

ized in the table and figure. No abnormal retention of dye in the blood was observed in the Thomas-type fistula dogs; abnormal retention occurred in 5 of 6 standard fistula dogs. Similarly, the unselected dogs with the Thomas-type fistula were superior to unselected dogs with the standard type fistula when judged by the other criteria enumerated above. Dogs in the latter group selected on the basis of satisfactory bromsulphalein excretion approached the former in this regard.

*Summary and Conclusions.* Evidence has been presented to indicate that dogs with the Thomas-type bile fistula are much more satisfactory than those with the Rous-McMaster-type fistula for studies of liver function, particularly those involving collection and examination of bile. Data are presented regarding the normal biliary excretion of bromsulphalein following intravenous injection of 2 mg and 5 mg of the dye per kilogram of body weight.

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### Urticarial Hypersensitivity to Sunlight.

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Urticarial hypersensitivity to sunlight or solar urticaria is a well recognized disease entity.<sup>1</sup> The reaction is analogous to the urticarial hypersensitivity reactions to foods, drugs, and such physical agents as mechanical, cold or heat stimuli. These reactions have all the characteristics of Thomas Lewis' "triple response".<sup>2</sup> It is generally assumed that in this type of hypersensitivity the antigen-antibody reaction leads to wheal formation

via the liberation of histamine. Solar urticaria has been regarded as one form of the "physical allergies" in which an antigen or allergen is produced by action of a physical agent. Recently two types of solar urticaria have been described.<sup>3,4</sup> In one type the sensitivity spectrum is between  $\lambda$  4000-5000 Å and in the other type it is below  $\lambda$  3700 Å.

*Experimental.* In this clinic 2 patients were studied who responded to sunlight exposure with severe urticarial reaction. In both cases

<sup>1</sup> Blum, H. F., *Photodynamic Action and Diseases Caused by Light*, New York, Reinhold Publ. Corp., 1941.

<sup>2</sup> Lewis, T., *Blood Vessels of the Human Skin and Their Response*, London, Shaw and Sons, 1927.

<sup>3</sup> Abramson, H. A., *Proc. Soc. Exp. Biol. and Med.*, 1940, **43**, 410.

<sup>4</sup> Blum, H. F., Baer, R. L., and Sulzberger, M. B., *J. Invest. Derm.*, 1946, **7**, 99.