

Effect of Cholecystectomy on Liver Function.

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The cholecystectomized animal or man remains in apparently good health over a long period of time. However, closer study has shown that the removal of the gallbladder may result in dilatation of the biliary tree and hepatitis (*cf.*¹). Cantarow, Gartman, and Ricchiuti² reported that cholecystectomy in man sometimes temporarily impaired the hepatic excretion of bromsulphalein when tested 24 hours after cholecystectomy. Bergh, Sandblom, and Ivy¹ found no change in the liver function of cholecystectomized dogs at intervals of from one week to 15 months after operation; they used the bromsulphalein test (2 mg dose), Van den Bergh, the icteric index as criteria. Since then the 5 mg dose of bromsulphalein has been shown to be more sensitive than the 2 mg dose in detecting hepatic damage. For detecting hepatic damage produced by CCl₄ in dogs³ the change in serum phosphatase has been shown to be nearly as sensitive as the bromsulphalein test (5 mg dose). Therefore, the effect of cholecystectomy on liver function was studied in dogs by means of the bromsulphalein test (5 mg dose) and serum phosphatase test.

Methods. Serum phosphatase was determined according to the method of Bodansky.⁴ Six units of phosphatase per 100 cc of serum was the upper limit of normal in control determinations. Five mg of bromsulphalein per kilo of body weight were injected intravenously and dye retention was determined in the serum one-half hour later, as described

in earlier experiments.⁵ A blue-glass filter was used in comparing the concentration of dye. Normal dogs vary from 2 to 12% retention of dye at the end of one-half hour, the upper limit of normal being taken as 15%.

Twelve cholecystectomized dogs, operated under ether anesthesia, were studied for 24 to 70 days post-operatively. Five of the dogs were fed the stock laboratory diet of meat scraps, bread, bones, cod liver oil, and yeast. Seven dogs were fed a modified form of Cowgill's casein diet,⁵ plus a daily supplement of yeast.

Results. Ten of the dogs showed a definite rise in serum phosphatase, values of 8 to 34 units per 100 cc of serum being found. One showed no change in serum phosphatase during 31 days of observation and a second only a transitory rise 43 days post-operatively, returning to normal after the 61st day. In only one of the 10 dogs did the serum phosphatase return to normal during the period of observation, even though studies were continued for 50 to 70 days in some of the dogs. (Table I.)

Of the 10 cholecystectomized dogs showing a rise in serum phosphatase only 4 dogs had consistent retention of bromsulphalein, the dye retention varying from 25 to 60% in these dogs. The dogs having an abnormal retention of bromsulphalein were not necessarily those having the highest serum phosphatase values.

That the increase in serum phosphatase is not merely a post-operative reaction is shown by the fact that 2 days after operation there was generally only a slight rise in phosphatase activity, the increase being greater 5 to 10 days post-operatively. Also, the increased serum phosphatase activity was maintained for as long as 70 days, the maximum period of observation.

Discussion. Following cholecystectomy the

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¹ Bergh, G. S., Sandblom, P., and Ivy, A. C., *Surg. Gyn. and Obstet.*, 1936, **62**, 811.

² Cantarow, A., Gartman, E., and Ricchiuti, G., *Arch. Surg.*, 1935, **30**, 865.

³ Drill, V. A., and Ivy, A. C., *Fed. Proc.*, 1943, **2**, 10.

⁴ Bodansky, A., *J. Biol. Chem.*, 1937, **120**, 167.

⁵ Drill, V. A., and Hays, H. W., *Proc. Soc. Exp. Biol. and Med.*, 1940, **43**, 450.

TABLE I.
Effect of Cholecystectomy on Serum Phosphatase and Bromsulphalein Retention.*

Dog No.	1		2		3		4		5	
	Brom. reten.	Serum phosphatase	Brom. reten.	Serum phosphatase	Brom. reten.	Serum phosphatase	Brom. reten.	Serum phosphatase	Brom. reten.	Serum phosphatase
Control	8	5.81	5	5.95	12	4.83	10	5.60	13	4.62
2	10	11.86	15	7.20	10	6.80	50	5.99	25	9.33
4-5	5	4.71	5	3.63	10	26.13	30	7.17	12	8.75
6-10	5	8.55	10	8.70	5	15.51	50	10.01	60	26.10
11-20	12	11.28	5	13.21	10	9.92	15	10.05	12	15.56
21-30	15	11.63	5	10.03	10	8.99	60	11.89	25	12.47
41-50	35	5.52	8	16.37	35	22.61				
51-70	12	10.25	10	9.87	10	12.09				

* More determinations were made at closer intervals than illustrated by these 5 dogs in the table.

biliary ducts are known to dilate and a slight hepatitis has also been observed. Cholecystectomy seems to cause incompetence of the sphincter of Oddi, thus allowing transmission of pressure into the ducts from the duodenum.^{1,6,7} Bergh *et al.*¹ reported that 8 of 11 cholecystectomized dogs still had grossly dilated ducts 9½ to 15 months after operation. It is thus not surprising that the serum phosphatase of cholecystectomized dogs was still above normal 70 days following operation. Since only 4 of the 10 dogs showing a rise in serum phosphatase had an increased retention of bromsulphalein, serum phosphatase is a more sensitive index than the bromsulphalein test for the slight functional biliary obstruction that is responsible for dilatation of the bile ducts. The mechanism by which the increased intraductal pressure raises serum phosphatase is unknown. Studies have been

reported on phosphatase excretion in the bile of cholecystectomized-bile fistula dogs.⁸ In such dogs the rise in serum phosphatase could be correlated with either a decreased excretion of bile phosphatase, presumably leading to a higher blood level of the enzyme, or with an increased biliary secretion of phosphatase which was also associated with a blood level above normal.

Summary. Ten of 12 cholecystectomized dogs showed a definite rise in serum phosphatase following operation. In one of the 10 dogs the serum phosphatase value returned to normal, whereas in the other dogs the rise in serum phosphatase was maintained throughout the period of observation, the maximum period being 70 days. Of the 10 cholecystectomized showing a rise in serum phosphatase, only 4 developed an increased retention of bromsulphalein.

⁶ Ivy, A. C., *Physiol. Rev.*, 1934, **14**, 1.

⁷ Sandblom, P., Bergh, G. S., and Ivy, A. C., *Ann. Surg.*, 1936, **104**, 702.

⁸ Drill, V. A., Annegers, J. H., Snapp, F. E., and Ivy, A. C., *Fed. Proc.*, 1943, **2**, 9.