Intrarenal Redistribution of the Organ Blood Flow, Induced by Bleeding or Hemorrhagic Shock

Although evidence was found[1] that renal hypoxia in the acute hemorrhagic shock is unlikely to occur, zonal ischaemia may possibly contribute to the pathogenesis of the shock kidney[2,3]. This paper is concerned with the intrarenal blood flow distribution in rats during bleeding and hemorrhagic shock. Therefore tissue ^{86}Rb distribution in the renal zones has been examined using a technique previously described[4,5], based on a method introduced by SAPIRSTEIN[6]. This technique could be employed for our purpose, as we found that the calculated equilibrium potentials for Rb distribution in renal cells, in our experimental conditions, are near to those actually measured[7] in ischaemic renal tissue. Determinations were performed generally 25 min after ending of the hemorrhage. Adequate indications had to be observed in hypotension[8].

Measurements comprised: cardiac output (CO), arterial pressure (AP), myocardial fraction (MF), renal cortex fraction (RCF), outer medulla fraction (RMF) and inner medulla fraction (RPF). Results have been expressed as % of CO. Blood flows were calculated in ml/g/min.

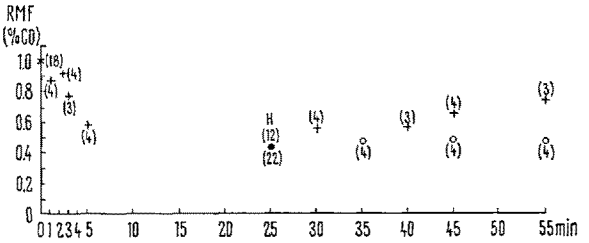
Results. Data reflecting shock state (MF, CO, AP) and intrarenal flow distribution are presented in the Table. Presentation of organ and zonal fractions are significant for our purpose and less affected by the error spreading.

Following a 3% hemorrhage, overall blood flow in the kidney decreases, while intraorgan distribution is altered: there is a more pronounced decrease of medullary blood flow than a cortical one. Decreased AP is associated with a more pronounced decrease of flow, while in normotensive animals, although the overall organ flow is less decreased, the intrarenal distribution is altered in the same manner. Little modification of the cortical flow can be recorded after a 1% hemorrhage, nevertheless the distribution of blood flows becomes altered by a significant decrease of the RMF. No action of hydergine could be observed. As presented in the Figure, redistribution of the flow follows the 1% hemorrhage in about 5 min, while normalization occurs in 60 min; after a 3% hemorrhage, the phenomenon still persists after 60 min.

Discussion. A decreased ^{86}Rb fixation in the outer medulla was found, which we assume to be a particular ischaemic reaction in this tissue. Thus we may suppose that within the renal blood flow, the medullary circulation has a peculiar reactivity, a view also shared by others[9]. Indirect evidence like urinary pO_2[10,11], also supports the existence of a medullary ischaemia in hemorrhagic shock.

The data obtained are in disagreement with those obtained by KRAMER[12] who, as a matter of fact, observed the blood flow of the inner medullary zone[13].

Our findings might complete recent works[14,15] on self-regulation of nephron circulation and Na excretion, as well as the alterations of these functions in shock. So, we assume that the selective ischaemia of the outer medulla



× controls, + hemorrhage 1%, H, hemorrhage 1% (S.E. ± 0.08), ○ hemorrhage 3%, ● hemorrhage 3% (S.E. ± 0.04). RMF, outer medulla fraction.

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	No.	CO (ml/100 g)	AP (mm Hg)	CF (% CO)	RCF (% CO)	RMF (% CO)	RPF (% CO)
Control	18	42.0 ± 2.6	120.0 ± 7.9	2.46 ± 0.32	12.27 ± 0.44	1.00 ± 0.05	0.25 ± 0.02
Hemorrhage 3%	22	30.4 ± 4.1[a]	78.0 ± 3.2[b]	3.68 ± 0.30[b]	8.45 ± 0.43[b]	0.45 ± 0.04[b]	0.12 ± 0.02[b]
Hemorrhage 3% (AP < 80 mm Hg)	9	19.3 ± 4.0[b]	56.0 ± 5.2[b]	4.21 ± 0.51[b]	6.60 ± 0.48[b]	0.37 ± 0.05[b]	0.10 ± 0.01[b]
Hemorrhage 3% (AP > 80 mm Hg)	13	37.9 ± 4.7	93.0 ± 11.5	3.32 ± 0.34	9.74 ± 0.35[b]	0.54 ± 0.07[b]	0.22 ± 0.06
Hemorrhage 1%	12	38.3 ± 5.1	105.0 ± 2.9	2.95 ± 0.21	10.66 ± 0.63	0.55 ± 0.08[b]	0.20 ± 0.02
Hemorrhage 3% (+ Hydergin 0.01 mg/kg)	6	35.8 ± 8.2	96.0 ± 10.8	1.29 ± 0.60	7.72 ± 0.80[b]	0.36 ± 0.09[b]	0.19 ± 0.02[c]

[a] $0.01 < P < 0.02$, [b] $P < 0.01$, [c] $0.02 < P < 0.05$.

might be the natural factor which, in hemorrhage, induces the damage of both the cortical circulation and of the glomerular function. The mechanism assumed is a functional disturbance of the thick segment of the ascending limb in the loop of Henle.

We must emphasize that medullary circulation in rats is more active than in other species[6,16].

Zusammenfassung. Es wird eine durch Blutung und hämorrhagischen Schock hervorgerufene intrarenale Neuverteilung der Durchblutung beschrieben. Der wesentliche Effekt ist eine verminderte Blutversorgung der äussern Markzone.

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Nephrectomy and Anaphylactoid Edema

It is known that certain organs play an important role in the formation of anaphylactoid edema (AE). Removal of the adrenals increases[1] while both exclusion of the insular apparatus[2] and hypophysectomy[3,4] prevent the development of the AE. On the basis of our earlier experiments we assumed that the kidneys may participate in the genesis of the AE. Therefore, in the present experiments we wanted to examine whether the AE can be influenced by nephrectomy in rats.

The experiments were carried out on female albino rats of the same strain weighing 150–165 g. Local and generalized AE were induced: by subplantar injection of dextran (900 μg Intradex in 0.1 ml), by i.p. administration of dextran (120 mg/kg body weight) and of egg white (25% in physiological saline given in a dose of 1 ml/100 g body weight). The changes of the volumina of the hind paws were measured by a method using displacement of mercury 90 and 120 min following the application of the edema-producing agents. The degree of inhibition produced by the manipulations was expressed as % of the control value. Nephrectomy and the sham operation were carried out in hexobarbital-Na anaesthesia (50 mg/kg body weight i.v.) 24 h before the experiments.

Nephrectomy inhibits, 24 h after removal of the kidneys, the edema-inducing effect of dextran given s.c. into the hind paws by 67%, while the sham operation only produces an 11% inhibition. Nephrectomy also inhibits to about the same extent (65%) the effect of compound 48/80 injected into the hind paws (25 μg in 0.1 ml), however, it does not influence the edema formation evoked by subplantar injection of 5-HT (serotonin-creatinine sulphate, 5 μg in 0.1 ml). Table I.

The generalized AE induced by dextran is suppressed by nephrectomy to an extent of 71% and in the case of the administration of egg white the inhibition is 77% as compared with the control values. The sham operation causes only a moderate inhibition (14%) of the dextran induced generalized AE (Table II).

Insulin increases in normal animals[5] and restores in diabetic rats[2] the effect of agents inducing AE. In our experiments insulin (4 IU s.c.; 10 times crystallized, glucagon-free, Novo[6] administered simultaneously with dextran counteracts the inhibiting effect of nephrectomy. In the insulin-treated animals, bilateral nephrectomy results in a 38% inhibition of the generalized AE only (see Table II).

The fasting blood sugar levels and the blood pressures measured in nembutal anaesthesia do not differ in nephrectomized animals from the control values. The blood urea nitrogen (BUN) is 103 ± 19 mg in 100 ml blood. Beside the elevation of the BUN there are no considerable changes in blood constituents 24 h following nephrectomy[7].

In addition, according to our preliminary observations, nephrectomy inhibits, to an extent of 85%, the formalin induced inflammation, too, while the sham operation increases the effect of formalin considerably (by 20%).

The mechanism of the AE is not yet cleared. A mediator role was attributed to histamine and 5-HT[8]. As the edema-

Table I. The volume of hind paws in ml before (A) and 90 min after (B) the local administration of edema producing agents

Treatment (No. of experiments)	Vol. of the hind paws in ml	Inhibition in % of control value	P
Dextran, control (20)	A 0.398 ± 0.006 B 0.665 ± 0.027	–	–
Dextran, sham operation (10)	A 0.383 ± 0.014 B 0.620 ± 0.018	11	$\cong 0.2$
Dextran, nephrectomy (10)	A 0.393 ± 0.004 B 0.485 ± 0.010	67	< 0.001
Compound 48/80, control (15)	A 0.410 ± 0.006 B 0.593 ± 0.027	–	–
Compound 48/80, nephrectomy (10)	A 0.398 ± 0.025 B 0.463 ± 0.042	65	< 0.001
5-HT, control (15)	A 0.396 ± 0.005 B 0.538 ± 0.050	–	–
5-HT, nephrectomy (10)	A 0.374 ± 0.018 B 0.504 ± 0.020	9	$0.5 > P > 0.2$

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