A STUDY OF THE EFFECTS OF HEMORRHAGE, TRAUMA, HISTAMINE AND SPINAL ANESTHESIA ON THE COMPOSITION OF THE BLOOD WHEN NO FLUIDS ARE INJECTED AND WHEN FLUIDS ARE INTRODUCED INTRAVENOUSLY

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In previous studies (1, 2) the composition of the blood has been determined before, during and after the injection of various fluids intravenously under normal and abnormal conditions. The abnormal conditions consisted of some experiments in which a decline in blood pressure was produced by trauma to the intestines and others in which probably due either to the anesthetic or to the fluid that was injected intravenously there was an early marked decline in the pressure. The results of these experiments led us to further studies on the composition of the blood of animals in which a decline in pressure was produced by other methods. These methods consisted of (1) graded hemorrhages, (2) trauma to an extremity, (3) the subcutaneous injection of histamine and (4) spinal anesthesia. These procedures were chosen because a large number of the instances of low blood pressures in patients are due to similar causes. Experiments were performed both with and without the introduction of fluids intravenously. The fluids that were chosen for study were normal salt solution and Evans' gum acacia-glucose-saline solution. These two fluids together with others were employed in the previous studies and in the present experiments they were used as examples of solutions of crystalloids and of colloids.

METHODS AND RESULTS

The experimental animals in all instances were dogs. They were anesthetized by morphine except in the experiments in which an extremity was traumatized. In the latter experiments, sodium barbital, 0.3 gram per kilogram of body weight, was administered intravenously. The animals gave no evidence of pain and were killed at the completion of the experiments. A cannula that was connected to a mercury manometer was placed in the carotid artery for the blood pressure determinations. Samples of blood for the various analyses were obtained from the femoral vein. The blood that was removed was replaced by an equal volume.

At the beginning of all experiments, specimens of blood were removed for determinations of the hemoglobin, the hematocrit, the blood volume, the total protein, albumin and globulin. These studies, except for those on the blood volume, were repeated after intervals of one, two and one-half, four, five and one-half and seven hours. Van Allen tubes were used for the hematocrit determinations. The method of Cohen and Smith (3) was employed in determining the percentage of hemoglobin. Vital red was used in the estimation of the control blood volume. These figures are placed in brackets in the tables. The changes in the blood volume during the course of the experiments were assumed to vary in an inverse ratio to the alterations in the percentage of hemoglobin. The hematocrit readings were used in calculating the volume of red blood cells and plasma. The nitrogen determinations on blood serum and urine were performed by the Kjeldahl-Gunning method. In the tables, nitrogen is expressed as protein. The absolute or entire amounts of total protein, albumin and globulin were obtained by multiplying the percentage of each by the volume of plasma.

A decline in blood pressure was produced by four different methods and for descriptive purposes the experiments are divided into four groups. In each group, studies were first performed on the effects of the procedure when no fluid was introduced intravenously. In subsequent studies, fluids were injected at a constant rate during the first four hours of the experiments. The volume of fluid introduced equalled 10 cc. per kilogram of body weight per hour. The fluids injected in the different experiments were normal salt solution and Evans' solution of 6.0 per cent gum acacia and 20 per cent glucose in normal saline. In addition in the experiments on histamine, the effects of injecting blood serum were studied also.

The results of all experiments are summarized in the text. Due to lack of space, the results of only one experiment are given in detail in the tables.

I. EXPERIMENTS ON THE EFFECTS OF GRADED HEMORRHAGE

The entire amount of blood that was withdrawn equalled 4.0 per cent of the body weight. Its removal was distributed as follows. After the control determinations had been performed, a volume of blood equal to 1.0 per cent of the body weight was removed. One hour later and two and one-half hours later just prior to the withdrawal of samples for the analyses, blood equalling 1.5 per cent of the body weight was removed.

Since blood was withdrawn from the circulation, the calculations were somewhat different from those in most of the other experiments. After calculating the alterations in the blood volume from the original by the use of the hemoglobin and hematocrit determinations, deduction was made for the amount of blood that had been removed. The absolute

amount of plasma protein was obtained by multiplying the volume of plasma by the percentage of protein. The sum of this figure and the amount of protein that was present in the blood that was removed is placed in parentheses in the tables.

A. The effects of graded hemorrhages alone on the composition of the blood

Three experiments were performed in which the effects of graded hemorrhage were studied. No fluid was introduced. In two of the experiments, there was a large decline in the arterial pressure. The alterations in the hemoglobin and hematocrit readings were very small and inconstant. There were decreases in the volumes of whole blood, of plasma and of red blood cells. The percentages of total protein, of albumin and of globulin decreased very slightly. The absolute amounts of the protein constituents in the blood plasma decreased. However, if one includes in these figures the amount of protein that was present in the withdrawn blood, it is to be seen in one experiment that there was an increase in the absolute amount of protein constituents, in another there was no alteration and in the third there was a slight decrease. The results of one of these experiments are given in Table I.

B. The effects of graded hemorrhages and of the intravenous injection of normal salt solution on the composition of the blood

Three such experiments were performed. In two of the three experiments there was a marked decline in the blood pressure. There was a decrease in the hemoglobin and hematocrit readings in all experiments. The volume of plasma declined rather markedly in two of the three experiments. A reduction of the percentages of total protein, albumin and globulin in the blood serum was found. The absolute amounts of the protein constituents in the blood plasma decreased. However, if one adds to that in the blood stream the protein that was present in the blood that was withdrawn, it is to be seen in two of the experiments that there was an increase in the absolute protein. The results of one of these experiments are to be found in Table I.

C. The effects of graded hemorrhages and of the intravenous injection of gum acacia-glucose-saline solution on the composition of the blood

Only one experiment of this type was performed. The blood pressure did not decline until after the injection of fluid was stopped. There was a decrease in the percentage of hemoglobin and in the hematocrit readings. The volume of plasma increased during the injection of the fluid and returned later to the original level. There was a marked decrease in the percentages of total protein, albumin and globulin. The absolute amounts of the protein constituents in the blood plasma decreased. The sum of the protein that remained in the plasma of the

TABLE I

The effects of hemorrhage on the composition of the blood

Experiment number and weight	Time from beginning	Amount of fluid given	Blood removed	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.	*cc.*	*per cent*	*grams*	*per cent*	*grams*	*per cent*	*grams*	*cc.*	*cc.*	*cc.*	*per cent*	*per cent*	*mm. Hg*
No fluid introduced															
T 102 20.0 kgm.	Control		0	5.88	72.1 (71.2)†	3.05	37.4 (35.5)†	2.83	34.7 (35.7)†	[832]*	[1225]*	[2057]*	40.4	89.3	137
	1°		200	5.78	64.1 (69.6)†	2.87	31.9 (35.5)†	2.91	32.2 (34.1)†	726	1108	1834	39.6	90.4	118
	2° 30′		500	5.60	52.0 (72.1)†	2.87	26.7 (36.4)†	2.73	25.3 (35.7)†	625	928	1553	40.2	89.3	107
	4°		655	5.60	49.3 (72.5)†	2.83	24.9 (36.9)†	2.77	24.6 (35.6)†	568	880	1448	39.2	86.2	106
	5° 30′			5.53	49.7 (69.6)†	2.83	25.4 (35.0)†	2.70	24.3 (34.6)†	550	898	1448	38.0	86.0	96
	7°			5.62	46.8	2.83	23.5	2.79	23.3	568	832	1400	40.6	89.0	90
Salt solution, 0.9 per cent, introduced intravenously															
T 99	Control	0	0	6.64	51.4 (50.9)†	4.06	31.4 (30.7)†	2.58	20.0 (20.2)†	[554]*	[774]*	[1328]*	41.8	93.5	135
16.4 kgm.	1°	164	164	6.48	44.6 (54.0)†	3.89	26.8 (32.7)†	2.59	17.8 (21.5)†	469	688	1157	40.5	94.0	135
	2° 30′	410	410	5.44	38.2 (55.9)†	3.29	23.1 (34.0)†	2.15	15.1 (21.9)†	383	702	1085	35.3	78.1	132
	4°	656	656	5.18	31.4 (57.4)†	3.16	19.2 (34.5)†	2.02	12.2 (22.9)†	286	606	892	32.0	73.5	125
	5° 30′			5.92	32.9 (56.3)†	3.54	19.7 (34.5)†	2.38	13.2 (22.8)†	287	556	843	34.0	77.3	116
	7°			5.66	31.8	3.51	19.7	2.15	12.1	290	562	852	34.0	76.5	101

TABLE I (*continued*)

Experiment number and weight	Time from beginning	Amount of fluid given	Blood removed	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.	*cc.*	*per cent*	*grams*	*per cent*	*grams*	*per cent*	*grams*	*cc.*	*cc.*	*cc.*	*per cent*	*per cent*	*mm. Hg*
Gum acacia-glucose-saline solution introduced intravenously															
T 109 12.7 kgm.	Control	0	0	6.35	47.8 (51.1)†	4.19	31.5 (34.5)†	2.16	16.3 (16.6)†	[482]*	[753]*	[1235]*	39.1	91.5	126
	1°	127	127	4.79	43.0 (54.7)†	3.25	29.2 (37.0)†	1.54	13.8 (17.7).	411	899	1310	31.5	77.3	128
	2° 30′	318	318	3.84	37.5 (54.6)†	2.61	25.5 (38.4)†	1.23	12.0 (16.3)†	389	978	1367	28.5	63.3	130
	4°	508	508	3.27	30.5 (50.7)†	2.35	21.9 (38.6)†	.92	8.6 (12.1)†	311	934	1245	25.0	59.1	130
	5° 30′			3.62	26.4 (53.4)†	3.03	22.1 (40.2)†	.59	4.3 (13.3)†	320	730	1050	30.4	71.1	113
	7°			3.75	29.3	3.03	23.7	.72	5.6	312	783	1095	28.5	68.2	85

* 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. Morphine as anesthetic in all experiments.

T 102. Total urine 99 cc. with a total protein equivalent of 8 grams. Stomach contained 45 cc. of fluid at completion of experiment.

T 99. Total urine 87 cc. with a total protein equivalent of 9.2 grams. Stomach contained 20 cc. of fluid with a total protein equivalent of 0.34 gram.

T 109. Total urine 495 cc. with a total protein equivalent of 10.5 grams. No fluid in stomach or peritoneal cavity at completion of experiment.

blood stream and that removed gave a figure in excess of that obtained during the control period. The results of this experiment are given in Table I.

II. EXPERIMENTS ON THE EFFECTS OF TRAUMA TO AN EXTREMITY

As has been stated, the animals were deeply anesthetized by sodium barbital. After the control determinations had been performed, one of the posterior extremities was traumatized by striking it with a hammer. In some instances, slight additional trauma was subsequently necessary since the blood pressure did not decline sufficiently as a result of the initial injury. At the completion of the experiments, the posterior portion of the body was divided into two parts by a method previously described (4). The difference in the weights of the two parts was considered a measure of the fluid that was lost from the blood stream into the injured area.

The various determinations were performed in these experiments as in all others that are reported in this paper. However, due to the fact that the amount of blood that was lost into the injured area could not be determined during the course of the experiments, some of the calculations were impossible. An attempt was made to calculate the blood volume and the absolute amounts of the protein constituents at the termination of the experiments. It is realized that the method employed is not in any sense absolute. As usual, the control blood volume and the alterations in the hematocrit and hemoglobin readings were used in computing the changes in the volumes of red blood cells, plasma and whole blood. From the blood volume thus obtained, the amount of fluid that was lost into the injured area as determined by the amputations was subtracted and the result was considered as the blood volume at the end of the experiment. The fluid that was lost into the extremity was considered as having an hematocrit which was the average of all those obtained on the venous blood throughout the experiment. With this assumption the volumes of red blood cells and of plasma in the injured area were calculated. These figures were subtracted from the volumes of red blood cells and of plasma which presumably would have been present in the blood stream had not the loss occurred.

A. The effects of trauma to an extremity on the composition of the blood

Two experiments on the effects of trauma to an extremity were performed. The arterial pressure declined markedly in both experiments. There was an increase in the hematocrit and hemoglobin readings. The volumes of whole blood, plasma and red blood cells decreased. The content of the serum in total protein, albumin and globulin was not altered significantly during the experiments. The absolute amount of the protein constituents was greatly diminished. The results of one of these experiments are given in Table II.

TABLE II

The effects of trauma to an extremity on the composition of the 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*	*per cent*	*grams*	*cc.*	*cc.*	*cc.*	*per cent*	*per cent*	*mm. Hg*
No fluid introduced														
T 112	Control		7.32	73.8	3.71	37.4	3.61	41.0	[610]*	[1007]*	[1617]*	35.4	86.2	135
18.9	1°		8.42		4.86		3.56					36.9	88.8	136
kgm.	2° 30′		7.74		3.81		3.93					37.7	90.4	122
	4°		7.78		3.81		3.97					38.7	90.9	84
	5° 30′		7.54		3.69		3.85					38.6	89.4	75
	7°		7.17	51.8	3.92	28.3	3.25	23.5	404	723	1067	37.5	85.2	66
	Injected blood		6.76		2.41		4.35					30.2	61.0	
Salt solution, 0.9 per cent, introduced intravenously														
T 134	Control	0	7.16	85.7	3.46	38.0	3.70	47.7	[670]*	[1096]*	[1766]*	37.9	82.4	175
17.9	1°	179	6.32		3.20		3.12					37.4	81.5	126
kgm.	2° 30′	447	6.04		2.87		3.17					35.0	78.1	86
	4°	716	5.70		3.16		2.54					33.1	73.9	85
	5° 30′		5.96		3.00		2.96					36.0	80.0	74
	7°		5.92	24.7	3.00	12.5	2.92	12.2	257	418	675	36.7	80.0	62
	Injected blood		7.04									41.2	83.8	

TABLE II (*continued*)

Experiment number and weight	Time from beginning	Amount of fluid given	Total protein		Albumin		Globulin		Blood volume			Hemotocrit	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*	*per cent*	*grams*	*cc.*	*cc.*	*cc.*	*per cent*	*per cent*	*mm. Hg*
Gum acacia-glucose-salt solution introduced intravenously														
T 117	Control	0	8.31	71.6	2.40	20.7	5.91	50.9	[443]*	[862]*	[1305]*	34.0	76.5	166
14.2	1°	142	6.25		1.92		4.33					29.7	69.4	155
kgm.	2° 30′	355	5.52		1.73		3.79					28.7	65.8	148
	4°	568	4.63		1.50		3.13					26.4	58.8	120
	5° 30′		4.95		1.62		3.33					24.2	61.5	75
	7°		5.00	28.8	1.68	9.7	3.32	19.1	257	576	833	30.0	65.1	59
	Injected blood		7.11		3.43		3.68					39.6	90.0	

* Determined directly by the dye method.

Protocols. Sodium barbital as anesthetic in all experiments.

T 112. Weight of traumatized extremity 2925 grams. Weight of non-traumatized extremity 2375 grams. Difference in weight 550 grams. Total urine during experiment 23 cc.

T 134. Slight additional trauma was carried out several times during the first 2 hours of the experiment. Weight of traumatized extremity 3295 grams. Weight of opposite non-traumatized extremity 2150 grams. Difference in weight 1145 grams. Total urine 5 cc. with a total protein equivalent of 0.1 gram.

T 117. The mean blood pressure declined to a mean level of 100 mm. Hg shortly after the leg was traumatized and it remained there for several minutes. Weight of traumatized extremity 2450 grams. Weight of non-traumatized extremity 1750 grams. Difference in weight 700 grams. Total urine 300 cc. with a total protein equivalent of 4.1 grams.

B. The effects of trauma to an extremity and of the intravenous injection of normal salt solution on the composition of the blood

Three experiments of this type were performed. A greater amount of trauma was necessary for the production of a low blood pressure than in the experiments in which no fluid was injected. In two of the present experiments, the blood pressure did not reach a low level until after the introduction of fluid had been terminated. The alterations in the hemoglobin and hematocrit readings were small and variable. The volume of blood plasma decreased markedly. There were small but definite decreases in the percentages of total protein, albumin and globulin in the blood serum. The absolute amounts of the protein constituents decreased markedly. The results of one of these experiments are contained in Table II.

C. The effects of trauma to an extremity and of the intravenous injection of gum acacia-glucose-saline solution on the composition of the blood

Two experiments of this type were performed. The blood pressure declined during the administration of fluid but did not reach a low level until after the injection was stopped. There was a marked decrease in the hemoglobin and hematocrit readings. The calculated volume of plasma increased in one experiment and decreased in the other. There were marked decreases in the percentages of total protein, albumin and globulin in the blood serum. The absolute amounts of the protein constituents decreased. The results of one of these experiments are to be found in Table II.

III. EXPERIMENTS ON THE EFFECTS OF HISTAMINE

The histamine solution that was injected subcutaneously contained one milligram of the drug per cubic centimeter of salt solution. It was given in sufficient amounts to maintain the blood pressure definitely depressed during the first four hours of the experiments.

A. The effects of the subcutaneous injection of histamine on the composition of the blood

Three experiments were performed in which the effects of the subcutaneous injection of histamine were studied. The blood pressure rose following the completion of the injections but did not return to the previous control level. The concentration of the red blood cells and the percentage of hemoglobin increased in all experiments. The volume of blood plasma diminished. There was a slight increase in the percentages of total protein, albumin and globulin in the blood serum. The absolute amounts of the protein constituents in the blood plasma decreased. The results of one of these experiments are given in Table III.

TABLE III

The effects of the subcutaneous injection of histamine on the composition of the blood

Experiment number and weight	Time from beginning	Amount of fluid given	Total histamine	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.	*mgm.*	*per cent*	*grams*	*per cent*	*grams*	*per cent*	*grams*	*cc.*	*cc.*	*cc.*	*per cent*	*per cent*	*mm. Hg*
No fluid introduced															
T 89	Control		0	6.99	51.8	4.62	34.2	2.37	17.6	[555]*	[740]*	[1295]*	42.8	113.6	130
15.1	1°		10	7.75	36.7	4.87	23.0	2.88	13.7	564	473	1037	54.4	144.2	117
kgm.	2° 30′		23	7.80	36.5	4.73	22.1	3.07	14.4	569	468	1037	54.8	144.2	99
	4°		53	8.05	36.0	4.98	22.2	3.07	13.8	553	447	1000	55.3	147.1	99
	5° 30′			7.54	36.2	4.59	22.0	2.95	14.2	560	480	1040	53.9	141.4	88
	7°			7.45	36.1	4.59	22.2	2.86	13.9	556	484	1040	53.5	141.4	107
	Injected blood			7.45		2.17		5.28					30.3	80.6	
Salt solution, 0.9 per cent, introduced intravenously															
T 95	Control	0	0	5.60	33.4	3.85	23.0	1.75	10.4	[403]*	[597]*	[1000]*	40.3	96.8	114
11.7	1°	117	25	4.94	25.2	3.30	16.8	1.64	8.4	404	509	913	44.2	106.0	94
kgm.	2° 30′	293	45	4.58	24.7	3.05	16.5	1.53	8.2	418	540	958	43.6	101.0	75
	4°	468	65	4.47	24.0	2.91	15.6	1.56	8.4	413	536	949	44.6	102.0	65
	5° 30′			4.72	21.8	3.10	14.3	1.62	7.5	404	461	865	46.7	111.9	98
	7°			4.90	25.0	3.15	16.0	1.75	9.0	404	509	913	45.2	106.3	110
	Injected blood			6.48		3.68		2.80					30.5	77.7	
Gum acacia-glucose-salt solution introduced intravenously															
T 108	Control	0	0	7.06	43.8	4.22	26.2	2.84	17.6	[372]*	[620]*	[992]*	37.4	92.0	135
13.9	1°	139	15	4.54	28.3	2.51	15.7	2.03	12.7	377	623	1000	37.7	91.2	70
kgm.	2° 30′	348	20	3.25	27.6	1.95	16.6	1.30	11.0	388	852	1240	31.4	73.5	80
	4°	556	25	2.78	27.9	1.65	16.5	1.13	11.4	392	1005	1397	28.0	65.2	56
	5° 30′			3.15	28.8	1.96	18.0	1.19	10.9	387	913	1300	29.8	70.1	46
	7°			3.59	30.5	2.12	18.1	1.47	12.4	381	852	1233	31.0	73.9	45
	Injected blood			6.10		3.42		2.68					33.4	76.1	

TABLE III (*continued*)

Experiment number and weight	Time from beginning	Amount of fluid given	Total histamine	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.	*mgm.*	*per cent*	*grams*	*per cent*	*grams*	*per cent*	*grams*	*cc.*	*cc.*	*cc.*	*per cent*	*per cent*	*mm. Hg*
Blood serum introduced intravenously															
T 107 15.5 kgm.	Control	0	0	6.01	49.3 (26.6)†	3.64	29.8 (13.1)†	2.37	19.5 (13.5)†	[580]*	[820]*	[1400]*	41.4	86.7	126
	1°	155	30	7.04	37.1 (25.5)†	3.61	19.0 (11.6)†	3.43	18.1 (13.9)†	559	526	1085	51.4	111.9	90
	2° 30′	388	50	6.84	51.8 (24.3)†	3.49	26.5 (9.6)†	3.35	25.3 (14.7)†	585	758	1343	43.5	90.4	78
	4°	620	135	6.78	66.4 (27.3)†	3.38	33.1 (10.8)†	3.40	33.3 (16.5)†	565	980	1545	36.6	78.5	55
	5° 30′			6.68	69.4 (14.7)†	3.30	34.3 (5.8)†	3.38	35.1 (8.9)†	560	1040	1600	35.0	75.8	55
	7°			6.78	56.8	3.49	29.3	3.29	27.5	572	838	1410	40.5	86.0	64
	Injected serum			6.78		3.78		3.00							

* 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. Morphine as anesthetic in all experiments.

T 89. Total urine 68 cc. with a total protein equivalent of 9.3 grams.

T 95. Total urine 77 cc. with a total protein equivalent of 11.2 grams. 190 cc. of fluid in stomach with a total protein equivalent of 0.9 gram. Small amount of bloody fluid was passed from rectum.

T 108. Total urine 61 cc. with a total protein equivalent of 0.8 gram. No fluid in stomach at completion of experiment. At autopsy, 150 cc. of fluid which clotted after removal was recovered from the peritoneal cavity. This fluid had a total protein content of 6.25 grams per 100 cc., an albumin content of 2.01 grams and a globulin content of 4.24 grams.

T 107. Total urine 10 cc. with a total protein equivalent of 0.2 gram. Stomach contained 195 cc. of fluid with a total protein equivalent of 3.9 grams.

B. The effects of the subcutaneous injection of histamine and of the intravenous injection of normal salt solution on the composition of the blood

Three experiments of this type were performed. A marked decline in the blood pressure was produced in all of them. There was a definite but not great increase in the hematocrit and hemoglobin readings in two of the experiments. In the remaining experiment, there was a slight decline. The volume of blood plasma decreased in two experiments and increased slightly in one. There was a decrease in the percentage of the protein constituents of the serum in all experiments. In none of these was the decrease very great. The absolute amounts of the protein constituents decreased in two experiments and remained at approximately the control level in the other one. At the completion of each of the experiments, the stomach contained a large amount of fluid. The results of one of these experiments are to be found in Table III.

C. The effects of the subcutaneous injection of histamine and of the intravenous injection of gum acacia-glucose-saline solution on the composition of the blood

Two experiments were performed. A marked decline in the blood pressure was produced in both. After a slight initial increase, there was a great decrease in the hemoglobin and hematocrit readings. The volume of blood plasma increased. There was a great decrease in the percentages of total protein, albumin and globulin in the blood serum. The absolute amounts of the protein constituents decreased. The results of one of these experiments are given in Table III.

D. The effects of the subcutaneous injection of histamine and of the intravenous injection of blood serum on the composition of the blood

Two experiments were performed in which the effects of the injection of histamine and of blood serum were studied. The serum was obtained from a normal dog the blood of which was not incompatible with that of the experimental animal. A marked decline in the blood pressure followed the injection of histamine in each experiment. There was an increase in the hemoglobin and hematocrit determinations during the early part of the experiments and a decrease later. The volume of blood plasma first decreased slightly and then increased. There was an increase in the percentages of total protein and globulin in the blood serum, except for an initial decrease in one experiment. The absolute amounts of the protein constituents in the blood plasma increased greatly. However, if one corrects for the protein that was present in the injected serum, a decrease in the absolute amount of plasma protein is found. The latter figures are placed in brackets in the table. The results of one of these experiments are to be seen in Table III.

IV. EXPERIMENTS ON THE EFFECTS OF SPINAL ANESTHESIA

A five per cent solution of procaine hydrochloride was used as the spinal anesthetic. With the animal lying on its side, the fluid was introduced into the canal in the lumbar region. Small amounts of the procaine were injected frequently until a marked decline in the blood pressure resulted. The animal was then placed on its back.

A. The effects of spinal anesthesia alone on the composition of the blood

Four experiments are reported in which the effects of spinal anesthesia were studied. In several others, either no significant decline in pressure was produced or death followed shortly after the injection of the procaine. The concentration of the blood and the percentage of hemoglobin increased in three of the four experiments but in no instance was the increase very great. In three of the experiments, there was a slight decrease in the volume of plasma. However, in two of these, the decline did not appear during the first hour of the experiment when the blood pressure was lowest. The percentages of the protein constituents in the blood serum remained practically unaltered during the experiments. In two of the experiments, the absolute amount of plasma protein remained at approximately the control level. In the remaining two, there was no alteration during the first hour, and following this there was a decline. The results of one of these experiments are given in Table IV.

B. The effects of spinal anesthesia and of the intravenous injection of normal salt solution on the composition of the blood

Two experiments of this type were performed. A marked decline in the blood pressure was produced in each. At the end of the first hour, there was a slight decrease in the hemoglobin and hematocrit readings in each. Following this, they rose to levels a little higher than those observed during the control periods. The plasma volume first increased and then decreased slightly. There were small decreases in the percentages of total protein, albumin and globulin in the blood serum. The absolute amounts of the protein constituents declined but not to a great extent. The results of one of these experiments are contained in Table IV.

C. The effects of spinal anesthesia and of the intravenous injection of gum acacia-glucose-saline solution on the composition of the blood

Two experiments were performed. In one of these, the blood pressure remained markedly depressed, while in the other it returned to the control level and remained there several hours. In one experiment the concentration of the red blood cells decreased during the injection of the fluid, and in the other the initial increase in the concentration was followed by dilution. The hematocrit and hemoglobin readings increased following the termination of the injections. There was a decrease in the percent-

TABLE IV

The effects of spinal anesthesia on the composition of the 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*	*per cent*	*grams*	*cc.*	*cc.*	*cc.*	*per cent*	*per cent*	*mm. Hg*
No fluid introduced														
T 131	Control		6.86	82.0	2.89	34.5	3.97	47.5	[716]*	[1194]*	[1910]*	37.5	84.3	150
20.0	1°		6.81	83.8	2.85	35.0	3.96	48.8	725	1230	1955	37.0	82.4	70
kgm.	2° 30′		6.97	79.2	2.92	33.2	4.05	46.0	733	1137	1870	39.1	86.2	138
	4°		6.86	78.2	2.89	33.0	3.97	45.2	738	1142	1880	39.2	85.7	130
	5° 30′		6.86	73.7	2.89	31.1	3.97	42.6	725	1075	1800	40.3	89.3	118
	7°		6.64	72.1	3.03	32.8	3.61	39.3	715	1085	1800	39.7	89.0	116
	Injected blood		5.07		2.78		2.29					22.9	51.0	
Salt solution, 0.9 per cent, introduced intravenously														
T 133	Control	0	6.77	76.3	3.29	37.1	3.48	39.2	[593]*	[1127]*	[1720]*	34.4	76.9	124
16.5	1°	165	6.33	80.7	3.08	39.3	3.25	41.1	575	1275	1850	31.0	71.5	80
kgm.	2° 30′	412	6.12	66.4	3.02	32.8	3.10	33.6	600	1085	1685	35.6	78.5	150
	4°	660	5.98	67.3	2.97	33.5	3.01	33.8	595	1125	1720	34.5	76.9	118
	5° 30′		6.37	70.0	3.04	33.3	3.33	36.7	608	1097	1705	35.7	77.5	102
	7°				3.00	32.1			595	1070	1665	35.7	79.4	100

TABLE IV (*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	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*
Gum acacia-glucose-salt solution introduced intravenously														
T 130	Control	0	7.64	61.8	3.04	24.6	4.60	37.2	[454]*	[808]*	[1262]*	36.0	89.0	125
15.6	1°	156	5.38	48.1	2.05	18.3	3.33	29.8	461	894	1355	34.0	82.9	56
kgm.	2° 30′	390	4.94	44.2	1.89	17.0	3.05	27.3	466	896	1362	34.2	82.4	144
	4°	624	4.16	43.6	1.56	16.3	2.60	27.3	448	1048	1496	30.0	75.0	132
	5° 30′		4.90	40.2	1.97	16.2	2.93	24.1	489	821	1310	37.3	85.7	120
	7°		4.98	40.5	2.05	16.7	2.93	23.8	511	814	1325	38.6	84.7	94
	Injected blood		6.63		2.71		3.92					28.5	67.9	

* Determined directly by the dye method.

Protocols. Morphine as narcotic in all experiments.

T 131. Total urine 210 cc. with a total protein equivalent of 1.9 gram.

T 133. Given 5.0 cc. of 5.0 per cent procaine hydrochloride over a period of one hour. Decline in blood pressure to 30 mm. Hg at completion of injection. Total urine 60 cc. with a total protein equivalent of 4.4 grams.

T 130. Procaine 1.6 cc. Total urine 250 cc. with a total protein equivalent of 8.9 grams.

ages of the total protein, albumin and globulin in the blood serum. The absolute amounts of the protein constituents in the blood plasma decreased. The results of one of these experiments are given in Table IV.

DISCUSSION

In a previous paper (2) experiments were reported in which the cause for the decline in blood pressure was not clearly understood, and in which the injection of fluids intravenously was usually associated with marked decreases in both the percentage and absolute amount of plasma protein. In view of these findings it seemed important to determine whether or not a decline in blood pressure produced in other ways would be associated with similar alterations. For example, if the intravenous injection of salt solution following a severe hemorrhage were associated with a marked decrease in the percentage and absolute amount of protein in the blood serum, its use might be harmful rather than beneficial. The four methods by which the decline in pressure was produced were arbitrarily chosen as being fairly representative of the different ways of causing such a condition.

The findings in the experiments on the effects of hemorrhage were quite different from those previously reported (2) in which the unexplained early decline in the pressure took place. When normal salt solution was injected into the animals from which blood was being removed, a decrease rather than an increase in the concentration of the red blood cells was found. The percentage of protein in the serum decreased but when the protein that was removed was added to that remaining in the blood stream, it was found that the absolute amount of plasma protein usually increased. Calculated in this manner, the increase in one experiment was five grams and in another six grams. In the experiments on hemorrhage the blood pressure readings as listed in the tables are not in all instances very low but they are somewhat misleading in this respect in that the pressure that existed just before the removal of the blood was the one used. During and shortly following the removal of blood, the blood pressure was frequently markedly depressed. The decline in pressure usually appeared much earlier in the experiments with the unexplained fall than in those in which blood was removed. It is possible that the vasoconstriction of the vessels which usually accompanies hemorrhage was responsible for the prevention of the loss of protein through the vessel walls in the present experiments, but we have no proof of this.

The addition of the protein that was removed to that remaining in the blood stream in the experiments on hemorrhage indicated an increase in the absolute amount of plasma protein in most of the experiments. Scott (5) from his studies on the mechanism of the absorption of fluid from the tissue spaces states: "The above results show that as large or larger increases in the nitrogenous bodies of the plasma occur after injecting

Ringer's fluid (when all backward filtration is excluded) as occur after hemorrhage. After hemorrhage, the fluid passing back into the blood must contain less protein than the plasma whether it passes back by osmosis or by filtration, it will then necessarily cause protein to pass from the cells into the plasma. Consequently an increase of protein in the plasma after hemorrhage is no evidence of backward filtration and is consistent with Starling's view that the fluid passes into the capillaries by osmotic action." In previous experiments in which the effects of the injection of solutions of crystalloids into normal dogs were determined, there was a slight increase in the absolute amount of the plasma protein in several of the experiments but in most of them it remained at the same level or decreased slightly. However, in the present experiments in which both the effects of hemorrhages and the injection of fluids were studied, there was usually an increase in the plasma protein. If Scott is correct in his statement that backward filtration is excluded when fluid that has been injected is passing through the vessels, then it follows that protein did not pass from the tissue spaces into the blood stream in our experiments because part of the fluid that was injected escaped through the vessel walls. However, it is not necessarily true that backward filtration is excluded simply because part of the fluid that was injected was leaving the blood stream. It would seem to be possible that at any given time fluid could be leaving the blood stream in some areas while at the same time fluid could be passing into the circulation in other areas.

The experiments on the effects of trauma to an extremity differ in the main from those on hemorrhage in that the latter type was usually associated with a decrease in the concentration of the red blood cells, whereas a slight increase usually occurred in the former. The difference is probably due to the fact that there was a greater proportional loss of plasma than of red cells in the studies on trauma whereas hemorrhage resulted in the loss of blood as it existed at the time in the blood vessels. The above remarks do not apply to the experiments in which the gum acacia solution was injected, since in both types a marked decrease in the concentration of the red blood cells was found. The increase in the concentration of the blood in the experiments on the effects of trauma and the introduction of salt solution was not nearly so marked as in the previous experiments (2), in which the unexplained declines in pressure occurred. Also, the decrease in the percentage of protein in the blood serum in the present experiments was not nearly so great as in the former ones. Unfortunately the absolute amounts of the protein constituents could not be determined accurately during the course of the experiments on trauma. Since the fluid that escaped from the blood stream into the injured area had approximately the same composition as whole blood and since there was such a marked difference in the weight of the traumatized

and non-traumatized parts, it is likely that most if not all of the protein was lost into the damaged tissues. The impression was gained that it took a greater amount of trauma to produce a decline in blood pressure when salt solution was injected than when no solutions were given. This observation would indicate that the salt solution was not exerting harmful effects.

Protein was usually lost from the blood stream when histamine and fluids were injected but it was surprising to us that the loss was not greater. The reduction in the percentage and absolute amount of plasma protein was usually not as great in these experiments as in the previous (2) ones with the unexplained decline in pressure. In the latter experiments the decline in pressure was frequently maintained for only a short while, whereas in the experiments on histamine the blood pressure was kept at a low level for a long time. At the completion of most of the experiments on histamine, the stomach contained large amounts of fluid. The content of this fluid in protein was quite low. It was sufficient to account for only a small part of the total loss of protein.

In the experiments on the effects of spinal anesthesia alone, there was either no loss in the absolute amount of plasma protein or the loss was not very great. When normal salt solution was introduced intravenously after producing a decline in pressure by spinal anesthesia, there was not a large loss of protein. The decline in the blood pressure in these experiments was similar to that observed in the experiments (2) in which the unexplained fall occurred. In both instances, a marked drop in the pressure was noted during the early part of the studies. It is possible that the absence of a large loss of protein in the experiments on spinal anesthesia was due to the fact that part rather than the whole of the body was affected by the anesthetic. In the experiments in which the unexplained decline in the pressure occurred and in those in which histamine was injected, the effects were probably general rather than local.

It is noted in some of the experiments reported in this paper that it is possible to have a marked decline in the blood pressure without an associated diminution in the absolute amount of plasma protein. This finding indicates that the unexplained decline in blood pressure in the experiments previously reported (2) was not entirely responsible for the loss.

SUMMARY

The effects on the composition of the blood of four different procedures which resulted in a decline in the blood pressure were determined in some dogs in which no fluid was injected and in others in which either normal salt solution or gum acacia-glucose-saline solution was introduced intravenously. The methods that were employed in reducing the blood pressure consisted of (1) the graded removal of blood, (2) trauma to an extremity, (3) the subcutaneous injection of histamine and (4) the injection

of procaine hydrochloride into the spinal canal. The studies included determinations of the carotid blood pressure, the percentage of hemoglobin, the concentration of the red blood cells, the volumes of whole blood, red blood cells and plasma, and the percentages of total protein, albumin and globulin in the blood serum. The absolute amounts of the protein constituents were calculated by multiplying the percentage of each in the serum by the volume of plasma.

Some of the results that were obtained are as follows:

1. In the experiments on the effects of hemorrhage, both with and without the introduction of fluids, the amount of protein that was present in the blood that was removed was usually more than sufficient to account for the decrease in the total amount of protein in the plasma of the blood stream. The results of most of the experiments indicate that protein passed into the blood vessels.

2. In both the experiments on hemorrhage and those on trauma to an extremity, there was a slight decrease in the concentration of the plasma protein associated with the introduction of normal salt solution. The total amount of protein that was lost from the blood stream in the experiments on trauma could not be determined with accuracy but the results indicate that most if not all of it escaped into the injured area.

3. In all of the experiments with one exception in which histamine was injected, there was a decrease in the absolute amounts of the protein constituents. However, the loss was not as great as was usually encountered in the previous experiments (2) in which the unexplained decline in blood pressure occurred.

4. There was a comparatively small loss of protein from the blood stream in the experiments in which a marked decline in the blood pressure followed the injection of procaine into the spinal canal. The findings were similar when in addition normal salt solution was introduced intravenously.

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