Effect of Carotid Artery Occlusion and Lung Inflation on the Main Pulmonary Artery[1] (36688)

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Supramaximal stimulation of stellate ganglia and posterior hypothalamic regions in dogs causes stiffening of large pulmonary arteries without increasing the pulmonary vascular resistance as demonstrated in lung lobes isolated and perfused *in situ* with a pulsatile pump (1, 2). When main pulmonary intra-arterial pressure and external diameter are measured simultaneously, the stiffening is reflected as a decrease in the pressure–diameter slope (3). The stiffening response is consistently abolished by pharmacologic alpha adrenergic blockade and is unaffected by both beta adrenergic and vagal efferent blockade (1–3).

The physiologic role of alpha adrenergic effects on large pulmonary arteries is uncertain. One reason for the uncertainty is that the response to direct supramaximal stimulation of sympathetic nerves might not be equivalent to the response to normally occurring and reflexly induced sympathetic efferent activity. Therefore, the present study was undertaken in order to assess whether stiffening of large pulmonary arteries occurs in response to efferent sympathetic nerve activity produced by means other than direct supramaximal stimulation.

Materials and Methods. Eleven mongrel dogs weighing between 14.1 and 23.4 kg were sedated with phencyclidine hydrochloride (Sernylan®, Parke-Davis & Co.) and anesthetized with α-chloralose (1.5 mg/kg im, and 80 mg/kg iv, respectively). Succinylcholine was infused at a rate sufficient to maintain neuromuscular blockade. The dogs were ventilated by a volume respirator (Harvard Apparatus Co.) through a cuffed endotracheal tube. The expiratory tube from the respirator was submerged under 3 cm water; the airway pressure was monitored by a lateral pressure tap in the endotracheal tube, connected to a Statham PR 23-2D-300 transducer, and tidal volume was adjusted to give airway pressures from +3 cm water at deflation to +12–15 cm water at peak inflation. Systemic arterial blood pressure was continuously monitored with a Statham P23Db strain gauge connected to a polyethylene cannula in the femoral artery.

After a left thoractomy, the left upper lobe was removed to allow access to the main pulmonary artery. The pericardium was then opened, and dissection was carefully done and kept to a minimum to preserve the innervation of the pulmonary vasculature. To record pulmonary arterial pressure, a vinyl catheter (10 cm long, i.d. 0.112 cm) was inserted into the left upper lobe arterial stump and directed toward the main pulmonary artery; pressure was determined with a Statham P23Db transducer. The end hole of the catheter was plugged, and several side holes were made near the tip. The dynamic response of the catheter manometer system was flat to at least 20 Hz.

Change in pulmonary arterial outer diameter was measured with a strain-gauge arch caliper (4) which measures displacement. The feet of the caliper were sutured securely with 5-0 silk on atraumatic needles so that the caliper spanned opposite sides of the wall of the main pulmonary artery. The caliper response was flat to 25 Hz, and its output was linear with strains encountered in these

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experiments. At the conclusion of each experiment, it was calibrated with a micrometer mounted on a bronze stand. The stability of the caliper output was checked at the conclusion of each experiment; the baseline before and after the experiment varied by not more than 0.01 cm. At the amplification used, the diameter measurement could be read to within ± 0.005 cm.

In nine dogs both carotid arteries were carefully dissected from the carotid sheath below the carotid sinuses, and soft surgical tape was passed around each artery for subsequent temporary bilateral occlusions. In two dogs the phrenic nerve was isolated in the neck, desheathed and cut distally. A bipolar platinum electrode was placed on the proximal portion of the cut nerve which was then covered with mineral oil warmed to 37°. The signal was recorded biphasically after passing through a filter of bandwidth 60–10, 000 Hz.

All data were recorded photographically with a multichannel oscillograph. The simultaneous pulmonary arterial pressure and diameter were also displayed as x–y plots on an oscilloscope and recorded photographically. The data are presented as the slopes ($\Delta D/\Delta P$) of the pressure–diameter plots, an example

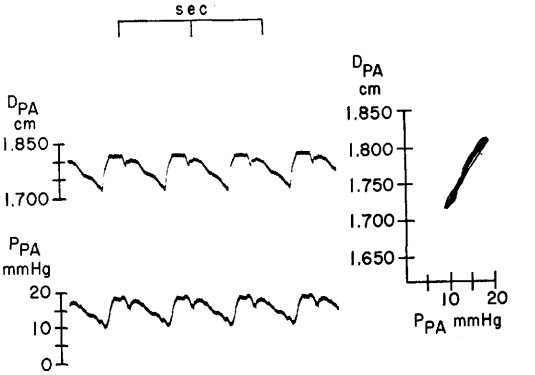

FIG. 1. Simultaneous main pulmonary arterial diameter (D_{PA}) and pressure (P_{PA}) measurements. The similarity in the two tracings is evident (left). The oscilloscopic tracing (right) of pressure–diameter relationship is linear.

of which is illustrated in Fig. 1. Each tabulated slope value represents a mean of at least ten cardiac cycles.

Phenoxybenzamine (10 mg/kg), an alpha adrenergic blocking drug, was administered to all dogs following initial measurement.

Results. Bilateral carotid artery occlusion resulted in a large decrease in $\Delta D/\Delta P$ which began in 1–2 sec as illustrated in Fig. 2. The slope changes during carotid occlusion at lung deflation are shown in Table I. The

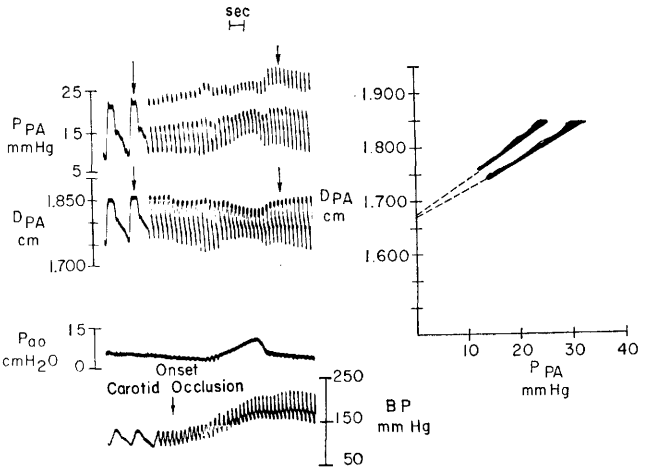

FIG. 2. The response to carotid artery occlusion is shown. The vertical arrow above the femoral arterial pressure (BP) indicates the onset of carotid occlusion which was maintained for 30 sec. The vertical arrows above pulmonary arterial pressure (P_{PA}) and diameter (D_{PA}) indicate the cycles for which the x–y plots are shown to the right. There is a large change in the pressure-diameter slope with a common extrapolated diameter intercept at zero transmural pressure. Pao represents pressure measured at the tracheal cannula.

TABLE 1. Pressure–Diameter Slopes Before and During Carotid Occlusion with the Lung at Deflation.

Experiment number	Control $\Delta D/\Delta P \times 10^{-3}$ cm/mm Hg	Carotid occlusion $\Delta D/\Delta P \times 10^{-3}$ cm/mm Hg	Percent change
1	5.8	4.1	—29
2	8.8	6.4	—27
4	10.6	8.4	—21
5	10.0	7.9	—21
6	10.7	6.6	—38
8	17.5	10.6	—40
9	16.4	9.8	—40
10	9.5	7.0	—26

decrease in $\Delta D/\Delta P$ averaged 32%. The extrapolated diameter intercept at zero pressure was unchanged which is identical to the results with stellate ganglion and hypothalamic stimulation (3).

During lung inflation in the absence of carotid occlusion the $\Delta D/\Delta P$ slope decreased with no change in the extrapolated diameter intercept at zero pressure. The slope change with inflation could be demonstrated over a range of respirator frequencies from 6/min to 30/min with tidal volume adjustments to give a relatively unchanging minute volume. Higher rates were associated, after several minutes, with inflational slope decreases on every second or third inflation. Occasionally at inflation rates of 16–18 per min the inflational slope decreases occurred on alternate pump cycles. In the two experiments in which phrenic nerve activity was measured, the slope decrease occurred only with those inflations associated with phrenic nerve efferent activity. An example is shown in Fig. 3. The $\Delta D/\Delta P$ decreases with lung inflation at a rate of 16–18 per min and at peak inflation pressures of 12–15 cm H_2O are shown in Table II. The average decrease with inflation was 18%. Between 5 and 15 min following phenoxybenzamine administration, the $\Delta D/\Delta P$ increased and did not decrease during either lung inflation or carotid occlusion. The results following phenoxybenzamine are also shown in Table II. Fig. 4 shows the $\Delta D/\Delta P$ decrease with lung inflation prior to phenoxybenzamine and the lack of $\Delta D/\Delta P$ change with lung inflation following phenoxybenzamine with a common diameter intercept for all slopes.

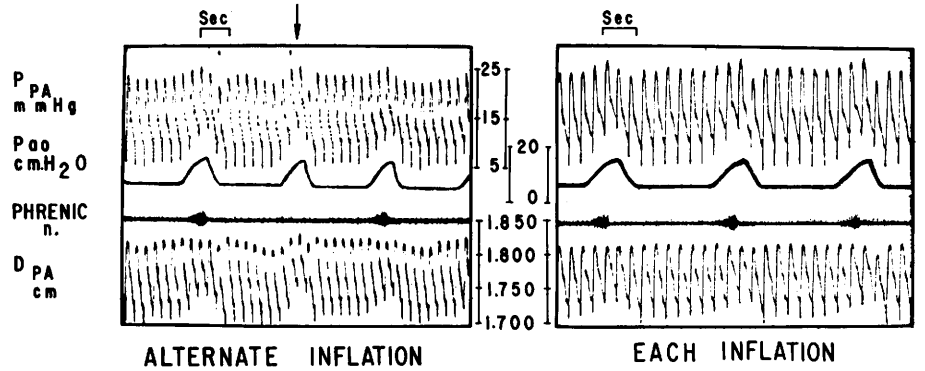

FIG. 3. Efferent phrenic nerve activity is shown in relation to lung inflation. Note that on the inflation unassociated with phrenic efferent activity (vertical arrow) diameter and pressure both increase; whereas on the inflations with phrenic efferent activity, diameter either fails to increase or actually decreases.

TABLE II. Pressure–Diameter Slope Changes with Lung Inflation Before and After Phenoxybenzamine.

	Control			After phenoxybenzamine		
Experiment number	Deflation $\Delta D/\Delta P \times 10^{-3}$ cm/mm Hg	Inflation $\Delta D/\Delta P \times 10^{-3}$ cm/mm Hg	Percent change with inflation	Deflation $\Delta D/\Delta P \times 10^{-3}$ cm/mm Hg	Inflation $\Delta D/\Delta P \times 10^{-3}$ cm/mm Hg	Percent change with inflation
1	5.8	4.6	−21	9.4	9.4	0
2	8.8	7.5	−15	14.3	15.0	+5
3	6.7	3.9	−42	7.2	7.1	−1
4	10.6	9.3	−12	11.8	11.7	−1
5	10.0	8.4	−16	13.1	12.9	−2
6	10.7	8.0	−12	16.4	16.6	+1
7	6.2	5.4	−13	13.4	13.6	+1
8	17.5	14.5	−18	21.1	21.5	+2
9	16.4	14.2	−13	17.1	17.8	+4
10	9.5	7.9	−17	10.1	10.2	+1
11	13.1	10.7	−18	14.2	14.4	+1

Discussion. Stiffening of large pulmonary arteries in response to direct sympathetic nerve stimulation has been well documented (1–3). That the sympathetic effects occur as a result of reflexly induced sympathetic efferent discharges is less well documented. The data reported by Grand and Downing suggest that reflex alpha adrenergic stiffening of large pulmonary arteries does occur (5). These authors employed a cat preparation with controlled pulsatile perfusion of the pulmonary circulation. Cerebral ischemia was induced by diverting blood from the carotid artery. This maneuver resulted in an increase in the pulmonary arterial pulse pressure without a change in mean pressure which is identical to earlier reported effects of direct sympathetic nerve stimulation in a similar dog preparation. Although the data of Grand and Downing are strongly suggestive of sympathetic efferent activity, the response was not tested following alpha adrenergic blockade. The present study clearly demonstrates that carotid occlusion stiffens the main pulmonary artery and that phenoxybenzamine blocks this effect.

The physiologic role of alpha adrenergically mediated vasomotor activity in the pulmonary circulation of the dog has been largely speculative. However, that such effects are seen with simulated defense reactions lends support to the idea that there is active neural control of the pulmonary circulation (2). The present investigation lends further support by demonstrating that large pulmonary artery stiffening occurs in response both to baroreceptor stimulation and to lung inflation when associated with phrenic nerve efferent activity.

The synchrony between sympathetic efferent effects on the pulmonary circulation and lung inflation associated with phrenic nerve efferent activity suggests a central coupling of respiratory and vasomotor neurons. Adrian *et al.* (6) and Cohen and Grootman (7) clearly demonstrated a coupling between phrenic and splanchnic sympathetic efferent nerve activities in cats. It was speculated that the coupling of the activities of the respiratory and vasomotor neurons was probably unimportant within one respiratory cycle but that the coupling might play a major coordinating role during changing physiologic conditions. The physiologic role of large pulmonary artery stiffening, however, may indeed be important within a single respiratory cycle. Intrapleural pressure-swings with breathing vary from approximately −1.0 mm Hg at end expiration to −7 mm Hg with peak inspiratory flow (8). The increase in transmural pressure with inspiration would have a distending effect on the pulmonary circulation

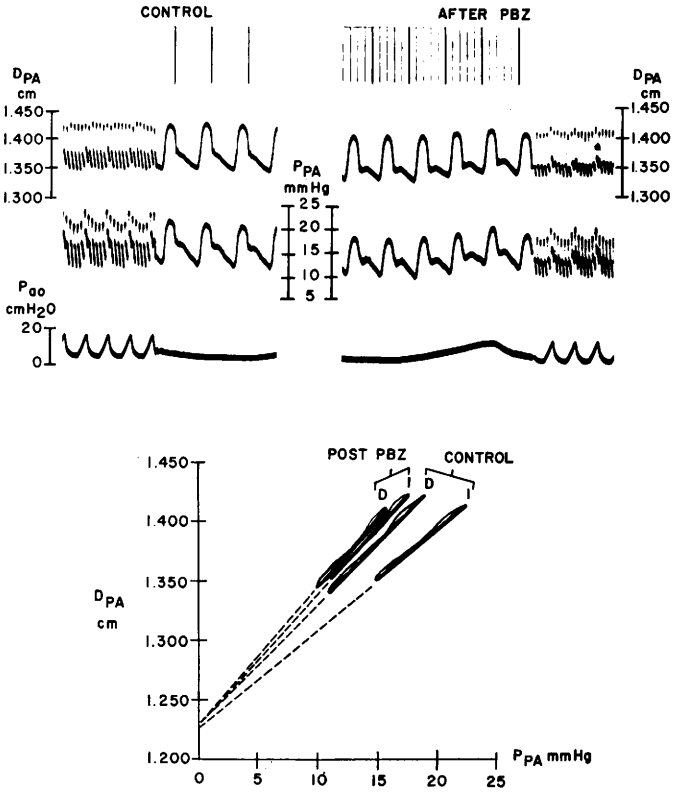

FIG. 4. The pressure–diameter relationships are shown before (left) and after (right) phenoxybenzamine (PBZ). Before PBZ, systolic diameter decreases with increases in pulmonary artery pressures during inflation. After PBZ, diameter and pressure both increase with lung inflation. The pressure–diameter slopes during deflation (D) and inflation (I) before and after PBZ are shown in the lower half of the figure.

and lead to a disparity between ventricular outputs during respiration. A decrease in left ventricular as compared to right ventricular stroke output during inspiration with a reversal during expiration would be the result. However, Yurugi *et al.* have shown in unanesthetized dogs that the ventricular outputs are in phase during the respiratory cycle and that the pulmonary blood volume change is minimal (8). The more rapid pulse wave transmission and decrease in vascular distensibility which characterize the alpha adrenergic effects on the pulmonary circulation (1) could well account for the maintenance of ventricular output balance during the respiratory cycle.

Summary. In anesthetized open-chest dogs stiffening of the main pulmonary artery reflected as a decrease in the pressure–diameter slope has been demonstrated during carotid artery occlusion and during lung inflation with associated phrenic nerve efferent activity. The response of the main pulmonary artery to both stimuli is blocked by phenoxybenzamine.

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