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

Date	Blood: Bilirubin mg%	Blood: Dye %*	Minutes: 15	30	45	60	75	90	105	120 (Mg dye per 100 cc bile)	Total Excretion: 1 hr %	2 hr %
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.

have been published dealing with the effect of the administration of solutions of acacia on the volume of the blood and plasma, the concentration of plasma proteins and the function of the liver. No report of its action on the functions of the kidney, however, has come to our attention. The present experiments were undertaken to obtain such information.

Experimental. A 5% solution of d-glucose was injected intravenously into dogs at a constant rate throughout the experiments. After steady diuresis had been established, an autoclaved salt-free 10% solution of acacia in 5% d-glucose was infused instead, without changing the rate of injection. At the end of this period, the fluid injected was changed so as to consist again of 5% d-glucose. Between 1.1 and 2.5 g of acacia per kilo of body weight has been administered in different experiments. The rates of excretion of creatinine, urea, water and chloride before, during and after the injection of solution of acacia were studied, as well as the hematocrit values and the concentration of the plasma proteins and of acacia in the plasma.

Results and Comment. Some of the results of 4 such experiments, comprising 11 periods of observation before the administration of acacia and 32 periods during its infusion and subsequent to it, have been represented in Fig. 1. In general, the experiments show the following features: (1) creatinine clearance remains essentially unchanged; (2) urea clearance shows more fluctuation than creatinine clearance; its larger changes appear definitely associated with changes in urinary volume; (3) urinary volume (water excretion) decreases as a solution of acacia is being infused but shows a tendency to return to its previous levels later in the experiments; (4) the concentration of chloride in the plasma decreases, obviously largely because of the increased volume of the plasma (a consequence of the injection of the salt-free solution of acacia); (5) the rate of excretion of chloride in the urine appears consistently increased after the injection of solution of acacia.

Chloride Excretion. The difference between the relative consistency of the creatinine clearance and the rather marked changes in the rate of excretion of chloride is obvious. In experiment D, the increase of the rate of excretion of chloride is the least striking; however, the maintenance of its rate of excretion at the original level appears significant, since the volume of urine excreted per minute following the injection of solution of acacia was diminished by 79%, and the concentration of chlorides in the plasma decreased from an average of 375 to 352 mg per 100 cc.

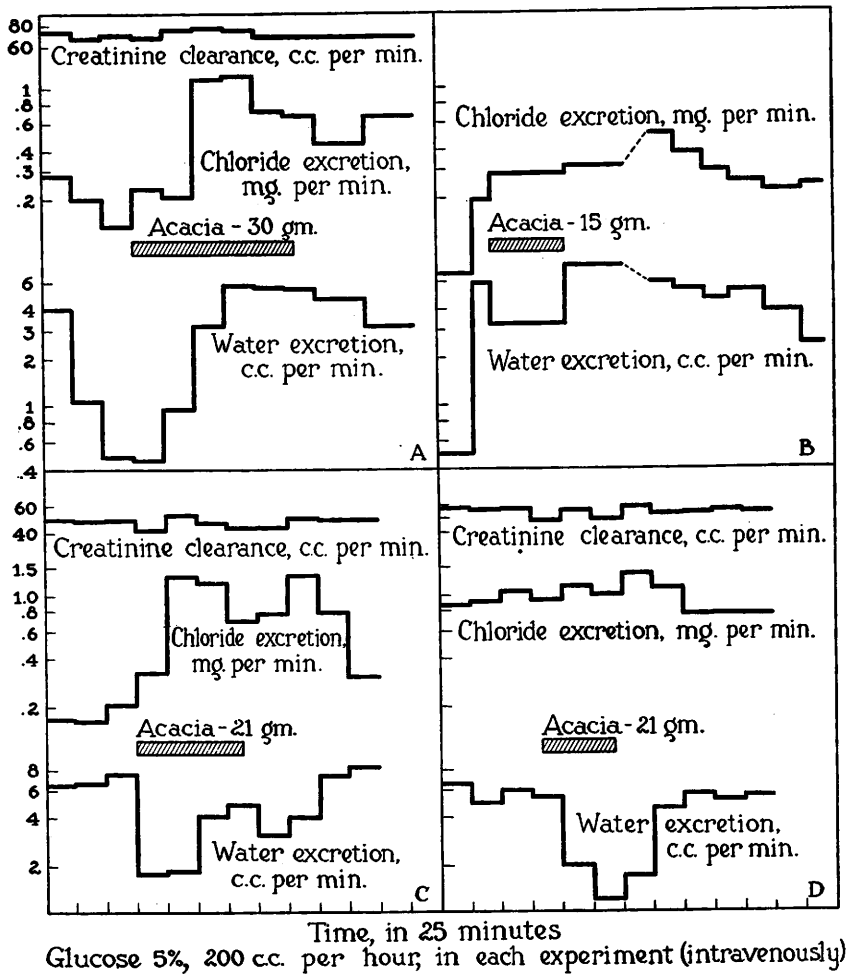

FIG. 1.

The influence of acacia on the renal excretion of water, chloride and creatinine (exogenous).

As an average for all the experimental periods, the increase of the rate of excretion of chloride observed amounted to 189%. In experiments B and C there was no overlapping of the values of chloride excretion before and after injection of the solution of acacia. Under the same circumstances, the creatinine clearance showed an average decrease of 3% and in all instances the values before and after the injection of solution of acacia showed appreciable overlapping.

Although the absolute change in terms of clearance of chloride

seems nearly infinitesimal when compared with the magnitude of the volume of the glomerular filtrate, it would seem important nevertheless from the point of view of chloride balance. Physiologically and pathologically, this appears significant, especially since, in the nephrotic syndrome, the excretion of sodium chloride is impaired, and its retention, along with water, gives rise to the pathologic accumulation of edema fluid. These considerations gain added importance, since Binger, Keith, and one of us (Goudsmit)[1] showed comparable increases of the rates of excretion of chloride in patients having nephrotic edema under treatment with solution of acacia.

Plasma Proteins. In all experiments, the concentration of plasma proteins was decreased, following the injection of a solution of acacia. This decrease was roughly proportional to the dose of acacia, and appears to have been caused chiefly by dilution, since the change in the concentration of plasma proteins can be rather satisfactorily predicted from the changes in the values of the hematocrit. The deviation of the average predicted change in plasma proteins from the average change observed is 3%. The concentrations of acacia in the plasma observed subsequent to the completion of its injection varied between 1210 and 3100 mg per 100 cc.

Summary. In experiments on dogs, after the intravenous injection of acacia, it was found that (1) the rate of glomerular filtration is essentially unchanged; (2) water excretion shows a diphasic response; (3) chloride excretion is markedly increased; (4) plasma proteins and hematocrit values diminish in comparable extent.

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Further Studies on a Frog Method for Assaying Gallbladder-Contracting-Substances.

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Cholecystokinin is usually assayed by the dog method,[1] incompletely described, and by the guinea pig method.[2, 3] Both are time

[1] Goudsmit, Arnoldus, Jr., Binger, M. W., and Keith, N. M., unpublished data.

[1] Ivy, A. C., and Oldberg, E., *Am. J. Physiol.*, 1928, **86**, 599.

[2] Agren, Gummar, *Skand. Arch. J. Physologie*, 1934, **69**, 1.

[3] Doubilet, H., and Ivy, A. C., *Am. J. Physiol.*, 1938, **124**, 379.