F_{cells} Value in Sympathectomized-Splenectomized Dogs after Hemorrhage.* (25970)

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The F_{cells} factor (overall cell percentage/venous cell percentage) is quite constant in splenectomized dogs, and is not apparently changed by variations in hematocrit level, transfusion or hemorrhage(1-3). It is well known that cardiac stimulation and vasoconstriction due to sympathetic activity constitute important circulatory adjustments to hemorrhage(4,5). Such compensatory mechanisms may conceivably adjust the distribution of cells and plasma in the circulation and contribute to the constancy of F_{cells} value after hemorrhage. To test this possibility, the F_{cells} factor in sympathectomized-splenectomized dogs is determined after hemorrhage and compared with the prehemorrhage value, which has been shown to be the same as that in splenectomized dogs(6).

Materials and methods. Twenty-five experiments were done on 19 unanesthetized mongrel dogs, sympathectomized and splenectomized(5) at least 4 weeks before experiments. Preparation of the animal, measurement of cell and plasma volumes, determination of hematocrit and plasma protein concentration, and removal of blood were performed as described elsewhere(3). The control blood volume of these experiments is given in the accompanying paper(6). One to 2 hours after removal of 146 to 362 ml of blood (19 to 43% of the control blood volume), posthemorrhage blood volume was measured.

Results. In Table I, results are tabulated in the descending order of percent of control blood volume remaining when posthemorrhage measurements were made. Posthemorrhage cell volume was either measured directly with Cr^{51} (CV in Table I), or calculated as the difference between control cell volume and volume of cells removed (CV'). In 6 dogs, both CV and CV' were determined, and they show very good agreement (Table I). In 19 of these 25 experiments, posthemorrhage F_{cells} value was within the control range of 0.82 to 0.92(6). The other 6 dogs had values lower than 0.80 after hemorrhage, the lowest value being 0.725 (dog #15). The relation between F_{cells} factor and % of initial blood volume remaining is shown in Fig. 1. The 6 low values were obtained in experiments where blood volume was reduced to 73-77% of the control.

Discussion. 1. F_{cells} factor after hemorrhage. Although the F_{cells} value is unchanged in splenectomized dogs after hemorrhage(1,3) or sympathectomy(6), it decreases in some sympathectomized-splenectomized dogs after hemorrhage. Therefore, the sympathetic activity after hemorrhage probably aids in redistribution of cells and plasma between large and small vessels such that a relationship similar to the prehemorrhage one can exist. That the sympathetic activity is not the only factor involved in this redistribution is evidenced by the fact that most sympathectomized-splenectomized dogs still have F_{cells} values after hemorrhage comparable to the control. Zweifach (7) has shown that the compensatory behavior to hemorrhage of the small vessels in

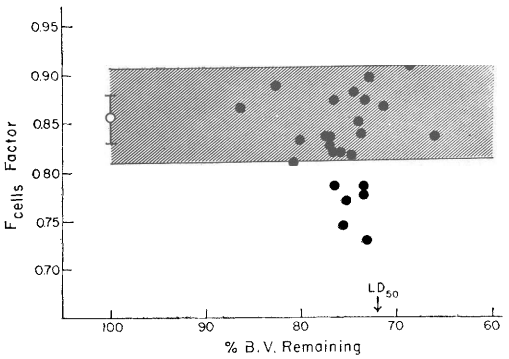

FIG. 1. Relationship between posthemorrhage F_{cells} factor and percent of control blood volume remaining. Open circle and vertical bars denote mean and stand. dev. of control F_{cells} factor. The two horizontal lines across the graph represent range of control F_{cells} factor. Note the 6 low F_{cells} values obtained in a range of 73-77% blood volume remaining. LD_{50} for sympathectomized-splenectomized dogs after hemorrhage is found with 72% of blood volume remaining(8), as indicated by the arrow.

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TABLE I. F_{cells} Factor in Sympathectomized-Splenectomized Dogs after Hemorrhage.

Dog No. and sex	Date of exp.	Body wt (kg)	Control: Art. cell %	Control: BV (ml)	Control: F_{cells}	Hemor. vol (ml)	Posthemorrhage: Art. cell %	Posthemorrhage: PV (ml)	Posthemorrhage: CV (ml)	Posthemorrhage: CV′ (ml)	Posthemorrhage: BV (ml)	Posthemorrhage: BV %	Posthemorrhage: F_{cells} factor
8 ♂	7/18/58	9.7	42.1	772	.898	146	41.3	426	—	241	667	86.4	.875
6 ♀	3/ 6/57	8.5	42.1	793*	.890†	155	40.0	420	235	—	655	82.6	.897
14 ♀	4/24/59	7.5	45.4	644	.866	187	42.4	340	184	177	521	80.8	.819
2 ♂	12/ 9/56	9.1	37.3	858*	.859†	209	34.1	491	198	—	690	80.1	.842
13 ♂	4/22/59	10.0	45.7	886	.848	255	41.2	441	234	234	675	77.4	.844
4 ♂	1/13/57	11.3	44.2	811*	.882†	247	39.3	419	208	—	627	77.3	.844
10 ♀	4/17/59	11.5	41.7	876	.875	267	37.0	467	208	210	676	77.1	.836
19 ♀	9/ 3/59	9.3	44.7	708	—	211	41.0	357	—	186	543	76.7	.828
1 ♂	11/24/56	10.0	41.4	880*	.890†	236	38.2	446	227	—	673	76.5	.882
20 ♀	11/19/59	8.1	41.9	641	—	193	39.4	338	149	155	490	76.5	.787
3 ♀	2/ 6/57	9.0	38.3	757*	.866†	252	33.4	416	159	—	575	76.0	.828
11 ♀	8/15/58	7.2	45.5	600	.819	201	40.2	318	—	136	454	75.7	.745
8 ♂	3/24/59	10.0	43.8	724	—	215	41.4	372	174	—	546	75.4	.771
9 ♂	8/25/58	9.7	40.0	901	.825	255	36.5	472	—	203	675	74.9	.825
5 ♀	1/ 8/57	9.3	35.7	782*	.892†	196	34.8	402	181	—	583	74.5	.891
12 ♂	8/27/58	10.7	41.2	1060	.867	356	36.1	542	—	244	786	74.1	.859
9 ♂	7/31/58	9.6	37.5	861	.861	241	34.9	448	—	188	636	73.9	.848
17 ♀	8/ 5/59	7.6	39.4	542	.838	180	36.4	286	—	113	399	73.6	.777
10 ♀	8/13/58	10.7	41.4	849	.860	328	35.5	450	—	174	624	73.5	.786
18 ♀	8/13/59	9.4	47.1	914	.870	285	42.5	420	—	251	671	73.4	.880
15 ♀	5/15/59	11.5	41.3	936	.850	379	36.0	505	174	182	683	73.0	.725
7 ♂	8/ 4/58	11.7	43.0	1038	.877	340	36.7	505	—	251	756	72.8	.905
12 ♂	12/29/59	12.9	49.8	1076	—	362	44.5	469	299	298	768	71.4	.874
10 ♀	8/29/58	10.9	42.7	996	.846	339	36.5	454	—	229	683	68.6	.918
11 ♀	11/10/58	8.5	47.4	646	.848	277	39.5	284	—	142	426	66.2	.843

* Control BV calculated from the equation $BV_1 = \frac{\text{Posthemor. CV} + \text{CV out}}{.87 \times \text{control art. cell \%}} \times 100$.

† Control F_{cells} value obtained at a different date.

the mesentery is a composite of the activity of renal, adrenal, and sympathetic homeostatic mechanisms superimposed on the intrinsic tone of the blood vessels themselves.

The critical level (LD_{50}) for sympathectomized-splenectomized dogs to survive hemorrhage is when blood volume is reduced to 72% of the control(8). This is close to the range of remaining blood volume where the low F_{cells} values are found. The decrease in F_{cells} value may be due to a relative increase in volume of blood in the small vessels and or a decrease in cell percentage there. It cannot be decided whether one or both of these factors are operating. But pooling of blood in small vessels may conceivably diminish venous return and become deleterious to the animal. It is interesting to note that histamine, a vasodilator probably causing increase in small vessel blood volume, decreases the F_{cells} value in splenectomized dogs(9).

2. Blood volume after hemorrhage. The agreement between posthemorrhage cell volume directly determined (CV in Table I) and that calculated by difference (CV′) validates the use of the latter. When there is a change of F_{cells} factor following hemorrhage, posthemorrhage plasma volume cannot be calculated from the posthemorrhage cell volume and hematocrit, as was done in the splenectomized dogs(5). In the present study, posthemorrhage plasma volume is always measured with T-1824. If replacement of plasma proteins is negligible within 2 hours after hemorrhage, the posthemorrhage plasma volume can also be calculated from changes in plasma protein concentrations(5):

$$PV_{2pp} = \frac{PV_1 \times (P.P.)_1 - \text{total plasma protein removed}}{(P.P.)_2}$$

where PV_1 is control plasma volume; $(P.P.)_1$ and $(P.P.)_2$ are respectively control and posthemorrhage plasma protein concentrations. In Table II, PV_{2pp} are thus estimated and compared with $PV_{2T\text{-}1824}$ directly measured with the dye. The results are generally in agreement, and there is no systemic difference. Therefore, when posthemorrhage plasma volume is not directly determined in sympathec-

TABLE II. Calculation of Posthemorrhage Plasma Volume from Changes in Protein Concentration.

Dog No. and sex	Date of exp.	% BV remaining	PV_1 (ml)	$(P.P.)_1$ (g %)	Total $(P.P.)_1$ (g)	P.P. out (g)	Total $(P.P.)_2$ (g)	$(P.P.)_2$ (g %)	PV_{2pp} (ml)	$PV_{2T-1824}$ (ml)	% dev.*
14 ♀	4/24/59	80.8	391	6.16	24.09	5.01	19.08	5.66	337	340	− .9
13 ♂	4/22/59	77.4	545	6.31	34.39	8.22	26.17	5.61	466	441	+5.7
10 ♀	4/17/59	77.1	556	6.36	35.36	9.76	25.60	5.20	492	467	+5.4
11 ♀	8/15/58	75.7	377	5.35	20.17	5.83	14.34	4.29	334	318	+5.0
8 ♂	3/24/59	75.4	447	5.66	25.30	6.56	18.74	5.30	354	372	−4.8
9 ♂	8/25/58	74.9	604	6.42	38.78	9.67	29.11	5.91	493	472	+4.4
12 ♂	8/27/58	74.1	682	6.62	45.15	13.99	31.16	5.81	536	542	−1.1
9 ♂	7/31/58	73.9	583	6.56	38.24	9.80	28.44	5.96	477	448	+6.5
17 ♀	8/ 5/59	73.6	363	5.15	18.69	5.23	13.46	4.60	293	286	+2.2
10 ♀	8/13/58	73.5	547	5.96	32.60	10.68	21.92	4.95	443	450	−1.6
18 ♀	8/13/59	73.4	538	5.30	28.51	7.98	20.53	4.60	446	420	+6.2
15 ♀	5/15/59	73.0	608	6.26	38.06	13.37	24.69	5.25	470	505	−6.8
7 ♂	8/ 4/58	72.8	647	6.31	40.83	11.89	28.94	5.45	531	505	+5.1
10 ♀	8/29/58	68.6	636	5.81	36.95	11.72	25.23	5.20	485	454	+6.8
11 ♀	11/10/58	66.2	386	5.76	22.23	8.57	13.66	5.05	270	284	−4.9

* % deviation $= \frac{PV_{2pp} - PV_{2T-1824}}{PV_{2T-1824}} \times 100.$

tomized-splenectomized dogs, it is better estimated from changes in plasma protein concentration than from cell volume and hematocrit.

Summary. In 6 out of 25 experiments on sympathectomized - splenectomized dogs, the posthemorrhage F_{cells} factor decreases to below the control range. The constancy of F_{cells} factor following hemorrhage in splenectomized dogs is partially due to sympathetic activity.

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Determination of N,N′-Diphenyl-p-Phenylenediamine in Animal Tissues.* (25971)

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Interest in the physiological activity of N,N′-diphenyl-p-phenylenediamine (DPPD) stems from its ability to substitute for Vit. E in prevention and cure of tocopherol deficiency diseases, including resorption gestation and muscular dystrophy(1,2). That this effect is not due to conservation of tocopherols in the tissues is evident from the fact that rate of decline of Vit. E in the liver of animals fed a diet deficient in the vitamin is not affected by DPPD administration, and that the antioxidant has curative as well as preventive activity(2). Following administration of d-α-tocopherol-5-methyl-C^{14} to rats, most of the radioactivity in the liver is present in the mitochondria as α-tocopherol, the remaining

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