TABLE I.
Acetylation of Sulfanilamide.

Exp. condition	% acetylated		Diff.	P‡
	Exp.	Control*		
Hyperthyroidism	30 ± 1.8 (11)†	39 ± 1.6 (11)	—23%	.01
Thyroidectomy	33 ± 2.2 (7)	39 ± 1.2 (6)	—15%	.05
Thiouracil treatment	44 ± 1.5 (11)	39 ± 1.4 (11)	—13%	.05

* For each experimental animal a control animal was run at the same time to minimize differences due to temperature, humidity, diet, etc.

† Figures represent mean values ± the standard error. Numbers in parentheses refer to number of rats per group.

‡ Probability of occurrence of deviation, obtain from Fisher "t" table.

ectomized- and thiouracil-treated groups just barely significant.

The results show that both hyperthroidism and thyroidectomy produced a decrease in the degree of acetylation of sulfanilamide, whereas thiouracil treatment caused an increase. It is difficult to interpret the variance in the effects of thyroidectomy and thiouracil. A possible explanation may be that thiouracil exerts other effects than those depressing the activity of the thyroid.

It may be noteworthy to compare these results with the changes observed in an entirely different experiment, in which the high energy containing phosphate compounds of the liver were determined under similar conditions;[14] hyperthyroidism was associated with a decrease in the specific activity of the labile phosphorus, thyroidectomy with no change in this value, and thiouracil treatment with an increased specific activity of the labile phosphorus.

Summary. The influence of the thyroid on the acetylation of sulfanilamide was studied. Hyperthyroidism and thyroidectomy caused a decrease in the amount of sulfanilamide acetylated; thiouracil treatment led to an increase.

[14] Greenberg, D. M., Fraenkel-Conrat, J., and Glendening, M. B., unpublished observations.

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Effect of Penicillin on Blood Coagulation.*

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Moldavsky, Hasselbrook and Caterno[1] have recently reported that both oral and intramuscular penicillin consistently shorten the coagulation time of normal blood and produce a nonretractile clot. These authors also observed decreased bleeding times in patients receiving penicillin. Hines and Kessler[2] demonstrated increased sensitivity to heparin in 2 of 10 cases receiving penicillin but found no changes in the platelet counts or prothrombin times.

The widespread use of penicillin makes this an important clinical problem. Therefore, it was decided to investigate more thor-

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[1] Moldavsky, L. F., Hasselbrook, W. B., and Caterno, C., *Science*, 1945, **102**, 38.

[2] Hines, L. E., and Kessler, D. L., *J. A. M. A.*, 1945, **128**, 794.

TABLE I.
In vitro Effect of Penicillin on the Coagulation Time of Normal and Hemophiliac Whole Blood.

Final conc. of penicillin (units) per 2 cc of blood	Coagulation time (min)	
	Normal	Hemophiliac
1000	6.5	33
250	6.5	32
25	6.5	33
5	8	30
2.5	8	30
1.25	8	32
0.75	7.5	32
0.5	7.5	32
0.25	7.5	32
0	7	30

Clot retraction normal in all tubes.

oughly the effects of penicillin on blood coagulation in both normal and hemophiliac subjects.

Methods and Material. Six normal and 6 hemophiliac subjects were studied: whole blood coagulation times by a modification[3] of the method of Lee and White at 37°C, prothrombin times by a modification[4] of the Quick Method[5] and clot retraction were determined repeatedly in all patients. Capillary bleeding times, platelet counts and plasma fibrinogen concentrations were determined in many of the experiments. Penicillin levels[6] were determined in all patients.

In vitro tests were performed to determine the effect of penicillin at various concentrations on the coagulation time of normal and hemophiliac blood. Two cc of whole blood was added to 0.1 cc of various 0.85% sodium chloride dilutions of penicillin and coagulation times measured.

Two normal and 2 hemophiliac subjects received oral penicillin in an initial dosage of 300,000 units, followed by 100,000 every 2 hours for 48 hours. Four normal and 4 hemophiliac patients received intramuscular sodium penicillin in single doses of 25,000, 50,000, 100,000 and 200,000 units each.

Results. In vitro: No effect was produced on the coagulation time of normal or hemophilic blood by the *in vitro* addition of various dilutions of penicillin. The results are shown in Table I.

In vivo: 1. Oral penicillin. No effect on the blood coagulation mechanism was observed after oral administration of penicillin in either normal or hemophiliac subjects. One typical case, a hemophiliac, is presented in Table II.

2. Intramuscular penicillin. Four normal and 4 hemophiliac patients received intramuscular penicillin in a single dose of 25,000, 50,000, 100,000 or 200,000 units without effect on coagulation time, clot retraction, prothrombin time, platelet count, bleeding time or fibrinogen concentration in spite of high plasma penicillin levels.

One normal and one hemophiliac subject, each of whom received 200,000 units of penicillin intramuscularly are presented in Tables III and IV.

Discussion. Penicillin is used with such frequency that any contraindication to its use should be thoroughly investigated. The suggestion that penicillin might alter the blood coagulation reaction to such an extent that intravascular coagulation could be produced or increased is important particularly in view of the frequency of penicillin ad-

TABLE II.
Effect of Oral Penicillin (100,000 Units Every 2 Hours) on the Blood Coagulation of a Hemophiliac Subject.

Time	Coagulation time, (min)	Clot retraction	Prothrombin time, (sec)	Fibrinogen, mg/100 cc	Penicillin level, units/cc
Before penicillin	150	normal	21	383	0
24 hr of penicillin	160	"	22	371	0.11
48 " " "	160	"	22	338	0.22

[3] Pohle, F. J., and Taylor, F. H. L., *J. Clin. Invest.*, 1937, **16**, 741.

[4] Souter, A. W., and Kark, R. M., *Am. J. Med. Sci.*, 1940, **200**, 603.

[5] Quick, A. J., Stanley-Brown, M., and Bancroft, F. W., *Am. J. Med. Sci.*, 1935, **190**, 501.

[6] Rammelkamp, C. H., PROC. SOC. EXP. BIOL. AND MED., 1942, **51**, 95.

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 demonstrate 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 investigators[1-3] 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 Findlay[5] 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.