PROCEEDINGS OF THE SOCIETY FOR EXPERIMENTAL BIOLOGY AND MEDICINE 170, 188–193 (1982)

Effect of Carotid Body Hypoxia and/or Hypercapnia on Pulmonary Vascular Resistance (41417)

N. C. OLSON,[1] N. E. ROBINSON, D. L. ANDERSON, AND J. B. SCOTT

Department of Physiology, 111 Giltner Hall, Michigan State University, East Lansing, Michigan 48824

Abstract. The effect of carotid body hypoxia and/or hypercapnia on pulmonary vascular resistance was investigated in anesthetized open-chested dogs. The carotid bodies were perfused bilaterally with hypoxic and/or hypercapnic blood in systemically normoxic and normocapnic dogs. This was accomplished by pumping arterial autologous blood through a ventilated extracorporeal lung to the common carotid arteries. Before vagotomy, carotid body hypoxia decreased cardiac output but did not alter any pulmonary vascular parameter measured or calculated. After vagotomy, carotid body hypoxia again decreased cardiac output while pulmonary vascular resistance increased. During hypoxia–hypercapnia mean pulmonary artery and pulmonary artery pulse pressures and pulmonary vascular resistance increased. Hypercapnia caused no change in any pulmonary vascular parameter measured or calculated. Following α-blockade with phentolamine pulmonary vascular resistance failed to increase during carotid body hypoxia or hypoxia–hypercapnia. We conclude that in the vagotomized dog carotid body hypoxia and hypoxia–hypercapnia reflexly increase pulmonary vascular resistance and that this effect is mediated by α-adrenergic receptors.

The hemodynamic effects of carotid body stimulation on the systemic circulation have been well documented (1) but the role of this chemoreceptor in reflex control of the pulmonary circulation remains unsettled (2). Some investigators (3, 4) have reported that hypoxemia stimulates the peripheral chemoreceptors to reflexly increase pulmonary vascular resistance (PVR). These preparations, however, could not distinguish between carotid and aortic body stimulation. While ventilating the left lower lobe with normoxic gases during systemic hypoxemia, Szidon and Flint (5) demonstrated a decrease in left lower lobe pulmonary vascular compliance but no change in PVR as determined from pressure–volume and pressure–flow curves, respectively. In a complicated preparation Daly and Daly (6) reported increased PVR during hypoxemic perfusion of the carotid bodies but this effect was consistently found only in the absence of bronchial flow. In another study, pharmacologic stimulation of the carotid bodies with nicotine failed to increase PVR but an increase in PVR was elicited during aortic body stimulation (7) and was later shown to be both pre- and postcapillary in origin (8). The objective of this investigation was to further evaluate the effects of carotid body hypoxia and/or hypercapnia on pulmonary vascular resistance both before and after vagotomy. Physiologic stimulation of the carotid bodies was achieved by altering gas tensions of blood perfusing the carotid bodies in systemically normoxic and normocapnic dogs.

Materials and Methods. Thirty mongrel dogs of either sex weighing 22.10 ± 0.50 kg were anesthetized with sodium thiamylal (17.6 mg/kg); anesthesia was maintained with a mixture of urethane (500 mg/kg) and chloralose (75 mg/kg) given intravenously. The dogs were intubated with a cuffed endotracheal tube and placed on positive pressure ventilation with 5 cm water positive-end expiratory pressure. They were ventilated with room air supplemented with one to two liters O_2 per minute. Tidal volume and respiratory rate were sufficient to maintain systemic gas tensions and pH within normal limits. Pancuronium bromide (0.08 mg/kg) and heparin sodium (10 mg/kg) were given intravenously to paralyze the

[1] To whom correspondence should be addressed: North Carolina State University, School of Veterinary Medicine, Department of Anatomy, Physiological Sciences, and Radiology, 4700 Hillsborough Street, Raleigh, North Carolina 27606.

0037-9727/82/060188-06$01.00/0

muscles of respiration and for anticoagulation, respectively.

Polyethylene catheters were placed into the aorta via the femoral artery and into the left atrial appendage (through a median sternotomy). A 7F thermistor-tip Swan-Ganz catheter was floated into the pulmonary artery. Left atrial (as measured in its appendage), pulmonary artery, pulmonary artery wedge, and aortic pressures were measured using Statham P23Gb pressure transducers referred to the level of the left atrium. All recordings were made continuously on a Hewlett–Packard polygraph recorder. Cardiac output was measured by the thermodilution technique. Four milliliters normal saline (1–2°) was injected into the right atrium via a side port in the Swan-Ganz catheter and the mean of three to five determinations was computed as right ventricular output.

The surgical procedure for isolation of the carotid bodies has been described (1). Hypoxic and/or hypercapnic stimulation of the carotid bodies was achieved by pumping arterial autologous blood through a ventilated extracorporeal lung (ECL) circuit that has also been described previously (1). Briefly, a lung was obtained from a donor dog which, approximately one hour prior to anesthesia, was given 300 mg aspirin intravenously to block prostaglandin synthesis that may occur in hypoxic lungs (9). Blood was pumped from the right femoral artery of the experimental animal into the pulmonary artery of the ECL at a rate sufficient to maintain its mean pulmonary venous pressure at 5 mm Hg. A second pump delivered this perfusate from the ECL, through a 38° water bath, and then to the cannulated common carotid arteries. Blood flow was maintained constant (100 to 125 ml/min) as was perfusion pressure. The latter was set equal to mean arterial pressure and was accomplished by adjusting outflow resistance by means of a screw clamp. The effluent perfusate was collected from the external carotid arteries and returned to the dog via the right femoral vein. The carotid sinus nerves were assumed to be functionally intact if, during temporary changes in carotid sinus perfusion pressure, mean arterial pressure changed in an opposite direction and if movement of respiratory muscles occurred (before neuromuscular blockade) out of phase with mechanical ventilation during hypoxemic stimulation of the carotid bodies.

The ECL was ventilated at a tidal volume of 500 ml and rate of 12 strokes/minute with the following: (i) a control gas mixture containing 15% O_2, 5% CO_2, 80% N_2; (ii) a hypoxic mixture containing 0% O_2, 5% CO_2, 95% N_2; (iii) a hypercapnic mixture containing 15% O_2, 15% CO_2, 70% N_2, and (iv) a hypoxic–hypercapnic mixture containing 0% O_2, 15% CO_2, 85% N_2. The ECL was ventilated with hypoxic, hypercapnic, or hypoxic–hypercapnic gas mixture for 5 min; each test gas was preceded by a ventilation period with the control gas mixture for at least 5 min. Sixty-two paired treatments were made on 30 dogs. With the vagi intact the ECL was ventilated with the hypoxic gas mixture ($N = 12$). Following vagotomy the ECL was ventilated with hypoxic ($N = 10$), hypercapnic ($N = 13$), or hypoxic–hypercapnic ($N = 10$) gas mixtures. The purpose of vagotomy was to eliminate buffering effects of the aortic baroreceptors and cardiac stretch receptors on the cardiovascular system (1).

In a separate set of experiments, after vagotomy, phentolamine (1 mg/kg) was infused as a slow iv bolus to block α-adrenergic receptors during carotid body hypoxia ($N = 7$) and hypoxia–hypercapnia ($N = 10$). An α agonist, phenylephrine (100 μg), was given iv as a bolus both before and after phentolamine. Adequate blockade was assumed when the response (i.e., increased P_{MA} and $\bar{P}_{PA}$) to the agonist given before α blockade was abolished after α blockade. In all experiments carotid sinus perfusion and pulse pressures were constant between control and test gas period.

Total pulmonary (PVR_T), pre-large venous (PVR_P), and venous resistances (PVR_V) were calculated by dividing the appropriate pressure gradient by cardiac output as follows: $(\bar{P}_{PA} - P_{LA}) / \dot{Q} = PVR_T$, $(\bar{P}_{PA} - P_{PAW}) / \dot{Q} = PVR_P$, and $(P_{PAW} - P_{LA}) / \dot{Q} = PVR_V$, where $\bar{P}_{PA}$ equals mean pulmonary artery pressure, P_{LA} equals left

atrial pressure, P_{PAW} equals pulmonary artery wedge pressure, $\dot{Q}$ equals cardiac output. The P_{PAW} represents downstream pressure at the point of the first postcapillary collateral venous vessel (10). Therefore, PVR_P represented resistance proximal to the point of the first collateral venous vessel and PVR_V represented resistance distal to the point of the first collateral venous vessel. Total peripheral resistance (TPR) was calculated by dividing $P_{MA} / \dot{Q}$, where P_{MA} equals mean arterial pressure.

Statistical analyses were performed using two-way analysis of variance (ANOVA) with comparison between paired means based on Student-Newman-Keuls' test. Data are expressed as mean ± standard error (SE). Treatment means were considered significantly different at $P < 0.05$.

Results. The use of the ECL permitted rapid changes in blood gas tensions of arterial blood supplying the carotid bodies while systemic gas tensions and pH were maintained within the normal range.

Table I shows the effects of carotid body hypoxia, before vagotomy, in which perfusate PO_2 was reduced from 96 to 23 Torr. Cardiac output decreased 10% and TPR increased 12%. None of the other measured or calculated variables changed.

TABLE I. EFFECT OF CAROTID BODY HYPOXIA BEFORE VAGOTOMY

	Control	Hypoxia	SE
PO_2 (Torr)	96	23	3.30*
PCO_2 (Torr)	33	33	1.00
pH	7.37	7.39	0.01
$P_{\overline{PA}}$ (mm Hg)	12.3	11.9	0.10
P_{PAW} (mm Hg)	4.9	4.8	0.10
P_{LA} (mm Hg)	2.7	2.7	0.10
P_{PAP} (mm Hg)	9.1	8.6	0.30
PVR_T (mm Hg/L/min)	4.70	5.04	0.20
PVR_P (mm Hg/L/min)	3.63	3.88	0.10
PVR_V (mm Hg/L/min)	1.07	1.16	0.10
$\dot{Q}$ (L/min)	2.09	1.89	0.06*
P_{MA} (mm Hg)	110	112	2.20
TPR (mm Hg/L/min)	54.9	61.7	1.90*

Note. $N = 12$. Values are means ± standard error (SE) based on error mean square from ANOVA. $P_{\overline{PA}}$, mean pulmonary artery pressure; P_{PAW}, pulmonary artery wedge pressure, P_{LA}, left atrial pressure; P_{PAP}, pulmonary artery pulse pressure; PVR_T, total pulmonary vascular resistance; PVR_P, pre-large venous pulmonary vascular resistance; PVR_V, venous pulmonary vascular resistance; $\dot{Q}$, cardiac output; P_{MA}, mean arterial pressure; TPR, total peripheral resistance.

* Significantly different from control at $P < 0.05$.

Table II shows the effects of carotid body hypoxia and hypoxia-hypercapnia following vagotomy. During hypoxia perfusate PO_2 decreased from 100 to 22 Torr. Total pulmonary vascular resistance, PVR_P, P_{MA}, and TPR increased 21, 26, 21 and 40%, respectively. Cardiac output decreased 12% while heart rate decreased from 172 to 161 beats/min (SE = 1.90). All other measured or calculated variables did not change. During hypoxia-hypercapnia, perfusate PO_2 decreased from 112 to 20 Torr, PCO_2 increased from 38 to 72 Torr, and pH decreased from 7.38 to 7.20. Pulmonary artery pulse pressure, $P_{\overline{PA}}$, PVR_T, PVR_P, P_{MA}, and TPR increased 17, 10, 14, 14, 46, and 42%, respectively. None of the other measured or calculated variables changed.

During hypercapnia perfusate PCO_2 increased from 38 to 83 Torr (SE = 2.30) and pH decreased from 7.36 to 7.10 (SE = 0.01). Mean arterial pressure increased from 79 to 90 mm Hg (SE = 1.90) while TPR increased from 40.9 to 49.5 mm Hg/liter/min (SE = 1.50). None of the other measured or calculated variables changed.

Table III shows the effects of carotid body hypoxia and hypoxia-hypercapnia following vagotomy and α blockade with phentolamine. Under these conditions carotid body hypoxia and hypoxia-hypercapnia failed to increase PVR_T and PVR_P. During hypoxia P_{MA} increased and during hypoxia-hypercapnia $\dot{Q}$, TPR, and P_{MA} increased.

Discussion. These data demonstrate that hypoxic and hypoxic-hypercapnic blood perfusing the carotid bodies can reflexly cause a small increase in PVR_T in vagotomized dogs. Increased PVR_T observed with hypoxia or hypoxia-hypercapnia was pre-large vein in origin and although precapillary vessels are the most likely sites of increased resistance, venules and small pulmonary veins cannot be ruled out because PVR_P includes the resistance of all vessels upstream from the first postcapillary collateral venous vessel. The increases

TABLE II. EFFECT OF CAROTID BODY HYPOXIA AND HYPOXIA–HYPERCAPNIA FOLLOWING VAGOTOMY

	Control	Hypoxia	SE	Control	Hypoxia–hypercapnia	SE
PO_2 (Torr)	100	22	4.60*	112	20	4.90*
PCO_2 (Torr)	35	36	1.00	38	72	2.90*
pH	7.35	7.37	0.01	7.38	7.20	0.01*
$P_{\overline{PA}}$ (mm Hg)	11.7	12.1	0.20	12.6	13.9	0.20*
P_{PAW} (mm Hg)	5.0	4.8	0.10	4.5	4.5	0.20
P_{LA} (mm Hg)	2.2	2.1	0.10	1.9	1.7	0.10
P_{PAP} (mm Hg)	9.4	9.5	0.30	9.8	11.5	0.20*
PVR_T (mm Hg/L/min)	4.66	5.63	0.20*	5.09	5.78	0.20*
PVR_P (mm Hg/L/min)	3.27	4.13	0.20*	3.83	4.36	0.10*
PVR_V (mm Hg/L/min)	1.39	1.50	0.10	1.26	1.42	0.20
$\dot{Q}$ (L/min)	2.19	1.93	0.04*	2.22	2.33	0.07
P_{MA} (mm Hg)	102	123	3.70*	74	108	4.50*
TPR (mm Hg/L/min)	48.3	67.8	3.40*	35.8	50.9	2.30*

Note. $N = 10$. Values are means ± standard error (SE) based on error mean square from ANOVA. $P_{\overline{PA}}$, mean pulmonary artery pressure; P_{PAW}, pulmonary artery wedge pressure, P_{LA}, left atrial pressure; P_{PAP}, pulmonary artery pulse pressure; PVR_T, total pulmonary vascular resistance; PVR_P, pre-large venous pulmonary vascular resistance; PVR_V, venous pulmonary vascular resistance; $\dot{Q}$, cardiac output; P_{MA}, mean arterial pressure; TPR, total peripheral resistance.

* Significantly different from control at $P < 0.05$.

in resistance must have resulted from active vasoconstriction because they cannot be explained by the passive effects of vascular transmural pressure. During hypoxia average prevenous vascular transmural pressure [i.e., $(P_{\overline{PA}} + P_{PAW})/2$] was unchanged from control (8.3 to 8.4 mm Hg) despite decreased $\dot{Q}$ and during hypoxia–hypercapnia it increased above control (8.5 to 9.2 mm Hg) without a change in $\dot{Q}$.

TABLE III. EFFECT OF CAROTID BODY HYPOXIA AND HYPOXIA–HYPERCAPNIA FOLLOWING VAGOTOMY AND α BLOCKADE

	Control	Hypoxia[a]	SE	Control	Hypoxia–hypercapnia[b]	SE
PO_2 (Torr)	104	25	3.30*	101	29	3.50*
PCO_2 (Torr)	43	40	1.60	38	76	1.50*
pH	7.40	7.40	0.01	7.37	7.11	0.01*
$P_{\overline{PA}}$ (mm Hg)	13.0	14.1	0.40	13.7	14.8	0.40
P_{PAW} (mm Hg)	6.0	6.4	0.20	5.4	5.4	0.10
P_{LA} (mm Hg)	2.8	2.9	0.30	2.0	2.1	0.20
P_{PAP} (mm Hg)	11.0	12.1	0.50	11.8	12.2	0.30
PVR_T (mm Hg/L/min)	7.91	7.36	0.30	8.67	8.18	0.20
PVR_P (mm Hg/L/min)	5.38	4.98	0.20	6.14	5.95	0.20
PVR_V (mm Hg/L/min)	2.53	2.38	0.20	2.53	2.23	0.10
$\dot{Q}$ (L/min)	1.41	1.82	0.14	1.45	1.76	0.09*
P_{MA} (mm Hg)	50	81	6.20*	54	87	6.30*
TPR (mm Hg/L/min)	37.6	50.3	4.20	40.0	53.7	2.90*

Note. Values are means ± standard error (SE) based on error mean square from ANOVA. $P_{\overline{PA}}$, mean pulmonary artery pressure; P_{PAW}, pulmonary artery wedge pressure, P_{LA}, left atrial pressure; P_{PAP}, pulmonary artery pulse pressure; PVR_T, total pulmonary vascular resistance; PVR_P, pre-large venous pulmonary vascular resistance; PVR_V, venous pulmonary vascular resistance; $\dot{Q}$, cardiac output; P_{MA}, mean arterial pressure; TPR, total peripheral resistance.

[a] $N = 7$.

[b] $N = 10$.

* Significantly different from control at $P < 0.05$.

The passive effects of increased transmural pressure would act to increase vessel diameter and decrease PVR_T (10) and this is the likely explanation for a lesser increase in PVR_T during hypoxia–hypercapnia than during hypoxia.

The increased PVR_T during carotid body hypoxia and hypoxia–hypercapnia agrees with the findings of other investigators (3, 4, 6). However, Daly and Daly (6) reported that increased PVR_T during carotid body hypoxia in a nonvagotomized preparation only occurred consistently in the absence of bronchial flow. They concluded the primary effect of carotid body hypoxia was to increase PVR_T but that this effect was masked by hemodynamic events associated with the bronchial circulation. Despite an intact bronchial circulation in our preparation PVR_T increased during hypoxia and hypoxia–hypercapnia but only after bilateral cervical vagotomy. Thus, it appears that vagotomy (which eliminates vagal afferent inhibition of central sympathetic outflow) might be a more important factor in eliciting increased PVR_T during carotid body hypoxia and hypoxia–hypercapnia than is exclusion of the bronchial circulation. Furthermore, Bruner and Schmidt (11) reported that approximately 1% of the $\dot{Q}$ drains into the pulmonary veins from the bronchial circulation. This small amount of flow negligibly affects the PVR values. In addition, results of more recent investigations involving changes in PVR (12) or vascular compliance (13) during electrical stimulation of stellate ganglion were not significantly different whether the bronchial circulation was intact or not. Thus, we believe an intact bronchial circulation in our preparation was of little or no consequence.

It is well known that changes in lung volume and active movement of respiratory muscles may passively influence PVR (6, 10). We minimized these factors by: (i) ventilating at constant volume, rate, and end-expiratory pressure; (ii) paralyzing the respiratory muscles; (iii) opening the thorax. It is unlikely local alveolar hypoxia caused the observed increases in PVR since P_aO_2 was unchanged from control values during carotid body stimulation (both > 100 Torr).

Since sympathetic innervation to the pulmonary vasculature has been clearly demonstrated (14), with α receptors predominating (15), it is likely that the increased PVR_T and PVR_P observed before α blockade was due to activation of α-adrenergic receptors either through stimulation of sympathetic nerves to the pulmonary circulation or release of catecholamines from the adrenal gland (16). This conclusion is supported by the fact that following α blockade with phentolamine, carotid body hypoxia and hypoxia–hypercapnia failed to increase PVR_T and PVR_P. However, it must be recognized that baseline PVR_T was greater in the α block compared to the non-α block control groups and this could have masked any further vasoconstriction during carotid body hypoxia and hypoxia–hypercapnia.

During hypoxic–hypercapnic stimulation of the carotid bodies an increased pulmonary artery pulse pressure was observed (without a significant change in stroke volume). This effect was also blocked by phentolamine suggesting that carotid body stimulation is capable of reflexly decreasing compliance of pulmonary vessels, an effect that has been previously reported (5).

Despite complete α blockade (as determined from blood pressure recordings) to an α agonist administered intravenously, an attenuated increase ($P < 0.05$) in TPR still occurred during hypoxia–hypercapnia. This is consistent with the concept that α-adrenergic antagonists are generally more effective in blocking responses to circulating α agonists than those resulting from adrenergic nerve activity (17).

The decreased $\dot{Q}$ during carotid body hypoxia, under conditions of controlled ventilation and intact vagus nerves, has been reported by other investigators (18, 19). This investigation demonstrates a similar decrease following vagotomy and suggests that the decrease in $\dot{Q}$ during carotid body hypoxia is due to withdrawal of sympathetic tone to the heart rather than increased vagal outflow. Although hypothesizing sympathetic withdrawal from the heart while the vasculature receives increased sympathetic tone is difficult to reconcile teleologically, this has been

previously reported. In vagotomized dogs, Downing *et al.*, (19) found a general sympathetic withdrawal from the heart and increased sympathetic tone to the vasculature during carotid body stimulation with hypoxic blood. Their evidence for this was increased TPR, decreased atrial and ventricular contractility, and decreased heart rate.

The authors are grateful for the technical assistance of Mr. William Stoffs. This work was supported in part by National Institutes of Health Grants 1F32HL05923 and HL10879.

1. Parker PE, Dabney JM, Scott JB, Haddy FJ. Reflex vascular responses in kidney, ileum, and forelimb to carotid body stimulation. Amer J Physiol **228**:46–51, 1975.
2. Downing SE, Lee JC. Nervous control of the pulmonary circulation. In: Edelman IS, ed. Annual Review of Physiology. Palo Alto, Calif: Annual Reviews, Vol 42:pp199–210, 1980.
3. Aviado DM Jr, Ling JS, Schmidt CF. Effects of anoxia on pulmonary circulation: Reflex pulmonary vasoconstriction. Amer J Physiol **189**:253–262, 1957.
4. Wilcox BR, Austen WG, Bender HW. Effect of hypoxia on pulmonary artery pressure of dogs. Amer J Physiol **207**:1314–1318, 1964.
5. Szidon JP, Flint JF. Significance of sympathetic innervation of pulmonary vessels in response to acute hypoxia. J Appl Physiol **43**:65–71, 1977.
6. Daly IdeB, Daly MdeB. The effects of stimulation of the carotid body chemoreceptors on the pulmonary vascular bed in the dog: The 'vasosensory controlled perfused living animal' preparation. J Physiol (London) **148**:201–219, 1959.
7. Stern S, Ferguson RE, Rapaport E. Reflex pulmonary vasoconstriction due to stimulation of the aortic body by nicotine. Amer J Physiol **206**:1189–1195, 1964.
8. Stern S, Braun K. Effect of chemoreceptor stimulation on the pulmonary veins. Amer J Physiol **210**:535–539, 1966.
9. Said SI, Yoshida T, Kitamura S, Vreim C. Pulmonary alveolar hypoxia: Release of prostaglandins and other humoral mediators. Science **185**: 1181–1183, 1974.
10. Fishman AP. Dynamics of the pulmonary circulation. In: Hamilton WF, Dow P, eds. Handbook of Physiology–Circulation. Washington DC, Amer Physiol Soc, Vol 2:pp1667–1743, 1963.
11. Bruner HD, Schmidt CF. Blood flow in the bronchial artery of the anesthetized dog. Amer J Physiol **148**:648–666, 1947.
12. Kadowitz PJ, Hyman AL. Effect of sympathetic nerve stimulation on pulmonary vascular resistance in the dog. Circ Res **32**:221–227, 1973.
13. Ingram RH, Szidon JP, Skalak R, Fishman AP. Effects of sympathetic nerve stimulation on the pulmonary arterial tree of the isolated lobe perfused in situ. Circ Res **22**:801–815, 1968.
14. Hebb C. Motor innervation of the pulmonary blood vessels of mammals. In: Fishman AP, Hecht HH, eds. The Pulmonary Circulation and Interstitial Space. Chicago, Univ of Chicago Press, pp195–222, 1969.
15. Bergofsky EH. Humoral control of the pulmonary circulation. In: Edelman IS, ed. Annual Review of Physiology. Palo Alto, Calif, Annual Reviews, Vol 42:pp221–233, 1980.
16. Anichkov SV, Malyghina EI, Poskalenko AN, Ryzhenkov VE. Reflexes from carotid bodies upon the adrenals. Arch Int Pharmacodyn **79**:156–165, 1960.
17. Nickerson M, Collier B. Drugs inhibiting adrenergic nerves and structures innervated by them. In: Goodman LS, Gilman A, eds. The Pharmacological Basis of Therapeutics. New York, MacMillan, 5th ed, pp533–564, 1975.
18. Daly MdeB, Scott MJ. The cardiovascular responses to stimulation of the carotid body chemoreceptors in the dog. J Physiol (London) **165**:179–197, 1963.
19. Downing SE, Remensnyder JP, Mitchell JH. Cardiovascular responses to hypoxic stimulation of the carotid bodies. Circ Res **10**:676–685, 1962.

Received November 9, 1981. P.S.E.B.M. 1982, Vol. 170.