CARBON MONOXIDE: INFLUENCE ON AVIAN RESPIRATORY CONTROL

by

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PART I. CARDIOPULMONARY RESPONSES TO CO BREATHING IN THE CHICKEN

Abstract

Effects of carbon monoxide (CO) in various cardiopulmonary parameters were determined in adult, male, White Leghorn type chickens (Babcock strain). Four groups of ten birds each were allowed to spontaneously breath 0, 0.01, 0.1, and 0.5% CO, respectively, while cardiopulmonary and carboxyhemoglobin (HbCO) measurements were obtained. No significant differences in respiratory frequency (f_{resp}), tidal volume (V_T), minute volume ($\dot{V}$), heart frequency (f_{card}), or systolic and diastolic blood pressure between birds receiving 0 to 0.01% CO for 60 minutes were detected (HbCO = 9%). Inhaling 0.1% CO for 60 minutes (HbCO = 39%) increased V_T and $\dot{V}$, and decreased blood pressure while f_{resp} was unchanged. Inhaling 0.5% CO was lethal after an average of 20.5 minutes (range, 17.5-24.5 min). That concentration increased V_T and $\dot{V}$ but decreased f_{resp}, blood pressure and f_{card} and resulted in HbCO concentrations of 52% in 15 minutes. The effects of CO on cardiopulmonary control cannot be explained by either direct or indirect action on peripheral chemorecptors (carotid body) because stimulation of those receptors increases f_{resp} as well as V_T. CO may, therefore, act directly on other peripheral receptors (intrapulmonary CO_2-sensitive receptors) or on the CNS.

INTRODUCTION

Carbon monoxide (CO) is an asphyxiant gas with three deleterious physiological effects. It binds to hemoglobin with an affinity ranging from 162 times greater than oxygen in sheep to 247 times greater in the opossum (Sendroy and O'Neal, 1955). The resulting complex, carboxyhemoglobin (HbCO), decreases the amount of hemoglobin available for O_2 transport. Furthermore, CO inhibits release of O_2 from the remaining unbound hemoglobin and, thus, causes the oxyhemoglobin dissociation curve to shift to the left (Stadie and Martin, 1925). Tissue hypoxia is thereby augmented and the partial pressure of O_2 in the tissue must be decreased far below normal before a significant amount of O_2 will diffuse from the hemoglobin. Finally, CO can inhibit cytochrome oxidase activity (Ball *et al.*, 1951) but high partial pressures of CO (600 torr) are required to stimulate carotid body chemoreceptors by CO (Joels and Neil, 1962).

Few studies have considered effects of CO on the cardiopulmonary system in birds. Acutely CO-poisoned chicks exhibit symptoms of uneasiness, stupor, drowsiness, and labored breathing (Stiles, 1940). Inhaling 0.016% CO for as long as 7 days (HbCO of 7-12%) resulted in no noticeable symptoms (Carlson and Clandinin, 1962). However, higher concentrations (0.06-0.1%) inhaled for 27 minutes to 7 days produced signs of poisoning (diarrhea, irritability, and dyspnea) with HbCO concentrations of 25-65%, but not death. CO concentrations of 0.2% and higher with HbCO of 63-75% killed many birds. Histopathological lesions of brains of chickens exposed to CO were similar to lesions in several other diseases that effect the central nervous system (Carlson and Clandinin, 1962).

Definitive measurements of CO effects on the cardiopulmonary system of chickens have not been made. We therefore studied the effects of inhaled CO and associated HbCO concentrations on that system with particular attention to alteration in control of the system.

METHODS

Animal preparation. Adult, male, White Leghorn type (Babcock strain, 1.75-2.25 kgs) chickens were anesthetized by injecting Equithesin (Jen-Sal Lab, 2.2 ml/kg) into three sites in both the right and left pectoralis muscles. A surgical plane of anesthesia (only a slight head movement to a strong comb pinch) was reached in approximately 15 minutes.

Both the right and left sciatic arteries were cannulated. The trachea was isolated and sectioned 8 cm caudal to the beak and was pulled into a glass cannula. The glass cannula was short enough so as to not add additional dead space to the respiratory system. The chicken was then placed in ventral recumbency by securing the legs, wings, head, and tail to a wooden frame (Fig. 1).

Cardiopulmonary recordings. All recordings were initiated one hour after administration of anesthetic. Tidal volume (V_T) and respiratory frequency (f_{resp}) were recorded using a closed system (Fig. 1). The tracheal cannula was connected to a 53.2 liter carboy. A pressure transducer (Statham, P23BB with the dome removed) was inserted through a rubber stopper in the top of the carboy. Pressure changes in the carboy, created by inspiration and expiration of the chicken, were recorded on a multi-channel pen recorder (Beckman, Type S). The system was calibrated by injecting into and withdrawing from the carboy known volumes of air with a 50 ml, gas-tight syringe so tidal volume could be measured.

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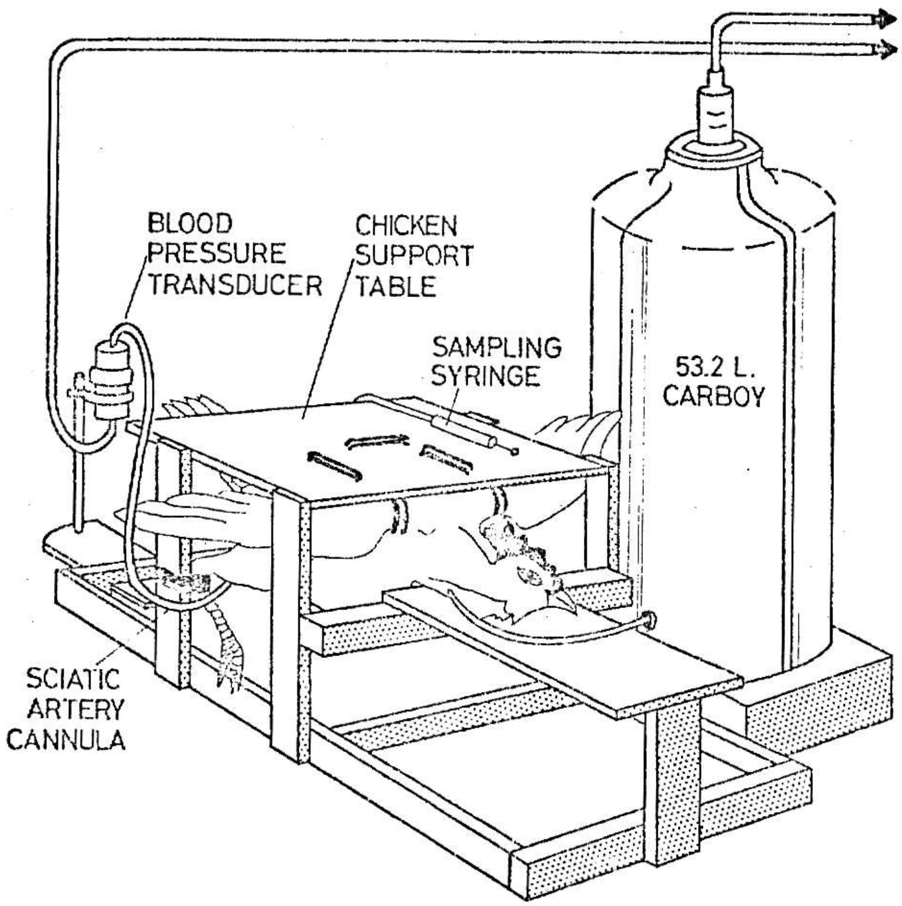

Fig. 1. Diagramatic arrangement of experimental animal and accompanying apparatus. Pressure changes in the carboy and blood were sensed by pressure transducers and recorded by a multi-channel pen recorder (arrows).

Blood pressure (P_b) and heart frequency (f_{card}) were detected by connecting the sciatic arterial cannula (Fig. 1) to a blood pressure transducer (Statham, P23Gb) and recording the signal on the multi-channel pen recorder. Rectal temperature was monitored by securing a thermistor 8 cm into the rectum. Body temperature was held at 40°C (± 0.5°C) with a hot water heating pad.

Exposure gases. Four groups of ten birds each were allowed to spontaneously breath 0, 0.01%, 0.1%, and 0.5% CO, respectively, in 20.4% O_2 from the carboy for 1 hour or until death. The carboy was flushed for 35 minutes with a gas mixture containing the desired concentration of CO. CO in the carboy was measured by a chemical method (Universal Pump, Mine Safety Appliances Co.). It varied less than 5% from one mixture of the same concentration to the next. Oxygen concentration in the inhaled gas mixture was determined by using a paramagnetic O_2 analyzer (Beckman, Modeal E 2). Build up of CO_2 in the carboy was prevented by suspending 0.1 kg of CO_2 absorbent, wrapped in cheese cloth, in the carboy. CO_2 concentrations in the carboy were monitored with an infrared CO_2 analyzer (Beckman, Model LB 1). They did not exceed 0.25% after the chicken had breathed into the carboy 1 hour.

Arterial HbCO concentrations were monitored every 15 minutes while CO was administered by withdrawing 1 ml of arterial blood from the sciatic cannula (Fig. 1) and analyzing it with a modified microdiffusion analysis (Lambert et al., 1972).

Record and data analysis. The respiratory parameters V_T, ml BTPS, and f_{resp}, min^{-1}, were measured from the recordings. The cardiovascular parameters, f_{card}, min^{-1}, and systolic and diastolic blood pressures, were measured at 15-minute intervals for 1 hour or until death, by reading 30 seconds of record. The differences in f_{resp}, and V_T, and $\dot{V}$ among 0, 0.01% and 0.1% CO treatment groups at 13 time periods were analyzed using split-plot analysis of variance. When significant values were obtained, the Duncan multiple range test was used to determine means that differed (Fryer, 1966).

RESULTS

Lethal exposures to CO. Cardiopulmonary responses to a high concentration of CO (0.5%) were determined in 10 birds. Typical records are shown in Fig. 2. V_T was more than doubled at maximum response, then decreased to 0 at 20.5 minutes. Blood pressure and f_{card} began to decrease 15 minutes after initiating CO inhalation.

Mean responses of the various cardiopulmonary parameters are shown in Fig. 3. Respiratory frequency did not change significantly during the first 10 minutes but both V_T and $\dot{V}$ increased. Tidal volume remained elevated until the chickens went into apnea (not shown in Fig. 3). Respiratory frequency and $\dot{V}$ decreased significantly from 10 until 1.5 minutes before death. Mean time to death was 20.5 minutes (range, 17.5--24.5 min.). Both blood pressure and f_{card} significantly decreased throughout inhalation. Fifteen minutes after 0.5% CO was administered carboxyhemoglobin in the arterial blood was 52.1% and averaged 55.4% at death (Fig. 4).

Sublethal exposure to CO. Inhalation of 0.01% CO for a one hour period did not produce differences, from those birds receiving 0% CO, in any of the cardiopulmonary parameters measured (Table 1). Changes did occur in f_{resp}, V_T, and $\dot{V}$, during the one hour period, within each group of birds indicating that they were not in a steady state condition. The changes may have resulted from alterations in the plane of anesthesia

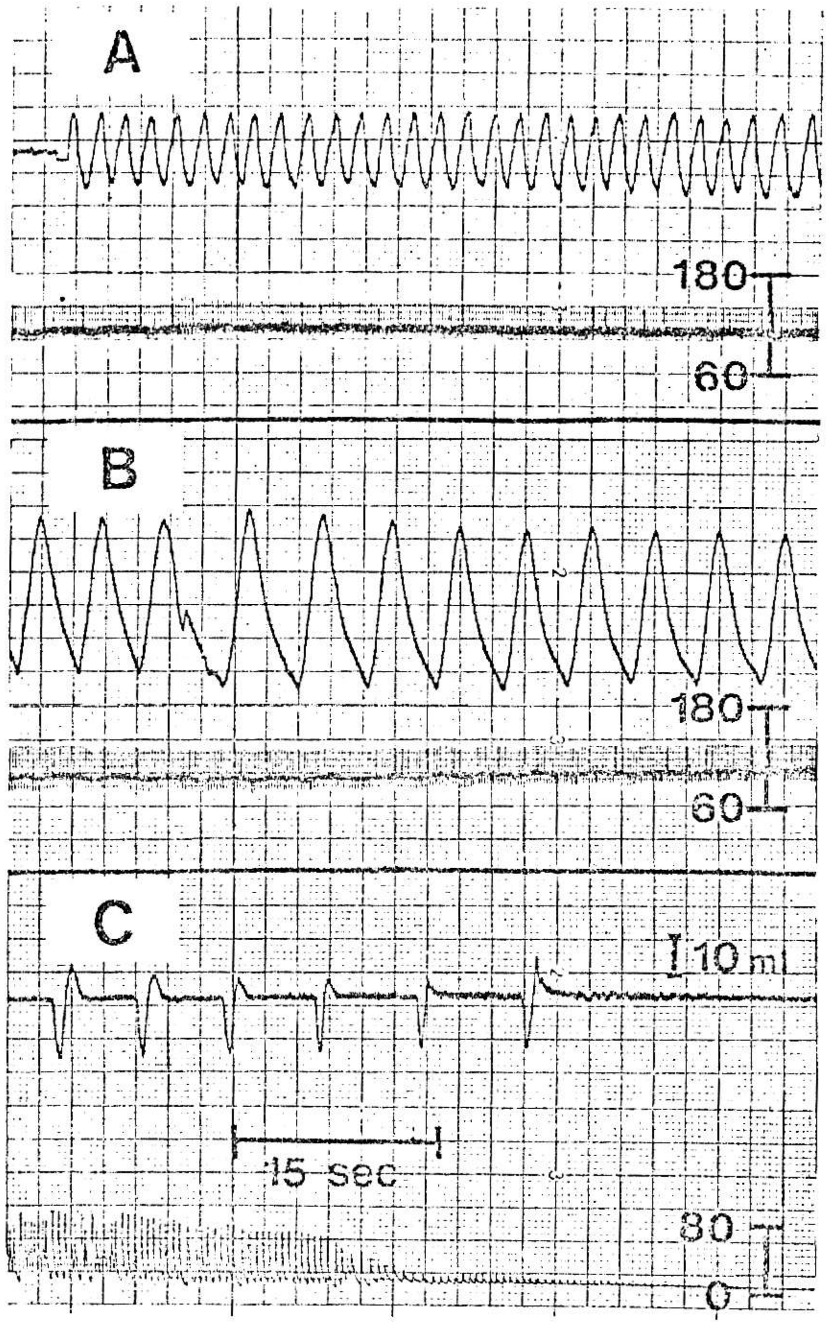

Fig. 2. Cardiopulmonary records while 0.5% CO was administered. Records A, B, and C were taken respectively at time 0, at maximum respiratory response (11 minutes), and 20 minutes after initiating CO inhalation. The top tracing in each record is respiratory activity (f_{resp} and V_T); the bottom line, blood pressure. Calibration for V_T is at the right of the respiratory tracing in record C; for blood pressure, at the right of each blood pressure tracing.

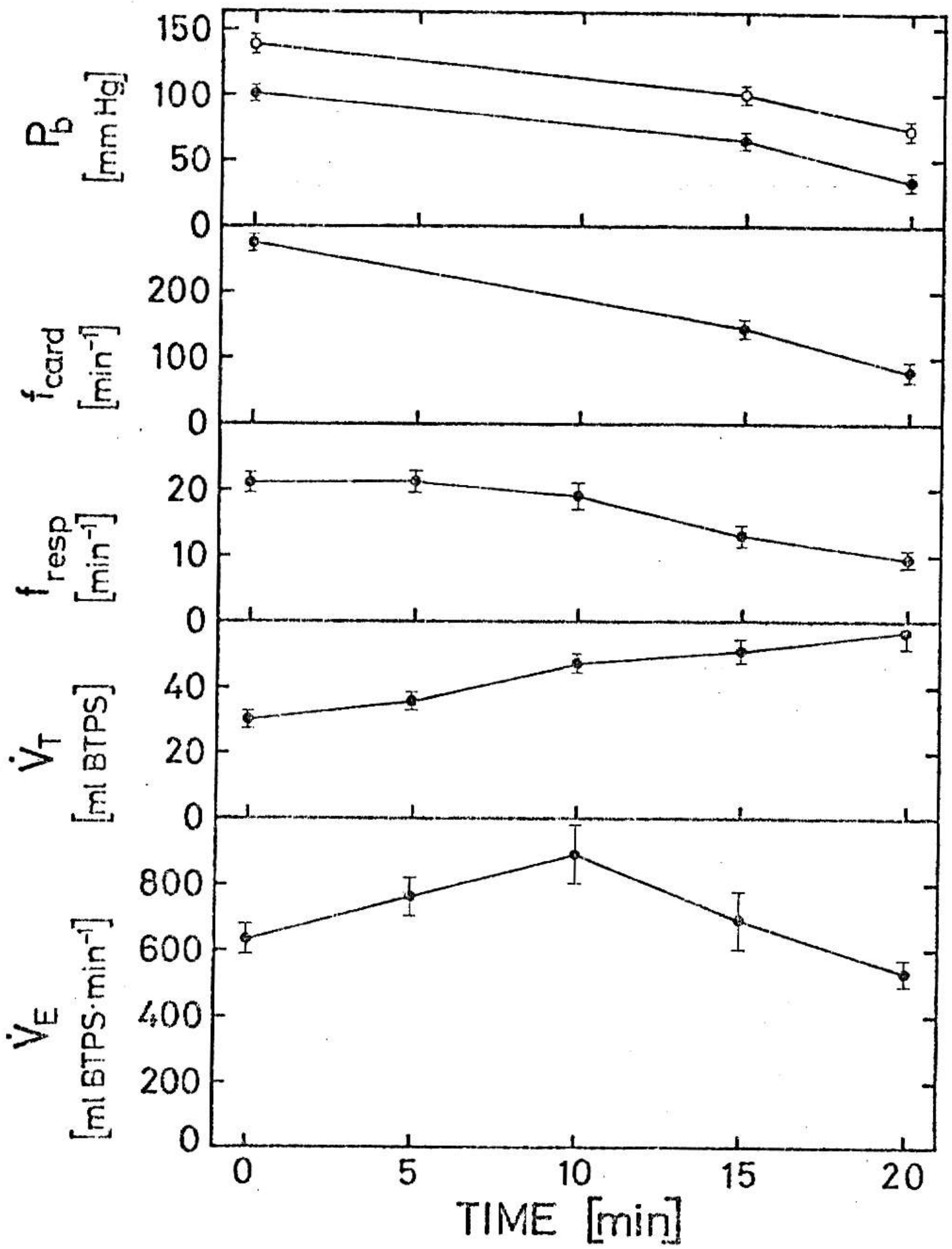

Fig. 3. Effect of 0.5% CO on cardiopulmonary parameters (mean ± SE). The mean of ten birds was used to plot values at times 0, 5, 10, and 15 minutes; the mean of seven (because three had died earlier) at 20 minutes of CO inhalation. Open circles in the blood pressure plot indicate systolic pressure; closed circles, diastolic pressure.

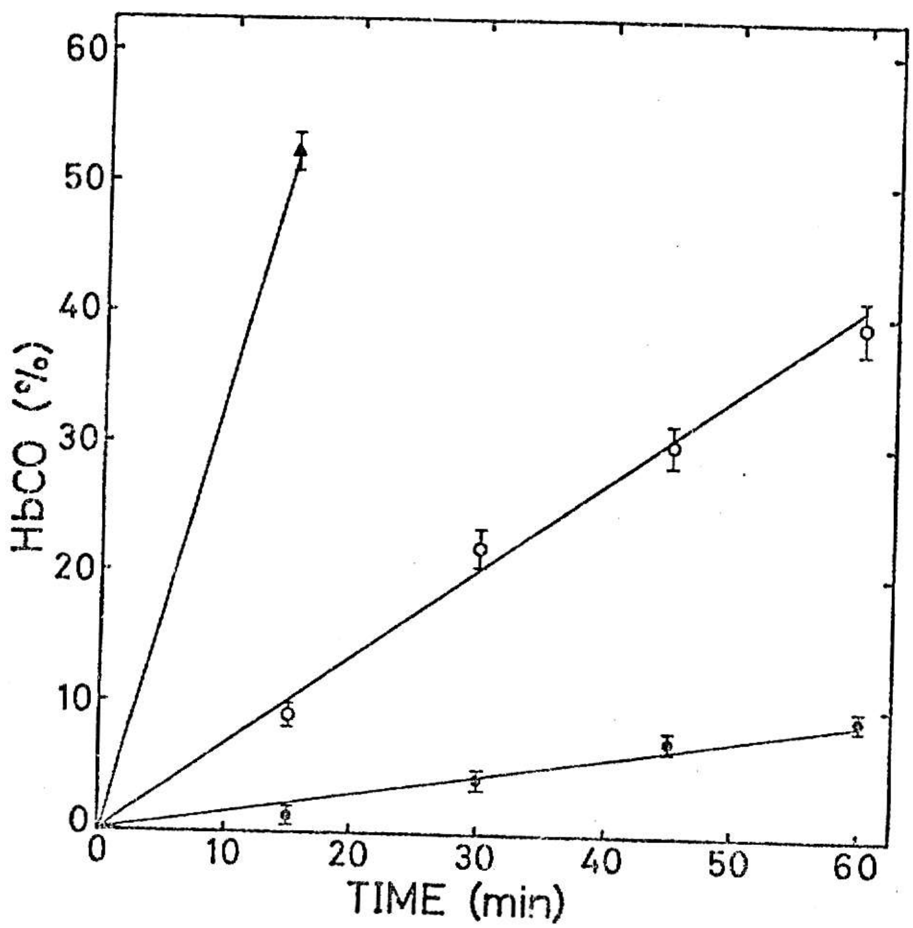

Fig. 4. Effects of inhaling 0.01% (closed circles), 0.1% (open circles) or 0.5% (closed triangle) CO on arterial carboxyhemoglobin concentrations. Mean ± SE.

TABLE 1

Influence of inhalation of 0.01% CO for 60 minutes on various cardiopulmonary parameters in the chicken. Mean ± SE.

Parameter	0% CO		0.01% CO	
	0 min	60 min	0 min	60 min
Systolic Pb, mmHg	136 ± 6	140 ± 3	134 ± 4	124 ± 6
Diastolic Pb, mmHg	98 ± 6	102 ± 4	107 ± 4	94 ± 3
f_{card}, min^{-1}	247 ± 2	253 ± 2	260 ± 5	266 ± 5
f_{resp}, min^{-1}	26.9 ± 2.5	23.8 ± 2.6	23.3 ± 1.8	19.7 ± 1.8
V_T, ml BTPS	24.4 ± 1.2	30.3 ± 1.4	25.3 ± 1.7	29.6 ± 2.2
$\dot{V}$, ml BTPS·min^{-1}	634 ± 44	695 ± 55	508 ± 35	608 ± 39

because additional drug was not administered. However, neither blood pressure nor f_{card} changed that hour.

HbCO concentration in the arterial blood in birds receiving 0% CO was never more than 1% after 60 minutes of breathing into the carboy, which is within analysis error. HbCO concentrations progressed linearly to 9% in 60 minutes in birds exposed to 0.01% CO (Fig. 4).

Spontaneous inhalation of 0.1% CO significantly increased V_T and $\dot{V}$, but did not change f_{resp} significantly from those chickens receiving 0% CO (Fig. 5). Increases in V_T and $\dot{V}$ occurred within 15 minutes after initiating 0.1% CO inhalation. The increase in $\dot{V}$ (571 to 885 $ml \cdot min^{-1}$) resulted entirely from an increase in V_T (23.7 to 44.5 ml) as f_{resp} was not significantly changed (24.6 to 20.2 $breaths \cdot min^{-1}$).

Changes in the cardiovascular system also occurred from inhaling 0.1% CO. Heart frequency increased from 278 to 292 $beats \cdot min^{-1}$ in 30 minutes, then decreased to 274 $beats \cdot min^{-1}$ after 60 minutes. Blood pressure continually decreased throughout the experiment. HbCO concentrations were 39% in 60 minutes (Fig. 4).

DISCUSSION

Cardiopulmonary changes in response to inhaled CO may be mediated by indirect or direct effects on both the peripheral and central nervous systems. However, our results do not support the idea that the indirect effect (hypoxia) is responsible for the ventilatory responses to CO. Chickens inhaling 0.1% CO f_{resp} did not significantly alter f_{resp} even though HbCO concentrations reached 39%, but V_T was increased significantly. That response is not like the response to hypoxia that Butler (1967) and Ray and Fedde (1969) reported in chickens. Hypoxia primarily increases f_{resp} with smaller increases in respiratory amplitude. Peripheral receptors,

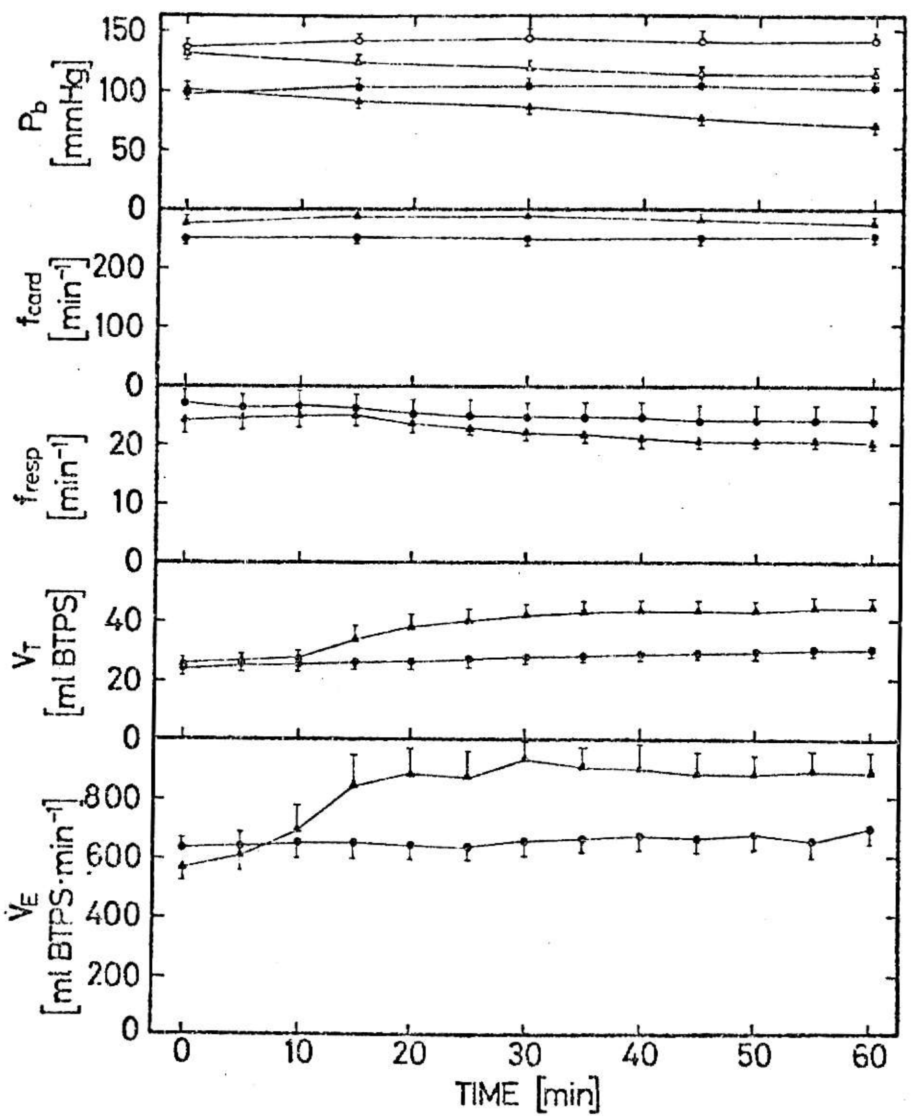

Fig. 5. Effects of 0% (circles) and 0.1% (triangles) CO on cardiopulmonary parameters (mean ± SE). Systolic blood pressure, open circles and triangles; diastolic blood pressure, closed circles and triangles.

such as the carotid body (Magno, 1973), which appear to be sensitive to hypoxia, therefore, appear not to be involved in the response. Furthermore, other peripheral receptors (intrapulmonary CO_2-sensitive receptors), which have been shown to be involved in control of avian respiration (Fedde and Peterson, 1970; Osborne, 1971; Molony, 1972), are not sensitive to hypoxia and therefore are probably not influenced indirectly by CO.

Direct effects of CO on peripheral chemoreceptors in the cat have been demonstrated by Joels and Neil (1962). They suggest that high CO tensions (600 mmHg) act on the cytochrome oxidase in the glomus cells and thereby increase the discharge frequency. Even though Mills and Edwards (1968) found that carotid body stimulation in the cat by 2-7 mmHg PCO did not result directly from the effect of CO on the cytochrome system, all cytochrome oxidases may not be identical. Substrate specificities of enzyme systems vary from tissue to tissue even in the same species (Mannering, 1971). Therefore, CO perhaps directly affects the intrapulmonary CO_2-sensitive receptors in birds. Increased CO_2 concentrations in the inhaled gas, which alter the activity of these receptors, predominantly alter amplitude of respiratory movements with minimal effects on f_{resp} (Ray and Fedde, 1969), a response similar to that produced by inhalation of 0.1% CO.

The cardiopulmonary response to CO also may result from a direct effect of CO on the central nervous system. Chiodi _et al._, (1941) indicated that CO depresses the respiratory centers, and Duke and Killick (1952) have suggested that CO inhibits contractility of vascular smooth muscle. The increased V_T due to inhaling 0.1% CO in our experiment might be explained by decreased sensitivity of the respiratory neuronal pool to the inhibitory input from the intrapulmonary CO_2-sensitive receptors. Further speculation on the site and mode of action of CO must await direct evidence of its effects on intrapulmonary CO_2-sensitive receptors.

REFERENCES

Ball, E. G., C. F. Strittmatter and O. Cooper (1951). The reaction of cytochrome oxidase with carbon monoxide. J. Biol. Chem. 193: 635-647.

Butler, P. J. (1967). The effect of progressive hypoxia on the respiratory and cariovascular systems of the chicken. J. Physiol. 191: 309-324.

Carlson, H. C. and D. R. Clandinin (1962). Carbon monoxide poisoning in chicks. Poultry Sci. 42: 206-213.

Chiodi, H., D. B. Dill, F. Consolazio and S. M. Horvath (1941). Respiratory and circulatory responses to acute carbon monoxide poisoning. Am. J. Physiol. 134: 683-693.

Duke, H. N. and E. M. Killick (1952). Pulmonary vasomotor responses of isolated perfused cat lungs to anoxia. J. Physiol. 117: 303-316.

Fedde, M. R. and D. F. Peterson (1970). Intrapulmonary receptor response to changes in airway-gas composition in Gallus domesticus. J. Physiol. 209: 609-625.

Fryer, H. C. (1966). Concepts and Methods of Experimental Statistics. Boston, Allyn and Bacon Inc., p. 329.

Joels, N. and E. Neil (1962). The action of high tensions of carbon monoxide on the carotid chemoreceptors. Arch. Int. Pharmacodyn. 139: 528-534.

Lambert, J. L., R. R. Tschorn and P. A. Hamlin (1972). Determination of carbon monoxide in blood. Analytical Chem. 44: 1529-1530.

Magno, M. (1973). Cardio-respiratory responses to carotid body stimulation with NaCN in the chicken. Respir. Physiol. 17: 220-226.

Mannering, G. J. (1971). Microsomal enzyme systems which catalyze drug metabolism. In: Fundamentals of Drug Metabolism and Drug Disposition. Ch. 12, edited by B. N. Ladu, H. G. Mandel and E. L. Way. Baltimore, Williams and Wilkins Co., p. 281.

Mills, E. and M. W. Edwards, Jr. (1968). Stimulation of aortic and carotid chemoreceptors during carbon monoxide inhalation. J. Appl. Physiol. 25: 494-502.

Molony, V. (1972). A study of vagal afferent activity in phase with breathing and its role in the control of breathing in Gallus domesticus. Ph.D. Thesis, University of Liverpool, England.

Osborne, J. L. (1971). Carbon dioxide-sensitive pulmonary afferent neurons in Gallus domesticus; static and dynamic response characteristics. Ph.D. Thesis, University of California, Davis.

Ray, P. J. and M. R. Fedde (1969). Responses to alterations in respiratory PO_2 and PCO_2 in the chicken. Respir. Physiol. 6: 135-143.

Sendroy, J. Jr., and J. D. O'Neal (1955). Relative affinity constant for carbon monoxide and oxygen in blood. Fed. Proc. 14: 137.

Stadie, W. C. and K. A. Martin (1925). The elimination of carbon monoxide from the blood. J. Clin. Invest. 2: 77-91.

Stiles, G. W. (1940). Carbon monoxide poisoning of chicks and poults in poorly ventilated brooders. Poultry Sci. 19: 111-115.

PART II. EFFECTS OF CARBON MONOXIDE ON AVIAN INTRAPULMONARY CO_2-SENSITIVE RECEPTORS

Abstract

The effects of carbon monoxide (CO) on intrapulmonary CO_2-sensitive receptors were investigated in unidirectionally ventilated chickens. Excluding CO_2 from the ventilating gas stream produced maximal stimulation of the CO_2-sensitive receptors and induced apnea. Single-unit, afferent vagal activity from the CO_2-sensitive receptors was not changed by including 0.1% CO in the ventilatory gas mixture; nor did CO alter static or dynamic CO_2-sensitivity curves, indicating the receptors' sensitivity to CO_2 was not altered. However, 6 minutes after CO was administered cyclic respiratory movements began. Rapid increases in HbCO to 50% with a simultaneous decrease in PaO_2 from 85 to 62 torr developed in 15 minutes.

The occurrance of respiratory movements during CO administration cannot be attributed to a direct action of CO on intrapulmonary CO_2-sensitive receptors nor to an increase in the activity of other chemoreceptors due to hypoxia. The movements may have resulted from a depressing action by CO on inhibitory interneurons in the CNS that normally are activated by intrapulmonary CO_2-sensitive receptors. Inactivity of those inhibitory interneurons would allow cyclic respiratory movements to resume from inherent rhythm of the respiratory neuronal pool even though continued high discharge of intrapulmonary CO_2-sensitive receptors occurred.

INTRODUCTION

Spontaneous inhalation of 0.1% carbon monoxide (CO) by the chicken increases tidal volume but produces no change in respiratory frequency (Part I of this thesis). The exact mechanism by which CO produces the response is not understood. In CO poisoning the degree of hypoxia is severer than expected from just the formation of HbCO because the release of O_2 by the remaining unbound hemoglobin is also inhibited (Stadie and Martin, 1925). However, hypoxia in the chicken increases respiratory frequency (Butler, 1967) with less effect on amplitude of breathing (Ray and Fedde, 1969). Because that response does not occur during CO intoxication, it is not likely that peripheral chemoreceptors, such as the carotid body, are responsible for the increased tidal volume produced by inhaled CO.

Intrapulmonary CO_2-sensitive receptors appear to be distributed throughout the avian lung, perhaps in the epithelium of the tubular system (Fedde and Peterson, 1970). Altering the activity of these receptors by inhaling various mixtures of CO_2 markedly influences amplitude of breathing with little effect on frequency (Ray and Fedde, 1969). Thus, altering the receptors activity might cause the respiratory changes observed during CO inhalation.

Our objective was to determine if CO influences respiratory control in the chicken by acting on intrapulmonary CO_2-sensitive receptors.

METHODS

<u>Animal preparation</u>. Adult, male, White Leghorn type chickens (Babcock strain, 1.7-2.0 kg) were anesthetized by injecting phenobarbital sodium (160mg/kg) through a cannulated left, cutaneous ulnar vein. Each bird was secured in dorsal recumbency, its trachea cannulated in the midcervical region, and its thoraco-abdominal cavity exposed by a midventral incision

through the skin, underlying muscles, and sternum (Fig. 6). The abdominal and thoracic air sacs were incised and a warmed, humidified gas was passed into the tracheal cannula, through the lungs, and out to the atmosphere through the opened air sacs. The unidirectional ventilation procedure has been previously described (Fedde et al., 1969). A constant flow rate (4 liters/min) of gas was used. The concentration of O_2, CO_2, and CO in the ventilating gas stream was monitored just before it entered the trachea by an oxygen analyzer (Beckman, Model E 2), an infrared CO_2 analyzer (Beckman, Model LB 1), and a CO Universal Sampling Pump (Mine Safety Appliance Co.). In all experiments, the chickens were unidirectionally ventilated with 20.4% O_2, balance N_2, with 0.1% CO added for 15 minutes. Body temperature held at 40° C ± 0.5° C, was monitored with a rectal thermistor inserted 8 cm.

Experiment 1. In experiment 1, single unit, afferent neuronal activity was recorded from intrapulmonary, CO_2-sensitive receptors in 5 birds during unidirectional ventilation with 0.1% CO. The left vagus nerve in the cervical region was exposed and immersed in a mineral oil pool formed by a ring of skin. All branches of the nerve except those from the lung were transected. The epineurium was removed and the nerve was placed on a mirror support. Small fasciculi were divided with the aid of a dissection microscope until a single active unit could be identified.

Single unit activity was detected by placing the dissected strand of nerve on a small bipolar hook electrode (90% platinum-10% iridium, 76μ in diameter). The signal was amplified (Grass Inst. Co., Model P-5), displayed on a multi-channeled oscilloscope (Tektronix, type 565), and recorded with an FM tape recorder (Hewlett-Packard, Model 3960).

Impulse activity was determined to be from CO_2-sensitive receptors by rapidly removing and adding CO_2 to the unidirectional ventilatory gas by

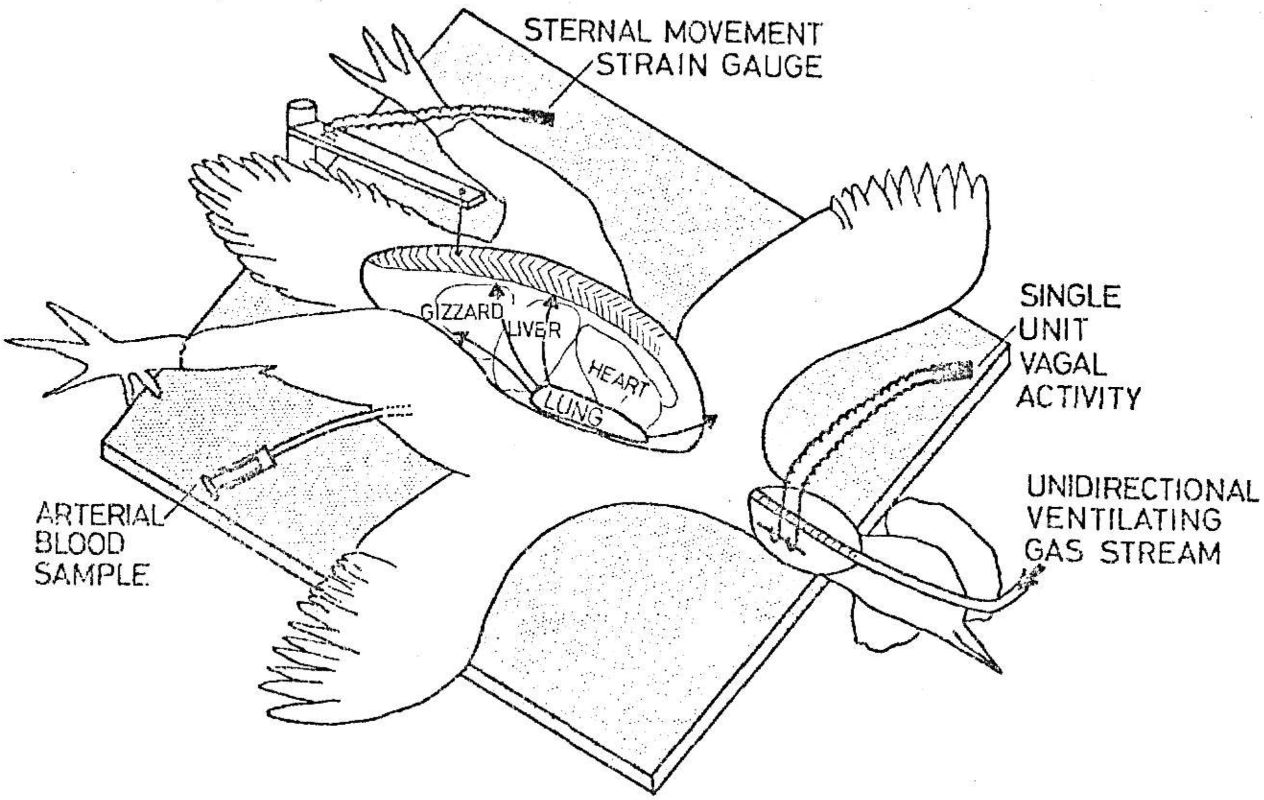

Fig. 6. Schematic diagram of arrangement of the chicken for single-unit vagal recordings from intrapulmonary CO_2-sensitive receptors.

using a solenoid valve in the CO_2 line. The rapid increase in impulse frequency when the intrapulmonary CO_2 concentration was reduced is a characteristic of those receptors (Fedde and Peterson, 1970).

Vertical sternal movement was detected with a strain gauge attached to the caudal tip of the sternum, displayed on the oscilloscope, and tape recorded. The neural activity and sternal movements were recorded on film from the tape with a kymographic camera (Grass Inst. Co., Model C-4) for analysis of data.

When we found a single intrapulmonary CO_2-sensitive unit, we followed the same protocol on 5 birds: 1) Obtained static and dynamic sensitivity curves; 2) removed CO_2 from the ventilating gas stream to produce maximal static discharge frequency; 3) approximately 5 minutes later, introduced 0.1% CO into the ventilatory gas stream; 4) ten minutes after beginning to administer CO, we again obtained static and dynamic CO_2 sensitivity curves; 5) removed CO from the ventilatory gas stream after 15 minutes of exposure; 6) obtained static and dynamic CO_2-sensitivity curves 1 minute and 30 minutes after removing CO.

Static CO_2-sensitivity curves were obtained by determining the impulse discharge frequency at steady CO_2 concentrations of 0, 2, 4, 6, and 8% in the ventilating gas stream. Recordings were taken only when the discharge frequency had stabilized (at least 30 seconds) after CO_2 concentration was changed. Dynamic CO_2-sensitivity curves were obtained by determining the change in discharge frequency as a function of time when the CO_2 concentration in the ventilating gas stream was abruptly reduced from 4 to 0%. The curves were used to determine if CO changed the sensitivity of the receptors to their adequate stimulus, CO_2.

The data were analyzed for significant changes by a split-plot analysis of variance (Fryer, 1966). Changes were considered significant when $P<0.05$.

Experiment 2. In experiment 2, the effects of CO of arterial blood gas tensions and HbCO concentrations were determined in 9 unidirectionally, ventilated chickens. Arterial oxygen tension, (PaO_2), pHa, and carbon dioxide tensions, ($PaCO_2$) were determined by withdrawing 3 ml of blood from a sciatic arterial cannula and analyzing it with a blood gas analyzer (Instrumentation Lab., Model 113). An equal volume of heated (40° C), air-equlibrated blood was returned to the bird immediately after the sample was withdrawn. Carboxyhemoglobin concentration was determined on the sample by a modified microdiffusion method (Lambert et al., 1972). Vertical sternal displacement was continuously monitored as described in experiment 1. We attempted to reproduce the protocol of experiment 1 as closely as possible to correlate the respiratory response to CO observed in that experiment with any changes in arterial blood gas tensions and HbCO.

One unidirectionally ventilated chicken in experiment 2 was given 6% CO_2 after CO administration was discontinued to determine if adding CO_2 would increase HbCO removal from the blood.

RESULTS

Experiment 1. Response of intrapulmonary CO_2-sensitive receptors to CO. Discharge frequency from intrapulmonary CO_2-sensitive receptors was determined for 10 seconds each minute for the first 10 minutes after 0.1% CO was added to the ventilating gas stream. A typical response is shown in Fig. 7. The discharge frequency for this receptor during ventilation with 0% CO_2 was 10.5 impulses per second before administering CO (2A); it was 11.0 impulses per second 7 minutes after (2B) and 11.5 impulses per second 10 minutes after (2C) CO was included in the ventilating gas. The mean discharge frequency of 5 receptors from 5 birds during CO administration is shown in

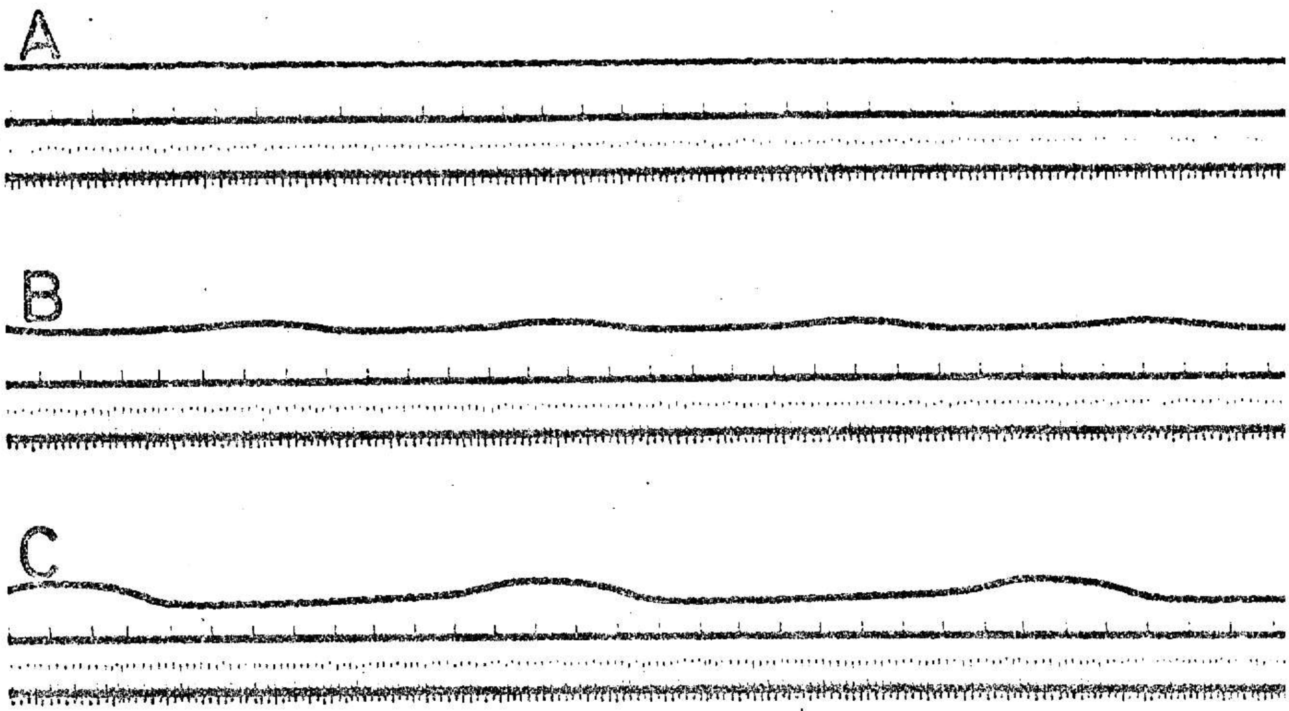

Fig. 7. Effect of CO on discharge frequency from an intrapulmonary CO_2-sensitive receptor and on cyclic respiratory movements. Unidirectional ventilation with 0% CO_2 in the ventilating gas: (A), before administration of CO; (B), 7 minutes after including 0.1% CO in ventilating gas; (C), 10 minutes after including CO. Top tracing in each record is sternal movement; middle tracing is a time line with 0.5 second intervals; bottom tracing is impulse discharge from intrapulmonary CO_2-sensitive receptor. Increases in sternal movements (tracings B and C) were observed without significant changes in discharge frequency of the intrapulmonary CO_2-sensitive receptor.

Fig. 8. Although the discharge frequency tended to increase as CO was administered, the change (9.4 ± 0.6 to 11.1 ± 0.9 SE) was not significant. The mean coefficient of variation for the discharge frequency during the 10 minute period for the 5 receptors was 8.0%.

Ten minutes after CO administration was begun and 1 and 30 minutes after 30 was removed, static and dynamic CO_2-sensitivity curves were determined to provide information about the receptors' response to changes in intrapulmonary CO_2 concentrations. The impulse frequency of the receptors decreased as the CO_2 concentration in the environment surrounding the receptor increased. Differences among curves did not differ significantly as a result of CO administration (Fig. 9 & 10). It thus appears that CO, at the partial pressure given, does not influence the discharge frequency of intrapulmonary CO_2-sensitive receptors nor their sensitivity to CO_2.

Experiment 2. Sternal movement, HbCO, and blood gas tensions during CO administration. For 5 minutes before and during the first 10 minutes of CO administration, the chickens were ventilated with a gas containing no CO_2. When CO_2 was removed from the ventilatory gas before CO was given, no cyclic respiratory motions were exhibited and the birds assumed hyperventilatory apnea. However, during CO administration, cyclic respiratory motions began (Fig. 11). These movements were studied more carefully in 6 birds in experiment 2. They began approximately 6 minutes after CO was included in the ventilating gas and, in most birds, increased in frequency (Fig. 11). The motions began when the HbCO concentration was approximately 25%. The amplitude of the movements also increased but our recording technique did not permit amplitude to be quantitated (Fig. 7). Removing CO from the ventilating gas stream put the birds again into apnea.

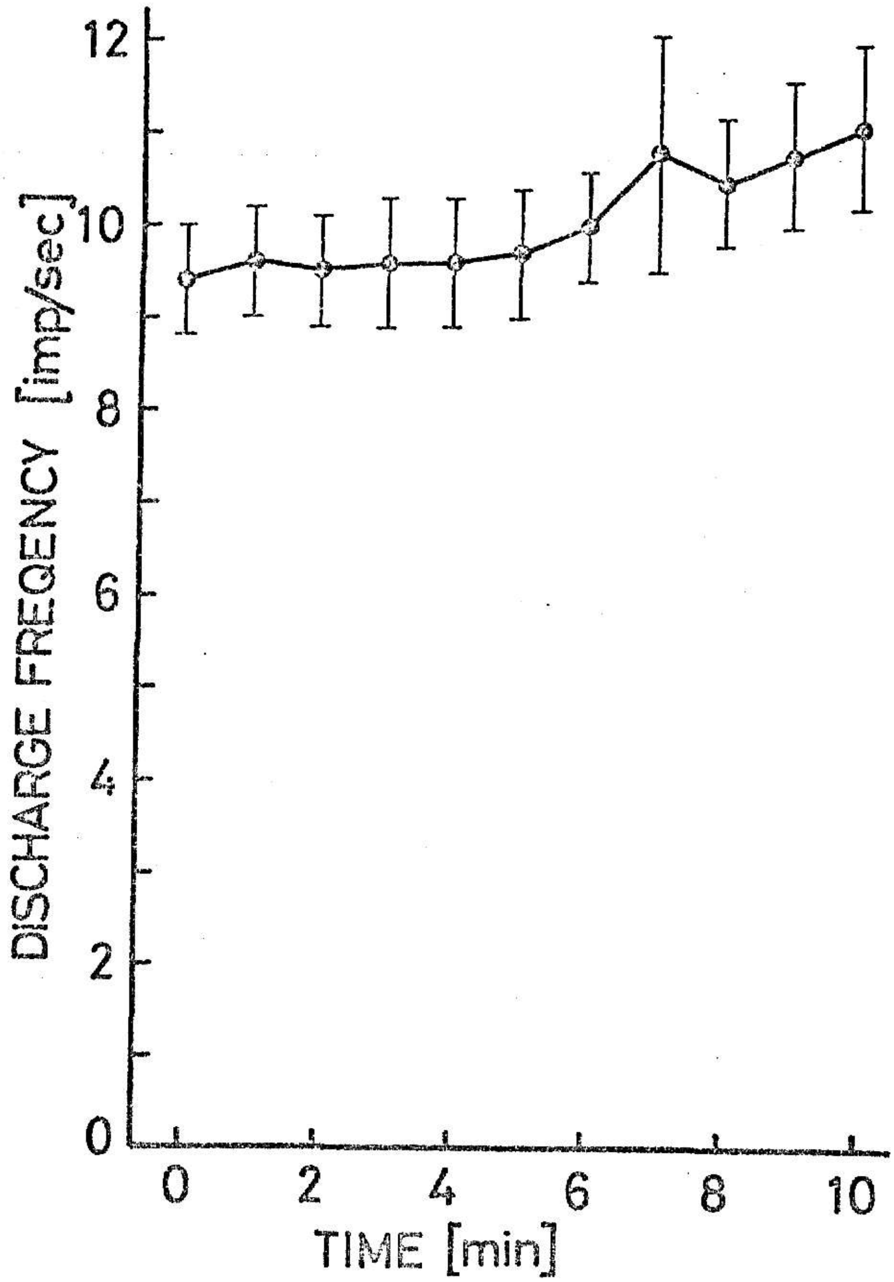

Fig. 8. Effect of 0.1% CO on discharge frequency of intrapulmonary, CO_2-sensitive receptors in 5 receptors (mean ± SE).

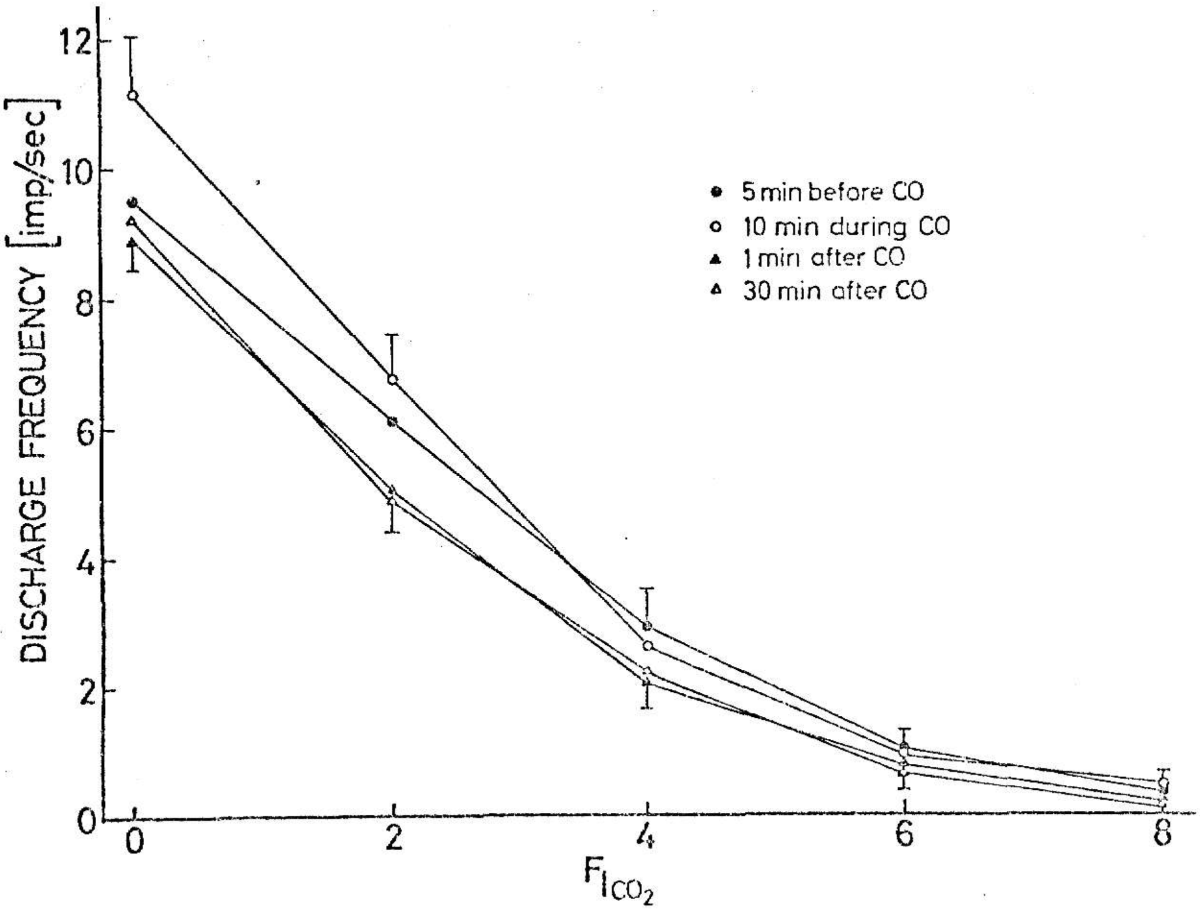

Fig. 9. Effect of 0.1% CO on static CO_2-sensitivity curves determined before, during, and after CO was administered. The mean, steady-state, impulse discharge frequency (± SE) of 5 receptors was plotted when 0, 2, 4, 6, and 8% CO_2 were introduced into the ventilatory gas.

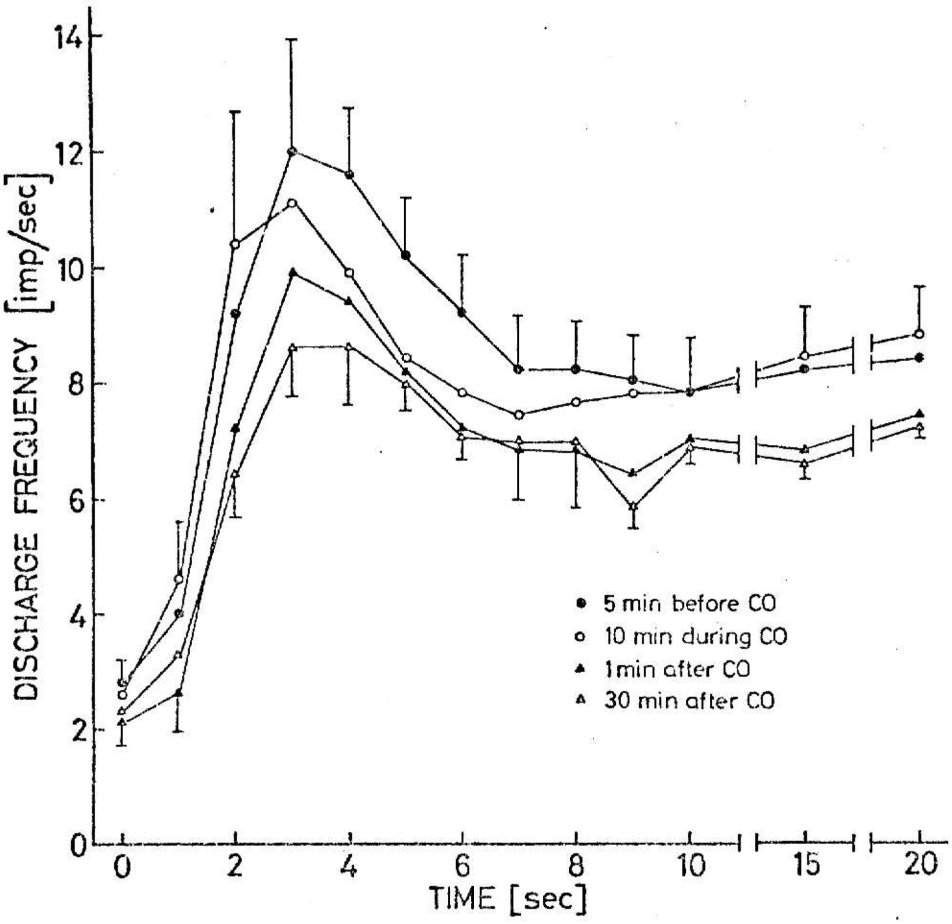

Fig. 10. Effect of 0.1% CO on dynamic CO_2-sensitivity curves before, during, and after CO was administered. The mean (± SE) impulse discharge frequency from 5 receptors is shown before (0 time) and after CO_2 concentration in the ventilating gas was abruptly decreased from 4 to 0%.

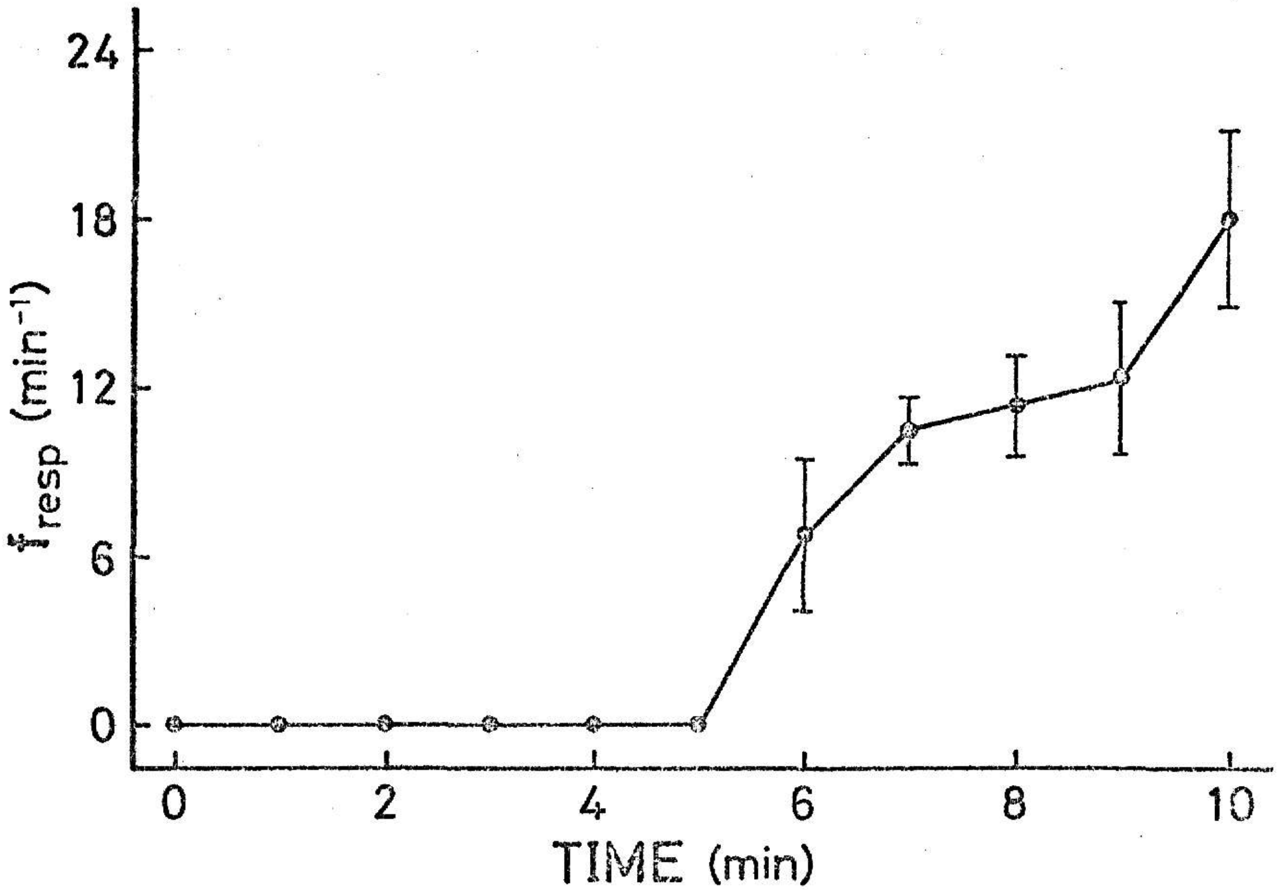

Fig. 11. Effect of 0.1% CO on respiratory frequency during unidirectional ventilation with 0% CO_2 in the ventilating gas. Mean (± SE) response of 6 birds is shown. The chickens were in apnea during the first 5 minutes of CO administration but they initiated cyclic respiratory movements about 6 minutes after CO administration began.

HbCO concentrations rose from 0 to 38% in only 10 minutes during unidirectional ventilation with 0.1% CO (Fig. 12). Likewise, one-half of the HbCO was lost within 25 minutes after CO administration ceased. One hour after CO was removed, HbCO concentrations were only 16.8 ± 0.6% (SE).

Two chickens, in which HbCO exceeded 47% in 10 minutes, died--one 10 minutes after CO administration began; the other, 15 minutes after CO was removed (Fig. 12). In both of these birds the rate of rise of HbCO was more rapid than in those birds that survived and the maximum HbCO was in excess of 50%.

Adding CO_2 to the inhaled gas has been reported to reduce the affinity of hemoglobin for CO (Best and Norman, 1966). To determine if the HbCO removal rate could be increased, we added 6% CO_2 to the ventilatory gas of 1 bird after CO was removed. The rate of removal of HbCO did not differ between that bird and the six that received no CO_2 (Fig. 12).

An unexpected change in PaO_2 occurred during the experiment. One minute before CO was introduced, PaO_2 was 84.8 ± 7.1 (SE) torr. It decreased (61.6 ± 7.8 torr) within 5 minutes after CO administration (Fig. 13) and appeared to increase slightly, but not to pre-exposure levels, after CO was removed from the ventilatory gas.

Because the ventilatory gas contained 0% CO_2 when the blood samples were taken, pHa was high (approximately 8.0) and $PaCO_2$ was low (below 10 torr) throughout the course of the experiment. Limitations in the blood gas analyzing system prevented exact measurements of pHa and $PaCO_2$.

DISCUSSION

Carbon monoxide poisoning seldom reduces PaO_2 until respiration is depressed by pronounced central hypoxia (Root, 1965; Lambertsen, 1968).

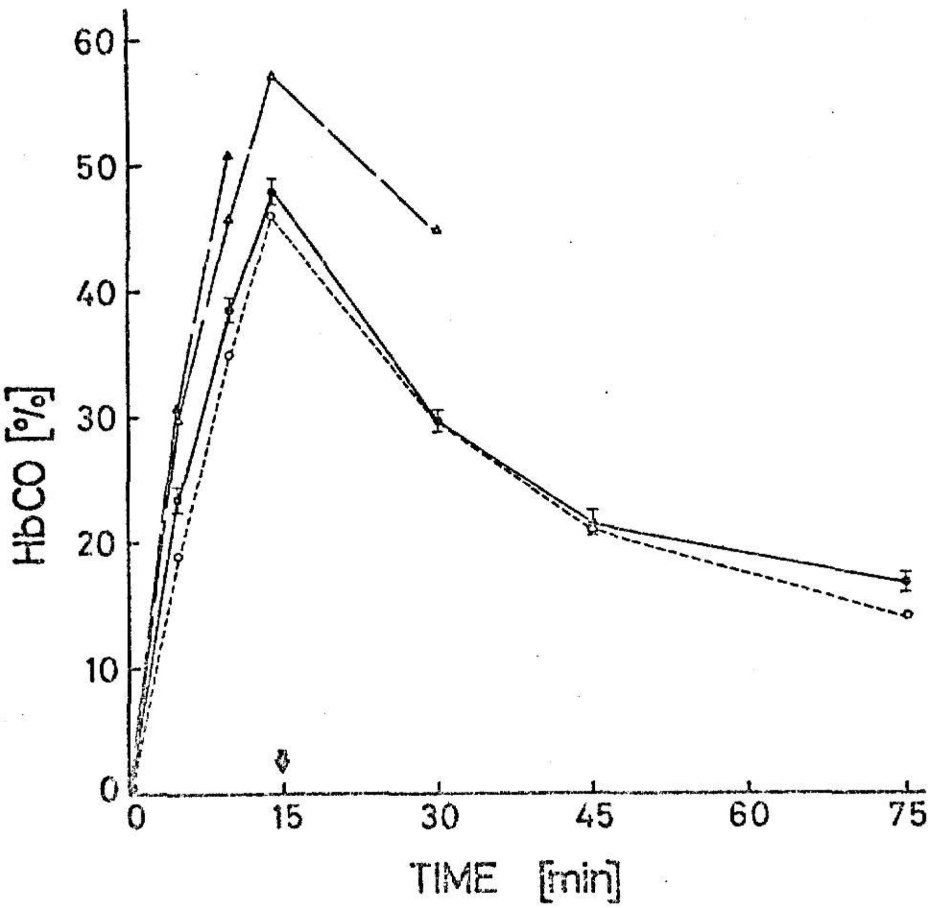

Fig. 12. Carboxyhemoglobin formation and dissociation in unidirectionally ventilated chickens, during and after administration of 0.1% CO. Solid line represents the mean (± SE) HbCO concentration of 6 birds receiving 0.1% CO in the ventilatory gas. Dotted line is the HbCO of 1 bird that received 6% CO_2 after CO was removed from the ventilatory gas. Dashed lines represent HbCO concentrations of 2 birds that died before the experiment ended. CO was added to the ventilatory gas mixture at 0 minute and removed at 15 minutes (arrow).

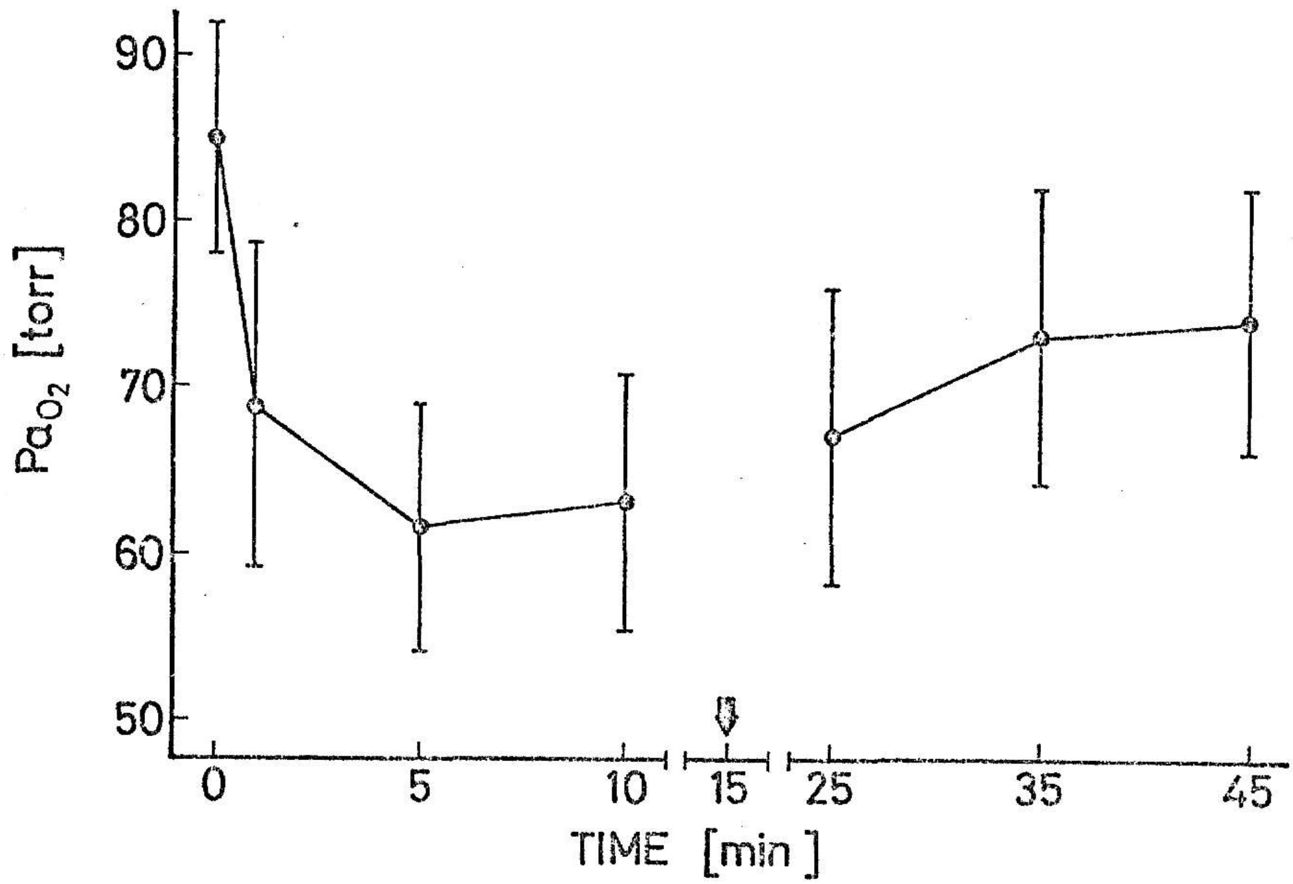

Fig. 13. Effects on PaO_2 during unidirectional ventilation with 0% CO_2 and 0.1% CO. The mean (± SE) of PaO_2 from 6 birds before (reading at time 0), during, and after CO administration. CO was introduced at time 0 and removed after 15 minutes (arrow). Values were not obtained during time indicated by the break in the graph.

The marked decrease in PaO_2 in the chickens receiving CO in our experiments most likely resulted from a facet of the experimental procedure other than adding CO. Removing CO_2 from the ventilating gas in unidirectionally ventilated chickens has been reported to increase tracheal pressure, probably via increased pulmonary airway resistance (Ray and Fedde, 1969). It appears that low intrapulmonary CO_2 concentration causes smooth muscle contraction, which is abundant in the avian lung, especially surrounding the parabronchi (King and Molony, 1971). Such action could shunt gas from the parabronchi and decrease parabronchial ventilation. In recent experiments, when we unidirectionally ventilated chickens first with 5.0% CO_2 and 20.0% O_2 then, for 15 minutes, with 0% CO_2 and 20.0% O_2, PaO_2 decreased from approximately 118 to 73 torr (Fedde, unpublished observations). In the current study, CO_2 was removed from the ventilating gas stream 4 minutes before PaO_2 was first measured. The mean PaO_2, 84.8 torr, was considerably less than expected during ventilation with 20.4% O_2 and it continued to drop (to a minimum of 61.6 torr) the next 5-6 minutes. Administration of CO likely was not involved in the response. Most probably, low intrapulmonary CO_2 concentration constricted parabronchial smooth muscle which decreased parabronchial ventilation and that, in turn, likely reduced PaO_2.

Intrapulmonary, CO_2-sensitive receptor activity was not influenced by 0.1% CO in the ventilatory gas mixture. Furthermore, the receptors' response to CO_2 remained unaltered in the presence of CO, as indicated by no changes in static or dynamic response curves. Thus, initiation of cyclic ventilatory motions, which began about 6 minutes after CO administration, could not have been caused by alterations of that receptor system's activity. Therefore, an alternate explanation of CO action on ventilatory control is needed.

The HbCO concentration reached 25% when cyclic ventilatory motions were initiated. A hypoxic stimulus sufficient to affect such peripheral chemoreceptors as the carotid body (Jones and Purves, 1970; Magno, 1973) may have been present. It is doubtful, however, that such a stimulus was responsible for cyclic ventilatory motions observed during CO administration, because the chickens were not receiving CO_2 in the ventilatory gas mixture during CO administration. The intrapulmonary CO_2-sensitive receptors were, therefore, discharging at relatively high frequency. An increase in discharge frequency of the receptors correlates with a decrease in respiratory motoneuronal activity and apnea (Fedde and Peterson, 1970). Furthermore, that receptor system's inhibitory influence is extremely strong. Fedde and Peterson (1970) showed that during apnea, produced by low intrapulmonary CO_2 concentrations, removing O_2 from the ventilatory gas mixture produced lethal hypoxia but did not induce cyclic ventilatory motions. Neither are those motions induced during less hypoxia (5% O_2 in the ventilating gas) nor by infusing epinephrine or norepinephrine so long as the intrapulmonary CO_2 concentration is low (Fedde, unpublished observations). Thus, all receptor systems, such as carotid and aortic bodies, which could be stimulated by hypoxia, cannot produce enough excitation on the central respiratory neuronal pool to overcome the strong inhibition from the intrapulmonary CO_2-sensitive receptor system. Therefore, even if hypoxia (due to increased HbCO, increased binding of O_2 by Hb, and decreased PaO_2) was strongly stimulating the carotid bodies, it is not likely that their activity could have been responsible for the cyclic ventilatory motions that occurred during CO administration.

To explain the influences of CO on the respiratory control system, its effect on other regions of the body must be considered. Chiodi *et al.* (1941)

found that a given concentration of CO_2 in inspired air induced less increase in ventilation in the hypoxia of CO poisoning than in the non-poisoned animal. They concluded that CO may depress centers in the CNS that control respiration. Barrios et al. (1969) extended that idea when they found latency of many reflexes, especially polysynaptic reflexes, increased during and after cats were exposed to various concentrations of CO.

Our results suggest a hypothesis to explain the site of depressing effect of CO on the CNS and resulting changes in ventilatory control (Fig. 14). Before CO is administered, inherent respiratory rhythmicity of inspiratory and expiratory centers is modulated by peripheral receptors and possibly by higher centers. When intrapulmonary CO_2 concentration is low, impulses from intrapulmonary CO_2-sensitive receptors inhibit respiratory rhythm and cause apnea in the chicken. During CO administration, a depression of inhibitory interneurons (which are activated by the intrapulmonary CO_2-sensitive receptors) would prevent the strong inhibitory influence of these receptors from reaching the respiratory centers. The action of CO must, however, be selective because generation of cyclic breathing movements shows the respiratory neuronal pool is still capable of activity. The inherent respiratory activity in the respiratory centers then could cause cyclic ventilatory motions.

The cardiovascular response of the chicken to spontaneous breathing of 0.1% CO is decreased blood pressure with constant heart frequency (Part 1 of this thesis). Those changes are also explained by the hypothesis that CO selectively depresses the CNS. If both sympathetic and parasympathetic control of the heart were depressed, the result could be negligible change in heart frequency. However, because vascular tone is predominantly provided by sympathetic activity, depressed activity of sympathetic fibers may produce

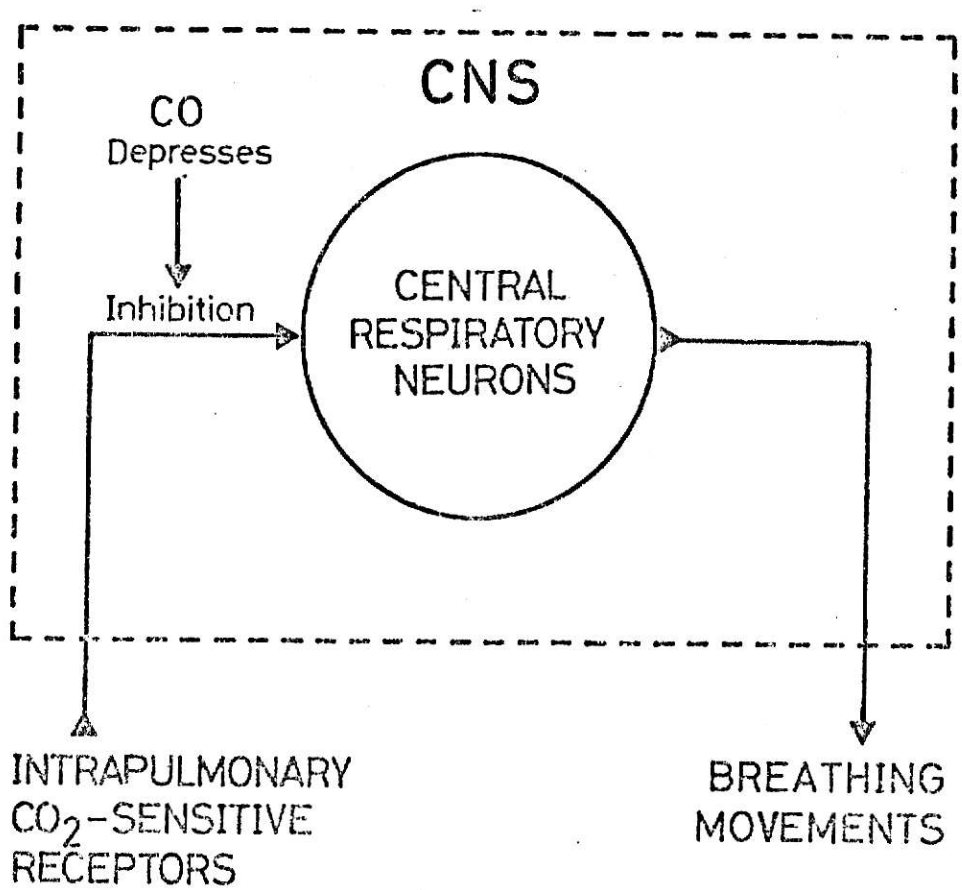

Fig. 14. Possible site and mode of action of CO on respiratory control.

vasodilitation and reduce cardiac output and, hence, the observed decrease in blood pressure. Confirmation or rejection of the hypothesis must await single-unit recordings from inhibitory interneurons activated by intrapulmonary CO_2-sensitive receptors. Perhaps a direct effect of CO on these neurons may thereby be shown.

REFERENCES

Barrios, P., W. Koll and G. Malorny (1969). Rückenmarksreflexe und afferente Nerveleitung der Katze unter dem Einfluss von Kohlenmonoxyd. Naunyn-Schmiebebergs Arch. Pharmak. 264: 1-17.

Best, C. H. and B. T. Norman (1966). Physiological Basis of Medical Practice. Baltimore, Williams and Wilkins Co., pp. 1030-1036.

Butler, P. J. (1967). The effect of progressive hypoxia on the Respiratory and cardiovascular systems of the chicken. J. Physiol. 191: 309-324.

Chiodi, H., D. B. Dill, F. Consolazio and S. M. Horvath (1941). Respiratory and circulatory responses to acute carbon monoxide poisoning. Am. J. Physiol. 134: 683-693.

Fedde, M. R., P. D. DeWet and R. L. Kitchell (1969). Motor unit recruitment pattern and tonic activity in respiratory muscles of Gallus domesticus. J. Neurophysiol. 32: 995-1004.

Fedde, M. R. and D. F. Peterson (1970). Intrapulmonary receptor response to changes in airway-gas composition in Gallus domesticus. J. Physiol. 209: 609-625.

Fryer, H. C. 91956). Concepts and Methods of Experimental Statistics. Boston, Allyn and Bacon Inc., p. 329.

Jones, D. R. and M. J. Purves (1970). The effect of carotide body denervation upon the respiratory responses to hypoxia and hypercapnia in the duck. J. Physiol. 211: 295-309.

King, A. S. and V. Molony (1971). The anatomy of respiration. In: Physiology and Biochemistry of the Domestic Fowl. Vol. I, edited by D. J. Bell and B. M. Freeman. New York, Academic Press, p. 162.

Lambert, J. L., R. R. Tschorn and P. A. Hamlin (1972). Determination of carbon monoxide in blood. Anal. Chem. 44: 1529-1530.

Lambertsen, C. J. (1968). Effects of excessive pressures of oxygen, nitrogen, carbon dioxide, and carbon monoxide: implications in aerospace and undersea environments. In: Medical Physiology. Vol. I, edited by V. B. Mountcastle, St. Louis, C. V. Mosby, p. 848.

Magno, M. (1973). Cardio-respiratory responses to carotide body stimulation with NaCN in the chicken. Respir. Physiol. 17: 220-226.

Ray, P. J. and M. R. Fedde (1969). Responses to alterations in respiratory PO_2 and PCO_2 in the chicken. Respir. Physiol. 6: 135-143.

Root, W. S. (1965). Carbon monoxide. In: Handbook of Physiology. Section 3. Respiration. Vol. II, edited by W. O. Fenn and H. Rahn. Washington, D.C., American Physiological Society.

Stadie, W. C. and K. A. Martin (1925). The elimination of carbon monoxide from the blood. J. Clin. Invest. 2: 77-91.

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APPENDIX TABLE 1

THE EFFECTS OF 0% CARBON MONOXIDE ON FREQUENCY (BREATHS MIN^{-1}) WITH MEANS (X), STANDARD DEVIATIONS (SD), AND STANDARD ERROR (SE)

TIME (MIN)	BIRD # 1	2	3	4	5	6	7	8	9	10	X	SD	SE
0	41.2	32.5	16.8	25.8	26.2	26.8	33.4	27.2	26.2	12.8	26.9	8.0	2.5
5	40.0	32.6	16.0	25.4	25.8	26.0	33.0	26.8	23.4	12.6	26.2	8.0	2.5
	-1.2*	0.1	-0.8	-0.4	-0.4	-0.8	-0.4	-0.4	-2.8	-0.2	-0.7	0.8	0.3
10	41.2	31.8	15.0	26.0	26.4	25.4	33.2	27.0	25.0	14.0	26.5	8.0	2.5
	0.0	-0.7	-1.8	0.2	0.2	-1.4	-0.2	-0.2	-1.2	1.2	-0.4	0.9	0.3
15	40.0	31.6	15.8	26.5	25.5	25.6	32.8	26.4	23.4	13.8	26.1	7.7	2.4
	-1.2	-0.9	-1.0	0.7	-0.7	-1.2	-0.6	-0.8	-2.8	1.0	-0.8	1.0	0.3
20	38.0	29.5	14.5	26.0	25.5	25.5	32.5	26.0	20.0	13.2	24.7	8.2	2.6
	-3.2	-3.0	-2.3	0.2	-0.7	-1.3	-0.9	-1.2	-4.2	0.8	-1.6	1.6	0.5
25	39.6	28.5	12.4	25.0	25.6	24.4	32.2	26.0	20.0	13.2	24.7	8.2	2.6
	-1.6	-4.0	-4.4	-0.8	-0.6	-2.4	-1.2	-1.2	-6.2	0.4	-2.2	2.0	0.6
30	38.0	30.0	13.4	24.8	24.8	24.0	32.4	25.6	19.2	12.8	24.5	7.9	2.5
	-3.2	-2.5	-3.4	-1.0	-1.4	-2.8	-1.0	-1.6	-7.0	0.0	-2.4	2.0	0.6
35	37.8	29.0	14.8	25.2	24.8	24.2	32.0	25.8	19.0	13.0	24.5	7.5	2.4
	-3.4	-3.5	-2.0	-0.6	-1.2	-2.6	-1.4	-1.4	-8.2	0.2	-2.3	2.1	0.7
40	38.2	29.0	13.6	26.0	24.4	24.2	32.0	25.2	18.0	13.0	24.4	7.9	2.5
	-3.0	-3.5	-3.2	0.2	-1.8	-2.6	-1.4	-2.0	-8.2	0.2	-2.5	2.4	0.7
45	39.6	28.5	13.0	25.8	23.8	23.8	31.6	24.8	17.0	13.6	24.2	8.2	2.6
	-1.6	-4.0	-3.8	0.0	-2.4	-3.0	-1.2	-2.4	-9.2	0.8	-2.7	2.7	0.9
50	39.0	29.0	12.5	26.5	23.2	23.8	31.2	24.4	17.0	13.6	24.0	8.2	2.6
	-2.2	-3.5	-4.3	0.7	-3.0	-3.0	-2.2	-2.8	09.2	0.8	-2.9	2.9	0.9
55	38.0	29.5	12.2	27.0	23.4	23.6	30.4	24.2	15.8	14.0	23.8	8.0	2.5
	-3.2	-3.0	-4.6	1.2	-2.8	-3.2	-3.0	-3.0	-10.4	1.2	-3.1	3.2	1.0
60	38.6	30.0	12.6	26.4	23.6	23.5	30.6	24.0	15.4	13.6	23.8	8.2	2.6
	-2.6	-2.5	-4.2	0.6	-2.6	3.3	-2.8	-3.2	-10.8	0.8	-3.1	3.2	1.0

*Absolute change values obtained by subtracting respiratory parameter at time period 0 from time periods 5, 10, 15...60.

APPENDIX TABLE 2

THE EFFECTS OF 0% CARBON MONOXIDE ON TIDAL VOLUME (ML BTPS)
WITH MEANS (X), STANDARD DEVIATIONS (SD), AND STANDARD ERROR (SE)

TIME (MIN)	BIRD # 1	2	3	4	5	6	7	8	9	10	X	SD	SE
0	20.7	21.8	31.4	28.0	23.0	20.7	23.5	23.3	21.8	29.7	24.4	3.8	1.2
5	22.4	21.8	31.4	29.1	23.5	21.3	23.5	24.2	22.4	31.4	25.1	3.9	1.2
	1.7*	0.0	0.0	1.1	0.6	0.6	0.0	0.9	0.6	1.7	0.7	0.6	0.2
10	21.3	22.4	31.9	28.6	24.1	21.3	24.1	24.6	24.1	31.9	25.4	3.9	1.3
	0.6	0.6	0.6	0.6	1.1	0.6	0.6	1.3	2.2	2.2	1.0	0.7	0.2
15	21.8	22.4	31.4	31.4	25.2	21.8	24.1	24.6	25.2	31.4	26.0	3.9	1.2
	1.1	0.6	0.0	3.4	2.2	1.1	0.6	1.3	1.1	1.7	1.3	0.9	0.3
20	22.4	23.0	33.6	30.8	26.3	21.3	24.6	25.1	23.0	31.9	26.2	4.4	1.4
	1.7	1.1	2.2	2.8	3.4	0.6	1.1	1.8	1.1	2.2	1.8	0.9	0.3
25	21.3	24.6	34.7	31.4	28.0	22.4	24.1	25.5	23.5	32.5	26.8	4.6	1.5
	0.6	2.8	3.4	3.4	5.0	1.7	0.6	2.2	1.7	2.8	2.4	1.4	0.4
30	22.4	25.8	34.2	31.9	29.7	23.0	24.6	26.3	24.6	34.7	27.7	4.6	1.4
	1.7	3.9	2.8	3.9	6.8	2.2	1.1	3.0	2.8	5.0	3.3	1.6	0.5
35	22.4	25.8	33.6	31.9	28.6	23.0	25.2	26.4	26.9	35.3	27.9	4.4	1.4
	1.7	3.9	2.2	3.9	5.6	2.2	1.7	3.1	5.0	5.6	3.5	1.5	0.5
40	23.0	26.3	39.2	30.8	29.1	23.5	25.8	26.9	27.4	35.3	28.7	5.1	1.6
	2.2	4.5	7.8	2.8	6.2	2.8	2.2	3.6	5.6	5.6	4.3	1.9	0.6
45	22.4	26.3	38.6	30.2	28.6	24.1	26.3	27.6	29.7	34.2	28.8	4.8	1.5
	1.7	4.5	7.3	2.2	6.2	3.4	2.8	4.3	7.8	4.5	4.5	2.1	0.6
50	23.0	26.3	38.6	30.8	29.7	23.5	26.9	38.4	32.5	34.7	29.4	4.9	1.5
	2.2	4.5	7.3	2.8	6.7	2.8	3.4	5.2	10.6	5.0	5.1	2.6	0.8
55	23.5	27.4	39.2	31.4	29.1	25.2	28.0	29.3	31.9	34.7	30.0	4.6	1.4
	2.8	5.6	7.8	3.4	6.2	4.5	4.5	6.0	10.1	5.0	5.6	2.1	0.7
60	23.5	28.0	37.5	31.9	30.8	24.6	28.6	30.2	33.0	34.7	30.3	4.3	1.4
	2.8	6.2	6.2	3.9	7.8	3.9	5.0	6.9	11.2	5.0	5.9	2.4	0.8

*Absolute change values obtained by subtracting respiratory parameter at time period 0 from time periods 5, 10, 15...60.

APPENDIX TABLE 3

THE EFFECTS OF 0% CARBON MONOXIDE ON MINUTE VOLUME (ML BTPS·MIN^{-1}) WITH MEANS (X), STANDARD DEVIATIONS (SD), AND STANDARD ERROR (SE)

TIME (MIN)	BIRD # 1	2	3	4	5	6	7	8	9	10	X	SD	SE
0	853	708	528	722	603	555	785	634	572	380	634	137	44
5	896	711	502	739	606	554	776	648	524	396	635	148	47
	43*	3	-26	17	3	-1	-9	14	-48	15	1	25	8
10	877	712	478	742	635	540	799	665	601	446	649	138	44
	23	3	-48	20	34	-15	14	32	29	67	16	31	10
15	874	708	495	831	642	559	789	650	537	432	652	148	47
	20	-2	-31	108	41	4	4	17	-35	52	18	42	13
20	851	677	487	800	671	542	800	652	505	434	642	146	46
	-2	-32	-39	78	70	-13	16	19	-67	54	8	48	15
25	843	702	431	784	723	547	775	664	470	429	637	155	49
	-11	-8	-96	61	121	-8	-10	30	-101	49	2	68	22
30	851	772	458	791	736	551	798	674	473	444	655	158	50
	-2	63	-69	69	134	-4	13	40	99	64	20	69	22
35	846	747	497	804	708	556	806	682	510	458	662	144	46
	-7	37	-30	82	107	0	21	48	61	78	40	44	14
40	877	763	533	801	711	569	824	677	494	459	671	149	47
	23	54	6	78	109	14	39	44	-78	78	36	52	16
45	887	750	502	780	680	573	832	683	505	465	666	149	47
	33	40	-25	58	78	18	46	50	-68	85	32	47	15
50	895	763	483	816	689	560	839	694	552	472	676	163	48
	42	53	-44	94	87	5	53	60	-20	92	42	47	15
55	894	809	478	511	681	595	851	710	502	486	652	160	51
	40	100	48	124	80	39	66	76	-68	106	61	54	17
60	908	840	473	843	727	579	875	726	509	472	695	173	55
	54	130	-55	120	125	24	88	92	-63	77	59	70	222

*Absolute change values obtained by subtracting respiratory parameter at time period 0 from time periods 5, 10, 15...60.

APPENDIX TABLE 4

THE EFFECTS OF 0.01% CARBON MONOXIDE ON FREQUENCY (BREATHS MIN^{-1}) WITH MEANS (X), STANDARD DEVIATIONS (SD) AND STANDARD ERROR (SE)

TIME (MIN)	BIRD # 1	2	3	4	5	6	7	8	9	10	X	SD	SE
0	19.5	17.3	24.7	26.1	26.1	25.4	15.6	21.6	36.0	20.4	23.3	5.8	1.8
5	18.0	16.8	25.0	25.8	26.6	25.0	15.0	21.8	36.2	21.2	23.1	6.1	1.9
	-1.5*	-0.5	0.3	-0.3	0.5	-0.4	-0.6	0.2	0.2	0.8	-0.1	0.7	0.2
10	17.4	16.2	24.8	26.0	26.8	24.2	14.4	21.0	38.0	20.7	23.0	6.8	2.1
	-2.1	-1.1	0.1	-0.1	0.7	-1.1	-1.1	-0.6	2.0	0.3	-0.3	1.2	0.4
15	17.0	15.9	24.5	25.5	26.1	23.8	15.4	21.2	37.5	20.1	22.7	6.5	2.1
	-2.5	-1.4	-0.2	-0.6	0.0	-1.6	-0.2	-0.4	1.5	-0.3	-0.6	1.1	0.3
20	16.4	16.0	24.9	25.4	25.6	23.5	14.8	20.4	35.8	19.8	22.3	6.2	1.9
	-3.1	-1.3	0.2	-0.7	-0.5	-1.9	-0.8	-1.2	-0.2	-0.6	-1.0	0.9	0.3
25	15.6	15.4	24.6	25.2	25.5	23.0	14.2	20.8	36.6	19.5	22.0	6.6	2.1
	-3.9	-1.9	-0.1	-0.9	-0.6	-2.4	-1.4	-0.8	0.6	-0.9	-1.2	1.3	0.4
30	15.0	15.7	24.1	24.9	25.0	22.4	14.0	20.5	37.2	19.2	21.8	6.8	2.1
	-4.5	-1.6	-0.6	-1.2	-1.1	-3.0	-1.6	-1.1	1.2	-1.2	-1.5	1.5	0.5
35	14.0	15.0	23.8	24.8	25.2	22.2	13.5	20.4	36.2	18.8	21.4	6.8	2.2
	-5.5	-2.3	-0.9	-2.3	-0.9	-3.2	-2.1	-1.2	0.2	-1.6	-2.0	1.6	0.5
40	13.5	15.2	23.7	24.4	24.7	21.6	13.8	20.0	36.4	18.8	21.2	6.8	2.2
	-6.0	-2.1	-1.0	-1.7	-1.4	-3.8	-1.8	-1.6	0.4	-1.6	-2.1	1.7	0.5
45	13.8	14.7	23.5	23.9	24.0	22.0	13.6	19.2	32.4	18.4	20.6	5.9	1.9
	-5.7	-2.6	-1.2	-2.2	-2.1	-3.4	-2.0	-2.4	-3.6	-2.0	-2.7	1.3	0.4
50	14.2	14.6	23.2	23.0	23.9	21.2	12.8	19.6	31.2	18.0	20.2	5.6	1.8
	-5.3	-2.7	-1.5	-3.1	-2.2	-4.2	-2.8	-2.0	-4.8	-2.4	-3.1	1.3	0.4
55	14.0	14.3	23.2	22.6	23.4	21.4	12.5	19.2	31.0	17.6	19.9	5.6	1.8
	-5.5	-3.0	-1.5	-3.5	-2.7	-4.0	-3.1	-2.4	-5.0	-2.8	-3.4	1.2	0.4
60	14.3	14.2	23.1	22.2	23.0	21.2	12.0	18.8	31.4	17.2	19.7	5.7	1.8
	-5.2	-3.1	-1.6	-3.9	-3.1	-4.2	-3.6	-2.8	-4.6	-3.2	-3.5	1.0	0.3

*Absolute change values obtained by subtracting respiratory parameter at time period 0 from time periods 5, 10, 15...60.

APPENDIX TABLE 5

THE EFFECTS OF 0.01% CARBON MONOXIDE ON TIDAL VOLUME (ML BTPS) WITH MEANS (X), STANDARD DEVIATIONS (SD), AND STANDARD ERROR (SE)

TIME (MIN)	BIRD # 1	2	3	4	5	6	7	8	9	10	X	SD	SE
0	26.9	31.4	23.5	22.4	23.1	33.6	30.8	23.5	15.7	21.8	25.3	5.4	1.7
5	29.1	31.4	23.5	23.5	23.9	34.2	31.4	24.1	15.7	21.3	25.8	5.6	1.8
	2.2*	0.0	0.0	1.1	0.9	0.6	0.6	0.6	0.0	-0.6	0.5	0.8	0.2
10	29.7	31.9	24.1	24.6	24.6	34.2	29.7	24.6	16.2	21.8	26.2	5.3	1.7
	2.8	0.6	0.6	2.4	1.6	0.6	-1.1	1.1	0.6	0.0	0.9	1.1	0.3
15	30.8	31.9	24.1	25.2	25.2	34.7	29.7	24.6	16.2	22.4	26.5	5.4	1.7
	3.9	0.6	0.6	2.8	2.1	1.1	-1.1	1.1	0.6	0.6	1.2	1.4	0.4
20	30.8	32.5	25.2	26.3	25.8	35.3	30.8	24.6	16.2	22.4	27.0	5.5	1.7
	3.9	1.1	1.7	3.9	2.7	1.7	0.0	1.1	0.5	0.6	1.7	1.4	4.3
25	34.2	33.0	25.2	26.9	25.8	35.3	32.5	25.2	16.8	23.0	27.8	5.8	1.8
	7.3	1.7	1.7	4.5	2.7	1.7	1.7	0.6	1.1	1.1	2.5	1.9	0.6
30	34.2	33.6	25.8	27.4	26.3	36.4	33.0	25.2	17.9	23.5	28.2	5.9	1.9
	7.3	2.2	2.2	5.0	1.0	2.8	1.7	1.7	1.7	1.1	2.9	1.9	0.6
35	34.7	33.6	25.7	27.4	26.3	36.4	33.0	25.2	17.9	23.5	28.4	5.8	1.8
	7.8	2.2	2.2	5.0	3.2	2.8	2.2	1.7	2.2	1.7	3.1	1.9	0.6
40	35.8	35.3	26.3	28.0	26.9	37.0	33.0	26.3	17.9	23.5	29.0	6.1	1.9
	9.0	3.9	2.8	5.6	3.8	3.4	2.2	2.8	2.4	1.7	3.7	2.1	0.7
45	35.8	34.7	26.9	29.1	26.9	36.4	33.6	26.9	18.5	24.1	29.3	5.8	1.8
	9.0	3.4	3.4	6.7	3.8	2.8	2.8	3.4	2.8	2.2	4.0	2.1	0.7
50	35.8	35.3	27.4	29.7	27.4	37.5	35.8	27.4	20.2	25.2	30.2	5.9	1.8
	9.0	3.9	3.9	7.3	4.4	3.9	5.0	3.9	4.5	3.4	4.9	1.8	0.6
55	35.3	35.8	28.0	30.2	38.6	38.6	36.4	28.6	23.0	26.3	31.1	5.1	1.6
	8.4	4.5	4.5	7.9	5.5	5.0	5.6	5.0	7.3	4.5	5.8	1.5	0.5
60	37.0	35.8	28.6	30.8	29.7	39.2	15.1	29.7	22.4	27.4	29.6	7.1	2.2
	10.1	4.5	5.0	4.8	6.6	5.6	6.7	6.2	6.7	5.6	6.6	1.6	0.5

*Absolute change values obtained by subtracting respiratory parameter at time period 0 from time periods 5, 10, 15...60.

APPENDIX TABLE 6

THE EFFECTS OF 0.01% CARBON MONOXIDE ON MINUTE VOLUME (ML BTPS·MIN^{-1}) WITH MEANS (X), STANDARD DEVIATIONS (SD) AND STANDARD ERROR (SE)

TIME (MIN)	BIRD # 1	2	3	4	5	6	7	8	9	10	X	SD	SE
0	524	543	580	585	602	8853	480	508	564	445	568	112	35
5	524	527	588	607	638	554	470	525	456	451	575	114	36
	0*	-16	7	21	35	1	-10	17	8	6	6	15	5
10	516	517	597	640	660	827	427	517	617	452	577	117	37
	- 8	-25	16	56	58	-27	53	9	52	6	19	34	10
15	524	507	590	642	658	826	457	522	609	450	579	113	36
	- 1	-35	9	58	56	-27	-23	14	44	5	10	34	11
20	505	452	627	667	659	629	456	547	581	444	577	123	39
	-19	-23	46	84	57	-24	-25	- 5	17	- 2	11	39	12
25	532	509	620	676	657	811	461	524	615	448	585	112	35
	8	-33	38	93	16	-42	-19	16	50	2	17	43	14
30	512	528	621	683	658	815	455	517	534	441	576	116	36
	-12	-15	40	99	56	-38	26	8	81	- 5	19	47	15
35	486	504	613	679	663	808	446	514	649	453	582	120	37
	-38	-39	32	95	61	-45	-34	6	84	7	13	53	17
40	484	536	624	683	663	798	456	526	652	442	587	116	37
	-40	- 6	42	99	62	-55	-25	18	87	- 3	18	53	17
45	495	510	632	696	645	801	457	516	599	604	595	105	33
	-30	-32	51	111	43	-53	-24	8	34	- 2	11	50	16
50	509	555	636	682	655	795	458	538	629	453	591	108	34
	-15	-27	55	98	54	58	22	30	65	8	19	50	16
55	494	513	650	683	668	827	455	548	708	463	601	124	39
	-30	-30	69	99	66	-27	-26	40	147	18	33	62	20
60	529	509	660	684	683	831	450	558	704	472	608	123	39
	4	-34	79	99	81	-22	-30	50	139	26	39	60	19

*Absolute change values obtained by subtracting respiratory parameter at time period 0 from time periods 5, 10, 15...60.

APPENDIX TABLE 7

THE EFFECTS OF 0.1% CARBON MONOXIDE ON FREQUENCY (BREATHS MIN^{-1}) WITH MEANS (X), STANDARD DEVIATIONS (SD), AND STANDARD ERROR (SE)

TIME (MIN)	BIRD # 1	2	3	4	5	6	7	8	9	10	X	SD	SE
0	16.4	26.2	15.8	21.2	24.5	35.2	28.6	22.8	17.7	37.8	24.6	7.5	2.4
5	16.8	26.4	16.0	22.0	25.0	35.8	29.0	22.5	17.8	37.8	24.9	7.6	2.4
	0.4*	0.2	0.2	0.8	0.4	0.6	0.4	-0.3	0.1	0.0	0.3	0.3	0.1
10	17.6	26.5	16.2	23.6	25.2	36.8	29.4	23.2	18.2	33.0	25.0	6.7	2.1
	1.2	0.3	0.4	2.4	0.6	1.6	0.8	0.4	0.5	-4.8	0.3	1.9	0.6
15	17.8	30.0	17.2	23.8	25.8	34.5	28.8	24.6	18.5	35.8	25.7	6.7	2.1
	1.4	3.8	1.4	2.6	1.2	-0.7	0.2	1.8	0.8	-2.0	1.1	1.6	0.5
20	17.6	29.2	17.5	23.5	24.2	31.2	28.4	24.0	19.2	26.0	24.1	4.8	1.5
	1.2	3.0	1.7	2.3	-0.4	-4.0	-0.2	1.2	1.5	-11.8	-0.6	4.4	1.4
25	17.3	23.0	17.4	23.2	24.2	28.8	28.0	23.8	19.2	25.6	23.1	4.0	1.3
	0.9	-3.3	1.6	2.0	-0.4	-6.4	-0.6	1.0	1.5	-12.2	-1.6	4.6	1.4
30	16.8	22.5	17.8	24.0	23.5	30.0	28.5	24.2	19.9	22.6	22.9	4.3	1.3
	0.4	-3.7	2.0	2.8	-1.1	-5.2	-0.1	1.4	1.3	-15.3	-1.8	5.4	1.7
35	15.5	21.5	17.8	22.6	22.4	28.0	27.6	24.0	18.0	20.8	21.8	4.1	1.3
	-2.9	-4.7	2.0	1.4	-2.2	-7.2	-1.0	1.2	0.9	-17.0	-3.0	5.8	1.8
40	14.5	18.5	16.4	22.5	20.0	27.5	27.5	23.8	18.8	21.4	21.1	4.4	1.4
	-1.9	-7.8	0.6	1.4	-4.6	-7.7	-1.1	1.0	1.1	-16.4	-3.5	5.7	1.8
45	15.0	18.6	16.8	21.4	19.8	25.0	26.4	23.5	18.2	21.0	20.6	3.6	1.1
	-1.4	-7.6	1.0	0.2	-4.8	-10.2	-2.2	0.7	0.5	-16.8	-4.1	5.9	1.9
50	16.0	19.8	16.0	22.0	19.8	24.0	26.2	22.6	18.0	21.2	20.6	3.3	1.1
	-0.4	-6.4	0.2	0.8	-4.8	-11.2	-2.4	-0.2	-0.3	-16.6	-4.1	5.8	1.8
55	15.5	20.2	16.5	22.8	20.0	22.4	25.5	20.2	17.8	21.4	20.2	3.0	1.0
	-0.9	-6.0	0.7	1.6	-4.6	-12.8	-3.1	-2.6	0.1	-16.4	-4.4	5.9	1.9
60	16.0	21.5	16.8	22.5	20.0	21.6	25.5	19.8	17.5	20.6	20.2	2.9	0.9
	-0.4	-4.7	1.0	1.3	-4.6	-13.6	-3.1	-3.0	-0.2	-17.2	-4.5	6.2	2.0

*Absolute change values obtained by subtracting respiratory parameter at time period 0 from time periods 5, 10, 15...60.

APPENDIX TABLE 8

THE EFFECTS OF 0.1% CARBON MONOXIDE ON TIDAL VOLUME (ML BTPS) WITH MEANS (X), STANDARD DEVIATIONS (SD), AND STANDARD ERROR (SE)

TIME (MIN)	BIRD # 1	2	3	4	5	6	7	8	9	10	X	SD	SE
0	29.7	17.9	20.2	28.0	22.4	24.1	20.7	26.3	27.4	20.2	23.7	4.0	1.3
5	31.4	19.0	20.7	29.1	24.6	25.2	21.3	26.9	28.0	23.5	25.0	3.9	1.2
	1.7*	1.1	0.6	1.1	2.2	1.1	0.6	0.6	0.6	3.4	1.3	0.9	0.3
10	36.4	19.0	21.8	29.7	25.2	31.4	22.4	27.4	28.6	35.8	27.8	5.8	1.8
	6.7	1.1	1.7	1.7	2.8	7.3	1.7	1.1	1.1	15.7	4.1	4.7	1.5
15	75.0	23.0	24.6	30.8	29.7	32.5	25.0	29.7	29.1	38.6	33.8	15.1	4.8
	45.4	5.0	4.5	2.8	7.3	8.4	4.5	3.4	1.7	18.5	10.1	13.3	4.2
20	73.9	29.7	31.9	33.0	33.6	35.8	27.4	33.6	30.8	47.5	37.7	13.8	4.4
	44.2	11.8	11.8	5.0	11.2	11.8	6.7	7.3	3.4	27.4	14.1	12.5	4.0
25	71.7	30.2	38.6	33.6	35.3	40.3	30.8	35.8	30.2	49.8	39.6	12.7	4.0
	42.0	12.3	18.4	5.6	12.9	16.2	10.1	9.5	2.8	29.7	16.0	11.8	3.0
30	66.6	34.2	41.4	36.4	37.0	40.9	34.2	37.5	33.0	56.0	41.7	11.0	3.5
	37.0	16.2	21.3	8.4	14.6	16.8	13.4	11.2	5.6	35.8	18.0	10.6	3.4
35	65.5	34.7	40.9	39.2	38.6	41.4	35.3	39.2	36.4	59.9	43.1	10.6	3.4
	35.8	16.7	20.6	11.2	16.2	17.4	14.6	12.9	9.0	39.8	19.4	10.3	3.2
40	68.9	33.0	33.0	42.6	40.3	43.7	35.8	40.3	35.3	60.5	43.3	12.0	3.8
	39.2	15.1	12.9	14.6	17.9	19.6	14.1	14.0	7.8	40.3	19.7	11.0	3.5
45	64.4	36.9	31.9	42.0	44.2	45.4	35.3	42.0	38.6	59.9	43.0	11.6	3.7
	34.3	9.0	11.8	14.0	21.8	21.3	14.6	15.7	11.2	39.8	19.3	10.2	3.2
50	61.6	28.6	33.6	42.0	45.4	42.6	36.4	40.9	40.3	58.2	43.0	10.2	3.2
	30.8	10.6	13.4	14.0	23.0	18.5	15.7	14.6	12.9	38.0	19.2	8.9	2.1
55	66.1	29.1	35.3	40.9	44.8	49.3	35.8	42.6	40.9	57.7	44.2	11.0	3.5
	36.4	11.2	15.1	12.9	22.4	25.2	15.1	16.2	13.4	37.5	20.6	9.6	3.0
60	65.0	29.1	37.0	41.4	44.8	48.7	35.8	42.0	40.3	61.0	44.5	11.1	3.5
	35.3	11.2	16.8	13.4	22.4	24.6	15.1	15.7	12.9	40.9	20.8	10.1	3.2

*Absolute change values obtained by subtracting respiratory parameter at time period 0 from time periods 5, 10, 15...60.

APPENDIX TABLE 9

THE EFFECTS OF 0.1% CARBON MONOXIDE ON MINUTE VOLUME (ML BTPS·MIN^{-1}) WITH MEANS (X), STANDARD DEVIATIONS (SD), AND STANDARD ERROR (SE)

TIME (MIN)	BIRD # 1	2	3	4	5	6	7	8	9	10	X	SD	SE
0	487	470	319	594	551	848	593	600	486	762	571	150	48
5	527	503	332	641	616	902	617	605	498	889	613	174	55
	40*	33	13	47	65	55	25	5	13	127	42	36	11
10	641	505	348	700	635	1154	659	637	520	1182	698	268	84
	154	35	30	107	84	306	66	36	34	421	127	133	42
15	1336	689	423	733	766	1121	726	730	539	1383	845	325	103
	849	219	94	139	214	273	133	130	53	621	273	257	81
20	1301	867	559	776	813	1118	779	806	591	1237	885	254	80
	814	397	240	115	262	271	187	206	106	476	307	212	67
25	1240	696	672	789	630	1161	862	852	581	1276	875	259	83
	753	226	354	186	303	314	270	252	95	514	327	186	58
30	1120	769	738	874	869	1226	974	908	628	1266	937	211	66
	633	299	419	280	318	379	381	307	142	504	366	134	42
35	1016	747	542	886	866	1160	974	941	677	1246	905	214	68
	529	276	223	292	314	313	381	341	191	484	335	106	34
40	999	608	536	958	806	1201	986	960	663	1294	901	248	78
	512	138	218	364	255	354	393	360	178	532	330	133	42
45	958	500	538	899	876	1134	931	987	703	1258	878	241	76
	471	30	219	305	325	386	339	387	106	496	296	147	46
50	968	565	582	924	898	1021	954	924	726	1235	880	204	65
	481	96	264	330	347	174	361	324	240	473	309	122	38
55	1024	588	621	932	896	1103	914	860	728	1234	890	204	65
	537	119	302	338	345	256	321	260	242	472	319	118	37
60	1039	626	582	932	896	1052	914	832	715	1257	885	207	65
	553	157	264	339	345	205	321	231	229	495	314	127	40

*Absolute change values obtained by subtracting respiratory parameter at time period 0 from time periods 5, 10, 15...60.

APPENDIX TABLE 10

THE EFFECTS OF 0.5% CARBON MONOXIDE ON FREQUENCY (f, BREATHS MIN^{-1}), TIDAL VOLUME (V_T, ML BTPS) AND MINUTE VOLUME ($\dot{V}$, ML BTPS$\cdot MIN^{-1}$), WITH MEANS (X), STANDARD DEVIATIONS (SD), AND STANDARD ERROR (SE)

TIME (MIN)	BIRD # 1	2	3	4	5	6	7	8	9	10	X	SD	SE
FREQUENCY													
0	19.2	24.8	27.2	17.3	28.5	19.2	17.2	15.6	21.2	18.3	20.9	4.5	1.4
5	20.0	25.0	27.8	18.7	30.0	19.3	17.5	16.0	20.2	19.0	21.3	4.6	1.5
	0.8*	0.2	0.6	1.4	1.5	0.1	0.3	0.4	-1.0	0.7	0.5	0.7	0.2
10	20.8	25.2	28.8	10.4	24.0	17.4	19.6	18.2	9.5	18.1	19.2	6.1	1.9
	1.6	0.4	1.6	-6.9	-4.5	-1.8	2.4	2.6	-11.7	-0.2	-1.7	4.7	1.5
15	15.4	19.5	19.5	6.0	14.8	12.2	11.8	10.5	3.7	15.6	12.9	5.2	1.6
	-3.8	-5.3	-7.7	-11.3	-13.7	-7.0	-5.4	-5.1	-17.5	-2.7	-7.2	5.9	1.5
20	10.2	12.6	9.9		11.4		8.5	6.4		7.5	9.5	2.2	0.8
	-9.2	-12.2	-17.3		-17.1		-8.7	-9.2		-10.8	-9.5	8.9	1.4
TIDAL VOLUME													
0	31.9	23.5	40.3	27.4	26.8	33.6	33.6	27.4	29.1	26.9	30.1	4.8	1.4
5	35.3	30.8	50.4	31.9	27.4	39.8	37.0	35.8	36.4	31.9	35.7	6.2	1.8
	3.4*	7.3	10.1	4.5	0.6	5.6	3.4	8.4	7.3	5.0	5.5	2.3	0.8
10	52.6	38.6	56.6	50.4	31.4	56.0	42.6	45.4	49.8	52.2	47.5	8.0	2.3
	20.7	15.1	16.2	23.0	4.5	22.4	9.0	17.9	20.7	25.2	17.5	6.5	1.7
15	59.9	49.9	59.4	56.0	37.5	67.2	56.0	53.7	20.2	52.1	51.2	13.4	3.8
	28.0	26.3	19.0	28.6	10.6	33.6	22.4	26.3	-9.0	25.2	21.1	12.2	3.5
20	56.0	47.6	58.2		38.6		84.0	58.2		54.9	55.8	13.9	4.7
	24.1	24.1	17.9		11.8		50.4	30.8		28.0	26.7	12.2	4.1
MINUTE VOLUME													
0	612	583	1096	474	766	645	577	428	617	491	629	190	53
5	705	770	1401	596	935	752	646	573	735	606	761	239	67
	93*	187	304	122	57	107	68	145	117	114	131	71	20
10	1094	973	1628	525	752	974	834	825	473	812	889	323	91
	482	390	532	49	-13	329	256	397	-138	320	260	222	63
15	922	972	1157	336	555	819	661	564	75	812	687	320	90
	309	388	60	-138	-211	175	82	136	542	320	166	233	66
20	572	600	576		440		714	361		411	525	124	42
	42	16	-520		-325		136	-55		-80	-112	230	78

*Absolute change values obtained by subtracting respiratory parameters at time period 0 from time periods 5, 10, 15 and 20.

APPENDIX TABLE 11

THE EFFECTS OF 0% CARBON MONOXIDE ON HEART RATE AND BLOOD PRESSURE

TIME (MIN)		BIRD # 1	2	3	4	5	6	7	8	9	10	X	SD	SE
0	HEART RATE	240	244	260	254	240	250	252	250	232	240	247.2	7.00	2.21
	DIASTOLIC PRESSURE	100	115	125	115	70	80	105	100	95	80	98.5	17.64	5.58
	SYSTOLIC PRESSURE	140	155	160	150	110	120	145	140	115	120	135.5	17.86	5.64
	MEAN BLOOD PRESSURE	113	128	136	126	83	93	118	113	101	93	110.4	17.39	5.50
15	HEART RATE	250	244	248	250	236	252	240	238	244	260	246.2	7.26	2.29
	DIASTOLIC PRESSURE	110	110	100	130	70	90	95	105	105	115	103.0	16.02	5.06
	SYSTOLIC PRESSURE	150	150	148	155	110	135	125	145	120	135	137.3	14.96	4.73
	MEAN BLOOD PRESSURE	123	123	116	138	83	105	105	118	110	121	114.2	14.70	4.64
30	HEART RATE	244	238	252	252	248	252	230	242	260	254	247.2	8.80	2.78
	DIASTOLIC PRESSURE	115	110	120	100	75	90	100	100	115	120	104.5	14.42	4.56
	SYSTOLIC PRESSURE	155	150	165	140	115	135	130	145	140	165	144.0	15.59	4.93
	MEAN BLOOD PRESSURE	128	123	135	113	88	105	110	115	123	135	117.5	14.50	4.58
45	HEART RATE	256	240	252	254	250	250	226	260	244	256	248.8	9.94	3.14
	DIASTOLIC PRESSURE	125	115	110	95	80	90	90	110	110	115	104.0	14.29	4.52
	SYSTOLIC PRESSURE	160	160	160	135	120	130	110	155	125	155	141.0	19.11	6.04
	MEAN BLOOD PRESSURE	136	130	126	108	93	103	96	125	115	128	116.0	15.21	4.81
60	HEART RATE	246	246	254	260	250	260	240	264	252	258	253.0	7.61	2.40
	DIASTOLIC PRESSURE	115	110	105	80	90	95	105	120	95	105	102.0	12.06	3.81
	SYSTOLIC PRESSURE	155	150	150	120	130	135	145	135	135	145	140.0	10.81	3.41
	MEAN BLOOD PRESSURE	128	123	120	93	103	108	118	125	108	118	114.4	11.00	3.49

APPENDIX TABLE 11a

THE EFFECTS OF 0% CARBON MONOXIDE ON CHANGES IN HEART FREQUENCY AND BLOOD PRESSURE WITH MEANS (X), STANDARD DEIVATIONS (SD) AND STANDARD ERROR (SE). VALUES OBTAINED BY SUBTRACTING THE CARDIOVASCULAR PARAMETER AT TIME 0 FROM TIME PERIODS 15, 30, 45 AND 60 ON TABLE 11.

TIME (MIN)		BIRD # 1	2	3	4	5	6	7	8	9	10	X	SD	SE
15	HEART RATE	10	0	-12	- 4	- 4	2	-12	-12	12	20	0.0	11.1	3.5
	DIASTOLIC PRESSURE	10	- 5	-25	15	0	10	-10	5	10	35	4.5	16.1	5.1
	SYSTOLIC PRESSURE	10	- 5	-12	5	0	15	-20	5	5	15	1.8	11.3	3.5
	MEAN BLOOD PRESSURE	10	- 5	-20	12	0	8	-13	5	9	28	3.4	13.6	4.3
30	HEART RATE	4	- 6	- 8	- 2	8	2	-22	- 8	28	14	1.0	13.7	4.4
	DIASTOLIC PRESSURE	15	- 5	- 5	-15	5	10	- 5	0	20	40	6.0	15.9	5.0
	SYSTOLIC PRESSURE	15	- 5	5	-10	5	15	-15	5	25	45	8.5	17.6	5.6
	MEAN BLOOD PRESSURE	15	- 5	- 1	-13	5	8	- 8	2	22	42	6.7	16.2	5.1
45	HEART RATE	16	- 4	- 8	0	10	0	-26	10	12	16	1.6	12.6	4.0
	DIASTOLIC PRESSURE	25	0	-15	-20	10	10	-15	10	15	35	5.5	18.0	5.7
	SYSTOLIC PRESSURE	25	5	0	-15	10	10	-35	15	10	35	6.0	19.7	6.2
	MEAN BLOOD PRESSURE	23	2	-10	-18	10	10	-22	12	14	35	5.6	17.9	5.6
60	HEART RATE	6	6	- 6	6	10	10	-12	14	20	18	7.2	9.9	3.1
	DIASTOLIC PRESSURE	15	- 5	-20	-25	20	15	0	20	0	25	4.5	17.4	5.5
	SYSTOLIC PRESSURE	20	- 5	-10	-30	20	15	0	- 5	20	25	5.0	17.8	5.6
	MEAN BLOOD PRESSURE	15	- 5	-16	-33	20	15	0	12	7	25	4.0	17.9	5.7

APPENDIX TABLE 12

THE EFFECTS OF 0.01% CARBON MONOXIDE ON HEART RATE AND BLOOD PRESSURE

TIME (MIN)		BIRD # 1	2	3	4	5	6	7	8	9	10	X	SD	SE
0	HEART RATE	280	262	240	232	272	260	260	282	256	252	259.6	15.96	5.04
	DIASTOLIC PRESSURE	100	115	125	115	95	100	95	100	125	100	107.0	11.83	3.74
	SYSTOLIC PRESSURE	125	135	145	140	110	125	130	135	160	135	134.0	13.29	4.20
	MEAN BLOOD PRESSURE	108	121	131	123	96	108	106	111	137	111	115.6	12.35	3.90
15	HEART RATE	272	260	252	260	280	272	256	272	256	250	263.0	10.20	3.22
	DIASTOLIC PRESSURE	85	115	110	100	90	95	95	110	100	105	100.5	9.35	3.02
	SYSTOLIC PRESSURE	125	135	123	123	115	115	125	150	150	145	131.0	13.29	4.20
	MEAN BLOOD PRESSURE	98	121	115	108	98	101	105	123	116	118	110.6	9.52	3.01
30	HEART RATE	274	262	260	252	292	264	248	288	264	254	265.8	14.71	4.65
	DIASTOLIC PRESSURE	95	120	105	105	95	100	95	115	100	100	103.0	8.56	2.70
	SYSTOLIC PRESSURE	125	135	125	130	110	115	125	155	140	130	129.0	12.64	4.00
	MEAN BLOOD PRESSURE	105	125	111	113	100	105	105	128	113	110	115.6	8.99	2.84
45	HEART RATE	286	272	264	248	286	264	264	292	260	264	270.0	13.85	4.38
	DIASTOLIC PRESSURE	95	100	110	100	95	85	100	125	120	95	102.5	12.30	3.89
	SYSTOLIC PRESSURE	120	125	125	135	100	120	125	155	165	110	128.0	19.46	6.15
	MEAN BLOOD PRESSURE	103	108	115	111	96	96	108	135	135	100	110.9	14.05	4.44
60	HEART RATE	280	258	250	240	284	264	268	284	262	270	266.0	14.45	4.57
	DIASTOLIC PRESSURE	80	90	95	100	85	85	100	115	105	85	94.0	11.00	3.48
	SYSTOLIC PRESSURE	115	120	135	135	105	105	125	155	145	100	124.0	18.27	5.81
	MEAN BLOOD PRESSURE	91	100	108	111	91	91	108	128	118	90	103.9	13.17	4.16

APPENDIX TABLE 12a

THE EFFECTS OF 0.01% CARBON MONOXIDE ON CHANGES IN HEART FREQUENCY AND BLOOD PRESSURE WITH MEANS (X), STANDARD DEVIATIONS (SD) AND STANDARD ERROR (SE). VALUES OBTAINED BY SUBTRACTING THE CARDIOVASCULAR PARAMETER AT TIME 0 FROM TIME PERIODS 15, 30, 45 AND 60 ON TABLE 12.

TIME (MIN)		BIRD # 1	2	3	4	5	6	7	8	9	10	X	SD	SE
15	HEART RATE	- 8	- 2	12	28	8	12	- 4	-10	0	- 2	3.4	11.5	3.7
	DIASTOLIC PRESSURE	-15	0	-15	15	- 5	- 5	0	10	-25	5	-3.5	12.2	3.8
	SYSTOLIC PRESSURE	0	0	-20	-15	5	-10	- 5	15	-10	10	-3.0	11.1	3.5
	MEAN BLOOD PRESSURE	-10	0	-16	-15	2	- 7	- 1	12	-20	7	-4.8	10.5	3.3
30	HEART RATE	- 6	0	20	20	20	4	-12	5	8	2	6.2	11.1	3.5
	DIASTOLIC PRESSURE	- 5	5	-20	10	0	0	0	15	-25	0	-2.0	12.3	3.9
	SYSTOLIC PRESSURE	0	0	-20	-10	0	-10	- 5	20	-20	- 5	-5.0	11.5	3.7
	MEAN BLOOD PRESSURE	- 3	4	-20	-10	4	- 3	- 1	17	-23	- 1	-3.6	11.7	3.7
45	HEART RATE	6	10	24	15	14	4	4	10	4	12	10.4	6.4	2.0
	DIASTOLIC PRESSURE	- 5	-15	-15	15	0	-15	5	25	- 5	- 5	-1.5	13.3	4.2
	SYSTOLIC PRESSURE	- 5	-10	-20	- 5	-10	- 5	- 5	20	5	-25	-6.0	12.4	3.9
	MEAN BLOOD PRESSURE	- 5	-13	-16	-12	0	-12	2	24	- 1	-11	-4.4	11.8	3.7
60	HEART RATE	0	- 4	10	8	12	4	8	2	6	18	6.4	6.3	2.0
	DIASTOLIC PRESSURE	-20	-25	-30	15	-10	-15	5	15	-20	-15	-10.0	16.1	5.1
	SYSTOLIC PRESSURE	-10	-15	-10	- 5	- 5	-15	- 5	20	-15	-25	-9.5	13.6	4.3
	MEAN BLOOD PRESSURE	-17	-21	-23	-12	- 5	-17	2	17	-18	-21	-11.5	12.7	4.0

APPENDIX TABLE 13

THE EFFECTS OF 0.1% CARBON MONOXIDE ON HEART RATE AND BLOOD PRESSURE

TIME (MIN)		BIRD # 1	2	3	4	5	6	7	8	9	10	X	SD	SE
0	HEART RATE	260	312	282	276	254	286	270	266	292	284	278.2	16.92	5.35
	DIASTOLIC PRESSURE	100	85	100	95	125	95	95	125	90	95	100.5	13.63	4.31
	SYSTOLIC PRESSURE	135	130	130	120	160	125	135	150	130	125	134.0	12.20	3.85
	MEAN BLOOD PRESSURE	111	100	110	103	136	105	108	133	103	105	111.6	12.77	4.03
15	HEART RATE	282	316	300	278	268	302	272	266	312	296	289.2	18.33	5.79
	DIASTOLIC PRESSURE	95	80	85	90	115	80	95	120	80	90	93.0	14.18	4.48
	SYSTOLIC PRESSURE	115	125	115	120	150	115	130	140	115	115	124.0	12.42	3.92
	MEAN BLOOD PRESSURE	101	95	95	100	126	91	106	126	91	98	103.3	13.11	4.14
30	HEART RATE	286	326	288	288	274	294	282	282	306	294	292.0	14.72	4.65
	DIASTOLIC PRESSURE	90	85	85	80	105	80	90	100	80	85	88.0	8.56	2.70
	SYSTOLIC PRESSURE	115	120	110	125	135	110	125	135	115	110	120.0	9.71	3.07
	MEAN BLOOD PRESSURE	98	96	93	95	115	90	101	111	91	93	98.6	8.45	2.67
45	HEART RATE	276	302	286	280	256	286	278	290	296	280	283.0	12.55	3.96
	DIASTOLIC PRESSURE	70	75	80	75	85	65	80	85	70	80	76.5	6.68	2.11
	SYSTOLIC PRESSURE	110	100	105	115	130	100	115	125	115	110	112.5	9.78	3.09
	MEAN BLOOD PRESSURE	83	83	88	88	100	76	91	98	85	90	88.4	7.05	2.23
60	HEART RATE	270	298	274	260	250	280	274	278	288	272	274.4	13.39	4.23
	DIASTOLIC PRESSURE	65	70	70	65	70	70	75	75	60	65	69.0	5.16	1.63
	SYSTOLIC PRESSURE	115	110	110	110	125	105	110	120	105	115	112.5	6.34	2.00
	MEAN BLOOD PRESSURE	81	83	83	80	91	81	86	90	75	81	83.4	4.86	1.53

APPENDIX TABLE 13a

THE EFFECTS OF 0.1% CARBON MONOXIDE ON CHANGES IN HEART FREQUENCY AND BLOOD PRESSURE WITH MEANS (X), STANDARD DEVIATIONS (SD) AND STANDARD ERROR (SE). VALUES OBTAINED BY SUBTRACTING THE CARDIOVASCULAR PARAMETERS AT TIME 0 FROM TIME PERIODS 15, 30, 45 AND 60 ON TABLE 13.

TIME (MIN)		BIRD # 1	2	3	4	5	6	7	8	9	10	X	SD	SE
15	HEART RATE	22	4	18	2	14	16	2	0	20	12	11.0	8.3	2.6
	DIASTOLIC PRESSURE	- 5	- 5	-15	5	-10	-15	0	- 5	-10	- 5	- 6.5	6.3	2.0
	SYSTOLIC PRESSURE	-20	- 5	-15	0	-10	-10	- 5	-10	-15	-10	-10.0	5.7	1.8
	MEAN BLOOD PRESSURE	-10	- 5	-15	- 3	-10	-14	- 2	- 7	-12	- 7	- 8.5	4.4	1.4
30	HEART RATE	24	14	6	12	20	8	12	16	14	10	13.6	5.3	1.7
	DIASTOLIC PRESSURE	-10	0	-15	-15	-20	-15	- 5	-25	-10	-10	-12.5	7.2	2.3
	SYSTOLIC PRESSURE	-20	-10	-20	5	-25	-15	-10	-15	-15	-15	-14.0	8.0	2.5
	MEAN BLOOD PRESSURE	-13	- 4	-17	- 8	-21	-15	- 7	-22	-12	-12	-13.1	5.8	1.8
45	HEART RATE	16	-10	4	4	2	0	8	24	4	- 4	4.8	9.6	3.0
	DIASTOLIC PRESSURE	-30	-10	-20	-20	-40	-30	-15	-40	-20	-15	-24.0	10.5	3.3
	SYSTOLIC PRESSURE	-25	-30	-25	- 5	-30	-25	-20	-25	-15	-15	-21.5	10.3	2.7
	MEAN BLOOD PRESSURE	-28	-17	-22	-15	-36	-29	-17	-35	-18	-15	-23.2	8.1	2.6
60	HEART RATE	10	-14	8	-16	- 4	- 6	4	12	- 4	-12	- 2.2	10.2	3.2
	DIASTOLIC PRESSURE	-35	-15	-30	-30	-55	-25	-20	-50	-30	-30	-32.0	12.3	3.9
	SYSTOLIC PRESSURE	-20	-20	-20	-10	-35	-20	-25	-30	-25	-10	-21.5	7.8	2.5
	MEAN BLOOD PRESSURE	-30	-17	-27	-23	-45	-24	-22	-43	-28	-24	-28.3	9.0	2.9

APPENDIX TABLE 14

THE EFFECTS OF 0.5% CARBON MONOXIDE ON HEART RATE AND BLOOD PRESSURE

TIME (MIN)		BIRD # 1	2	3	4	5	6	7	8	9	10	X	SD	SE
0	HEART RATE	288	300	310	264	252	270	272	264	280	260	276.0	18.45	5.83
	DIASTOLIC PRESSURE	85	95	110	110	105	95	120	115	85	100	102.0	12.06	3.81
	SYSTOLIC PRESSURE	120	135	140	160	150	145	135	140	125	135	138.5	11.55	3.65
	MEAN BLOOD PRESSURE	96	108	120	126	120	111	125	123	98	111	113.8	10.80	3.41
15	HEART RATE	204	128	196	88	204	190	132	100	90	122	145.4	48.15	5.22
	DIASTOLIC PRESSURE	65	55	70	45	60	65	85	60	45	90	64.1	14.10	4.70
	SYSTOLIC PRESSURE	115	110	110	85	100	95	115	90	75	110	100.5	13.83	4.37
	MEAN BLOOD PRESSURE	81	73	83	58	73	75	95	70	55	95	75.9	13.56	4.28
20	HEART RATE	74	82	62		104		78	68		112	82.9	18.5	6.9
	DIASTOLIC PRESSURE	40	35	35		45		25	30		30	34.2	6.7	2.5
	SYSTOLIC PRESSURE	95	85	45		90		75	55		60	72.1	19.1	7.2
	MEAN BLOOD PRESSURE	58	52	38		60		42	38		40	46.9	9.6	3.6

APPENDIX TABLE 15

CARBOXYHEMOGLOBIN CONCENTRATIONS (%) DURING SPONTANEOUS INHALATION OF 0%, 0.01%, 0.1%, AND 0.5% CARBON MONOXIDE WITH MEANS (X), STANDARD DEVIATIONS (SD) AND STANDARD ERROR (SE)

TREATMENT

	0 ppm CO	100 ppm CO				1000 ppm CO				5000 ppm CO	
	TIME (MIN)	TIME (MIN)				TIME (MIN)				TIME (MIN)	
BIRD #	60	15	30	45	60	15	30	45	60	15	Death
1	0	0.0	6.0	7.0	11.0					48.0	51.5
2	0	1.0	1.0	5.0	7.0	13.0	28.0	36.5	48.5	58.0	60.0
3	1	1.0	4.5	7.0	7.5	7.5	25.0	36.5	50.0	55.5	57.0
4	1	1.0	5.0	7.0	9.5	7.0	15.5	28.0	35.5	50.0	58.0
5	0	3.5	3.5	7.0	8.5	11.0	26.5	31.5	36.5	51.5	56.5
6	1	0.0	3.5	7.0	7.0	8.5	20.0	26.5	40.0	58.0	60.0
7	0	1.0	5.0	8.5	8.5	12.5	23.5	25.5	41.5	46.0	51.5
8	0	1.0	5.0	8.5	9.5	5.0	16.0	26.5	33.0	48.0	50.0
9	0	3.5	5.0	7.5	12.5	10.0	24.0	35.0	33.0	56.5	62.0
10	1	0.0	4.5	7.0	10.0	7.0	20.0	25.0	36.5	50.0	48.0
X	0.40	1.20	4.30	7.15	9.10	9.05	22.05	30.11	39.38	52.15	55.45
SE	0.51	1.29	1.37	0.97	1.77	2.73	4.44	4.81	5.26	4.47	4.83
SE	0.61	0.41	0.43	0.36	0.56	0.91	1.47	1.60	2.08	1.41	1.53

APPENDIX TABLE 16

STATIC CO_2 SENSITIVITY CURVES OF PULMONARY-CO_2-SENSITIVE RECEPTORS BEFORE, DURING AND AFTER UNIDIRECTIONAL VENTILATION WITH 0.1% CARBON MONOXIDE WITH MEAN (X), STANDARD DEVIATION (SD) AND STANDARD ERROR (SE).

	BEFORE CO ADMINISTRATION					10 MINUTES DURING CO ADMINISTRATION				
	% CO_2					% CO_2				
BIRD #	0	2	4	6	8	0	2	4	6	8
5	10.0	7.0	4.3	1.2	0.3	12.8	8.6	3.8	2.2	1.0
		-3.0*	-5.7	-8.8	- 9.7		-4.2	-9.0	-10.6	-11.8
6	8.1	5.5	2.3	0.8	0.0	9.2	6.6	2.3	0.3	0.0
		-2.6	-5.8	-7.3	- 8.1		-2.6	-6.9	- 8.9	- 9.2
7	7.9	3.9	1.0	0.0	0.0	9.2	4.2	1.2	0.0	0.0
		-4.0	-6.9	-7.9	- 7.9		-5.0	-8.2	- 9.2	- 9.2
27	10.4	7.0	4.0	8.1	0.5	13.6	7.6	2.6	1.0	0.0
		-3.4	-6.4	-8.6	- 9.9		-6.0	-11.0	-12.0	-13.6
28	11.0	7.2	3.0	1.1	0.2	11.0	6.8	3.2	1.4	0.2
		-3.8	-8.0	-9.9	-10.8		-4.2	-7.8	- 9.6	-10.8
X	9.48	6.12	2.92	0.98	0.20	11.16	6.76	2.62	0.98	0.24
SD	1.39	1.41	1.33	0.65	0.21	2.02	1.63	0.98	0.87	0.43
SE	0.62	0.63	0.59	0.29	0.09	0.90	0.72	0.43	0.38	0.19
X*		-3.36	-6.56	-8.50	- 9.28		-4.40	-8.54	-10.18	-10.92
SD*		0.57	0.93	0.98	1.24		1.24	1.56	1.49	1.86
SE*		0.25	0.41	0.43	0.55		0.55	0.69	0.66	0.83

*Change values obtained by subtracting impulses per second at 0% CO_2 from impulses per second at 2, 4, 6 and 8% CO_2.

APPENDIX TABLE 16 CONTINUED

	1 MINUTE AFTER CO OFF ($\% CO_2$)					30 MINUTES AFTER CO OFF ($\% CO_2$)				
BIRD #	0	2	4	6	8	0	2	4	6	8
5	8.1	4.6	2.4	1.8	1.0	10.0	5.0	2.6	1.0	0.1
		-3.5	-5.7	-6.3	- 7.1		-5.0	-7.4	-9.0	- 9.9
6	8.7	4.9	1.9	0.4	0.0	8.4	4.5	2.1	0.7	0.0
		-3.8	-6.8	-8.3	- 8.7		-3.9	-6.3	-7.7	- 8.4
7	8.3	4.0	0.5	0.0	0.0	8.5	3.5	0.9	0.0	0.0
		-4.3	-7.8	-8.3	- 8.3		-5.0	-7.6	-8.5	- 8.5
27	8.8	5.6	2.8	1.3	0.0	8.8	5.6	2.8	1.3	0.0
		-3.2	-6.0	-7.5	- 8.8		-3.2	-6.0	-7.5	- 8.8
28	10.6	6.2	2.6	1.2	0.3	10.6	6.2	2.6	1.2	0.3
		-4.4	-8.0	-9.4	-10.3		-4.4	-8.0	-9.4	-10.3
X	8.90	5.06	2.04	0.94	0.26	9.26	4.96	2.20	0.84	0.08
SD	0.99	0.85	0.92	0.72	0.43	0.98	1.03	0.77	0.52	0.13
SE	0.44	0.38	0.41	0.32	0.19	0.43	0.46	0.34	0.23	0.05
X*		-3.84	-6.86	-7.96	- 8.64		-4.30	-7.06	-8.42	- 9.18
SD*		0.51	1.03	1.14	1.14		0.77	0.86	0.81	0.86
SE*		0.22	0.40	0.50	0.50		0.34	0.38	0.36	0.38

APPENDIX TABLE 17

DYNAMIC CO_2 SENSITIVITY CURVES BEFORE UNIDIRECTIONAL VENTILATION WITH 0.1% CARBON MONOXIDE WITH MEAN (X), STANDARD DEVIATION (SD) AND STANDARD ERROR (SE).

TIME (SEC)

BIRD #	0	1	2	3	4	5	6	7	8	9	10	15	20
5	3.4	3	4	7	10	9	9	8	8	8	7	8	9
		-0.4*	0.6	3.6	6.6	5.6	5.6	4.6	4.6	4.6	3.6	4.6	5.6
6	2.0	2	4	8	8	8	7	5	6	6	5	6	6
		0.0	2.0	6.0	6.0	6.0	5.0	3.0	4.0	4.0	3.0	4.0	4.0
7	1.6	2	14	17	14	10	8	8	7	7	8	8	8
		0.4	12.4	15.4	12.4	8.4	6.4	6.4	5.4	5.4	6.4	6.4	6.4
27	4.0	6	12	13	12	10	9	9	9	8	8	8	8
		2.0	8.0	9.0	8.0	6.0	5.0	5.0	5.0	4.0	4.0	4.0	4.0
28	3.0	7	12	15	14	14	13	11	11	11	11	11	11
		4.0	9.0	12.0	11.0	11.0	10.0	8.0	8.0	8.0	8.0	8.0	8.0
X	2.8	4.0	9.2	12.0	11.6	10.2	9.2	8.2	8.2	8.0	7.8	8.2	8.4
SD	0.98	2.34	4.81	4.35	2.60	2.28	2.28	2.16	1.92	1.87	2.16	1.78	1.81
SE	0.43	1.04	2.15	1.94	1.16	1.01	1.01	0.96	0.84	0.83	0.96	0.79	0.80
X*		1.3	6.4	9.2	8.8	7.4	6.4	5.4	5.4	5.2	5.0	5.4	5.6
SD*		2.34	4.95	4.68	2.78	2.29	2.09	1.89	1.54	1.66	2.11	1.75	1.69
SE*		1.04	2.21	2.09	1.24	1.02	0.93	0.84	0.68	0.74	0.94	0.78	0.75

*Change values obtained by subtracting value at time 0 from time 1, 2, 3...20.

APPENDIX TABLE 18

DYNAMIC CO_2 SENSITIVITY CURVES 10 MINUTES DURING UNIDIRECTIONAL VENTILATION WITH 0.1% CARBON MONOXIDE WITH MEAN (X), STANDARD DEVIATION (SD) AND STANDARD ERROR (SE).

	TIME (SEC)												
BIRD #	0	1	2	3	4	5	6	7	8	9	10	15	20
5	3.8	4	7	8	9	8	8	7	7	8	8	9	10
		0.2*	3.2	4.2	5.2	4.2	4.2	3.2	3.2	4.2	4.2	5.2	6.2
6	2.2	8	15	14	11	9	9	8	8	8	8	8	9
		5.8	12.8	11.8	8.8	6.8	6.8	5.8	5.8	5.8	5.8	5.8	6.8
7	1.2	5	16	18	12	9	6	7	6	7	7	8	8
		3.8	14.8	16.8	10.8	7.8	4.8	5.8	4.8	5.8	5.8	6.8	6.8
27	2.6	2	4	5	6	5	6	5	6	6	6	6	6
		-0.6	1.4	2.4	3.4	2.4	3.4	2.4	3.4	3.4	3.4	3.4	3.4
28	3.2	4	10	11	11	11	10	10	11	10	10	11	11
		0.8	6.8	7.8	7.8	7.8	6.8	6.8	7.8	6.8	6.8	7.8	7.8
X	2.6	4.6	10.4	11.2	9.8	8.4	7.8	7.4	7.6	7.8	7.8	8.4	8.8
SD	0.98	2.19	5.12	5.06	2.38	2.19	1.78	1.81	2.07	1.48	1.48	1.81	1.92
SE	0.43	0.97	2.28	2.26	1.06	0.97	0.79	0.80	0.92	0.66	0.66	0.89	0.85
X*		2.0	7.8	8.6	7.2	5.8	5.2	4.8	5.0	5.2	5.2	5.8	6.2
SD*		2.69	5.85	5.82	2.92	2.40	1.54	1.89	1.89	1.37	1.37	1.66	1.66
SE*		1.20	2.61	2.60	1.30	1.07	0.68	0.84	0.84	0.61	0.61	0.74	0.74

*Change values obtained by subtracting value at time 0 from time 1, 2, 3...20.

APPENDIX TABLE 19

DYNAMIC CO_2 SENSITIVITY CURVES 1 MINUTE AFTER 0.1% CARBON MONOXIDE WAS REMOVED FROM THE UNIDIRECTIONAL VENTILATORY GAS WITH MEAN (X), STANDARD DEVIATION (SD) AND STANDARD ERROR (SE)

	TIME (SEC)												
BIRD #	0	1	2	3	4	5	6	7	8	9	10	15	20
5	2.4	3	4	4	5	6	6	4	6	5	5	5	6
		0.6*	1.6	1.6	2.6	3.6	3.6	1.6	3.6	2.6	2.6	2.6	3.6
6	2.1	2	6	11	12	10	8	7	8	6	7	6	7
		-0.1	3.9	8.9	9.9	7.9	6.9	5.9	6.9	4.9	5.9	4.9	5.9
7	0.5	1	10	15	12	8	5	6	4	6	6	6	7
		0.5	9.5	14.5	11.5	7.5	4.5	5.5	3.5	5.5	5.5	5.5	6.5
27	2.8	2	6	8	7	7	6	7	6	5	7	7	7
		-0.8	3.2	5.2	4.2	4.2	3.2	4.2	3.2	2.2	4.2	4.2	4.2
28	2.6	5	10	11	11	10	11	10	10	10	10	10	10
		2.4	7.4	8.4	8.4	7.4	8.4	7.4	7.4	7.4	7.4	7.4	7.4
X	2.08	2.6	7.2	9.8	9.4	8.2	7.2	6.8	6.8	6.4	7.0	6.8	7.4
SD	0.92	1.51	2.68	4.08	3.20	1.78	2.38	2.16	2.28	2.07	1.87	1.92	1.51
SE	0.41	0.67	1.19	1.82	1.43	0.79	1.06	0.96	1.01	0.92	0.83	0.85	0.67
X*		0.52	5.12	7.72	7.32	6.12	5.32	4.92	4.98	4.52	5.12	4.92	5.52
SD*		1.19	3.23	4.78	3.78	2.04	2.24	2.17	1.98	2.14	1.81	1.75	1.58
SE*		0.53	1.44	2.13	1.69	0.91	1.00	0.97	0.88	0.95	0.89	0.78	0.70

*Change values obtained by subtracting value at time 0 from time 1, 2, 3...20.

APPENDIX TABLE 20

DYNAMIC CO_2 SENSITIVITY CURVES 30 MINUTES AFTER 0.1% CARBON MONOXIDE WAS REMOVED FROM THE UNIDIRECTIONAL VENTILATORY GAS WITH MEAN (X), STANDARD DEVIATION (SD) AND STANDARD ERROR (SE)

TIME (SEC)

BIRD #	0	1	2	3	4	5	6	7	8	9	10	15	20
5	2.6	5	4	6	7	8	7	6	7	5	6	6	7
		2.4*	1.4	3.4	4.4	5.4	4.4	3.4	4.4	2.4	3.4	3.4	4.4
6	2.1	2	6	11	12	10	8	7	8	6	7	6	7
		-0.1	3.9	8.9	9.9	7.9	5.9	4.9	5.9	3.9	4.9	3.9	4.9
7	0.9	2	8	10	10	7	8	6	6	6	7	7	8
		1.1	7.1	9.1	9.1	6.1	7.1	5.1	5.1	5.1	6.1	6.1	7.1
27	2.8	2	6	8	7	7	6	7	6	5	7	7	7
		-0.8	3.2	5.2	4.2	4.2	3.2	4.2	3.2	2.2	4.2	4.2	4.2
28	2.8	4	8	8	7	8	8	8	7	7	8	7	7
		1.2	5.2	5.2	4.2	5.2	5.2	5.2	4.2	4.2	5.2	4.2	4.2
X	2.24	3.3	6.4	8.6	8.6	8.0	7.4	6.8	6.8	5.8	7.0	6.6	7.2
SD	0.80	1.41	1.67	1.94	2.30	1.22	0.89	0.83	0.83	0.83	0.70	0.54	0.44
SE	0.35	0.63	0.74	0.86	1.02	0.54	0.39	0.37	0.37	0.37	0.31	0.24	0.19
X*		0.76	4.16	6.36	5.76	5.76	5.16	4.56	4.56	3.56	4.76	4.36	4.96
SD*		1.24	2.14	2.52	2.88	1.37	1.47	0.75	0.10	2.37	1.02	1.02	1.23
SE*		0.55	0.95	1.12	1.28	0.61	0.65	0.33	0.04	1.05	0.45	0.45	0.55

*Change values obtained by subtracting value at time 0 from time 1, 2, 3...20.

APPENDIX TABLE 21

CARBOXYHEMOGLOBIN CONCENTRATIONS (%) 5, 10, AND 14 MINUTES DURING AND 30, 45, AND 60 MINUTES AFTER UNIDIRECTIONAL VENTILATION OF 0.1% CO WITH MEAN (X), STANDARD DEVIATION (SD) AND STANDARD ERROR (SE).

	TIME (MINUTES) DURING AND AFTER CO ADMINISTRATION					
BIRD #	5 DURING	10 DURING	14 DURING	30 AFTER	45 AFTER	60 AFTER
1	27	42	52	30	20	17
4	24	41	50	28	22	19
5	25	40	48	33	25	16
8	21	35	45	28	19	16
9-1	21	37	47	29	20	18
9-2	23	37	46	31	24	15
X	23.50	38.66	48.00	29.83	21.66	16.83
SD	2.34	2.73	2.60	1.94	2.42	1.47
SE	0.95	1.11	1.06	0.79	0.98	0.60

APPENDIX TABLE 22

PULMONARY-CO_2-SENSITIVE RECEPTOR ACTIVITY (impulses per second) AT 0% CARBON DIOXIDE BEFORE, DURING AND AFTER UNIDIRECTIONAL VENTILATION WITH 0.1% CARBON MONOXIDE WITH MEAN (X), STANDARD DEVIATION (SD) AND STANDARD ERROR (SE)

TIME (MINUTES)

	BEFORE CO	DURING CO											AFTER CO OFF							
BIRD #	0	1	2	3	4	5	6	7	8	9	10	14	1	5	10	15	20	25	30	60
5	10.2	10.4	9.7	10.4	10.1	10.4	10.6	11.0	11.6	12.8	12.8	6.8	8.1	4.7	7.1	7.5	8.8	9.4	10.0	10.4
		0.2*	-0.5	0.2	-0.1	0.2	0.4	0.8	1.4	2.6	2.6	-3.4	-2.1	-5.5	-3.1	-2.6	-1.4	-0.8	-0.2	0.2
6	8.2	8.4	8.2	8.2	8.0	8.4	8.6	8.6	8.8	9.0	9.2	7.4	8.7	7.3	7.9	8.8	7.9	9.3	8.4	8.6
		0.2	0.0	0.0	-0.2	0.2	0.4	0.4	0.6	0.8	1.0	-0.8	0.5	-0.8	-0.3	0.6	-0.3	1.1	0.2	0.4
7	8.0	8.0	8.0	8.0	7.8	7.6	8.4	8.0	8.6	9.0	9.2	7.0	8.3	6.5	7.6	8.1	8.6	8.3	8.5	8.1
		0.0	0.0	0.0	-0.2	-0.4	0.4	0.0	0.6	1.0	1.2	-1.0	0.3	-1.5	-0.4	0.1	0.6	0.3	0.5	0.1
27	10.2	10.4	10.4	10.4	10.6	11.2	11.2	11.4	11.6	11.8	13.6	8.2	8.8	4.2	8.6	9.6	10.0	10.2	10.2	10.2
		0.2	0.2	0.2	0.4	1.0	1.0	1.2	1.4	1.6	3.4	-2.0	-1.4	-6.0	-1.6	-0.6	-0.2	0.0	0.0	0.0
28	10.8	11.2	11.2	11.4	11.4	11.2	11.2	15.4	12.0	11.6	11.0	7.6	10.6	10.4	10.8	8.0	6.2	7.6	6.6	7.4
		0.4	0.4	0.6	0.6	0.4	0.4	4.6	1.2	0.8	0.2	-2.6	-0.2	-0.4	0.0	-2.8	-4.2	-3.2	-4.2	-3.4
X	9.4	9.6	9.5	9.6	9.6	9.7	10.0	10.8	10.5	10.8	11.1	7.4	8.9	6.6	8.4	8.4	8.3	8.9	8.7	8.9
SD	1.3	1.3	1.3	1.5	1.6	1.6	1.4	2.9	1.6	1.7	2.0	0.5	1.0	2.5	1.4	0.8	1.4	1.0	1.4	1.3
SE	0.58	0.58	0.58	0.67	0.71	0.71	0.62	1.29	0.71	0.76	0.89	0.24	0.44	1.10	0.64	0.36	0.62	0.45	0.64	0.58
X*		0.20	0.02	0.20	0.10	0.28	0.52	1.40	1.04	1.36	1.68	-1.96	-0.58	-2.86	-1.08	-1.06	-1.10	-0.52	-0.74	-0.54
SD*		0.14	0.33	0.24	0.37	0.50	0.27	1.84	0.40	0.76	1.29	1.08	1.12	2.67	1.28	1.55	1.87	1.64	1.95	1.60
SE*		0.06	0.14	0.10	0.16	0.22	0.12	0.82	0.17	0.33	0.57	0.48	0.50	1.19	0.57	0.69	0.83	0.73	0.87	0.71

*Changes values (impulses per second) obtained by subtracting pulmonary-CO_2-sensitive receptor activity at time 0 from time 1, 2, 3,...60.

ADDENDUM TO APPENDIX TABLE 22

AVERAGE COEFFICIENT OF VARIATION OF THE IMPULSE FREQUENCY FROM CO_2 SENSITIVE RECEPTORS. BEFORE, DURING, AND AFTER CO ADMINISTRATION.

BIRD #	$\bar{X}$*	SD	SE	COEF. OF Y_{AR} (%)
5	10.9	1.055	.318	9.7
6	8.5	.373	.112	4.4
7	8.2	.504	.152	6.1
27	11.2	.979	.295	8.7
28	11.7	1.275	.384	10.9
			$\bar{X}$ of CV	8.0
			SD	2.7
			SE	1.2

*$\bar{X}$ = mean discharge frequency over 10 minutes for each receptor and coefficient of variation is SD/$\bar{X}$ x 100. Average coefficient of variation gives an idean of the variability over this time period within a receptor.

APPENDIX TABLE 23

AVIAN ARTERIAL OXYGEN TENSION (torr) BEFORE, DURING AND AFTER UNIDIRECTIONAL VENTILATION WITH 0.1% CARBON MONOXIDE WITH MEAN (X), STANDARD DEVIATION (SD) AND STANDARD ERROR (SE)

TIME (MINUTES)

	BEFORE CO	DURING CO				AFTER CO OFF								
BIRD #	1	1	5	9	14	1	5	10	15	20	25	30	45	60
5	91.0	52.3	45.0	31.5	32.0	42.5	57.5	54.6	60.5	63.8	63.8	68.0	62.5	64.5
		-38.7*	-46.0	-59.5	-59.0	-48.5	-33.5	-36.4	-30.5	-27.2	-27.2	-23.0	-28.5	-26.5
4	98.0	59.8	63.8	55.8	35.5	36.5	59.0	49.0	53.4	50.3	49.0	48.0	42.0	43.0
		-29.2	-25.2	-33.2	-53.5	-52.5	-30.0	-40.0	-35.6	-38.7	-40.0	-41.0	-47.0	-46.0
5	49.3	31.8	35.0	56.9	36.0	31.0	65.5	40.0	40.0	45.0	43.0	55.4	37.5	35.5
		-17.7	-14.5	7.4	-13.5	-18.5	16.0	- 9.5	- 9.5	- 4.5	- 6.5	5.9	-12.0	-14.0
8	94.0	97.0	69.5	80.3	58.5	61.0	72.8	84.5	89.6	90.5	84.5	90.0	81.0	89.3
		3.0	-24.5	-13.9	-35.5	-33.0	-21.2	- 9.5	- 4.5	- 3.5	- 9.5	- 4.0	-13.0	- 4.7
9-1	93.3	83.5	71.5	78.0	47.0	64.2	78.8	88.0	92.5	94.8	97.0	93.0	92.8	96.0
		- 9.8	-21.8	-15.3	-46.3	-29.1	-14.5	- 5.3	- 0.8	1.5	3.7	- 0.3	- 0.5	2.7
9-2	92.0	88.5	85.0	78.0	73.8	72.0	85.5	90.3	92.0	93.0	89.5	90.0	89.9	92.3
		- 3.5	- 7.0	-14.0	-18.2	-20.0	- 6.5	- 1.7	0.0	1.0	- 2.5	- 2.0	- 2.0	0.3
X	84.80	68.81	61.63	63.41	47.13	51.20	69.85	67.73	71.33	72.90	71.13	74.06	67.61	70.10
SD	17.38	24.98	18.41	19.13	16.30	16.71	11.16	22.33	22.93	22.55	22.45	19.65	24.08	26.43
SE	7.09	10.20	7.51	7.81	6.65	6.82	4.55	9.11	9.36	9.24	9.16	8.02	9.83	10.79
X*		-15.89	-23.16	-21.38	-37.66	-33.60	-14.95	-17.06	-13.46	-11.90	-13.66	-10.73	-17.18	-14.70
SD*		15.79	13.15	22.67	18.69	14.23	18.10	16.66	15.61	16.87	16.56	17.74	17.70	18.69
SE*		6.44	5.36	9.25	7.63	5.81	7.39	6.80	6.37	6.88	6.76	7.24	7.22	7.63

*Changes values (mmHg) obtained by subtracting the arterial oxygen tension value at time 1 from time 2, 3, 4,...14.

APPENDIX TABLE 24

AVIAN ARTERIAL CARBON DIOXIDE TENSION (torr) BEFORE, DURING AND AFTER UNIDIRECTIONAL VENTILATION WITH 0.1% CARBON MONOXIDE WITH 0.1% CARBON MONOXIDE WITH MEAN (X), STANDARD DEVIATION (SD) AND STANDARD ERROR (SE)

TIME (MINUTES)

	BEFORE CO	DURING CO				AFTER CO OFF								
BIRD #	1	1	5	9	14	1	5	10	15	20	25	30	45	60
1	10.0*	10.0	10.0	10.0	11.8	10.0	14.2	10.0	10.0	10.0	10.0	11.2	10.0	10.0
		0.0**	0.0	0.0	1.8	0.0	4.2	0.0	0.0	0.0	0.0	1.2	0.0	0.0
4	10.0	10.0	10.0	10.0	11.3	10.0	15.0	10.0	10.0	10.0	10.0	10.0	10.0	10.0
		0.0	0.0	0.0	1.3	0.0	5.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
5	10.0	10.0	10.0	10.0	15.4	10.7	14.1	10.0	10.0	10.0	10.0	11.6	10.0	10.0
		0.0	0.0	0.0	5.4	0.7	4.1	0.0	0.0	0.0	0.0	1.6	0.0	0.0
6	10.0	10.0	10.0	10.0	12.2	10.0	14.3	10.0	10.0	10.0	10.0	10.0	10.0	10.0
		0.0	0.0	0.0	2.2	0.0	4.3	0.0	0.0	0.0	0.0	0.0	0.0	0.0
9-1	10.0	10.0	10.0	10.0	10.7	10.0	13.5	10.0	10.0	10.0	10.0	10.0	10.0	10.0
		0.0	0.0	0.0	0.7	0.0	3.5	0.0	0.0	0.0	0.0	0.0	0.0	0.0
9-2	10.0	10.0	10.0	10.0	11.3	10.0	14.8	10.0	10.0	10.0	10.0	10.0	10.0	10.0
		0.0	0.0	0.0	1.3	0.0	4.8	0.0	0.0	0.0	0.0	0.0	0.0	0.0
X					12.1	10.1	14.3					10.5		
SD					1.67	0.29	0.54					0.73		
SE					0.68	0.11	0.22					0.29		
X**					2.1	0.1	4.3					0.5		
SD**					1.67	0.28	0.53					0.73		
SE**					0.68	0.11	0.21					0.29		

*All 10.0 values actually below 10.

**Change values (mmHg) obtained by subtracting the arterial carbon dioxide tension values at time 1 from time 2, 3, 4,...14.

APPENDIX TABLE 25

AVIAN ARTERIAL Ph VALUES BEFORE, DURING AND AFTER UNIDIRECTIONAL VENTILATION WITH 0.1% CARBON MONOXIDE WITH MEAN (X), STANDARD DEVIATION (SD) AND STANDARD ERROR (SE)

TIME (MINUTES)

	BEFORE CO	DURING CO				AFTER CO OFF								
BIRD #	1	1	5	9	14	1	5	10	15	20	25	30	45	60
1	7.930	7.981	7.991	7.986	7.615	7.741	7.552	7.675	7.680	7.687	7.708	7.619	7.800	7.827
		0.051*	0.062	0.056	-0.315	-0.189	-0.378	-0.255	-0.250	-0.243	-0.222	-0.311	-0.130	-0.103
4	8.000**	8.000	8.000	8.000	7.723	7.810	7.615	7.797	7.782	7.818	7.829	7.788	7.909	7.918
		0.000	0.000	0.000	-0.277	-0.190	-0.385	-0.203	-0.218	-0.192	-0.171	-0.212	-0.091	-0.082
5	7.976	7.970	7.972	8.000	7.715	7.804	7.721	7.816	7.850	7.861	7.890	7.799	7.890	7.899
		-0.006	-0.004	-0.024	-0.261	-0.172	-0.255	-0.160	-0.126	-0.115	-0.086	-0.177	-0.086	-0.077
8	8.000	8.000	8.000	8.000	7.797	7.900	7.714	7.910	7.979	8.000	8.000	7.906	8.000	8.000
		0.000	0.000	0.000	-0.203	-0.100	-0.286	-0.090	-0.021	0.000	0.000	-0.094	0.000	0.000
9-1	8.000	8.000	8.000	7.985	7.674	7.835	7.613	7.832	7.840	7.890	7.920	7.850	7.959	7.980
		0.000	0.000	-0.015	-0.326	-0.165	-0.387	-0.168	-0.160	-0.110	-0.080	-0.150	-0.041	-0.020
9-2	8.000	8.000	7.955	7.942	7.687	7.771	7.609	7.817	7.855	7.850	7.880	7.820	7.904	7.900
		0.000	-0.045	-0.058	-0.313	-0.229	-0.391	-0.183	-0.145	-0.150	-0.120	-0.180	-0.096	-0.100
X	7.984	7.991	7.986	7.985	7.701	7.810	7.637	7.807	7.831	7.849	7.871	7.797	7.910	7.920
SD	0.028	0.013	0.018	0.022	0.060	0.054	0.066	0.076	0.098	0.102	0.097	0.096	0.067	0.062
SE	0.011	0.004	0.007	0.008	0.024	0.022	0.027	0.030	0.040	0.041	0.039	0.039	0.027	0.025
X*		0.007	0.002	0.001	-0.282	-0.174	-0.347	-0.176	-0.153	-0.135	-0.113	-0.187	-0.074	-0.063
SD*		0.021	0.034	0.038	0.046	0.042	0.060	0.054	0.079	0.082	0.077	0.072	0.046	0.043
SE*		0.008	0.013	0.015	0.018	0.017	0.024	0.022	0.032	0.033	0.031	0.029	0.018	0.017

*Change values (Ph units) obtained by subtracting the arterial Ph value at time 1 from time 2, 3, 4,...14.

**All 8.000 values were greater than 8.

APPENDIX TABLE 26

CYCLIC VENTILATORY MOTION DURING UNIDIRECTIONAL VENTILATION WITH 0.1% CARBON MONOXIDE WITH MEAN (X), STANDARD DEVIATION (SD), AND STANDARD ERROR (SE).

	TIME (MIN) DURING CO									
Bird #	1	2	3	4	5	6	7	8	9	10
1	0	0	0	0	0	20	10	6	10	25
4	0	0	0	0	0	0	15	12	12	17
5	0	0	0	0	0	15	10	20	25	30
8	0	0	0	0	0	0	12	15	11	10
9-1	0	0	0	0	0	7	9	9	8	20
9-2	0	0	0	0	0	0	7	6	8	15
X	0	0	0	0	0	7.0	10.5	11.4	12.3	19.5
SD						8.7	2.7	5.5	6.4	7.2
SE						3.6	1.1	2.2	2.6	2.9

CARBON MONOXIDE: INFLUENCE OF AVIAN RESPIRATORY CONTROL

by

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B.S., Kansas State University, 1969

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ABSTRACT

The effect of carbon monoxide (CO) on avian cardiopulmonary control was determined in adult, male White Leghorn type chickens (Babcock strain). In one series of experiments, four groups of ten birds each were allowed to spontaneously breath 0%, 0.01%, 0.1% and 0.5% CO in air, respectively, for 60 minutes or until death while respiratory frequency (f_{resp}, breaths min^{-1}), tidal volume (V_T, ml BTPS), minute volume ($\dot{V}$, ml BTPS-min^{-1}), systolic and diastolic blood pressure (mmHg), carboxyhemoglobin (HbCO) concentrations and heart frequency (f_{card}) were recorded. Inhalation of 0.5% CO produced increases in V_T and $\dot{V}$ while f_{resp}, blood pressure and f_{card} decreased. The HbCO levels reached 52% in 15 minutes and mean death time was 20.5 minutes with a range of 17.5 to 24.5 minutes. No significant differences in the cardiopulmonary parameters were detected between birds receiving 0 and 0.01% CO for a 60 minute period (HbCO = 9%). However, inhalation of 0.1% CO for 60 minutes (HbCO 39%) increased V_T and $\dot{V}$ and decreased blood pressure while f_{resp} was unchanged. The effects of CO on cardiopulmonary control cannot be experienced by either direct or indirect action on peripheral chemoreceptors (carotid body) because stimulation of those receptors increases f_{resp}, as well as V_T. CO may, therefore, act directly on other peripheral receptors (intrapulmonary CO_2-sensitive receptors) or on the CNS. The possible effect of CO on the CNS is discussed.

In order to further explain why CO affected the control of avian ventilation, 14 chickens were unidirectionally ventilated for 75 minutes with a gas mixture containing 20.4% O_2, balance N_2, with 0.1% CO being administered for 15 minutes during this period. Excluding CO_2 from the ventilatory gas stream produced maximal stimulation of CO-sensitive

receptors and produced Apnea. Afferent vagal activity from intrapulmonary CO_2-sensitive receptors and vertical sternal movements were recorded in five birds, while carboxyhemoglobin (HbCO) concentrations, arterial oxygen tension (PaO_2) and vertical sternal movements were monitored in 9 birds. Intrapulmonary CO_2-sensitive receptor activity was not changed by the presence of 0.1% CO in the ventilatory gas mixture. Furthermore, CO did not significantly alter the CO_2-sensitive receptor's sensitivity to CO_2. However, 6 minutes after CO was administered cyclic respiratory movements began. Rapid increases in HbCO values to 50% with a simultaneous decrease in PaO_2 from 85 to 62 torr developed in 15 minutes.

The occurrence of respiratory movements during CO administration cannot be attributed to a direct action of CO on intrapulmonary CO_2-sensitive receptors nor to an increase in the activity of other receptors due to hypoxia. The movements may have resulted from a depressing action of CO on inhibitory interneurons in the CNS that normally are activated by intrapulmonary CO_2-sensitive receptors. Inactivity of those inhibitory interneurons would allow cyclic respiratory movements to resume from inherent rhythm of the respiratory neuronal pool even though continued high discharge of intrapulmonary CO_2-sensitive receptors occurred.