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THE DIRECT ACTION

OF

CALCIUM, SODIUM, POTASSIUM, AND AMMONIUM SALTS ON THE BLOODVESSELS.

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THE experiments of Ringer on the influence of certain calcium and potassium salts on the contractility of the frog's ventricle, have attracted well-deserved attention from the profession.

In the several papers published in the *Journal of Physiology*, he has shown that very minute quantities of potassium and calcium salts possess the power of greatly modifying the contractility of the heart. He pointed out that even so minute a quantity of potassium chloride as 1 in 15,000, and of calcium chloride as 1 in 10,000, is capable of promoting the normal cardiac contractility, provided they are brought in contact with the ventricle in the presence of a three-quarter per cent. saline medium.

Ringer, while not attempting to explain how such minute quantities of inorganic salts can influence so profoundly the organized structures of the heart, thinks it not improbable that the salts do not enter into direct combination with the molecules of the muscular tissue, or, if any combination does take place, that it is of an extremely loose character, since the salts are easily dislodged and washed away by the mere circulation of a fluid devoid of these salts.

Kronecker, and some of his pupils, find that if a ventricle is fed with a 0.6 per cent. normal saline solution, contractility soon ceases, and a strong induction-shock will not excite contractions. They conclude that the suspension of contractility depends on the saline solution washing out all the nutritive material from the cavities of the heart and the meshes of its spongy substance.

Merunowicz (quoted by Ringer) found that the dissolved ash of incinerated blood furnishes a good fluid for supporting the heart's contractility, and Gaule concluded that the essential agent in the ash which sustains the contractility is an alkaline carbonate. Gaule also found that the addition of an alkaline sodium salt, even in small quantity, to saline solution, enables it to sustain contractility longer than when simple saline solution is used.

Gaule, therefore, differs from Kronecker, and maintains that the heart can feed on its own tissues, and derive from them all the materials necessary for a contraction. Kronecker, on the other hand, insists that the frog's heart does not feed on its own substance, and that as soon as nutritive fluid is withdrawn its contractility ceases.

We think that Ringer has shown conclusively that certain alkaline salts will prolong the contractility of the heart, and calcium salts prolong it more than sodium salts. Ringer very correctly observed that the character of the contractions underwent much alteration under the influence of these salts, but that the addition to the circulating fluid of a physiological quantity of a potassium salt entirely obviated these alterations, adding greatly to the duration of the contractility. It was found that while calcium salts promoted the contractility, potassium salts favored the relaxation of the ventricle.

Thus, by adding to normal saline solution certain small quantities of bicarbonate of sodium, chloride of potassium, and chloride of calcium, Ringer finally succeeded in obtaining a circulating medium by means of which normal contractility could be maintained for hours.

On looking over the literature of the subject, I found that very little indeed had been done to ascertain the nature of the action of these salts on the vascular system. The interest and importance which attaches to the results of Ringer's experiments on the heart made it appear very desirable that something more should be done with a view of ascertaining the exact influence of these salts on the vascular system.

With this object in view, the experiments which follow were made.

On account of the great scarcity of frogs in midwinter these experiments were all made with terrapins. My method consisted in cutting out the heart and inserting canulas into the aortic trunks, and one canula into the sinus. The aortic canulas were connected with Mariotte's flasks, placed at a certain height above the body of the animal, from which flasks liquid was made to flow into the arteries. This liquid, after circulating through the capillaries and veins, was drained off from the sinus into a beaker, and measured at definite intervals. After this outflow had become constant, circulating fluid, plus the drug, was substituted for the normal circulating fluid, and the action of the drug on the vessels determined from the change which took place in the amount of the outflow in a unit of time. A decreased outflow indicated increased resistance to the flow of the fluid through the vessels, or, in other words, a constriction of them, and an increased outflow, a dilatation of them.

In most of my published experiments on the action of drugs on the heart and bloodvessels, I made use of a circulating fluid which I termed "Ringer's saline," on account of his having first proposed it as a good substitute for the normal salt solution wherever the use of the latter might be indicated. As a diluent for mammalian blood to be used in experiments on the isolated heart of cold-blooded animals, it certainly was found to surpass by far the ordinary seventy-five one-hundredths per cent. salt solution in keeping the heart active and alive to the action of drugs as well as to other influences.

But in experimenting with different alkaline salts on the bloodvessels, I was naturally obliged to fall back upon normal salt solution as the standard, and, therefore, the first experiments were made with a view of ascertaining the influence on the bloodvessels of Ringer's saline as compared with that of normal salt solution.

EXPERIMENT XLI.—March 23, 1886. Terrapin 1250 grms. Inflow canulas in right and left arterial trunks. Outflow canula in sinus. Arterial pressure 18 c.m. Venous pressure 0. Circulating fluids: Ringer's saline and normal salt solution (0.75 per cent.).

Time P. M. from	to	Temp. Cent.	Total outflow	Outflow per min.	Circulating fluids were supplied to the vessels at the time mentioned on same line in second column.
3.14	3.16	16°	49	24.5	On normal salt solution.
16	18	...	50	25	
18	20	...	49	24.5	
20	22	...	52	26	
22	24	16	52	26	
24	26	...	52	26	On Ringer's saline.
26	28	...	53	26.5	
28	30	...	52	26	
30	32	16	26	13	
32	34	...	30	15	
34	36	...	30	15	

Time P. M. from	to	Temp. Cent.	Total outflow.	Outflow per min.	Circulating fluids were supplied to the vessels at the time mentioned on same line in second column.
36	38	...	32	16	
38	40	16	30	15	
40	42	...	29	14.5	On normal salt solution.
42	44	...	20	10	
44	46	...	24	12	
46	48	16	26	13	
48	50	...	26	13	
50	52	...	28	14	
52	54	...	30	15	
54	56	16	32	16	
56	58	...	35	17.5	
58	4.00	...	37	18.5	
4.00	02	...	38	19	
02	04	...	38	19	
04	06	...	40	20	
06	08	16	40	20	On Ringer's saline.
08	10	...	35	17.5	
10	12	...	30	15	
12	14	...	21	10.5	
14	17	16	31	10.3	
17	19	...	21	10.5	
19	21	...	21	10.5	
21	23	...	20	10	
23	25	16	18	9	On normal salt solution.
25	27	...	16	8	
27	29	...	19	9.5	
29	31	...	22	11	
31	33	16	25	12.5	
33	35	...	30	15	
35	37	...	32	16	
37	39	...	34	17	
39	41	16	38	19	
41	43	...	40	20	
43	45	...	42	21	Ended.

Experiment XLI. is one out of the three experiments made with regard to the influence of Ringer's saline on the bloodvessels as compared with that of normal salt solution. They all show very clearly that Ringer's saline possesses over normal salt solution the power of greatly contracting the bloodvessels. This contraction, as shown in this experiment, takes place gradually, but the dilatation which follows the re-admission of normal salt solution is very slow.

The composition of this fluid is as follows:

Normal salt solution . . .	(0.75 per cent.)	100	c. c.
Calcium chloride solution .	(1 : 390)	5	"
Sodium bicarbonate solution	(0.50 per cent.)	2.5	"
Potassium chloride solution	(1.0 per cent.)	0.75	"

Mix and filter.

The question naturally arose as to which one of the different constituents of this fluid gave rise to the contraction of the vessels. Several experiments were made with regard to this point, but Experiment XLII. will suffice to show that it was the chloride of calcium. As indicated in the heading, three different circulating fluids were made use of: First, normal salt solution; second, normal salt solution to which had been added potassium chloride in the exact proportion in which this was contained in Ringer's saline; third, Ringer's saline, the potassium chloride left out. Potassium chloride, therefore, was used in extremely small quantities, the solution containing less than 1 : 10,000.

This experiment shows very clearly that normal salt solution and potassium chloride give rise to great dilatation of the bloodvessels, while, on the other hand, Ringer's saline without potassium chloride causes their contraction. As may be seen in the experiment, the vessels, contracted by Ringer's saline minus potassium chloride, are gradually dilated by normal salt solution, and this dilatation is still further increased upon the admission of normal salt solution plus potassium chloride. Ringer's saline now re-admitted, within a very few minutes may be noticed to reduce the quantity of the outflow to one-third its former amount, therefore, also reducing the calibre of the vessels in about the same proportion ; normal salt solution reëstablished the normal calibre of these vessels, while potassium chloride, again, caused them to dilate.

From this and other experiments, all concordant, it is plain that everything pointed to the chloride of calcium as being the cause of the contraction of the vessels, and, at the same time, to the potassium chloride as causing their dilatation. Both having been used in the same proportion in which they are contained in Ringer's saline—that is, in very minute quantities—we may conclude (1) that calcium chloride, even in very small doses, gives rise to contraction, and potassium chloride in equally minute doses to dilatation of the bloodvessels in the terrapin.

EXPERIMENT XLII.—March 24, 1886. Terrapin 990 grms. Inflow canulas in right and left arterial trunks. Outflow canula in sinus. Arterial pressure 18 c.m. Venous pressure 0. Circulating fluids: (*a*) normal salt solution, (*b*) normal salt solution + potassium chloride, (*c*) Ringer's saline —potassium chloride.

Time P. M. from	Time P. M. to	Temp. Cent.	Total outflow.	Outflow per min.	The circulating fluids were supplied to the vessels at the time mentioned on the same line in the second column.
3.07	3.09	16°	28	14	Normal salt solution(*a*).
09	11	...	30	15	
11	13	...	30	15	
13	15	16	29	14.5	
15	17	...	31	15.5	Normal salt solution + potassium chloride(*c*).
17	19	...	35	17.5	
19	21	...	48	24	
21	23	16	48	24	
23	25	...	50	25	
25	27	...	45	22.5	
27	29	...	35	17.5	
29	31	16	31	15.5	
31	33	...	30	15	
33	35	...	32	16	

Time from	P. M. to	Temp. Cent.	Total outflow	Outflow per min.	The circulating fluids were supplied to the vessels at the time mentioned on the same line in the second column.
35	37	...	32	16	On normal salt solution(*a*).
37	39	16	36	18	
39	41	...	40	20	
41	43	...	42	21	
43	45	...	47	23.5	
45	47	16	46	23	
47	49	...	48	24	
49	51	...	48	24	
51	53	...	48	24	On normal salt solution +
53	55	16	52	26	[potassium chloride(*c*).
55	57	...	62	31	
57	59	...	62	31	
59	4.01	...	63	31.5	
4.01	03	...	67	33.5	On Ringer's saline — potas-
03	06	16.5	76	25.3	[sium chloride(*b*).
06	08	...	36	18	
08	10	...	24	12	
10	12	...	22	11	
12	14	...	23	11.5	
14	16	16.5	23	11.5	
16	18	...	22	11	On normal salt solution(*a*).
18	20	...	26	13	
20	22	...	30	15	
22	24	...	32	16	
24	26	16.5	30	15	
26	28	...	31	15.5	On normal salt solution +
28	30	...	36	18	[potassium chloride(*c*).
30	32	...	42	21	
32	34	16.5	48	24	
34	36	...	54	27	[slight œdema.
36	38	...	60	30	Observations discontinued;

In order to test still further the action of lime salts on the vessels, a saturated solution of sulphate of lime was made, and the solution converted into normal salt solution by simply adding the required amount of chloride of sodium. In addition, a solution of bromide of potassium was made containing one gramme of the bromide in 3000 cubic centimetres of normal saline solution. Several observations were made with the solution of bromide of potassium, but since they were all concordant, one will here suffice to show the effect it produces on the vessels.

Experiment XLV. clearly shows the influence of both calcium and potassium salts on the vessels in larger doses than had been used in previous experiments. It was found that under sulphate of lime the quantity of the outflow was gradually diminished to about one-fifth normal, and that, therefore, the calibre of the vessels must have become reduced in about the same proportions. Bromide of potassium, on the other hand, gave rise to an increased outflow, hence must have dilated the vessels.

The conclusions, therefore, are obvious, namely, calcium salts, in comparatively large doses, cause contraction, and potassium salts, in medium doses, cause dilatation of the bloodvessels, in the case of the terrapin.

EXPERIMENT XLV.—March 27, 1886. Terrapin 460 grms. Inflow canulas in right and left aortic trunks. Outflow canula in sinus. Arterial pressure 16 c.m. Venous pressure 0. Circulating fluids: normal salt solution, saturated solution of calcium sulphate made into normal salt solution (0.75 per cent.), normal salt solution and bromide of potassium 3000 c. c. : 1.

Time P. M. from	to	Temp Cent.	Total outflow.	Outflow per min.	
3.06	3.08	16°	28	14	Normal salt solution.
08	10	...	28	14	
10	12	...	29	14.5	
12	14	...	28	14	
14	16	...	29	14.5	On calcium sulphate solution
16	18	16	24	12	
18	20	...	21	10.5	
20	22	...	14	7	
22	24	...	8	4	On normal salt solution.
24	26	...	7	3.5	
26	28	...	7	3.5	
28	31	16	12	4	
31	33	...	12.5	6.2	
33	36	...	31	10.3	

Time P. M. from	to	Temp Cent.	Total outflow.	Outflow per min.	
36	38	...	23	11.5	
38	40	...	27	13.5	
40	42	...	28	14	On calcium sulphate solution.
42	44	16	26	13	
44	46	...	21	10.5	
46	48	...	13	6.5	
48	50	...	11	5.5	On normal salt solution.
50	53	...	13	4.3	
53	55	...	8	4	
55	57	...	11	5.5	
57	59	...	13	6.5	
59	4.01	...	15	7.5	
4.01	03	...	18	9	
03	05	...	20	10	
05	08	...	31	10.3	
08	10	...	24	12	
10	12	...	25	12.5	On solution of bromide of
12	15	...	39	13	[potassium.
15	17	...	28	14	
17	20	...	46	15.3	
20	22	...	35	17.5	
22	24	...	36	18	
24	26	...	41	20.5	[considerable œdema.
26	28	...	48	24	Observations discontinued;

EXPERIMENT L.—April 1, 1886. Terrapin 1205 grms. Inflow canulas in right and left aortic trunks. Outflow canula in sinus. Venous pressure 0. Arterial pressure 14 c.m. Circulating fluids: Normal salt solution, solution of sodium iodide in normal salt solution 1 : 1000, solution of sodium bromide in same proportion.

Time P. M. from	to	Temp Cent.	Total outflow.	Outflow per min.	Circulating fluids were supplied to the vessels at the time mentioned on the same line in the second column
2.55	2.57	18°	18	9	On normal salt solution.
57	59	...	18	9	
59	3.01	...	18	9	
3.01	03	...	18	9	
03	05	18	19	9.5	
05	07	...	18	9	On sodium iodide solution.
07	09	...	20	10	
09	11	...	26	13	
11	13	...	32	16	
13	15	18	24	12	
15	17	...	16	8	
17	19	...	10	5	On normal salt solution.
19	21	...	8	4	
21	23	...	10	5	
23	25	18	15	7.5	
25	27	...	14	7	
27	29	...	14	7	
29	31	...	14	7	
31	33	...	14	7	
33	35	18	14	7	On sodium iodide solution.
35	37	...	15	7.5	
37	39	...	16	8	
39	41	...	16		
41	43	...	18		
43	45	...	22		
45	47	18.5	26	...	On normal salt solution.
47	49	...	14		
49	51	...	13		
51	53	...	18		
53	55	...	19		
55	57	18.5	18	...	On sodium bromide solution.
57	59	...	18		
59	4.01	...	18		
4.01	03	...	32		
03	05	...	36		
05	07	18 5	34		
07	09	...	24		
09	11	...	20		
11	13	...	12		
13	15	...	10	...	On normal salt solution.
15	17	...	12		
17	19	18 5	15		
19	21	...	15		
21	23	...	14		
23	25	...	14	...	On sodium bromide solution.

Time P. M. from	to	Temp. Cent.	Total outflow.	Outflow per min.	Circulating fluids were supplied to the vessels at the time mentioned on the same line in the second column
25	27	...	15		
27	29	18.5	22		
29	31	...	28		
31	33	...	33		
33	35	...	38		
35	37	18 5	28		
37	39	...	24	...	On sodium iodide solution.
39	41	...	20		
41	43	...	15		
43	45	...	13		
45	47	...	10		
47	49	18.5	11		
49	51	...	10		
51	53	...	9		
53	55	...	9	...	On normal salt solution.
55	57	...	5.5		
57	59	...	6		
59	5.03	...	16		
5.03	07	...	26		
07	09	...	12		
09	11	...	14		
11	13	...	14		
13	15	19	15	...	Observations discontinued.

The observations recorded in Experiment L. show that bromide and iodide of sodium in large doses give rise to dilatation of the bloodvessels, which dilatation is followed by contraction of the same. The same result was obtained when these salts were used in the proportion of 1 : 5000, with the exception that the dilatation produced lasted longer, and the contraction came on much later, and was much more gradual. Sodium salts, therefore, differ materially from those of calcium and potassium in their effects upon the bloodvessels.

Experiment XLVII. — March 30, 1886. Terrapin 1370 grms. Inflow canulas in right and left aortic trunks. Outflow canula in sinus. Arterial pressure 16 c. m. Venous pressure 0. Circulating fluids: Normal salt solution, sodium bicarbonate in normal salt solution 1 : 1000, potassium iodide in normal salt solution 1 : 1500.

Time P. M. from	to	Temp. Cent.	Total outflow.	Outflow per min.	
2.40	2.42	16°	20	10	On normal salt solution.
42	44	...	20	10	
44	46	...	20	10	
46	48	...	21	10.5	
48	50	...	22	11	On sodium bicarbonate solu-
50	52	16	24	12	[tion.
52	54	...	28	14	
54	56	...	35	17.5	
56	58	...	41	20.5	On normal salt solution
58	3 00	...	33	16.5	
3 00	02	16	24	12	
02	04	...	24	12	On sodium bicarbonate solu-
04	07	...	40	13.3	[tion.
07	09	...	32	16	
09	11	16	28	14	
11	13	...	22	11	
13	15	...	20	10	
15	17	...	16	8	
17	20	...	18	6	
20	23	...	12	4	On normal salt solution.
23	26	...	14	4.6	
26	28	16	11	5.5	
28	30	...	14	7	
30	32	...	16	8	On potassium iodide solu-
32	34	...	16	8	[tion.
34	36	...	19	9.5	
36	38	16.5	21	10.5	
38	40	...	23	11.5	
40	42	...	24	12	
42	44	...	26	13	
44	46	...	28	14	
46	48	...	30	15	
48	50	16.5	35	17.5	
50	52	...	36	18	
52	54	...	40	20	On normal salt solution.
54	56	...	33	16.5	
56	58	...	29	14.5	
58	4.00	...	27	13.5	
4 00	02	17	20	10	
02	04	...	20	10	On potassium iodide solu-
04	06	...	24	12	[tion.
06	08	...	26	13	
08	10	...	29	14.5	
10	12	...	31	15.5	
12	14	...	33	16.5	
14	16	17	36	18	
16	18	...	42	21	[œdema.
18	20	...	48	24	Observations discontinued ;

Experiment XLVII. shows that bicarbonate of sodium, like bromide and iodide of sodium, causes dilatation of the bloodvessels, which dilatation is followed by a contraction; it shows, furthermore, that iodide of potassium, like chloride of potassium, gives rise to a dilatation of the bloodvessels, which dilatation, even when very large doses are used, is permanent, and at no time followed by contraction. We may, therefore, safely conclude that sodium salts give rise to dilatation followed by contraction of the bloodvessels, and that potassium salts, in large as well as small doses, always cause dilatation of the vessels.

In the next experiment the bromide of potassium was used in the proportion of 1 of the bromide to 3000 cubic centimetres of normal salt solution, or about half the strength of the potassium iodide solution used in previous experiments. The effect on the bloodvessels may be seen to be identical with that produced by the iodide, thus showing that it is not due to the iodine or bromine in combination with potassium, but rather to the potassium part of these salts. This may also be inferred from the fact that the chloride of potassium, too, produces the same effect upon the bloodvessels, namely, it causes their dilatation in small as well as large doses.

In connection with the dilatation of the vessels produced by potassium salts, considerable œdema was invariably noticed; this was absent in experiments with calcium and sodium salts.

Experiment XLIV.—March 26, 1886. Terrapin 650 grms. Inflow canulas in right and left aortic trunks. Outflow canula in sinus. Arterial pressure 18 c.m. Venous pressure 0. Circulating fluids: Normal salt solution, solution of potassium bromide 1 in normal salt solution 3000.

Time P. M. from	to	Temp. Cent.	Total outflow.	Outflow per min.	
3.08	3.10	18°	11	5.5	Normal salt solution.
10	12	...	11	5.5	
12	14	...	10	5	
14	16	...	10	5	
16	18	...	12	6	
18	20	...	12	6	
20	24	18	24	6	On potassium bromide solu-
24	26	...	14	7	[tion.
26	28	...	17	8.5	
28	30	...	18	9	
30	32	...	24	12	
32	34	...	30	15	On normal salt solution.
34	36	18	18	9	
36	38	...	16	8	
38	40	...	11	5.5	
40	42	...	11	5.5	On potassium bromide solu-
42	44	...	13	6.5	[tion.
44	46	...	17	8.5	
46	48	18	24	12	
48	50	...	30	15	On normal salt solution.
50	52	...	24	12	
52	54	...	13	6.5	
54	56	...	9	4.5	
56	58	...	9	4.5	
58	4.00	...	10	5	
4.00	02	...	10	5	On potassium bromide solu-
02	04	...	12	6	[tion.
04	06	...	15	7.5	
06	08	...	18	9	
08	10	...	23	11.5	
10	12	...	29	14.5	On normal salt solution.
12	14	...	16	8	
14	16	...	14	7	
16	18	...	10	5	
18	20	...	9	4.5	
20	22	...	8	4	
22	24	...	9	4.5	[great œdema.
24	26	19	10	5	Observations discontinued;

Experiment XLVIII. has been selected from three experiments made with ammonium salts on the bloodvessels, because it represents in a typical manner what took place in all, namely, great dilatation followed by slight contraction; the latter, though rarely observed as coming on during the time the ammonium salt solution is in the bloodvessels, must nevertheless be looked upon as an effect of ammonium salts, for the vessels ultimately recover their normal calibre under the influence of normal salt solution. Hence, the salts of ammonium resemble those of sodium in their effects on the bloodvessels.

EXPERIMENT XLVIII.—March 31, 1886. Terrapin 1210 grms. Inflow canulas in right and left arterial trunks. Outflow canula in sinus. Arterial pressure 12 c.m. Venous pressure 0. Circulating fluids: Normal salt solution—chloride and bromide of ammonium in normal salt solution, each in the proportion of 1 : 1000.

Time P. M. from	to	Temp. Cent.	Total outflow.	Outflow per min.	
2.55	2.57	16°	30	15	Normal salt solution.
57	59	...	30	15	
59	3.01	...	31	15.5	
3.01	03	...	30	15	
03	05	...	30	15	
05	07	...	29	14.5	
07	09	16	29	14.5	On ammonium chloride solution.
09	11	...	29	14.5	
11	13	...	37	18.5	
13	15	...	42	21	
15	17	...	48	24	On normal salt solution.
17	19	...	38	19	
19	21	...	18	9	
21	23	...	20	10	
23	25	...	25	12.5	
25	27	16	30	15	
27	29	...	30	15	
29	31	...	32	16	On ammonium chloride solution.
31	33	...	40	20	
33	35	...	59	29.5	
35	37	...	74	37	On normal salt solution.
37	39	...	61	30.5	
39	41	...	45	22.5	
41	43	...	42	21	
43	45	...	41	20.5	
45	47	...	42	21	
47	49	...	41	20.5	On ammonium bromide.

Time P. M. from	to	Temp. Cent.	Total outflow	Outflow per min.	
49	51	...	46	23	
51	53	...	66	33	
53	55	...	78	39	On normal salt solution.
55	57	...	60	30	
57	59	...	55	27.5	
59	4.01	...	50	25	
4.01	03	...	38	19	
03	05	...	28	14	
05	07	..	36	18	
07	09	...	35	17.5	On ammonium bromide.
09	11	...	45	22.5	
11	13	...	90	45	On normal salt solution.
13	15	...	73	37.5	
15	17	...	58	29	
17	19	...	52	26	
19	21	...	48	24	
21	23	...	41	20.5	[no œdema.
23	25	...	41	20.5	Observations discontinued:

The amount of chloride and bromide of ammonium used in this experiment was larger than that used in the remainder of them. The effect, however remained the same. The dilatation produced by ammonium salts, in large or small doses, is prompt and extensive.

With the exception of Ringer's experiments, referred to above, very little indeed is found in literature on the physiological characteristics of calcium salts. The same may be said of the salts of sodium so far as their effect on the circulatory apparatus is concerned.

Potassium salts have been found to cause death by heart-paralysis, being both nerve and muscle poisons. The primary effect of the potassium salts on the circulation is said to be a transient decrease in blood-pressure, together with a slowing of the pulse-rate, but a rise in pressure and an increase in the rate quickly follow. The rate, however, again begins to go down while the pressure may still be on the rise.

Finally, large doses have been found to cause immediate and permanent lowering of blood-pressure, as well as slowing of the pulse-rate, which may culminate in diastolic arrest.

Drs. Lauder Brunton and Cash, in their experiments with potassium salts on the bloodvessels, found that potassium chloride gave rise to great contraction, which exceeded even that produced by calcium and strontium salts. This certainly is not the *direct* action of these salts in the case of the terrapin.

The salts of potassium, as is well known, are frequently employed by practitioners in combination with digitalis for the diuretic effects which they produce. If, now, they did produce dilatation of the renal vessels in man as they do in the terrapin, which, I think, is more than probable from the foregoing experiments, their combination with cardiac tonics like, for instance, digitalis, would certainly go far to explain their salutary diuretic effects which they are known to produce in dropsies of all kinds.

According to Funke and Deahne, the salts of ammonium cause temporary contraction of the bloodvessels owing to their stimulating influence upon the vasomotor centres in both brain and spinal cord; the same authors also state that these salts possess a stimulating influence on the inhibitory centre in the brain, thereby causing slowing in the pulse-rate, in larger doses, diastolic cardiac arrest.

In conclusion, we offer the following explanations for the phenomena observed in the foregoing experiments:

1. Calcium salts cause the vessels to contract by virtue of their stimulating influence on the vasomotor ganglia.

2. Sodium and ammonium salts excite, first, the ganglia of the vasodilators; next, those of the vasomotors; hence producing at first dilatation, and afterward contraction of the vessels.

3. Potassium salts stimulate the ganglia of the vasodilators only, and consequently produce dilatation; if, however, as was shown in two observations, the dilatation which they produce is followed by contraction, this contraction is so extremely slight that it may practically be neglected; therefore, any stimulating influence on the vasomotor ganglia which they might possess is insignificant when compared with that which they exert over the vasodilators.