Catecholamine Release After Spinal Cord Section* (33610)

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For many years physiologists and pharmacologists have used the spinal animal preparation in various experiments. The method of dividing the spinal cord described by Burn (1) or spinal cord section combined with division of the vagus nerves in the neck bilaterally offer the advantage of total autonomic denervation. Although it is known that transection of the spinal cord elicites first a transient pressor response, this fact has not been particularly emphasized (2, 3). The present study was undertaken to test the supposition that the genesis of this immediate cardiovascular reaction might be due to the release of catecholamines.

Methods. Twenty-six mongrel dogs (8.0–21.0 kg) were anesthetized with 30 mg/kg of pentobarbital given intravenously. A Y-shaped cannula was inserted into the trachea and respiration maintained with a Harvard respirator. Both carotid arteries and vagus nerves were ligated and divided. The spinal cord was exposed at the level of the second cervical vertebra. After a right-sided thoracotomy a strain-gauge arch was sutured to the right ventricle in order to measure the myocardial contractile force (CF). The mean femoral arterial blood pressure (MABP) was measured with a Statham pressure gauge and the heart rate (HR) was obtained from the CF tracings. All parameters were recorded continuously with a E&M Physiograph. Four groups of animals were studied.

Group I consisted of 6 dogs that underwent the procedure described above including spinal cord section. The animals of this group comprised the controls.

Group II and Group III consisted of 6 and 8 dogs respectively, pretreated with hexamethonium chloride (Hexameton) or (2-octahydro-1-azocinyl)-ethyl)-guanidine sulfate (Guanethidine) prior to spinal cord section. Both drugs were administered in the amount of 10 mg/kg by injection into the femoral vein over an interval of 1–5 min. Section of the spinal cord in these animals (group II and III) was performed after CF, MABP, and HR had returned to or were below their preinjection values, except that HR was still elevated above preinjection rates in the animals that had received guanethidine.

Group IV consisted of 6 dogs in which blood samples for catecholamine analysis were drawn pior to section of the spinal cord and 1 and 3 min after section of the cord by means of a catheter advanced through the right external jugular vein into the right atrium. The amount of blood withdrawn for analysis was replaced with an equal volume of blood given intravenously.

The plasma was absorbed on Dowex resin as described by Vendsalu (4) and the catecholamines were determined according to the tryhydroxy-indole method as outlined by Bertler, Carlsson, and Rosengreen (5). The catecholamines are expressed as the equivalent of norepinephrine in micrograms/liter of plasma. Recoveries of norepinephrine standards yielded 79.8 ± 3.6%.[1]

Results and Discussion. Figure 1 presents the increase in CF, MABP, and HR expressed as percentage of increase over the respective values before section of the cord in groups I, II, and III. The mean increase of CF was 98 ± 11% in the control group of animals, whereas the MABP and the HR rose by 89 ± 4 and 33 ± 7% respectively. The CF, MABP, and HR increased by 28 ± 9, 30 ± 1, and 4 ± 1% in the animals pretreated with Hexameton. In the animals that had received Guanethidine the increases in these parameters were 12 ± 5, 21 ± 5, and

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[1] Values are means ± standard error.

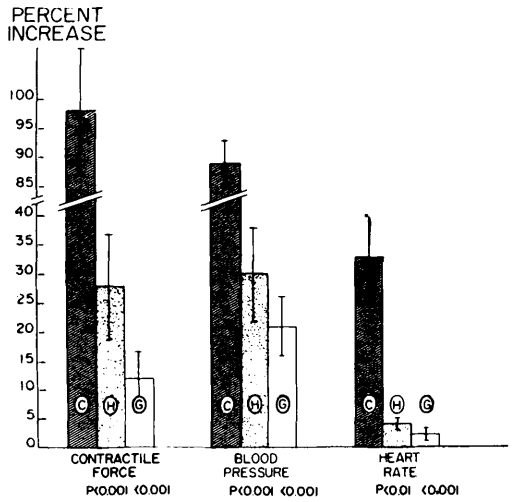

FIG. 1. Increase in contractile force, mean arterial blood pressure, and heart rate (mean± standard error) after spinal cord section in a control group (C) of dogs and in dogs pretreated with Hexameton (H) and Guanethidine (G). The p values (t test nonpaired experiments) represent the difference between the control and pretreatment groups.

2 ± 1%. It is evident that spinal cord section produced a marked rise in CF, MABP, and HR, which was significantly diminished by prior administration of Hexameton and Guanethidine.

Transection of the cervical spinal cord has been classically described as being followed by fall in arterial blood pressure and loss of vasomoter reflexes (2, 3). Hypotension persists for several days after which the arterial pressure is often found to have returned nearly to pretransection levels (2, 3, 6). However it is evident from this study and others (6, 7) that the cardiovascular changes that occur immediately after spinal cord section consist of a prompt increase in arterial blood pressure, myocardial contractile force, cardiac output, heart rate, and peripheral resistance which persist for several minutes. Thereafter, all parameters fall below control levels except for the peripheral resistance which changes little and increases in time (6, 7).

The present study indicates that the increase in CF, MABP, and HR immediately after spinal cord section is due to stimulation of the sympathetic nervous system. This is suggested by the decrease in cardiovascular responses after cord transection by sympatholytic agents, Hexameton and Guanethidine (8, 9), and is confirmed by the rise in blood catecholamine levels (Fig. 2).

The studies of Beattie *et al.* and Chen *et al.* (10, 11) have shown that pressor responses and cardiac-stimulant actions can be repeatedly obtained by stimulation of the posterior hypothalamus and medullary sympathetic area as well as the ventrolateral columns of the spinal cord. The latter constitute the descending pathways of cerebral sympathetic functions, and seem to be markedly stimulated by cord transection resulting in the release of norepinephrine. It is now accepted that the physiologic activity of catecholamines released by nerve stimulation is terminated by uptake and rebinding within tissue stores, their metabolism to relatively inactive compounds, and the removal of

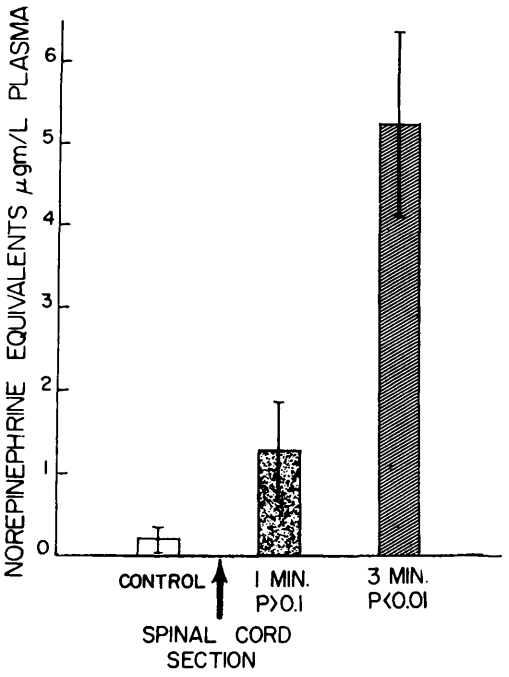

FIG. 2. Plasma catecholamine level (mean± standard error) in blood withdrawn from the right atrium prior to spinal cord section and 1 and 3 min after section of the spinal cord. The p values (t test paired experiments) represent the difference between the control and post-spinal cord section catecholamine levels.

small amounts from the receptor area by "wash out" (12–14). After spinal cord section the portion of norepinephrine removed from the receptor area by the circulation increased progressively (Fig. 2), apparently due to saturation of the other mechanisms of inactivation. It is not surprising that the significant rise of norepinephrine 3 min after cord section was concomitant with the peak cardiovascular responses. Thereafter CF, BP, and HR decreased but remained above control levels for from 4–10 min, indicating that the discharge of norepinephrine was continuing. It is suggested that the release of catecholamines after spinal cord section might interfere with physiological and pharmacological studies in which it is presumed that a steady state is present. This seems to be particularly true of studies pertaining to the mechanism of action of sympathometic amines, since it is known that change in receptor saturation and catecholamine content of the neurotransmiter store can alter the effect of these agents (15).

Summary. Cervical spinal cord section causes an immediate rise in CF, MABP, and HR. The increase in these cardiovascular parameters is due to stimulation of the sympathetic nervous system, as indicated by the diminished response after treatment with sympatholytic agents, Hexameton and Guanethidine, and by the rise in blood catecholamines.

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