with carbon. Carbon-laden phagocytes were not found in the atheromata.

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Comparative Blood Volume Changes in Anti-Platelet Serum Shock and Other Types of Shock.* (19411)

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Haematological changes observed(1) in anti-platelet serum shock, have indicated that haemodilution occurred in this type of shock. It seemed desirable, therefore, to study changes in the absolute volumes of red cells and plasma, respectively. Studies are presented in this paper which show results in anti-platelet serum, histamine, trypsin and peptone shock.

Methods. All experiments were done with dogs. Plasma volumes were determined by the injection of Evans blue dye (T-1824). Since radioactive substances were not available, another method was employed(2) for the determination of total cell volume, using red blood cells with methaemoglobin. The amount of anti-platelet serum injected for inducing shock varied with the titer of the serum.

Results. Table I shows plasma, red blood cell, and total blood volume determinations in different types of shock. In all observations the total blood volume diminished in anti-platelet serum shock. Identical results were observed in histamine shock. These results are in agreement with those of other authors who have studied histamine and other types of shock. Increase of total blood volume was observed in 2 dogs shocked by trypsin; the significance of these data requires further study.

Plasma volume diminished in all the animals, except those shocked by trypsin, in which it increased. The total red cell volume increased in both animals with tryptic shock, in one case of anti-platelet serum shock and in one of histamine shock. In all other observations (11 out of 16) the total red cell volume diminished (Table II). The ratio between the decreases of plasma and red cell volumes varied according to the type of shock. In anti-platelet serum shock the red cell volume decreased more than the plasma volume. This occurred occasionally in histamine shock also, but generally the reverse was observed, *i.e.*, a more accentuated decrease of the plasma than the red cell volume.

When methaemoglobin-labeled red cells were injected after shock had been induced, a greater proportion of methaemoglobin remained in the circulation than when a comparable amount of labeled cells were injected in normal animals (Table III). Since the number of labeled cells given before and after shock was not identical, a correction was used assuming that there was a linear relationship between the amount of methaemoglobin administered and that found in the peripheral blood. That such an assumption is valid is shown by the following experiment performed 3 times on the same dog:

Day of exp.	MetHb inj.	Circulating MetHb/100 g Hb
1	1.5	3.6
2	2.5	5.2
3	5.2	10.3

* Aided by a grant from Dr. Guilherme Guinle.

TABLE I. Absolute Values of Blood Volume Determinations Before and After Different Types of Shock in 16 Dogs.

Dog No.	Body wt, kg	Type of shock	Dose/kg body wt	Normal: Haemoglobin, g	Normal: Haematocrit, %	Normal: Blood vol (ml) Plasma	Normal: Blood vol (ml) Cells	Normal: Blood vol (ml) Total	Normal: Body haematocrit, %	Shock: Haemoglobin, g	Shock: Haematocrit, %	Shock: Blood vol (ml) Plasma	Shock: Blood vol (ml) Cells	Shock: Blood vol (ml) Total	Shock: Body haematocrit, %
1	9	A.P.S.	.3 ml	8.4	33	563	253	816	31	—	—	493	178	671	27
2	6.3		.6	12.4	44	292	191	483	40	—	—	283	72	355	20
3	8.2		.6	13.4	42	301	321	622	52	—	—	290	101	391	26
4	6.8		.8	13.8	45	328	451	779	58	8.3	27	271	170	441	39
5*	7		.4	11	38	471	338	809	42	12.7	44	320	367	687	53
6	9.3		1	9.8	34	434	172	606	28	8.4	29	378	100	478	21
7	10.1	H	2 mg	7.2	21	806	133	939	14	8.9	26	526	150	676	22
8	9.5		2	6.8	27	581	165	746	22	8.3	33	242	142	384	37
9	8.3		1.5	10.8	35	416	285	701	41	12.7	41	373	126	499	25
10	7.7		1.5	6.2	26	409	151	560	27	8.1	34	324	115	439	26
11	7.7		1.5	6.8	24	396	235	631	37	9.1	32	294	105	399	26
12	6.7		2	11	41	330	187	517	36	9.4	35	186	187	373	50
13	12.8		2	12.8	40	531	416	947	44	16.6	52	297	257	554	46
14*	8.3	T	5	11.2	37	333	156	489	31	13.9	46	384	200	584	34
15	5.5		5	11.4	42	250	259	509	51	13.8	51	290	342	632	54
16	9.1	P	300	11.2	41	471	330	801	41	—	—	312	318	630	51

* Since in these animals the blood pressure, 10 min after inj., returned to a level above 50 Hg mm, they were not computed in the analysis of results.
A.P.S. = Anti-platelet serum, H = Histamine, T = Trypsin, P = Peptone.

TABLE II. Percent Differences of Blood Volume Determinations Before and After Different Types of Shock in 16 Dogs.

Dog No.	Type of shock	Blood volume: Plasma	Blood volume: Cells	Blood volume: Total	Total body haematocrit (%)
1	A.P.S.	—12	—30	—18	—13
2		— 3	—62	—26	—50
3		— 4	—69	—37	—50
4		—17	—62	—43	—33
5*		*—32	+ 8	—15	+26
6		—13	—42	—21	—25
7	H	—35	+12	—28	+57
8		—76	—14	—49	+68
9		—10	—56	—29	—39
10		—21	—24	—22	— 4
11		—26	—55	—37	—30
12		—44	0	—28	+39
13		—44	—38	—41	+ 5
14*	T	*+15	+13	+72	+10
15		+16	+32	+24	+ 6
16	P	—34	— 4	—21	+24

* See Table I.

TABLE III. Circulating Methaemoglobin % (Ratio $\frac{MHb \times 100}{Hb}$) Before and After Different Types of Shock, Supposing the Same Amount of MHb Were Injected in Both Instances.

Dog No.	Type of shock	Avg MHb used before and after shock (g)	Methaemoglobin (%): Before shock	Methaemoglobin (%): After shock	% diff.
1	A.P.S.	3.4	5.4	6.3	+ 17
2		2.3	4.3	10.7	+168
3		2.3	2.8	7.5	+166
4		2.8	2	5.3	+165
5*		5	4.7	5.1	+ 6
6		2.6	5.5	9.5	+ 73
7	H	2.9	6.4	7	+ 9
8		3.7	9	9.1	+ 1
9		3.3	3.9	9.4	+ 49
10		3	8.2	11.2	+ 37
11		2.5	3.8	8.5	+124
12		3.6	7.4	7.4	0
13		3.2	2.4	3.9	+ 63
14	T	2	4.2	3.5	— 17
15		2.4	3.4	2.5	— 26
16	P	3	2.6	2.7	+ 4

* See Table I.

It is noteworthy that in anti-platelet serum shock, the proportion of circulating methaemoglobin was greater than that observed in other types of shock. A lesser proportion of circulating methaemoglobin was found in the 2 animals with tryptic shock.

Discussion. It is evident that the blood volume decreased in anti-platelet serum shock

(Table I) as well as in histamine and peptone shock as shown by others. Decrease in blood volume is one of the most common features in shock and has been found by many workers in several types of shock. There is no agreement on the mechanism of the decrease; one of the most widely accepted theories suggests leakage through the capillaries with loss of plasma. More recently, however, this theory has been criticized on the basis of the work of Fine and collaborators(3), who while studying shock induced by hemorrhage, burn and trauma observed stagnation of plasma within the capillaries in the peripheral blood. These authors found that after the injection, during deep shock, of a known amount of plasma tagged with radioactive substances (S, I, Br), the plasma volume determination was always less than that expected from the plasma volume before shock plus the amount of plasma injected. After previous washing with saline to remove the tagged plasma from the vessels, these tissues showed no radioactivity, indicating that no leakage of plasma occurred under the conditions studied. They described the situation picturesquely in these words: "If in the late phase of shock the peripheral blood is not in active circulation, in the same sense as the peripheral waters of a swamp through whose center a brook runs, are not in active circulation, complete mixing may not occur in the time interval allowed." Regarding red blood cells, Gibson, Seligman, Evans and Fine (4) found that after the injection of red blood cells tagged with radioactive iron administered into animals in deep shock, the untagged and tagged red cell content of the tissues indicated that one fifth of the capillary blood becomes stagnant or trapped out of the active circulation.

Our results, excepting in tryptic shock, indicated a decrease of both plasma and red cell volumes, the absolute changes varying according to the type of shock; in anti-platelet serum shock the red cell volume decreased more than the plasma volume, leading to an apparent striking hemodilution; on the other hand, in histamine and peptone shock the plasma volume decreased more than the red cell volume, leading to the classical hemoconcentration described by others. The two exceptions observed in the dogs shocked by histamine, where hemodilution was found, could perhaps be explained by the anemic condition of the animal, since it is known that the ratio between capillary and total body hematocrit is even greater in anemic than in normal dogs(5). Our observations in 2 dogs shocked by trypsin seem to indicate a condition peculiar to this type of shock, in which an unexpected increase of plasma and red cell volumes was found. These observations should be confirmed.

Since hemolysis or hemorrhage did not occur during the phase of shock observed and the decrease of red blood cells of samples taken from great vessels occurs one or two minutes after the administration of anti-platelet serum(1), trapping seems to be a justifiable explanation of such rapid blood changes. The evidence presented by Fine and collaborators(4) for trapping of red blood cells in the peripheral bed, and of Chambers and Zweifach(6) for trapping of plasma, offers a new explanation of the mechanism of the changes in the relationship between red cell and plasma volumes.

The results obtained by the injection of methemoglobin labeled red cells before and after the induction of shock (Table III) support the possibility of red blood cell trapping. A relative increase of the circulating methemoglobin, greater than would be expected, was observed in all our experiments excepting in tryptic shock.

These results make it clear that the determination of the jugular hematocrit is far less significant than is usually accepted. Even the total body hematocrit is not enough to describe the whole picture of the blood changes. For instance, dogs 13 and 15, respectively shocked by trypsin and histamine, both presented practically the same blood concentration (+6% and +5%), notwithstanding the decrease of the red blood cell and plasma volumes in the animal shocked by histamine and the increase in red blood cell and plasma volumes in the animal shocked by trypsin. The different conditions in these two animals is clearly shown in Table III. The increase

of circulating red cells and plasma in dog 15 is evident in the result of —26% below the expected methemoglobin figure, while dog 13 shows plasma trapping in the result of +63% above the expected methemoglobin value. Thus, it is incorrect to accept the occurrence of hemodilution or hemoconcentration from determination of the hematocrit of blood in the great vessels. On the contrary, the results of these experiments indicated that different concentration of red cells can occur in the vessels; hemoconcentration in the great vessels with hemodilution in some of the capillaries and vice versa. Thus to explain the apparent hemoconcentration observed in the great vessels it is not necessary to assume extravasation of plasma or water nor to explain hemodilution is it necessary to assume loss of red cells from the circulatory system. To explain hemodilution in the great vessels by trapping, presupposes the stagnation of hemoconcentrated blood in the capillaries of some regions of the body and vice versa for hemoconcentration.

Summary. Total red blood cell volume (using red cells tagged with methemoglobin as a tracer) and plasma volume (using Evans blue dye T-1824) of dogs in different types of shock have been determined. Decreases in total red cell and plasma volumes have been observed in anti-platelet serum shock. The decrease in the red cell volume was greater than of the plasma volume, while in histamine shock the reverse was observed. Assumption has been made that trapping of red cells explains the apparent hemodilution in the great blood vessels in anti-platelet serum shock. The degree of trapping of the red cells, was determined by the proportion of circulating methemoglobin before and after shock. Analysis of the results shows the greater importance of the consideration of absolute values of red cell and plasma volumes rather than the acceptance of results indicated by the hematocrit of the blood from the great vessels, for the interpretation of the pathogenesis of shock.

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Experimental Porphyria. I. Isolation of Uroporphyrin I from Bone Marrow of Lead Poisoned Rabbits.* (19412)

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It is generally believed that lead interferes with hemoglobin synthesis. Associated abnormalities in porphyrin metabolism, namely, the presence of increased erythrocyte protoporphyrin and of urinary coproporphyrin III have been repeatedly documented. More recently, studies in this laboratory have revealed the occurrence of marked increases in the concentration of coproporphyrin III in the bone marrow of lead-poisoned rabbits(1). In the course of these studies, large amounts of an ether-insoluble, uro-type porphyrin were found in the marrow of the same animals. The present report is concerned with the iso-

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