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Research Article

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In the alpha adrenergic blockade group, vascular pressures did not increase after elevation of CSF pressure. Cardiac output increased or did not change, stroke volume increased, systemic resistance decreased, and pumonary resistance did not change.

In the beta adrenergic blockade group, the vascular pressures all increased significantly when CSF pressure was elevated, but cardiac output did not change. Systemic resistance increased and pulmonary resistance decreased. Central blood volume increased in all three groups when CSF pressure was 200 mm Hg. The data suggest that a large and distinct alpha and beta adrenergic stimulus occurred when CSF pressure was increased to 200 mm Hg.

Hemodynamic Effects of Elevated Cerebrospinal Fluid Pressure: Alterations with Adrenergic Blockade

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ABSTRACT The cardiovascular effects of elevated cerebrospinal fluid (CSF) pressure were studied in 18 dogs, 6 in a control group, 6 after alpha adrenergic blockade, and 6 after beta adrenergic blockade. Vascular pressures did not change until CSF pressure was increased from 100 mm Hg to 200 mm Hg.

In the control group, the aortic, pulmonary arterial, wedge, and right atrial pressures increased significantly. Cardiac output, heart rate, and stroke volume increased but systemic and pulmonary vascular resistances did not change.

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INTRODUCTION

The maintenance of the blood supply to the cerebrum and the medulla is one of the important functions of the circulation. Cushing (1), in 1901, found that an increased intracranial tension produced a rise in blood pressure which tended to find a level slightly above that of the pressure exerted against the medulla. The activity of the central nervous system in the regulation of blood pressure and cardiac function has been studied with varying results. Several recent reviews (2–4) discuss many facets of this regulation. Pulmonary edema and hypertension, in association with increased intracranial pressure, have been described (5, 6) but their relationships are not well understood. This study was done to better define the hemodynamic responses to elevated cerebrospinal fluid (CSF) pressure and the role of alpha and beta adrenergic receptors.

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METHODS

18 mongrel dogs were anesthetized with pentobarbital, 30 mg/kg intravenously. Cardiac catheters were placed in the main pulmonary artery, right atrium, and wedge position through the jugular veins and in the ascending aorta just distal to the aortic valve through the carotid artery. Catheter locations were confirmed fluoroscopically and by pressure contours. The wedge catheter was checked repeatedly during the procedure by attempting to aspirate blood. At the conclusion of the procedure, the wedge catheter was slowly withdrawn and the catheter tip was observed to snap out of its wedge location. Statham pressure transducers were used with an Electronics for Medicine recorder. Pressures were measured at end expiration. Heart rate was determined from an electrocardiogram. Cardiac outputs and mean transit times were determined in duplicate by the indicator-dilution technique using Indocyanine Green. Cardiac output is expressed as milliliters per minute per kilogram of body weight and stroke volume as milliliters per beat per kilogram. Central blood volume (ml/kg) was measured from the main pulmonary artery to the ascending aorta just distal to the aortic valve.

Mean pressures were used to calculate vascular resistances. Systemic vascular resistance (units) = arterial pressure − right atrial pressure (mm Hg)/cardiac output (ml/min per kg). Pulmonary vascular resistance (units) = pulmonary artery pressure − wedge pressure (mm Hg)/cardiac output (ml/min per kg). Arterial blood pH, P_{O_2}, and P_{CO_2} were determined by conventional electrodes (Instrumentation Laboratory, Inc.). Hematocrit was determined with Wintrobe tubes and blood oxygen capacity was determined spectrophotometrically by the method of Hickam and Frayser (7).

Ventilation with periodic hyperinflation was controlled through a cuffed endotracheal tube with a Harvard constant volume ventilator and end-tidal CO_2 was determined with a Beckman LB-1 analyzer. The ventilator was initially adjusted to maintain end-expired CO_2 at 5.0–5.5% and then not changed during the remainder of the study. The

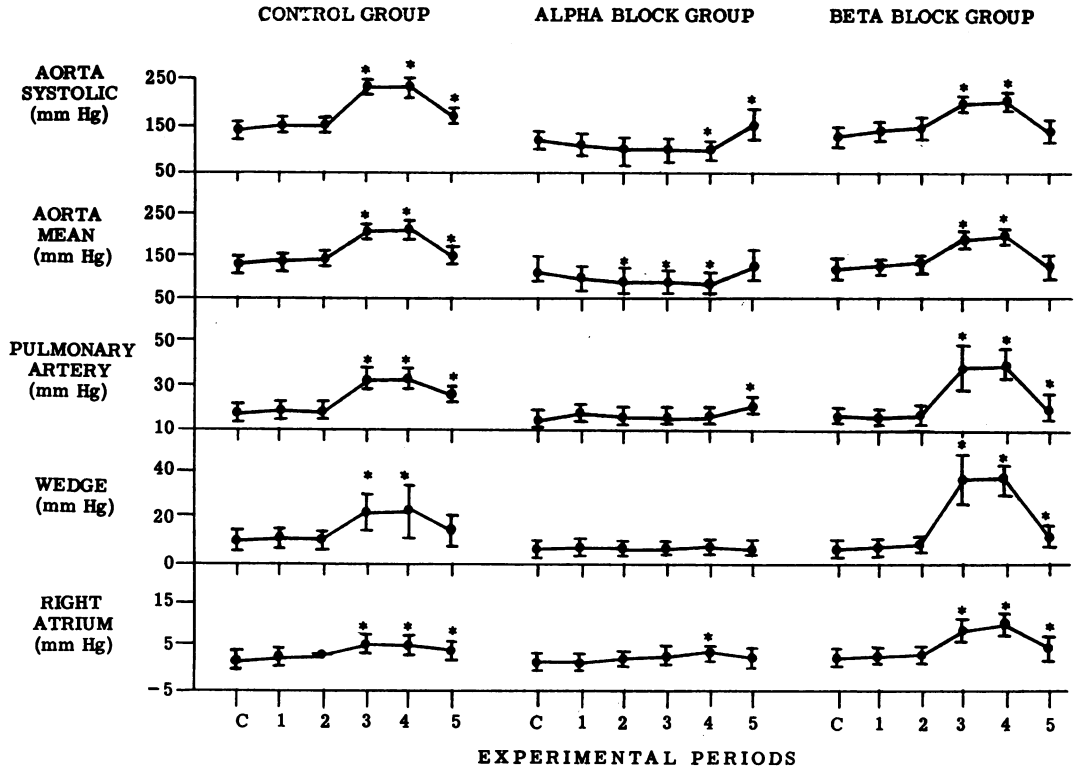

FIGURE 1 Mean ±SD of systolic aortic pressure, mean aortic pressure, pulmonary arterial pressure, pulmonary capillary (wedge) pressure, and right atrial pressure in the three groups. Experimental periods: (C), control period; (1), 5 min after elevating CSF pressure to 100 mm Hg; (2), 10 min after elevating CSF pressure to 100 mm Hg; (3), 5 min after elevating CSF pressure to 200 mm Hg; (4), 10 min after elevating CSF pressure to 200 mm Hg; (5) 10 min after CSF pressure elevation was discontinued and CSF pressure returned to control period levels. The asterisk indicates a significant ($P < 0.05$) change from the control period.

dogs were placed in the left decubitus position and paralyzed with intravenous gallamine triethiodide, 2.0 mg/kg. A No. 18 needle was percutaneously placed into the cisterna magna (8) and a free flow of clear cerebrospinal fluid indicated proper placement. Dogs with bloody spinal fluid were not used. The needle was connected to a Statham pressure transducer and the recorder. Control pressures, heart rate, cardiac output, arterial pH, and gas tensions were obtained after placement of the needle in the cistern.

Cerebrospinal fluid pressure was elevated by connecting the needle to a pressure reservoir of saline (37°C) that had been buffered with $NaHCO_3$ to pH of 7.4. Cerebrospinal fluid (CSF) pressure was monitored with a Statham pressure transducer and pressure in the saline reservoir was monitored with a mercury manometer.

After control period values were obtained, the CSF pressure was increased during a period of 1 min to 100 mm Hg and maintained for 10 min. Pressures, heart rate, and cardiac output were determined after 5 min of CSF pressure elevation and repeated with blood gas determinations after 10 min. The CSF pressure was then increased to 200 mm Hg for 10 min and the determinations repeated. The CSF pressure was then returned to normal by permitting fluid to drain from the needle. 10 min after the CSF pressure returned to control level, the previously mentioned determinations were repeated. Fluid was clear or slightly pink at the conclusion of the procedure.

There were six dogs in the control group (22 ±3 kg, mean ±SD), six dogs in the alpha adrenergic blockade group (21 ±3 kg), and six dogs in the beta adrenergic blockade group (20 ±1 kg). The alpha adrenergic blockade group received phenoxybenzamine hydrochloride (courtesy of Smith Kline & French Laboratories), 3 mg/kg in 100 ml saline intravenously over a 60 min period, before obtaining control measurements. After the study, the blockade was challenged with norepinephrine base (0.1 mg in 20 ml saline) during a 2 min period intravenously. Aortic pressure and heart rate were recorded before and after norepinephrine. The beta adrenergic blockade group received propranolol hydrochloride, 0.5 mg/kg in 30 ml saline intravenously, over a 5 min period before obtaining control measurements. Additional propranolol, 0.25 mg/kg in 30 ml saline, was continuously infused during the remainder of the study. After the study, the blockade was challenged with isoproterenol hydrochloride, 0.01 mg in 20 ml saline intravenously during a 2 min period. Aortic pressure, heart rate, and cardiac output were determined before and after the isoproterenol.

Four dogs (19 ±3 kg), not included in the previously described studies, were used to compare the direct left atrial pressure and wedge pressure. They had a left thora-

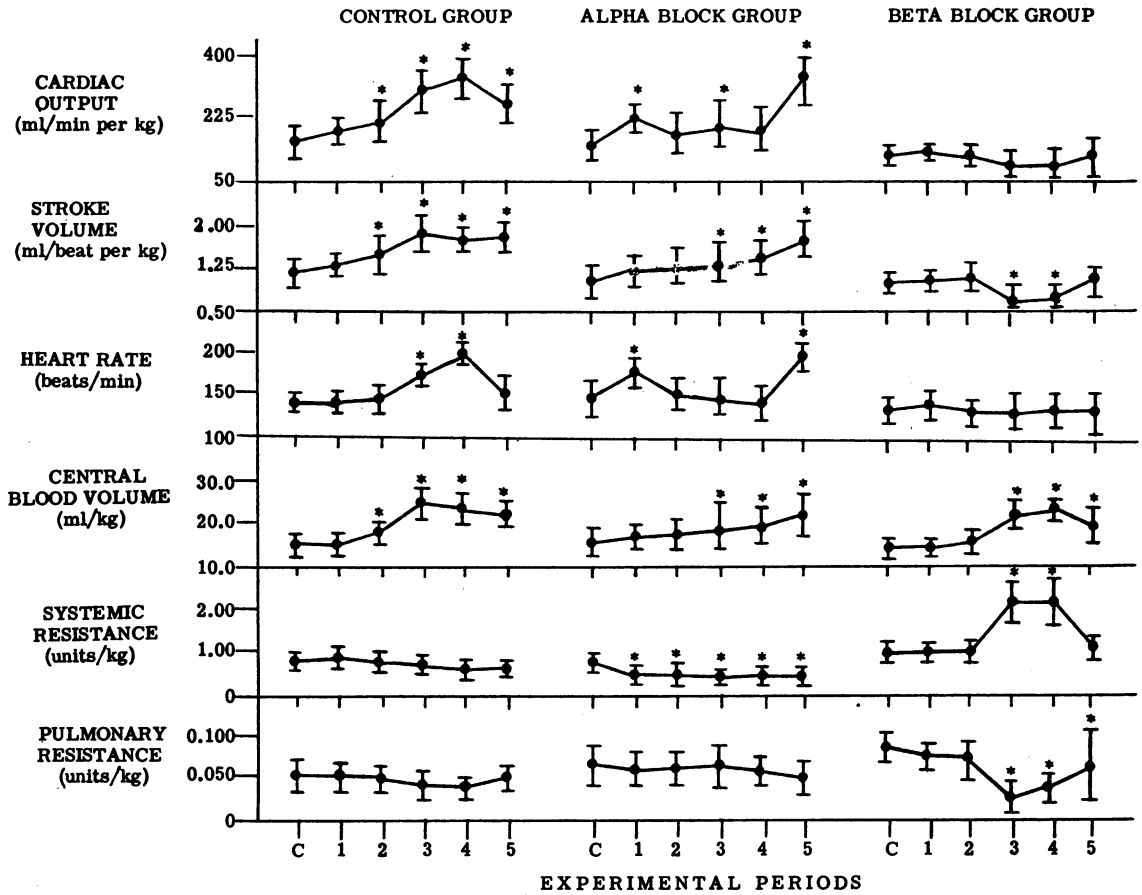

FIGURE 2 Mean ±SD of cardiac output, stroke volume, heart rate, central blood volume, systemic vascular resistance, and pulmonary vascular resistance in the three groups. Experimental periods and asterisk same as Fig. 1.

cotomy and were ventilated with 100% oxygen. A catheter was positioned in the left atrium through the atrial appendage under direct vision. Another catheter was placed through the jugular vein in the wedge position in the right lung under fluoroscopic control. Pulmonary arterial pressure and right atrial pressure were also recorded. The dogs received propranolol and the procedure was otherwise the same as the six dogs in the beta adrenergic blockade group.

In another group of four dogs (22 ±2 kg), a total of 100 ml of saline at 37°C (pH 7.4 with $NaHCO_3$) was slowly injected into the cistern in 5-ml amounts. Each 5 ml was permitted to drain out of the cistern needle before the next 5 ml was injected, so CSF pressure was not increased. The procedure required 20–25 min. Pressures, heart rate, and cardiac output were determined before and 2 and 10 min after the procedure. This was done to detect changes due to properties of the fluid independent of increased CSF pressure.

The significance of the change from the control period to each of the subsequent periods was evaluated by Dunnett's *t* test (9) at the 5% level for each of the three different groups (control, alpha blockade, and beta blockade). The variance among the three different groups was determined by Newman-Keul's test for multiple comparisons (9) at the 5% level. The comparison in the control period for the three different groups was evaluated using absolute values. The comparison among the three groups for the experimental periods after the control period was evaluated using the change from the control period. Other comparisons were made by the paired *t* test.

RESULTS

The effects of elevated CSF pressure are illustrated in Figs. 1–3. The experimental periods are: (C), control period before elevating CSF pressure; (1, 2), 5 and 10 min after elevating CSF presure to 100 mm Hg, respectively; (3, 4), 5 and 10 min after elevating CSF pressure to 200 mm Hg, respectively; and (5) 10 min after CSF pressure elevation discontinued and the CSF pressure returned to control levels.

Systolic and mean aortic pressure were increased significantly ($P < 0.05$) by elevated CSF pressures in the control group and the beta blockade group. There were no significant differences in periods 2, 3, and 4 between the increases in pressures in these two groups but both

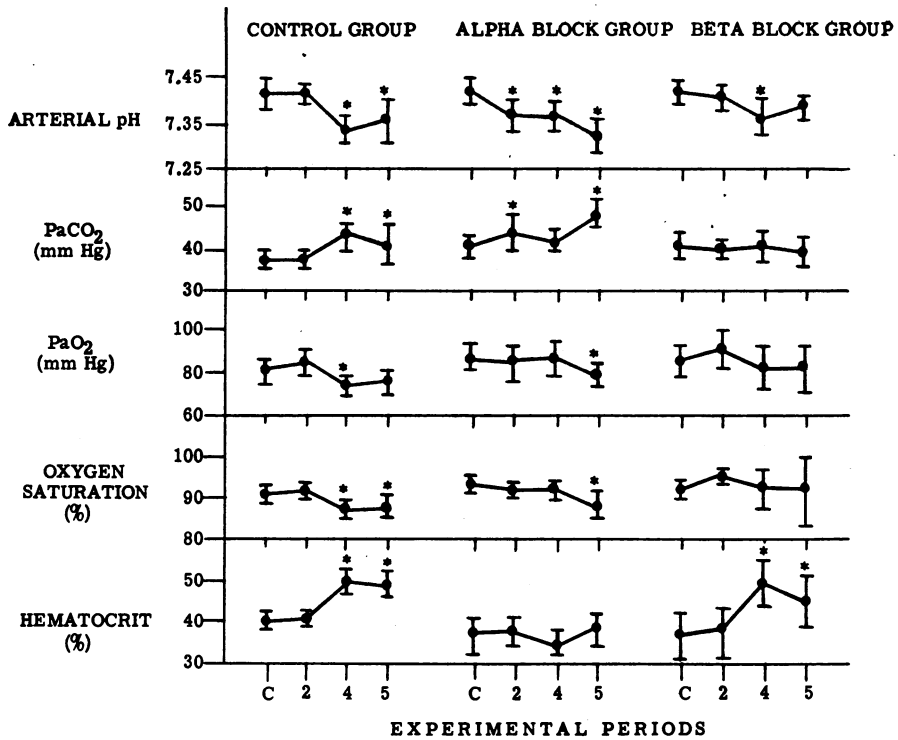

FIGURE 3 Mean ±SD of arterial pH, Pa_{CO_2}, Pa_{O_2}, oxygen saturation, and arterial hematocrit in the three groups. Experimental periods and asterisk same as Fig. 1.

groups were significantly ($P < 0.05$) different from the alpha blockade group.

Pulmonary arterial pressure and wedge pressure were increased significantly by elevated CSF pressures in the control group and the beta blockade group. The comparisons between the control group, beta blockade group, and alpha blockade group were all significantly different in periods 3 and 4.

Right atrial pressure was increased significantly by elevated CSF pressures in the control group and the beta blockade group. The beta blockade group was significantly different compared to the control group and the alpha blockade group in periods 3 and 4.

Cardiac output was increased significantly by elevated CSF pressures in the control group, but not in the beta blockade group. The control group was significantly different compared to the alpha blockade group and the beta blockade group in periods 3, 4, and 5. In periods 3 and 5, the alpha blockade group compared to the beta blockade group was significantly different.

Stroke volume was increased significantly by elevated CSF pressures in the control group and the alpha blockade group. The beta blockade group was significantly different compared to the control group and alpha blockade group in periods 3, 4, and 5.

Heart rate was increased in the control group by elevated CSF pressures, but was not changed in the beta blockade group. The control group was significantly different compared to the alpha blockade group and the beta blockade group in period 4. The alpha blockade group was significantly different compared to the control group and beta blockade group in period 5.

Central blood volume was increased significantly by elevated CSF pressures in all three groups and there were no significant differences among the three groups.

Systemic vascular resistance was decreased in the alpha blockade group and was increased in the beta blockade group with elevated CSF pressures. The beta blockade group was significantly different from the control group in periods 3 and 4 and the alpha blockade group in periods 3, 4, and 5.

The pulmonary vascular resistance was decreased significantly by elevated CSF pressures in the beta blockade group, but did not change in the other two groups. The beta blockade group was significantly different from the control group and the alpha blockade group in periods 3 and 4.

Arterial blood changes were variable. The only significant differences in pH and CO_2 tension among the three groups occurred in the alpha blockade group compared

TABLE I

Simultaneous Left Atrial and Wedge Pressures in Four Dogs with Beta Adrenergic Blockade and Elevated CSF Pressure

	Control period (C)	5 min 100 mm Hg (1)	10 min 100 mm Hg (2)	5 min 200 mm Hg (3)	10 min 200 mm Hg (4)	10 min control (5)
Left atrium, *mm Hg*	6 ±4	6 ±5	7 ±6	34 ±8	25 ±9	12 ±7
Wedge, *mm Hg*	6 ±4	7 ±5	7 ±6	34 ±8	26 ±9	11 ±7
Pulmonary artery, *mm Hg*	15 ±2	15 ±3	15 ±4	40 ±8	33 ±10	20 ±5
Right atrium, *mm Hg*	4 ±2	3 ±2	3 ±2	7 ±2	6 ±1	4 ±2

All values mean ±SD, experimental periods same as Figs. 1–3.

to the beta blockade group in period 5. There were no differences among the three groups for oxygen tension or oxygen saturation. A significant difference in the hematocrit occurred in the alpha blockade group compared to the beta blockade group and the control group in period 4.

The results in four dogs with thoracotomy, elevated CSF pressure, and propranolol are illustrated in Table I. There was no difference between the wedge pressure and direct left atrial pressure. The propranolol had been found to produce a marked increase in wedge pressure and pulmonary arterial pressure after elevation of CSF pressure. We were concerned that the elevation of pulmonary arterial pressure may have caused the wedge catheter to become temporarily unwedged, so the wedge catheter was not reflecting left atrial pressure.

The total amount of fluid (ml, mean ±SD) infused into the cistern during the 10 min of 100 mm Hg CSF pressure was 60 ±22 control group, 58 ±20 alpha blockade group, and 48 ±12 beta blockade group. The total amount of fluid (ml) infused into the cistern during the 10 min of 200 mm Hg CSF pressure was 216 ±59 control group, 203 ±36 alpha blockade group, and 182 ±50 beta blockade group. Only 10 ±2 ml was drained from CSF at end of procedure to return CSF pressure to control levels.

The norepinephrine challenge in the alpha blockade group increased aortic pressure 6 ±7 mm Hg (mean ±SD) and heart rate 2 ±3 beats per min; neither change was significant.

The isoproterenol challenge in the beta adrenergic blockade group decreased aortic pressure 1 ±3 mm Hg (NS), increased heart rate 1 ±5 beats per min (NS), and increased cardiac output 12 ±10 ml/min per kg ($P < 0.05, > 0.025$).

In the four dogs, with the 100 ml irrigation in and out of the cistern in 5-ml amounts, the CSF pressure (mm Hg) changed from 7 ±2 to 6 ±3 and 5 ±3, pulmonary arterial pressure (mm Hg) changed from 14 ±2 to 15 ±3 and 14 ±3, aortic pressure (mm Hg) changed from 140 ±11 to 147 ±12 and 140 ±14, heart rate changed from 152 ±33 to 155 ±40 and 137 ±24, and cardiac output (ml/min per kg) changed from 205 ±64 to 222 ±78 and 203 ±63 at 2 min and 10 min after completion of the irrigation. None of the changes were statistically significant.

DISCUSSION

The present study has demonstrated that elevation of the cerebrospinal fluid pressure to 200 mm Hg will result in pulmonary arterial and systemic hypertension with increased cardiac output. Alpha adrenergic blockade prevented the hypertensive response and beta adrenergic blockade prevented the increase in cardiac output. Other investigators have found a similar elevation of systemic blood pressure and pulmonary venous pressure after elevating intracranial pressure with bags, balloons (5, 6, 10, 11), and mineral oil (12). Similar hemodynamic changes can be produced by the intracisternal injection of veratrine (13, 14), kaolin (15), a thrombin-fibrinogen mixture (16–18), and the injection of aconitine in the preoptic areas (19). The mechanisms that have been suggested for these hemodynamic changes accompanying elevated intracranial pressure or intracisternal injections include: ischemia (1, 20), release of a pressor material (21), venocontriction (22, 23), a myocardial intoropic response (22), and somatic and splanchnic shunting (24).

In this study, attempts have been made to further define the hemodynamic responses to elevated CSF pressure. The three different groups demonstrated a similar increase in central blood volume. This increase in central blood volume could possibly represent a shift of blood from the systemic to the pulmonary circulation as previously described by Sarnoff and Sarnoff (17) and Sarnoff and Berglund (18). The increase in central blood volume could also result from alpha and beta adrenergic stimulation. Alpha stimulation results in an elevated left atrial pressure and passive distension of the pulmonary vascular bed whereas beta stimulation increases pulmonary blood volume by vasodilation, reenforced by a

rise in pressure secondary to increased cardiac output (25). The increase in central blood volume occurring in the alpha adrenergic blockade group is probably not due to a passive shift in blood from the systemic to the pulmonary circulation because it occurs with a decrease in systemic vascular resistance and no elevation of systemic blood pressure. A systemic venoconstriction probably did not occur as reflected by the minimal changes in right atrial pressure. The unopposed beta adrenergic stimulation apparently results in sufficient vasodilation and distension of the pulmonary blood vessels to significantly elevate the central blood volume. The change in central blood volume in the alpha adrenergic blockade group was not significantly different from the beta blockade group. The elevated systemic blood pressure and systemic vascular resistance in the beta blockade group could result in a shift of blood into the pulmonary circulation. However, this would not adequately explain the marked elevations in wedge pressure in this group. The prominent increase in the wedge pressure must reflect the unopposed alpha stimulation resulting in elevated left atrial pressure and passive distention of the pulmonary vascular bed. Alpha adrenergic stimulation may elevate left atrial pressure by decreasing compliance of the left ventricle (26). The control group probably represents a combination of alpha and beta adrenergic stimulation. It seems likely that the changes in central blood volume are more related to the effects of alpha and beta adrenergic stimulation on the myocardium and pulmonary circulation than to the effects of a large shift in blood volume from the systemic to the pulmonary circulation.

The wedge pressure, during the CSF pressure of 200 mm Hg, was significantly higher in the beta blockade group (unopposed alpha adrenergic effect) compared to the control group (alpha and beta adrenergic effects). There was no change in the wedge pressure in the alpha blockade group (unopposed beta adrenergic effect). This change in wedge pressure possibly reflects a specific alpha adrenergic effect on the left ventricle.

Some of the changes may have been the result of the adrenergic blocking agents. However, before elevating CSF pressure, only the pulmonary vascular resistance in the beta blockade group demonstrated a statistically significant difference compared to the control group. The higher wedge pressure with 200 mm Hg CSF pressure in the beta blockade group compared to the control group might represent some impairment of the myocardium. A decreased diastolic distensibility of the left ventricle in dogs after propranolol has been described (27).

The intracranial location of this pressor response has been ill defined and is not further localized by this study which is concerned with effector mechanisms. Bard (28) has reviewed some of the neural channels over which the central nervous system can influence the heart and blood vessels. The medulla, particularly the reticular formation, contains pressor areas with paramount control of the circulatory system (28, 29). Electrical stimulation of the hypothalamus produces a discharge of sympathetic outflow with vasoconstriction and rises in arterial pressure (28, 30). A number of cortical regions also yield pressor responses to local stimuli (28, 31).

Vascular pressures did not change until CSF pressure was increased from 100 to 200 mm Hg. These results could reflect pressure-sensitive areas with a threshold near systemic blood pressure or the production of disturbed cerebral perfusion and areas of cerebral ischemia. Kety, Shenkin, and Schmidt (32) also noted that in acute animal experiments the blood pressure did not begin to rise until CSF pressure approached systemic pressure. More recent work describes very localized pressure-sensitive structures in the medulla and spinal cord with thresholds for the responses close to systolic blood pressures (33). The results of our study do not answer the question about whether pressure alone is responsible for the hemodynamic changes accompanying elevated CSF pressure or whether disturbed cerebral perfusion is primarily responsible. It is possible that the fluid (saline, 37°C, pH adjusted to 7.4) which was used to elevate CSF pressure could have caused stimulation by alternations in CSF electrolytes and composition. To exclude this possibility, an irrigation with 100 ml of fluid was done through the cistern and there were significant hemodynamic changes.

All dogs survived the procedures and none developed grossly detectable pulmonary edema. The dogs in the alpha blockade group obviously survived 20 min of essentially no cerebral perfusion. Neely and Youmans (34) demonstrated that ventilated dogs could survive 25 min with the CSF pressure elevated to 400 mm Hg.

In summary, the CSF pressure was probably not effective as a stimulus until it significantly reduced cerebral perfusion. However, stimulation of some pressure-sensitive area cannot be excluded. Acute elevations of CSF pressures to 100 mm Hg had little effect and elevations to 200 mm Hg produced a profound increase in vascular pressures and cardiac output. The hemodynamic response to elevated CSF pressure was a massive alpha and beta adrenergic stimulation. The vascular pressure changes were effectively eliminated by alpha adrenergic blockade and the cardiac output changes effectively eliminated by beta adrenergic blockade.

APPENDIX

Effects of Elevated Cerebrospinal Fluid Pressure with and without Adrenergic Blockade

		Control group	Alpha block group	Beta block group	Control vs. alpha block	Control vs. beta block	Alpha vs. beta block
Aorta, systolic, *mm Hg*							
Control period	(C)	146 ±19	121 ±19	137 ±20	NS*	NS	NS
5 min, 100 mm Hg	(1)	153 ±14	112 ±26	150 ±16	NS	NS	NS
10 min, 100 mm Hg	(2)	157 ±16	101 ±28	157 ±18	0.05	NS	0.05
5 min, 200 mm Hg	(3)	244 ±10‡	102 ±18	228 ±10‡	0.05	NS	0.05
10 min, 200 mm Hg	(4)	245 ±21‡	99 ±15‡	228 ±7‡	0.05	NS	0.05
10 min, control	(5)	175 ±7‡	154 ±36‡	159 ±19	NS	NS	NS
Aorta, mean, *mm Hg*							
Control period	(C)	133 ±14	112 ±20	127 ±18	NS	NS	NS
5 min, 100 mm Hg	(1)	142 ±12	98 ±29	136 ±14	NS	NS	NS
10 min, 100 mm Hg	(2)	144 ±12	87 ±29‡	143 ±15	0.05	NS	0.05
5 min, 200 mm Hg	(3)	209 ±8‡	88 ±18‡	205 ±4‡	0.05	NS	0.05
10 min, 200 mm Hg	(4)	209 ±16‡	87 ±17‡	208 ±9‡	0.05	NS	0.05
10 min, control	(5)	156 ±7‡	131 ±31	145 ±19	NS	NS	NS
Pulmonary artery, *mm Hg*							
Control period	(C)	16 ±2	13 ±2	16 ±2	NS	NS	NS
5 min, 100 mm Hg	(1)	17 ±2	17 ±3	15 ±3	NS	NS	NS
10 min, 100 mm Hg	(2)	17 ±1	16 ±3	16 ±3	NS	NS	NS
5 min, 200 mm Hg	(3)	32 ±4‡	16 ±2	40 ±13‡	0.05	0.05	0.05
10 min, 200 mm Hg	(4)	33 ±4‡	16 ±1	41 ±5‡	0.05	0.05	0.05
10 min, control	(5)	25 ±2‡	21 ±2‡	22 ±6‡	NS	NS	NS
Wedge, *mm Hg*							
Control period	(C)	8 ±5	4 ±2	5 ±3	NS	NS	NS
5 min, 100 mm Hg	(1)	10 ±5	5 ±1	5 ±2	NS	NS	NS
10 min, 100 mm Hg	(2)	9 ±4	5 ±1	6 ±3	NS	NS	NS
5 min, 200 mm Hg	(3)	22 ±9‡	5 ±2	38 ±13‡	0.05	0.05	0.05
10 min, 200 mm Hg	(4)	22 ±12‡	6 ±2	38 ±6‡	0.05	0.05	0.05
10 min, control	(5)	13 ±7	5 ±1	15 ±4‡	NS	NS	NS
Right Atrim, *mm Hg*							
Control period	(C)	1 ±1	1 ±1	2 ±1	NS	NS	NS
5 min, 100 mm Hg	(1)	2 ±1	1 ±2	2 ±1	NS	NS	NS
10 min, 100 mm Hg	(2)	2 ±0	2 ±1	2 ±1	NS	NS	NS
5 min, 200 mm Hg	(3)	5 ±2‡	2 ±1	8 ±2‡	NS	0.05	0.05
10 min, 200 mm Hg	(4)	5 ±2‡	3 ±1‡	9 ±2‡	NS	0.05	0.05
10 min, control	(5)	4 ±2‡	2 ±2	4 ±2‡	NS	NS	NS
CSF, *mm Hg*							
Control period	(C)	9 ±2	9 ±2	9 ±2	NS	NS	NS
5 min, 100 mm Hg	(1)	103 ±6‡	100 ±3‡	97 ±9‡	NS	NS	NS
10 min, 100 mm Hg	(2)	104 ±9‡	102 ±5‡	98 ±8‡	NS	NS	NS
5 min, 200 mm Hg	(3)	204 ±7‡	198 ±3‡	200 ±11‡	NS	NS	NS
10 min, 200 mm Hg	(4)	200 ±7‡	202 ±6‡	195 ±4‡	NS	NS	NS
10 min, control	(5)	12 ±3	11 ±2	10 ±1	NS	NS	NS

Values are means ±SD. Periods are: (C), contro. period; (1, 2), 5 and 10 min after elevating CSF pressure to 100 mm Hg, respectively; (3, 4), 5 and 10 min after elevating CSF to 200 mm Hg, respectively; and (5), 10 min after CSF pressure elevation was discontinued and the CSF pressure returned to control levels.

* Comparison among the three groups comparing absolute values in the control period and comparing the change from control period in each subsequent time period. Significant at 0.05 level or not significant (NS).

‡ Change from control period to each subsequent time period for each group significant at 0.05 level, other changes not significant.

		Control group	Alpha block group	Beta block group	Control vs. alpha block	Control vs. beta block	Alpha vs. beta block
Cardiac output, *ml/min per kg*							
Control period	(C)	163 ±39	146 ±22	128 ±17	NS	NS	NS
5 min, 100 mm Hg	(1)	182 ±32	211 ±32‡	131 ±13	NS	NS	NS
10 min, 100 mm Hg	(2)	208 ±46‡	175 ±47	139 ±25	NS	NS	NS
5 min, 200 mm Hg	(3)	308 ±42‡	191 ±57‡	96 ±26	0.05	0.05	0.05
10 min, 200 mm Hg	(4)	334 ±51‡	187 ±50	104 ±33	0.05	0.05	NS
10 min, control	(5)	260 ±60‡	331 ±72‡	135 ±34	0.05	0.05	0.05
Stroke volume, *ml/beat per kg*							
Control period	(C)	1.13 ±0.26	1.01 ±0.17	0.98 ±0.12	NS	NS	NS
5 min, 100 mm Hg	(1)	1.28 ±0.24	1.20 ±0.20	0.98 ±0.12	NS	NS	NS
10 min, 100 mm Hg	(2)	1.43 ±0.30‡	1.14 ±0.27	1.07 ±0.17	NS	NS	NS
5 min, 200 mm Hg	(3)	1.76 ±0.20‡	1.29 ±0.22‡	0.73 ±0.16‡	NS	0.05	0.05
10 min, 200 mm Hg	(4)	1.71 ±0.23‡	1.36 ±0.22‡	0.77 ±0.16‡	NS	0.05	0.05
10 min, control	(5)	1.73 ±0.25‡	1.69 ±0.32‡	1.06 ±0.21	NS	0.05	0.05
Heart rate, *beats/min*							
Control period	(C)	143 ±7	146 ±21	131 ±16	NS	NS	NS
5 min, 100 mm Hg	(1)	143 ±14	178 ±21‡	135 ±18	NS	NS	NS
10 min, 100 mm Hg	(2)	146 ±14	153 ±24	130 ±16	NS	NS	NS
5 min, 200 mm Hg	(3)	175 ±12‡	145 ±23	133 ±22	NS	NS	NS
10 min, 200 mm Hg	(4)	195 ±9‡	137 ±23	135 ±26	0.05	0.05	NS
10 min, control	(5)	150 ±21	196 ±15‡	129 ±26	0.05	NS	0.05
Central blood volume, *ml/kg*							
Control period	(C)	15.6 ±2.9	15.2 ±3.3	14.5 ±1.3	NS	NS	NS
5 min, 100 mm Hg	(1)	15.6 ±2.3	17.3 ±2.8	14.8 ±1.0	NS	NS	NS
10 min, 100 mm Hg	(2)	18.1 ±3.3‡	17.5 ±3.7	15.7 ±1.7	NS	NS	NS
5 min, 200 mm Hg	(3)	24.4 ±3.9‡	18.6 ±4.9‡	22.4 ±3.1‡	NS	NS	NS
10 min, 200 mm Hg	(4)	24.0 ±3.7‡	18.8 ±4.3‡	22.7 ±3.2‡	NS	NS	NS
10 min, control	(5)	21.9 ±3.7‡	22.0 ±5.2‡	19.4 ±3.2‡	NS	NS	NS
Systemic resistance, *units/kg*							
Control period	(C)	0.837 ±0.144	0.767 ±0.144	0.977 ±0.110	NS	NS	NS
5 min, 100 mm Hg	(1)	0.787 ±0.151	0.457 ±0.130‡	1.027 ±0.125	NS	NS	NS
10 min, 100 mm Hg	(2)	0.714 ±0.177	0.488 ±0.100‡	1.035 ±0.156	NS	NS	NS
5 min, 200 mm Hg	(3)	0.678 ±0.112	0.471 ±0.111‡	2.164 ±0.529‡	NS	0.05	0.05
10 min, 200 mm Hg	(4)	0.629 ±0.138	0.469 ±0.115‡	2.062 ±0.602‡	NS	0.05	0.05
10 min, control	(5)	0.608 ±0.127	0.402 ±0.111‡	1.067 ±0.199	NS	NS	0.05
Pulmonary resistance, *units/kg*							
Control period	(C)	0.055 ±0.024	0.065 ±0.026	0.086 ±0.017	NS	0.05	NS
5 min, 100 mm Hg	(1)	0.053 ±0.020	0.056 ±0.016	0.077 ±0.015	NS	NS	NS
10 min, 100 mm Hg	(2)	0.049 ±0.016	0.065 ±0.021	0.071 ±0.020	NS	NS	NS
5 min, 200 mm Hg	(3)	0.039 ±0.018	0.066 ±0.024	0.021 ±0.016‡	NS	0.05	0.05
10 min, 200 mm Hg	(4)	0.042 ±0.018	0.063 ±0.016	0.036 ±0.017‡	NS	0.05	0.05
10 min, control	(5)	0.053 ±0.021	0.053 ±0.021	0.062 ±0.040‡	NS	NS	NS
Arterial pH							
Control period	(C)	7.42 ±0.03	7.42 ±0.03	7.42 ±0.03	NS	NS	NS
10 min, 100 mm Hg	(2)	7.42 ±0.02	7.36 ±0.04‡	7.41 ±0.03	NS	NS	NS
10 min, 200 mm Hg	(4)	7.33 ±0.03‡	7.36 ±0.03‡	7.36 ±0.03‡	NS	NS	NS
10 min, control	(5)	7.35 ±0.05‡	7.31 ±0.04‡	7.39 ±0.03	NS	NS	0.05
Arterial P_{CO_2}, *mm Hg*							
Control period	(C)	37 ±2	40 ±2	40 ±3	NS	NS	NS
10 min, 100 mm Hg	(2)	37 ±2	43 ±4‡	39 ±2	NS	NS	NS
10 min, 200 mm Hg	(4)	43 ±3‡	41 ±3	40 ±4	NS	NS	NS
10 min, control	(5)	40 ±4‡	47 ±4‡	39 ±4	NS	NS	0.05

		Control group	Alpha block group	Beta block group	Control vs. alpha block	Control vs. beta block	Alpha vs. beta block
Arterial P_{O_2}, *mm Hg*							
Control period	(C)	81 ±5	86 ±6	85 ±8	NS	NS	NS
10 min, 100 mm Hg	(2)	84 ±5	85 ±9	91 ±9	NS	NS	NS
10 min, 200 mm Hg	(4)	73 ±4‡	86 ±9	81 ±11	NS	NS	NS
10 min, control	(5)	75 ±7	78 ±6‡	81 ±14	NS	NS	NS
Oxygen saturation, %							
Control period	(C)	91 ±2	93 ±1	93 ±1	NS	NS	NS
10 min, 100 mm Hg	(2)	92 ±1	92 ±2	95 ±1	NS	NS	NS
10 min, 200 mm Hg	(4)	88 ±2‡	92 ±2	92 ±5	NS	NS	NS
10 min, control	(5)	88 ±3‡	88 ±3*	91 ±8	NS	NS	NS
Arterial hematocrit, %							
Control period	(C)	40 ±2	37 ±4	37 ±6	NS	NS	NS
10 min, 100 mm Hg	(2)	41 ±2	38 ±3	38 ±6	NS	NS	NS
10 min, 200 mm Hg	(4)	50 ±3‡	35 ±3	49 ±5‡	0.05	NS	0.05
10 min, control	(5)	49 ±3‡	39 ±3	45 ±6‡	NS	NS	NS

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