

## INTRAVENOUS INJECTIONS

### A STUDY OF THE EFFECTS ON THE COMPOSITION OF THE BLOOD OF THE INJECTION OF VARIOUS FLUIDS INTO DOGS WITH NORMAL AND WITH LOW BLOOD PRESSURES

BY ALFRED BLALOCK, J. W. BEARD, AND CHARLES THUSS

*(From the Department of Surgery, Vanderbilt University, Nashville)*

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In a previous study (1) in which the composition of the blood was determined in experiments in which fluid was injected continuously while the intestines were being traumatized, it was found that there was a great decrease in the protein content as well as in the volume of the blood plasma. The object of the experiments reported in this paper is to determine the effects of the intravenous injection of fluids on the composition of the blood of normal dogs.

After a few experiments had been performed, it was observed that the results following the injection of the same type of solution were somewhat variable. For example, in some experiments the concentration of the red blood cells increased while in others it decreased. In the experiments in which the arterial pressure remained normal the results obtained were different from those if the pressure declined, even though the drop was only temporary.

We do not know why there was a decline in the blood pressure in many of the experiments. No trauma was instituted in any of them. It seems most likely that it was usually caused by the fluid that was being injected but this was not always the case as in some experiments the decline appeared before the introduction was begun. Probably the morphine or the barbital that was used as anesthetic caused the decline in some experiments. The dosage of these was not great, being only sufficiently large to maintain the animals quiet and free from pain. In many of the experiments the decline in pressure appeared almost simultaneously with the beginning of the introduction of fluid. It frequently returned later to its previous normal level. Vincent and Thompson (2) have described the effects on the arterial pressure of the injection of salt solution into the veins of decerebrate cats. They found that the injection of 10 cc. of salt solution in some instances produced an elevation or a decline in the pressure equivalent to as much as 60 mm. Hg. The temperature of the fluid was thought to be the most important factor in determining the response.

## METHODS

Dogs were used in all experiments. Morphine or sodium barbital was used as the anesthetic. The results did not seem to be influenced by the anesthetic. After the animals became quiet a cannula that was connected to a mercury manometer was placed in the carotid artery in order to determine the blood pressure. Samples of blood were obtained from the femoral veins. The blood volume was determined at the beginning of most of the experiments by the dye method as outlined by Rowntree, Brown and Roth (3). The blood that was withdrawn was replaced in all instances by an equal quantity of blood obtained from another dog. In most experiments tests were performed in order to be sure that the blood of the donor and recipient were not incompatible. Urine was collected through a catheter in the bladder. Small pieces of muscle were obtained at the beginning and end of some of the experiments for determinations of the water content.

When all of the specimens for the control determinations had been obtained, fluid was introduced at a constant speed and at body temperature through a cannula that had been placed in either the external jugular or the femoral vein. The fluid was usually injected at the rate of 10 cc. per kilogram of body weight per hour. In most of the experiments the duration of the introduction of the fluid was four hours, and the various samples for the analyses were collected one hour, two and one-half hours and four hours after the beginning of the injection. At one and three hour intervals after the termination of the injection, more samples were obtained. In a few of the experiments fluid was introduced throughout the entire period of observation and specimens for the analyses were collected at approximately two hour intervals. The following fluids were used in the different experiments; (1) 0.9 per cent salt solution, (2) 3.0 per cent salt solution, (3) 6.0 per cent glucose, (4) 20.0 per cent glucose, (5) 6.0 per cent gum acacia, (6) Evans' solution of 6.0 per cent gum acacia and 20 per cent glucose in normal saline, (7) blood serum and (8) whole blood.

The hematocrit determinations were performed by the use of the Van Allen tubes. The method of Cohen and Smith (4) was employed for the estimation of the hemoglobin. The initial blood volume was determined in most of the experiments by the dye method and the values obtained are placed in brackets in the tables. When not determined the blood volume was assumed to be ten per cent of the body weight and the volumes of red blood cells and plasma were calculated from the hematocrit readings. The alterations in the whole blood, red blood cell and plasma volumes that occurred in the experiments were estimated in the following manner. When both hemoglobin and hematocrit readings were obtained, the alterations in the total blood volume were assumed to vary in an inverse ratio to the changes in the percentage of hemoglobin, and from the total blood volume the quantity of red blood cells was calculated from the hematocrit readings. In the few experiments in which the hemoglobin was not determined, it was assumed that the volume of red blood cells remained constant throughout the experiments and alterations in the plasma volume were computed from the changes in the hematocrit readings. The various determinations were performed on the blood that was injected to replace that removed for the studies. Any differences between that removed and that injected were not considered in the various calculations. This introduced very little error. In the experiments in which the effects of the injection of whole blood were studied, the calculations were slightly more complicated. If blood is used, one is adding a fluid that contains red blood cells and consequently the changes in the hematocrit readings and hemoglobin are not measures of al-

terations in the blood volume. The calculations were made in the following manner. From the initial whole blood volume, the succeeding volume was calculated by the use of the percentage of hemoglobin as in other experiments. The actual volume of blood injected was reduced to that volume which would represent a blood with an hematocrit reading the same as the circulating blood at the time of the injection. The resulting value was then added to the tentative volume calculated initially from the hemoglobin changes and the sum was considered as the true blood volume. Each succeeding volume was calculated not from the control volume but from the one immediately preceding it since the hematocrit reading was constantly changing.

The total protein, the albumin and the globulin were determined by the same methods used in the experiments described in a previous paper (1). The absolute amounts of the protein constituents were obtained by multiplying the percentage of each by the plasma volume. The water content of blood and of muscle was determined by drying them to a constant weight.

## RESULTS

The results of the experiments with the different solutions that were used will be described separately. These groups will be subdivided into those in which the blood pressure remained at approximately the normal level throughout the experiments and those in which there was a definite decline in the pressure. Because of lack of space, only one experiment of each type will be given in detail in the tables.

### I. THE EFFECTS OF THE INJECTION OF NORMAL SALT SOLUTION

#### *A. Essentially normal blood pressure*

Two experiments of this type were performed. During the injection of the fluid there was a decrease in the concentration of the red blood cells and a diminution of protein per unit volume of blood serum. After the injection was terminated, there was a return towards the previous control level. The volume of plasma increased slightly during the injection and decreased later. In one of the experiments at no time was there any appreciable alteration in the absolute amount of protein in the circulation. In the other a decrease in the entire amount of protein was found during the last half of the experiment. The alterations in the albumin and globulin content of the serum paralleled closely those in the total protein. The results of one of these experiments are given in Table I. In this and in the succeeding tables "Injected blood" refers to that which was introduced in order to replace that withdrawn for the analyses.

#### *B. Low blood pressure*

Two experiments of this type were performed. The blood pressure in each declined early and never returned to the original control level. Fluid was injected during the entire duration of both experiments. There was an increase in the concentration of red blood cells, a decrease in the volume of plasma and a great decrease in both the percentage and abso-

TABLE I  
*The effects of the intravenous injection of normal salt solution*

Experiment number and weight	Time from beginning	Amount of fluid given	Total protein		Albumin		Globulin		Blood volume			Hematocrit	Hemoglobin	Mean blood pressure
			Serum	For total serum volume	Serum	For total serum volume	Red blood cells	Plasma	Whole					
		cc.	per cent	grams	per cent	grams	per cent	grams	cc.	cc.	cc.	per cent	per cent	mm. Hg
Normal blood pressure														
T 64 15.1 kgm.	Control	0	6.20	50.2	3.87	31.3	2.33	18.9	[665]*	[810]*	[1475]*	45.0	105.6	122
	1°	151	5.78	50.7	3.54	31.0	2.24	19.7	644	878	1522	42.3	102.3	116
	2° 30'	375	5.63	50.2	3.31	29.5	2.32	20.7	643	891	1534	41.9	101.6	138
	4°	604	5.29	49.6	3.15	29.5	2.14	20.1	655	935	1590	41.2	98.0	120
	5°		5.68	52.6	3.32	30.8	2.36	21.8	636	924	1560	40.8	99.3	136
	7°		5.75	50.6	3.34	29.7	2.41	20.9	648	888	1536	42.2	101.3	120
	Injected blood		6.07		2.84		3.23					35.1	86.9	
Lowered blood pressure														
T 32 13.4 kgm.	Control	0	5.30	39.0	2.37	6.3	1.82	4.8	602	736	1338	45.0		120
	1° 30'	225	4.19	11.1	2.09	6.5	1.45	4.5	602	364	966	62.3		79
	3° 30'	500	3.54	11.0	2.09	7.2	1.45	4.5	602	310	912	66.0		110
	5° 30'	825	3.63	12.4	2.11	7.2	1.52	5.2	602	339	941	64.0		76
	7° 30'	1125	3.30	13.2	1.83	7.3	1.47	5.9	602	398	1000	60.2		80

\* Determined directly by the dye method.

Protocols. T 64. Morphine as anesthetic. Total amount of urine collected during experiment was 180 cc. with a total protein equivalent of 7.79 grams.

T 32. Morphine as anesthetic. Total amount of urine collected during experiment was 162 cc. with a total protein equivalent of 8.08 grams. Died 6 hours later.

lute amounts of total protein, albumin and globulin. It is interesting that almost the entire loss of protein occurred during the first part of the experiment at the time that the blood pressure declined so markedly. The results of one of these experiments are to be found in Table I.

## II. THE EFFECTS OF THE INJECTION OF 3.0 PER CENT SALT SOLUTION

In no experiment in which 3.0 per cent salt solution was injected did the blood pressure remain entirely normal during the whole period of study. For this reason the experiments are divided into those in which the decline in blood pressure was great and those in which it was not so marked. In several instances bloody fluid was passed from the rectum.

### *A. Fairly well sustained blood pressure*

Four experiments of this type were performed. There was a decrease in the concentration of red blood cells during the injection followed by a marked increase after the cessation of the injection. The plasma volume increased during the injection and declined markedly later. In the two instances in which the injections were continued throughout the experiments there was an increase in the hematocrit reading and a decrease in the plasma volume at the conclusion. The diminution in the percentage of total protein, albumin and globulin was usually progressive up to the time that the injection was stopped. During the early part of the experiments there was usually very little reduction in the absolute amount of plasma protein but the decline later was usually marked. The results of one of these experiments are enumerated in Table II.

### *B. More marked decline in blood pressure*

Two experiments were performed. The findings are similar in most respects to those in the preceding group except that the changes were more pronounced. The loss of protein was greater in experiment T 38 in which a very marked decline in blood pressure occurred than in any other experiment reported in this paper. There was not only a large decrease in the concentration of total protein, albumin and globulin in the serum but also a great diminution in the plasma volume. The absolute amount of plasma protein was least when the blood pressure was lowest which was during the early part of the experiment. The results of one of these experiments are given in Table II.

## III. THE EFFECTS OF THE INJECTION OF 6.0 PER CENT GLUCOSE SOLUTION

### *A. Essentially normal blood pressure*

Two experiments of this type were performed. In one of these, T 65, there was no loss of protein. During the injection period, there was a slight increase in the plasma volume and a slight decrease in the percentage of protein. After the injection was terminated the plasma volume

TABLE II  
*The effects of the intravenous injection of 3 per cent salt solution*

Experiment number and weight	Time from beginning	Amount of fluid given	Total protein		Albumin		Globulin		Blood volume			Hematocrit	Hemoglobin	Mean blood pressure
			Serum	For total serum volume	Serum	For total serum volume	Red blood cells	Plasma	Whole					
		cc.	per cent	grams	per cent	grams	per cent	grams	cc.	cc.	cc.	per cent	per cent	mm. Hg
Fairly well sustained blood pressure														
T 60 12.6 kgm.	Control	0	5.99	43.7	4.14	30.2	1.85	13.5	[813]*	[729]*	[1542]*	52.7	124.5	184
	1°	126	5.28	38.9	3.38	24.9	1.90	14.0	830	736	1566	53.0	122.0	150
	2° 30'	315	4.40	38.0	2.79	23.8	1.98	16.9	855	855	1710	50.0	112.4	105
	4°	504	4.10	39.2	2.55	24.4	1.95	18.6	874	956	1830	47.7	104.9	115
	5°		4.37	35.6	2.81	22.9	1.56	12.7	880	815	1695	51.9	113.2	130
	7°		4.20	30.6	2.62	19.1	1.68	12.3	921	729	1650	55.8	116.3	80
	Injected blood		5.25			3.38		1.87					36.2	78.5
Lowered blood pressure														
T 38 11.5 kgm.	Control	0	4.70	26.4	2.90	16.3	1.80	10.1	591	565	1153	51.3		130
	1° 30'	225	3.16	7.5	1.94	4.6	1.22	2.9	591	235	826	71.5		65
	3° 30'	525	3.16	10.1	1.84	5.9	1.32	4.2	591	318	909	65.0		100
	5° 30'	825	3.18	9.3	1.90	5.6	1.28	3.7	591	292	883	66.0		80
	7° 30'	1125	3.07	9.5	1.84	5.7	1.33	3.8	591	311	902	65.5		75

\* Determined directly by the dye method.

Protocols. T 60. Barbital as anesthetic. Total amount urine 400 cc. with a total protein equivalent of 6.44 grams.

T 38. Morphine as anesthetic. Total amount of urine was 376 cc. Passage of a large quantity of fluid from rectum.

TABLE III  
*The effects of the intravenous injection of 6 per cent glucose solution*

Experiment number and weight	Time from beginning	Amount of fluid given	Total protein			Albumin			Globulin			Blood volume			Hematocrit	Hemoglobin	Mean blood pressure
			Serum	For total serum volume	grams	Serum	For total serum volume	grams	Serum	For total serum volume	grams	Red blood cells	Plasma	Whole			
		cc.	per cent	grams	per cent	grams	per cent	grams	cc.	cc.	cc.	per cent	per cent	mm. Hg			
Normal blood pressure																	
T 65 14 kgm.	Control	0	7.15	65.7	4.05	37.2	3.10	28.5	[710]*	[918]*	[1628]*	43.6	96.8	130			
	1°	141	6.98	63.6	3.83	34.9	3.15	28.7	702	911	1613	43.5	97.7	130			
	2° 30'	352	6.85	65.1	3.82	36.3	3.03	28.8	690	950	1640	42.1	96.1	130			
	4°	564	6.58	66.2	3.62	36.3	2.96	29.9	698	1004	1702	41.0	92.6	130			
	5°		6.99	68.9	3.80	37.4	3.19	31.5	694	986	1680	41.3	93.8	135			
	7°		7.00	67.4	3.91	37.6	3.09	29.7	703	962	1665	42.2	94.6	125			
	Injected blood		6.14		4.16		1.98					34.0	82.0				
Lowered blood pressure																	
T 59 13 kgm.	Control	0	6.14	58.5	3.28	31.2	2.86	27.2	[548]*	[952]*	[1500]*	36.5	82.0	150			
	1°	130	5.28	55.1	2.94	30.7	2.34	24.4	556	1044	1600	34.8	76.9	90			
	2° 30'	325	5.37	54.5	2.97	30.1	2.40	24.3	560	1015	1575	35.6	78.1	100			
	4°	520	4.84	50.9	2.94	30.9	2.36	24.8	545	1052	1597	34.1	77.0	113			
	5°		5.34	51.2	2.98	28.6	2.36	22.7	550	960	1510	36.4	81.5	122			
	7°		5.20	50.3	3.06	29.6	2.14	20.7	549	967	1516	36.2	81.1	106			
	Injected blood		5.64		3.33		2.31					35.8	80.9				

\* Determined directly by the dye method.

Protocol. T 59. Sodium barbital as anesthetic. Total amount of urine 97 cc. with a total protein equivalent of 5.71 grams.

decreased and the percentage of protein increased. In the second experiment, T 78, there was a slight loss in the absolute amount of plasma protein even though the blood pressure remained at approximately the normal control level. This was encountered in very few of the experiments in which the blood pressure remained elevated. The results of one of these experiments are given in Table III.

#### *B. Decline in blood pressure*

Two experiments of this type were performed. In each there was a decline in the blood pressure during the early part of the experiment. Later the pressure approached but never reached that which was found in the control studies. In one experiment, T 59, there was a slight increase in the plasma volume, a decrease in the percentage of protein and a reduction in the absolute amount of plasma protein. In the other experiment, T 35, in which the mean blood pressure declined to 70 mm. Hg simultaneously with the beginning of the injection and remained there for a short while, there was a great decrease in the plasma volume, percentage of protein and absolute amount of plasma protein. The results of one of these experiments are given in Table III.

### IV. THE EFFECTS OF THE INJECTION OF 20.0 PER CENT GLUCOSE SOLUTION

#### *A. Normal blood pressure*

Two experiments of this type were performed. The findings in each are almost identical. The blood pressure remained at approximately the same level throughout the experiments. There was a slight decrease in the plasma volume and a slight increase in the percentage of total protein, albumin and globulin in the serum. In one experiment there was a slight increase in the absolute amounts of total protein, albumin and globulin in the circulation and in the other there was practically no alteration. The results of one of these experiments are to be seen in Table IV.

#### *B. Decline in blood pressure*

There was an early decline in the blood pressure in both of the experiments. During the injection there was a slight increase in the volume of plasma and a reduction in the percentage and absolute amount of plasma protein. After the introduction of fluid was terminated the percentage of protein in the serum increased but due to the fact that the plasma volume decreased, the absolute amount of plasma protein in the circulation did not rise appreciably. The results of one of these experiments are given in Table IV.



TABLE IV  
*The effects of the intravenous injection of 20 per cent glucose solution*

Experiment number and weight	Time from beginning	Amount of fluid given	Total protein		Albumin		Globulin		Blood volume			Hematocrit	Hemoglobin	Mean blood pressure
			Serum	For total serum volume	Serum	For total serum volume	Red blood cells	Plasma	Whole					
										per cent	grams			
Normal blood pressure														
T 66 13.9 kgm.	Control	0	6.44	58.4	2.39	21.6	4.05	36.8	[667]*	[908]*	[1575]*	42.3	96.6	126
	1°	139	5.25	55.7	2.03	21.6	3.22	34.1	657	1058	1715	38.3	88.8	132
	2° 30'	348	5.52	58.7	2.15	22.9	3.37	35.8	646	1064	1710	37.8	89.0	132
	4°	556	6.62	58.8	2.63	23.1	4.17	35.7	660	888	1548	42.6	98.3	130
	5°		7.20	59.0	2.86	23.2	4.54	35.8	694	818	1512	45.9	106.0	132
	7°		6.95	58.4	2.81	23.5	4.39	35.5	666	850	1516	44.0	100.3	128
	Injected blood			5.70								26.9	66.4	
Lowered blood pressure														
T 61 9.0 kgm.	Control	0	5.54	27.8	3.32	16.7	2.22	11.1	[311]*	[502]*	[813]*	38.3	93.2	130
	1°	90	3.49	20.2	2.06	11.9	1.43	8.3	308	578	886	34.8	85.5	50
	2° 30'	225	3.36	21.9	1.84	12.0	1.42	9.3	311	652	963	32.3	75.8	63
	4°	360	3.56	21.9	2.07	12.7	1.31	8.1	308	614	922	33.4	82.2	74
	5°	Injected blood	4.33	23.3	2.46	13.2	1.71	9.2	326	538	864	37.7	87.8	54
	7°		4.84	22.7	2.79	13.1	2.05	9.6	315	469	784	40.2	96.5	54
					2.46						32.0	74.7		

\* Determined directly by the dye method.

Protocols. T 66. Morphine as anesthetic. Total amount of urine 900 cc. with a total protein equivalent of 19.26 grams.  
T 61. Barbitol as anesthetic. Total urine 66 cc. with a total protein equivalent of 1.85 grams.

TABLE V  
*The effects of the intravenous injection of 6 per cent gum acacia solution*

Experiment number and weight	Time from beginning	Amount of fluid given	Total protein		Albumin		Globulin		Blood volume			Hematocrit	Hemoglobin	Mean blood pressure
			Serum	For total serum volume	Serum	For total serum volume	Red blood cells	Plasma	Whole					
		cc.	per cent	grams	per cent	grams	per cent	grams	cc.	cc.	cc.	per cent		mm. Hg
Essentially normal blood pressure														
T 77 13.8 kgm.	Control	0	6.24	43.1	3.65	25.2	2.59	17.9	[388]*	[690]*	[1078]*	36.0	84.7	138
	1°	138	4.98	38.6	3.12	24.2	1.86	14.4	380	776	1156	32.9	79.0	140
	2° 30'	345	4.18	37.2	2.54	22.7	1.64	14.5	383	892	1275	30.2	71.6	160
	4°	552	3.77	40.2	2.37	25.2	1.40	15.0	390	1065	1455	26.8	62.7	168
	5°		3.95	40.5	2.43	24.9	1.52	15.6	410	1025	1435	28.4	63.7	156
	7°		3.95	45.6	2.40	27.7	1.55	17.9	335	1155	1490	22.6	61.2	128
	Injected blood		5.47		2.48							27.1	64.7	
Lowered blood pressure														
T 74 14 kgm.	Control	0	6.27	51.4	3.46	28.4	2.81	23.1	[665]*	[820]*	[1485]*	44.8	107.7	124
	1°	140	5.02	32.2	2.75	17.9	2.27	14.8	654	661	1315	49.7	120.5	100
	2° 30'	350	4.11	36.6	2.25	20.0	1.86	16.6	604	891	1495	44.5	107.1	124
	4°	560	3.41	36.2					728	1062	1790	40.7	97.7	100
	5°		3.61	34.8	2.03	17.0	1.65	13.8	663	957	1620	40.9	98.7	96
	7°		3.68	30.8	2.42		2.06		658	837	1495	44.0	107.1	90
	Injected blood		4.48									31.2	75.4	

\* Determined directly by the dye method.

Protocols, T 77. Morphine as anesthetic. Shortly after first injection of fluid, blood pressure declined to a mean of 110 mm. Hg but rose almost immediately. Total urine 260 cc. with a total protein equivalent of 7.46 grams.

T 74. Morphine as anesthetic. Shortly before injection of fluid, mean blood pressure declined to 90 mm. Hg and remained at that level for about 15 minutes.

## V. THE EFFECTS OF THE INJECTION OF 6.0 PER CENT GUM ACACIA SOLUTION

### *A. Essentially normal blood pressure*

Several attempts were made before we were successful in performing an experiment in which the blood pressure did not decline markedly during the early part of the injection of the gum acacia solution. Except for boiling it, no effort was made to purify this solution. In the experiment that is reported the mean blood pressure declined to 110 mm. Hg simultaneously with the beginning of the injection but it rose almost immediately to its previous level. A marked increase in the plasma volume and a large decrease in the percentage of protein were associated with the giving of the gum acacia. The absolute amount of plasma protein decreased slightly. Following the cessation of the injection the volume of plasma did not decrease as was found in most of the experiments in which salt and glucose solutions were employed. At the end of the experiment the absolute amount of plasma protein was slightly greater than at the beginning. The results of this experiment are given in detail in Table V.

### *B. Decline in blood pressure*

Only one complete experiment of this type was performed. At the end of the first hour of the injection there was a small but definite decline in the blood pressure and a decrease in the plasma volume. Following this the blood pressure rose and the plasma volume became greater than it had been during the control studies. There was a large drop in the protein content of the blood plasma and despite the fact that the volume of plasma increased, there was a great decrease in the absolute amount of plasma protein. The results of this experiment are to be seen in Table V.

## VI. THE EFFECTS OF THE INJECTION OF GUM ACACIA-GLUCOSE-SALINE SOLUTION

### *A. Essentially normal blood pressure*

Two experiments of this type were performed. There was a great increase in the plasma volume and a marked decrease in the percentage of protein in the serum in both. During the early part of the experiments there was a small loss in the absolute amount of protein in the circulation in one and a small gain in the other. Later in one experiment an excessive amount of fluid was injected and the absolute amount of plasma protein diminished markedly. The results of one of these experiments are given in Table VI.

### *B. Decline in blood pressure*

Two experiments of this type were performed. During the injection period in each there was an increase in the volume of plasma but the decrease in the percentage of protein was so great that there was a marked

TABLE VI  
*The effects of the intravenous injection of gum acacia-glucose-saline solution*

Experiment number and weight	Time from beginning	Amount of fluid given	Total protein		Albumin		Globulin		Blood volume			Hematocrit	Hemoglobin	Mean blood pressure
			Serum	For total serum volume	Serum	For total serum volume	Serum	For total serum volume	Red blood cells	Plasma	Whole			
Essentially normal blood pressure														
T 71 12.8 kgm.	Control	0	7.77	49.6	5.12	32.7	2.65	16.9	[729]*	[638]*	[1367]*	53.3	120	130
	1°	128	5.63	44.8	3.48	27.7	2.13	16.9	705	795	1500	47.1	109.5	137
	2° 30'	320	4.99	46.3	3.05	28.3	1.94	18.0	672	928	1600	44.2	102.4	140
	4°	512	4.26	40.1	2.74	25.8	1.52	14.3	708	942	1650	42.9	99.3	144
	5°		4.64	35.8	2.90	22.4	1.74	13.4	703	772	1475	47.7	111.1	115
	7°		4.84	32.4	2.90	19.4	1.90	12.7	730	670	1400	52.2	117.1	60
	Injected blood		5.96		3.47		2.49					42.7	102	
Lowered blood pressure														
T 63 13.3 kgm.	Control	0	5.10	37.9	2.78	20.6	2.32	17.3	[335]*	[743]*	[1078]*	31.2	75.2	157
	1°	133	3.17	24.8	1.65	12.9	1.52	11.9	316	784	1100	28.7	73.7	117
	2° 30'	333	2.76	27.0	1.58	15.6	1.18	11.4	327	978	1305	25.1	62.1	146
	4°	532	2.58	28.8	1.37	15.3	1.21	13.5	315	1115	1430	22.0	56.7	148
	5°		2.78	26.9	1.57	16.1	1.81	10.8	327	968	1295	25.2	62.6	156
	7°		3.06	28.1	1.65	15.1	1.41	13.0	319	918	1237	25.8	65.6	136
	Injected blood		5.98		3.56		2.42					28.8	73.1	

\* Determined directly by the dye method.

Protocols. T 71. Morphine as anesthetic. The mean blood pressure declined to 105 mm. Hg immediately after first fluid was injected. It remained there for 5 minutes, then rose to 120. Total amount of urine was 322 cc. with a total protein equivalent of 8.96 grams.

T 63. Barbitol as anesthetic. The mean blood pressure was 77 mm. Hg when injection was begun. Total amount of urine was 481 cc. with a total protein equivalent of 6.54 grams.

decrease in the absolute amount of plasma protein. After the introduction of fluid was terminated the plasma volume decreased, the protein content of the serum increased, and the absolute amount of plasma protein remained approximately the same as it had been at the time of the previous determination. The alterations in the amounts of albumin and globulin paralleled those in the total protein. In these experiments as in many of the others it is interesting that the greatest decrease in the amounts of total protein, albumin and globulin took place in the periods when the most marked decline in the blood pressure occurred. The results of one of these experiments are enumerated in Table VI.

## VII. THE EFFECTS OF THE INJECTION OF BLOOD SERUM

### *A. Normal blood pressure*

In the one experiment in which blood serum was injected in the presence of a normal blood pressure there was an increase in the plasma volume and in the content of total protein, albumin and globulin in the blood serum. Following the termination of the injection the plasma volume decreased slightly and the percentage of protein increased slightly. The absolute amount of plasma protein in the blood stream progressively increased during the injection and then decreased very slightly. If one subtracts from the absolute amount of plasma protein a figure that represents the amount of protein that was present in the serum that had been injected, it is to be seen that very little of the protein that was already in the vessels or that was introduced in the serum was lost from the blood stream.

The results of this experiment are given in Table VII. The figures for total protein, albumin and globulin that are placed in parentheses in the table indicate the entire amount that would have been present in the blood stream had protein not been present in the fluid that was injected. In other words, the figures in the parentheses were obtained by subtracting the amount that was injected from the amount that was actually present.

### *B. Decline in blood pressure*

One experiment of this type was performed. The decline in the blood pressure appeared in the early part of the experiment and it was not very great. However, during the first hour of the experiment there was a tremendous decrease in the entire amount of protein in the blood stream despite the fact that protein was present in the fluid that was being injected. This decrease was due to the loss of plasma and not to a diminution in the percentage of protein. Later the plasma volume and the absolute amount of plasma protein increased, but if one makes allowance for the amount of protein that was injected, the loss was considerable. The results of this experiment are to be found in Table VII.

TABLE VII  
*The effects of the intravenous injection of blood serum*

Experiment number and weight	Time from beginning	Amount of fluid given	Total protein		Albumin		Globulin		Blood volume			Hematocrit	Hemoglobin	Mean blood pressure
			Serum	For total serum volume	Serum	For total serum volume	Serum	For total serum volume	Red blood cells	Plasma	Whole			
		cc.										per cent	per cent	mm. Hg
Normal blood pressure														
T 70 8.6 kgm.	Control	0	4.33	24.8 (23.3)†	3.16	18.2 (14.5)†	1.17	6.71 (9.8)†	[326]*	[574]*	[900]*	36.2	87.7	100
	1°	86	5.34	29.0 (25.2)†	3.30	17.6 (15.4)†	2.14	11.4 (7.3)†	324	544	868	37.4	90.9	108
	2° 30'	214	5.64	39.4 (23.2)†	3.58	24.9 (13.0)†	2.09	14.5 (6.3)†	360	695	1035	34.1	83.1	104
	4°	422	5.77	46.0 (22.5)†	3.54	28.2 (12.5)†	2.23	17.8 (6.1)†	341	795	1138	30.0	77.1	102
	5°		5.81	45.3 (20.5)†	3.55	27.7 (12.2)†	2.26	17.6 (4.3)†	351	779	1130	31.1	77.7	99
	7°		5.91	43.3	3.74	27.4	2.17	15.8	368	732	1100	33.4	79.6	98
	Blood injected Serum injected		6.66 6.66			3.79 3.79		2.87 2.87					54.8	132.7

TABLE VII (continued)

Experiment number and weight	Time from beginning	Amount of fluid given	Total protein		Albumin		Globulin		Blood volume			Hematocrit	Hemoglobin	Mean blood pressure
			Serum	For total serum volume	Serum	For total serum volume	Red blood cells	Plasma	Whole					
										per cent	grams			per cent
Lowered blood pressure														
T 72 14.5 kgm.	Control	0	5.99	92.5 (61.3)†	3.47	53.6 (32.9)†	2.52	38.9 (25.5)†	[687]*	[1545]*	[2232]*	30.8	74.9	120
	1°	145	6.19	68.2 (66.9)†	3.44	37.9 (32.6)†	2.75	30.3 (32.0)†	703	1102	1805	38.9	92.6	100
	2° 30'	363	6.68	86.9 (73.0)†	3.38	44.6 (40.2)†	3.30	43.6 (33.1)†	690	1320	2010	34.4	83.1	130
	4°	580	6.75	105.3 (70.5)†	3.43	53.6 (39.1)†	3.32	51.8 (32.3)†	672	1560	2232	30.1	75.0	118
	5°		6.83	102.5 (75.0)†	3.50	52.5 (41.6)†	3.33	50.0 (33.5)†	680	1500	2180	31.0	75.8	113
	7°		7.07	107.0	3.65	55.0	3.44	52.2	705	1515	2220	31.6	75.4	120
	Replaced blood Injected serum		5.64 5.53		2.79 2.31		2.85 3.22						25.2 70.1	

\* Determined directly by the dye method.

† Indicates the entire amount that would have been present in the blood stream had protein not been present in the fluid that was injected.

Protocols. T 70. Morphine as anesthetic. Total amount of urine 64 cc. with a total protein equivalent of 6.66 grams.  
 T 72. Morphine as anesthetic. Total amount of urine 185 cc. with a total protein equivalent of 7.31 grams.

Where two sets of figures are given, those in brackets were obtained by subtracting the amounts of protein that were injected from the quantity that was actually present in the blood stream.

#### VIII. THE EFFECTS OF THE INJECTION OF WHOLE BLOOD

##### *A. Normal blood pressure*

Only one experiment was performed. There was an increase in the concentration of red blood cells, an increase in the percentage and in the absolute amounts of total protein, albumin and globulin in the serum. If one makes a deduction for the protein that was injected in the serum, there was a slight decrease in the absolute amount of plasma protein. These figures are placed in brackets in Table VIII in which the results appear.

##### *B. Decline in blood pressure*

In the experiment of this type, the blood pressure declined to a mean of 95 mm. Hg shortly before the beginning of the introduction of blood and it remained at that level for approximately one hour. There was a great increase in the concentration of red blood cells, a diminution in the volume of plasma, and a slight increase in the percentage of protein in the serum. Despite the fact that almost 17 grams of protein were present in all of the serum that was introduced the absolute amount of plasma protein was no greater at the end of the injection than during the control period. The results of this experiment are to be found in Table VIII.

In twenty of the experiments the water content of skeletal muscle was determined at the beginning and end of the studies. The results may be summarized briefly as follows. In the experiments in which isotonic solutions of salt or glucose were injected, there was a slight increase in the water content of muscle. In those instances in which hypertonic solutions of salt or glucose were used, there was usually a slight decrease in the water content of muscle. The injection of the gum acacia-glucose-saline solution was associated with a decrease in the water content of muscle. The results of these experiments are given in Table IX.

#### DISCUSSION

The results of these experiments may be divided into two rather definite groups. In those instances in which there was practically no alteration in the blood pressure, there was little or no loss in plasma protein. When solutions of salt or glucose were injected, they were lost from the blood stream rapidly and protein was usually not carried with them. When solutions containing gum acacia were injected, there was an increase in the plasma volume due to the fact that a large part of the solution remained in the blood stream. The percentage of protein was decreased but the absolute amount of plasma protein remained approximately the



TABLE VIII  
*The effects of the intravenous injection of whole blood*

Experiment number and weight	Time from beginning	Amount of fluid given	Total protein		Albumin		Globulin		Blood volume			Hematocrit	Hemoglobin	Mean blood pressure
			Serum	For total serum volume	Serum	For total serum volume	Serum	For total serum volume	Red blood cells	Plasma	Whole			
		cc.			per cent	grams	per cent	grams	cc.	cc.	cc.	per cent	per cent	mm. Hg
Normal blood pressure														
T 68	Control	0	5.92	38.6 (36.9)†	3.85	25.1 (25.0)†	2.07	13.5 (11.9)†	[463]*	[652]*	[1115]*	41.6	104.5	125
10.3 kgm.	1°	103	6.52	40.7 (34.6)†	4.25	26.5 (26.3)†	2.27	14.2 (8.3)†	505	624	1129	44.7	111.9	140
	2° 30'	258	6.64	46.2 (29.9)†	4.32	30.0 (22.2)†	2.32	16.2 (7.7)†	568	695	1263	44.0	111.8	155
	4°	412	6.66	45.2 (33.1)†	4.14	28.1 (23.7)†	2.52	17.1 (9.4)†	627	678	1305	48.1	119.0	166
	5°		6.65	48.4 (29.1)†	4.06	29.6 (20.7)†	2.59	18.8 (8.4)†	621	728	1349	46.1	115.4	160
	7°		6.66	44.4	3.99	26.6	2.67	17.8	633	667	1300	48.7	119.5	128
	Injected blood		5.99		2.30		3.40					37.9	91.1	

TABLE VIII (continued)

Experiment number and weight	Time from beginning	Amount of fluid given	Total protein		Albumin		Globulin		Blood volume			Hematocrit	Hemoglobin	Mean blood pressure
			Serum	For total serum volume	Serum	For total serum volume	Red blood cells	Plasma	Whole					
		cc.	per cent	grams	per cent	grams	per cent	grams	cc.	cc.	cc.	per cent		mm. Hg
Lowered blood pressure														
T 75 11.5 kgm.	Control	0	5.46	32.1 (20.8)†	4.12	24.2 (16.0)†	1.34	7.9 (4.8)†	[444]*	[511]*	[955]*	46.5	111.1	164
	1°	115	6.18	25.0 (16.6)†	4.56	18.4 (12.3)†	1.62	6.6 (4.3)†	473	404	877	53.9	132	110
	2° 30'	288	5.94	27.1 (11.5)†	4.09	18.7 (8.7)†	1.85	8.4 (2.8)†	540	457	997	54.2	130.1	142
	4°	460	6.28	28.3 (7.5)†	4.09	18.4 (6.3)†	2.19	9.9 (1.2)†	602	450	1052	57.3	136.3	130
	5°		6.14	24.3 (8.3)†	4.06	16.0 (7.3)†	2.08	8.3 (1.0)†	596	396	992	60.1	145	104
	7°		6.14	25.1	4.17	17.0	1.97	8.1	598	409	1007	59.4	142.8	117
	Injected blood		5.51		3.20							34	85.7	

\* Determined directly by the dye method.

† Indicates the entire amount that would have been present in the blood stream had protein not been present in the fluid that was injected.

Protocols. T 68. Morphine as anesthetic. Total urine 123 cc. with a total protein equivalent of 11.23 grams.

T 75. Morphine as anesthetic. Thirty minutes before the injection of fluid was begun, the blood pressure declined to a mean of 95 mm. Hg and remained there for approximately one hour. Total urine 46 cc. with a total protein equivalent of 3.3 grams.

TABLE IX

*The effects of the administration of fluids on the water content of blood and muscle—no trauma*

Fluid injected	Experiment number	Time	Mean blood pressure	Hematocrit	Water			Amount fluid given
					Blood	Pectoral muscle	Thigh muscle	
<i>per cent</i>			<i>mm. Hg</i>	<i>per cent</i>	<i>per cent</i>	<i>per cent</i>	<i>per cent</i>	<i>cc.</i>
0.9 Saline.....	T 31	Control	127	36.0	80.80	75.25	73.22	0
		7° 30'	53	37.0	81.10	75.80	73.95	1125
0.9 Saline.....	T 32	Control	120	45.0	80.75	75.42	74.75	0
		7° 30'	80	60.2	77.20	75.90	75.00	1125
0.9 Saline.....	T 41	Control	115	57.3	77.18	75.55	74.90	0
		7° 5'	104	47.3	79.90	76.30	75.20	1091
0.9 Saline.....	T 58*	Control	132	42.0	78.10	74.90	76.00	0
		7°	120	46.6	78.80	76.60	77.20	488
Average...		Control	123.5	45.1	79.21	75.28	74.72	
		Later	89.3	47.8	79.25	76.15	75.34	
3.0 Saline.....	T 33	Control	150	43.5	79.98	77.38	76.50	0
		7° 5'	0	53.6	79.50	74.40	75.50	1063
3.0 Saline.....	T 42	Control	164	49.2	77.95	75.80	74.22	0
		6° 45'	116	44.8	78.60	74.80	71.75	1094
3.0 Saline.....	T 38	Control	130	51.3	79.40	75.50	74.70	0
		7° 30'	75	65.5	76.60	74.25	74.00	1125
3.0 Saline.....	T 60*	Control	184	52.7	75.40	76.00	75.10	0
		7°	80	55.8	75.50	75.40	72.70	504
Average...		Control	157	49.2	78.18	76.17	75.13	
		Later	68	54.9	77.55	74.71	73.49	
6.0 Glucose....	T 34	Control	146	37.0		76.20	73.95	0
		7° 5'	150	40.0		81.30	75.80	1125
6.0 Glucose....	T 35	Control	130	50.6	78.40	76.10	74.40	0
		7° 30'	112	53.8	78.80	77.80	75.60	1125
6.0 Glucose....	T 59*	Control	150	36.5	80.20	77.80	75.50	0
		7°	106	36.2	81.40	78.10	76.90	520
Average...		Control	142	41.4	79.30	76.70	74.62	
		Later	123	43.3	80.10	79.07	76.10	

TABLE IX (continued)

Fluid injected	Experiment number	Time	Mean blood pressure	Hematocrit	Water			Amount fluid given
					Blood	Pectoral muscle	Thigh muscle	
<i>per cent</i>			<i>mm. Hg</i>	<i>per cent</i>	<i>per cent</i>	<i>per cent</i>	<i>per cent</i>	<i>cc.</i>
20.0 Glucose . . .	T 37	Control 7° 30'	120 122	45.4 46.2	79.60 79.80	79.50 75.00	75.60 73.50	0 1125
20.0 Glucose . . .	T 36	Control 7° 30'	160 108	38.0 40.6	81.40 81.40	77.00 75.50	75.60 75.30	0 1125
20.0 Glucose . . .	T 61*	Control 7°	130 54	38.3 40.2	80.40 79.80	74.80 76.60	73.40 73.90	0 360
Average . . .		Control Later	137 95	40.6 42.3	80.47 80.33	77.10 75.70	74.87 74.23	
6.0 Gum acacia	T 39	Control 7° 20'	152 111	46.3 35.0	78.6 82.6	75.70 75.60	79.70 75.40	0 1100
Acacia-glucose-saline	T 11	Control 6° 30'	164 60	52.0 35.0	76.77 81.90	68.05 64.95	65.40 62.75	0 975
Acacia-glucose-saline	T 13	Control 18° 50'	125 0	47.0 49.0	78.85 80.10	74.35 73.50	75.10 73.20	0 1250
Acacia-glucose-saline	T 12	Control 6°	128 20	58.0 49.0	75.05 78.60	67.20 54.40	67.30 69.75	0 900
Acacia-glucose-saline	T 62*	Control 7°	190 96	44.5 43.3	78.10 78.00	77.20 74.80	74.90 73.40	0 508
Average . . .		Control Later	152 44	50.4 44.1	77.19 79.65	71.70 66.91	70.68 69.78	
Whole blood. . .	T 40	Control 7° 20'	154 165	43.0 51.0	79.80 76.90	76.80 76.30	75.20 75.20	0 1100

\* In experiments T 58, T 59, T 60, T 61, and T 62, the injection of fluid was discontinued after four hours and the samples were obtained three hours later. In the remaining experiments with the exception of T 13, fluid was injected during the entire duration of the experiments.

same. When blood serum or whole blood was injected, there was practically no loss either of the protein that was already in the blood stream or of that which was injected. In the other group in which there was a temporary or sustained decline in the pressure, the results were quite different. When solutions of salt or glucose were injected, there was a loss not only of a large part of the fluid that was injected but also a loss of blood plasma. It appeared in these experiments as though the mixture of the blood plasma and the injected solution passed through the vessel walls in the same composition as it existed in the blood stream. It seems

that the loss was similar in this respect if gum acacia, whole blood or blood serum were injected. The results were different in that gum acacia and blood are colloidal solutions and that the portion of the fluid which was left in the blood stream exerted an osmotic pressure. Although there was a decrease in both the percentage and absolute amounts of plasma protein following the introduction of gum acacia, the latter due to the size of its molecule probably compensated for part of the loss. No attempt was made to determine the amount of gum acacia in the serum. Due to the fact that the injected blood serum and whole blood had approximately the same content in protein as the plasma in the blood stream, their injection was associated with only the decrease in the absolute amount of protein and not with a reduction in the concentration of protein.

It has been known for a long time that solutions of crystalloids leave the blood stream shortly after having been introduced. Most of the evidence has indicated that the walls of the blood vessels are normally impermeable to the passage of proteins. White and Erlanger (5) found that the injection of a strongly hypertonic solution of glucose and gum acacia into normal dogs was associated with an increase in the plasma volume, a decrease in the percentage of plasma protein and very little alteration in the absolute amount of plasma protein. The blood pressure was not determined in these experiments. It is rather generally believed that plasma is lost from the blood stream in shock. In the preceding study it was found that the intravenous introduction of protein free fluids into dogs in which tissues had been injured is associated usually with a decrease both in the plasma volume and in the percentage of protein in the serum. The present experiments show that protein may be lost from the blood stream without gross injury to tissues. As to the mechanism of the loss, we can make no definite statements. Protein may have been lost because of the decline in the arterial pressure or both the decline in pressure and the loss of protein may have resulted from a common cause. It is possible that the passage of red blood cells from the spleen into the general circulation caused an increase in the concentration of red cells in the latter. That the spleen was not entirely responsible was demonstrated in two experiments in which the spleen was removed and normal salt solution was injected after a decline in blood pressure had been produced by the introduction of a small amount of gum acacia. In both instances a concentration of the blood and a marked loss of protein was found. The results of these experiments are given in Table X.

The observations on the water content of skeletal muscles showed that most of the fluid that left the blood stream did not pass into them. Analyses were not performed on other tissues but it seems likely that the greater part of the fluid escaped into the intraperitoneal structures. No free fluid was present in the peritoneal cavity in any of the experiments. In most instances in which 3.0 per cent salt solution was injected, there

TABLE X  
*The effects of the intravenous injection of normal salt solution after removal of the spleen (Lowered blood pressure)*

Experiment number and weight	Time from beginning	Amount of fluid given	Total protein		Albumin		Globulin		Blood volume			Hematocrit	Hemoglobin	Mean blood pressure
			Serum	For total serum volume	Serum	For total serum volume	Serum	For total serum volume	Red blood cells	Plasma	Whole			
T 104 13.5 kgm.	Control	cc.	per cent	grams	per cent	grams	per cent	grams	cc.	cc.	cc.	per cent	per cent	mm. Hg
	1°	0	6.38	53.0	4.49	37.2	1.89	15.8	[550]*	[830]*	[1380]*	40.0	89.3	150
	2° 30'	135	5.58	39.2	3.99	28.0	1.59	11.2	543	702	1245	43.6	99.0	146
	4°	338	5.58	36.5	3.88	25.4	1.70	11.1	539	654	1193	45.2	103.4	148
	5° 30'	540	5.58	35.3	3.95	25.0	1.63	10.3	542	633	1175	46.1	105.6	140
	7°		6.28	35.0	4.53	25.2	1.75	10.8	536	558	1094	49.0	112.7	126
T 103 14.4 kgm.	Injected blood		6.37	36.5	4.43	25.4	1.94	11.1	537	573	1110	48.4	110.0	105
			6.10		3.53		2.57					34.5	82.4	
	Control	0	6.80	58.9	3.80	32.9	3.00	26.0	[426]	[866]	[1292]	32.9	73.4	168
	1°	144	5.98	51.2	3.65	31.2	2.33	20.0	415	855	1270	32.7	74.0	138
	2° 30'	360	5.60	48.8	3.18	27.7	2.42	21.1	420	872	1292	32.5	73.2	139
	4°	576	5.60	45.3	3.31	26.8	2.29	18.5	435	810	1245	34.9	76.2	130
	5° 30'		5.88	43.3	3.51	25.8	2.37	17.5	434	736	1170	37.2	81.1	123
	7°		6.00	43.8					433	730	1163	37.2	81.5	130
	Injected blood		5.57		2.74		1.83					39.1	89.4	

\* Determined directly by the dye method:

Protocols. Sodium barbital as anesthetic in both experiments.

T 104. Shortly before the introduction of salt solution was begun the animal was given 6 cc. of 6 per cent gum acacia solution in the external jugular vein. The blood pressure declined to a mean of 70 mm. Hg, remained there for about 5 minutes and returned in 15 minutes to the previous normal level. Total urine 997 cc. with a total protein equivalent of 18.1 grams.

T 103. After removal of the spleen, 10 cc. of 6.0 per cent gum acacia were injected into the external jugular vein. The blood pressure declined to a mean of 86 mm. Hg almost immediately. The injection of normal salt solution was then begun. Shortly thereafter the blood pressure rose rapidly. Total urine 537 cc. with a total protein equivalent of 13.9 grams.

was a passage of fluid from the rectum. In several instances, the lungs were definitely edematous.

#### SUMMARY

The effects on the composition of the blood of the injection of various solutions was determined in normal dogs and in dogs in which due to the anesthetic or unknown reason the blood pressure at some time during the experiments declined. No trauma was instituted in any of the experiments. The solutions that were injected in the different experiments included (1) 0.9 per cent salt solution, (2) 3.0 per cent salt solution, (3) 6.0 per cent glucose, (4) 20.0 per cent glucose, (5) 6.0 per cent gum acacia, (6) 6.0 per cent gum acacia and 20.0 per cent glucose in normal saline, (7) blood serum and (8) whole blood. The solutions were injected continuously usually at the rate of 10 cc. per kilogram of body weight per hour for four hours. Determinations were performed before, during and after the completion of the injections.

Some of the findings are summarized below.

I. Experiments in which the blood pressure remained at essentially the normal level.

(a) The injection of solutions of salt or glucose was usually associated with a slight increase in the volume of blood plasma, a slight decrease in the percentage of protein and very little alteration in the absolute amount of plasma protein in the circulation.

(b) When solutions containing gum acacia were injected, there was a definite increase in the plasma volume, a rather large decrease in the percentage of protein and very little alteration in the absolute amount of plasma protein.

(c) The introduction of blood serum or whole blood was associated with an increase in the plasma volume and in the percentage and absolute amounts of plasma protein.

II. Experiments in which there was a temporary or well sustained decline in the blood pressure.

(a) The injection of solutions of salt or glucose was usually associated with a decrease in the volume of plasma, a decrease in the percentage of protein and a marked diminution in the absolute amount of plasma protein.

(b) The introduction of solutions containing gum acacia was associated with very little alteration in the plasma volume, a great decrease in the percentage of protein and a reduction in the absolute amount of plasma protein.

(c) When whole blood or blood serum was injected the alterations in the plasma volume were not marked and there was a slight increase in the percentage of protein. If deductions are made for the protein that was present in the whole blood or blood serum that was injected, a great decrease in the absolute amount of plasma protein is found.

The alterations in the percentage and absolute amounts of albumin and globulin paralleled fairly closely the changes in the total protein.

Removal of the spleen in some experiments did not seem to affect the results indicating that the spleen was not in the main responsible for the alterations in the proportion of red blood cells to plasma.

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