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Excretion of Bromsulfalein in the Bile.

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Bromsulfalein, injected intravenously in a dosage of 2 mg per kilo of body weight, is rapidly removed from the blood stream (85-95% in 5 minutes; 100% in 30 minutes), but its elimination in the bile continues over a period of several hours. This suggests that two separate or related mechanisms are involved and that simultaneous investigation of the rapidity of removal of the dye from the blood and the curve of its elimination in the bile might yield information of interest.

The concentration of bromsulfalein in the bile was determined as follows: 0.1 cc of bile was added to 15 cc of distilled water and 0.1 cc of 10% NaOH, and mixed by inversion. A blank was prepared for each specimen, containing 0.1 cc of bile, 15 cc of water and 0.1 cc of 10%NaCl. If turbidity developed the mixtures were filtered. After 10 minutes, readings were made in the Evelyn photoelectric colorimeter, using filter 580, and the concentration of bromsulfalein determined on the basis of a calibration curve obtained by adding known amounts of the dye to bile. In the case of very high concentrations, 30-45 cc water may be used instead of 15 cc.

Studies were made upon 6 cholecystectomized, bile-fistula dogs (45 determinations), 10 patients with T-tubes in the common bile duct (32 determinations), and 24 subjects in whom bile was obtained by duodenal intubation (60 determinations). Bromsulfalein was injected intravenously (2 mg per kilo), blood was withdrawn at the end of 30 minutes for estimation of the degree of retention of dye and determination of the serum bilirubin concentration, and bile was collected by continuous drainage in 15-minute fractions over a period of at least 2 hours. In patients in whom the gall bladder was present, the bladder bile was withdrawn (magnesium sulfate stimulation) before injection of the dye.

Under normal conditions, none of the dye remained in the blood at the end of 30 minutes after injection, and it usually appeared in the bile during the first 15-minute collection period. A maximum concentration in the bile (24-200 mg per 100 cc in human subjects;

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42-292 mg per 100 cc in dogs) was reached in 45-75 minutes, the quantity of dye subsequently falling to a relatively low level at 2 hours, some frequently being still present after 5-6 hours. Normally, 50-83% of the quantity injected was excreted in the bile during the first hour and 67-100% within 2 hours. The highest concentration observed in the entire series (normal and abnormal) in bile obtained directly from the common duct was 532 mg per 100 cc in dogs and 369 mg per 100 cc in human subjects, while the highest concentration in material obtained by duodenal intubation was 200 mg per 100 cc. The frequently lower concentrations in the latter cases in the presence of normal total excretion values is probably due to admixture of the bile with pancreatic, duodenal and, occasionally, gastric secretions. Contamination with gastric juice, which may cause considerable turbidity in the specimen, may be minimized by the use of a double lumen tube (Diamond),[1] permitting continuous removal of gastric secretion under negative pressure through one channel simultaneously with withdrawal of duodenal contents through the other.

Abnormal excretion of the dye was evidenced by one or more of the following phenomena: (1) delayed removal from the blood; (2) delayed entrance into the bile; (3) delayed attainment of maximum concentration in the bile; (4) prolonged high curve of excretion in the bile; (5) subnormal concentration in the bile; (6) abnormally low excretion within one or 2 hour periods following the injection.

In 9 patients with other evidence of hepatic or biliary tract disease, significantly abnormal findings were obtained in the absence of abnormal retention of bromsulfalein in the blood. In these cases, the one-hour excretion ranged from 6 to 45% and the 2-hour excretion from 30 to 75% of the amount administered. Similar findings were obtained on 11 occasions in bile-fistula dogs, the total excretion at one hour being 25.7-41.1% and at 2 hours, 36-61% of the quantity administered.

Observations were made during a period of progressive partial obstruction to the flow of bile in a bile-fistula dog. The latter findings are presented in Table I.

These data indicate that considerable flattening of the curve of dye excretion in the bile, and progressive diminution in the total quantity excreted during the 2-hour period may occur before there

[1] Diamond, J. S., Siegel, S. A., Gall, M. B., and Karlen, S., *Am. J. Digest. Dis.*, 1939, **6**, 355.

TABLE I.
Bromsulfalein Excretion in a Bile-Fistula Dog During Progressive Partial Biliary Obstruction.

	Blood		Minutes								Total Excretion	
Date	Bilirubin mg%	Dye %*	15	30	45	60	75	90	105	120	1 hr %	2 hr %
			Mg dye per 100 cc bile									
2-4	.1	0	29	292	210	100	97	95	95	77	83	91
2-6	.1	0	1	59	159	150	127	111	76	55	35	61
2-10	.3	0	2	19	46	45	45	33	25	30	26	36
2-14	.9	0	0	3	4	19	18	33	35	38	4	18

*30 minutes after injection of 2 mg per kilo.

is any significant interference with removal of the dye from the blood.

There is some evidence that Kupffer and other reticuloendothelial cells are concerned with the removal of bromsulfalein from the blood,[2-5] whereas its elimination in the bile must be accomplished by the hepatic cells. The procedure presented here affords a means of clinical investigation of these two phases of the elimination of bromsulfalein from the body. The data suggest that dissociation of Kupffer and hepatic cell function may be demonstrated frequently, particularly during periods of increasing and decreasing bile stasis. Other studies are in progress which are concerned with the effects of reticuloendothelial "blockade" and the administration of various cholagogic and choleretic agents.

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Some Effects of Injection of Acacia: With Special Reference to Renal Function.

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In recent years numerous reports have appeared in the literature relative to the diuretic activity of acacia in certain forms of renal disease associated with edema. Similarly, many experimental studies

2 Herlitz, C., *Acta, pædiat.* (supp. 5), 1931, **12**, 1.

3 Klein, R., and Levinson, S. A., PROC. SOC. EXP. BIOL. AND MED., 1933, **31**, 179.

4 Mills, M. A., and Dragstedt, C. A., PROC. SOC. EXP. BIOL. AND MED., 1936, **34**, 228.

5 Mills, M. A., and Dragstedt, C. A., *Arch. Int. Med.*, 1938, **62**, 216.