ESTIMATION OF THE VASCULAR PERMEABILITY IN SHOCK BY DETERMINING THE ARTERIOVENOUS DIFFERENCE OF THE CONCENTRATION OF SERUM PROTEIN AND ITS FRACTIONS

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Considerable importance has been attached to the general [10, 12] and local [8, 9] increase in vascular permeability in shock, although some workers [1, 5], while admitting the importance of changes in permeability in the genesis of shock, ascribe only a secondary role to them.

Vascular permeability is determined either from the rate of migration of substances introduced into the vessels and changes in their concentration in the blood and tissues after injection [3, 11], or from changes in the composition of the blood itself [6, 7]. Methods based on the latter principle include the determination of the capillary permeability from the arteriovenous difference in the concentration of the serum proteins, the hematocrit index, or the concentration of hemoglobin [6]. The object of the present investigation was to evaluate the vascular permeability in the various phases of shock from the arteriovenous difference in the constituents of the blood (serum protein and its fractions, dry residue, and hematocrit index).

EXPERIMENTAL METHOD

Experiments were carried out on unanesthetized cats and dogs. Shock was produced in the cats by stimulation of localized receptor fields by a pulsed electric current using A. M. Dubinskii's method [2], and in the dogs by pulping the thigh muscles. On the basis of observations on the general condition of the animals, pulse rate, arterial pressure, respiration, and body temperature, the following phases of shock were distinguished: erectile, torpid (first and second), and terminal. Besides recording the arterial pressure and respiration of the animals, the venous pressure was measured in the femoral vein in the cats and in the external jugular vein in the dogs. Blood for investigation was taken in the cats from the femoral artery and vein, and in the dogs from the common carotid artery and the external jugular vein. The total protein was determined by the biuret reaction, and its fractions were estimated by paper electrophoresis. The paper strips were stained with bromphenol blue and eluted with a 0.1 N solution of NaOH, and colorimetry was carried out using a green filter. The results were analyzed statistically.

EXPERIMENTAL RESULTS

Altogether three series of experiments were conducted, two on cats and one on dogs. The first series consisted of control experiments on ten cats fixed to the bench for 3 h. No significant changes were found in the vascular permeability.

The second series of experiments was carried out on 20 cats, in which shock was induced. It will be seen from Table 1 that in the first torpid phase of shock the protein concentration was increased, together with that of all its fractions, in both the arterial and the venous blood, and the excess of the increase in concentration in the venous blood over that in arterial blood was significant ($P < 0.001$); analogous changes were found in the dry residue and hematocrit index. These findings evidently indicate that considerable amounts of water had passed out of the vessels, i.e., that the vascular permeability was increased in this phase of shock. It must also be remembered that the total protein concentration may have been increased as a result of arrival from the liver and tissues, especially at the beginning of shock. However, the fact that the increase in the protein concentration was so large, and moreover that

TABLE 1. Concentration of Serum Protein and Its Fractions in Arterial and Venous Blood of Cats during Shock (compared with controls)

Criteria	Statistical criterion	Control		Shock					
				torpid phase				terminal phase	
				1st		2nd			
		A	V	A	V	A	V	A	V
Total protein (in g%)	M ± m	7.43	7.48	9.02	9.62	7.2	6.92	8.52	8.34
		0.096	0.086	0.246	0.27	0.02	0.089	0.22	0.47
Albumins (in g%)	M ± m	2.46	2.5	2.9	2.93	2.35	1.95	2.7	2.67
		0.052	0.043	0.109	0.138	0.03	0.036		
Globulins (in g%) α_1	M ± m	0.37	0.37	0.42	0.53	0.39	0.40	0.38	0.4
		0.025	0.024	0.028	0.055	0.058	0.062		
Globulins (in g%) α_2	M ± m	1.41	1.42	1.85	1.95	1.35	1.36	1.84	1.82
		0.043	0.049	0.082	0.141	0.052	0.052		
Globulins (in g%) β	M ± m	1.02	1.03	1.25	1.35	1.10	1.03	1.05	1.06
		0.028	0.025	0.069	0.077	0.085	0.037		
Globulins (in g%) γ	M ± m	2.17	2.16	2.6	2.86	2.01	2.18	2.55	2.39
		0.062	0.058	0.111	0.138	0.099	0.083	0.234	0.311
Albumin-globulin ratio		0.5	0.5	0.47	0.44	0.48	0.39	0.46	0.47
Dry residue of serum (g%)	M ± m	8.66	8.68	10.31	10.84	8.42	8.17	9.8	9.63
		0.098	0.095	0.191	0.230	0.107	0.091	0.234	0.739
Hematocrit		38	38	41	43	38	36	38	41

Legend: A—arterial blood; V—venous blood.

TABLE 2. Concentration of Serum Protein and Its Fractions in Arterial and Venous Blood in Dogs Before (Controls) and During Shock

Criteria	Control		Shock					
			torpid phase				terminal phase	
			beginning of phase		end of phase			
	A	V	A	V	A	V	A	V
Total protein (in g%)	6.38	6.18	5.85	6.55	5.78	5.29	5.96	6.42
Albumins (in g%)	2.76	2.64	2.45	2.31	1.99	1.77	2.39	2.54
Globulins (in g%) α_1	0.12	0.17	0.16	0.29	0.17	0.23	0.25	0.30
Globulins (in g%) α_2	0.55	0.81	0.81	1.23	0.70	0.65	0.76	0.92
Globulins (in g%) β	1.51	1.38	1.47	1.84	1.49	1.34	1.57	1.55
Globulins (in g%) γ	1.44	1.18	0.96	0.88	1.43	1.30	0.99	1.11
Albumin-globulin ratio	0.76	0.75	0.72	0.71	0.53	0.50	0.67	0.65
Dry residue of serum (in g%)	7.45	7.30	6.97	7.74	6.87	6.53	7.04	7.56
Hematocrit	38	38	40	42	39	37	38	40

Legend: A—arterial blood; V—venous blood.

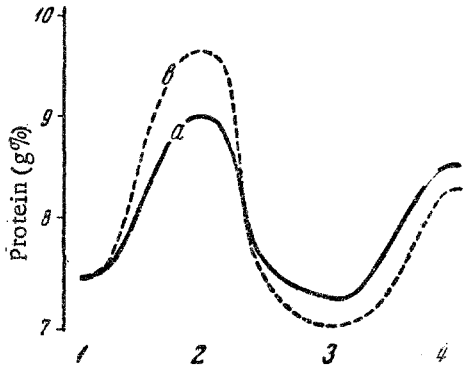
it was significantly larger in the venous than the arterial blood, coupled with the analogous changes in the hematocrit in association with the reduction in the circulating blood volume, justify the explanation that these changes are mainly due to extravasation of water.

In the second torpid phase the serum protein concentration actually fell below the initial level, but its concentration in the venous blood became significantly lower ($P < 0.001$) than in the arterial blood, this decrease being mainly an account of the albumin fraction (significance $P < 0.01$). The relative proportions of the α_1- and α_2-globulins were unchanged. The concentration of β-globulins was slightly decreased and that of γ-globulins increased in the venous blood by comparison with the arterial, although the differences were not statistically significant. The changes in the dry residue corresponded to the protein changes. The hematocrit index fell. These findings evidently demonstrated that mainly protein had left the blood stream, i.e., that a new, qualitative change had taken place in the vascular permeability in this phase of shock.

In the terminal phase the serum protein concentration again increased, but no significant differences could be found between the concentrations of the protein and its fractions in the arterial and venous blood, although the decrease in the γ-globulin fraction in the venous blood was quite noticeable by comparison with the arterial blood (see Table 1).

These changes suggest not only that the vascular permeability was disturbed and that a new increase in the extravasation of water had occurred, but also that highly dispersed serum proteins may have escaped from the vessels or disintegrated.

In the third series of experiments, conducted on nine dogs, the character of the changes taking place in the vascular permeability (Table 2) was substantially the same as in the second series of experiments on the cats.



Protein concentration in the serum of arterial (a) and venous (b) blood from cats in different phases of shock. 1) Before shock; 2) in the first torpid phase; 3) in the second torpid phase; 4) in the terminal phase.

The only difference was that in the dogs there was no marked increase in the serum protein at the beginning of the torpid phase of shock (the first torpid phase in cats), presumably because of the more rapid local escape not only of water, but also of protein, from the blood stream at the site of injury.

The findings demonstrate an association between the changes in vascular permeability and the phases of development of shock: at the beginning of the torpid phase the increase in permeability is accompanied by the escape mainly of water from the blood vessels, and at the end of this phase, mainly of protein, while in the terminal phase it is again mainly water that escapes. If it is remembered that areas of the blood stream forming part of the system of the superior and inferior venae cavae were investigated, it may be assumed that the observed disturbances of vascular permeability were evidently fairly general in character.

In certain areas of the vascular system, however, increased permeability may lead to an increased entry of fluids into the blood stream, depending on the hemodynamic conditions [4]. Our investigations into the absorption of salt solutions in the gastrointestinal tract of cats during shock also support this suggestion [2].

In conclusion, we refer again to the results of the second series of experiments (see figure). These clearly show that, despite the progressive deepening of the shock, the protein composition of the serum has its balance restored twice, or, in other words, even during this severe pathological process the organism remains capable of maintaining the constancy of its internal milieu.

SUMMARY

The present work was conducted on cats and dogs. The vascular permeability was assessed by the arteriovenous difference in the content of serum protein, its fractions, dry residue and of the hematocrit reading.

The data obtained demonstrated the relation of the vascular permeability changes to the phases of shock development: at the beginning of the torpid phase the rise of the vascular permeability was accompanied by the es-

cape of water from the vessels, and at the end – largely of protein, mostly at the expense of albumin fraction: at the terminal phase it was again water that was mainly extravasated, but at this phase some reduction of macrodispersive proteins was noted.

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