Responses of Systemic Arterial Pressure and Heart Rate to Increased Intrapulmonary Pressure in Anesthetized Dogs (33893)

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Since the original description of the Valsalva maneuver, the cardiovascular response to increased intrapulmonary pressure has attracted the attention of many physiologists and clinicians. It has been used as a simple test for cardiac function (1), in analyzing left-sided and right-sided cardiac events (2, 3) and in studies of abnormalities of the autonomic nervous system (4, 5).

We have attempted to simulate the Valsalva test in anesthetized dogs by increasing intrapulmonary pressure with inflation of the lungs through an endotracheal tube. The changes in heart rate and arterial pressure were quite similar to those observed during the Valsalva maneuver in normal subjects, although in phase 3 a further decrease in systemic arterial pressure was not uniformly encountered. When higher intrapulmonary pressure was applied, certain abnormal responses occurred, which were thought to be related to muscle relaxation from anesthesia. The present communication describes arterial pressure and heart rate responses to a range of inflation pressures in a series of anesthetized dogs. The role of mechanical and neural regulatory factors is analyzed and discussed.

Materials and Methods. Thirteen mongrel dogs weighing 9–20 kg were studied. Pentobarbital sodium (initial dose 25–50 mg/kg), chloralose (initial dose 40–80 mg/kg), and sodium methohexital (10 mg/kg) followed by chloralose were used in 9, 1, and 3 dogs, respectively. Chloralose solution was prepared by dissolving 3.2 g in 80 ml of warmed polyethylene glycol. Femoral artery and femoral vein were isolated and cannulated. Arterial pressure was measured through a Statham strain gauge (either P23AA or P23DB), connected to a no. 964 Sanborn direct writing 4-channel recorder. An ECG limb lead was recorded. A recording paper speed of 2.5 mm/sec was employed primarily for arterial pressure, and 25 mm/sec for heart rate recordings.

A double-lumen tube with a pneumatic cuff was intubated into the trachea. The smaller outlet of the tube was connected to a second strain gauge to record endotracheal pressure. The animals continued their own respiration. Intrapulmonary pressure inflation (IPPI) was accomplished by blowing into a long rubber tube with a mouth piece connected to the main lumen of the endotracheal tube. Sudden cessation of the applied pressure was accomplished by disconnecting the rubber tube from the endotrocheal tube. The four phases during intrapulmonary pressure inflation are shown in Fig. 1.

The following observations and interventions were made:

1. *Anesthesia.* The effects of pentobarbital and chloralose anesthesia were compared in regard to the reflex changes due to IPPI. In one dog on pentobarbital, deep anesthesia was applied and the changes were observed over a 2-hr period.

2. *Inflation pressure.* A range of inflation pressures (5 mm Hg to 75 mm Hg) was applied and the responses were observed in the same as well as in different dogs.

3. *Drug.* The effects of atropine 0.2 mg/kg iv both at high and low pressure inflations were observed.

4. *Mechanical intervention.* Thoracic and abdominal distention due to inflation was prevented by thoracic and abdominal binding

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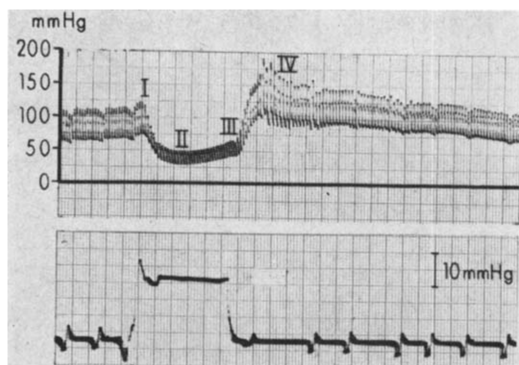

FIG. 1. Response to increased intrapulmonary pressure: I, phase 1: Note an arterial pressure rise. There is little or no change in heart rate and pulse pressure. II, phase 2: Note a reduction of arterial mean and pulse pressures. Toward the end of this phase a slight increase in mean arterial pressure is recorded. Reflex tachycardia is present. III, phase 3: In this dog, there is no further well-defined reduction in arterial pressure as that observed in normal subjects during the Valsalva maneuver except for one heart beat. IV, phase 4: Note an overshoot of arterial pressure above the control level and reflex bradycardia. (upper), femoral artery pressure; (lower) endotracheal pressure; paper speed, 2.5 mm/sec; magnification factor 10/23.

by tapes and also manually during the inflation.

Results. 1. Anesthesia. Normal sympathetic responses characterized by phase 2 reflex tachycardia and phase 4 arterial pressure overshoot were observed with low pressure inflation in all modes of anesthesia studied (pentobarbital sodium, chloralose, sodium methohexital and chloralose) when a light-to-moderate depth of anesthesia was applied. Chloralose-anesthetized dogs showed prominent sinus arrhythmia in the control phase and marked bradycardia in phase 4. In one dog on pentobarbital sodium anesthesia, a deeper anesthesia was induced by adding additional pentobarbital sodium (6.8 mg/kg). Normal response changed to a pattern without phase 4 overshoot. After 2 hr of observation, however, the normal pattern was again noted.

2. Inflation pressure. Responses to graded inflation pressure under pentobarbital sodium anesthesia are shown in Fig. 2. Whenever the inflation pressure was increased to 45 mmHg or greater, a qualitatively different pattern of response was observed. Salient features on high pressure inflation may be summarized as follows:

a. Bradycardia was present in phase 1 through 4, being most marked in phase 1–2. This was exaggerated in dogs with chloralose anesthesia. Despite a marked narrowing of the pulse pressure and a decline of the mean arterial pressure, there was no reflex tachycardia in phase 2 and heart rate was slower than that observed during the control phase.

b. No rise in blood pressure was observed toward the end of phase 2 and blood pressure overshoot in phase 4 was absent. In fact, it took a long time (up to several minutes) for the pressure to return to the normal control level.

c. There was a prolonged apnea in phase 4.

d. The diastolic pressure was markedly lowered in phase 4.

3. Atropine abolished phase 4 bradycardia in response to low inflation pressure. It suppressed the reflex bradycardia in phases 1 through 4 due to high pressure inflation. Lack of overshoot in phase 4, prolonged apnea, markedly lowered diastolic pressure, and its slow return to control level in response to high pressure inflation were not affected by atropine (Fig. 3).

4. Mechanical intervention. When thoracic and abdominal distention due to high pressure lung inflation was prevented, phase 4 arterial pressure overshoot was again demonstrated. In addition, phase 1 arterial pressure increase was better defined and especially phase 3 arterial pressure drop was now clearly present as in the normal Valsalva phenomenon. Heart rate in phase 2, however, was slower when compared with the control phase, indicating a vagal reflex activity due to lung inflation despite lowered mean arterial and pulse pressures in this phase which are potent triggering factors for reflex sympathetic activity.

Discussion. As inflation pressure was increased, normal pattern of the Valsalva phenomenon gradually changed into a qualitatively different pattern. Ventilating the dog

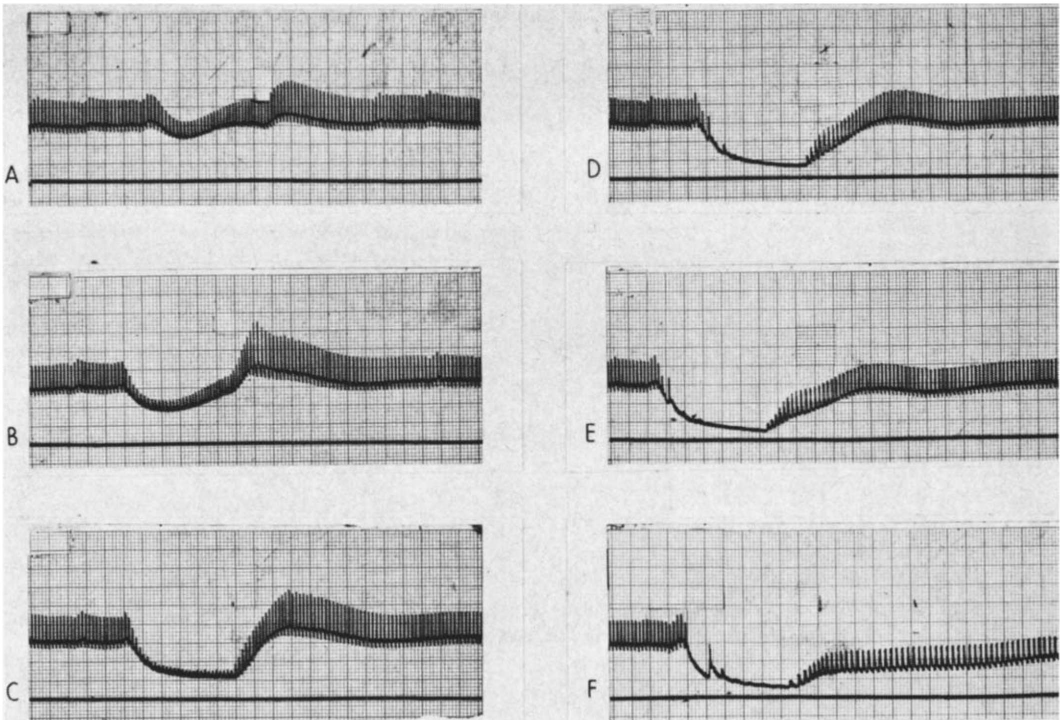

FIG. 2. Response to graded inflation pressures (mmHg): (A), 15; (B), 25; (C), 35; (D), 40; (E), 50; (F), 75; pressure calibration and paper speed are the same as in Fig. 1; magnification factor 1/2; similar trend was observed in all the dogs studied.

by a Harvard respirator immediately following the discontinuation of inflation did not change the pattern. It is, therefore, unlikely that anoxic changes due to apnea are responsible for the described response. The high inflation pressure pattern is characterized by the absence of phase 2 reflex tachycardia despite a marked reduction in arterial mean and pulse pressures, and the absence of phase 4 arterial pressure overshoot. These are consistent with depressed sympathetic reflex activities that are mediated through carotid sinus and aortic baroreceptors. It is also characterized by bradycardia (especially prominent with chloralose anesthesia) throughout the period of pressure application extending to phase 4. This indicates a parasympathetic activity. The active suppression of the sympathetic activities is suggested by the finding that atropine almost completely blocked phase 2 bradycardia but did not evoke tachycardia. These observations suggest that the afferent impulse transmission is not blocked by atropine and that the central suppression of the sympathetic system may take place upon high pressure pulmonary inflation. A central mechanism of sympathetic

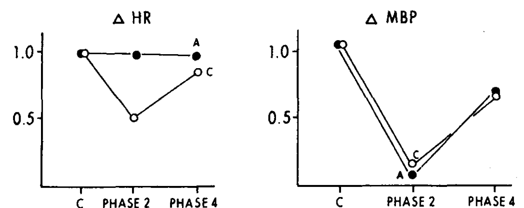

FIG. 3. Atropine effect on high pressure inflation pattern: (C), control period; (A), after 0.2 mg/kg of atropine iv; (C on abscissa), control phase; (Δ HR and Δ MBP), heart rate, and mean blood pressure changes. The mean blood pressure was calculated as diastolic pressure plus ⅓ of pulse pressure. The maximum pressure during 15 sec following the cessation of IPPI was taken as the phase 4 pressure. Note absence of bradycardia in phase 2 after atropine. Pressure patterns with and without atropine are similar and both lack phase 4 overshoot. The values are means from 2 dogs.

suppression was demonstrated in detail by Löfving (6), who showed the presence of a sympatho-inhibitory center in the rostral parts of the cingulate gyrus, surrounding the genu of the corpus callosum, and a medullary depressor area (medial part of the bulbar reticular formation) in cats. Bronk and associates (7) reported that action potentials recorded from the cut proximal end of the cardiac accelerator nerve in cats were decreased coincident with lung inflation.

Aside from the neural mechanism, a mechanical factor is known to play a role in the production of the Valsalva phenomenon. Phase 4 arterial pressure overshoot is considered to be due to sympathetic reflex and also due to increased venous return, which is provided by the pooling of blood during phase 2, and now allowed to return to the thorax without impediment. The model under study differs from the Valsalva maneuver in that anesthesia is used and intrathoracic pressure is raised passively rather than actively. To simulate the Valsalva maneuver, abdominal and thoracic pressure was applied simultaneously with intrapulmonary inflation. This added mechanical factor changed the arterial pressure responses at high inflation pressure. Most strikingly, it restored phase 4 arterial pressure overshoot, which otherwise would have been absent at the inflation pressure employed. It also made phase 1 and phase 3 arterial pressure changes more evident.

It is interesting to note that paradoxical changes in the Valsalva phenomenon have also been reported in man. Bürger *et al.* (8) noted in 3 of 145 individuals presence of bradycardia instead of tachycardia in phase 2 of the Valsalva test. Dern and Fenn (9) reported that the secondary rise of blood pressure in phase 4 of the Valsalva test did not occur if the intrathoracic pressure was too high, but no specific explanation was offered.

Conclusion. Effects of varying pulmonary inflation pressure upon heart rate and arterial blood pressure were observed in anesthetized dogs. Mechanical, sympathetic and parasympathetic factors are believed to be involved in the responses observed as in the Valsalva phoenomenon. A high inflation pressure caused paradoxical bradycardia in phase 2, and a lack of arterial pressure overshoot in phase 4. From the evidences available, the bradycardia in phase 2 is interpreted as due to reflex vagal activity plus an active suppression of the sympathetic reflex. The lack of arterial pressure overshoot in phase 4 is considered to be the result of the mechanical effect of muscle relaxation due to anesthesia associated with peripheral blood pooling.

When a low pulmonary inflation pressure was employed under mild to moderate anesthesia, and when the mechanical factor caused by anesthesia was eliminated, the responses observed were quite similar to the Valsalva phenomenon in man. The preparation used in this experiment appears to provide a useful tool for the study of the cardiovascular sympathetic and parasympathetic reflex activities under various experimental hemodynamic states with or without pharmacological interventions.

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