Ventilatory response to transient perfusion of carotid chemoreceptors

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Since soon after the discovery by J. F. and C. Heymans in 1927-1930 of the carotid and aortic chemoreceptors, controversy has existed regarding their relative contribution to the control of resting ventilation at sea level and their sensitivity to small changes in Po2, Pco2, and pH. C. Heymans and colleagues concluded early that the peripheral chemoreceptors contributed actively to ventilation during normoxia at rest (16), but Schmidt and Comroe (33) believed that the role of the peripheral chemoreceptors was to meet hypoxic or asphyctic emergencies. There has been much evidence to support both views, as ably reviewed by Ileymans and Neil (17) and by Dejours (7). Part of the controversy may have originated from limitations in two of the methods traditionally used to study the chemical regulation of respiration. Dejours has pointed out that with the “steady-state” method whereby ventilation is measured after several minutes of breathing a given gas mixture, the response may be modified by secondary effects. For example, when breathing pure O2, less reduced hemoglobin is present in capillary blood to buffer the hydrogen ions from carbonic acid, causing the acidity of the respiratory centers to increase. The second traditional method, involving measurement of action potentials from the peripheral chemoreceptors, tests their responses but not their actual effects on ventilation.

These complications are largely avoided by the ingenious unsteady-state technique devised and perfected by Dejours and his colleagues (8, 9), which involves determining the transient effect on respiratory minute volume of one or two breaths of pure O2, of a CO2 mixture, or of pure N2. Evidence for a tonic ventilatory drive for O2 in unanesthetized human subjects breathing air at rest at sea level was provided by the finding that ventilation was transiently decreased 12% by a single breath of O2, no such reduction occurring when the subjects breathed 33% O2 previously. Marked sensitivity of the peripheral chemoreceptors to CO2 was demonstrated in unanesthetized man and in both anesthetized and unanesthetized dogs. In the latter a 20-30% transient increase in ventilation followed two breaths of 6% CO2 in 35% O2, only a 6% delayed increase occurring after chemodenervation (4).

Intrigued by Dejours’ method, we decided to modify it so as to permit determination of the effect on ventilation of a transient infusion of blood of known Po2, Pco2, and pH into the common carotid arteries and thence to the carotid bodies, blood flow from below being temporarily cut off.
METHODS

Dogs weighing from 12 to 20 kg were anesthetized with pentobarbital sodium (26 mg/kg). One femoral artery and vena cava were catheterized in order to allow blood to flow at certain times through an extracorporeal system for measuring pH, \( \text{Paco}_2 \), and \( \text{Pao}_2 \). A second venous catheter was used for renewing anesthesia. A midline incision was made in the neck for the insertion of a tracheal cannula and exposure of both common carotid arteries. A pneumotachograph (model 00, Instrumentation Associates, Inc.) and a differential pressure transducer (model PT-5, Grass Instrument Co.) were used to measure airflow. The airflow during expiration was integrated (unit integrator, model UI-I-A and integrator preamplifier, model 5U-2A, Grass Instrument Co.) to give tidal volume (\( V_T \)). End-tidal \( \text{Paco}_2 \) was measured by infrared analyzer (Beckman Instruments, Inc., Spinco Division). These three parameters and blood pressures measured by strain gauges (Statham model P23AC) at three sites as described below were recorded on a six-channel Grass polygraph. To obtain breath by breath \( V_T \) as used by Dejours, the \( V_T \) of each breath was multiplied by the reciprocal of the period of a given respiratory cycle.

For infusing blood transiently into the carotid arteries three-way stopcocks were placed in series with each common carotid artery as shown in Fig. 1. Syringes held at body temperature by means of water jackets were connected to the stopcocks by water-jacketed catheters. A side arm at the rostral end of each stopcock was provided for monitoring blood pressure in each carotid artery. The effects of the infusion procedure on systemic blood pressure were determined by measuring femoral artery pressure.

Two types of infusion were used alternately, the control infusion in which blood from a femoral artery was drawn directly into the syringes, and the experimental infusion in which the blood was specially modified before being placed in the syringes. An infusion was carried out as follows: After respiration had been recorded for a control period of 40 sec the stopcocks were turned, stopping flow from below, and blood from the syringes was pushed into the carotid arteries in a rostral direction. In order to minimize the influence of the pressoreceptors on respiration a pulsatile force was manually applied to both syringe plungers by two operators so as to provide pressures approximating the systolic and diastolic pressures existing in the carotid arteries prior to infusion. The pulsations in pressure, which were monitored on the polygraph as shown in Figs. 1 and 2, were made to occur at essentially the same rate as the heartbeat. In spite of the development of a certain skill in this technique, some pressoreceptor influence on respiration persisted, as manifested by a reduction of approximately 5% in the breath-by-breath \( V_T \) during a control infusion. Part of the effect may have been caused by the action of a rise in systemic (femoral) blood pressure (as seen in Fig. 2, resulting from the infusion of blood) upon the aortic pressoreceptors.

Arterial blood was modified for the experimental infusion by placing it in a rotating tonometer kept at the animal’s body temperature, through which warmed, humidified gases of desired composition were passed for approximately 3 min. The blood was then placed in the water-jacketed syringes and, after a control period of 40 sec, was infused. In later experiments, the water-jacketed catheters were filled with blood up to the stopcocks. Just before the blood was infused, the \( \text{Paco}_2 \), \( \text{Pao}_2 \), and pH of a sample of arterial blood were measured by

![Fig. 1. Experimental setup for transient perfusion of the carotid bodies by infusing blood of known \( \text{Paco}_2 \), pH, and \( \text{Pao}_2 \) into the common carotid arteries via three-way stopcocks, while stopping blood flow from below. Simulated polygraph record shows transient decrease produced by infusion of hypocapnic, hyperoxic blood (which reduces carotid chemoreceptor drive) in airflow (measured by pneumotachograph) and in tidal volume (integrated airflow) and corresponding rise in end-tidal \( \text{Paco}_2 \) (measured by infrared analyzer). Breath-by-breath respiratory minute volume (\( V_T \)) is calculated by multiplying \( V_T \) by \( 1/period \) of respiratory cycle. DPC = differential pressure gauge for pneumotachograph; SG = strain gauge for blood pressure.](http://ajplegacy.physiology.org/attachment.php/ajplegacy/59/4/1306/F1.jpg)

![Fig. 2. Record illustrating how by manual pulsing of infusion syringes systolic and diastolic carotid blood pressures existing prior to infusion (carried out between dashed vertical lines) are mimicked, and at rates approximating pulse rate. Pressoreceptor effects on respiration are thereby minimized. Hypocapnic, hyperoxic blood was infused, with decrease in \( V_T \) and respiratory frequency resulting.](http://ajplegacy.physiology.org/attachment.php/ajplegacy/59/4/1306/F2.jpg)
means of a Severinghaus PO_{2} electrode (National Welding Equipment Co.), and by a Beckman PO_{2} electrode (model 31550, Beckman Instruments, Inc., Spinco Division) and a pH electrode (model 46850, Beckman Instruments, Inc., Scientific and Process Instruments Division). PO_{2}, PO_{2}, and pH of the infused blood (referred to henceforth as PinfCO_{2}, PinfO_{2}, and pHinf) were measured immediately after infusion, a sample having been removed from the water-jacketed syringes at this time.

The time required for 50 ml of blood to be infused into each common carotid artery by this technique varied from 15 to 60 sec in different animals, owing to variability in the hemodynamic resistance of the vascular beds fed by the common carotid artery. As an experiment progressed, the time required for the infusion of a given volume of blood increased. This was because the infusion pressure was deliberately kept as close as possible to the pressure in the carotid arteries, which fell as the animal's condition gradually deteriorated. With decreased infusion pressure the flow decreased, and was presumably reduced still further by reflex vasoconstriction of the vascular bed supplied by the carotids.

Chemodenervation of the carotid chemoreceptors was carried out in some animals by exposing the carotid bifurcations and cutting all the nerves originating from them. Completeness of the procedure was tested by injecting 2 ml of a solution of 0.003 M sodium cyanide into the common carotid arteries while recording airflow and tidal volume.

RESULTS

Data Indicating That the Transient Infusion Technique Measures Carotid Body Responses Alone

The animals with denervated carotid bodies were used in order to determine whether a portion of the blood infused into the common carotid arteries passed via the circle of Willis or other collateral channels to the medullary chemoreceptors, causing them to participate in the ventilatory response to infusion. Infusion of severely hypercapnic, normoxic blood (PinfCO_{2} = 250-300 mm Hg, PinfO_{2} > 100 mm Hg) produced a huge increase in ventilation in the intact animal (Fig. 3) but none in the denervated preparation which retained internal carotid arteries intact and open. Sometimes the infusion of severely hypercapnic blood caused a slight ventilatory depression in the denervated animal which appeared 15-20 sec after the onset of the infusion. With moderately hypercapnic blood (PinfCO_{2} = 60-90 mm Hg) the intact animal exhibited a marked ventilatory response, but there was neither an increase nor a decrease in ventilation in the chemodenervated preparation. The infusion of hypoxic, hypercapnic blood (PinfCO_{2} > 500 mm Hg, PinfO_{2} < 10 mm Hg) which depressed respiration in the intact animal (Figs. 2, 4) had no effect in the chemodenervated animal (Fig. 4). The responses to cyanide were abolished by chemodenervation as one would expect (Figs. 3, 4).

Infusion of hypercapnic blood was carried out before and after chemodenervation in four animals in which the occipital artery had been ligated in the process of denervation, and in four animals in which the occipital and adjacent arteries were purposely left intact. The latter group was studied in order to determine whether hypercapnic blood infused into the common carotid arteries could pass via collateral channels known to exist between occipital and vertebral arteries to the medulla. No increase in ventilation occurred in either group. This finding, together with evidence cited in the DISCUSSION, suggests that the transient infusion technique can be used, at least in the dog, to study the effects on ventilation of the carotid chemoreceptors alone, apparently because the infused blood does not reach the medullary chemoreceptors.
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FIG. 4. Upper records demonstrate infusion-to-response delays of similar value for cyanide and for hypocapnic, hyperoxic blood which transiently decreased ventilation (to 58% of the control value, causing end-tidal PCO$_2$ (PACES) to rise). Following carotid chemodenervation (middle records; chart speed for cyanide infusion = one-half usual), neither infusion had any measurable effect.

Ventilatory Response to Infusion of Hypercapnic, Normoxic Blood—Quantitative Aspects

Time course. Transient infusion of hypercapnic, normoxic blood produced a prompt response (Figs. 3, 5). The first breath which was statistically greater than the control values was completed in about 4 sec (mean 3.8; range 1.0–7.4) after the beginning of infusion, in 18 infusions performed in 4 experiments. For ten test infusions of cyanide the delay was of the same order of magnitude (mean 2.7; range 1.6–4.6). A major portion of the delay was undoubtedly caused by the time required for the infused blood or cyanide to pass from the stopcocks to the carotid bodies. Cropp and Comroe (6) found a delay of approximately 0.5 sec in the ventilatory response to hypercapnic blood when the latter was introduced via a small catheter into the region of the carotid bifurcation. Once started, the ventilatory response to hypercapnic blood increased rapidly, as shown for the group in Fig. 6. The scatter of the points prevented fitting a curve to these data. However, that breath representing the maximal response began on an average within 8 sec (mean 7.3; range 2.8–10.1) after the beginning of infusion, and in 16 of 18 infusions was the second or third breath following the breath during which the infusion was begun. In one infusion it was the fourth, and in the other, the fifth. In some of the experiments, as shown in Fig. 5, the tidal volume decreased even while the perfusion of hypercapnic blood continued.

Minimal effective CO$_2$ stimulus (Fig. 7). The PCO$_2$ of the infused blood (Pinf$_{CO_2}$) was varied relative to arterial (P$_{ACO_2}$) until the value of the smallest increment (Pinf$_{CO_2}$ − P$_{ACO_2}$, referred to as “ΔPCO$_2$”) capable of stimulating ventilation was determined. The P$_{ACO_2}$ of the infused blood was kept close to that of arterial blood with the animal breathing air (Pinf$_{O_2}$ ≈ P$_{AO_2}$ ≈ 100 mm Hg). V$_E$ was increased significantly (24%, P < 0.001) when ΔPCO$_2$ averaged 2.3 mm Hg (range 1–4). (In this experiment, the pH of the infused blood fell more during equilibration with the CO$_2$ mixture than the usual ratio of approximately 0.01 pH U/1 mm Hg increase in PCO$_2$ (see DISCUSSION).)

$\dot{V}_E$ versus ΔPCO$_2$ (Fig. 8). The ability of various values of ΔPCO$_2$ transiently to increase ventilation was studied in animals breathing air. In those which happened to have lower values of P$_{ACO_2}$ before infusion, the graph relating $\dot{V}_E$ to ΔPCO$_2$ was curvilinear. When arterial P$_{CO_2}$ was spontaneously higher in the animal breathing air, thus exposing the carotid chemoreceptors to a higher P$_{CO_2}$ before infusion, the curve relating $\dot{V}_E$ to ΔPCO$_2$ was steeper and more nearly linear. At present we have no data for higher values of resting P$_{ACO_2}$ or for higher values of ΔPCO$_2$.

Effects of Infusing Hypocapnic, Hyperoxic Blood (Pinf$_{O_2}$ > 500 mm Hg, Pinf$_{CO_2}$ < 10 mm Hg)

Figures 2 and 4 show the decrease in VT and respiratory frequency resulting from this procedure, which greatly minimizes and possibly eliminates carotid body activity. Effects on breath-by-breath V$_E$ were studied in four situations as follows:

Breathing O$_2$ (Fig. 9A). Infusion of hypocapnic, hyperoxic blood produced a slight transient increase in breath-by-breath V$_E$. (Actually, a slight decrease in breathing would have been anticipated since Pinf$_{CO_2}$, which was less than 10 mm Hg, was below the value of P$_{ACO_2}$ (~18–28 mm Hg) existing before infusion.)

FIG. 5. Ventilatory response to infusion of hypercapnic, normoxic blood was (as in Fig. 3) as fast as to cyanide. Fall-off in response to sustained infusion of hypercapnic blood observed in lower tracing is commonly present. Part of it may represent adaptation to the stimulus.
...was observed by Cropp and Comroe (6), who infused carotid arteries of eight chemodenervated animals in blood with a PCO$_2$ of 330 mm Hg into the common carotid arteries of a chemodenervated dog. There is a considerable body of literature supporting the view that the lack of response can be attributed to failure of blood infused into the carotid arteries to reach the medullary respiratory chemoreceptors. Kramer (22) in 1912 assembled the first evidence to disprove the 250-year-old view, since Willis in 1664, that it was the function of the circle of Willis to equalize the blood to all parts of the brain. He showed that the circle was a potential anastomotic channel brought into play only when one of its contributing vessels was obstructed. Kramer found that methylene blue injected into the common carotid arteries of anesthetized dogs and monkeys was distributed over the cerebral hemispheres and anterior portions of the brain via the anterior and middle cerebral arteries and their branches, but did not reach the medulla. Dye injected into the vertebral arteries stained the medulla, cerebellum and posterior portions of the brain via the basilar, posterior cerebral, superior cerebellar, and posterior inferior cerebellar arteries. Kramer found that alcohol or ether injected into the carotid arteries had no effect on respiration, but caused it to cease temporarily when the injection was made into the vertebral arteries. Finally, by means of a hemodynamic model, made of glass and rubber tubes, he showed that there is a “dead point” in both posterior communicating arteries of the circle of Willis where the opposing streams from the carotid and vertebral arteries (through the basilar) meet, but since the pressure in the two systems is equal here, the streams do not mix, and there is no flow in either direction.

The data were placed in three subgroups (Fig. 9, B1, B2, B3) on the basis of the PacO$_2$, which existed just prior to infusion, in order to determine whether the chemoreceptor drive was related to this factor. However, no statistical difference in the values of V̇E for a given time interval was found between the three groups except in the 15- to 20-sec interval in B3, in which the infusion lasted only 15 sec. The control infusions represented in B2 caused an increase in ventilation, which was unusual. A slight depression of ventilation, possibly from pressor-receptor influence, as seen in A, B1, B3, and C (Fig. 9), occurred in the majority of instances. During hypoxia (Fig. 9C). When the animal was rendered hypoxic by the inhalation of approximately 10% oxygen in nitrogen (Pao$_2$ = 32–55 mm Hg), infusion of hypocapnic, hyperoxic blood into the carotid arteries reduced breath-by-breath V̇E by an average of 62% of the mean V̇E for the control period. Apnea ensued in two of eight infusions.

During asphyxia. In some experiments not diagrammed here the animal inhaled an asphyxic gas mixture. Infusions of hypocapnic, hyperoxic blood produced less depression of ventilation than with hypoxia. Thus, of 14 infusions performed during asphyxia only 3 caused a depression greater than the 62% observed in hypoxia, a depression of no greater than 27% occurring in the remaining 11. (A graphical or tabular summation of the data for the group was not possible owing to wide variations in the parameter, PacO$_2$, Pao$_2$, and duration of infusion.)

**Discussion**

**Evidence That the Transient Perfusion Technique Measures Responses of Carotid Chemoreceptors Alone**

Moderately or severely hypcapnic blood failed to stimulate ventilation when infused into the common carotid arteries of eight chemodenervated animals in our experiments. Similarly, no increase in ventilation was observed by Cropp and Comroe (6), who infused blood with a PacO$_2$ of 330 mm Hg into the common carotid arteries of a chemodenervated dog. There is a considerable body of literature supporting the view that the lack of response can be attributed to failure of blood infused into the carotid arteries to reach the medullary respiratory chemoreceptors. Kramer (22) in 1912 assembled the first evidence to disprove the 250-year-old view, since Willis in 1664, that it was the function of the circle of Willis to equalize the blood to all parts of the brain. He showed that the circle was a potential anastomotic channel brought into play only when one of its contributing vessels was obstructed. Kramer found that methylene blue injected into the common carotid arteries of anesthetized dogs and monkeys was distributed over the cerebral hemispheres and anterior portions of the brain via the anterior and middle cerebral arteries and their branches, but did not reach the medulla. Dye injected into the vertebral arteries stained the medulla, cerebellum and posterior portions of the brain via the basilar, posterior cerebral, superior cerebellar, and posterior inferior cerebellar arteries. Kramer found that alcohol or ether injected into the carotid arteries had no effect on respiration, but caused it to cease temporarily when the injection was made into the vertebral arteries. Finally, by means of a hemodynamic model, made of glass and rubber tubes, he showed that there is a “dead point” in both posterior communicating arteries of the circle of Willis where the opposing streams from the carotid and vertebral arteries (through the basilar) meet, but since the pressure in the two systems is equal here, the streams do not mix, and there is no flow in either direction.

Essentially all of Kramer’s findings have been confirmed by intracranial angiography in man (21, 24) and by injection of dyes or other agents in experimental animals (27), and modern writers on the cerebral circulation concur on these essential points (19, 20, 31, 32, 34).

The possibility still exists that in dogs a collateral circulation known to be located between the occipital and vertebral arteries (1, 10) could carry part of the blood infused into the common carotid arteries to the vertebrales and thence to the medulla. Here again hemodynamic factors appear to make this unlikely. Hypocapnic blood did not stimulate ventilation when infused at arterial pressure into the common carotid arteries in the four of our experiments in which all blood vessels of any significant size remained intact after chemodenervation. Presumably there is a “dead point” in this collateral system too, located somewhere between the occipital and vertebral arteries. Even if the hypocapnic blood had reached the medulla, but in diluted form, it should have had some stimulating effect on ventilation, but it did not, just as the alcohol or ether injected into the carotid arteries in Kramer’s experiments on dogs had no depressant effect.

The possibility that in the above experiments some of the hypocapnic blood which was infused reached the medullary chemoreceptors but remained for too short a period to excite them seems unlikely. That they may re-
CO₂. The accompanying fall in pH of 0.08 units in these particular experiments is larger than to be expected for a rise in Pₐ₉₀ of 2.3 mm, possibly as a result of glycolysis in the blood. Whether the CO₂ is acting as an acid, as a molecular species, or both, cannot be told from our studies.

The rapid response of the carotid chemoreceptors to hypercapnic blood and their high sensitivity to it is consistent with the hypothesis of Yamamoto and Edwards (35), of Grodins and James (14), and of Riley et al. (30), according to which oscillations in arterial Pₐ₉₀ during exercise may contribute through stimulation of the carotid and aortic chemoreceptors to the hyperventilation of exercise.

Curves relating Vₑ to ΔPₐ₉₀. As indicated in Fig. 8, the slope of the curves relating Vₑ to ΔPₐ₉₀ are steeper at higher (25–33 mm Hg) initial values of Pₐ₉₀ than the animal breathing air but 21 mm Hg. Thus, during normoxia, the “sensitivity” in terms of increase in ventilation produced by the carotid chemoreceptors in response to a given ΔPₐ₉₀ appears to be greater as one approaches the normal range of Pₐ₉₀.

The curves of Eyzaguirre and Lewin (11) and of Hornbein, Griffio, and Roos (18), relating impulse frequency in the carotid sinus to Pₐ₉₀, have maximum slopes in the physiological range of Pₐ₉₀, though those of Bartels and Witzleb (2) are linear. However, one cannot directly compare effects of chemical respiratory stimuli on ventilation with their effects on impulse traffic. The relation of the latter to ventilation is not well established, and may be nonlinear. Thus, when Loeschcke et al. (26) stimulated one carotid sinus nerve with maximal shocks at varying frequencies, they found an approximately linear relation between Vₑ and stimulation frequency at low frequencies (ca. 1–10/sec), but the response leveled off and reached a maximum at about 20 cycles/sec. Moreover, with the nerve fibers firing synchronously...
in this way the situation differs from that when the carotid bodies are stimulated physiologically by chemical agents and the nerve fibers fire asynchronously at frequencies up to 800 impulses/sec for the whole nerve (11).

Infusion of Hypocapnic, Hyperoxic Blood for Estimating Ventilatory Drive of Carotid Bodies

**Rationale.** Dejours (7) has stated that “the fall in ventilation recorded a few seconds after the start of pure O2 breathing does not afford an accurate estimate of the magnitude of the ventilatory O2 drive prior to the O2 inhalation.” He explains that, at the time of the maximal fall in ventilation, the Po2 of the blood perfusing the carotid bodies may not be above the threshold of stimulation—i.e., may not be high enough to abolish chemoreceptor drive, and if the O2 inhalation is prolonged further, secondary effects such as hypocapnia resulting from the transient hyperventilation intervene. Nevertheless, Dejours’ “O2 test” has provided the best evidence to date on “O2-dependent” peripheral chemoreceptor drive during normoxia.

Infusion of hypocapnic, hyperoxic blood into the common carotid arteries might be expected to inactivate the carotid bodies more completely than a single breath of O2. The Po2 of the infused blood exceeds 500 mm Hg, and because of the very prompt responses of the carotid bodies to infusions of hypercapnic blood, and because of their small size and enormous blood flow, one should expect rapid equilibration of gases between their tissues and the blood perfusing them. If the Po2 inside the carotid bodies does indeed rise to high levels during the infusion, their activity should be greatly minimized. Thus, Hesser (15) found but a slight decrease in ventilation on cold blocking the carotid sinus nerve in anesthetized dogs breathing O2, though there was a considerable decrease during breathing of air. That the infused blood is hypocapnic as well as hyperoxic tends further to reduce carotid body drive, in view of the interaction between CO2 and O2 tensions below certain levels, as first demonstrated by Nielsen and Smith (28) and by others (5, 25, 29). For these reasons we believe that the degree of decrease in ventilation produced by transient infusion of hypocapnic, hyperoxic blood provides a reasonable approximation of carotid body drive in a given situation. It is true that the contribution of the aortic bodies to ventilation is not eliminated, but this
does not interfere with the estimation of carotid body drive.

Evaluatation of data. The data we obtained with this type of infusion during O₂ breathing are not entirely satisfactory. There is no explanation for the slight, but apparently statistically significant, increase in VE occurring during five infusions in two animals. At least there was no decrease in VE.

With the animal breathing air, the fact that the infusion transiently decreased VE by an average of 24% is consistent with the concept of Bjurstedt (3), of Hesser (15), and of Dejours (7) that the carotid chemoreceptors exert an "oxygen-dependent" respiratory drive at rest even during normoxia. Our use of anesthesia does not necessarily invalidate the above conclusion, since there was no indication of respiratory depression, the Pao₂ even during normoxia. Our use of anesthesia does not interfere with the estimation of carotid body drive before infusion is greater than with hypoxia because of the interaction between CO₂ and hypoxia (assuming Pao₂ the same in each), the high Pco₂ drives the intracranial receptors and marked respiratory depression or apnea is less from the infusion.

CONCLUSIONS

Transient perfusion of blood of known Pao₂, Pco₂, and pH into the common carotid arteries produces a transient change in ventilation via the carotid bodies. There is evidence that the infused blood does not reach the medullary chemoreceptors; thus the technique permits studying the properties of the carotid bodies alone, as they actually modify respiration. Infusion of hyperoxic, hypocapnic blood largely eliminates the activity of the carotid bodies, permitting estimation of their relative contribution to breathing during hyperoxia, normoxia, hypoxia, and asphyxia.

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