7. Rafajko, R., Fed. Proc., 1966, v25, 249.
8. Wigand, R., Wunn, W., Virology, 1966, v28, 484.
9. Brandt, C. D., Wassermann, F. E., Fox, J. P., Proc. Soc. Exp. Biol. & Med., 1966, v123, 513.
10. Hatch, M. H., Siem, R. A., Am. J. Epid., 1966, v84, 495.
11. Parks, W. P., Melnick, J. L., Queiroga, L., Ali Kahn, H., Am. J. Epid., 1966, v84, 382.
12. Lucas, J. B., Johnston, J. G., Kaye, H. S., Bucca, M. A., Robinson, R. Q., Pub. Health Reports, 1965, v80, 647.
13. Pereira, H. G., Kelly, B., J. Gen. Microbiol., 1957, v17, 517.
14. Henry, M., Chardonnet, M., Sohier, R., Ann. Inst. Pasteur, 1963, v105, 54.
15. Rowe, W. P., Hartley, J. W., Huebner, R. J., Proc. Soc. Exp. Biol. & Med., 1958, v97, 465.
16. Van der Veen, J., Dijkman, J. H., Am. J. Hyg., 1962, v76, 149.
17. Green, M., Pinã, M., Proc. Nat. Acad. Sci. U. S., 1963, v50, 44.
18. Cramblett, H. G., Kasel, J. A., Langmark, M., Wilken, F. D., Pediat., 1960, v25, 282.
19. Behbehani, A. M., Lee, L. H., Melnick, J. L., Proc. Soc. Exp. Biol. & Med., 1964, v116, 661.

Received March 2, 1967. P.S.E.B.M., 1967, v125.

Influence of Bradykinin on Water, Sodium, Potassium, Magnesium and Calcium Content of Segments of Arteries and Veins of Dogs *in vitro*.* (32131)

C. C. HUANG, N. P. DEPASQUALE, AND G. E. BURCH
Department of Medicine, Tulane University School of Medicine and the Charity Hospital of Louisiana, New Orleans

Bradykinin is a powerful vasoactive polypeptide. Its role in inflammation, tissue injury, reactive hyperemia, and the regulation of the circulation has received attention from many laboratories including our own(1,2,3). Because of its strong vasoactivity and because of our interest in its action on postcapillary blood vessels including A-V shunts, it was considered of interest to learn the effects of bradykinin upon electrolyte content of arteries and veins which were available from dogs under study of hemodynamic phenomena. Such information is of importance because of the role of sodium, potassium, magnesium and calcium in smooth muscle metabolism and contraction.

Material and methods. Dogs were anaesthetized with pentobarbital, and their femoral arteries and veins were rapidly dissected and placed in Krebs bicarbonate solution(4), oxygenated by bubbling a mixture of 95% oxygen and 5% carbon dioxide. The temperature of the water bath was maintained at 38.5°C(5). Two beakers, each containing about 50 ml of oxygenated Krebs bicarbonate solution, were also kept in the water bath, and to one was added 1 μg/ml synthetic bradykinin.† Two segments of femoral artery and two segments of vein were transferred simultaneously, one of each into both beakers, and removed 10 minutes later. Any solution adhering to these vessels was blotted away with filter paper. After weighing, the samples were placed in an oven at 105°C for 48 hours and were then reweighed. The samples were digested over an open flame with HNO_3, H_2SO_4 and $HClO_4$, as previously described (6). The sodium, potassium, magnesium, and calcium contents of the vessel segments were determined by flame photometry (Zeiss PMQII, double monochromator)(7).

Results. The water content of the arteries and veins was not significantly changed by bradykinin (Table I). After treatment with bradykinin there were statistically significant changes in the electrolyte content in the arterial wall (Table I). The amount of sodium decreased from 155.5 ± 20.7 mEq/kg

* Supported by grants from USPHS, Rowell A. Billups Fund for Research in Heart Disease and the Rudolph Matas Fund for the Kate Prewitt Hess Laboratory.

† Bradykinin obtained through the courtesy of Dr. Rudolph Bircher of Sandoz Co.

TABLE I. Water, Sodium, Potassium, Magnesium and Calcium Content of Normal Dog Blood Vessel with and without Bradykinin Added to Krebs Bicarbonate Solution. (water: % of wet weight of vessel — electrolyte: mEq. per Kg of fresh vessel)

	Control			Bradykinin			P value
	No.	Mean	SD	No.	Mean	SD	
Artery							
water	23	74.465	±3.545	15	74.298	±3.829	>.8
sodium	21	155.463	20.660	15	120.784	13.330	<.001
potassium	22	31.309	10.810	13	29.607	4.876	>.5
magnesium	22	8.609	2.883	13	8.492	2.672	>.9
calcium	18	7.698	2.088	14	11.003	3.776	<.01
Vein							
water	25	74.146	4.194	15	74.577	5.094	>.7
sodium	25	182.215	36.330	14	137.087	25.560	<.001
potassium	23	17.913	4.562	13	16.131	4.576	>.2
magnesium	21	8.043	2.625	12	10.167	3.876	<.05
calcium	19	7.292	1.770	8	12.371	2.178	<.001

of fresh artery to 120.8 ± 13.3 mEq/kg, with a p value of <0.001. The amount of calcium increased from 7.7 ± 2.09 mEq/kg of fresh artery to 11.0 ± 3.8 mEq/kg, with a p value of <0.01. There was no significant change in the content of potassium or of magnesium.

Bradykinin produced similar changes in the venous wall, the only difference being that the magnesium content also increased significantly (Table I). The sodium content was decreased from 182.2 ± 36.3 mEq/kg of fresh vein to 137.1 ± 25.6 mEq/kg, with a p value of <0.001; the calcium was increased from 7.29 ± 1.77 mEq/kg of fresh vein to 12.37 ± 2.18 mEq/kg, with a p value of <0.001; and the magnesium increased from 8.04 ± 2.63 mEq/kg of fresh vein to 10.17 ± 3.88 mEq/kg, with a p value of <0.05.

Discussion. From *in vitro* studies of arteries and veins of the dog, it was found that bradykinin will change the absolute and/or relative content of sodium, potassium, magnesium and calcium in the walls of these vessels. The mechanisms by which this occurs are unknown but are probably related in part to the action of this polypeptide on muscle contraction as well as cellular permeability. There was a slight difference beween the effects on the arteries and veins. This is also true for the action of bradykinin on the smooth muscle of pre- and postcapillary blood vessels(3). Whether or not these differences are related to smooth muscle function could not be determined from these studies. Although bradykinin did not increase the water content of the arterial and venous segments there was a change in the electrolyte content. Bradykinin increases the rates of diffusion of sodium (Na^{22}) and potassium (traced by Rb^{86}) into and across the wall of these vessels. Thus, these studies show that bradykinin can alter the electrolyte metabolic state of both arteries and veins of dog.

Summary. From *in vitro* studies of vessel segments, bradykinin has been shown to decrease the sodium content of arteries and veins and increase the calcium content of both arteries and veins, whereas it increased the magnesium content of veins only. However, in spite of the changes in the electrolyte content noted, the water content of the veins and arteries was not altered by bradykinin.

1. Huggins, C. G., Walaszek, E. J., Am. Heart J., 1960, v60, 976.

2. Burch, G. E., DePasquale, N. P., Am. Heart J., 1963, v65, 116.

3. ———, Circulation Res., 1962, v10, 105.

4. Furchgott, R. F., Methods in Med. Res., 1960, v8, 177.

5. Siegmund, O. H., Merck Veterinary Manual, ed. 2. Rahway, N. J., Merck & Co., 1961, p1441.

6. Burch, G. E., Lazzara, R. K., Yun, T. K., Proc. Soc. Exp. Biol. & Med., 1965, v118, 581.

7. MacIntyre, I., Adv. Clin. Chem., 1961, v4, 1.

Received March 3, 1967. P.S.E.B.M., 1967, v125.