Effect of Bilateral Adrenalectomy on the Cardiovascular Response to Induced Tachycardia.* (28949)

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It has been shown that electrically induced tachycardia of sufficiently high rate results in an immediate decrease of cardiac output and mean arterial blood pressure which recover partially or completely through both myocardial and vascular mechanisms(1,2). Since during such bouts of tachycardia, there occurs a marked rise in the catecholamines blood level(2), it was thought of interest to investigate the importance of the adrenal medulla in the compensation of the cardiovascular system to induced tachycardia by studying the response of the cardiovascular system to tachycardia immediately before and after bilateral adrenalectomy, in order to gain more insight into the respective role of the adrenal medulla and the sympathetic nervous system.†

Methods. Eleven dogs (22.3 kg-33.4 kg) were anesthetized by intravenous administration of 100 mg of chloralose per kg. The methods used to measure and record continuously the output of the left ventricle (CO) and mean arterial blood pressure (MABP) as well as the formula used to calculate total peripheral resistance (TPR) have been described(4). Heart rate (HR) was determined from electrocardiographic tracings. To reduce to a minimum the extraneous effect of the surgical manoeuvres at the time of actual removal of the adrenals, the following procedure was adopted. Two threads were threaded under the upper and lower pole of each adrenal with a minimal amount of dissection so as not to disturb either innervation or circulation of the adrenals. Then after the control observations had been made, gentle pulling of the 4 loose ends of the threads permitted easy lifting of the adrenals, with rapid tying and then tight clamping with a curved hemostat of all the tissues beneath the glands, followed in the first 5 dogs by extirpation of both adrenals in quick succession. Ventricular tachycardia of approximately 220 to 240 per minute was induced electrically with a Grass stimulator, short DC stimuli of minimal intensity being applied to the apex of the left ventricle through 2 fishhook electrodes. Essentially the experiments were conducted as follows. After a control period, ventricular tachycardia was induced and maintained for approximately 2 to 3 minutes. Then a period of recovery was observed. The adrenals were then removed and after a period of 4½ to 14½ minutes to permit recovery from the manipulations involved in bilateral adrenalectomy, the effects of a comparable bout of ventricular tachycardia lasting approximately 2 to 3 minutes were observed. In 2 of the 11 dogs, 2 control bouts of tachycardia instead of one were induced before adrenalectomy. In 5 of the 11 dogs, one bout of tachycardia was induced after adrenalectomy whereas 2 and 3 bouts were induced respectively in 5 and 1 of the 11 dogs. The first, second, and third bouts of post-adrenalectomy tachycardia were initiated respectively 4½ to 14½ minutes, 14½ to 22½

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† It seems legitimate to assume that the ablation of the adrenal cortex which was removed during total bilateral adrenalectomy played no role in the present acute experiments of very short duration, lasting approximately 22 to 59 minutes from the beginning of the first control period and *9 to 47 minutes from the end of the adrenalectomy*. Some of the post-adrenalectomy bouts of tachycardia were initiated purposely this long after the end of the adrenalectomy to insure the disappearance from the blood of the catecholamines which might have been released in the blood stream during the adrenalectomy, although it is most unlikely that catecholamines were released into the blood stream during adrenalectomy with the technique used(3).

minutes and 35 minutes after the end of adrenalectomy.

Results and discussion. The results observed are summarized in Tables I and II. In Exp. 1, during the control period, heart

TABLE I. Effect of Ventricular Tachycardia on Mean Arterial Blood Pressure (MABP; expressed in mm Hg), Cardiac Output (CO; expressed in cc/min) and Total Peripheral Resistance (TPR; expressed in arbitrary units) Before and Immediately After Bilateral Adrenalectomy. DT, duration of tachycardia in sec; HR, ventricular rate per min. C, control values; T_1, values at time of lowest cardiac output during induced tachycardia and T_2, values at time of maximal recovery of cardiac output during induced tachycardia; R, values after recovery period.

Dog No.		DT	HR	MABP	CO	TPR
1	C	—	162	120	1230	97.6
	T_1	—	228	55	390	141.0
	T_2	120	228	105	1000	105.0
	R	—	162	124	1230	100.8
Adrenalectomy						
	C	—	156	108	940	114.9
	T_1	—	228	55	300	183.3
	T_2	150	228	98	740	132.4
	R	—	156	105	870	120.7
2	C	—	120	132	2020	65.3
	T_1	—	216	105	1420	73.9
	T_2	179	216	127	1730	73.4
	R&C	—	138	135	2020	66.8
	T_1	—	234	110	1700	64.7
	T_2	176	234	133	2000	66.5
	R	—	150	137	2020	67.8
Adrenalectomy						
	C	—	156	145	1730	83.8
	T_1	—	240	102	830	122.9
	T_2	163	240	145	1700	85.3
	R&C	—	150	146	1715	85.1
	T_1	—	240	113	1100	102.7
	T_2	167	240	137	1430	95.8
	R	—	156	145	1700	85.3
3	C	—	96	133	2220	59.9
	T_1	—	222	68	990	68.7
	T_2	151	222	102	1620	63.0
	R	—	96	130	2130	61.0
Adrenalectomy						
	C	—	102	120	1860	64.5
	T_1	—	222	55	580	94.8
	T_2	161	222	105	1500	70.0
	R	—	102	125	1860	67.2
4	C	—	180	128	960	133.3
	T_1	—	228	63	380	165.8
	T_2	174	228	68	400	170.0
	R	—	162	122	820	148.8
Adrenalectomy						
	C	—	162	109	740	147.3
	T_1	—	228	57	320	178.1
	T_2	177	228	66	380	173.7
	R	—	162	103	670	153.7
5	C	—	160	118	1140	103.5
	T_1	—	225	70	380	184.2
	T_2	160	225	106	730	145.2
	R	—	168	119	1120	106.3

TABLE I (continued)

Dog No.		DT	HR	MABP	CO	TPR
Adrenalectomy						
	C	—	180	108	810	133.3
	T_1	—	225	57	300	190.0
	T_2	110	225	72	410	175.6
	R	—	184	102	800	127.5
6	C	—	144	140	2150	65.1
	T_1	—	240	95	1350	70.4
	T_2	171	240	129	1750	73.7
	R&C	—	138	140	2150	65.1
	T_1	—	210	93	1200	77.5
	T_2	173	210	130	1425	91.2
	R	—	144	135	2075	65.1
Adrenalectomy						
	C	—	165	98	1360	72.1
	T_1	—	210	57	350	162.9
	T_2	172	210	63	600	105.0
	R	—	180	86	1150	74.8
7	C	—	168	165	1875	88.0
	T_1	—	234	73	120	608.3
	T_2	169	234	164	1340	122.4
	R	—	180	173	1875	92.3
Adrenalectomy						
	C	—	174	135	1380	97.8
	T_1	—	234	64	50	1280.0
	T_2	171	234	127	800	158.8
	R	—	180	133	1220	109.0
	C	—	174	133	1220	109.0
	T_1	—	234	58	25	2320.0
	T_2	169	234	121	720	168.1
	R	—	180	131	1200	109.2
8	C	—	130	132	1800	73.3
	T_1	—	220	65	500	130.0
	T_2	202	220	113	1200	94.2
	R	—	144	142	1950	72.8
Adrenalectomy						
	C	—	170	115	1475	78.0
	T_1	—	240	48	200	240.0
	T_2	189	240	98	975	100.5
	R	—	160	120	1625	73.8
	C	—	180	125	1625	76.9
	T_1	—	240	55	275	200.0
	T_2	204	240	110	1000	110.0
	R	—	160	120	1800	66.7
9	C	—	115	195	1275	152.9
	T_1	—	228	95	400	237.5
	T_2	175	228	165	900	183.3
	R	—	120	192	1200	160.0
Adrenalectomy						
	C	—	132	153	950	161.1
	T_1	—	228	55	50	1100.0
	T_2	170	228	118	425	277.6
	R&C	—	156	152	900	168.9
	T_1	—	228	42	25	1680.0
	T_2	172	228	110	400	275.0
	R	—	138	143	775	184.5
10	C	—	160	127	1860	68.3
	T_1	—	220	63	410	153.7
	T_2	164	220	99	1340	73.9
	R	—	150	143	2050	69.8
Adrenalectomy						
	C	—	160	121	1550	78.1
	T_1	—	225	68	440	154.5
	T_2	169	225	98	1120	87.5
	R	—	160	112	1480	75.7
	C	—	165	116	1570	73.9

TABLE I (continued)

Dog No.		DT	HR	MABP	CO	TPR
	T_1	—	225	67	530	126.4
	T_2	170	225	100	1280	78.1
	R	—	165	114	1650	69.1
	C	—	180	115	1715	67.1
	T_1	—	225	60	465	129.0
	T_2	172	225	98	1260	77.8
	R	—	160	116	1715	67.6
11	C	—	130	160	2025	79.0
	T_1	—	230	75	575	130.4
	T_2	168	230	138	1525	90.5
	R	—	130	155	1925	80.5
Adrenalectomy						
	C	—	130	129	1450	89.0
	T_1	—	230	63	225	280.0
	T_2	171	230	122	1025	119.0
	R&C	—	150	128	1300	98.5
	T_1	—	230	47	250	188.0
	T_2	167	230	115	825	139.4
	R	—	144	121	1200	100.8

rate, mean arterial blood pressure, cardiac output, and total peripheral resistance were 162 beats per minute, 120 mm of mercury, 1230 cc per minute and 97.6 units respectively. Electrically induced ventricular tachycardia of a frequency of 228 per minute promptly lowered mean arterial blood pressure and cardiac output to minimal values of 55 mm of mercury and 390 cc per minute respectively, the peripheral resistance rising to 141.0 units. By the end of the 2 minutes of tachycardia, blood pressure and cardiac output had recovered partially and stabilized at respective levels of 105 mm of mercury and 1000 cc per minute, and the peripheral resistance had decreased to 105.0 units, a value still higher than the control value of 97.6. Upon cessation of the tachycardia, mean arterial blood pressure, cardiac output and total peripheral resistance returned essentially to their control levels. Approximately 3 minutes after termination of the bout of tachycardia, bilateral adrenalectomy was begun and done in 6½ minutes. Within 9½ minutes of the end of the adrenalectomy, heart rate, mean arterial blood pressure and cardiac output had stabilized around respective values of 156 beats per minute, 108 mm of mercury and 940 cc per minute and total peripheral resistance had risen to 114.9 units. A bout of ventricular tachycardia of a frequency of 228 lowered mean arterial blood pressure and cardiac output to respective minimal values of 55 mm of mercury and 300 cc per minute, the total peripheral resistance rising to 183.3 units. By the end of the 150 seconds bout of tachycardia, blood pressure, cardiac output and peripheral resistance had returned toward their control levels and upon cessation of the tachycardia, they returned to or further toward control values.

Essentially similar results were observed in all experiments (Table I). Analysis of the phenomena observed during tachycardia before adrenalectomy would seem to indicate that the initial phenomenon produced by the tachycardia is the abrupt reduction of systolic and minute cardiac output caused by the shortening of diastole and the abnormal intraventricular excitation(1,5). This decrease in systolic and minute cardiac output produces a prompt fall in mean arterial blood pressure. The return of the cardiac output to or toward its control level presumably is due to the accumulation of blood in the atria and large veins which results in a higher filling pressure and better filling of the ventricles. Hence the systolic and minute cardiac output rise from their minimal value and return to or toward control level. Obviously, other factors are involved in the recovery of the systolic and minute cardiac output from their minimal levels. Sympathetic stimulation resulting from the fall of mean arterial

TABLE II. Percentile Changes (means ± standard errors) from Control Values of Mean Arterial Blood Pressure (MABP), Cardiac Output (CO) and Total Peripheral Resistance (TPR) During Bouts of Ventricular Tachycardia Electrically Induced Before and After Adrenalectomy (Table I). T_1, values at time of lowest cardiac output and T_2, values at time of maximal recovery during tachycardia. P, P-values vs. control.

	Before adrenalectomy			After adrenalectomy					
	MABP	CO	TPR	MABP	P	CO	P	TPR	P
T_1	−43.1±3.5	−58.6±5.9	+85.6±43.3	−50.4±2.8	<.2	−75.0±4.0	<.05	+334.0±126.3	<.1
T_2	−13.8±3.4	−27.0±3.7	+19.7± 3.9	−16.2±2.6	<.6	−34.3±3.6	<.2	+ 31.4± 5.1	<.1

blood pressure must be considered as a factor responsible for recovery of the cardiac output through its direct cardiac effect(6,7) as well as release of catecholamines in the blood stream(2). The recovery of the arterial blood pressure must be ascribed partly to the recovery of the cardiac output and partly to peripheral vasoconstriction resulting from the reflex stimulation of the sympathetic by the fall in mean arterial blood pressure(6,8). Indeed the increase in total peripheral resistance observed to occur in practically all experiments during the tachycardia, and to be especially marked at the beginning of the period of tachycardia when cardiac output and arterial blood pressure are generally minimal, confirms the occurrence of peripheral vasoconstriction. The present observation as well as work previously reported(2) emphasize the importance of the sympathetic nervous system in the compensatory mechanisms triggered by a decrease in cardiac output and/or mean arterial blood pressure. This work supports the view that sympathetic stimulation probably plays a role in any clinical condition resulting in "forward failure" such as sufficiently severe cases of myocardial infarction(9), paroxysmal tachycardia(2), severe hemorrhagic hypotension (10-12) and hemorrhagic shock(13).

Bilateral adrenalectomy was followed by a decrease in cardiac output and mean arterial blood pressure and an increase in total peripheral resistance in practically all experiments. It is most probable that these changes were caused by the adrenalectomy and were not the result of spontaneous deterioration of the preparation, as indicated by the sudden occurrence of these cardiovascular changes and by the degree of stability of the preparation before and after adrenalectomy in those 2 experiments in which 2 controls were obtained before adrenalectomy, and in those 6 experiments in which 2 or 3 post-adrenalectomy bouts of tachycardia were studied. The constancy of the occurrence of these cardiovascular changes after adrenalectomy also makes it most likely that they were due to a specific effect of the removal of the adrenals, presumably the adrenal medulla, and not to the effect of the surgical manoeuvres inherent to the adrenalectomy which were minimal in intensity and duration when the adrenalectomy was actually performed, as explained in the methodology used. The most logical interpretation of this series of syndromic events is that adrenalectomy resulted in a primary decrease of cardiac output tending to cause a decrease of arterial blood pressure, which induced peripheral vasoconstriction presumably through reflex stimulation of the sympathetic nervous system.

Comparison of the effects of tachycardia before and after bilateral adrenalectomy would seem to indicate that the cardiovascular compensation in response to the bouts of tachycardia studied in the present work can remain relatively unmodified by bilateral adrenalectomy, at least insofar as the decrease in mean arterial blood pressure resulting from the induced tachycardia is corrected essentially to the same extent by the end of the bout of tachycardia after, as well as before adrenalectomy (Tables I and II). Furthermore, this recovery of the mean arterial blood pressure in post-adrenalectomy as well as pre-adrenalectomy tachycardia, is mediated through an increase both in cardiac output and total peripheral resistance. Whether adrenalectomy modifies the effect of induced tachycardia in some other manner, such as by making the cardiovascular compensation to tachycardia more contingent upon an increase in cardiac output than upon vasoconstriction or vice versa, is difficult to ascertain and to draw such a conclusion from the data of Tables I and II would be hazardous. However, these data seem to indicate that the maximal decrease in cardiac output occurring at the beginning of the bout of tachycardia is greater during post-adrenalectomy tachycardia than during pre-adrenalectomy tachycardia. It should be added that even a quantitatively similar recovery of the cardiac output such as that which takes place by the end of the post-adrenalectomy as well as pre-adrenalectomy tachycardias, does not necessarily indicate that recovery of the cardiac output is mediated through the same mechanism(s) during post- and pre-adrenalectomy tachycardias, and it is conceivable that be-

fore adrenalectomy the recovery of the cardiac output is mediated *via* the operation of the Starling law of the heart(1), the action of the sympathetic nervous system of the heart(2,6,7) and adrenal medulla, whereas obviously after adrenalectomy the last mechanism of cardiac output recovery is not available. If such is the case, the reserve of compensation to induced tachycardia may well be reduced by adrenalectomy and it is possible that induced tachycardia of higher frequency might reveal such a reduction of the reserve of cardiovascular compensation.

As it was not possible to determine the catecholamines blood level during the present experiments, it cannot be stated whether the increase in catecholamines blood level which occurs in similar bouts of tachycardia(2), still occurs after bilateral adrenalectomy, or whether the compensatory mechanisms observed during pre- and post-adrenalectomy induced tachycardias may be independent of an increase in the catecholamines blood level. Whatever future investigation reveals concerning the origin of the increase in catecholamines blood level during such bouts of tachycardia, it seems that the extent of the cardiovascular compensation in response to bouts of tachycardia can remain relatively unaffected by bilateral adrenalectomy, at least under experimental conditions of this work.

Summary. Relatively short bouts of electrically induced ventricular tachycardia of sufficiently high rate to result at least initially in a marked decrease in cardiac output and mean arterial blood pressure were induced in anesthetized dogs before and immediately after bilateral adrenalectomy. This study reveals that, although adrenalectomy affects the circulation under the experimental circumstances described, the degree of cardiovascular compensation in response to such bouts of tachycardia can remain relatively unaffected by bilateral adrenalectomy. Whether this remains true with bouts of higher rate tachycardia remains to be determined.

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