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Research Article

THE EFFECTS ON THE COMPOSITION OF THE BLOOD OF THE SUBCUTANEOUS INJECTION OF NORMAL SALT SOLUTION INTO NORMAL DOGS AND INTO DOGS SUBJECTED TO INTESTINAL TRAUMA, GRADED HEMORRHAGES AND HISTAMINE INJECTION

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In previous studies (1, 2, 3), the effects on the composition of the blood of the introduction of fluids intravenously have been determined on normal animals and on animals in which a decline in blood pressure had been produced by a variety of means. Another method frequently employed by which fluids may be introduced consists of injection into the subcutaneous tissues. For this purpose, normal salt solution is used most often. The present studies were undertaken in order to determine the effects on the composition of the blood of the subcutaneous injection of normal salt solution into normal dogs and into dogs in which a decline in blood pressure was produced by several different methods. Also we were interested in determining how much of the fluid that was placed in the tissues was absorbed into the general circulation. For this reason all of the fluid was injected into the tissues of one posterior extremity, groin and flank. At the completion of the experiments, the difference in the weights of the two posterior portions of the body was determined.

METHODS

Dogs were used in all experiments. Morphine sulphate was employed as an anesthetic in all experiments except those in which the intestines were traumatized. Sodium barbital was used in these. The animals gave no evidence of pain during the course of the experiments. The blood pressure was determined by placing a cannula that was connected to a mercury manometer into the carotid artery. Specimens of blood for the various analyses were obtained from the femoral vein of the extremity into which no fluid was injected and this blood was replaced by an equal amount obtained from a normal dog.

Four different types of experiments were performed. In all of these, following the replacement of the blood which was removed in order to determine the blood volume, hemoglobin, hematocrit, total protein, albumin and globulin, normal salt solution was injected continuously into the tissues of one of the posterior extremities, groin and flank. It was given at body temperature at the rate of 10 cc. per kilogram of body weight per hour for four hours. Samples of blood for the various analyses were obtained one and two and one-half hours

following the beginning of the injection and at its completion. Further samples were obtained after intervals of one and one-half and three hours. The animals were then killed and the difference in the weights of the two posterior portions of the body was determined. In the first group of experiments, the effects on the composition of the blood of the introduction of fluids into the subcutaneous tissues of normal animals were studied. In the second group, after making a midline abdominal incision, the intestines were traumatized during the four hours while fluid was being injected by gently passing them between the fingers. At the end of this time, the incision was closed, and two further series of determinations were performed during the following three hours. In the third group of experiments, the effects of graded hemorrhages at the same time that fluid was being introduced subcutaneously were studied. As in all experiments normal salt solution was injected at the rate of 10 cc. per kilogram of body weight per hour for four hours and samples of blood were obtained at the usual times. After performing the control determinations, whole blood which equalled one per cent of the body weight was removed from the femoral artery. Blood equalling approximately one and one-half per cent of the body weight was withdrawn one hour later and two and one-half hours later. The volume of the blood that was removed was slightly less than the volume of salt solution that was introduced. The observations were continued for three hours after the completion of the injection of salt solution. In the fourth group of experiments, histamine was injected intermittently into the subcutaneous tissues during the four hours that salt solution was being introduced. It was given in amounts sufficiently large to produce a definite decline in the blood pressure. The usual determinations were performed during the three hours following the termination of the injections.

Van Allen tubes were used in the hematocrit determinations. Hemoglobin estimations were performed by the method of Cohen and Smith (4). The control blood volume was determined by the dye method as employed by Rowntree, Brown and Roth (5). These figures are placed in brackets in the tables. During the course of the experiments, excepting those on hemorrhage, the alterations in the total blood volume were assumed to vary in an inverse ratio to the changes in the percentage of hemoglobin. The volumes of red blood cells and of plasma were calculated from the hematocrit readings. In the experiments in which graded hemorrhages were performed, the calculations were different in that after determining the volume by the method described above, subtraction was made for the amount removed. The determinations of the nitrogen were performed on blood serum. Albumin and globulin were separated by the use of 22.2 per cent sodium sulphate as recommended by Howe (6). The Gunning (7) modification of the Kjeldahl method was employed for determining the albumin and total protein nitrogen of the serum. The total nitrogen of the urine was also determined by this method. In all the tables the nitrogen is expressed as protein. The figures for the entire or absolute amounts of protein were obtained by multiplying the percentage of protein per unit volume of serum by the total amount of plasma in the blood stream. In the experiments on hemorrhage, the figures in brackets represent the addition of the total protein, albumin and globulin that were removed at the time of the bleedings to the calculated absolute amounts of each that remained in the blood stream. Analyses were performed on the blood that was injected in order to replace that removed for the various determinations. The differences between the blood removed and that injected were ignored in the calculations. This introduced very little error.

The method (8) by which the posterior part of the body was divided into two parts was as follows. An abdominal incision was made in the midline line. The symphysis pubis was divided with a saw. The bladder and rectum were removed. The abdominal aorta and vena cava were doubly ligated and divided. The iliac vessels were clamped. A transverse abdominal incision was made at approximately the level of the umbilicus. This was extended through the vertebral column and the front part of the body was discarded. Using a knife and a saw, the structures on either side of the vertebral column of the posterior part were divided in a longitudinal direction. This resulted in a separation of the spinal column and tail from the two posterior portions of the body. The difference in the weight of the part into which fluid had been injected and the opposite part was determined.

RESULTS

1. The effects of the subcutaneous injection of normal salt solution

Three experiments were performed in which the effects on the composition of the blood of the subcutaneous injection of normal salt solution were determined. The blood pressure remained at approximately the control level in all of the experiments. There was usually a slight diminution in the concentration of red blood cells, and in the percentage of hemoglobin. There was a slight but definite increase in the volume of plasma in all experiments. The alterations in the percentages of total protein, albumin and globulin in the blood serum were very minor. There was an increase in the absolute amounts of total protein, albumin and globulin in the blood plasma in all experiments. Determinations of the difference in the weights of the two posterior extremities in the three experiments indicated that 29 per cent of the fluid that was injected was absorbed into the general circulation. The results of these experiments are given in Table I.

2. The effects of continuous trauma to the intestines and of the subcutaneous injection of normal salt solution

Continuous trauma to the intestines and the subcutaneous injection of normal salt solution were associated with varying degrees of decline in the blood pressure. There was an increase in the concentration of the red blood cells and an increase in the percentage of hemoglobin. The volume of blood plasma decreased in all experiments. The percentages of total protein, albumin and globulin in the blood serum remained at approximately the control levels throughout the experiments. There were rather marked decreases in the absolute amounts of the protein constituents in all experiments. Comparison of the weights of the posterior extremities indicated that 17 per cent of the fluid that was injected in the three experiments was absorbed. The results of these experiments are enumerated in Table II.

TABLE I

The effects of the subcutaneous injection of normal salt solution on the composition of the blood

Experiment number and weight	Time from beginning	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*
T 79	Control	0	5.22	59.0	2.67	30.2	2.55	28.8	[630]*	[1130]*	[1760]*	35.8	90.5	116
16.9	1°	169	5.22	60.6	2.74	31.8	2.48	28.8	660	1160	1820	36.6	88.2	100
kgm.	2° 30′	422	5.32	62.7	2.81	33.2	2.41	29.5	640	1180	1820	35.0	88.2	122
	4°	676	5.13	66.2	2.73	35.2	2.40	31.0	670	1290	1960	33.8	81.5	126
	5° 30′		5.04	64.1	2.62	33.2	2.42	30.9	690	1270	1960	34.8	81.4	114
	7°		4.95	64.4	2.59	33.6	2.36	30.8	700	1300	2000	34.8	79.8	113
	Injected blood		5.67		2.56		3.11					26.1	65.5	
T 80	Control	0	6.18	75.2	3.53	42.9	2.65	32.3	[750]*	[1215]*	[1965]*	38.1	86.7	124
18.7	1°	187	6.22	80.6	3.60	46.7	2.62	33.9	724	1296	2020	35.9	84.2	122
kgm.	2° 30′	467	6.53	82.3	3.75	47.3	2.78	35.0	705	1260	1965	36.5	86.7	129
	4°	748	6.30	83.2	3.50	46.2	2.80	37.0	740	1320	2060	35.9	82.7	120
	5° 30′		6.34	87.0	3.87	53.1	2.47	34.9	730	1370	2100	34.8	81.1	120
	7°		6.12	78.8	3.43	44.0	2.69	34.8	715	1285	2000	36.7	85.2	120
	Injected blood		4.97		3.56		2.41					33.6	76.9	

TABLE I (*continued*)

Experiment number and weight	Time from beginning	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*
T 81	Control	0	7.20	66.6	4.82	44.6	2.38	22.0	[724]*	[926]*	[1650]*	44.0	100.0	127
21.6	1°	216	7.15	71.5	4.73	47.3	2.42	24.2	715	1000	1715	41.7	96.1	130
kgm.	2° 30′	540	6.93	67.0	4.59	44.3	2.34	22.7	729	966	1695	43.0	97.4	135
	4°	864	6.79	68.4	4.49	45.3	2.30	23.1	724	1008	1732	41.8	95.2	128
	5° 30′		6.70	72.4	4.32	46.6	2.38	25.8	735	1080	1815	40.6	90.9	118
	7°		6.25	73.4	4.25	50.0	2.00	23.4	740	1175	1915	38.5	86.2	120
	Injected blood		6.08		3.46		2.62					37.0	80.2	

* Determined directly by the dye method.

Protocols. Morphine as anesthetic in all experiments.

T 79. Weight of extremity into which fluid was injected was 2540 grams. Weight of opposite extremity was 2020 grams. Difference in weight 520 grams. Total fluid injected was 676 cc. Amount of fluid absorbed was approximately 156 cc. Total urine 105 cc. with a total protein equivalent of 4.7 grams.

T 80. Weight of extremity into which fluid was injected was 2880 grams. Weight of opposite extremity was 2325 grams. Difference in weight 555 grams. Total fluid injected was 748 grams. Amount of fluid absorbed was approximately 193 cc. Total urine 112 cc. with a total protein equivalent of 17 grams.

T 81. Weight of extremity into which fluid was injected was 3405 grams. Weight of opposite extremity was 2840 grams. Difference in weight 565 grams. Total fluid injected was 864 cc. Amount of fluid absorbed was approximately 299 cc. Total urine 85 cc. with a total protein equivalent of 12.3 grams.

TABLE II

The effects of trauma to the intestines and the subcutaneous injection of normal salt solution on the composition of the blood

Experiment number and weight	Time from beginning	Fluid given	Total protein			Albumin			Globulin			Blood volume			Hematocrit	Hemoglobin	Mean blood pressure
			Serum	For total serum volume	Fluid	Serum	For total serum volume	Fluid	Serum	For total serum volume	Fluid	Red blood cells	Plasma	Whole			
		cc.	*per cent*	*grams*	*per cent*	*per cent*	*grams*	*per cent*	*per cent*	*grams*	*per cent*	*cc.*	*cc.*	*cc.*	*per cent*	*per cent*	*mm. Hg*
T 85	Control	0	7.08	77.4		4.33	47.3		2.75	30.1		[871]*	[1094]*	[1965]*	44.3	112.7	154
20.3	1°	203	7.11	63.0	6.80	4.33	38.4	4.75	2.78	24.6	2.05	858	886	1744	49.2	127.0	128
kgm.	2° 30′	507	7.20	58.2	5.90	4.29	34.7	4.01	2.91	23.5	1.89	876	808	1684	52.0	131.5	117
	4°	812	7.46	43.0	5.48	4.50	25.9	3.73	2.96	17.1	1.75	840	576	1416	59.4	156.2	117
	5° 30′		7.46	39.7	5.48	4.50	23.9	3.59	2.96	15.8	1.89	813	532	1345	60.4	164.8	38
	Injected blood		6.72			4.34			2.38						36.2	91.5	
T 86	Control	0	7.96	69.4		3.63	31.7		4.33	37.7		[694]*	[872]*	[1556]*	44.0	108.7	130
21.3	1°	213	7.46	57.0	7.98	3.20	24.4	4.75	4.26	32.6	3.23	733	733	1466	48.0	115.4	87
kgm.	2° 30′	533	7.88	55.8	6.98	3.49	24.7	4.03	4.39	31.1	2.95	722	708	1430	50.5	119.0	76
	4°	852	8.00	58.2	6.66	3.67	26.7	3.87	4.33	31.5	2.79	703	727	1430	49.2	119.0	66
	5° 30′		7.88	54.2	6.46	3.53	24.3	3.60	4.35	29.9	2.86	722	688	1410	51.2	120.0	68
	7°		6.78	52.6	6.02	3.03	23.5	3.50	3.75	29.1	2.52	747	776	1523	49.0	111.9	54
	Injected blood		6.12			3.63			2.49						29.9	71.8	

TABLE II (*continued*)

Experiment number and weight	Time from beginning	Fluid given	Total protein			Albumin			Globulin			Blood volume			Hematocrit	Hemoglobin	Mean blood pressure
			Serum	For total serum volume	Fluid	Serum	For total serum volume	Fluid	Serum	For total serum volume	Fluid	Red blood cells	Plasma	Whole			
		cc.	*per cent*	*grams*	*per cent*	*per cent*	*grams*	*per cent*	*per cent*	*grams*	*per cent*	*cc.*	*cc.*	*cc.*	*per cent*	*per cent*	*mm. Hg*
T 87	Control	0	6.25	39.0		3.90	24.3		2.35			[312]*	[624]*	[936]*	33.3	78.5	164
12.5	1°	125	6.40	29.7	5.87	4.20	19.5	4.26	2.20		1.61	320	464	784	40.8	93.8	148
kgm.	2° 30′	313	6.59	27.0	5.56	4.16	17.1	3.73	2.43		1.83	304	410	714	42.5	103.0	134
	4°	500	6.40	26.5	5.56	4.00	16.6		2.40			302	414	716	42.2	102.7	153
	5° 30′		6.03	24.4	5.18	3.73	15.1	3.59	2.30		1.59	312	404	716	43.5	102.7	139
	7°		5.87	25.5	4.91	3.69	16.0	3.87	2.18		1.04	309	435	744	41.6	98.7	125
	Injected blood		6.30			3.54			2.76						33.4	78.5	

* Determined directly by the dye method.

Protocols. Sodium barbital as anesthetic in all experiments.

T 85. Weight of extremity into which fluid was injected 3230 grams. Weight of opposite extremity 2635 grams. Difference in weight 595 grams. Total fluid injected 812 cc. Amount of fluid absorbed approximately 217 cc. Total urine 97 cc. with a total protein equivalent of 13.8 grams. The loss of fluid from the peritoneum was probably greater after the trauma was stopped than before. The intestines were very black in color at end of experiment.

T 86. Weight of extremity into which fluid was injected 3800 grams. Weight of opposite extremity 3050 grams. Difference in weight 750 grams. Total fluid injected 852 cc. Amount of fluid absorbed approximately 102 cc. Total urine 14 cc. with a total protein equivalent of 0.7 gram.

T 87. Weight of extremity into which fluid was injected 2105 grams. Weight of opposite extremity 1645 grams. Difference in weight 460 grams. Total fluid injected 500 cc. Amount of fluid absorbed approximately 40 cc. Total urine 32 cc.

TABLE III

The effects of hemorrhage and of the subcutaneous injection of salt solution on the composition of the blood

Experiment number and weight	Time from beginning	Fluid given	Blood removed	Total protein		Albumin		Globulin		Blood volume			Hematocrit	Hemoglobin	Mean blood pressure
				Serum	For total serum protein	Serum	For total serum protein	Serum	For total serum protein	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*
T 82 14.0 kgm.	Control	0	0	5.85	50.1 (55.8)†	3.20	27.4 (27.9)†	2.65	22.7 (27.9)†	[724]*	[856]*	[1580]*	45.3	109.0	138
	1°	140	140	6.18	51.4 (56.3)†	3.07	25.5 (28.0)†	3.11	25.9 (28.4)†	608	832	1440	43.3	107.0	100
	2° 30′	350	350	6.00	47.0 (57.3)†	2.95	23.1 (28.3)†	3.05	23.9 (29.0)†	567	783	1350	42.0	103.0	100
	4°	560	420	5.68	39.6 (58.1)†	2.85	19.8 (29.2)†	2.83	19.8 (28.9)†	478	697	1175	40.7	101.0	113
	5° 30′			5.45	39.2 (58.1)†	2.73	19.6 (29.2)†	2.72	19.6 (28.9)†	457	718	1175	39.0	95.0	110
	7°			5.45	39.2	2.73	19.6	2.72	19.6	467	718	1185	39.4	94.3	98
T 83 16.4 kgm.	Control	0	0	5.81	49.3 (50.7)†	3.69	31.3	2.12	18.0	[882]*	[848]*	[1730]*	51.0	120.0	136
	1°	164	164	5.94	46.0 (54.1)†					792	774	1566	51.0	119.0	126
	2° 30′	410	410	6.35	42.3 (52.5)†	3.88	25.8	2.47	16.5	669	665	1334	50.5	119.0	120
	4°	656	636	5.65	33.5 (53.0)†	3.58	21.2	2.07	12.3	516	592	1108	48.2	115.4	114
	5° 30′			5.46	34.0 (53.2)†	3.36	20.9	1.20	13.3	553	622	1175	47.1	112.0	108
	7°			5.45	34.2	3.35	21.0	2.10	13.2	568	628	1196	47.6	110.0	100

TABLE III (*continued*)

Experiment number and weight	Time from beginning	Fluid given	Blood removed	Total protein		Albumin		Globulin		Blood volume			Hematocrit	Hemoglobin	Mean blood pressure
				Serum	For total serum protein	Serum	For total serum protein	Serum	For total serum protein	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*
T 84 16.0 kgm.	Control	0	0	6.08	58.2 (61.5)†	3.62	34.6 (36.6)†	2.46	23.6 (24.9)†	[617]*	[958]*	[1575]*	39.2	93.1	143
	1°	160	160	6.01	55.6 (63.9)†	3.58	33.1 (38.6)†	2.43	22.4 (25.3)†	490	925	1415	37.3	89.3	124
	2° 30′	400	400	5.67	49.0 (63.6)†	3.44	29.7 (38.7)†	2.23	19.3 (24.9)†	371	864	1235	34.8	83.3	80
	4°	640	550	5.47	43.1 (62.8)†	3.37	26.5 (38.1)†	2.10	16.6 (24.7)†	387	788	1175	32.9	78.1	120
	5° 30′			5.54	42.3 (65.1)†	3.37	25.8 (40.5)†	2.17	16.5 (24.6)†	391	764	1155	33.9	79.4	120
	7°			5.60	44.6	3.55	28.2	2.05	16.4	390	796	1186	33.0	77.3	123

* 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 82. Weight of extremity into which fluid was injected 2335 grams. Weight of opposite extremity 1960 grams. Difference in weight 375 grams. Total fluid injected 560 cc. Fluid absorbed was approximately 185 cc. Total urine during experiment was 28 cc.

T 83. Weight of extremity into which fluid was injected 2750 grams. Weight of opposite extremity 2245 grams. Difference in weight 505 grams. Total fluid injected 656 cc. Fluid absorbed was approximately 151 cc. Total urine 80 cc. with a total protein equivalent of 7.2 grams.

T 84. Weight of extremity into which fluid was injected 2490 grams. Weight of opposite extremity 1980 grams. Difference in weight 510 grams. Total fluid injected 640 cc. Fluid absorbed was approximately 130 cc. Total urine 110 cc.

3. The effects of graded hemorrhages and of the subcutaneous injection of normal salt solution

In the three experiments in which the effects of graded hemorrhages and the subcutaneous injection of salt solution were studied, the removal of blood was sufficient to cause a definite decline in the blood pressure. There was a decrease in the hematocrit readings and in the percentage of hemoglobin in all experiments. The volumes of whole blood, plasma, and red blood cells decreased when the amount of blood that was removed is taken into consideration. There was a slight decrease in the percentages of total protein, albumin and globulin in the blood serum. The absolute amounts of the protein constituents that remained in the blood plasma decreased. However, if one adds to that remaining in the blood stream the amount corresponding to the protein removed by bleeding, it is to be noted that protein probably passed into the vessels during the course of the experiments. These figures are placed in brackets in the tables. Approximately 25 per cent of the fluid that was injected into the extremities was absorbed. The results of these experiments are given in Table III.

4. The effects of the subcutaneous injection of histamine and of normal salt solution

A marked decline in the blood pressure was produced in the three experiments in which the effects of the subcutaneous injection of histamine and salt solution were studied. The blood pressure rose after the injections were terminated. There were marked increases in the concentration of the red blood cells and in the percentage of hemoglobin. There was a rather large diminution in the volume of plasma in the blood stream. The content of the blood serum in total protein, albumin and globulin altered very little. However, due to the loss of plasma, there was a great decrease in the absolute amounts of total protein, albumin and globulin. The difference in weight of the posterior extremities in the three experiments indicated that approximately 22 per cent of the fluid that was injected was absorbed. The results of these experiments are given in Table IV.

DISCUSSION

The significant alterations that accompanied the subcutaneous injection of salt solution into normal dogs consisted of a slight increase in the volume of plasma and in the absolute amount of plasma protein. The findings differ in the main from those previously reported (2) in which the fluid was given intravenously to normal dogs in that an appreciable decrease in the percentage of protein in the blood serum was not encountered in the present experiments. Less than one-third of the fluid that

TABLE IV

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

Experiment number and weight	Time from beginning	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*
T 91	Control	0	0	6.62	48.9	4.31	31.8	2.31	17.1	[628]*	[738]*	[1366]*	46.0	121.0	118
13.3	1°	133	30			4.10	26.2			660	640	1300	50.8	127.0	110
kgm.	2° 30′	332	40	6.94	32.4	4.48	20.9	2.50	11.5	657	467	1124	58.4	147.1	74
	4°	532	55	6.39	27.9	4.28	18.7	2.11	8.2	644	436	1080	59.7	153.0	80
	5° 30′			6.39	29.8	4.10	19.5	2.29	10.7	657	467	1124	58.4	147.1	95
	7°			6.30	33.4	4.05	21.5	2.25	11.9	693	531	1224	56.6	135.1	95
	Injected blood			6.93		3.31		3.62					32.0		
T 93	Control	0	0	6.24	48.1	3.75	28.9	2.49	19.2	[541]*	[771]*	[1312]*	41.3	109.1	150
13.7	1°	137	20	5.62	28.9	3.53	18.2	2.09	10.7	536	514	1050	51.0	136.3	124
kgm.	2° 30′	343	45	5.98	29.6	3.62	18.0	2.36	11.6	539	496	1035	52.0	138.5	110
	4°	548	95	5.98	29.6	3.67	18.2	2.31	11.4	539	496	1035	52.0	138.5	90
	5° 30′			5.98	29.6	3.75	18.6	2.23	11.0	539	496	1035	51.7	138.8	135
	7°			6.12	30.3	3.77	18.7	2.35	11.6	539	496	1035	51.5	138.5	134
	Injected blood			5.86		3.25		2.61					30.4	81.5	

TABLE IV (*continued*)

Experiment number and weight	Time from beginning	Fluid given	Total histamine	Total protein		Albumin		Globulin		Blood volume			Hematocrit	Hemaglobin	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*
T 94	Control	0	0	7.13	48.1	3.92	26.5	3.21	21.6	[570]*	[675]*	[1245]*	45.8	100.0	112
12.8	1°	128	25	6.81	34.9	3.98	20.4	2.83	14.5	567	512	1079	52.4	115.4	90
kgm.	2° 30′	320	60	6.93	34.0	3.87	19.0	3.06	15.0	572	491	1063	53.8	117.1	97
	4°	512	100	6.62	33.1	3.82	19.1	2.80	14.1	563	500	1063	53.0	117.1	73
	5° 30′			7.20	34.1	4.00	19.0	3.20	15.1	564	473	1037	54.4	120.0	116
	7°			6.97	33.1	3.78	18.0	3.19	15.1	562	475	1037	54.2	120.0	103
	Injected blood			5.94		3.53		2.41					30.0	66.1	

* Determined directly by the dye method.

Protocols. Morphine as anesthetic in all experiments.

T 91. Weight of extremity into which fluid was injected was 2085 grams. Weight of opposite extremity 1680 grams. Difference 405 grams. Total fluid injected was 532 cc. Total amount of urine was 68 cc.

T 93. Weight of extremity into which fluid was injected was 2100 grams. Weight of opposite extremity 1670 grams. Difference 430 grams. Total fluid injected was 548 cc. Total amount of fluid absorbed was approximately 118 cc. Total urine 63 cc. with a total protein equivalent of 4.2 grams. Stomach contained 370 cc. of fluid at completion of experiment with a total protein equivalent of 1.6 grams.

T 94. Weight of extremity into which fluid was injected was 2020 grams. Weight of opposite extremity 1620 grams. Difference 400 grams. Total fluid injected was 512 cc. Total amount of fluid absorbed was approximately 112 cc. Total urine 26 cc. Stomach contained 335 cc. of darkly bile-stained fluid with a total protein equivalent of 9.9 grams.

was injected was absorbed and the greater part of this could be accounted for by the urine that was passed.

The findings in the experiments in which the intestines were traumatized and those in which histamine was injected were quite similar. In each there was an increase in the concentration of the red blood cells, an increase in the percentage of hemoglobin, a decrease in the volume of plasma, very little alteration in the percentage of the protein constituents in the blood serum and a marked decrease in the absolute amounts of each. The proportion of the fluid that was absorbed was approximately the same in the two types of experiments. The percentage of fluid that was absorbed was less with these animals than with the normal ones. Similar experiments (1, 3) previously performed in which fluids were introduced intravenously instead of subcutaneously showed a decrease in the concentration of the protein constituents in the blood serum but otherwise essentially the same findings. It seemed to require more trauma to produce a given decline in the blood pressure when fluids were administered subcutaneously than was necessary in similar experiments in which no fluid was introduced.

In the studies on the effects of graded hemorrhages and the subcutaneous injection of normal salt solution, there was a decrease in the concentration of the red blood cells. The decrease was not quite as great as was usually found when the intravenous introduction of salt solution accompanied hemorrhage. The decrease in the plasma volume was not as great as the quantity of plasma removed. The decrease in the percentage of protein in the serum was less than was found when the fluid was given intravenously. If the protein that was removed with the blood is included, there was a definite increase in the absolute amount of plasma protein. This increase varied from five to eight grams in the different experiments.

The fact that the plasma protein increased in the experiments in which salt solution was injected subcutaneously in normal dogs and in dogs that were bled is of interest from a physiological viewpoint. The question arises as to whether the increase can be explained on the basis of osmosis alone or whether it is necessary to include backward filtration as accounting for part of it. This question we fear cannot be answered from our experiments and no attempt will be made to do so. The recent experiments of Field and Drinker (9) give information on this point. They state, " 1. The capillaries under normal conditions are not concerned with the absorption of protein from the subcutaneous tissues. 2. After plasmapheresis, with substantial reduction of total blood protein, foreign protein placed in the subcutaneous tissues can be detected serologically in the blood when entrance by lymphatic routes has been blocked."

Speculation as to the comparative values of administering fluids intravenously and subcutaneously is not without interest. The intravenous

route presents a disadvantage in some instances in which there is a marked decline in the blood pressure in that a marked decrease in the percentage of plasma protein results which is not due to an increase in the plasma volume and hence the osmotic pressure in the blood vessels is lowered. This disadvantage apparently does not exist when the decline in pressure results from hemorrhage. The main objection to the subcutaneous introduction of fluids is that the absorption is slow and especially so when the blood pressure is at a low level. This latter method is not as apt to result in a reduction of the percentage of protein in the serum. It would seem in the absence of a favorable response in the blood pressure following the intravenous introduction of a moderate amount of a solution such as normal salt solution that the injection should be discontinued before a marked decline in the concentration of protein is produced. Possibly the subcutaneous injection of fluids would be of some assistance in maintaining the level in pressure until arrangements for a blood transfusion could be made. Certainly the subcutaneous injection of fluids will tend to prevent the drop in pressure following procedures that are frequently associated with a slow decline.

SUMMARY

The effects on the composition of the blood of the subcutaneous introduction of normal salt solution into dogs have been determined repeatedly under the following experimental conditions: (1) control studies on the injection alone, (2) trauma to the intestines, (3) the graded removal of blood and (4) the subcutaneous injection of histamine. The studies included determinations of the arterial pressure, the percentage of hemoglobin, the concentration of the red blood cells, the blood volume, the percentages of total protein, albumin and globulin in the blood serum and the volume of salt solution absorbed by the circulation.

The following are some of the results that were obtained.

1. In normal animals in which salt solution was injected under the skin, there was a slight increase in the volume of plasma, practically no alteration in the concentration and an increase in the absolute amounts of the protein constituents.

2. Trauma to the intestines and the subcutaneous injection of histamine were associated with a decrease in the volume of plasma, no definite change in the concentration of total protein, albumin and globulin and a marked decrease in the absolute amounts of the protein constituents. A smaller amount of the salt solution was absorbed by the circulation in these experiments than in the other ones.

3. The graded removal of blood was associated with a decrease in the concentration of the red blood cells, a slight diminution in the percentages of total protein, albumin and globulin in the blood serum, and an increase in the absolute amounts of the protein constituents if the amount of protein that was removed is included.

BIBLIOGRAPHY

1. Beard, J. W., and Blalock, Alfred, J. Clin. Invest., 1932, xi, 249. Intravenous Injections. A Study of the Composition of the Blood During Continuous Trauma to the Intestines When No Fluid is Injected and When Fluid is Injected Continuously.
2. Blalock, Alfred, Beard, J. W., and Thuss, Charles, J. Clin. Invest., 1932, xi, 267. 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.
3. Beard, J. W., Wilson, H., Weinstein, B. M., and Blalock, A., J. Clin. Invest., 1932, xi, 291. 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.
4. Cohen, B., and Smith, A. H., J. Biol. Chem., 1919, xxxix, 489. The Colorimetric Determination of Hemoglobin.
5. Rowntree, L. G., Brown, G. E., and Roth, G. M. The Volume of the Blood and Plasma in Health and Disease, Mayo Clinic Monographs, 1929, W. B. Saunders Company, Philadelphia.
6. Howe, P. E., J. Biol. Chem., 1921, xlix, 109. The Determination of the Proteins in Blood—A Micro Method.
7. Gunning, J. W., Ztschr. f. Anal. Chem., 1889, xxviii, 188. Ueber eine Modification der Kjeldahl-Methode.
8. Blalock, Alfred, Arch. Surg., 1930, xx, 959. Experimental Shock. The Cause of the Low Blood Pressure Produced by Muscle Injury.
9. Field, M. E., and Drinker, C. K., Am. J. Physiol., 1931, xciii, 66. Conditions Governing the Removal of Protein Deposited in the Subcutaneous Tissues of the Dog.