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INFLUENCE OF THE AORTIC AND CAROTID SINUS NERVES UPON THE HEIGHT AND FORM OF THE RISE OF BLOOD-PRESSURE PRODUCED BY PERIPHERAL STIMULATION OF THE SPLANCHNIC NERVE.

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THE experimental work of H. E. Hering [1927*a*] and collaborators [Koch, 1929*a*] has proved conclusively that the aortic[2] and carotid sinus nerves together represent the centripetal path of a reflex self-regulating mechanism of the aortic pressure, and that a controlling action upon variations of blood-pressure is exerted by cardiac and vascular reflexes originating in the special pressure receptors of these nerves [Hering, 1927*d*].

Nevertheless, the experimental demonstration of the blood-pressure regulating rôle of the sinus and aortic nerves has been based until now on methods which consist essentially in varying locally the pressure in the carotid sinus [Hering, 1927*a*, 1929; Heymans, 1929*a*]. Experiments have been lacking to show that the aortic and carotid sinus nerves come into play when physiological variations of the general blood-pressure take place in the organism.

A convenient method for producing a rise in the general blood-pressure is to stimulate the peripheral end of the splanchnic nerve. The vaso-pressor effect thus produced may be regarded as normal. The resulting increase in peripheral resistance takes place in a vascular territory totally independent of that in which the sinus nerves are located. Thus by stimulating the peripheral end of the splanchnic nerves by a constant faradic stimulus under similar conditions, first with the aortic and carotid sinus nerves intact and then with the nerves eliminated, results were obtained which not only confirmed the controlling function

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[2] The name "depressor nerve" was enough to designate the centripetal nerves running from the aorta, as long as no other centripetal path for depressor cardio-vascular reflexes was known. But since the sinus nerves were shown to have the same functions, it is better to revert to the older name of "aortic" nerves [Hering, 1927*a*; Schumacher, 1902].

of these nerves but gave a more detailed picture of this control under physiological conditions.

METHODS.

Ten 2·5–3·7 kg. rabbits; four 3·6–3·8 kg. hares; four 5·0–18·5 kg. dogs and five 3·2–4·0 kg. cats were used for these experiments.

About half an hour before the beginning of the experiments with rabbits, hares and dogs urethane and morphine hydrochloride were subcutaneously injected. (Rabbits, 0·35–0·55 cg. morphine and 0·35–0·55 g. urethane per kg. body weight; hares, 0·54–0·84 cg. morphine and 0·40–0·55 g. urethane per kg.; dogs, 0·5–1·0 cg. morphine and 0·27–0·30 g. urethane per kg.) With cats urethane alone was injected (0·70–1·25 g. per kg. of body weight).

To eliminate the influence of muscular movements and to obtain more regular curves curaril (rabbits 0·54–0·80 c.c., and dogs 0·27–0·32 c.c. of the original solution per kg. of body weight[1]) was administered in a few instances, and the animals artificially ventilated. This obviated the prolonged arrest of the respiratory movements which is often seen, especially in the dog, after stimulating the sinus nerves. Hyper-ventilation, which is known to depress the vasomotor centre [Henderson and Haggard, 1918], was also avoided.

The animals were kept warm by an electric heating pad. The preparation consisted usually of the following steps: Longitudinal medial incision in the neck in order to put cannulas in the trachea and in the external maxillary vein; isolation of both vagi, in special cases the aortic and sinus nerves, and, in all, isolation of both common carotids, around which loops of thread were passed by means of which they could be easily lifted and clamped. One of the splanchnic nerves (usually the left) and, in a few cases, both right and left were prepared extra-peritoneally by a procedure which was essentially the same as that described by the earlier investigators [Asp, 1867] and in recent books [Sherrington, 1919]. The nerves were severed and their peripheral ends placed on platinum-shielded electrodes, similar to those described by Samojloff [1925]. The electrode with the nerve was fixed in position by stitching it to the neighbouring muscles and, to prevent any escape of current to the surrounding tissues, it was packed around with dry gauze before sewing

[1] These doses of curaril are definitely smaller than those which paralyse the smaller arterioles, capillaries and small veins of the splanchnic area [Koch and Nordmann, 1928b].

together the edges of the wound. An inductorium with a 10,000 turns secondary coil, and an interrupter giving about 50 double oscillations per second, connected to a 4-volt accumulator, were used. The weakest stimulus was selected which gave a maximal blood-pressure effect (this generally occurred with coil distances between 12 and 8 cm.), and was continued until the blood-pressure curve had reached its maximum. As a routine the Hg manometer was connected with the right A. femoralis. In cases in which it was desired to follow the variation in heart-rate, a Hürtle's membrane tonometer registered simultaneously upon the smoked surface of a sliding kymograph (E. Hering). In a number of experiments the suprarenal glands were prepared: in dissecting them and arranging the loops of thread preparatory to tying them off, care was taken to see that no damage was done to the splanchnic fibres coursing close by [Gley and Quinquaud, 1918; Pearlman and Vincent, 1919]. To test this, the operation was performed before any other and a control curve of the effect of splanchnic stimulation was obtained before tying off the suprarenals.

RESULTS.

General remarks. The relation between the height reached by the rise of blood-pressure during stimulation of the peripheral end of the splanchnic nerve and the influence of the blood-pressure regulating nerves upon this rise has not yet been investigated.

Moreover, although the typical form of the curve has been the object of numerous investigations, no investigation has been made upon the influence of these nerves upon its general features. Since Johansson [1891], Bayliss and Starling [1899] and Lehndorff [1908], many experimenters have shown that the form of the blood-pressure curve produced by stimulation of the splanchnic nerve is characterized by a "step" or a "dip" which occurs shortly after the beginning of the rise, and breaks the smooth ascent of the curve.

For a long time this form has been considered as typical for the cat and the dog. It was denied later for the rabbit, and predicted that it would not be found in other species [Gley and Quinquaud, 1921], but finally it was reported to be more or less constant in different mammals in which it was investigated [Gley and Quinquaud, 1922; Vincent and Wright, 1924]. It appears that to register the "dip," attention must be paid to the conditions under which the experiments are carried out. The nature and the doses of the anæsthetic used must be carefully considered. In animals deeply anæsthetized or which have received excessive doses of morphine or curare the "dip" is not observed [Pearlman and Vincent, 1919; Vincent and Wright, 1924; McGuigan and Hyatt, 1919].

As far as my observations go, the "dip" in the curve varies both in its character and form, not only from animal to animal but also in the same animal. A more or less marked "dip" is seen most frequently (Figs. 1 A, 8 A to D). It may be, however, as Johansson showed [1891], only a simple "step." Nevertheless, wide variations of these two types are also found and the "dip" can be so slight as only to be represented by a notch (Figs. 2 B, 3 A and C) or, on the contrary, so exaggerated as to sink to (Fig. 7 A) or even below the initial level of pressure. In the four hares not only was the "dip" observed, but it was followed very constantly by a second depression (Figs. 4 and 5 B). Thus to judge upon and compare its experimental variations, all these gradations must be borne in mind.

The experiments reported in this paper show that both the height and the form of the blood-pressure curve resulting from splanchnic stimulation are very considerably modified by the aortic and carotid sinus nerves.

The following descriptions are typical of the variations observed in the curves from rabbits, hares and dogs. Results of the same type are obtained in the cat after suppression of the suprarenal glands, but when these glands are intact, as reported below, they are found to differ in several respects.

A. *Influence of the aortic and carotid sinus nerves together.*

(*a*) *Upon the height of the curve.* The existing evidence upon the functions of the aortic and sinus nerves suggests that the rises of blood-pressure following identical stimulations of the peripheral end of the

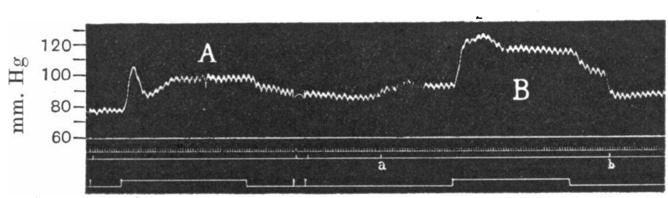

Fig. 1. Rabbit 5. Both suprarenals tied off and both splanchnic nerves severed. Stimulation of the peripheral end of the right splanchnic nerve (coil distance = 12). A. Both common carotids open. B. Both common carotids closed at *a* and re-opened at *b*. 1 second time intervals in this and other curves. The duration of stimulation is recorded at the bottom of the figures.

splanchnic nerve when both aortic and sinus nerves are intact would be smaller than those obtained after one or more of these nerves have been eliminated. The maximal differences were naturally to be expected between the conditions in which all the four blood-pressure regulating units are active and those in which all are eliminated. My observations which confirm this are tabulated in Table I.

TABLE I. Rise of blood-pressure produced by stimulating the splanchnic nerve before and after suppression of the aortic and carotid sinus nerves.

	Splanchnic nerve		Aortic and carotid sinus nerves intact				Aortic and carotid sinus nerves eliminated			
				Rise of pressure in mm. Hg				Rise of pressure in mm. Hg		
Animal	Sectioned	Side stimulated and coil distance in cm.	Time	From	To	Increase	Time	From	To	Increase
Rabbit 5	Both	R_{12}*	10.51	78	104	26	11.16	81	135	54
Rabbit 9	Both	R_8	11.12	46	66	20	11.46	98	147	49
Rabbit 15	Both	L_{12}	9.38	73	104	31	9.47	88	169	81
Hare 17	Left	L_{12}	10.21	116	153	37	10.32	179	296	117
Dog 12†	Left	L_{10}	11.4	126	143	17	12.46	169	256	87
Dog 22	Left	L_8	10.6	150	178	28	11.8	234	282	48
Cat 13	Left	L_{12}	10.39	122	149	27	12.15	153	194	41
Cat 25†	Left	L_{10}	10.5	161	190	29	10.39	163	215	52

* R = right splanchnic nerve. L = left splanchnic nerve. † Vagi also severed.

From inspection of this table it is seen that with two similar stimulations of the splanchnic peripheral end, the one made after the aortic and sinus nerves are eliminated brings about a rise of blood-pressure considerably greater than those obtained when all these nerves are intact.

(*b*) *Upon the form of the curve.* After suppressing the two aortic and the two sinus nerves the form of the curve is simpler (Figs. 4D, 5A and 7B) and without the slightest suspicion of a "dip."

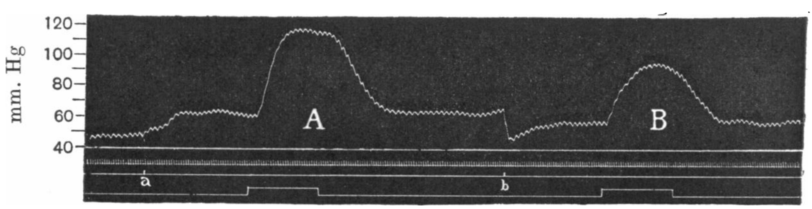

Fig. 2. Rabbit 7. Both suprarenal glands tied off and both splanchnic nerves severed. Stimulation of the left splanchnic nerve (coil distance = 6). A. Both common carotids closed at *a*. B. Both common carotids open at *b*.

Having thus observed the maximal variations, it was next determined what variations occurred when either the aortic or carotid sinus nerves were suppressed in turn leaving the other pair of nerves active.

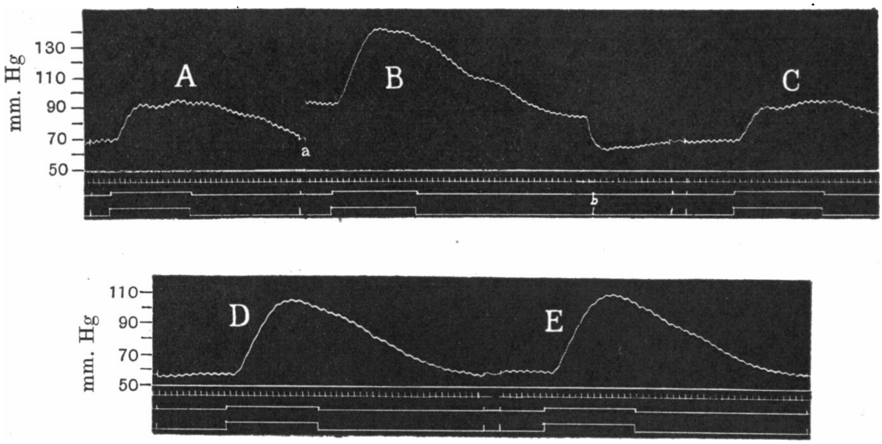

Fig. 3. Rabbit 9. Both splanchnic nerves severed and simultaneously stimulated (coil distance = 6). The three upper curves were taken after both aortic nerves were severed. A and C. Common carotids open. B. Common carotids closed. Between A and B carotids closed at *a* and 2 minutes' pause; at *b* carotids opened. Sinus nerves sectioned before taking the two lower records. D. Both carotids open. E. After they had been closed at the beginning of a 1·5 minutes' interval between the two curves.

B. *Influence of the aortic nerves alone.*

(*a*) *Upon the height of the curve.* A very simple method for suppressing the functions of the two carotid sinus nerves consists in merely clamping both common carotids, thus bringing the blood-pressure values in the carotid sinus below threshold. Under these conditions the two aortic nerves only are left active. Examples of the observed differences in the height reached by the splanchnic pressure curve when both carotid sinuses and aortic nerves or when only the later are active are given in Table II and Figs. 1, 2, 4 A, B and 6.

With the exception of the cases in the cat to which reference is made below, from inspection of the table it is seen that the rise of the splanchnic pressure curve is higher when only the two aortic nerves are in action than when the two sinus nerves are in action as well. The observation in dog 22, which is an exception, is to be explained by the high values reached by the blood-pressure after clamping the carotids, values so high that no further increase could be expected.

Attention must be drawn also to another result, obtained on several occasions, of which dog no. 20 is an example: stimulation of the splanchnic

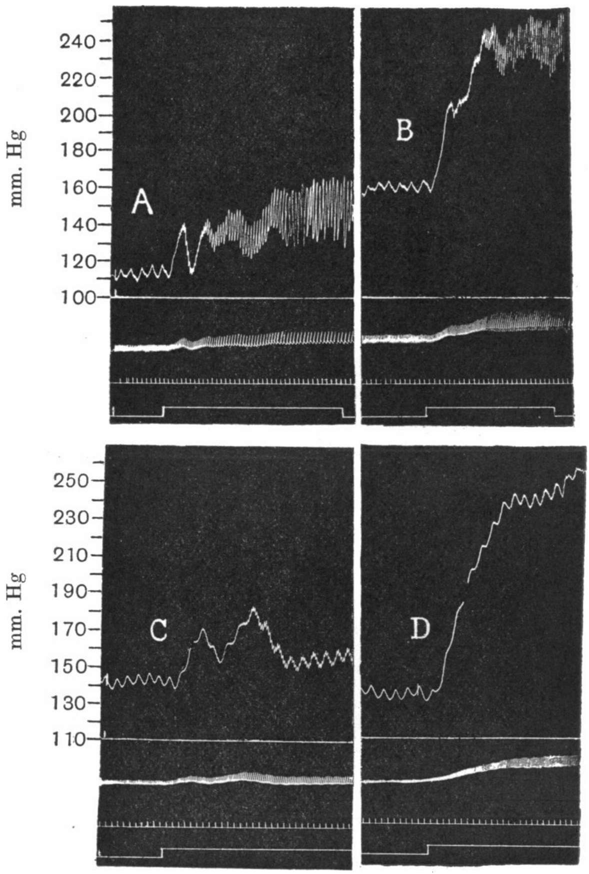

Fig. 4. Hare 17. Both splanchnics severed. Left stimulated (coil distance = 12). A. Both common carotids open. B. Both closed. Both aortic nerves then severed and the other two records taken. C. Both common carotids open. D. Both closed. Upper curve, Hg manometer; lower curve, Hürtle's membrane tonometer, in each case.

nerves was so ineffective in raising the blood-pressure (Fig. 6 A) that at first the correct position of the electrodes was questioned. That such was not the case was easily proved by clamping both common carotids, upon which, by repeating the same stimulation, the pressure definitely rose (Fig. 6 B). This clearly shows that the inhibitory influence of the aortic and carotid sinus nerves, and especially of the latter, upon the

Table II. Rise of blood-pressure produced by stimulating the splanchnic nerve when both aortic and carotid sinus nerves, or when only the aortic nerves are active.

	Splanchnic nerve		Aortic and carotid sinus nerves intact				Aortic nerves only active			
				Rise of pressure in mm. Hg				Rise of pressure in mm. Hg		
Animal	Sectioned	Side stimulated and coil distance in cm.	Time	From	To	Increase	Time	From	To	Increase
Rabbit 5	Both	R_{12}	10.51	78	104	26	10.53	90	124	34
Rabbit 7	Both	L_6	11.35	57	94	37	11.33	62	105	43
Rabbit 9	Both	R_8	11.12	46	66	20	11.20	47	78	31
Rabbit 15	Both	L_{12}	9.38	73	104	31	9.34	69	126	57
Hare 16	Left	L_{12}	10.27	132	169	37	10.36	162	254	92
Hare 16	Left	L_{12}	10.59	130	153	23	10.57	202	254	52
Hare 17	Left	L_{12}	10.12	112	152	40	10.15	156	236	80
Hare 17	Left	L_{12}	10.21	116	153	37	10.23	157	223	66
Dog 12	Left	L_{10}	11.4	126	143	17	11.2	153	194	41
Dog 20	Left	L_{10}	10.14	128	128	0	10.17	173	194	21
Dog 22	Left	L_8	10.6	150	178	28	10.8	224	243	19
Cat 13	Left	L_{12}	10.37	122	149	27	10.39	132	168	36
Cat 21	Left	L_{12}	9.50	170	197	27	9.52	197	224	27
Cat 25	Left	L_{10}	10.00	161	190	29	10.6	166	202	36
Cat 26	Left	L_{10}	10.38	151	176	25	10.35	151	192	41

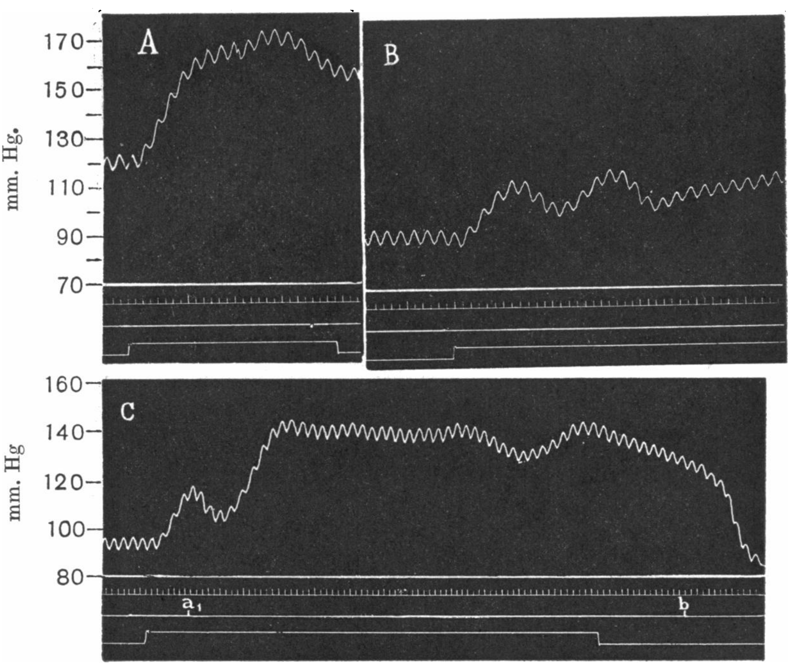

Fig. 5. Hare 10. Both splanchnic nerves severed. Both aortic nerves and right carotid sinus nerve severed (only left sinus nerve intact). Stimulation of the left splanchnic nerve (coil distance = 12). A. Left common carotid closed. B. Left common carotid open. C. Left common carotid closed. By unclosing it at a_1, shortly after the beginning of the stimulation, a definite "dip" is produced in the curve which otherwise would have risen as in A. 2 minutes' interval between A and B and C.

rise of pressure can be so strong that a stimulation of the splanchnic nerve fails to produce any appreciable rise in blood-pressure.

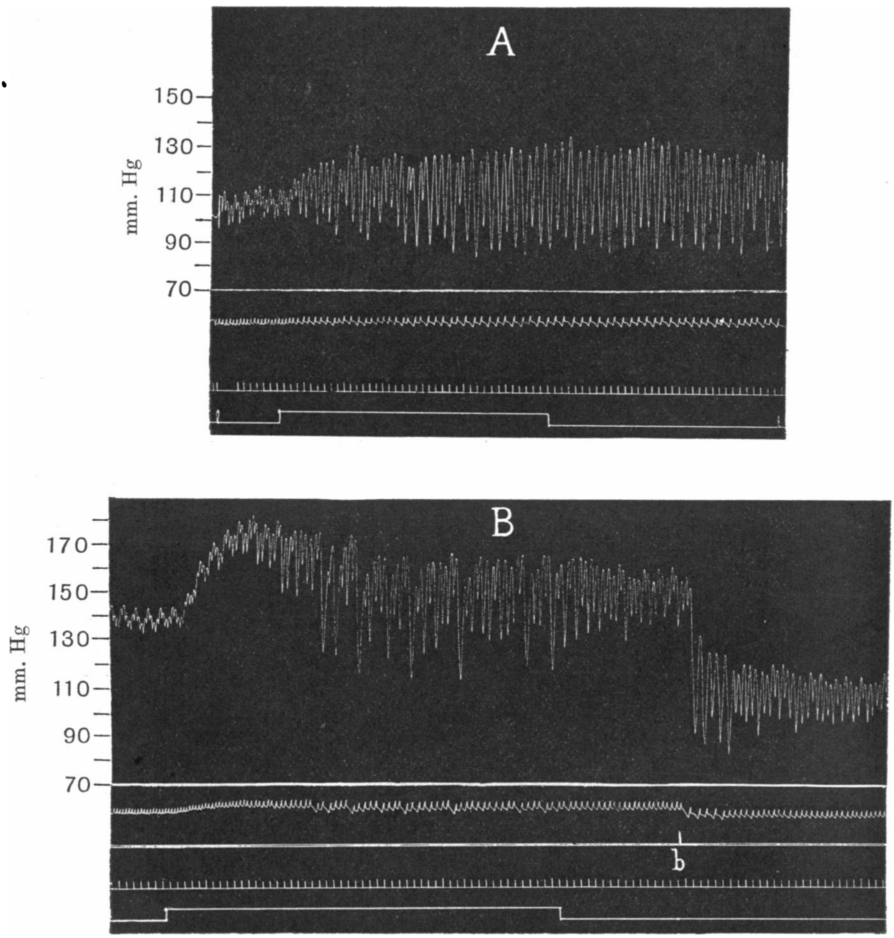

Fig. 6. Dog 18. Left splanchnic severed and stimulated (coil distance = 12). Aortic and sinus nerves intact. A. Both common carotids open. B. Both closed. At *b* both carotids opened. Between the A and B, 2 minutes' interval. Upper curve, Hg manometer; lower curve, Hürtle's membrane tonometer, in each case.

(*b*) *Upon the form of the curve.* If the form recorded by the rise of pressure when only the aortic nerves are active (both common carotids closed) is compared with another obtained only a few minutes before or afterwards when, in addition, both sinus nerves are also active, it is discovered that in the former condition the notch in the curve is usually much less pronounced and frequently has entirely disappeared (Figs. 3B, 4B), this coinciding with the greater steepness of the curve and its ascent to a higher level. In the hare, the double hump does not disappear but becomes much less obvious (Fig. 4B). Only in the cat the form of the curve remains practically unchanged (Figs. 8A, B).

In the cases in which the stimulation of the splanchnic nerve only produced a small rise of pressure as long as the aortic, sinus and vagus nerves fully exerted their functions, it was observed that as soon as the influence of the sinus nerves was removed, the "step" was but brief or unnoticeable (Figs. 6A, B) and followed by the second rise.

C. *Influence of the sinus nerves alone.*

(*a*) *Upon the height of the curve.* To test the action of the carotid sinus nerves alone, both aortic nerves were carefully prepared in the neck and severed. The result was, as shown by the measurements given in Table III, that the height reached by the splanchnic pressure curve

TABLE III. Rise of blood-pressure produced by stimulating the splanchnic nerve when both aortic and carotid sinus nerves were intact, when only the sinus nerves were active and when both the aortic and sinus nerves were suppressed.

	Splanchnic nerve		Aortic and carotid sinus nerves active				Carotid sinus nerves only active				Both aortic and carotid sinus nerves suppressed			
				Rise of pressure in mm. Hg				Rise of pressure in mm. Hg				Rise of pressure in mm. Hg		
Animal	Sectioned	Side stimulated and coil distance in cm.	Time	From	To	Increase	Time	From	To	Increase	Time	From	To	Increase
Rabbit 5	Both	R_8	10.51	78	104	26	11.11	70	108	38	11.16	81	135	54
Rabbit 9	Both	R_8	11.12	46	66	20	11.49	68	93	25	11.52	91	138	47
Rabbit 15	Both	L_{12}	9.38	73	104	31	10.6	65	106	41	10.9	78	162	84
Hare 17	Left	L_{12}	10.12	112	152	40	10.44	140	180	40	10.40	157	264	107
Cat 25	Left	L_{10}	10.5	133	185	52	10.55	102	137	35	10.39	163	215	52

is greater after section of the aortic nerves than when all the blood-pressure regulating nerves were intact. Again, it was observed in some experiments in which, prior to severing the aortic nerves, stimulation of the splanchnic nerve only produced slight rises of pressure, that immediately after the nerves were cut more or less conspicuous rises followed. By finally clamping both common carotids after the double section of the aortic nerves and again repeating the stimulation a final group of measurements was obtained, which, together with those secured before, made a comparison possible of the vaso-pressor responses with both aortic and sinus nerves intact, and when aortic and sinus nerves had been suppressed, one pair after the other. As will be appreciated from Table III, as the nerves are gradually eliminated the rise of blood-pressure becomes greater and greater.

The greater rises of pressure observed after closing both common carotids are not the result of the vaso-constriction produced by the stimulation of the splanchnic nerve acting upon a confined vascular bed. Table IV contains measurements of the rises observed after the aortic

TABLE IV. Rise of blood-pressure produced by stimulating the splanchnic nerve after both carotid sinus and aortic nerves had been severed.

	Splanchnic nerve		Both carotids opened				Both carotids closed			
				Rise of pressure in mm. Hg				Rise of pressure in mm. Hg		
Animal	Sectioned	Side stimulated and coil distance in cm.	Time	From	To	Increase	Time	From	To	Increase
Rabbit 9	Both	$Both_6$	12.23	58	103	45	12.55	59	108	49
Rabbit 9	Both	$Both_6$	12.28	55	99	44	12.30	55	100	·45
Dog 12	Left	L_8	13.54	122	176	54	13.56	149	205	56
Dog 22	Left	L_8	13.19	187	224	37	13.21	185	222	37

nerves were severed and the carotid sinus nerves eliminated by sectioning between ligatures the tissues in the angle between the external and internal carotids. It is seen that, under these conditions, closing the common carotids did not appreciably alter the height of the splanchnic pressure curve.

If the differences observed after elimination of both aortic nerves (Table II) are compared with those seen after suppression of the two sinus nerves (Table III), it is seen quite clearly that of the two pairs of nerves, the sinus nerves are those which exert the more important inhibitory effect. This fully corroborates earlier findings [E. Koch, 1929*c*] according to which the reflex vascular action of the carotid sinus nerves upon the blood-pressure is greater than the one exerted by the aortic nerves.

(*b*) *Upon the form of the curve.* Section of both aortic nerves does not appreciably modify the form of the curve as it may be seen in Figs. 3A and C, 4C, 7A and 8B. But if then the functions of the sinus nerves are suppressed by closing the two common carotids, as will be noticed in the corresponding section of the same figures, then the "dip" is more or less eliminated from the curve.

If the observations reported on the influence of the aortic and sinus nerves upon the form of the curve are compared with each other, it is clear that the more profound "dip" in the curve is the result of the action of the carotid sinus nerves, which agrees with findings from different animals showing that the reflex action of the

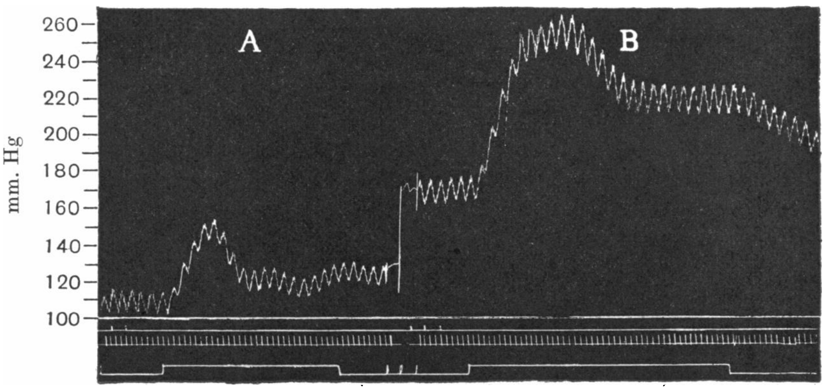

Fig. 7. Dog 12. Left splanchnic nerve severed and stimulated (coil distance = 8). Both vago-sympathetic trunks sectioned in the neck. Between A and B both common carotids closed and 2 minutes, interval.

carotid sinus nerves upon the blood-pressure is greater than that exerted by the aortic nerves [Koch, 1929*c*].

D. *Influence of a single carotid sinus nerve.*

(*a*) *Upon the height of the curve.* After sectioning both aortic nerves and one of the two carotid sinus nerves, it was possible to study the influence exerted by the remaining sinus nerve upon the rise of pressure evoked by the stimulation of the splanchnic nerve. Thus, in hare 10, with only the left sinus nerve remaining, two identical stimulations of the splanchnic nerve (coil distance = 6) gave the following rises of pressure:

At 12.18 when the left carotid was closed, from 111 to 182, *i.e.* 71 mm. Hg.
At 12.22 when the left carotid was open, from 93 to 127, *i.e.* 34 mm. Hg.

These results agree with the well-known observation that, after suppression of one or more blood-pressure regulating nerves, those which remain function more intensely [Hering, 1927*b*; Koch, 1929*b*].

(*b*) *Upon the form of the curve.* Even after double section of the aortic nerves and suppression of one of the carotid sinus nerves the blood-pressure curve is interrupted by the usual "dip" (Fig. 5B). But, if the remaining sinus is put out of action by closing the corresponding common carotid, then the "dip" disappears (Fig. 5A). This last result confirms once more the great influence that a single sinus nerve can exert upon the rise in blood-pressure.

E. *The part played by the cardiac and vascular reflexes.*

(*a*) *Upon the height of the curve.* It was observed that the rise of blood-pressure produced by stimulation of the peripheral end of the splanchnic nerve, especially in the dog and hare, more rarely in the rabbit and cat, was accompanied by a more or less pronounced slowing of the heart, which, as is well known, is the result of a reflex originating in the pressure receptors of the aortic and carotid sinus nerves. In the cases reported above, for example, the one seen in Fig. 6A, in which almost no rise of pressure followed the stimulation of the splanchnic nerve, the profound slowing of rhythm suggests that the cardiac reflexes co-operate with the vascular reflexes in reinforcing the "pressure depressing effect," following the stimulation of the splanchnic nerve. Therefore, to examine the part played by the cardiac and vascular reflexes respectively, the effects of the stimulation of the splanchnic nerve were also studied after suppressing the cardiac reflex.

In several experiments mere section of the aortic nerves was enough to suppress it, agreeing with already reported findings [Koch, 1929*c*] which indicate that the aortic nerves are a more important and effective path for provoking the reflex than the sinus nerves. In others both vagi were severed in the neck.

TABLE V. Rise of blood-pressure produced by stimulating the splanchnic nerve after section of the vagi when the carotid sinus nerves were in function, and when they were suppressed by closing both common carotids.

	Splanchnic nerve		Carotid sinus nerves only active				Carotid sinus nerves suppressed			
				Rise of pressure in mm. Hg				Rise of pressure in mm. Hg		
Animal	Sectioned	Side stimulated and coil distance in cm.	Time	From	To	Increase	Time	From	To	Increase
Rabbit 5	Both	R_{12}	12.47	43	79	36	12.48	47	111	64
Rabbit 14	Left	L_{12}	10.31	96	110	14	10.33	103	128	25
Dog 12	Left	L_{8-10}	12.32	109	131	22	12.33	169	258	89
Dog 18	Left	L_{10}	11.26	81	136	55	11.41	94	157	63
Cat 26	Left	L_{10}	11.26	85	99	14	11.22	104	137	33

From measurements given in Table V (see also Figs. 7, 8A and B) it is clear that after suppression of the two vagi, the quantitative differences in the height reached by the blood-pressure curve during stimulation of the peripheral splanchnic nerve remain fundamentally the same, *i.e.* they are mainly determined by the vascular reflexes, and especially by those which originate from the carotid sinus nerves.

It must be noted that, occasionally, after double section of the vagi or atropinization, the rise of pressure in the dog is still accompanied by a slight slowing of the heart rate, but this is thought to be due to a reflex decrease of tone of the cardio-sympathetic nerves.

(*b*) *Upon the form of the curve.* The form of the curve remains essentially unchanged after double section of the vagi (Figs. 7, 8A, C). That the typical form of the curve is independent of the integrity of the vagi has been reported by many other observers [Johansson, 1891; Lehndorff, 1908; Vincent and Wright, 1924; McGuigan and Hyatt, 1919; Elliott, 1912].

F. *Influence of the suprarenal glands.*

(*a*) *Upon the height of the curve.* When both suprarenal glands were extirpated at the beginning of the experiment and then the suppression of the different nerves carried out, the results in the rabbit, hare and dog remained exactly as described above. All measurements given in the tables for rabbits 5, 6 and 7 and for cat 26 were secured after both suprarenals had been tied off and are indistinguishable from those from animals in which the suprarenals had not been touched. The result confirms again the older evidence [Houssay, 1920; Gley and Quinquaud, 1913; Tournade and Chabrol, 1921] showing that vasoconstrictor and adreno-secretory fibres run independently from each other in the splanchnic nerve, although their functions are so intimately correlated that they have been considered as forming together a functional unit [Cannon, 1928].

In the same manner, when the suprarenal glands were prepared prior to the experiment but were not tied off until the aortic and sinus nerves had been severed, unless the nerve had been damaged, no appreciable change was noticed in the height reached by the rise of pressure. For example:

Rabbit 14. Both splanchnic nerves severed. Similar stimulation of the peripheral end of the left splanchnic nerve (coil distance = 12) gave:

At 10.12 when no experimental operation had been made yet, rise from 78 to 93, *i.e.* 15 mm. Hg.

At 10.56 after the right adrenal gland had been tied off, from 82 to 96, *i.e.* 14 mm. Hg.

At 11.26 after the left adrenal gland had been tied off, from 77 to 94, *i.e.* 17 mm. Hg.

In the cat with the two adrenals intact the observations just described are not constantly found, in fact the reverse is more frequently seen. Out of the five cats used only one conformed (no. 24) during the whole experiment with the findings from dogs, hares and rabbits, but in the other four the results of the stimulation of the splanchnic nerve were frankly of an opposite character, *i.e.* smaller rises took place when the carotid sinus nerves were out of function and only became greater after ipsilateral tying off of the suprarenal gland (in two of them) or after double section of the aortic nerves (in the other two).

As an example of the reversed reactions observed (to be compared with tables before) the following observation from cat 13 is given (0·75 g. urethane per kg. of body weight; left splanchnic nerve severed and its peripheral end stimulated; coil distance = 12):

	Rise of blood-pressure mm. Hg		
	From	To	Increase
Before any experimental operation was carried out:			
At 10.39 when both aortic and sinus nerves active	132	168	36
At 10.43 with only aortic nerves active (carotids closed)	122	149	27
At 11.22 after double section of the vagi and aortic nerves (only sinus nerves free for action)	102	145	43
At 11.27 when sinus nerves were in addition suppressed	162	192	30
After in addition both external carotids were tied and both sinus nerves severed:			
At 12.15 with both common carotids open	153	194	41
At 12.18 with both common carotids closed	177	199	22
After tying off the left suprarenal gland:			
At 12.33 with both carotids open	158	196	38
At 12.36 with both carotids closed	160	194	34

(*b*) *Upon the form of the curve.* In four rabbits and also in the hares in which the two adrenals were tied at the beginning of the experiment, the variations observed in the form of the curve when the aortic and carotid sinus nerves were sectioned afterwards did not differ appreciably from those reported above.

In the dog the results reported by Gley and Quinquaud [1918] and Anrep [1912] are conflicting; while the former investigators, although using a method which has been criticized [Cannon, 1919], reported that double adrenalectomy does not modify the form of the curve, according to the latter after elimination of only the suprarenal of the side stimulated the typical form of the curve is not seen any more. In the present experiments it was not thought necessary to eliminate the suprarenals in the dog, because by simple suppressing the aortic and sinus nerves the "dip" in the curve disappeared. In this respect the cat deviates still more from the other species. As Figs. 8A to D will show, suppression of the aortic and carotid sinus nerves, one after the other, did

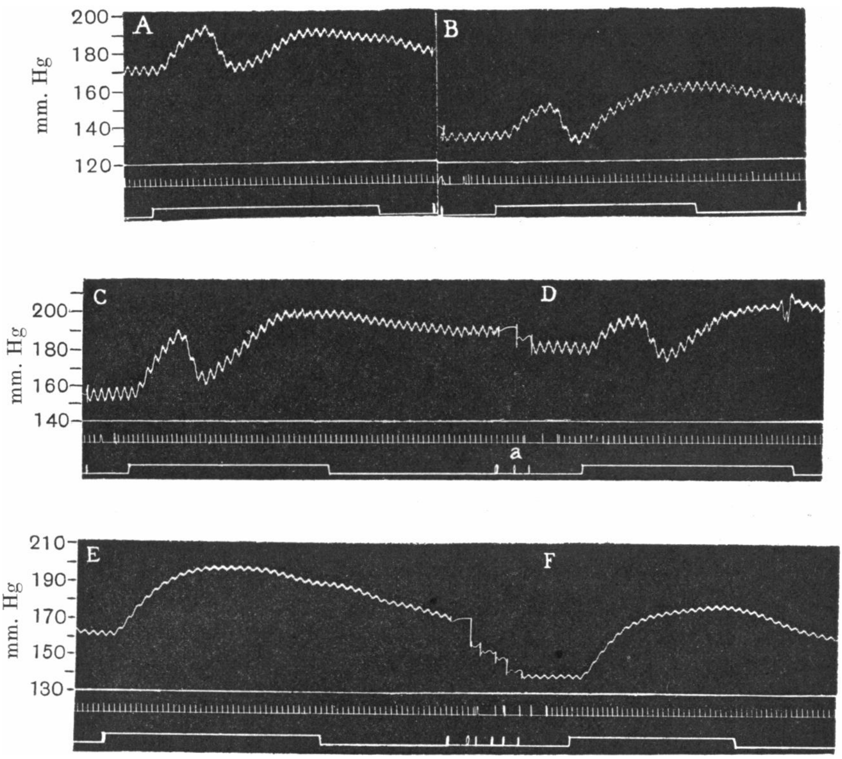

Fig. 8. Cat 13. Left splanchnic nerve severed and stimulated (coil distance = 12). Records A and B taken after double section of the aortic, vagal and sympathetic nerves in the neck. A. Both common carotids opened. B. Both carotids closed at the beginning of the 2 minutes' interval between these two records. Records C and D taken 15 minutes later after both carotid sinus nerves had been severed. Between them both common carotids closed at *a* and 2 minutes' interval. Records E and F taken 18 minutes after latter, after tying off the left suprarenal gland. Both carotids open between E and F and 2·5 minutes' interval.

not suppress the "dip," but as soon as the suprarenal gland of the side stimulated[1] was tied off, the "dip" entirely disappeared (Figs. 8E and F). This result agrees with others reported by previous investi-

[1] If each splanchnic can innervate also the suprarenal gland of the other side [Cannon, 1919] this is not the general rule, as evidenced by this and the other observation reported above. Elliott [1912] could not observe any dilatation of the denervated pupil by stimulation of the ipsilateral glandless splanchnic nerve.

gators [Elliott, 1912; Pearlman and Vincent, 1919], except those from others already referred to [Houssay, 1920; Gley and Quinquaud, 1921; Vincent and Wright, 1924].

DISCUSSION.

Evidence has been brought forward which shows that the height and form of the pressure curve resulting from stimulation of the splanchnic nerve are modified by reflexes originating in the blood-pressure receptors in the aortic and carotid sinus walls, and particularly the latter.

Considering generally the results observed in rabbits, hares and dogs, it is seen not only that the changes are of a very uniform character, but that if the two variations, namely notch and rise of blood-pressure, are considered together for the same animal, they are found to develop simultaneously and in the opposite direction, *i.e.* the gradual attenuation and final disappearance of the notch in the curve are accompanied by the progressive increase in the height reached by the curve as the influence of the aortic and carotid sinus nerves, especially of the latter, is progressively suppressed.

Therefore it can be accepted:

1. That the typical and constant feature in the normal splanchnic pressure curve (simple "notch," "step" or "dip") is related to the activities of the aortic and carotid sinus nerves.

Hering [1927*c*] had already predicted that the "dip" is the "result of the blood depressing action of the aortic and carotid sinus nerves (*Blutdruckzügler*) which are strongly brought in action by the increasing effect of the splanchnic stimulation." The evidence in this paper not only confirms his view, but shows in addition that of the vascular reflexes which are evoked during the rise of pressure, those originating in the carotid sinus are more closely related to the production of the "dip" than those originating in the aortic nerves.

2. That in the normal conditions, the height reached by the splanchnic pressure curve is notably reduced, also by the action of the aortic and carotid sinus nerves, particularly the latter.

The older evidence [Bayliss, 1893; François-Frank, 1896; Bunch, 1899] and the more recent direct microscopical observations of Koch and Nordmann [1928*a*] show that the splanchnic arterioles and capillaries dilate when the aortic nerves are stimulated, or the carotid sinus nerves stimulated by unclamping the carotids, and indicate that the splanchnic vessels participate in these reflexes. Moissejeff

[1926] reported that the vaso-dilator reflexes were not observed after section of both splanchnic nerves, and concluded that the regulation was mainly visceral. The part played by the general and visceral areas in these reflexes is still undecided. My observations suggest that the general areas must play an important part, as no definite difference in the height or form of the curve was noted whether one or both splanchnic nerves were severed. It would appear, therefore, that the vaso-pressor effects produced by a stimulation of the peripheral end of the splanchnic nerve cannot be considered as due solely to a vaso-constriction in the splanchnic area. The splanchnic pressure curve represents a balance between two factors working in the opposite directions: the direct vaso-constrictor effect due to the stimulation of the splanchnic nerve and the indirect reflex vaso-dilatation[1] resulting from the rise of pressure.

Numerous tracings have been published [Oliver and Schäfer, 1895; Heymans, 1929*a*; McGuigan and Hyatt, 1919] showing that with considerable rises in blood-pressure, produced under conditions fundamentally the same as those here considered, the curves have essentially the same features as those described in this paper. During the production of the curves the inhibitory mechanism was obviously active. It would appear, however, that not only considerable rises of pressure bring the reflex vaso-dilatation into play, but even minor variations are effective, especially if they occur in the neighbourhood of the normal blood-pressure level [Koch, 1929*c*; Heymans and Bouckaert, 1929]. This view is supported by some tracings published by Heymans [1929*b*] which show how the blood-pressure curve of a dog, whose isolated sinus is perfused by the circulation of another dog, presents inverted variations which correspond to the vaso-motor and respiratory pressure variations in the latter.

The inhibitory action of the carotid sinus reflexes upon the height

[1] The findings of McGuigan and Hyatt [1919], who observed that "after ablation of the head or pithing of the brain in the cat the primary fall and secondary rise were absent," as well as those of Vincent and Wright [1924], who concluded that the characteristic curve is "uncommon in the decapitate animal," become clarified. In making the decapitate preparation "each carotid artery is ligated close posterior to its tyroid branch" and the neuraxis severed "about 4 mm. behind the point of the calamus scriptorius" [Sherrington, 1919; Liddell and Sherrington, 1929]. Such a procedure interrupts the reflex channels, thus making the preparation only suitable for studying the part played by the suprarenal gland on the height and the form of the curve. The carotids being ligated in the same way in the decerebrate preparation, this can only serve the purpose of studying the effects mediated by the aortic nerves but not of the reflexes originating in the sinus nerves. Again this explains why "the dip does not occur" [Thompson, 1928] in the decerebrate preparation.

and the form of the splanchnic curve can be readily shown by bringing the reflex into play at different moments in the ascent of the curve, and exactly the same variations can be produced as in the normal animal.

The results are especially clear cut by using a preparation in which only one of the two carotid sinuses has been left in relation with its nerve. The splanchnic nerve is stimulated when both carotids are closed, then shortly after the beginning of the stimulation they are successively opened: opening the carotid leading to the denervated sinus has no effect on the rise of the curve, but by opening the one leading to the normally innervated sinus a typical "dip" is obtained (Fig. 5C).

Another way of demonstrating the carotid sinus inhibitory reflexes is shown in Fig. 9. The splanchnic nerve is stimulated, and both carotids suddenly closed at the very beginning or early during the ascent of the curve (curves A and B). In both these cases the rise of pressure is almost as large as when made with the carotids closed, and no "dip" or only very slight "dip" is seen, because the rise of pressure in the carotid sinus has been inappreciable or lasted too short a time to evoke the reflex. But if made later, as in curve C, then an obvious "dip" is produced in the curve and its height also lessened.

Occasionally the relations of the inhibitory reflex effect to the height of the rise of pressure from which it originates can be demonstrated by varying the length of the stimulation of the splanchnic nerve. Thus, if a series of similar stimulations of progressively increasing duration is made at convenient intervals, it is found that with a very short stimulation (Fig. 10A), the reflex depressant wave coincides with the fall of the pressure curve and this drops below its initial level. But, as the stimulations are lengthened (Figs. 10B to E), then the fall due to the reflex vaso-dilatation is counterbalanced, and the curve kept high for longer and longer periods of time.

The features of the splanchnic pressure curve have already been artificially reproduced by other means. Anrep [1912] reproduced the "step" after ligating the suprarenals (1) by stimulating the splanchnic nerve "first with a weak current and then with a strong one"; (2) by "injection of a small dose of adrenaline shortly after the commencement of the stimulation." As these results were observed only after both adrenal glands had been tied off, they were considered as proof of the relation of the second rise to the secretion of adrenaline. But the conclusion would have been legitimate only if the intensity of the stimulation had been kept constant, as in the ordinary experiment. If the

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intensity or the frequency of the stimulation are increased (and both methods used by Anrep consist in increasing the stimulation of the

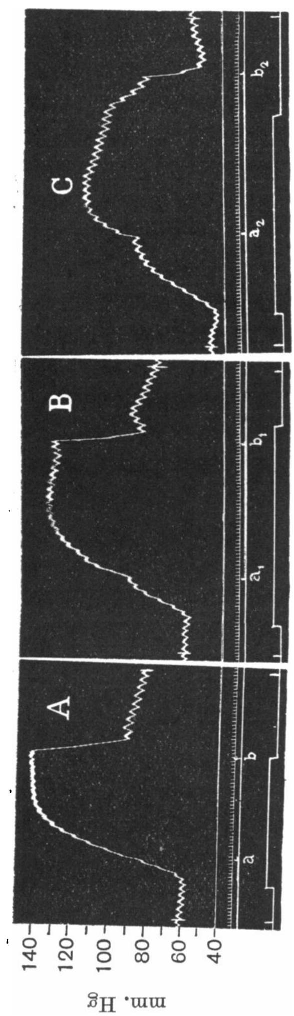

Fig. 9. Rabbit 5. Both splanchnic and aortic nerves severed. Stimulation of the right splanchnic nerve (coil distance =5). From A to C at progressively longer intervals after the beginning of the stimulation, both carotids are closed at a, a_1 and a_2, respectively. At b, b_1 and b_2 they are reopened.

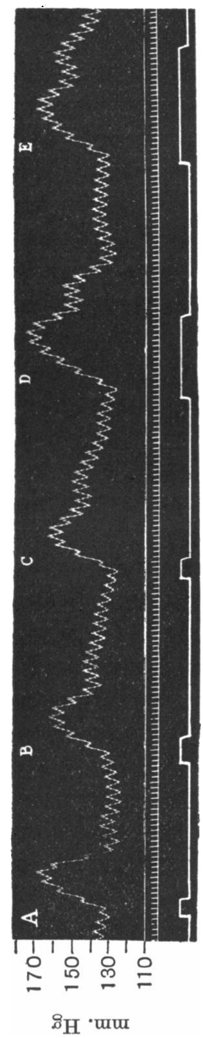

Fig. 10. Dog 12. Left aortic-vago-sympathetic trunk severed. Left splanchnic nerve severed. Successive stimulations of increasing duration (coil distance =8).

splanchnic vaso-motor endings at a certain moment) even when the adrenal glands are intact the steepness of the curve becomes greater, as is well known from the work of Johansson [1891].

The cat. The results on the cat, reported in this paper, offer an explanation as to why in most of the literature on the splanchnic pressure curve, based on experiments on the cat, the "dip" has been mainly referred to the suprarenals. As to the mechanism of the action of the secreted adrenaline, views have differed. It is supposed that the "dip" is produced, either by its general vaso-dilator action in small amounts [Cannon and Lyman, 1913; Pearlman and Vincent, 1919] or by a direct effect upon the heart, causing a secondary rise [Anrep, 1912; Vincent and Wright, 1924]. Some even maintain that it acts in both ways [Sherrington, 1919]. It is surprising to discover in some tracings in which a period of acceleration of the heart is found at the beginning of the secondary rise, how closely these two features in the curve coincide in time with the duration of the latent period for the adrenaline secretion, which has been estimated at 8–11 seconds [Pearlman and Vincent, 1919; Stewart, Rogoff and Gibson, 1916; Tournade and Chabrol, 1921; Cannon and Carrasco-Formiguera, 1922]. But, judging from the experiments reported here, as well as from some of the tracings illustrating Sherrington's book [1919], in which this acceleration is also absent, it is clear that, as Lehndorff [1908] already has shown, the period of acceleration is not as constant as Johansson [1891] thought. Its absence, in any case, does not prove either that no adrenaline has been secreted, because, even by using the denervated heart which is a very sensitive test organ [Anrep, 1912; Cannon and Carrasco-Formiguera, 1922], minute doses of adrenaline can make the heart beat stronger without affecting the rate [Anrep and Daly, 1925].

The anomalies found in the cat become fewer after extirpation of the suprarenals. At the moment we can only point out the relation of these anomalies to the glands, because the existing data upon the relations between the suprarenals and the blood-pressure regulating nerves [Heymans, 1929*a*; Richards and Wood, 1916] do not offer any material for further discussion.

Conclusions.

By stimulating the peripheral end of the splanchnic nerves by a constant faradic stimulus under similar conditions, first with the two sets of aortic and carotid sinus nerves intact and then with these nerves partially or totally eliminated, the following results were obtained:

1. When the aortic and sinus nerves are eliminated the blood-pressure curve is considerably higher and simpler in form than when both sets of nerves are intact.

2. When only the two aortic nerves are active the curve is higher

and its "dip" less pronounced than when in addition the two carotid sinus nerves are in action.

3. When only the two carotid sinus nerves are active the height reached by the curve is higher than when in addition the aortic nerves are in action, but its form is not appreciably modified.

4. When a single carotid sinus nerve is left active its effects upon the height and form of the splanchnic pressure curve are often considerable.

5. When both aortic and carotid sinus nerves are active, their joint inhibitory action can be so strong that a stimulation of the splanchnic nerve may fail to give any appreciable rise of blood-pressure.

6. Comparison of the effects observed after elimination of both aortic nerves or both carotid sinus nerves alone, shows that the carotid sinus nerves exert the more important inhibiting effect upon the height of the curve and are the main factors in producing the "dip" in the splanchnic pressure curve.

7. Tying off of both adrenals at the beginning of the experiment or after partial or total suppression of the aortic and carotid sinus nerves does not modify the results in the rabbit, the hare and the dog. But in the cat the "dip" more frequently disappears after the ipsilateral gland is tied off.

8. The two variations, namely, in the height and "dip" in the curve develop simultaneously and in contrary sense, *i.e.* the gradual attenuation and final disappearance of the "dip" keeps pace with the gradual increase in the height reached by the curve. Therefore, both series of changes are compatible with the view that the curve of the rise of blood-pressure produced by stimulation of the splanchnic nerve consists of two superimposed elements, (*a*) the direct vaso-pressor effect (vaso-constriction in the splanchnic area), and (*b*) the indirect vaso-depressor effect (aortic and more especially carotid sinus reflexes) evoked by the rise of blood-pressure.

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[1] A preliminary report by the author has already been published in the *Z. ges. exp. Med.* **72**, 415 (1930).

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