

TABLE III.
Effect on Blood Coagulation of 200,000 Units of Penicillin Intramuscularly in a Normal Subject.

Time (hr after injection)	Coagulation time (min)	Prothrombin time (sec)	Clot retraction	Bleeding time (min)	Fibrinogen, mg/100 cc	Penicillin, unit/cc
Initial	8½	22	normal	1	243	0
½	9	19	"	1	236	7.15
2	7½	21	"	1¼	232	0.45
3	7½	22	"	1¼	204	0.11
4	8	22	"	1	231	0.05

TABLE IV.
Effect on Blood Coagulation of 200,000 Units of Penicillin Intramuscularly in a Hemophiliac Subject.

Time (hr after injection)	Coagulation time (min)	Prothrombin time (sec)	Clot retraction	Bleeding time (min)	Platelet count, × 1000	Fibrinogen, mg/100 cc	Penicillin, unit/cc
Control	79	20	normal	1½	252	224	0
1	110	20	"	1¾	289	339	7.15
2	80	20	"	2¼	250	336	0.90
3	97	19	"	2¼	258	256	0.11
4	105	21	"	2	262	286	0.05

ministration to patients suffering from thrombophlebitis, coronary artery disease and bacterial endocarditis. We were unable to demonstrate any effect of penicillin on either the normal or hemophiliac blood coagulation reaction, and therefore do not feel that consideration of intravascular blood coagulation offers any contraindication to the clinical use of penicillin.

Conclusions. We were able to demon-

strate any *in vitro* or *in vivo* effect of penicillin on the blood coagulation reaction. No significant changes were observed in coagulation time, clot retraction, prothrombin concentration, fibrinogen concentration, platelet count or bleeding time of normal or hemophiliac subjects.

We are indebted to Clare Wilcox for the penicillin determination.

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Studies of the Thoracic Duct Lymph in Experimental Liver Injury in Dogs.

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The purpose of the present communication is to report comparative studies of the bilirubin, alkaline phosphatase, cholesterol, bile acids and intravenously-administered bromsulfalein content of the blood and thoracic duct lymph of dogs acutely poisoned with carbon tetrachloride or manganous

chloride. A number of investigators¹⁻³ have used carbon tetrachloride by stomach tube to produce liver injury. A marked increase in its toxicity can be obtained by simultaneous administration of ethyl alcohol.⁴ Manganous chloride was shown by Findlay⁵ to

¹ Meyer, J. R., and Pessoa, B. S., *Am. J. Trop. Med.*, 1923, **3**, 177.

² Lamson, P. D., and McLean, A. J., *J. Pharm. and Exp. Therap.*, 1923, **21**, 237.

³ Freeman, S., Chen, Y. P., and Ivy, A. C., *J. Biol. Chem.*, 1938, **124**, 79.

⁴ Lamson, D. P., Gardner, G. H., Gustafson, R. K., Maire, E. D., McLean, A. J., and Wells, H. S., *J. Pharm. and Exp. Therap.*, 1923, **22**, 215.

⁵ Findlay, G. M., *Brit. J. Exp. Path.*, 1924, **5**, 92.

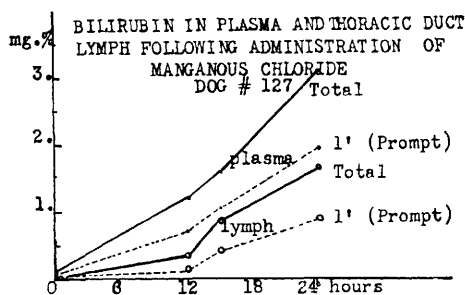


FIG. 1.

be toxic to the liver of rabbits, rats, and guinea pigs.

Material and Methods. Seven male dogs were used, ranging from 18 to 20 kg in weight. The anesthetic employed was pentobarbital sodium in an amount of 35 mg per kg of body weight. The thoracic duct lymph was secured in the following manner: In accordance with the Markowitz technic⁶ the left subclavius vein was ligated, as were also the veins entering the external jugular just above its junction with the subclavius. Instead of ligating the innominate vein, as recommended by Markowitz, a string was placed around it just below the entrance of the thoracic duct. The left external jugular was then ligated and cut at a distance of 6-7 cm above the clavicle. A plastic can-

nula 3 cm in length* was introduced in the proximal cut end of the external jugular vein. A sample of thoracic duct lymph could then be secured by pulling the string upward, thus impeding the flow of lymph into the general circulation. At other times, the lymph flows through its natural channel, the string being loose and a small cork stoppering the cannula.

Four of the dogs were given 5 cc each of carbon tetrachloride, together with 5 cc of 95% ethyl alcohol by stomach tube immediately following thoracic duct cannulation and again after 24 hours. Each of the re-

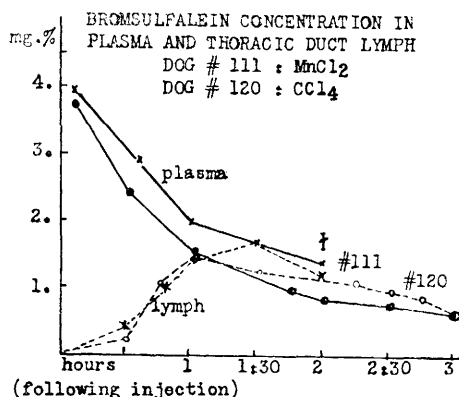


FIG. 3.

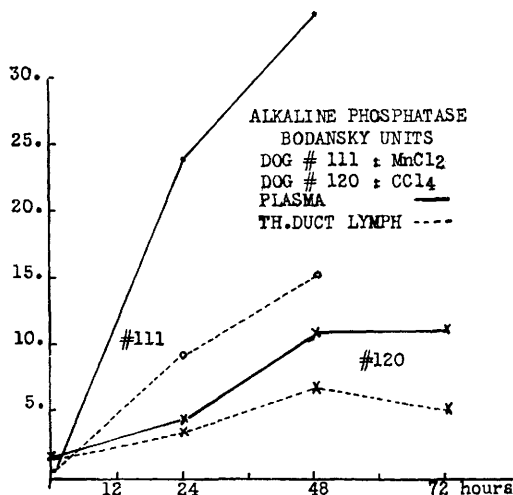


FIG. 2.

maining 3 dogs were given 800 mg of $MnCl_2$ dissolved in 20 cc of physiological saline. Twenty-four hours later a second dose of 400 mg was injected into each of 3 dogs. These amounts were injected intramuscularly.

The laboratory methods used were the same as those described in a previous communication,⁷ except for the alkaline phosphatase which was determined by the Bodansky method.⁸

Results. The bilirubin increased in both blood and lymph 12 hours following the first

* The author is indebted to Dr. J. H. Grindley, of the Mayo Clinic, Rochester, Minn., for suggesting the use of this type of cannula, and to the Irvington Varnish and Insulator Co., Irvington, N.J., for making it available.

⁷ Gonzalez-Oddone, Miguel V., *Proc. Soc. Exp. Biol. and Med.*, 1946, **63**, 144.

⁸ Bodansky, A., *J. Biol. Chem.*, 1937, **120**, 167.

⁶ Markowitz, J., *Textbook of Experimental Surgery*, William Wood and Co., 1937.

dose of MnCl_2 and 24 hours following the first dose of CCl_4 . The main component of the blood and lymph bilirubin was the 1' or prompt reacting type.^{9,10} Fig. 1, from one of the MnCl_2 dogs is a typical example. The alkaline phosphatase increased as early as 12 hours following the first dose of MnCl_2 in both lymph and blood, and a definite increase was noted in all of the dogs 24 hours following the administration of either of the toxic substances. Fig. 2 compares the typical results from MnCl_2 and CCl_4 (one dog for each).

The total cholesterol changed very little in any of the experiments, either in blood or lymph, if anything showing a slight tendency to decrease. The same might be said for the cholesterol esters. The bile acid concentrations in blood and lymph showed no significant alterations in the experiments with either of the 2 toxic substances. The behavior of the intravenously-injected bromsulfalein was similar in all 6 of the dogs in which it was administered (3 MnCl_2 and 3 CCl_4 dogs). As noted in Fig. 3, the bromsulfalein was retained in the blood at relative high concentration, a delayed increase appearing in the thoracic duct lymph similar to that previously described for the 32-hour stage following common duct ligation.

Discussion. The present results differ in a number of respects from those previously described for experimental obstructive jaundice.⁷ The increase of serum bilirubin in

the lymph was not as early nor as marked, and the same was true for bromsulfalein, although, as noted above, there was a delayed increase in the lymph, similar to that seen 32 hours following common duct ligation. The behavior of the bile acids was quite different in that, in the present experiments, no increase was noted, while in the experimental obstructive jaundice, the bile acids rose rapidly and to a marked degree in the lymph. The alkaline phosphatase behaved quite similarly in the 2 groups of experiments. While no attempt will be made to explain these observations, the possibility is considered that the differences are due to a relatively greater hepatocellular and lesser cholangiolar injury in the present experiments than in the experimental obstructive jaundice.

Summary. A method is described that allows collection of thoracic duct lymph over a period of days, the lymph circulating through its natural channel during the intervals in which it is not being collected. Liver injury caused by either CCl_4 or MnCl_2 were qualitatively comparable in dogs, the changes being more marked with the latter. An elevation of the alkaline phosphatase activity and bilirubin content of both blood and thoracic duct lymph were noted. The main component of the bilirubin was the 1' or prompt reacting type.^{9,10} The behavior of the injected bromsulfalein was comparable to that of the 32-hour stage, following common bile duct ligation.⁶ No significant changes were observed as regards the bile acids, total cholesterol or cholesterol esters.

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Effect of Meals on the Electrocardiogram of Cardiac Patients.*

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In a previous communication,¹ we reported, for 12 normal men, the effect of meals on

electrocardiograms recorded 30 and 60 minutes later. Most of the electrocardiographic functions, especially the T-wave, showed sta-

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1 Simonson, E., Alexander, H., Henschel, A., and Keys, A., *Am. Heart J.*, 1946, **32**, 202.