

TABLE I. Summary of Hematological Data of Rats Exposed to Cold Environment for 30 Days; 18 Rats/Series.

	Body wt, g		Hemato- crit, %	Hemoglo- bin conc., g/100 ml blood	Total blood vol, ml	Total red cell vol			Total circulating hemoglobin		
	Initial	Final				ml	% change	P*	g	% change	P
Controls	400	428	45.5	13.2	20.22	9.20	12.9	.001	2.67	10.9	.001
Cold exposed 30-days	400	413	47.2	13.4	22.01	10.39			2.96		

* Fisher's "t" test(10).

posure to cold. However, they suggest that possibly 5 days is not a long enough time in which to expect acclimatization to appear. The present study would also suggest that concentration studies alone are perhaps not as conclusive as the observation of a net increase in red cell volume in response to a particular stimulation.

That an increase in red cell volume is observed in animals exposed to a cold environment is not altogether unexpected when one considers that it is accompanied by a physiologically increased requirement of oxygen. Such a stimulation of red cell production, possibly secondary to an increased oxygen consumption, is interesting since in many different endocrine states variations in the red cell picture are seen accompanied by variations in oxygen consumption.

Summary. An increase in total red cell volume and total circulating hemoglobin was observed in rats exposed to a cold environ-

ment for a period of 30 days.

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Bromsulphalein Dye Retention Test in Toxicological Investigations. (23180)

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Routine toxicologic investigations demand evaluation of liver function in the experimental animal as an indication of possible hepatotoxicity. The method employed should give results which can be read quan-

titatively. This report describes a procedure by which concentrations of the bromsulphalein dye in the blood are obtained which can easily be determined by standard electrophotometric methods. Moses *et al.*(1) have reported that bromsulphalein at doses of 5, 10 and 20 mg/kg intravenously in dogs yielded reproducible and quantitatively similar curves. Gornall *et al.*(2) showed that a 10

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TABLE I. 15 Minute B.S.P. Retention Values for 5 Rabbits Fed CCl_4 .

Control	% bromsulphalein retention				Liver damage
	After 2 doses CCl_4	After 4 doses CCl_4	7 days following 4th dose	14 days following 4th dose	
4.6	30	64	8.5	6.4	Mild
4.0	9.7	36*	—	7.0	"
6.5	Dead	—No autopsy performed—			
4.5	"	—Autopsy			Very marked
5.7	45.6	92	Sacrificed, autopsy performed		Marked

* Retention at 18 min.

mg/kg dose administered intravenously gave more satisfactory results than the 5 mg/kg dose. Smith *et al.* (3) showed that in many instances 15 minutes after administering the dye none was found in the blood, indicating rapid removal of the dye from the blood stream.

To evaluate possible hepatotoxicity of agents with potential chemotherapeutic value, an indication of altered liver function should be of diagnostic significance. The bromsulphalein dye retention test serves as a useful method for evaluation of liver function.

Materials and methods. Male and female adult albino rabbits were used in these experiments. Bromsulphalein dye was given intravenously at a dose of 10 mg/kg. 20 mg of dye per 100 ml of blood was considered 100% retention (2).

Results. Control bromsulphalein retention value at 15 minutes after injection of the dye was determined on 63 rabbits, with a mean value of $3.8\% \pm 1.6$.[‡] Five of the rabbits were given 5 mg/kg of a 10% (v/v) solution of CCl_4 in peanut oil by gavage, twice weekly, to produce liver impairment (4). Two of the 5 rabbits died after receiving 2 doses of the CCl_4 , the other 3 received a total of 4 doses (Table I). Retention values at 5, 10, 15, 30, and 60 minutes were obtained on 2 of the 5 rabbits to establish control curves (Table II and Fig. 1).

After 2 and 4 doses of CCl_4 , 15 minute retention values were determined on the 3 remaining rabbits (Table I). Simultaneously, retention values at 5, 10, 15, 30, and 60 minutes were obtained on rabbit 142, on which

a control curve had already been established (Table II). All tests were done approximately 24 hours after the CCl_4 was given. The rabbits were fasted overnight prior to the determinations.

Autopsy was performed on rabbit 140, which died after receiving 2 doses of CCl_4 , and on rabbit 142, which was sacrificed after receiving the 4 doses. Gross examination revealed marked liver damage in rabbits 140, and 142. The findings were corroborated on examining tissue sections of the liver. Liver

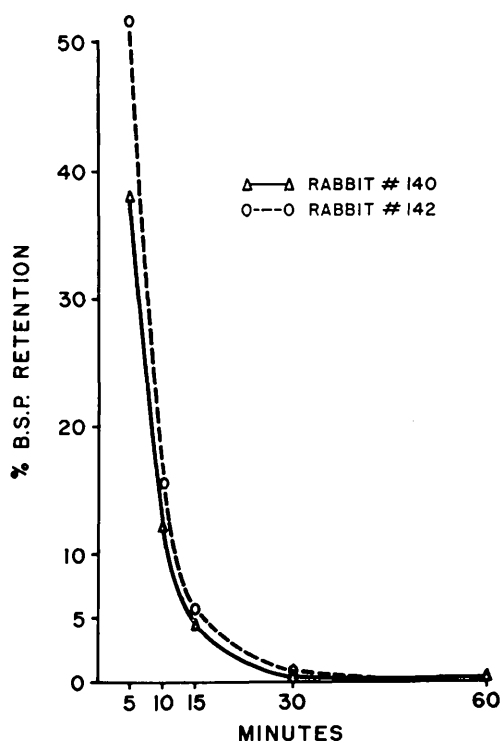


FIG. 1. Control B.S.P. retention values for rabbits No. 140 and 142.

[‡] Stand. dev.

TABLE II. Bromsulphalein Value at Selected Time Intervals for Rabbits Fed CCl_4 .

Speci- men	% bromsulphalein retention				
	5 min.	10 min.	15 min.	30 min.	60 min.
Control	51.2	15.7	5.7	.7	0
After 2 doses	91.2	69.8	45.6	33.8	5.2
After 4 doses		110.6	92	50	22
Control	38	12.2	4.5	.5	.3

sections from rabbit 140 revealed greater liver damage than that of rabbit 142. Liver sections from rabbits 139 and 148 which were killed 14 days following the fourth dose of CCl_4 revealed milder liver damage (Table I). No tissue was obtained from rabbit 138 as death occurred on a weekend and the rabbit

was disposed of by error.

Summary. 1) Fifteen minutes after administration of bromsulphalein at a dose of 10 mg/kg i.v. in rabbits, dye was present in the blood and a satisfactory determination of the dye concentration was possible. 2) Liver damage was reflected by an increased retention of bromsulphalein 15 minutes after injection of the dye.

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Excretion of Urinary "Epinephrines" in Psychiatric Disorders.* (23181)

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Physiologic changes which resemble those following injection of epinephrine and norepinephrine frequently occur in response to many types of noxious stimuli. The recent introduction of bio-assay and chemical procedures for estimation of epinephrine has made it possible to confirm physiologic evidence of increased sympathetic medullary activity under these circumstances. Since fear or anxiety is one of the most prominent symptoms in both neurotic and psychotic patients, such a study is of particular interest in these individuals. The purpose of this report is to present preliminary observations on excretion of urinary epinephrine in this group.

Materials and methods. Seventeen psychiatric patients, none of whom was receiving a course of tranquillizing drugs, insulin treatment or electric shock therapy, were studied

on one or more occasions. Diagnoses of the nature of the disorders were made by the psychiatric staff of McLean Hospital. In some cases, the illness was acute, while in others it was chronic. Some, but not all, patients complained of severe anxiety and often showed physiological evidence of increased epinephrine activity such as clammy hands and tachycardia. Their blood pressures, however, were within normal limits. The method used in determination of the urinary "epinephrines"† has been described elsewhere(1). Minor refinements in the chromatographic technics were made during the course of the investigation. In a control series comprising 45 patients, values ranged from 0 to 59.5 μg per 24 hours; average value was 20.0 and standard error was 2.9. Values in patients

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‡ "Epinephrines", as used in this paper, includes all compounds detected by the method employed. These substances include epinephrine, norepinephrine, certain other alpha-hydroxy catechol amines, trihydroxyindoles, and 3,5 hydroxy-6-oxy indoles.