A METHOD FOR ESTIMATING THE DISTRIBUTION
OF THE PULMONARY BLOOD FLOW
IN THE DOG

by

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A THESIS

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TABLE OF CONTENTS

LIST OF TABLES

LIST OF ILLUSTRATIONS

Introduction:

The pulmonary circulation has been a neglected factor in evaluation of pulmonary function, probably because of the greater difficulty and hazard involved in attempting to measure the circulatory parameters. Nevertheless, methods must be developed so that the pulmonary circulation and lung function relationship can be adequately assessed. A logical parameter of the circulation to be investigated would be that of blood flow and its distribution in the vascular bed of the lung. Conventional methods of measuring blood flow utilize the Fick Principle. The Fick Principle can be applied to any organ provided three facts are known: (1) the concentration of some substance, X, in the blood entering the organ, (2) the concentration of X in the mixed venous blood leaving the organ and (3) the total amount of X removed from the blood by the organ each minute.

Kety and Schmidt (6) have utilized low concentrations of nitrous oxide to determine cerebral blood flow in man. Bromsulphalein has been employed by Bradley and Inglefinger (1) to estimate the hepatic blood flow in man. Lee and Dubois (8) measured pulmonary capillary flow with nitrous oxide and found it to be pulsatile with the heart beat, but were unable to assess the distribution of the pulmonary blood flow.

Regardless of the substance employed in the application of the Fick Principle, this method has the following limitations: (1) distribution of organ blood flow cannot be estimated, (2) intravascular sampling is required, (3) there is an inherent analytical error in the determinations and (4) the assumption has to be made that the concentration difference, flow rate and extraction rate are all constant over the time of measurement. (19)

The effects of non-uniform distribution of blood flow in the lungs is recognized as having a pronounced influence upon pulmonary gas exchange. This study is devoted to the development of a method of analysis of distribution of blood flow in the lungs. From the foregoing discussion, it is apparent that conventional applications of the Fick Principle are not suitable for this purpose. The method investigated in this study concerns the evaluation of blood flow by observing the changes in gas composition which are related to the blood flow during the development of atelectasis in an occluded lobe of the lung. The inspired gas composition, total lobe volume and blood flow were studied to determine the effect of these factors on the period of changing gas composition during the early stages of the development of atelectasis.

Historical Review:

In 1879, Lichtheim (9) showed that the ligation of a bronchus is followed by absorption of the gases in the occluded lobe and atelectasis; but a combined ligature of the bronchus to a lobe and its corresponding pulmonary artery is not followed by atelectasis. This was the first definite demonstration that blood circulation through the lung is an indispensible factor concerned with the absorption of the gases in the alveoli. Moreover, he observed, oxygen and carbon dioxide were absorbed faster than nitrogen. Coryllos and Birnbaum (3) account for the different rates of absorption of nitrogen, oxygen and carbon dioxide on the basis of the individual gas solubility, diffusion rate and their chemical affinities with blood.

Blood combines with oxygen in two ways, (1) in physical solution as dissolved oxygen in the watery parts of the blood and (2) in chemical combination with hemoglobin. In each case, the amount of oxygen taken up depends upon the partial pressure of oxygen to which the plasma or blood is exposed. The mean values of the partial pressure of oxygen in normal young men are 95 mm Hg. for arterial blood and 40 mm Hg. for venous blood. (2)

In the case of hemoglobin, the amount of oxygen is not linearly related to the partial pressure of oxygen as it is in the case of dissolved oxygen. This factor will be discussed in greater detail in subsequent portions of this thesis.

Blood combines with carbon dioxide in three ways: (1) in physical solution as dissolved carbon dioxide in the watery parts of the blood, (2) in chemical combination with hemoglobin and (3) in physical solution as bicarbonate ion in the erythrocyte and plasma. These three factors may be considered to affect blood carbon dioxide concentrations in an approximately linear fashion with changes in partial pressures over the physiological range of pressures dealt with here. The values of the partial pressure of carbon dioxide in healthy young men is 41 mm Hg. in arterial blood and 46.5 mm Hg. in venous blood. (2)

Nitrogen combines with the blood by physical solution in proportion to the partial pressure in the environment. The blood and tissues equilibrate with the nitrogen concentration in the atmosphere and consequently the partial pressure of nitrogen in arterial and venous blood is essentially the same in the steady state (no change in the inspired nitrogen partial pressure and no change in the overall respiratory gas exchange ratio).

Water vapor is the fourth gas in equilibrium with blood. It has a partial pressure of 47 mm Hg. at 37 degrees centigrade in both arterial and venous blood.

Entrapped lobar air rapidly undergoes marked changes in composition as shown by Loewy and von Schroetter. (10) . The percentage of oxygen decreases and carbon dioxide increases so that the respective partial pressures tend to come into equilibrium with the corresponding gases of the systemic blood entering the lung. In this context, the blood entering the pulmonary artery will be referred to as mixed venous blood.

Dale and Rahn (4) state that "...the absorption of the gas is due to the pressure difference between the gases of the occluded lobe and those of the surrounding tissue or blood. While the total pressure in the lobe remains essentially atmospheric, the sum of the partial pressures in the venous blood and tissues is always less than atmospheric. This peculiar circumstance is attributable to the nature of the hemoglobin saturation curve which allows a far greater pressure drop for a given quantity of oxygen removed than is gained from a similar quantity of carbon dioxide added to the blood. Thus the total gas pressure in mixed venous blood is always less than the total gas pressure in the alveoli.

This pressure differential thus developed between lung gas and venous blood gas tensions is the driving force of gas absorption. In a lung breathing air it may total about 54 mm Hg. (assuming an arterio-venous oxygen difference of 60 and a venous-arterial carbon dioxide difference of 6 mm.)"

Two principle phenomena occur in the occluded lobe. First, there is an initial adjustment of the composition of the gas in the lobe until a state of constant composition is reached. Secondly, following the achievement of constant composition, the volume of the lobe decreases at a constant rate. (18)

In this context, the period of changing gas composition within the occluded lobe will be referred to as the unsteady state. The duration of the unsteady state in a closed chest preparation, in which the occluded lung of the dog was attached to a 610 ml. spirometer, was approximately 6 minutes. (4)

In summary of the foregoing discussion, the following three generalizations can be made: (1) The pressure of the occluded lobe remains essentially atmospheric while the sum of the partial pressures of all the gases in the blood-tissue environment is always less than atmospheric. (2) The gas composition in the occluded lobe will eventually become constant provided the gas tension of the blood-tissue environment remains unchanged. This is the state of constant composition. (3) During this state of constant composition the gas volume is absorbed at a constant rate. These generalizations lead to two further inferences. (1) The partial pressure of each gas in an occluded lobe must be higher than that of the blood-tissue environment. (2) Each particular gas disappears at a rate proportional to its fractional concentration during the period of constant composition.

Thus for example, in Dale and Rahn's study (4) of gas absorption during atelectasis in the dog, they were able experimentally to show that the composition of the gases within the occluded lung becomes constant after approximately 6 minutes. At that time, when the dog was breathing air in the left lung, for every 86.48 volumes of nitrogen absorbed, 5.64 volumes of oxygen and 7.88 volumes of carbon dioxide disappeared from the occluded right lung. Since there is continued absorption of each gas, each partial pressure must be higher than the corresponding partial pressure in the blood-tissue environment.

The above gas concentrations expressed in mm Hg. is 605 for nitrogen, 40 for oxygen and 55 for carbon dioxide when the gas tensions are computed on a basis of a barometric pressure of 747 mm Hg. and 47 mm Hg. alveolar water vapor tension.

Let us assume, in the gas mixture in the occluded lobe, that the partial pressure of carbon dioxide and oxygen are identical with those in the blood; but the partial pressure of nitrogen is higher in the lung than in the blood. The partial pressure in the blood would be 560 mm Hg. when the animal is breathing air and the partial pressure is calculated on the basis of the above barometric pressure.

Because the partial pressure gradient for nitrogen exists, nitrogen will be absorbed by the blood. By the absorption of some of the nitrogen, the percentages and partial pressures of carbon dioxide and oxygen are augmented and they too begin to be absorbed. In this manner the volume of gas in the occluded lobe is absorbed until the lung becomes atelectatic.

It can be predicted that the principle driving pressure to remove gas from the occluded lung by the blood is that of the least soluble gas, nitrogen. This unique situation develops, as will be demonstrated later, as a result of the rapid influx of the very soluble gas, carbon dioxide, immediately following occlusion of the lung. The concentration of carbon dioxide in the occluded lobe will rapidly approach the concentration in the blood. This dilutes the nitrogen and oxygen concentration in the occluded lobe. However, the oxygen concentration still exceeds that of the blood and consequently it will be absorbed by the blood until the partial pressure of oxygen in the occluded lobe nearly equals that of the blood. Nitrogen was in equilibrium with the blood at the onset of the occlusion of the lung and then was concentrated by the absorption of oxygen. Consequently, during the unsteady state, the very soluble blood gases, oxygen and carbon dioxide tend to equilibrate with the blood, while the nearly inert nitrogen is concentrated in the trapped gas. The concentration of nitrogen thus accounts for the larger share of the pressure difference existing between the occluded lung and mixed venous blood during the period of constant composition.

Dale and Rahn (4) correlated pulmonary blood flow with the rate of change in volume of the spirometer, which was attached to the occluded right lung, after the state of constant composition had been reached. The surface area of the lung during the experiment was considered to be unchanged since all of the measurements were made before the spirometer was exhausted.

The volume change was then a function of pressure difference between alveolus and mixed venous blood, absorption coefficient and blood flow. The absorption coefficient was a measure of physical solubility and chemical affinity of a gas with blood and was expressed as cubic centimeters of gas absorbed per liter of blood flow per mm. pressure increment. The absorption coefficient values were different for oxygen, carbon dioxide and nitrogen and were determined by Dale and Rahn under the conditions of their experiment to be 0.0185 for nitrogen, 3.5 for oxygen and 4.0 for carbon dioxide when the dog was breathing air. The foregoing relationships to the rate of gas absorption (rate of spirometer volume change) were defined quantitatively by Dale and Rahn utilizing the blood flow equation of Fick as follows: Let:

$\dot{Q}$ equal rate of blood flow through the occluded lung

P_A equal the partial pressure of alveolar gas in the occluded lung

P_a equal the partial pressure of gas in blood leaving occluded lung

P_v equal the partial pressure of gas in mixed venous blood

$\dot{V}$ equal the total volume absorbed per unit time

F equal the fractional concentration of gas in the occluded lung

α equal the absorption coefficient of nitrogen expressed as cc/liter blood flow/mm pressure difference

β equal the absorption coefficient of oxygen

γ equal the absorption coefficient of carbon dioxide

O_2, CO_2, and N_2 equal the particular molecular species

If one assumes P_A equals P_a then according to Fick's equation

$$\dot{Q} = \frac{\dot{V}F_{O_2}}{(P_{A_{O_2}} - P_{v_{O_2}})\beta} = \frac{\dot{V}F_{CO_2}}{(P_{A_{CO_2}} - P_{v_{CO_2}})\gamma} = \frac{\dot{V}F_{N_2}}{(P_{A_{N_2}} - P_{v_{N_2}})\alpha}$$

By rearrangement, the rate of lung collapse expressed as volume absorbed per unit time may be expressed as follows:

$$\dot{V} = \dot{V}F_{O_2} + \dot{V}F_{CO_2} + \dot{V}F_{N_2} \quad \text{or}$$

$$\dot{V} = \dot{Q}\left[(P_{A_{O_2}} - P_{v_{O_2}})\beta + (P_{A_{CO_2}} - P_{v_{CO_2}})\gamma + (P_{A_{N_2}} - P_{v_{N_2}})\alpha\right]$$

Thus when the gases in the occluded lung have reached constant composition, the rate of collapse, for a given mixed venous blood composition, will be directly proportional to the blood flow through the occluded lung.

Dale and Rahn's estimation of the pulmonary blood flow during atelectasis was unsatisfactory for the following reasons: (1) The rate of atelectasis formation was measured by the volume change of both the occluded lung and the spirometer. Since they were able to increase the rate of atelectasis formation 63 fold by changing the inspired gas composition, the rate of change volume was dependent to a greater extent on the inspired gas composition than on blood flow per se. (2) The duration of the unsteady state was prolonged by the tendency of the gases in the spirometer to equilibrate with the blood perfusing the occluded right lung. (3) Since they observed volume changes, they could not describe the rate of gas composition changes. (4) The method was not ideally suited to measure blood flow on a lobar basis. If this was attempted, the controlled ventilation to the segment would compromise the ventilation of the remaining lung because of the size of the catheter required to insure adequate ventilation of the obstructed lobe.

Farhi (5) studied the lobar distribution of the pulmonary circulation in the supine and erect rat. He occluded the bronchial tree so that gas was trapped in the lobes and therefore could not exchange their gas contents with other lobes. The gas was absorbed by the blood which continues to flow through the lungs until the death of the animal. The speed of gas resorption is proportional to the amount of blood flowing through the area. He varied the inspired oxygen concentration from 50 volumes percent to 100 volumes percent. At the lower oxygen concentration, the rats died before any atelectasis developed; however, rats breathing 100 percent oxygen died with atelectasis in all parts of the lung. When 70-80 percent oxygen was inspired, survival time of the rat was sufficient to permit atelectasis to develop in some parts of the lung before death. These were obviously the better perfused parts relative to the volume of lung.

In supine rats, atelectasis was encountered in the right upper lobe more often than in the right lower lobe and the statistical difference was statistically significant. ($P < 0.001$) In the erect position, the same results were obtained; thus showing that the upper lobe of the rat was better perfused than the lower lobe regardless of posture.

Mattson and Carlens (12) demonstrated spirometrically that the oxygen uptake in the upper and basal lobes of the right lung in man was influenced by posture. The oxygen uptake decreased in the right upper lobe with a change from supine to the erect position, while the ventilation in this lobe remained unchanged. Rahn and Sadoul (16) reported similar results in the dog. The discrepency between work on man and the dog (which indicates shifts in perfusion to the dependent parts of the lung on the assumption of erect posture) and the rat, was attributed to the small size of the rats (in which changes in hydrostatic pressure differences between upper and lower lobes is necessarily small).

The distribution of pulmonary blood flow has been studied in relation to the ventilation of the lungs. The following method was used to determine the alveolar carbon dioxide and oxygen concentrations in man.

Oxygen uptake by the lobe of a lung was measured by the placement of a small catheter in the bronchus of the lobe. Near the end of expiration a gas sample is aspirated via the catheter and analyzed. This sample would be equivalent to that of the alveolar gas in that the dead space gas would be flushed from the bronchus at the beginning of expiration. If two or more catheters are used, comparisons of lobar oxygen uptake and the carbon dioxide output could be made.

The knowledge of the oxygen uptake and the carbon dioxide released in a period of time, enables one to calculate the respiratory exchange ratio of the individual lobes. (13) The respiratory exchange ratio is the ratio of carbon dioxide output divided by the oxygen uptake.

Martin <u>et. al.</u> (11) found that in man in the upright position, the respiratory exchange ratio and end-expiratory oxygen were higher and carbon dioxide was lower in the right upper lobe than in the right lower lobe. When the subject was placed in a supine position, the end-expiratory oxygen was higher and the carbon dioxide concentration was lower in the right lower lobe than in the right upper lobe, and the respiratory exchange ratio showed no significant difference between the two lobes. Apparently, ventilation-perfusion relationships are not greatly different in the two lobes in this position compared to the differences found in the upright position.

The ventilation-perfusion ratio is an expression of the volume of gas reaching the alveolus and the volume of blood perfusing the alveolus per unit of time. This ratio will determine the alveolar gas concentration. Rahn and Fenn (15) related this ratio to the partial pressure of alveolar carbon dioxide, respiratory exchange ratio and arterio-venous oxygen difference. When these values are known, the predicted ratio can be calculated over the physiological range of the partial pressures of oxygen and carbon dioxide in the lung.

The relationship of the ventilation-perfusion ratio to the respiratory exchange ratio is shown in figure 1. (16)

As can be seen, the higher the gas exchange ratio, the larger is the ventilation-perfusion ratio. If at any time one can demonstrate that the exchange ratio in any two regions are different, the ventilation-perfusion ratio must also be different.

Rahn, Sadoul _et. al._ (16) studied the distribution of ventilation and perfusion in the dog. They measured the respiratory exchange ratio in the right upper lobe and right lower lobe and found that a change in posture gave them similar results as those found in man by Martin _et. al._ (11)

Figure 1

Relationship between the ventilation-perfusion ratio of an alveolus or larger unit and the corresponding exchange ratio, R. (16).

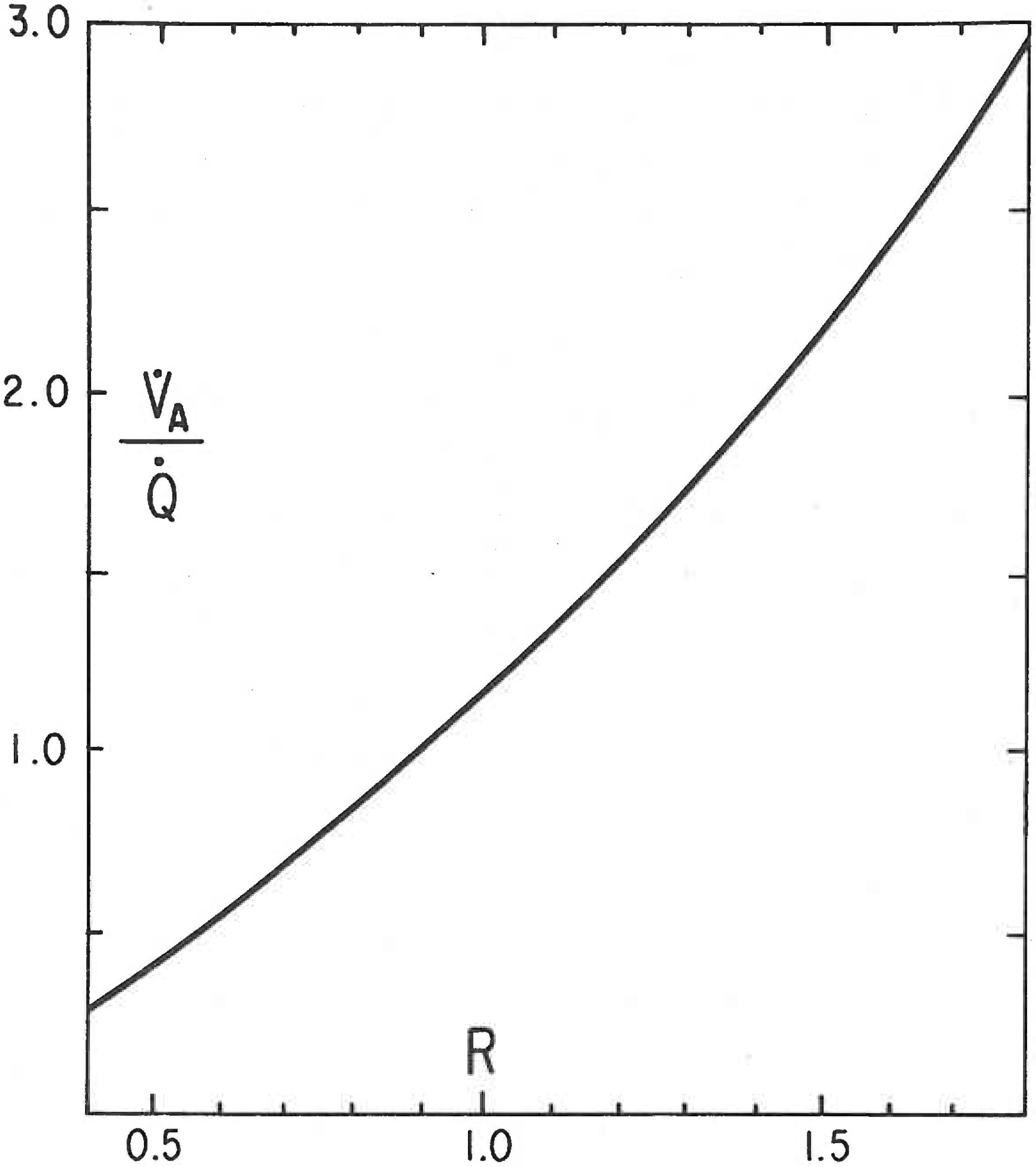

Figure 1

They also measured the distribution of ventilation by employing a radioactive aerosol. Their findings indicated that in the supine position, less activity per unit of lung was found in the lower lobes than in the upper lobes. In the erect position, this situation was reversed. On the assumption that that the radioactive count was proportional to the ventilation, they substituted ventilation figures into the ventilation-perfusion ratio which they had determined, and arrived at approximate values of the relative blood flow to each lobe. Their analysis showed that perfusion per unit lung was nearly the same for both upper and lower lobes in the supine position. In the erect position, however, the perfusion per unit lung of the right lower lobe was greater than that for the right upper lobe.

From these studies and bronchospirometry studies in man, it appears that gravity produces an uneven distribution of blood flow favoring the dependent portions of the lung.

Rahn and Bahnson (14) were able to calculate differences in blood flow to each lung caused by making one lung hypoxic. This phenomenon was due to the vasoconstriction of the pulmonary vessels in the hypoxic lung with a shunting of blood to the oxygenated lung.

West and Hugh-Jones (20) observed the rate of fall of oxygen tension in a lobe of the dog's lung after bronchial occlusion. Gas tensions were measured with a mass spectrometer. Cannulas were placed in the branch of the pulmonary artery which allowed the blood flow to the lobe to be continuously monitored by a rotameter, and direct measurements of flow were made by collection of timed samples. The rate of fall of oxygen tension following occlusion was approximately linear initially and the rate correlated well with the direct measurement of perfusion when the animal was in a steady state.

West and Hugh-Jones's efforts in relating the fall in oxygen tension in an occluded lobe with blood flow has the following feature. They were working with a high sampling rate (20 cc/minute), and therefore, were obliged to sample for only a short period of time. This time period may well be too short, as will be mentioned in the discussion, to accurately relate the fall of oxygen tension to the blood flow.

Methods:

The experiments were carried out on boxer dogs weighing 13-31 kilograms. The animals were anesthetized with intravenous pentobarbital 30 mgm./kg. A bronchoscope serving as an endotracheal tube was placed so that the distal tip of the scope was one to two centimeters above the carina. All dogs were placed in a supine position during the experiments.

The catheter was 80 centimeters in length and consisted of an 8 french, balloon tip Foley catheter with polyethylene and vinyl tubing extensions. The catheter had an external diameter of 2.5 to 3.5 millimeters and was consequently small enough not to interfere with the ventilation of the lungs.

For balloon inflation, a 5 cc. syringe with a three-way stopcock was attached to the balloon inlet and 3 cc. of air or water was injected.

The principal lumen of the catheter was connected through a 2 cc. moisture trap to the sampling cell of a Beckman fast response carbon dioxide analyzer. The trap served to prevent aspiration of the bronchial secretions into the carbon dioxide analyzer. This analyzer operates by the detection of non-dispersive infra-red radiation transmitted through the sample gas. The gas sample was directed from the carbon dioxide analyzer into the sampling system of a fast response nitrogen meter (Nitralyzer).

The Nitralyzer is a continuous sampling meter for measuring the percentage of nitrogen in a gas mixture. The instrument is connected to a vacuum pump which draws the sample gas through an ionization chamber from the sampling system. The sampling system includes a needle valve, adjustment of which will control the pressure in the system and the ionization chamber. Its adjustment also controlled the rate at which gas was aspirated from the lung or lobe. Ionized nitrogen is intensely luminescent. The light output is detected by a photocell, the output of which is proportional to the nitrogen concentration.

Both the Nitralyzer and carbon dioxide analyzer were connected to the Sanborn AC-DC Preamplifiers where the changing nitrogen and carbon dioxide concentrations were recorded on paper.

The response times for each component of the analysis system was 0.1 second or less. The response time of the entire sampling system including the catheter was 7-12 seconds.

The instruments were calibrated to yield dry gas composition even though saturated gas was aspirated.

The catheter was placed under direct visualization by a bronchoscope telescope into the left main bronchus. The distal 2 centimeters of the catheter contained the balloon. The ideal placement of the catheter was to have the inflated balloon just beyond the left apical bronchial orifice and the tip in the left lower lobe bronchus. This site was chosen because it is the most convenient in the dog's bronchial system in that the inflated balloon did not occlude any segmental bronchi.

Complete bronchial occlusion could be determined by direct visualization of the inflated balloon occluding the bronchus during several respiratory cycles or by auscultation over the occluded lobe where no breath sounds were heard. If for some reason, such as breakage or movement, the balloon did not occlude the bronchus during the experiment, it would be detected immediately by observing no change or fluctuating changes in the nitrogen and carbon dioxide concentrations coincident with the respiratory cycles following inflation of the balloon.

The proximal end of the bronchoscope formed a slip joint with a Y tube. One arm was in direct alignment with the longitudinal axis of the scope and the other arm was curved so that its orifice was 90 degrees to this axis. The straight arm was fitted with a slip ring collar which forms an air tight junction around the catheter. The angulated arm of the Y tube serves as the airway orifice. This slips into a set of rubber valves which prevents the animal inspiring the previous expired gas volume.

The inspiratory valve system was connected by large rubber tubing to a gas reservoir. This reservoir is a 75 liter weather balloon. Known gas mixtures were made up in compressed gas cylinders and then bled off into the weather balloon. Oxygen-nitrogen mixtures ranging from air (21% oxygen) to 70% oxygen were used.

The dogs were allowed to equilibrate with the gas mixture until constant alveolar gas concentration was attained before the experiments were begun. The minimum equilibration time was 20 minutes.

The sampling system aspirated 4-5 cc. of gas in the occluded lobe per minute. The aspiration pressure which was controlled by the needle valve of the Nitralyzer was always adjusted to 1 mm. of Hg.

In some experiments a 50 centimeter balloon tip, vinyl catheter was utilized in occluding part of the pulmonary vascular bed. This catheter was constructed in this laboratory following the design of Lategola *et. al.* (7) The catheter was inserted via the external jugular vein, through the right heart to the pulmonary vascular system. The bronchus was occluded and the pulmonary artery was occluded during the unsteady state.

The decrease in the total lobe volume during the period of the unsteady state was estimated by attaching a 200 cc. spirometer to the proximal end of the bronchial catheter. The balloon was inflated and the rate of decrease in spirometer volume was measured. The gas in the spirometer was always that inspired by the dog. The inspired gases were 100 percent oxygen, and several mixtures of oxygen in the 40 to 80 percent range.

Results:

Figure 2 depicts a typical recording. One should note the following: (1) the changing concentration of nitrogen, (2) the changing concentration of carbon dioxide, (3) the duration of the unsteady state of nitrogen and carbon dioxide and (4) the time lag following bronchial occlusion before changes in nitrogen and carbon dioxide can be observed.

Since we were able to determine the concentration of carbon dioxide and nitrogen, the calculation for the oxygen concentration becomes a simple matter. The concentrations of nitrogen and carbon dioxide were substracted from 100 and the value determined was equal to the oxygen concentration. If the change in the log of the oxygen concentration was plotted against time, the curve in figure 3 was obtained. The linear segment of the two curves illustrates a first order reaction in that the oxygen concentration decreased at a constant rate with time during this period.

The dotted lines represent extensions from the straight line portions of the curve. The point where they crossed was chosen to be more accurate estimation of the time for the lobe gas to reach constant composition. A comparison of the estimation of the unsteady state time was made with and without the knowledge of the carbon dioxide concentration. As can be seen in figure 3, the time predicted was very nearly the same.

When the inspired nitrogen concentration was decreased, the unsteady state was altered in two ways. First the duration of the unsteady state was increased. Secondly the potential range of

Figure 2

A typical recording. Note:

(1) The changing concentration of nitrogen,
(2) The changing concentration of carbon dioxide,
(3) The duration of the unsteady state of nitrogen and carbon dioxide and
(4) The time lag of the sampling system, the average duration of which is depicted by the dark line near the time scale.

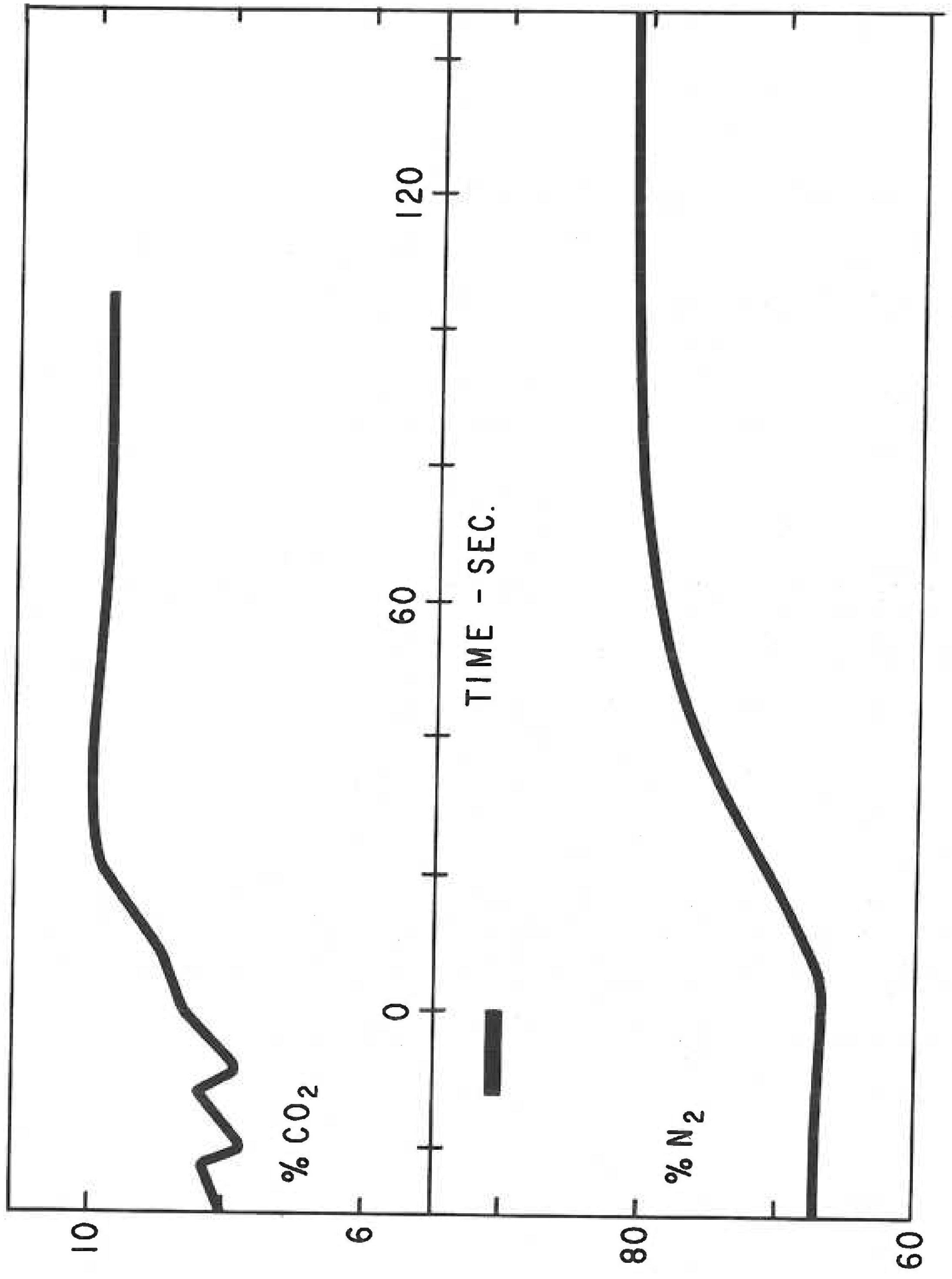

Figure 2

Figure 3

The changing oxygen concentration during the unsteady state.

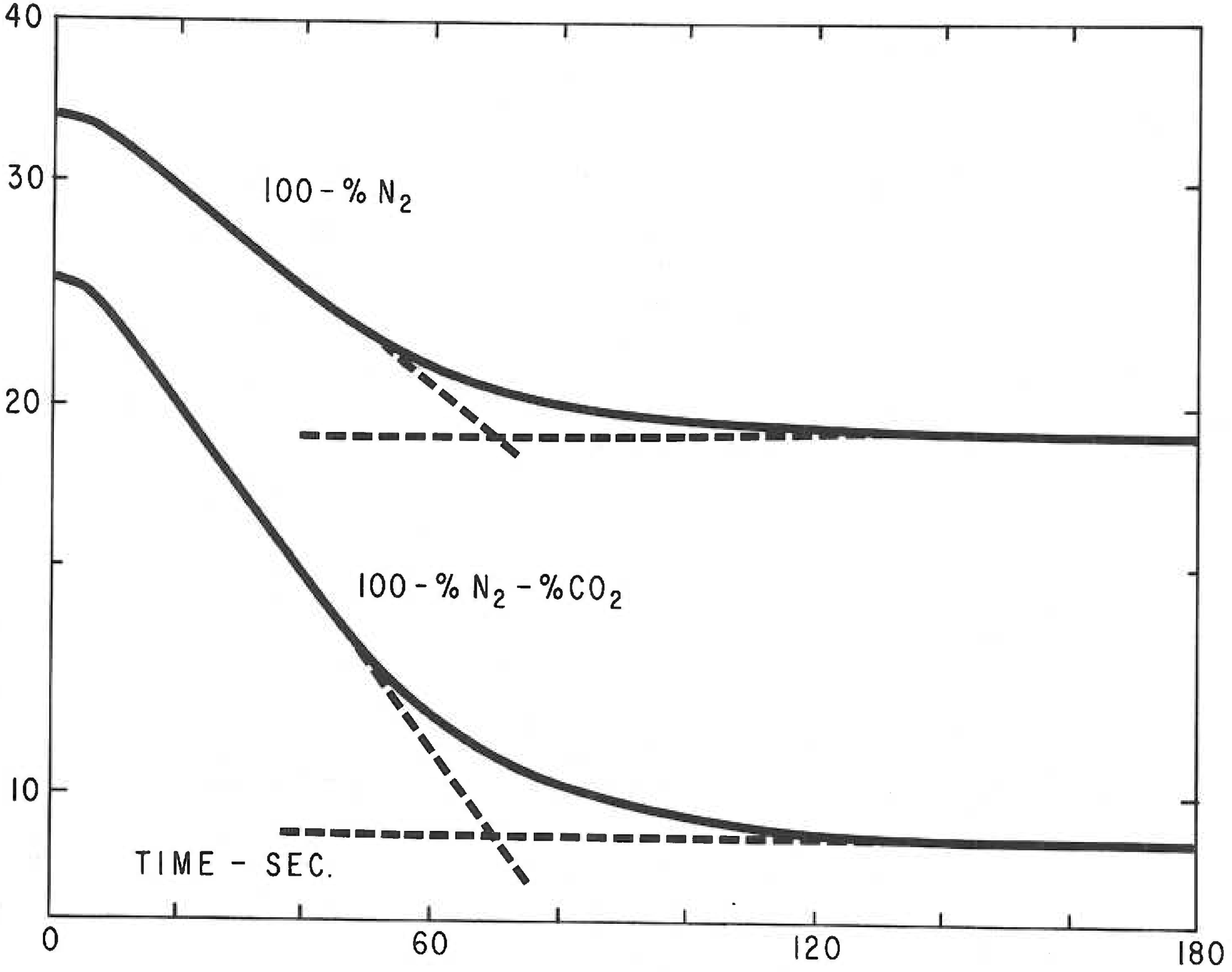

Figure 3

changing nitrogen concentration in the occluded lobe was increased because the venous nitrogen concentration remains virtually constant during the state of changing gas composition. Both these factors are illustrated in figure 4.

The inspired nitrogen concentrations were studied over the range of 30 to 79 percent. It can be seen in figure 5 that the duration of the unsteady state time was increased from 30 seconds when the animal was inspiring air to 160 seconds when the dog was inspiring 30 percent nitrogen.

The straight line was drawn by eye. However, the regression line was calculated and the values for "b" and "a" are -0.28 and 85.67 respectively. The slope, b, of this line demonstrates an approximate increase in time to reach constant composition of 10 seconds for each 2.8 percent decrease in the initial nitrogen concentration. It is also of interest to note that the intercept, a, is at the approximate concentration of nitrogen which exists during the period of constant composition. The large scatter of points around the straight line is apparently due to the variations in rate of blood flow through the occluded lobes of the several dogs used in this series of experiments.

The effect of occluding the blood flow to the occluded lobe during the unsteady state is shown in figure 6. Oxygen absorption from the lobe was halted only to continue again when the perfusion of the lobe was resumed.

If the balloon tip, pulmonary catheter occludes a portion of the pulmonary vasculature other than that of the left lower lobe, results were obtained as in figure 7. Here the duration of the unsteady state

Figure 4

The duration of the unsteady state is increased with a decrease in the inspired nitrogen concentration. The potential range of changing nitrogen concentration in the occluded lobe is increased with a decrease in the inspired nitrogen concentration.

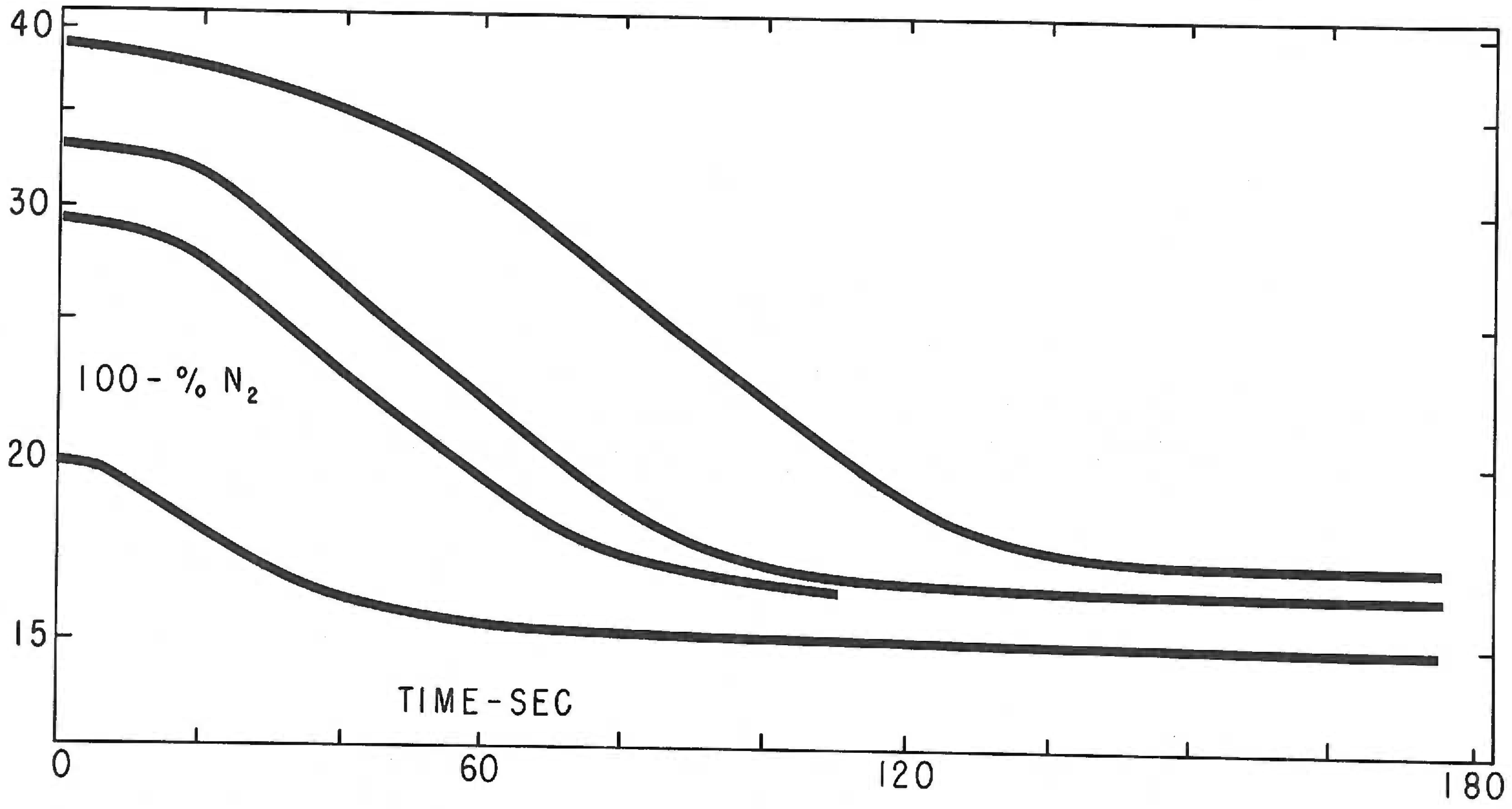

Figure 4

Figure 5

Increase in the duration of the unsteady state with a decrease in the inspired nitrogen concentration. For every 2.8 percent decrease in the initial nitrogen concentration, the unsteady state time is increased by 10 seconds.

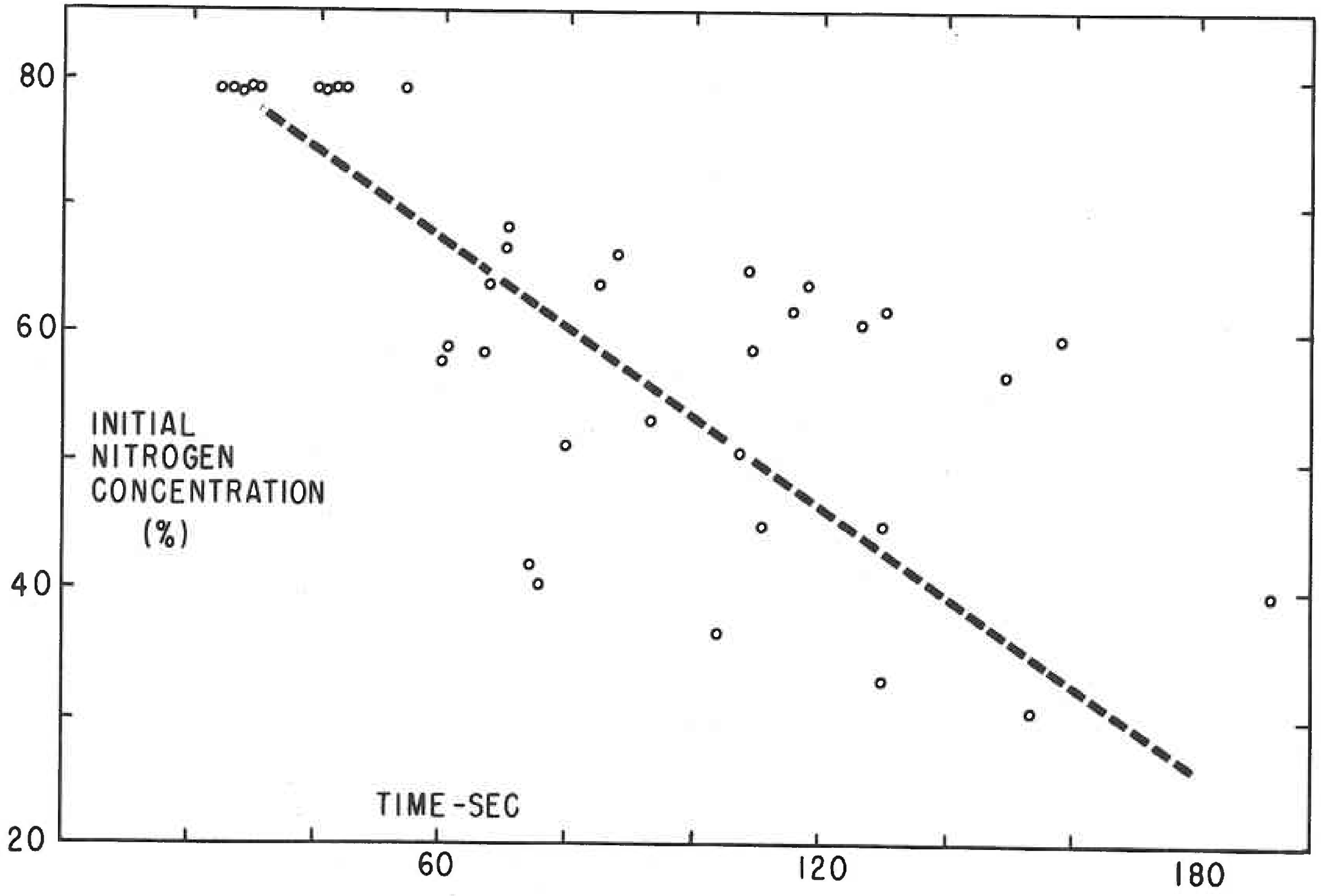
80
60
40
20
INITIAL NITROGEN CONCENTRATION (%)
TIME-SEC
60
120
180

Figure 5

Figure 6

The decreasing oxygen concentration during the unsteady state is interrupted by the occlusion of the lobar blood flow. When lobar perfusion resumes, the shape of the falling oxygen tension is parallel to the slope prior to occlusion.

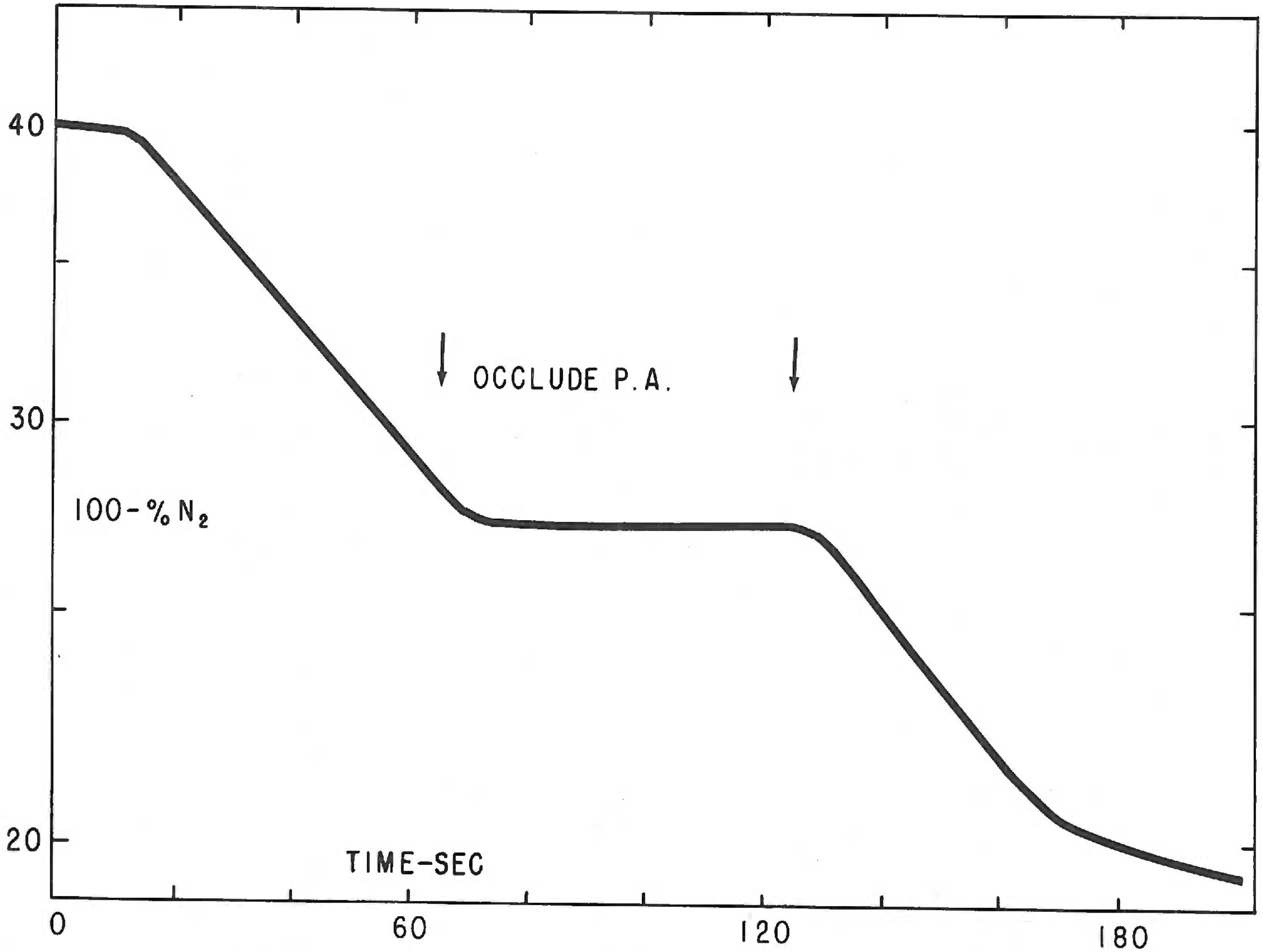

Figure 6

Figure 7

Partial occlusion of the blood flow to the lungs other than the left lower lobe. The dotted lines illustrate the decrease in the duration of the unsteady state due to the shunt of more blood through the occluded lobe.

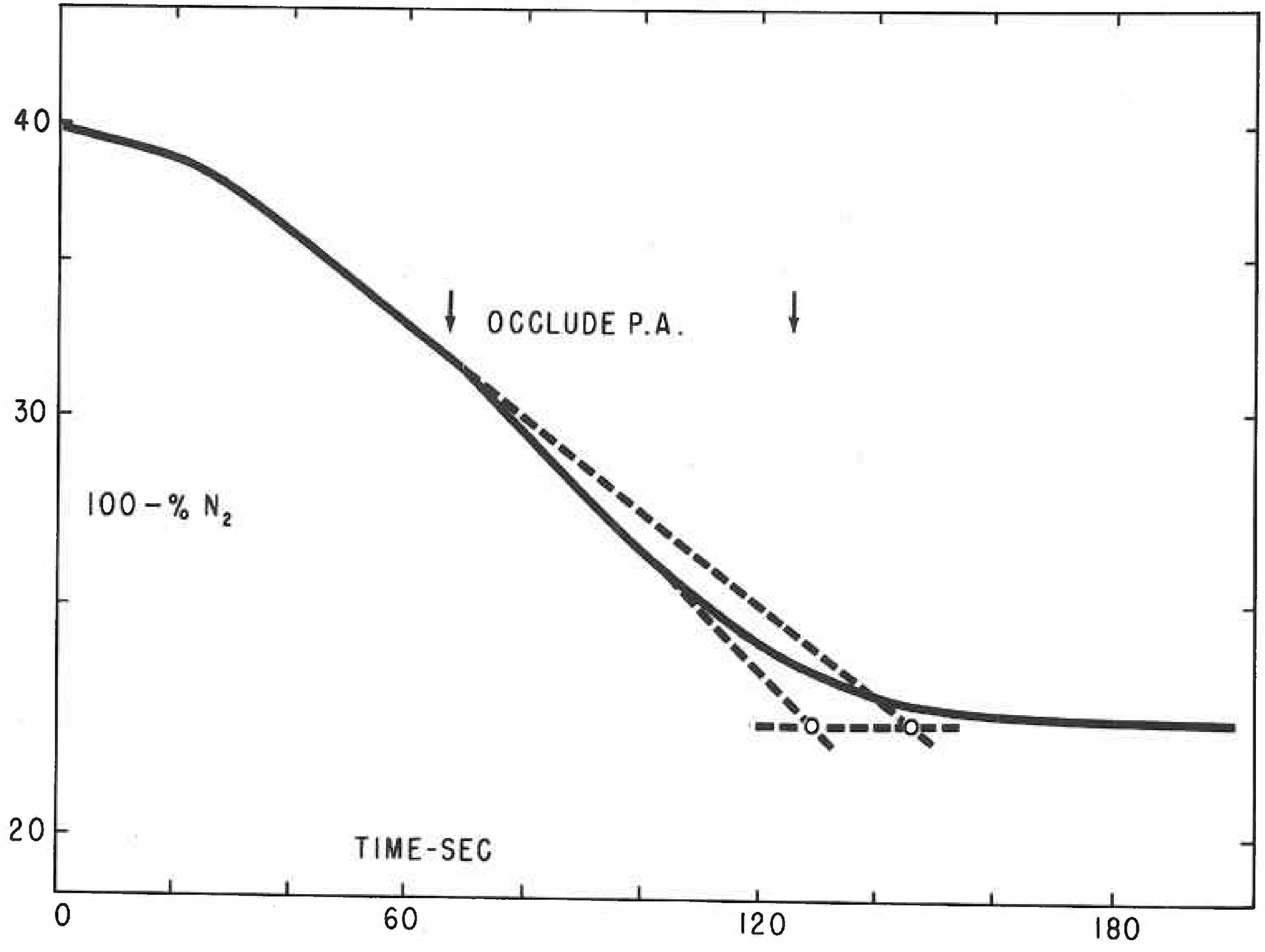

Figure 7

was decreased, indicating a shunt of more blood flow through the occluded lobe.

The total volume change in the spirometer during the first three minutes following bronchial occlusion increased as the inspired oxygen increased up to the 80 percent concentration. The spirometer volume change with 100 percent oxygen was the same as the 80 percent oxygen. The three minute time was chosen because 160 seconds was the longest unsteady state time recorded.

Table 1 identifies the volume change of the spirometer with time for two dogs with various oxygen-nitrogen gas mixtures.

The volume changes in each column are the means of two separate determinations which were run in succession following a twenty to thirty minute period in which the dog's alveolar nitrogen became constant.

The rate of change of volume was related to the composition of the gas breathed by the animal. The volume transferred to the occluded lobe at the end of 5 minutes was considerably greater when the dog breathed 100 percent oxygen, than when 42.3 percent oxygen was breathed. This finding agrees with that of Dale and Rahn (4), in which the spirometer volume change was compared with air and 100 percent oxygen. The gas volume transferred from the spirometer to the occluded lobe when the dog was breathing 42.3 percent oxygen was less than the volume aspirated by the sampling system for the same period of time.

When a known 3 mm. Hg. pressure gradient was applied between the spirometer and the tip of the bronchial catheter, the rate of spirometer volume decrease was 64 cubic centimeters per minute. This value far exceeds any rate shown in the following table and proves that a

Table 1

Gas % Oxygen	100		80		60		42.3	
Dog	1	2	1	2	1	2	1	2
	Spirometer volume change - cc.							
Time in minutes								
1	7.5	8	9.5	5	4.5	2	3.5	2
2	14.5	20.5	15	18	8	14	4.5	1.5
3	15	21.5	14.5	26.5	15	20.5	4.5	5.5
4	21.5	29	18.5	22.5	15	13.5	5.5	4.5
5	22.5	28.5	18	21	12	10	6	5

small pressure gradient between the occluded lobe and the spirometer was sufficient to empty the spirometer.

Discussion:

A frequent criticism of this method of estimating blood flow has been that the developing atelectasis would impair the blood flow as well as decrease the surface area for gas absorption. To evaluate the surface area of the lobe, the volume change of the occluded lobe was estimated during the unsteady state. Alteration in the blood flow is discussed later in this section.

It was predicted that the decreasing lobe volume during the unsteady state would not be greater than the volume occupied by the nitrogen initially present in the occluded lobe. For example: If the animal was inspiring 40 percent oxygen in 60 percent nitrogen, the volume of the lobe at the end of the unsteady state would be at least 60 percent of the unoccluded lobe volume. This approximation excludes the volume lost from the lobe by the sampling process. The basis for this hypothesis is obvious when noting the changing nitrogen concentration in the occluded lobe in figure 2. The nitrogen concentration at the onset of occlusion is in equilibrium with the perfusing blood. However, the concentrations of oxygen and carbon dioxide are not in equilibrium with the perfusing blood at the beginning of occlusion. The trend towards equilibrium of oxygen and carbon dioxide within the occluded lobe with blood has a net concentrating effect on the nitrogen. Consequently, at the end of the unsteady state, nitrogen is the farthest from equilibration with the blood as compared to the oxygen and carbon dioxide.

Therefore, the partial pressure difference between the lobe and blood is principally that of nitrogen. The rate of nitrogen absorption would be proportional to its partial pressure. Since this partial pressure gradually increases during the unsteady state to a maximum level during the state of constant composition, the nitrogen absorption rate would be greater during the period of constant composition. Consequently, little nitrogen is absorbed by the blood during the unsteady state and the volume of nitrogen present prior to occlusion remains in the lobe during the phase of changing gas composition.

The foregoing hypothesis has been confirmed by the estimation of lobe volume change during the unsteady state by a 200 cubic centimeter spirometer. The greatest volume change of the spirometer during the unsteady state was 50 cubic centimeters. Assuming the spirometer volume change to be proportional to the lung volume change, the lung volume decreased 50 cubic centimeters during the unsteady state.

Rahn and Ross (17) estimated the volume of the various lobes of the dog's lungs by weighing the air dried lobes. They predicted the left lower lobe to have a volume of approximately 250 cubic centimeters. The sampling rate was 4-5 cubic centimeters per minute. Since our maximum unsteady state time was 160 seconds, the three minute duration of the unsteady state was purposely chosen here so that all experiments definitely had as a minimum the following calculated value for lobe volume at the end of the unsteady state. Adding 15 cubic centimeters of gas for sampling to the 50 cubic centimeter volume of gas absorbed during the unsteady state equals the total volume change of the occluded lobe. The 65 cubic centimeter volume change is equivalent to a 26 percent decrease in the initial lobe volume. The volume decrease in the spirometer during the initial lobe three minute period was calculated using 80 percent oxygen as the inspired gas. We were never able to successfully complete an experiment with a higher inspired gas oxygen concentration than 70 percent. As noted in table 1, the spirometer volume change was the largest with either inspired 80 percent oxygen or 100 percent oxygen.

Since under the most adverse conditions, the lobe volume does not change by more than 26 percent of its initial volume, it may be argued that any associated change in surface area is not expected to alter the diffusion properties of the alveolar membranes. The argument is tenuous but then, it is not established that there is a fixed relation between lung volume and exchange surface area.

The S shaped curve of the falling oxygen tension during the unsteady state (Figure 8) indicates different rates of oxygen absorption during the unsteady state. However, there was a period in the mid-section of the curve in which the slope is a straight line; in this area it was considered to be proportional to the blood flow.

The changes in slope in each segment of the curve were interpreted as follows: (1) In segment 1, there was no change in the oxygen concentration due to the lag time of the sampling system. It took several seconds for the gas in the sampling system to be flushed out by the gases in the occluded lobe. It was in this manner that the lag time was determined for our sampling system---in all the experiments it varied from 7-12 seconds. (2) There is a rapid influx of carbon dioxide from the blood into the occluded lobe during segment 2. (See figure 2) In this same period, the intralobar oxygen concentration begins to decrease because of dilution by carbon dioxide and by the

Figure 8

The S shaped curve of the falling oxygen tension during the unsteady state. The numbers refer to the different slopes of the curve.

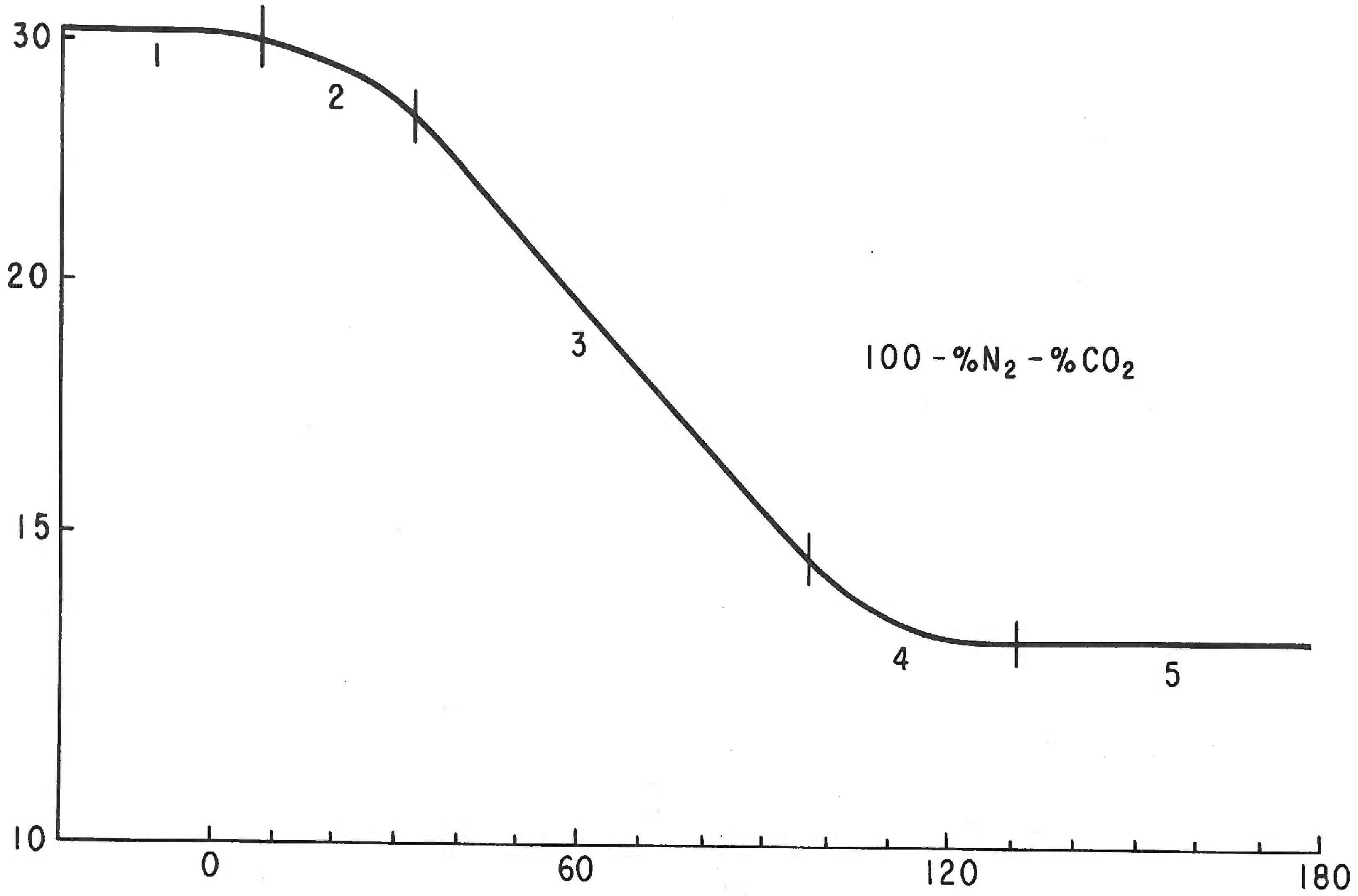

Figure 8

initial absorption of oxygen by the blood. At the end of segment 2, the carbon dioxide has reached the level of its constant composition. (3) Segment 3 was representative of the decreasing oxygen concentration since carbon dioxide had reached its state of constant composition and nitrogen was being concentrated only by virtue of the decrease in oxygen content of the contained lobar gas. The amount of nitrogen absorbed during this period of the unsteady state was negligible as was mentioned in the foregoing discussion. (4) The straight line is altered in segment 4 for several possible reasons. (a) The developing atelectasis of the lobe may interfere with the lobar blood flow. (b) Mixing of the gases in the segments of the occluded lobe could occur. (c) There is a possibility that the diffusing capacity of the gases is decreased because of the decreasing volume of the lobe and corresponding contraction of the surface area. (d) The oxygen tension in the occluded lobe probably has decreased beyond the linear segment of the S shaped hemoglobin saturation curve. (5) Segment 5 represented the state of constant composition for oxygen.

Because of the foregoing discussion, segment 3 of the curve was chosen to relate blood flow to the falling oxygen tension within the occluded lobe. West et. al. (20) came to the same conclusion that blood flow could be estimated by the falling oxygen tension during bronchial occlusion, but their methods of rapid sampling limited them to 10-12 seconds of sampling time and consequently their sample was taken during segments 1 and 2 of the curve in Figure 8. Their methods limited their observation of a fall in oxygen tension to the time interval when it was being partly decreased by the rapid influx of carbon dioxide into the lobe from the blood. Since they were able to correlate blood flow quantitatively with the decreasing oxygen tension, including the above error; the possibility exists that correlating the falling oxygen tension during segment 3 with the lobar blood flow could be more accurate.

This method of estimating lobar blood flow could find direct application in comparing perfusion in individual lobes and in lobes which perfusion has been altered by posture or hypoxia.

The greatest deficiency in this experiment is that there is no direct quantitative correlation of the rate of blood flow to the slope of the decreasing oxygen tension during the unsteady state. This could be done in an open chest preparation much like the method of West and Hugh-Jones. (20) Perhaps, if this were done and the mid-section of the unsteady state oxygen curve was correlated with the blood flow, a reasonably accurate method of estimating blood flow would be established.

There was no attempt in this experiment to evaluate changes in the diffusing capacity of the gases in the occluded lobe other than estimation of the lobe volume change during the unsteady state. It was assumed that the alveolar membrane offered little resistance to the absorption of gases from the lobe by the blood.

The rate of fall in oxygen tension is dependent upon the lobar volume. West et. al. (20) found in small lung volumes a steeper slope of the decreasing oxygen concentration during the unsteady state. Consequently, if two different lobes were studied for perfusion rates, the blood flow could be identical, but the smaller lobe volume would produce a steeper slope of the falling oxygen tension. This would give the investigator the false impression of a higher blood flow rate to the smaller lobe. Therefore, lobar blood flow must be expressed as perfusion per unit lobe volume. For this reason, the lobes should be occluded at the same time during the respiratory cycle.

Conclusions:

1. A method of estimating pulmonary blood flow has been outlined. The method is based upon the observation of the rate of change in oxygen concentration in an occluded lobe which is dependent upon the rate of perfusion of that segment.
2. The duration of the period of changing gas composition and the potential range of change were both increased by decreasing the initial alveolar nitrogen concentration.
3. This method could be employed to compare the individual lobar perfusion rates in the lungs.

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