DISTRIBUTION OF THE OSMOTIC LOAD BETWEEN THE BODY FLUIDS AFTER INTRAVENOUS INJECTIONS OF HYPERTONIC SOLUTIONS

O. G. Karandeeva

UDC 612.117.2+612.014.462.1

During recent years, for the investigation of the water and salt metabolism of mammals, the method of determining the water volumes of distribution of certain substances has often been used [5]. In a previous report [2], the author showed that after intravenous injection of a hypertonic solution of NaCl into cats, the osmotic concentration of the blood was balanced extremely rapidly (in the course of 30 sec). It was suggested that this was achieved by the osmotic redistribution of water and of osmotically active substances between the blood and the body tissues. This process, called by the author a primary osmoregulatory reaction, does not involve the participation of the kidneys and it comprises the passive movement of water into the blood and the movement of salts outside the vascular system. The second of these is evidently an active process, controlled by the subcortical osmoregulatory centers in the hypothalamic region. It has been found that a measured osmotic loading with NaCl causes the same change in osmotic pressure as if it had been distributed over a volume similar to the volumes of distribution of the Na and Cl ions.

The object of the present investigation was to attempt to discover the character of the primary osmoregulatory reaction after injection of substances of different permeabilities into the blood stream and after different degrees of osmotic loading. For this purpose, cats were given intravenous injections of hypertonic solutions of sucrose, the true distribution volume of which is equal to the volume of the extracellular fluid, for practically no sucrose penetrates through the cell membranes [5], of urea, which penetrates readily into cells and is distributed throughout the total volume of water capable of dilution [13], and of NaCl. The Na ion is known to penetrate into cells comparatively well [11], and it is continuously eliminated from them by means of the "sodium pump" [9]. With high degrees of loading, the distribution volume of NaCl approximates to the total volume of the body water [4,6].

EXPERIMENTAL METHOD

Hypertonic solutions of NaCl, sucrose, and urea were injected into the femoral vein of adult cats anesthetized with urethane. The experiments of series I were set up in a similar manner to those described earlier [2]: the injections, which lasted 15 sec, were given every 5 min; at each injection 5.25 milliosmoles/kg body weight was injected. After the first three injections of NaCl* solutions of sucrose or urea of the same osmotic concentration were injected. In control experiments, NaCl was injected four times altogether. Blood samples were taken from the carotid artery before the fourth injection, then every 3 sec during the first 30 sec after the fourth injection, and then at less frequent intervals until the end of the first 5 min. The osmotic concentration of the blood in the samples was determined by means of an electrocryoscope [3] and the dilution of the blood by the hematocrit. In the experiments of series II, the animals received injections of hypertonic equilibrated NaCl solutions of different concentrations continuously for 20 min. During and after the injection, blood samples were taken and the urine collected for determination of their osmotic pressure. The volumes of the injected solution and urine were recorded. Some animals were decerebrated at the level of the corpora quadrigemina.

EXPERIMENTAL RESULTS AND DISCUSSION

In the experiments of series I, results on the whole analogous to those described previously [2] were obtained: the osmotic concentration of the blood at first rose sharply, reaching a maximum 15-20 sec after the beginning of the injection, and then it fell rapidly to a certain stable level, which was regarded as the establishment of osmotic

*NaCl was injected as a 5% equilibrated solution with the addition of KCl and $CaCl_2$ in the same proportions as in Ringer's solution.

Division of Physiology of Aquatic Organisms, A. O. Kovalevskii Institute of Biology of the Southern Seas, Academy of Sciences of the UkrSSR, Sevastopol' (Presented by Academician V. N. Chernigovskii). Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 62, No. 8, pp. 19-23, August, 1966. Original article submitted July 8, 1964. The research was carried out in the laboratory of general physiology, Institute of Normal and Pathological Physiology, Academy of Medical Sciences of the USSR (Moscow), under the direction of Professor A. M. Ugolev, to whom the author is deeply grateful.

TABLE 1. Changes in Osmotic Concentration (in % of Original Level) and Dilution of Blood after Intravenous Injections of Hypertonic Solutions of NaCl, Sucrose, and Urea

Conditions of experiments	No. of experiments	Index	4½ min after 3rd injection	At point of maximum after 4th injection	4½ min after 4th injection
4 injections of NaCl	13	Osmotic concentration of blood	108.7 ± 0.5	136.5 ± 2.5	111.9 ± 2.0
		Dilution of blood	1.27± 0.02	1.43± 0.03	1.31± 0.02
		Osmotic concentration of blood × dilution	138.0 ± 2.4	195.2 ± 2.5	146.6 ± 2.6
3 injections of NaCl, 1 injection of sucrose	7	Osmotic concentration of blood	108.9 ± 1.5	148.7 ± 4.2	111.9 ± 1.0
		Dilution of blood	1.35± 0.07	1.47± 0.02	1.40± 0.02
		Osmotic concentration of blood × dilution	147.0 ± 4.9	218.6 ± 9.3	156.6 ± 5.3
3 injections of NaCl, 1 injection of urea	7	Osmotic concentration of blood	108.6 ± 0.5	127.4 ± 2.3	111.3 ± 1.1
		Dilution of blood	1.31± 0.02	1.33± 0.02	1.28± 0.03
		Osmotic concentration of blood × dilution	142.3 ± 1.7	169.4 ± 4.5	142.5 ± 2.1

equilibrium. The osmotic concentration of the blood before the beginning of the injections was on the average 349.0 ± 2.8 milliosmoles/liter. The values of the osmotic concentration of the blood as percentages of the initial level and the dilution of the blood as determined by the hematocrit 4.5 min after the 3rd and 4th injections and at the maximum of osmotic pressure after the 4th injection are given in Table 1. The values of the osmotic concentration of the blood calculated in relation to the initial blood volume (the product of the osmotic concentration and the dilution characterizing the osmotic concentration which would be produced in undiluted blood) are also given in Table 1.

Because the blood accounts for 12.5% of the body weight and the plasma for about 60% of the blood volume, the injection of 5.25 milliosmoles/kg increased the total concentration of osmotically active substances in the plasma by roughly 20% (if the salts were not eliminated from the blood stream while they were being administered). The increase in the osmotic concentration of the blood by more than 20% in the course of an injection (calculated in relation to the initial blood volume) therefore indicated that at that particular moment the injected solution had not been distributed throughout its volume. Such a phenomenon was observed at the point of the maximum of the osmotic concentration of the blood after injection of NaCl and sucrose. Urea was distributed (or excreted) more quickly. A large proportion of the total amount of the salts had been eliminated from the blood stream 4.5 min after the injections of all three substances. In the case of the injection of sucrose, the blood dilution was greatest. A considerable movement of fluid into the blood was also caused by NaCl. Conversely, injection of urea, which penetrates readily into the tissues, did not lead to dilution of the blood. However, despite the differences in the permeability of the injected substances and the variation in the role of the dilution component, the total osmotic effect of the primary osmoregulatory reaction was the same for all three solutions; the osmotic concentration of the blood rose as a result of each injection on the average by 2.9%.

If the injected osmotic load of 5.25 milliosmoles was divided by the mean increase in osmotic concentration of the blood (2.9% of 349 milliosmoles/liter) and the result expressed per kilogram body weight, the mean volume of osmotic distribution was obtained, amounting to 52% of the body weight. As might be expected from the concept of the isoosmolarity of the extracellular and intracellular fluids [4,10,15], the volume of the osmotic distribution calculated as described above was of the same order as the total volume of water in the body. According to various authors, using special methods for its determination, this value in cats is 59-70.6% of the body weight [6-8,16], in dogs 48-75.7% [12-14,16], and in rabbits 58.35-77.8% [7,12,14].

The results of the experiments of series II are given in Table 2. The value of the osmotic load as a percentage of the total volume of salts in the plasma was calculated from the concrete values of the osmotic concentration of the blood and the hematocrit of individual animals. When the volume of the osmotic distribution was calculated, a correction was made for the amount of salts injected and for the volume of fluid injected and excreted. The part played by the kidneys in the primary osmoregulatory reaction was negligible; they excreted only a part of the injected fluid and a few percent of salts. Despite the considerable differences in the concentration and volume of the injected solutions, and in the relative role of renal excretion, the dilutions of the blood and the rate of elimination of salts from the blood stream, the osmotic load injected into the blood was distributed extremely quickly whatever its magnitude.

TABLE 2. Volume of Osmotic Distribution in Control and Decerebrate Cats, Calculated from the Osmotic Concentration of the Blood, Its Dilution, and the Volume and Concentration of the Urine after Injection of Hypertonic Equilibrated Solutions of NaCl

Animals	Animal No.	Initial blood concentration (in milliosmoles/liter, 100%)	During injection (20 min): injected: volume (in ml/kg)	During injection: injected: amount of salts: milliosmoles/kg	During injection: injected: amount of salts: % of concentration in plasma	During injection: excreted: volume of urine (in ml/kg)	During injection: excreted: amount of salts (in milliosmoles/kg)	At end of injection: osmotic concentration of blood (% of initial)	At end of injection: dilution of blood	At end of injection: volume of osmotic distribution (% of body weight)	After injection: excreted during 0-20 min: volume of urine (in ml/kg)	After injection: excreted during 0-20 min: amount of salts (in milliosmoles/kg)	After injection: 20 min: osmotic concentration of blood (% of initial)	After injection: 20 min: dilution of blood	After injection: 20 min: volume of osmotic distribution (% of body weight)	After injection: excreted during 20-40 min: volume of urine (in ml/kg)	After injection: excreted during 20-40 min: amount of salts (in milliosmoles/kg)	After injection: 40 min: osmotic concentration of blood (% of initial)	After injection: 40 min: dilution of blood	After injection: 40 min: volume of osmotic distribution (% of body weight)
Control	1	321	6.10	15.2	57	0.6	0.8	109	1.41	49.2	1.0	1.1	108	—	51.8	1.7	0.9	107	1.31	55.4
	2	319	22.40	38.3	135	8.3	4.7	129	1.57	34.9	4.5	2.1	124	1.35	40.2	—	—	—	—	—
	3	346	32.10	54.8	192	7.8	5.0	127	1.51	51.0	11.3	6.6	119	1.10	64.4	—	—	—	—	—
	4	355	8.55	66.8	255	1.5	2.2	138	2.28	47.2	3.5	2.7	130	1.82	56.9	3.0	2.1	128	1.82	60.1
	5	340	11.52	76.6	310	2.2	2.5	148	2.16	44.5	3.3	6.4	145	—	43.8	1.5	1.3	145	1.65	43.0
Decerebrate	6	336	7.08	53.3	215	4.3	2.6	148	2.15	31.1	3.0	3.0	133	1.78	43.0	1.5	1.4	131	1.74	44.6
	7	333	7.28	54.8	220	2.5	1.9	141	1.82	38.3	2.7	1.9	127	1.29	56.5	1.0	0.8	126	1.27	57.7
	8	343	10.78	69.9	233	0.3	0.3	154	2.46	36.6	0.4	0.4	143	2.36	46.0	—	—	—	—	—
	9	349	7.38	55.6	195	0.1	0.4	141	2.22	37.8	0.1	0.3	127	—	57.4	—	—	125	1.38	—

In the control animals, the primary osmoregulatory reaction was largely completed during the injection. In the decerebrate animals, this process took place much more slowly. The volume of the osmotic distribution during the period of the observations approximated to a relatively stable value close to that calculated for the experiments of series I.

Hence, in the case of intravenous injections of hypertonic solutions into cats, the primary osmoregulatory reaction took place extremely quickly, irrespective of the size of the osmotic load injected, its chemical composition, the time of the injection, and the rate of excretion by the kidneys, leading to equilibration of the osmotic concentration of the blood. Decerebration slowed, but did not stop this process. In the period of established osmotic equilibrium, the increase in the osmotic pressure of the blood was determined entirely by the size of the injected osmotic load and was independent of the concentration and permeability of the substance injected.

The volume of distribution of the osmotic load was close to the total volume of water capable of diluting (to the total water of the body). These facts suggest that the primary osmoregulatory reaction takes place as a result of the establishment of osmotic equilibrium between the tissues and the extracellular fluid, which is reached both on account of the passive movement of water [1] and by the redistribution of osmotically active components along the osmotic gradient. With an excess of a substance in the blood for which the cell membranes are impermeable or only slightly permeable, a redistribution of other substances with higher permeability may take place.

LITERATURE CITED

1. A. G. Ginetsinskii, Physiological Mechanisms of Water-Salt Balance [in Russian], Moscow-Leningrad (1963).
2. O. G. Karandeeva, DAN SSSR, 139, 3, 755 (1961).
3. O. G. Karandeeva, Lab. Delo, 8, 52 (1961).
4. E. J. Conway and J. I. McCormack, J. Physiol. (Lond.), 120, 1 (1953).
5. N. Deane, Meth. Med. Res., 5, 159 (1952).
6. M. G. Eggleton, J. Physiol. (Lond.), 115, 482 (1951).
7. J. M. Foy and H. Schnieden, J. Physiol. (Lond.), 154, 169 (1960).
8. M. Hetherington, J. Physiol. (Lond.), 73, 184 (1931).
9. A. L. Hodgkin, Biol. Rev., 26, 339 (1952).
10. A. Leaf, Ann. N. Y. Acad. Sci, 72, 398 (1959).
11. H. McLennan, Biochim. Biophys. Acta, 24, 333 (1957).
12. C. R. Richmond, W. H. Langham, and T. T. Trujillo, J. cell. comp. Physiol., 59, 45 (1962).
13. P. R. Schloerb, Am. J. Physiol., 199, 661 (1960).
14. R. J. Soberman, Proc. Soc. Exp. Biol. (N.Y.), 74, 789 (1950).
15. A. G. Swan and A. T. Miller, Jr., Am. J. Physiol., 199, 1227 (1960).
16. A. V. Wolf and M. E. McDowell, Am. J. Physiol., 176, 207 (1954).

All abbreviations of periodicals in the above bibliography are letter-by-letter transliterations of the abbreviations as given in the original Russian journal. *Some or all of this periodical literature may well be available in English translation.* A complete list of the cover-to-cover English translations appears at the back of the first issue of this year.