The influence of age, sex and weight on respiratory function in the sedate canine

by

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INTRODUCTION

The increased acceptance of physiologic tests in clinical veterinary medicine has improved our diagnostic, therapeutic, and prognostic capabilities. With the incidence of pulmonary disease rising, and with respiratory failure being a significant surgical complication, it is readily apparent that knowledge of the deranged mechanisms in the pulmonary patient is extremely valuable to the practitioner.

In the past three decades, a large number of physiologic tests has been developed that has allowed qualitative and quantitative evaluation of pulmonary function in patients with cardiopulmonary disturbances. Recently, the quality and availability of apparatus for pulmonary function testing in clinical medical practice has remarkably improved the physicians ability to diagnose, evaluate and understand pulmonary irregularities. These tests have enabled the physician to gain a better understanding of the factors that control lung function and have allowed for early implementation of prophylactic measures or ventilator support that has significantly reduced mortality resulting from respiratory complications during surgery.

Although the veterinary practitioner has attempted to parallel the success the human physician has experienced in handling pulmonary disease and acute respiratory disturbances, he has received little clinical benefit from pulmonary function tests.

The veterinarian recognizes the importance of pulmonary function tests and blood gas analysis in evaluating animals with pulmonary

abnormalities, but at this time testing is impractical and less exacting than that available to human medicine.[42,113]

Unfortunately, many of the diseases and respiratory disturbances that have been effectively diagnosed and evaluated by pulmonary function testing in man, are also major concerns to the veterinarian. The ease with which obstructive lesions and lower airway pathology is evaluated in medical practice cannot be appreciated by the veterinary clinician. The disparity exists because many of the pulmonary function studies require voluntary cooperation from the patient during testing procedures. For example, the expiratory flow-volume curve (EFVC) is a relatively new but very effective tool available to the physician for evaluating both obstructive and restrictive pulmonary disturbances.[53,73,135] Flow and volume are two parameters that can easily be measured in an animal, but for the EFV curve to have clinical significance, maximum forced expiratory efforts are necessary. One of the major complaints of physicians is that patients fail to cooperate and do not provide reproducible ventilation efforts. Therefore, it is absurd to think a veterinarian could get the necessary cooperation from a dog or cat to allow this test to have diagnostic significance.

As a result, many of the pulmonary function tests currently available to veterinary medicine are too difficult and dangerous to routinely conduct since they require complete control of the animal, making anesthesia necessary. Certainly, it is contraindicated to risk anesthesia on a clinically ill respiratory patient for the sake of evaluating the nature and extent of the disturbance.

Recently, several investigators have utilized pulmonary function tests in evaluating lung mechanics in induced disease situations in dogs and cats. They have found that lung volumes, lung compliance and resistance, and blood gases are sensitive and reliable indicators of respiratory deficit.[22,31,33,96] More importantly, the unanesthetized dog model was used in several of the procedures.[31,33] The creativity and inventiveness of the investigators involved in pulmonary function studies in animals must not be underestimated. The possibility of existing human tests being modified or new procedures being developed that will enable routine clinical evaluation of respiratory diseased animals seems imminent.

In anticipation of this, it is apparent that in order to evaluate the pulmonary function in a diseased animal, comparison with baseline parameters of normal healthy animals is necessary. Several investigators have provided respiratory function parameters in normal dogs.[31,33,40,50,104] The models used in obtaining these parameters are numerous and variable, several offering clinically applicable possibilities.[31,33,104]

In order for pulmonary function testing to have clinical application, the procedure must place minimal stress on the animal, avoiding any unnecessary physical activity or excessive restraint. Many investigators elect to avoid stress and obtain respiratory stability by studying pulmonary function in anesthetized animals. Parameters obtained under these conditions must be carefully evaluated and seldom represent normal values since lung function is extremely sensitive to anesthetic agents.[16,74,124] With these limitations in mind, it was the intention of this investigator to measure respiratory function in the normal dog,

modifying existing procedures in order to minimize stress without drastic sacrifice of the normal physiological respiratory state.

Before attempting these measurements, two major experimental design features had to be considered. First, a respiratory model had to be selected that would provide parameters that could be useful for eventual comparison with obtained clinical values. Second, the experimental design must enable the influences of age, sex and weight on respiratory function to be studied and allow for appropriate statistical analysis of these variables.

There are only two respiratory models to choose from: the unanesthetized dog using either a facemask or body plethysmograph, and the intubated animal that has been either tranquilized, sedated or anesthetized. The facemask model has been an efficient and consistent method of producing normal respiratory parameters in the unanesthetized dog.[104] Similarly, the body plethysmograph has been a useful tool in studying respiratory physiology, but both have clinical limitations in that the animal must undergo adaptation periods to adjust to the mask or chamber before normal respiratory measurements can be made.[40] The second choice, the anesthetized model, has been an invaluable method to study respiratory function in the dog, but the level of anesthesia has been often abused and results obtained seldom can be used to simulate respiratory parameters in an awake, normal dog.

Preliminary studies in this laboratory revealed that a combination of a mild tranquilizer with an ultra-short acting barbiturate anesthetic produced a sedate animal that facilitated testing procedures without a severe compromise of lung function. Although drug combinations have

been used before in studying pulmonary function, no investigators have manipulated the dosage of the agents so that respiratory parameters such as frequency and tidal volume approach values established for normal awake dogs. Although tranquilizers and anesthetic agents are contra-indicated in an acutely ill pulmonary disease patient, sedation has been found to be helpful in eliminating the characteristic anxiety in chronic patients.[42] A further benefit of this model is that a patent airway is assured by the endotracheal tube, allowing for immediate respiratory therapy if necessary. However, clearly the value of this model is not its clinical applicability but its ease with which respiratory function can be measured.

A major consideration of this study was to examine the influence of age, sex and weight on respiratory function. Although many investigators have found significant correlations between weight and several respiratory parameters, and several have studied age influences on respiratory function in dogs, few have examined sex effects. Further, there is no literature available that looks at age, sex and weight effects and possible interactions simultaneously. It is likely that certain respiratory function changes attributed to weight or age effects have been misinterpreted. Consideration of these effects and interactions enables charts of normal values to be established based on the age, sex and weight of the animal. These charts would allow the clinician to rapidly define respiratory irregularities in clinical situations.

It is the purpose of this study to examine and evaluate the influence of age, sex and weight on respiratory function in the sedate canine.

LITERATURE REVIEW

Introduction

Pulmonary function studies occupy a unique position in physiological testing in that almost all the procedures and methods have been developed specifically for human studies, and only recently have pulmonary function testing methods become popular in animal studies. The amount of literature available on pulmonary function testing in man compared to that in animal bears this out.

As early as 1849 static pressure-volume measurements were being performed on human lungs.[90] Hutchinson described and measured vital capacity in the early 19th century.[37] Shortly after, vital capacity measurements and other lung volume studies were being performed in patients with breathing difficulties and by 1925 many of these function tests were being performed on patients with a variety of cardiorespiratory disorders.[7] During the past four decades many investigators have modified and perfected pulmonary function studies enabling them to be moved from experimental research laboratories into clinical situations where today a number of these tests are performed routinely in most teaching hospitals and in many private clinics. Progressive methodologies have allowed valuable information to be gained from new tests that are more sensitive to minor ventilatory disorders and peripheral airway disease.[68,84,145] Besides being an important diagnostic and therapeutic tool, human function testing has made important contributions to acquiring basic physiologic knowledge of pulmonary function in healthy man as affected by age, sex, size, and physical training status.

Unlike physiological tests of renal, cardiovascular, and hepatic function, little of the foundation of pulmonary function knowledge was obtained by animal research. Significant functional differences exist in the respiratory systems of the various species.[30,130] As a result, much of the information obtained from human studies is of little benefit to understanding respiratory function in animals.

It is obvious that there is a disparity between the benefits gained from pulmonary function studies in medical practice compared to veterinary medicine when one considers that it was not until the past decade that procedures and methods borrowed from medical practice had found their way into laboratory animal and domestic animal studies. Thirty years after clinicians began using physiological testing as a diagnostic aid in pulmonary disease, Guyton initiated quantitative studies of different laboratory animals in order to evaluate respiratory disease.[47,48] Following this initial work, a number of manipulative studies utilizing mechanical respiration and anesthesia in the dog contributed much to our understanding of pulmonary physiology in the canine.[2,19,88,108]

Recently, several investigators have developed respiratory models that permit efficient measurements of lung mechanics and ventilation parameters in the unanesthetized dog.[31,40,104] The innocuous nature of these procedures and the minimal cooperation required of the dog suggests potential use in veterinary clinical diagnosis and in evaluation of therapy.

Although information about the clinical significance of pulmonary measurements in naturally occurring disease of dogs is lacking, control

values and the effects of experimentally induced disease have been reported.[19,21,40,50,94,104]

With the incidence of lung disease increasing, and with the growing suspicion that the inhalation of a variety of noxious agents within our environment is related to this incidence, animal models have become important for the evaluation of toxicity of inhaled noxious agents. Therefore, veterinary clinical medicine is not the only beneficiary of advancements in pulmonary function studies in animal.

The primary concern of this survey is a review of canine pulmonary function studies. To permit full appreciation of the subsequent discussion, it is necessary to define some of the principles and describe techniques involved in pulmonary function studies. The second section of the survey is an inclusive review of specific pulmonary studies reported in the literature involving the canine. Because the majority of these studies utilized anesthetized respiratory models, the third section examines the effects of preanesthetic and anesthetic agents on pulmonary function. The final section of the survey reviews the influences of age, sex, and weight on pulmonary function.

Pulmonary Function Testing: Definitions, Principles, and Techniques

The primary function of the respiratory system is to provide oxygenation of mixed venous blood to the cells of the body and to eliminate excess carbon dioxide from them. It is admittedly arbitrary to divide lung function into components, but to facilitate discussion of pulmonary

function testing, it is useful to subdivide lung function into five components; (1) lung volumes, (2) ventilation, (3) pulmonary mechanics, (4) distribution of ventilation, and (5) pulmonary blood flow and blood gas analyses.

Lung volume tests

For many years, the only tests of pulmonary function were measurements of lung volumes. These are measured under static (no air flow) conditions and do not evaluate function but are essentially anatomic measurements. Alterations in physiological processes cause changes in lung volumes,[17] therefore it is necessary to know normal values and how to interpret abnormal deviations. Table 1 below defines the volumes and capacities pertinent to lung volume studies.[17]

Table 1. The Lung Volumes and Capacities

A. VOLUMES. There are four primary volumes which do not overlap
   1. Tidal Volume, or the depth of breathing, is the volume of gas inspired or expired during each respiratory cycle.
   2. Inspiratory Reserve Volume (formerly complemental or complementary air minus tidal volume) is the maximal amount of gas that can be inspired from the end-inspiratory position.
   3. Expiratory Reserve Volume (formerly reserve or supplemental air) is the maximal volume of gas that can be expired from the end-expiratory level.
   4. Residual Volume (formerly residual capacity or residual air) is the volume of gas remaining in the lungs at the end of a maximal expiration.

B. CAPACITIES. There are four capacities, each of which includes two or more of the primary volumes
   1. Total Lung Capacity (formerly total lung volume) is the amount of gas contained in the lung at the end of a maximal inspiration.
   2. Vital Capacity is the maximal volume of gas that can be expelled from the lungs by forceful effort following a maximal inspiration.
   3. Inspiratory Capacity (formerly complemental or complementary air) is the maximal volume of gas that can be inspired from the resting expiratory level.
   4. Functional Residual Capacity (formerly functional residual air, equilibrium capacity or mid-capacity), is the volume of gas remaining in the lungs at the resting expiratory level. The resting end-expiratory position is used here as a base line because it varies less than the end-inspiratory position.

Vital capactiy (VC), the volume of a forced expiration following a maximal inspiration, is the oldest pulmonary function measurement, having been described by Hutchinson in the early 19th century.[37] Although a simple test requiring a spirometer or pneumotachograph, an enormous number of clinical measurements have been collected with it.

Vital capacity and its subdivisions, inspiratory capacity (IC) and expiratory reserve volume (ERV) are dependent on the voluntary ventilatory pattern of the subject.[115] The same individual may vary as much as 20% from predicted normal values from one testing period to the next.[16,17,37]

Modification of VC testing, forces vital capacity (FVC), is a maneuver used as a screening test for early detection of pulmonary or cardiopulmonary disease and has been useful in the differentiation of restrictive and obstructive lung disease.[18]

Although vital capacity maneuvers are severely limited in their ability to detect minor restrictive or obstructive lesions in the peripheral airways,[51,68] they are a valuable pulmonary function screening method for demonstrating volume disturbances associated with pulmonary edema, emphysema, pneumonia, bronchiogenic carcinoma, pulmonary congestion, and atelectasis.[17,18,37,69,118] Therefore, it is apparent that VC maneuvers provide significant diagnostic information for the medical practitioner. However, because of the necessity of patient cooperation and voluntary breathing patterns, measurements of VC and associated maneuvers cannot routinely be employed in canine function studies.

Gillespie and Hyatt[40] measured VC in six dogs utilizing a volume-displacement body plethysmograph, but the procedures were accomplished

only after extensive training and conditioning periods. As a result, VC measurements, easy and routine in medical practice, are an example of the frustration respiratory investigators encounter when attempting to evaluate pulmonary function in animals.

Functional residual capacity (FRC) and residual volume (RV) are two lung volumes usually measured simultaneously.[17] Residual volume is the only one of the four lung volumes that is not measured by direct methods and is calculated by subtracting ERV from FRC (RV = FRC - ERV).

FRC, the volume of the respiratory tract at the end of normal expiration, is measured by either the open-circuit nitrogen washout method[33,40,104,129] or closed-circuit methods.[129] Because these procedures require little patient cooperation, FRC determinations have been successfully accomplished in the canine. Although information about the clinical significance of this measurement in dogs is lacking, normal values and effects of experimental manipulations in anesthetized and unanesthetized dogs have been reported.[2,19,21,33,40,65,66,104] In man, FRC is significantly altered in emphysema, asthma, pulmonary fibrosis, and other restrictive disease and in most obstructive conditions.[16,37]

Other lung volume tests that are used in the evaluation of human lung function include measurements of thoracic gas volume (TGV) and total lung capacity (TLC). Both measurements are helpful in assessing function disturbances, but because voluntary breathing patterns are required, values are rarely reported for the canine.[40]

It is apparent the only lung volume test routinely utilized in canine function studies is the measurement of FRC. Although changes in lung volume may indicate changes in the lung parenchyma associated with

disease, pulmonary gas exchange does not depend on these volumes over a wide range of values.[37] Therefore, the inability to apply all the lung volume tests to canine function studies is not a serious restriction.

Ventilation tests

Ventilation, the cyclic process of inspiration and expiration, is responsible for maintaining partial pressure gradients of O_2 and CO_2 in the pulmonary alveoli and in the arterial blood.

Ventilation measurements such as respiratory rate (f), tidal volume (V_T), and minute volume (MV) have been important diagnostic aids in evaluating pulmonary disease in both man and animals. Although tidal volume and rate can change significantly during pulmonary disturbances,[94] by themselves they are not an adequate indicator of alveolar ventilation and should never be considered outside the context of minute volume.[16,17,37]

Minute volume, long recognized as an effective indicator of ventilation efficiency when used in conjunction with blood gas analysis, is the sum of both the dead space and effective alveolar ventilation. Therefore, absolute values of MV are not necessarily indicative of hypo- or hyperventilation.[17] Respiratory dead space (V_D), the volume of the lungs which is ventilated but not perfused by pulmonary capillary blood flow,[115] is made up of two compartments; anatomic dead space or the space which is in the conduction airways, and alveolar dead space which is the nonfunctioning alveoli.[38] V_D, also referred to as physiological dead space, can be measured by either the Bohr's equation[115] or by single breath analysis methods.[8] Although both methods can be applied in canine pulmonary function studies, measurements are rarely reported. It is reported that the anatomic dead space depends upon the size and posture

of the individual,[140] and is approximately numerically equal in milliliters to the weight of the subject in pounds.[37]

Alveolar ventilation, the volume of inspired air that reaches the alveoli, considers both tidal volume and dead space. [Alveolar ventilation = frequency (MV - anatomic dead space)]. The magnitude of alveolar ventilation has been shown to be a better indicator of respiratory gas exchange than the magnitude of minute volume.[16,37,42]

The most effective evaluation of pulmonary gas exchange is to combine alveolar ventilation measurements with arterial P_{CO_2} analysis.[37] Arterial P_{CO_2} is in equilibrium with alveolar gas even in severe lung disease provided the alveolus is aerated.[37,49] The magnitude of arterial P_{CO_2} generally depends only on pulmonary function; an increased arterial P_{CO_2} means a decrease in alveolar ventilation (hypoventilation), a decreased arterial P_{CO_2} indicated hyperventilation.

Therefore, ventilation measurements such as minute volume and alveolar ventilation, when combined with blood gas analysis, are excellent methods of evaluating pulmonary function in man and animals and are of tremendous clinical utility.[37,40,104]

Pulmonary mechanics

Although lung volumes do change with disease and are useful diagnostic measures, pulmonary gas exchange does not depend on these volumes over a wide range of values. The forces and resistances which determine the flow of gas in and out of the lungs are ultimately responsible for alveolar ventilation. The most frequently reported measurements of these pulmonary forces and resistances in the canine are dynamic lung compliance, airway resistance, and respiratory work.

Compliance is defined as the volume change per unit of pressure change and is a measure of the distensibility of the chest and/or lungs--the ease with which the lung volume is changed.[122] Total pulmonary compliance (C_{LT}) is made up of lung compliance (C_L) and compliance of the thorax (C_T).[115] Lung compliance (C_L), the change in lung volume per change in pressure across the lung, is an index of the distensibility of the lung and is useful clincally because it gives a measure of the change in lung elasticity with disease.[37,42,113] C_L is the slope of the line when lung volume vs intrapleural pressure is graphed. It is conveniently measured in the dog with either a spirometer or pneumotach and an esophageal balloon on the end of a fine plastic tube to record pleural pressure.[115] Changes in intraesophageal pressure have been found to equal changes in intrapleural pressure.[31,40,91]

The validity of intraesophageal measurements has been investigated with contradictory results. Several investigators find that although there are differences in the absolute pressure as measured in the esophagus as compared to direct intrapleural measurement, changes in intrapleural pressure are faithfully reflected by intraesophageal pressure changes.[1,2,23,31,40,41,91] Others find considerable variance between pressure changes in these two sites.[4,10,13] Several factors are responsible for these discrepancies. Studies have shown that pressure gradients exist along the esophagus[4,31,91,138] and at different sites of direct intrapleural measurements.[4,23] In addition to these variations of pressure with in the thoracic cavity, esophageal wall compliance,[91] mechanical conformation of the pressure recording system,[31] and the influence of

mediastinal structures[72,138] affect the fidelity of intraesophageal pressure measurements.

Recent compliance studies in the anesthetized dog revealed that lung compliance differed by as much as 50% when measured at the intrapleural and intraesophageal sites.[31,41] Changes in lung compliance during induced hypovolemic shock and central vascular engorgement in dogs, were in the same direction and equal in magnitude when either esophageal or intrapleural sites were used for pressure measurement.[2,10] It is concluded that since compliance values determined with esophageal pressure were extremely variable, but lower and less variable during anesthesia than values with intrapleural procedures, the transpleural pressure changes are uniformly transmitted to the interior of the esophagus in anesthetized dogs.[31]

Compliance terminology has been confused by the introduction of such terms as "effective," fast, slow, dynamic, and specific compliance. Even though the definition of compliance requires that measurements be made under static conditions, measurements can be made during uninterrupted breathing. Such measurements are referred to as dynamic compliance and is defined as the ratio of tidal volume to the difference in intrapleural (intraesophageal) pressure at end inspiration and end expiration at the instants of no airflow during breathing.[31] Although actual static measurements can be made with patient cooperation and voluntary breathing patterns, canine function studies using unanesthetized animals require that dynamic compliance be measured.

Pulmonary compliance varies with the volume of the lungs at the end expiratory level, the functional residual capacity (FRC).[16,115]

To compare the compliance of disease lungs to that of normal lungs, the FRC in each case should be known.[16] This is often stated as the compliance/FRC ratio and is referred to as specific compliance.[31] If specific compliance is decreased, the tissues of the lung must be more rigid and less distensible.[16] This may occur with some types of interstitial or pleural fibrosis because collagen and fibrous tissue have different length-tension (pressure-volume) relationships than elastic fibers.[37] In diseases where pulmonary compliance is normally decreased as in pulmonary edema, atelectasis, pneumonia, and pulmonary congestion, these decreases can in part be attributed to a reduction in FRC.[115] Emphysema usually results in an increase in compliance since elastic fibers are lost or damaged and not replaced by collagen or fibrous tissue. Since less pressure is required to maintain the FRC in the lungs, compliance is increased.[115]

Until recently, it has been thought that the recoil force of the lung was due entirely to the elastic tissue elements in the walls of the alveoli. This is not the case, and it is important that the components of recoil force are understood when considering normal pulmonary function and dysfunction that occurs with disease. Recoil force includes the elastic force due to tissue elements and in addition, the surface tension forces.[42] There is a surface tension at the tissue-gas boundary which tends to collapse the alveoli, and which increases the force required to expand the lung, decreasing the compliance. The magnitude of surface tension is dependent upon the fluid that lines the alveolar membrane. A material, dipalmitoyl lecithin complexed with protein, known as pulmonary surfactant, has been extracted from saline lavages of normal dog

lungs, and is essential to the stability of the lung and thereby effective ventilation and gas exchange.[34] Abnormally low production of surfactant is the likely cause of newborn respiratory distress in some species of animals and in premature human infants. Consequently, when one finds change in the compliance/FRC ratio (specific compliance), these changes cannot immediately be attributed to alterations in the lung elastic tissue without consideration of surfactant disturbances. Although surfactant measurements can be accomplished using a Langmuir trough or Wilhelmy balance,[37] clinical procedures that quickly and efficiently evaluate surfactant levels are presently not available.

A modification of conventional compliance measurements, frequency dependence of compliance, is a relatively new pulmonary function test that has been found to be sensitive to peripheral airway pathology.[16,77,84,145] Although this procedure has been helpful in evaluating bronchitic and asthmatic conditions in man,[140,145] the rigorous voluntary ventilation pattern this procedure demands elminates its application to canine pulmonary function study.

Airway resistance (R_A), the pressure difference required for a unit flow change, is a parameter frequently measured in canine pulmonary function studies and is quite useful clinically. The pressure difference is created by the friction of flowing molecules coming in contact with the conducting airways, and therefore can only be measured during the time when air is flowing into and out of the lung; dynamic conditions. Airway resistance and tissue resistance constitute total pulmonary resistance (R_P), with airway resistance (R_A) contributing most of the total resistance.[37,77]

R_A has been shown to be dependent upon the following factors: (1) number of patent airways to the alveoli, (2) cross-sectional area of the airways, and (3) collapse of the airways.

When the number of patent airways to the alveoli decreases as in the destruction of lung tissue in tumors, tuberculosis, and atelectasis, a higher driving gradient of pressure between alveoli and mouth results, rate of flow in the remaining patent airways increases, and airway resistance is increased.

According to the Poiseuille relationship for viscous flow, airway resistance should decrease as the fourth power of the effective radius of the airways.[16] This makes the resistance to airflow at each level very sensitive to slight changes in radius. Although airways bifurcate 18 to 22 times between the trachea and the alveoli with each division resulting in branches with a smaller radius, the combined total cross-sectional area of the new airways is greater than the cross-sectional area of the parent airway.[113,140] As a result, the major portion of total airway resistance lies in the large airways.[79] A number of investigators confirm that the contribution of the smaller airways (peripheral airways) is only 10-15% of the total airway resistance at low lung volumes.[45,51,68,79,145] Therefore, widespread involvement of these peripheral airways could occur with little alteration in total R_A. Using the retrograde catheter technique of Macklem and Mead,[79] Hogg and associates[51] demonstrated little increase in total airway resistance in chronic obstructive airway disease patients but a four-fold increase in peripheral resistance.[51] Further, measurements of total airway

resistance in vagal stimulation studies in the dog gave little information about the caliber of the smaller peripheral airways.[113]

The third factor affecting R_A, collapse of the airways, is responsible for much of the peripheral resistance that goes unmeasured by the usual tests of ventilatory function. Even in healthy individuals, some bronchioles close when lung volume is reduced during expiration to 5 to 10 percent of VC. This is designated as "closing volume."[37,84]

Measurements of "closing volume" can be accomplished using procedures that deliberately create a different composition of gas in the upper and lower lobes of the lung.[84,115,135] These procedures provide a test which detects small airway abnormalities much earlier than the conventional lung function tests of airway resistance. Although clinical application of "closing volume" procedures are presently not available to veterinary medicine, the retrograde catheter technique has been successfully developed and applied to open chest living dogs and cats.[79]

Although not sensitive to early peripheral airway problems, traditional methods of measuring airway resistance are extremely helpful clinical diagnostic tools. Airway resistance is increased in asthma patients, increased in emphysema because of airway narrowing and collapse, and is increased in bronchitic conditions proportionate to the degree of obstruction.[113] Because resistance is decreased by increased lung volume,[113] it is often advantageous to ascertain the FRC at the time of resistance measurements.

The work of breathing is another mechanical parameter that can be measured during pulmonary function testing. It requires energy to pump the minute volume into and out of the lungs. During inspiration, as

muscles increase the volume of the thorax, elastic tissue is stretched and deformed and surface tension is overcome, creating a subatmospheric intrapulmonary pressure so that air flows into the lungs. To generate the necessary pressure, resistance to airflow and elastic resistance of lung and thorax must be overcome. The concept of work is useful in expressing the energy required or expended for breathing.[120]

Since pressure x volume (g/sq cm x cu cm = g x cm) has the same dimensions as work (force x distance), it is most convenient to measure work of breathing as pressure x volume.[38]

The work of breathing is calculated from records of transpulmonary pressure and volume. The principle is illustrated by the pressure-volume curve in Figure 1. Point A is the plot of pleural pressure at the end of expiration when flow is zero, and volume is the FRC. During inspiration, the intrapleural pressure follows the curve ABC and the total work done on the lung is given by the area OABCD. Of this, the trapezoid OAECD represents the work required to overcome the elastic forces, the elastic work (pressure x volume) done on the lungs. The hatched area ABCE represents the work overcoming airway and tissue resistance (viscous). The higher the airway resistance or the inspiratory flow rate, the more negative would be the intrapleural pressure excursion between A and C and the larger the area.[120,140] Area AECF is the work required to overcome airway and tissue resistance on expiration. This normally falls within the OAECD area, thus this work can be accomplished by the energy stored in the expanded elastic structures and released during a passive expiration.[140]

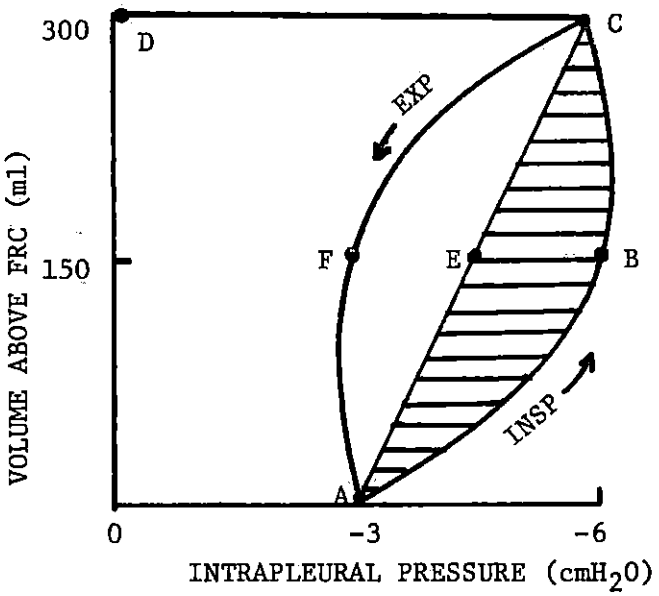


Figure 1. Pressure-volume curve of the lung illustrating respiratory work.

A crude estimate of the work of breathing can be obtained simply by calculating the product of tidal volume and maximum esophageal pressure. Ventilating 1 liter of air with a force of 1 cm of water pressure is equivalent to moving 1 ml of water 1000 cm or doing 1 g-m of work.[120] Because the work of breathing is also dependent upon the frequency of respiration, work has been expressed as g-m/min.[21] Tidal volume has been demonstrated to be weight dependent, therefore, it is appropriate to express work on a body weight basis (g-m/min/kg body weight).[21]

Studies of lung mechanics have made it possible to offer rational explanations of breathing patterns in patients with pulmonary disease.[16] The optimal frequency and depth of breathing should be that which produces the required alveolar ventilation with the minimal amount of work on the part of the respiratory muscles.[17] It is reported that for a given level

of alveolar ventilation there is a particular frequency which is least costly in terms of respiratory work.[87] In normal subjects, breathing is most economical when the balance of elastic and resistive work yields the lowest sum of these forces compatible with ventilation sufficient to meet the body's metabolic requirements.[120] This occurs in man at about 15 respirations per minute and in dog at 22 breaths per minute.[136]

In patients with very stiff lungs (decreased compliance), the best combination is small rapid breaths, minimizing the elastic factor.[17,140] Patients with obstructive disease often breathe slowly but with increased tidal volume. Asthmatic patients, where increased airway resistance is the dominant mechanical problem, select slow rates, greater minute volume, and therefore higher rates of air flow.

One final method of evaluating pulmonary mechanics, the flow-volume loop, is a relatively new test now being utilized in several laboratories in this country but has had limited use in canine function studies.[12,53,73,93]

The flow-volume loop is a graphic analysis of the flow generated during a forced expiratory volume maneuver followed by a forced inspiratory volume versus the volume expired (Figure 2). The main advantage of plotting flow versus volume is that significant decreases in higher flow or volume or both are available in a single graphic display, so as to aid in the diagnosis of the nature of a particular lesion.[115]

The shape of the F-V loop offers a qualitative diagnostic tool in that abrupt changes in flow, rather than decreased peak flows, are characteristic of air trapping. The flow-volume loop has been most useful in evaluating changes in the lower peripheral airways.[53,133]

It has been shown to be relatively insensitive to upper airway problems.[53,73]

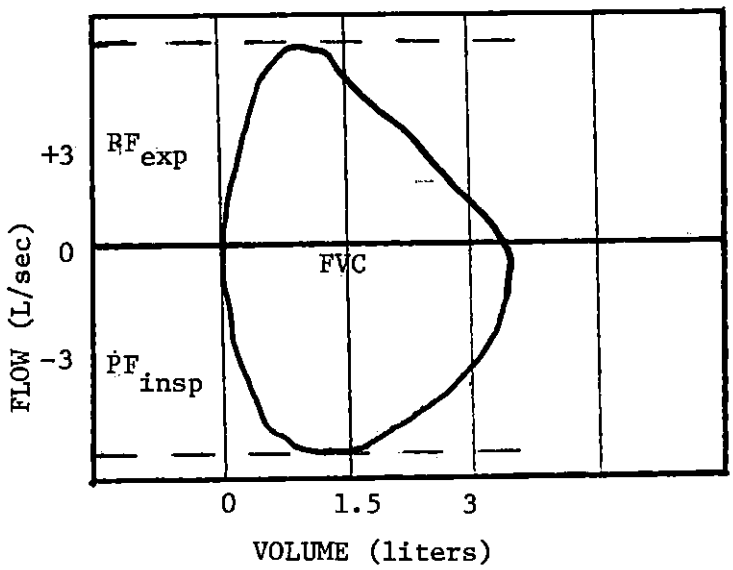


Figure 2. Flow-volume loop. Flow rate is plotted on the vertical axis and volume on the horizontal axis. FVC and peak flows for inspiration and expiration are shown.

F-V loops are also helpful in distinguishing between restrictive and obstructive pulmonary disease. Since both lung volumes and lung mechanics are measured simultaneously, the extent of obstruction or restriction or the amount of overlap between the two are indexed. Lord[73] found that flow-volume loops for restrictive and obstructive disease are distinctive, and that in obstructive disease the F-V curve correlates well with the degree of clinical and physiological disability.

In canine function studies, it is necessary to record flow-volume loops during spontaneous quiet breathing, since voluntary forced breathing maneuvers are impossible. Unfortunately, by themselves, without accompanying MVV and FVC flow-volume loops to compare, the quiet breathing flow-volume loops are of little diagnostic value.[133] However, no investigators have compared spontaneous quiet breathing flow-volume loops of normal and pulmonary diseased dogs. Until these studies are pursued, it is premature to eliminate the flow-volume loop from subsequent canine pulmonary function evaluations.

Gas distribution tests

Screening tests are now available to show whether there is normal distribution of inspired air to the airways and pulmonary alveoli, normal distribution of blood flow to the pulmonary capillaries, or normal matching of gas and blood to the pulmonary alveoli. Local mechanisms for control of airway resistance and capillary blood flow intricately balance ventilation/blood flow ratios between the apices and bases of the lungs preventing excessive changes in normal blood gases.[37] However, this delicate adjustment is easily deranged in pulmonary disease situations. Alveoli with decreased compliance, either due to alteration in surfactant or surrounding parenchymal pathology, will take a smaller volume of gas than normal. Pathology that results in increases in airway resistance can increase the time necessary for alveolar filling and at normal rates, the alveoli supplied by these resistant airways will not be completely inflated before expiration begins resulting in inadequate alveolar ventilation and possible impairment of gas exchange.

Tests that evaluate ventilation distribution include the nitrogen washout test, helium distribution, single breath oxygen test, and single-breath xenon test.[18,115] Currently, there is renewed interest in the single-breath nitrogen test because it offers promise of detecting airway obstruction at potentially reversible stages.[8] These procedures are simple, rapid, and painless. Further, because gas concentration measurements are performed on expired gas during normal breathing, consideration of these procedures in canine function studies is in order.

Pulmonary blood flow/blood gas analysis

Among the most useful and efficient tests that assess the physiopathologic status of the pulmonary system are blood flow tests such as percent shunt calculation and blood gas analysis to include blood gas partial pressure measurements and pH.

The Pa_{CO_2} is a measure of the partial pressure exerted by CO_2 in arterial blood and is expressed in mm Hg.[16] Pa_{CO_2} is an excellent index of alveolar ventilation. Rise in CO_2 tension is usually associated with hypoventilation, a fall with hyperventilation. Because CO_2 diffuses twenty times as readily across the alveolar-capillary membrane than O_2, small changes in ventilatory pattern of distribution of gas will show little change in Pa_{CO_2}.[115] Therefore, since diffusion defects rarely raise Pa_{CO_2}, high CO_2 tension strongly suggests that advanced pulmonary disease is present. When correlated to alveolar ventilation, O_2 tension, and blood pH, elevated CO_2 tension serves as a definitive indication of disturbed gas exchange. Because of the variation reported in canine blood gas tension and pH values,[35,106,107] multiple determination are necessary.

Canine Pulmonary Function Studies

In the last few years, extensive study has been directed toward gaining an understanding of the pathogenesis and pathophysiology of pulmonary disease. As our knowledge of normal respiratory physiology in animals progresses, the necessity of utilizing animal models to develop the mechanisms involved in pulmonary disease is recognized.

The dog, with his normally cooperative behavior, has become an especially popular respiratory model for studying diseases such as pulmonary edema, allergic asthma, and inhalation of toxic substances. Further, significant information has already been gained in the fields of anesthesia and aerosol therapy.

Normal parameters

Until the past decade, only a handful of investigators had described normal respiratory parameters for the various characteristics of ventilation and little was known of the physiology of respiration in the dog. Still, investigations in the awake dog are limited but respiratory function in the anesthetized dog has been extensively studied.

In 1947, Guyton initiated a study of respiratory patterns in a number of laboratory animals, but the canine species was not examined.[47] In 1961, Crosfill and Widdicombe examined different patterns of breathing in animals with emphasis on the physical characteristics of the chest and lungs and the work of breathing.[21] Dogs were anesthetized with pentobarbital, intraesophageal pressure measured and airflow monitored with gauze-screen pneumotachographs. Besides establishing normals, these investigators found that lung resistance tended to increase with

the size of the dog, but that as a species, dogs had relatively low resistance.[21] Calculations of optimal mechanical breathing rates by Mead[87] compare favorably to the observed rates in the Crosfill study. Parameters are listed in Table 2. In 1967, Hamlin and Smith, using anesthetized dogs, designed a study to provide base-line information against which data obtained from diseased animals could be compared.[50] Hamlin is the only investigator that looked at the effects of age and sex on characteristics of respiration. However, Hamlin's finding that lung compliance increased with age has since been contradicted by several investigators.[31,33,40,104] As in many of the studies conducted in anesthetized dogs, respiratory rates were greatly depressed by pentobarbital anesthesia, complicating some of the respiratory characteristics.[50]

Drorbaugh[30] determined relaxation pressure-volume curves from the lungs and thorax of dogs. Measurements of compliance, magnitude of elastic work in breathing, vital capacity and several other ventilation parameters are described.[30] This is the one of the few reports of vital capacity measurements in the dog available.

Stahl[130] collected data from the literature on respiratory variables and correlated these against body weight on the assumption of log-log relationships with the use of computer regression analysis. Statistically validated power law formulas for vital capacity, functional residual capacity, lung compliance, tidal volume, respiratory flow resistance, etc. were presented. (See Table 2)

It has been demonstrated that lung volumes are proportional to body weight whereas various measures of lung function such as rate of doing work, are proportional to the 3/4 power of the body weight.[30,47,48,130]

However, using this constant, experimental results within individual species such as cat or dog often differ by as much as 100% because of animal variations.[130]

Investigators have observed that anesthesia has profound effects on respiratory function and that many of the normal parameters in the literature cannot be applied to the awake dog.[31,33,34,40,104]

Anesthesia, especially barbiturate anesthesia commonly used in canine pulmonary function studies, has been shown to significantly decrease lung compliance,[15;31,88] increase airway resistance,[88,104] and increase functional residual capacity.[33] Alterations in pulmonary diffusing capacity[108] and increased venous admixture have been reported in anesthetized dogs.[36,132] The changes in FRC, lung compliance, and airway resistance are quite rapid with the large portion of the change being observed in the first 10 minutes after induction.[88] Compliance and FRC changes are not progressive, decreasing only slightly after 45 minutes but airway resistance continues to increase throughout the period of anesthesia.[88]

Part of the emphasis on using the anesthetized dog model is attributed to the desirability of defining the relationship between respiratory function and effective safe anesthesia.[104] However, studies presenting normal parameters in the anesthetized model have not been effective in simulating an awake animal since the respiratory system is the system most deranged by anesthesia.[127] Therefore, a number of investigators have eliminated any pulmonary impairment from the effects of anesthesia by studying respiratory function in the unanesthetized dog.

Two models have been utilized in obtaining reproducible respiratory parameters; (1) face mask and mouthpiece model,[32,104] and (2) the body plethysmograph.[40]

Pickrell and Dubin measured f, V_T, FRC, C_L, and R_A, and blood gases in unanesthetized beagle dogs.[104] Their face mask model has been extremely efficient in measurements of lung mechanics. Functional residual capacity and lung compliance measurements are reported.[31,33] Qualities of comfort and fixed low dead space permits animals to adapt quickly to the testing procedure with short time exposure. This model is particularly useful in long-term toxicity experiments where anesthesia procedures are high risk.[83]

Gillespie and Hyatt[39,40] trained mongrel dogs to adapt to a body plethysmograph and examined the effects of anesthesia and body position on certain respiratory parameters. The necessity of pre-conditioning each dog to the body chamber makes this model unsatisfactory for clinical use. As a research tool, measurements of lung gases and lung volumes are obtained that pneumotach and spirometric methods cannot measure.

Canine function studies in disease

Recent reports indicate that the measurements of lung compliance, airway resistance, and functional residual capacity are sensitive and reliable indicators of mechanical respiratory deficit under disease conditions.[31] Because of the innocuous nature of the face mask procedures[31,33,104] and the minimal cooperation required of the dog, consideration of this model for evaluating pulmonary disease is in order.

It has been demonstrated that comparison of lung-compliance measurements made in diseased animals with the values for normal dogs are helpful in defining the types of pulmonary disease.[113]

Macklem[77] suggests that compliance measurements are influenced by lung volume, respiratory frequency and time. Unless these variables are rigorously controlled, compliance measurements are difficult to interpret. It is necessary to look at more than just the slope of the pressure-volume curve since many pulmonary diseases that alter lung elasticity frequently alter the shape and position of the P-V curve, and are not detected by measurements of slope.[77] For these reasons, it is best to evaluate the lungs elastic properties by observation of the whole curve--its shape, position and slope.

Inspite of reports that question the reliability of measuring pulmonary mechanics in dogs without all variables controlled, a number of studies have indicated that lung mechanics measurements do provide evidence of diagnostic significance.[22,51,83,94,96,121]

Miyamoto et al. reports that the respiratory changes in passively sensitized dogs and sub-primates as models for allergic asthma studies.[94] Although only certain ventilatory parameters were examined, they demonstrated marked respiratory changes including increased frequency, decreased tidal volume, decreased flow rate and prolongation of expiration. This evidence supports their model as a reproducible method of studying human allergic asthma.[94]

In experimental asthma in dogs, respiratory resistance increased 262% of control, pulmonary compliance decreased 23.7% and arterial P_{O_2} decreased significantly.[43] The changes in airway structure and function

are similar to those in human asthmatic patients, offering further support that the respiratory dog model is suitable for study of human asthma.[2,43,64]

Patients and experimental animals with pulmonary edema exhibit marked changes in mechanical properties of the lungs.[19] Early research by Cook suggested that surface phenomena are responsible for the mechanical behavior of the lungs during edema rather than vascular congestion or instrinsic tissue changes.[19] The decrease in lung compliance as demonstrated in anesthetized dogs with induced edema, falls directly proportional to rising lung water in pulmonary edema. Pulmonary resistance does not rise until alveolar edema was present as indicated by the extra-vascular thermal volume indicator technique used in measurements of pulmonary edema.[96] These are among the many concepts that have been gained about the pathophysiology of pulmonary edema. Again, this demonstrates the necessity of having reliable normal parameters for which to compare the disease values.

Canine pulmonary function studies have been beneficial in examining the effects of inhalation of particles. Mauderly et al. reports that the unanesthetized face mask model is excellent for studying the pathogenesis of pulmonary disorders resulting from the inhalation of radioactive particles.[83]

The canine respiratory model has been helpful in evaluating therapeutic techniques such as aerosol therapy and pulmonary lavage. Pulmonary lavage studies in the canine have verified the lavage technique as being a useful diagnostic and treatment tool in pulmonary disease.[34]

Inhalation therapy as a method of treating respiratory diseases of animals has been largely overlooked. In human medicine, where extensive trials have been done, controversy regarding its use still exists. As aerosol studies in the dog continues,[83,104] it is predicted that practical principles of aerosol science will be developed that will benefit both veterinary and human medicine.

Manipulative studies

Extensive manipulative studies have been reported.[10,51,66,139] Much of our understanding of pulmonary physiology in animals has been gained from canine respiratory models.

The relationship between total dynamic compliance, functional residual capacity, and alveolar-arterial oxygen gradients has been described.[66] Valuable concepts about metabolic acidosis and lung mechanics,[121] ventilatory mechanics and hypovolemic shock,[10] and ventilation during hemorrhagic shock[101] have been gained by studying canine respiratory function.

Mechanical ventilation is critical in many surgical procedures. Although the foundation for artificial ventilation was established in medical practice, certain concepts such as the effects of lung inflation on pulmonary blood volume were left unexamined.[139] Pulmonary mechanics during changes in ventilation and blood volume has been examined in the dog.[2]

As more becomes known about the physiology of the respiratory system in the canine, the importance of this model in veterinary medicine for studying the pathophysiology of pulmonary disease is evident.

Table 2. Reported Values for Respiratory Parameters in the Dog

Source	Weight (Kg)	Anesthesia	Rate	Tidal volume (ml)	Minute Volume (ml/min)	Compliance (ml/cmH_2O)	Airway resistance ($cmH_2O/L/sec$)
2	10-15	pentobarb	-	-	-	51	-
10	9-16	pentobarb	-	-	-	84	-
21	12.6	pentobarb	21	144	3100	40	-
31	5-14	none	-	-	-	46	-
40	18.6	none	13	309	3878	97	1.30
50	19.1	pentobarb	13	203	2819	-	-
81	9.1	none	20	186	3720	73	10.0
81	10.9	none	19	170	3230	53	13.0
83	-	none	-	-	-	75	8.6
94	-	pentobarb	11	180	-	-	-
104	9.1	none	24	220	-	48	10.44
130	-	pentobarb	-	-	-	30-75	-
136	12.0	pentobarb	22	149	-	63	-

Effects of Preanesthetic and Anesthetic Agents on Pulmonary Function

In order for the lung to accomplish the essential function of gas exchange, four components of function; ventilation, distribution, diffusion, and perfusion, must be recognized. General anesthesia alters the efficiency of these components and in turn disturbs the effectiveness of gas exchange. Numerous factors determine the magnitude of respiratory dysfunction. Among these are the preanesthetic condition of the subject, the type and amount of preanesthetic and anesthetic agents, the method of administration, and body position.[130]

Preanesthetic and anesthetic agents are commonly used in canine pulmonary function studies since investigators must substitute controlled ventilation for voluntary cooperative breathing cycles. Since effects of these agents on pulmonary function are profound, it is important that significant alterations be recognized when interpreting function parameters.

Three agents, acetylpromazine maleate, methohexital sodium, and atropine sulfate were administered in this investigation and their effects and mechanisms reviewed. Because the results of this study are compared to those obtained under various types and levels of general anesthesia, it is necessary to review its effect on lung function.

Most investigators agree that general anesthesia interfers with pulmonary gas exchange.[109,117,124,132] This may result from increased venous admixture, or changes in cardiac output, changes in O_2 carrying characteristics of hemoglobin, dead space, or other factors. How much

of this impairment of pulmonary gas exchange can be attributed to alterations in pulmonary mechanics and the effects of these alterations on intrapulmonary gas distribution is still unanswered.

Arterial P_{O_2} can be reduced by an increased venous admixture, or physiological shunt, which commonly occurs during general anesthesia.[109,124,132] Venous admixture results from anatomic shunts and from "shunt-like" effects, i.e. perfusion of poorly ventilated or nonventilated alveoli and perfusion of alveoli in which diffusion is impaired resulting in low $\dot{V}/\dot{Q}$ ratios.[124]

Anatomic shunting through right to left vascular connections (bronchial and thebesian veins) occurs in the heart and lungs and constitutes a shunt of approximately two percent of total cardiac output in normal conscious man.[109] This shunt varies from 1-10% in dogs.[36] This blood passes through unventilated areas of the lung which represents a $\dot{V}/\dot{Q}$ of zero. Anatomic pathways less frequently considered for shunting through the lungs have been proposed.[109] He describes "sperrarterien" blocking arteries that could increase right to left shunt to 20%. Blood flow through these vessels in man seems to be small, and at present nothing is known concerning their function during anesthesia or if such structure exist in other species.[109]

One of the popular explanations of the increase in venous admixture during anesthesia is the contribution of mismatching of ventilation to perfusion. Campbell and co-workers[11] in 1958 suggested that ventilation/perfusion ($\dot{V}/\dot{Q}$) mismatching was a probable cause for the increased venous admixture and widened (Alveolar-arterial) P_{O_2} pressure difference [$(A-a)P_{O_2}$] during general anesthesia.[11] But despite much work in this

area since Campbell, controversy continues regarding the contribution of $\dot{V}/\dot{Q}$ mismatching to impaired oxygenation during general anesthesia.

Finley and co-workers, on the basis of indirect evidence obtained in dogs during pentobarbital anesthesia, suggested that spontaneous collapse of lung area caused the major part of the observed $(A-a)P_{O_2}$ during spontaneous breathing.[36] The theory of atelectasis is supported by Mead and Collier.[88] They found that the appearance of the lungs of the dogs on post mortem suggested that atelectatic lung areas were present. The concept of airway closure has rekindled the interest in the mechanism for increased shunting and increased $\dot{V}/\dot{Q}$. Airway closure is believed to affect pulmonary gas exchange either by creating poorly ventilated regions, as occurs within the tidal breathing range, or by leading to cessation of ventilation if opening volume exceeds end-inspiratory lung volume.[20,71] If the distribution of pulmonary blood flow is not adjusted to this altered gas distribution, areas with low or zero $\dot{V}/\dot{Q}$ would develop leading to overall impaired oxygenation. Although airway closure may seem an attractive explanation for impaired oxygenation during anesthesia, evidence for its occurrence in anesthesia is incomplete and valid experimental proof for its contribution to hypoxemia is lacking.[109]

Other explanations for impaired oxygenation during anesthesia include diffusion disturbances. Piiper and associates[108] found that unequal distribution of diffusion capacity of the lung (D) to perfusion ($\dot{Q}$) was the main factor increasing $(A-a)P_{O_2}$, resulting in increased venous admixture.[108] The definitive mechanism involved in this unequal

distribution of diffusing capacity to perfusion is unknown since position, exercise, and lung volume all alter $D/\dot{Q}$.[46]

Evidence is accumulating that CO and O_2 transfer may be partially carrier-mediated in the human lung.[132] If such facilitated diffusion occurs, and effect of anesthetic on CO and O_2 transfer might be anticipated offering possible explanations for poor oxygenation during anesthesia.

It has been proposed that reductions in cardiac output without major changes in either shunt fraction or $\dot{V}/\dot{Q}$ matching are responsible for increases in $(A-a)P_{O_2}$ during anesthesia.[62] The possible contribution of reduced cardiac output as a cause for impaired oxygenation has not been confirmed.

Although no influence on blood gas transport is accorded specific to anesthetic agents, several phenomena have been associated with the state of anesthesia. A reduction of as much as 30% in PCV red cell and Hb in various species during constant and variable anesthetic depth has been reported.[130] The possibility that anesthetics cause a left shift of O_2 dissociation curve leading to an increase $(A-a)P_{O_2}$ has been examined, but evidence strongly suggests no shift in the curve during anesthesia.[109]

Increases in dead space brought about by general anesthesia has been thought to contribute to impaired oxygenation. The alveolar dead space has been found to be increased from 15 to 231 ml in anesthetized man.[99] Further, atropine, a common agent used in preparation for anesthesia, increases dead space by as much as 50% during spontaneous breathing.[118] However, the possible effect increased dead space has on impaired oxygenation is clouded because alveolar dead space can

increase as a result of an increase in anatomic shunt or an altered ventilation-perfusion relationship or both.[109]

One can only conclude that gas exchange is impaired during general anesthesia. Increased venous admixture, increased alveolar dead space, altered ventilation-perfusion relationships and atelectasis are all possible contributing factors to this impairment.

It has been demonstrated that general anesthetics result in an altered intrapulmonary gas distribution. Although this altered gas distribution may be partly explained by the alterations in FRC, and is greatly influenced by position, changes in the mechanics of the respiratory system seems to be involved.[109]

Reports regarding the effects of anesthesia on respiratory mechanics in man are conflicting. Some investigators have reported no change in lung or chest wall compliance,[97] while the majority have shown a decrease in one or the other of these parameters.[15,19,31,36,88,109,124,141] Disagreement as to whether functional residual capacity is decreased or remains unchanged exists.[141] Evidence indicates low or reduced functional residual capacity and lowered compliance occurs during general anesthesia.

Canine function studies are uniform in that lung compliance and FRC are decreased and airway resistance is increased during anesthesia.[31,33,39,117] Mechanisms involved in the changes of these mechanics are not understood. Possibilities for the reduction in FRC include an increase in central blood volume, a change in chest-wall mechanical properties, gas trapping and increased elastic recoil of the lung as may occur with atelectasis.[109] FRC values are also significantly affected by position of the subject. It is reported that both the prone

and supine positions for anesthetized dogs that are used by investigators may cause a forward displacement of the diaphragm by the abdominal viscera or deformation by gravity of the thoracic wall, resulting in reduced FRC as compared to the standing position.[33] The FRC is apparently not reduced in sitting, anesthetized man, but this is unconfirmed.[109]

Airway closure may reduce lung compliance by decreasing the number of distensible units assessible to ventilation. Evidence does indicate that increased airway closure leading to gas trapping does occur during anesthesia.[109] Reduced lung compliance during anesthesia has frequently been attributed to atelectasis.[88,109] Mead and Collier found that lung compliance in anesthetized dogs decreased rapidly shortly after induction but was not progressive.[88]

A number of investigators have reported a disproportionately larger reduction in lung compliance than in lung volume in anesthetized dogs. This suggests that another mechanism, such as a change in surface tension in lung units may have contributed to a reduced lung compliance.[15,88] Depressed surfactant action has been found when lipid-soluble anesthetics such as halothane and chloroform are used.[131] Whether this is a combination of direct effect upon surfactant or if in fact there is another mechanism that is engaged during general anesthesia to cause a depressed surfactant action is not known.

The possibility that lung mechanical properties changes are secondary to those in the chest wall has been reported, but the few investigators that have separated compliance into components cannot agree on this.[109]

Methohexital sodium (Brevane) is an ultrashort-acting barbiturate. Barbiturates are a widely used and very versatile group of agents,

classified as hypnotic-sedatives and general anesthetics according to their use. The principal effect of a barbiturate is depression of the central nervous system by interference with passage of impulses to the cerebral cortex. In hypnotic doses, the barbiturates have little effect upon respiration while in anesthetic doses, respiration is depressed.[74]

As depressants, barbiturates affect both the respiratory drive and the mechanism responsible for the rhythmic characteristics of respiratory movements.[119]

In the waking state, normal ventilation is largely controlled by neurogenic drive, and responds to a wide variety of sensory or alerting stimuli.[16] This drive is most sensitive to depression by hypnotics, is reduced by drug-induced sleep, and control of respiration is then dominated by the direct action of CO_2 and hydrogen ions on medullary chemical centers.[119] The effects of a hypnotic dose of a barbiturate closely resemble those of natural sleep, with a decrease in alveolar ventilation, an increase in alveolar CO_2 tension (3 to 5 mm Hg), and a slight decrease in the O_2 saturation of arterial blood.[119]

As a dose of barbiturate is increased, the hypoxic and chemical drives to respiration are diminished roughly in proportion to dose. At levels of deep anesthesia, a shift in control of respiration from CO_2 sensitive areas of the medullary centers to more primitive peripheral chemoreceptors of the carotid and aortic bodies takes place and sensitivity to increases in CO_2 decreases markedly.[16,119]

As with inhalation agents, it is difficult to define the specific depth of anesthesia in an individual at a given moment in the time

course of barbiturate anesthesia. The effect of barbiturates on the CNS is progressive in nature.[123]

A somewhat arbitrary division of the signs and stages of anesthesia has been developed.[11,74] These are described as: stage I, analgesia; stage II, delirium; stage III, surgical anesthesia divided into four planes; and stage IV, respiratory paralysis.[74] It is quite difficult to routinely produce a consistent level of barbiturate anesthesia. As a result, many of the canine pulmonary function studies using the anesthetized model experience respiratory depression. Table 3 illustrates some physiological values in dogs in stage III, plane three of barbiturate anesthesia.[126] Although the depression demonstrated is extreme, it is not uncommon for function parameters obtained from anesthetized models to show ventilatory depression with reduced frequency, tidal volume, and marked respiratory acidosis.[21,50,94]

Table 3. Dogs in deep surgical anesthesia with sodium pentobarbital.

Sign	Value
Respiratory rate (breaths/min)	5.3 ± 0.37
Exhaled minute volume (ml/kg/min)	98.4 ± 9.15
Arterial pH	7.25 ± 0.019
Arterial carbon dioxide tension (Torr)	53.0 ± 2.13
Arterial oxygen tension (Torr)	71.1 ± 5.29
Standard bicarbonate (mEq/liter)	20.2 ± 0.45
Heart rate (beats/min)	141.5 ± 1.99
Systolic pressure (Torr)	150 ± 3.61
Oxygen consumption (ml/kg/min)	6.8

*Mean dose of the drug administered with no preanesthetic medication. Data are the mean values for 14 dogs ± 1 S.E. of the mean.

Methohexital sodium (Brevane) has a short duration and there is a quick recovery, but may be accompanied by muscular tremors and violent excitement which detract for the usefulness of the drug.[74] Dogs are usually ambulatory 30 minutes after administration.

However, by combining Brevane with acetylpromazine maleate (Acepromazine), a smaller dosage is required and the recovery is still quick but quite smooth with no tremors and little or no excitement.

Acetylpromazine (Acepromazine) is a potent neuroleptic agent with low toxicity. It is a member of the group of phenothiazine derivatives that have been used extensively for sedation and preanesthetic medication in a variety of animals. As a group, phenothiazine derivatives are notorious for their hypotensive action and in many species, their inconsistent effect.[128] Phenothiazines produce variable changes on cardiovascular parameters. A close relative of Acepromazine, promazine produces minimal hypotension and tachycardia, with a rise back toward control levels within 20 minutes.[128] Some derivatives show a decrease in respiratory rate, and increased tidal volume but specific information for Acepromazine is not available.

Like other tranquilizers, phenothiazine derivatives potentiate the respiratory, cardiovascular and anesthetic effects of all barbiturates. When used in combination with short acting barbiturates, the return time of the righting reflex is reduced by 60%. The opposite effect occurs when used with ultra-short acting barbiturates like Brevane where hypnotic effects can be more than doubled.[127]

Atropine sulfate is an anticholinergic (parasympatholytic) drug which is most frequently used to reduce secretions from the respiratory

tract and salivary glands and to inhibit the effects of vagal stimulation on the cardiovascular and respiratory systems.[74,128]

In the dog, it produces a decrease in heart rate at lower doses (0.006 mg/kg) and a progressive increase as the dose increased.[128] The initial cardiac slowing may be due to central parasympathomimetic activity on the vagal nucleus.[55] With the larger, more commonly used doses, atropine produces an increase in heart rate by blocking the effects of the vagus on the sinoatrial node.[55]

Atropine will effectively block bradycardia and helps prevent laryngospasm upon tracheal intubation.[74,128] Contrary to former belief, atropine does not block laryngeal skeletal muscle responsible for laryngospasm, but does depress respiratory tract secretions that can precipitate spasm.[55] This effect is especially appreciated when barbiturates are used since during induction there is increased likelihood of laryngospasm, bronchospasm, and other undesirable respiratory effects due to increase in the sensitivity of the larynx and trachea to vagal stimulation.[128]

Besides atropine's inhibitory action on glandular secretions of respiratory tract, oral and nasal cavities, it causes relaxation of bronchial and tracheal smooth muscle, resulting in bronchodilation. In man and dog atropine causes an increase in both anatomical and physiological dead space.[118] However, recent studies in the dog indicate that this increase in dead space has little clinical significance with no significant alteration in blood gases.[124]

Influence of Age, Sex, and Weight on Pulmonary Function

Age

Lung volume changes in aging humans have been extensively investigated. There is an increase in residual volume and in functional residual capacity with little change in total lung capacity.[17,37,49,115] Changes in lung mechanics with age have also been reported. The elastic properties of the human lung indicate a shift of the lung pressure-volume curve progressively to the left, indicating an increase in lung compliance.[16,37] Airway resistance has been found to increase with age in man.[16]

In contrast to the large number of reports on man, there are few reports on lung volumes and the mechanical properties of the lungs of dogs in relation to age changes. Prior to anyone investigating age effects in the dog, static compliance and airway resistance changes with age were examined in the rabbit.[24]

The first report that took age into consideration when measuring pulmonary function was Hamlin and Smith.[50] However, these investigators found only one significant effect of age on respiratory function; compliance increases with age. Although this agrees with compliance changes in man and in rabbit, this has since been contradicted in dog.[81,111,112]

Mauderly observed a significant decrease in compliance with increase in age.[81] Robinson and Gillespie found decreased lung compliance in older dogs but were unable to show a significant decrease in chest wall compliance.[111]

With increasing age, an increase in the ratios residual volume/total lung capacity (RV/TLC) and functional residual capacity/total lung capacity (FRC/TLC) have been reported.[111,112] The increased FRC/TLC appeared due to both a loss of lung elastic recoil in dogs over 1500 days of age and an increase in the resting volume of the thoracic cage. The RV/TLC in young dogs was determined by the mechanical limitations of the thoracic cage while in old dogs it was determined by factors within the lungs.[111] By examining lung volume ratios, the effect of varying body weights on lung volumes was eliminated.[112] The changes in volume ratios in older dogs are similar to those seen in aging people, but in the dog they cannot be explained by increase lung compliance.[112]

It is reported that young dogs have higher ventilation, larger resting lung volume, and consume more O_2 per kilogram than do older dogs.[81] This is probably reflected in the higher metabolic rate known to exist in young growing animals than in adults.[81,128]

A slightly lower diffusing capacity was observed in older dogs.[81] This is similar to the age-related change in diffusing capacity reported in man.[16]

One report indicates that blood gas partial pressures change with age. Although none of the changes are significant from age group to group, young dogs had lower arterial pH and increased arterial CO_2 tension with no change in O_2 tension among the groups.[81]

With such few reports available, many of the changes in lung function with age are unexplained at this time. Of the studies done, there was no concern of possible age and weight interactions, rate of breathing, and inspiratory and expiratory rate of flow.[47]

Weight

Stahl utilized power law formulas based on weight to predict various respiratory parameters in different sizes and species of mammals.[130] Predictions based on equations in animals have been found to lack accuracy and errors as great as 100% may occur since animals differ in other respects than merely size.[30] Surprisingly, prediction formulas are less accurate predicting respiratory function parameters within species than they are across species.[30]

In the dog, lung volumes increase with the weight of the animal.[40,50,104] Lung compliance is reported to increase with the weight of the dog.[31,42,104] Several investigators have reported a highly significant correlation between body weight and lung compliance.[42,81]

In man, useful formulas have been developed that allow expected respiratory parameters to be calculated on the basis of height and age of the patient, and a constant.[16,115]

Unfortunately, no reports of size and age interaction effects on pulmonary function in the canine are available.

Sex

Differences in respiratory function in human males and females have been demonstrated.[16,17,37,49,115]

Hamlin and Smith report a significant difference in minute volume and tidal volume/kg body weight between male and female dogs.[50] No explanation for this difference is given, but it is noted that the female dogs are of similar weight as the males but are significantly younger.[50] This demonstrates the necessity of examining the influence of age, sex, weight, and possible interactions on respiratory function.

METHODS AND MATERIALS

Pulmonary function studies were performed on thirty mongrel dogs randomly selected from an animal colony. The animals were grouped according to age and sex.

Two sex classes were considered; intact females and males. Although accurate histories were not available for all dogs in the colony, each was closely examined and palpated for evidence of prior surgery. Any animals suspected of not being intact were omitted from the study.

The two sex classes were further divided into three age groups. Group 1 were young dogs, less than a year of age. The second group were young adult dogs, one to five years of age, and the third group were aged animals, at least eight years old. The groups were divided according to the presence of deciduous and permanent teeth, cusp wear, occlusal surfaces, and colony records.

The animals ranged in weight from 8.2 to 21.4 kg. Some randomness was sacrificed to assure that each class contained animals of variable weights.

Experimental Protocol

Acetylpromazine maleate (Acepromazine, Ayerst Laboratory, 0.05 mg/lb) was administered subcutaneously forty-five minutes prior to initiating function testing. The tranquilized animals were then given an intravenous injection of atropine sulfate (Atropine, Burns-Biotee Laboratory, 0.05 mg/lb), and then sedated with methohexital sodium (Brevane, Elanco Products Co., 1.25 mg/lb) intravenously.

The animals were quickly placed into the supine position and the laryngeal area sprayed with a topical anesthetic (Cetacaine, Cetylite Industries, Inc.). The animals were then intubated with an appropriate endotracheal tube (9 mm - 11 mm) and recording initiated.

Inspiratory and expiratory velocity was measured with a Fleisch #0 pneumotachograph having a linear response to 27 L/minute. A Statham PM5 differential pressure transducer was connected to the pneumotachograph and recordings were made on a four channel Beckman Type R dynograph recorder. Tidal volume was determined simultaneously by electronic integration of the flow signal. Compliance, resistance, and flow-volume loops were simultaneously produced by a Hewlett Packard 7035B X-Y recorder.

Intraesophageal pressure, an estimate of intrapleural pressure changes, was measured by a catheter latex balloon system. The balloon, 4.0 cm long and 1 cm in diameter, containing approximately 3 ml of water, was sealed over the end of a polyethylene catheter. The catheter was connected to a Statham P23Db pressure transducer and pressure changes recorded on the Dynograph. Attempts were made to place the balloon catheter in the same relative area of each dog, the lower middle third of the esophagus. If too much cardiac interference appeared on the recording, attempts were made to minimize this by adjustment in balloon position.

Values for tidal volume (channel 4), respiratory rate, inspiratory and expiratory velocities (channel 3), and esophageal pressure (channel 2), were obtained directly from the recording. Heart rate was measured directly from channel 1 EKG recording, lead II. These are demonstrated in Figure 3.

Lung compliance was determined as the ratio of tidal volume to the difference in intrapleural (intraesophageal) pressure at end inspiration and end expiration at the instants of no airflow during breathing. Lung compliance was also determined by measuring directly from the pressure-volume loop plotted by the X-Y recorder. Airway resistance was calculated dividing maximum expiratory velocity by the esophageal pressure difference between points of end inspiration and end expiration. This method compared favorably to resistances obtained directly from the X-Y resistance loop. (See Figure 4)

Arterial blood samples were obtained by femoral arterial puncture. The femoral triangle was shaved and swabbed with 70% alcohol, the femoral artery palpated, and a 20 gauge one inch needle attached to a 5 cc plastic syringe inserted into the artery. Confirmation of arterial source was made by the entrance of bright crimson blood into the syringe with little or no traction applied. The dead space in the syringe was completely filled with a heparin solution (1000 units/ml). After three to five milliliters of blood was obtained, the syringe was sealed with a rubber cap, any air bubbles excluded, and placed in an ice bath prior to analysis. Pressure was applied to the groin area after puncture in order to minimize subcutaneous extravasation.

Blood gas analysis was performed on a IL513 analyzer. P_{O_2}, P_{CO_2}, and pH measurements were automatically printed out on a IL315 ticket printer. HCO_3^-, BE, and CO_2ct. were compiled by analyzing existing information and were included on the printout.

Two other blood parameters, PCV and hemoglobin concentration were determined, using micro hematocrit centrifugation and cyanomethemoglobin methods.

Recording Periods

Recordings were obtained from three different test periods. Although recording was initiated shortly after administration of Brevane, these recordings were not statistically evaluated.

The initial recording (period 1) occurred when respiratory rate appeared to reach and stabilize at normal levels (18-24 breaths/minute). This occurred routinely three to four minutes after Brevane administration.

The second group of recordings (period 2) were made less than two minutes after period one. At this time, compliance, resistance, and flow-volume loops were made. During period two, femoral artery blood samples were obtained. The dog at this time was able to maintain sternal recumbency, eyes were open, but exhibited no movement.

The third group of recordings (period 3) began shortly after the blood sample was taken and proceeded until the dog began to resist the endotracheal tube or esophageal balloon or made attempts to move from the table.

Comparison of the data obtained from these three periods provides valuable information as to determining the extent of respiratory depression present in this model.

Other Procedures

Ten dogs were selected from the colony on the basis of their temperment and response to handling. The dogs were restrained in lateral recumbency, the groin area swabbed with alcohol, the course of the

femoral artery palpated, and femoral puncture performed. Respiratory rate during the sampling period was recorded. Care was taken to handle the blood samples obtained from these unanesthetized dogs in the same way that earlier samples were handled and blood gas analyses was performed. An initial attempt of infiltrating the femoral triangle area with Lidocaine prior to puncture seemed to irritate the animals more than the arterial puncture itself. The blood gas values are compared in the subsequent section.

Statistical Analysis

The thirty animals were divided into groups according to age and sex; three age classes and two sex groups. Age, sex, and weight were considered as main effects (independent variables) and each respiratory parameter was a dependent variable.

The initial analysis of the data was based on the statistical assumption that every value of each dependent variable could be determined from contributions due to (1) a population mean of the variable under consideration, (2) an effect of animal age classification, (3) an effect of the sex of the animal, (4) an effect of age by sex interaction, (5) a quantitative change in the dependent variable as a function of animal weight, i.e. a regression of the dependent variable on body weight, and (6) inherent experimental variability (error).

In statistical notation, the model was in the form:

$$Y_{ijk} = \mu + A_i + S_j + AS_{ij} + b(x-\bar{x}) + E_{ijk}.$$

Y_{ijk} represents the value of the dependent variable for a dog of i'th age, j'th sex and $x-\bar{x}$ weight. μ represents the true mean of the dependent variable population among dogs of all ages, sex, and weights.

The regression coefficient (b), represents the change observed in the dependent variable with each unit of change in body weight. Error, or E, represents a measure of experimental error.

Accordingly, a series of analyses of variance were computed for each dependent variable to partition the total sums of squares of deviations from the means and determine the variance contributions due to each main effect (age, sex, age by sex, and the regression of the dependent variable on weight). These analyses permitted use of the F test to determine whether the various independent variables significantly influenced the values of the dependent variables, or were merely reflections of experimental error.

The results of this initial analysis permitted independent variables that failed to have significant effects on dependent variables to be removed, increasing the power of the tests of significance for the remaining main effects.

Simple statistics (means, range, standard deviation) were performed on each of the respiratory parameters (dependent variables) and on individual groups. Tests of least significant difference (lsd) was applied to treatment means where specific treatment comparisons were planned.

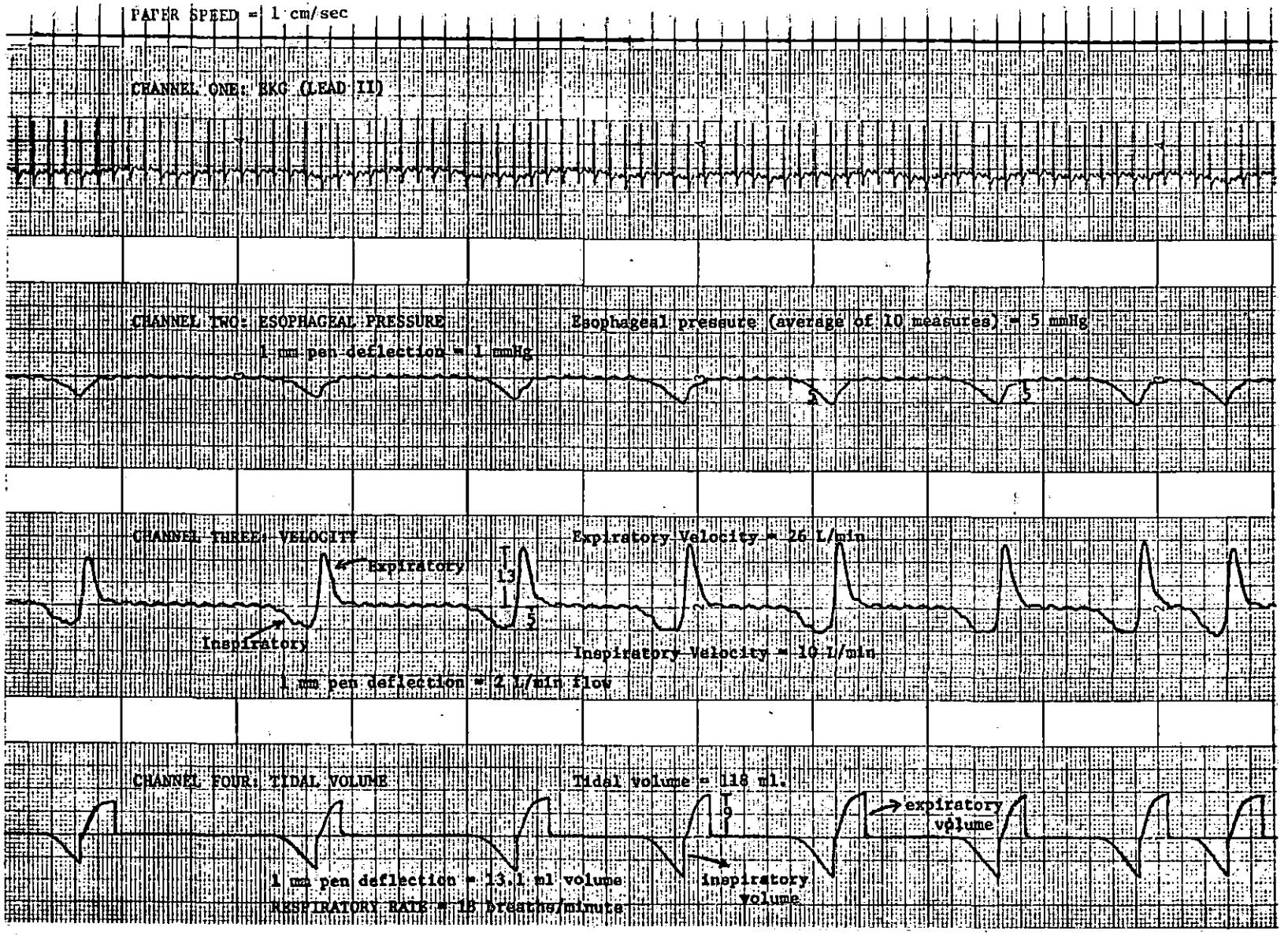
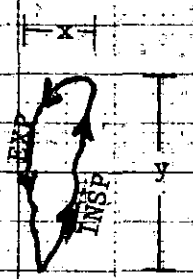


Figure 3. Recorder Output

PRESSURE-VOLUME LOOP



x axis (pressure); 1mm=0.67 mmHg

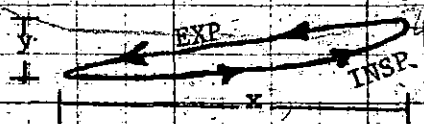
y axis (volume); 1mm= 10 ml V_T

Dynamic Lung compliance = 19.5 mm or 195 ml tidal volume/ (6.5 mm x 0.67 mmHg/mm x 1.36 cmH_2O/mmHg) = 195 ml V_T/5.92 cmH_2O = 32.94 ml/cmH_2O

PRESSURE-FLOW LOOP

y axis (pressure); 1 mm = 0.67 mmHg

x axis (flow); 1 mm = 0.9 L/min



Airway Resistance = (6 mm x 0.67 mm/mmHg x 1.36 cmH_2O)/ 5 mm x 0.9 L/min/60 sec/min) = 10.50 cm H_2O/L/sec.

FLOW-VOLUME LOOP

y axis (flow); 1 mm=1.1 L/min

x axis (volume); 1mm= 10 ml.

y' = inspiratory velocity

y" = expiratory velocity

x = tidal volume

Tidal volume = 18mm or 180 ml.

Expiratory velocity = 23.1 L/min

Inspiratory velocity = 15.7 L/min

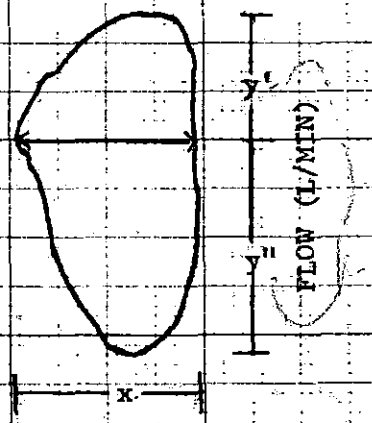


Figure 4. X-Y Respiratory Loop Studies

RESULTS

The first part of this section is devoted to simple statistics. The means, ranges, and standard deviations of each of the respiratory parameters based on all thirty animals regardless of age, sex and weight for each specific measurement period are shown in Table 4. Tables 5-7 are comparisons of means according to sex group and age class. These means were tested for significance using Fisher's Protected Least Significant Difference (LSD), this being applied only if the F-test demonstrates significance.[124]

A matrix of significant correlations of coefficients is shown in Table 8. The level of significance ($p<0.05$, $p<0.01$, $p<0.001$) is indicated.

Table 9 is a comparison of means of selected respiratory parameters for each of the measurement periods.

The next part of this section contains ANOVA procedures and graphical illustrations of the effects of age, sex and weight on each of the respiratory parameters. The model used for the ANOVA procedure was previously discussed. The initial analysis of variance indicated that with none of the dependent variables (respiratory parameters) did the contributions due to either sex or the age by sex interaction approach significance. On this basis the data was reanalyzed with the effects of sex and age by sex interaction pooled into the experimental error, thus increasing the power of the test of significance for the remaining independent variables; the effects of age and the regressions of the dependent variable values on weight.

The initial analysis, including age, sex, age by sex interaction, and regression with weight for each dependent variable is shown in the A tables. The B tables are those with insignificant main effects removed.

Graphical illustrations of each respiratory parameter versus body weight are presented. The first graph of each section represents the linear regression (best line) fit for all observations, while the second graph demonstrates the three linear regression (best line) fits for each of the age groups. The means for each parameter in the three measurement periods were tested for significant differences. Only the means for MV_1 and MV_3 were found to be significantly different ($p \leq 0.05$). As a result, all the other period means for each parameter could be grouped together increasing the number of observations (n) upon which simple linear regression analyses were performed.

Graphical analysis provided the further suggestion that the regression coefficient values for the regressions of the dependent variables on body weight were influenced by the age group considered, evidence of interactions which were not tested for significance by the analysis of variance procedures. On this basis, simple linear regression analyses were performed on the data from each age group of animals and for each of the dependent variables. The analyses provided the linear regression equations of the form; $\hat{Y} = a + bx$. $\hat{Y}$ represents the estimate of the dependent variable, a is the intercept of Y at x (Wt) equal to zero, and b is the rate of change (slope) in the dependent variable per unit change of weight.

The linear regression analyses provided estimates of mean and

regression coefficient variances so that confidence bands could be drawn around the plots of the linear regression (best line) fits.

Other investigators[30,129] have suggested that the allometric (log-log) relationship is the most appropriate for expressing relationship of respiratory variables to body weight. However, when attempts were made to express the data of the present study in log-log, less significant correlation coefficients were obtained. Graphically, log-log plots were found to be less efficient. As a result, allometric relationships are not utilized in this paper.

A parameter key with explanations of subscripts, abbreviations and units of measure utilized in the various figures and tables is shown below.

PARAMETER	ABBREVIATION	UNIT
Weight	WT or Kg	(Kg)
Heart rate	HT RT	(beats/min)
Respiratory rate$_1$*	F_1	(breaths/min)
Tidal volume$_1$	V_{T1}	(ml)
Minute volume$_1$	MV_1	(ml/min)
Expiratory velocity$_1$	$\dot{V}_{E1}$	(L/min)
Inspiratory velocity$_1$	$\dot{V}_{I1}$	(L/min)
Esophageal pressure$_1$	P_{E1}	(cm H_2O)
Lung compliance$_1$	C_{L1}	(ml/cm H_2O)
Airway resistance$_1$	R_{A1}	(cm H_2O/L/sec)
Work/Kg$_1$	WK/Kg_1	(g.-m/Kg)
Work/minute/Kg$_1$	$WK/min/Kg_1$	(g.-m/min/Kg)
Respiratory rate$_2$	F_2	(breaths/min)
Tidal volume$_2$	V_{T2}	(ml)
Minute volume$_2$	MV_2	(ml/min)
P_{O2}	P_{O2}	(mmHg)
P_{CO2}	P_{CO2}	(mmHg)
pH	pH	(pH)
Hemoglobin	Hb	(g./100 ml)
Hematocrit	PCV	(percent)
Respiratory rate$_3$	F_3	(breaths/min)
Tidal volume$_3$	V_{T3}	(ml)
Minute volume$_3$	MV_3	(ml/min)
Esophageal pressure$_3$	P_{E3}	(mmHg)
Expiratory velocity$_3$	$\dot{V}_{E3}$	(L/min)
Lung compliance$_3$	C_{L3}	(ml/cm H_2O)
Airway resistance$_3$	R_{A3}	(cm H_2O/L/sec)
Work/Kg$_3$	WK/Kg_3	(g.-m/Kg)
Work/minute/Kg$_3$	$WK/min/Kg_3$	(g.-m/min/Kg)

*The subscripts identify the specific time periods during which each parameter was measured. Those marked with a 1 as in F_1 indicate a period 1 measurement, F_2 is a period 2 measurement and F_3 was measured during period 3.

Simple Statistics

Mean values for the various respiratory parameters, along with their ranges and standard deviations, are presented in Table 4. The subscripts on certain parameters represents the time period in which the measurement was taken. Most of the values recorded or calculated need no explanation. An estimate of respiratory work was obtained by two separate calculations. Pressure x volume have the same dimensions as work (force x distance), therefore respiratory work was calculated by multiplying tidal volume by the maximum esophageal pressure change. Since tidal volume has been demonstrated to be a weight dependent respiratory parameter, it is necessary to place work on a body weight basis. The first calculation, Work/Kg, is an estimate of the respiratory work/breath/Kg of body weight. Because respiratory rates are not constant in all dogs, it is necessary to multiply the result of the first calculation by respiratory rate to obtain an estimate of the respiratory work/minute for each dog. Although this is not as exacting as pressure-volume loop integration techniques, it does allow the effects of age, sex and weight on respiratory work to be evaluated.

Table 5 is a comparison of age group means. Superscripts represent means that are significantly different as tested by the Fisher's Protected Least Significant Difference. These levels of significance are at the $p<0.05$ level. Old dogs have significantly lower tidal volumes and minute volumes than young or adult dogs. Part of this difference can be attributed to the lower weights of the aged dogs. Dynamic lung compliance and airway resistance means were also found to be significantly

different between age groups. Compliance is significantly lower in the aged dogs compared to the other two groups and airway resistance is significantly greater. These significant differences in age groups means are in evidence through the three testing periods. Airway resistance, the ratio of change in esophageal pressure to expiratory velocity, is greater in aged dogs primarily because esophageal pressures in the aged animals are significantly larger than the other two groups.

The sex group means are shown in Table 6. Only one significant difference was demonstrated between male and female dogs; P_{CO_2} was significantly lower in females than in males. This difference is unexplained. Comparisons of means indicate that respiratory function is not significantly influenced by sex in the canine. This fact is further demonstrated in ANOVA procedures.

Table 7 demonstrates the extent of variability within the age but sex groups. Because of the small number of observations involved, no significant differences are indicated within the three age by sex groups.

Table 8 is a matrix of statistically significant coefficients of correlation. Most of these correlations need not be explained but several are less obvious. Weight is correlated to tidal volume, minute volume, inspiratory velocity and expiratory velocity at the $p<0.001$ level. Weight and compliance are correlated at the $p<0.025$ level. This correlation coefficient is much lower than reported by other investigators.[40,81,104]

All ventilation parameters (volumes and velocities) were highly correlated with each other and were also significantly correlated with

compliance. Compliance is negatively correlated with airway resistance and this relationship is explained by age effects in a subsequent section. The expected negative correlation in blood gas tensions is demonstrated and they also correlate in the appropriate directions with minute volume.

Additional correlations not displayed in this table are shown in the graph section for each parameter.

Table 9 is a comparison of means from the three sample periods. Period 1 measurements were taken within two to four minutes of induction. Period 2 measurements were recorded to coincide with blood sampling and occured within several minutes of the first period. The final recording period was initiated shortly after the femoral blood sample was taken and recording continued until the dog actively resisted the measurement procedures. Although mean values for MV_1 and MV_3 were the only significantly different means for the three periods, some interesting trends are demonstrated. Frequency, tidal volume, minute volume, work/min/Kg body weight and lung compliance consistently increase across the three periods (periods 1-3), however, only minute volume means were significantly different ($p<0.05$). Conversely, esophageal pressure and airway resistance consistently decrease during the same time periods. The physiological implications of these trends are discussed in the subsequent section.

Table 4. Simple Statistics

PARAMETER	RANGE (DISTRIBUTION LIMITS)	MEAN	STANDARD DEVIATION
Weight (kg)	13.18 (8.18 - 21.36)	13.9363	3.8490
Heart rate$_1$	88 (116 - 204)	158.7333	23.0530
Respiratory rate$_1$(breaths/min)	26 (14 - 40)	22.3333	5.6283
Tidal volume$_1$(ml)	170 (100 - 270)	163.9000	38.0538
Minute volume$_1$(ml/min)	4440 (2040 - 6480)	3623.6666	1122.8390
Expiratory velocity$_1$(L/min)	12.50 (15 - 2.75)	20.2133	2.8375
Inspiratory velocity$_1$(L/min)	16.50 (7.50 - 24)	12.3633	3.5888
Esophageal pressure$_1$(cm H_2O)	3.88 (3.40 - 7.28)	4.9300	1.1600
Lung compliance$_1$(ml/cm H_2O)	30.72 (18.77 - 49.49)	34.4310	7.4116
Airway resistance$_1$(cm H_2O/L/sec)	14.38 (10.10 - 24.48)	14.7814	3.4185
Work/Kg$_1$(g.-m/Kg)	0.08(0.0267-0.01086)	0.0607	0.0209
Work/min/Kg$_1$ (g.-m/min/Kg)	2.04(0.5642-2.6076)	1.3338	0.4381
Respiratory rate$_2$ (breaths/min)	26 (14 - 40)	24.1666	6.1143
Tidal volume$_2$ (ml)	170 (100 - 270)	163.6667	43.3926
Minute volume$_2$ (ml/min)	4440 (2040 - 6480)	3915.6000	1371.1673
PO_2 (mm Hg)	31.40 (74.80 - 106.20)	89.8767	9.2069
P_{CO_2} (mm Hg)	21.20 (34.90 - 56.10)	43.8900	5.8017
pH	0.16 (7.294 - 7.457)	7.3465	0.0544
Hb (g/100 ml)	12.10 (8.3 - 20.4)	13.8100	2.2620
PCV	20.1 (26.0 - 46.1)	34.9233	4.6386
Respiratory rate$_3$ (breaths/min)	26 (14 - 40)	24.4700	5.3158
Tidal volume$_3$ (ml)	200 (110 - 310)	170.7333	48.6663
Minute volume$_3$ (ml/min)	5044 (2156 - 7200)	4126.0667	1308.1913
Expiratory velocity$_3$ (L/min)	12.5 (15.00 - 27.50)	20.4467	2.8344
Esophageal pressure$_3$(cm H_2O)	4.62 (2.72 - 7.34)	4.7440	1.2941
Lung compliance$_3$(ml/cm H_2O)	47.35 (18.82 - 66.17)	37.4117	10.3797
Airway resistance$_3$(cm H_2O/L/sec)	11.73 (8.666 - 20.402)	14.0274	3.8114
Work/Kg$_3$ (g.-m/Kg)	0.08(0.0272-0.1065)	0.0595	0.0202
Work/min/Kg$_3$ (g.-m/min/Kg$_3$)	1.7216(0.6587-2.4803)	1.4145	0.4821

Table 5. Age Group Means +Standard Deviations

PARAMETER	N=14 YOUNG	N=11 ADULT	N=5 AGED
WT(Kg)	14.77±3.61	14.23±3.91	10.95±3.57
HT RT_1	162.86±22.92	153.64±24.73	158.40±22.01
F_1(breaths/min)	24.14±7.32	20.82±3.15	20.60±2.96
V_{T1}(ml)	168.57±40.12[a]	173.45±35.48[b]	129.80±18.37[ab]
MV_1(ml/min)	3979.36±1283.21[a]	3611.54±898.71[b]	2654.40±390.05[ab]
V_{E1}(L/min)	20.48±3.06	20.62±2.14	18.60±3.50
V_{I_1}(L/min)	12.73±4.30	12.84±2.80	10.30±2.64
P_{E_1} (cm H_2^0)	4.59±1.17[a]	5.04±0.98	5.68±1.29[a]
C_{L_1} (ml/cm$H_2$0)	37.12±6.53[a]	34.89±4.98[b]	24.12±5.30[ab]
R_{A_1} (cm$H_2$0/L/sec)	13.53±4.35[a]	14.62±2.09[b]	18.64±4.34[ab]
WK/Kg_1 (g.-m/Kg)	0.05±0.02[ab]	0.07±0.02[a]	0.07±0.02[b]
$WK/min/Kg_1$	1.22±0.40	1.37±0.57	1.33±0.48
F_2 (breaths/min)	25.64±7.33	23.27±4.77	22.00±4.84
VT_2(ml)	167.71±50.04[a]	171.64±38.53[b]	134.80±22.97[ab]
MV_2(ml/min)	4264.00±1794.76[a]	3893.64±727.66[b]	2988.40±986.63[ab]
P_{O_2}	88.54±9.88	90.00±8.89	93.38±8.81
P_{CO_2}	44.18±5.76	43.94±6.13	42.94±6.38
pH	7.36±0.05	7.33±0.05	7.34±0.04
Hb (g/100 ml)	13.95±2.46	13.82±1.81	13.40±2.95
PCV (percent)	33.21±4.24	37.13±5.30	34.86±1.88
F_3 (breaths/min)	25.78±6.51	22.27±4.11	25.60±2.19
V_{T_3} (ml)	174.28±54.13[a]	183.00±43.29[b]	133.80±28.25[ab]
Mv_3 (ml/min)	4446.43±1614.73[a]	4022.18±904.09	3457.60±970.84[a]
P_{E_3} (cm$H_2$0)	4.36±1.32[a]	4.83±1.17	5.63±1.20[a]
V_{E_3} (L/min)	20.70±3.02	20.87±2.10	18.80±3.63
C_{L_3} (ml/cm$H_2$0)	40.91±10.17[a]	38.86±7.69[b]	24.14±6.06[ab]
R_{A_3} (cm$H_2$0/L/sec)	12.63±3.16[a]	13.82±2.80[b]	18.40±4.70[ab]
WK/Kg_3(g.-m/Kg)	0.05±0.02	0.06±0.02	0.07±0.01
$WK/min/Kg_3$	1.30±0.48[a]	1.39±0.47[b]	1.79±0.38[ab]

Superscripts represent significant difference ($p<0.05$).

Table 6. Sex Group Means ±Standard Deviations

PARAMETER	M=16 M	N=14 F
WT	13.30±3.88	14.66±3.81
HT RT_1	155.00±22.65	163.00±23.59
F_1(breaths/min)	22.25±3.97	22.43±7.23
V_T (ml)	159.63±40.13	168.78±36.37
MV_1^1(ml/min)	3551.19±1133.93	3706.50±1146.74
$\dot{V}_{E1}$(L/min)	20.03±3.56	20.42±1.79
$\dot{V}_I$ (L/min)	12.24±4.20	12.50±2.93
$P_{E_1}^1$(cmH_2O)	4.89±1.40	5.01±0.83
C_L^1 (ml/cmH_2O)	34.33±8.25	34.54±6.62
R_{A1}^1(cmH_2O/L/sec)	14.74±3.80	14.83±3.06
WK/Kg_1(g.-m/Kg)	0.06±0.025	0.06±0.016
WK/min/Kg_1 (g.-m/min/Kg)	1.40±0.594	1.26±0.319
F_2(breaths/min)	24.38±4.32	23.93±7.76
VT_2(ml)	165.50±49.12	161.57±37.51
MV_2(ml/min)	4030.37±1527.46	3784.43±1211.29
P_{O_2} (mmHg)	89.23±10.36	90.61±8.00
P_{CO_2}(mmHg)	45.97±6.70[a]	41.51±3.42[a]
pH	7.36±0.05	7.33±0.04
Hb (g./100ml)	14.12±2.61	13.46±1.81
PCV (percent)	34.39±3.59	35.53±5.68
F_3 (breaths/min)	25.31±4.14	23.50±6.43
V_{T_3}(ml)	163.25±52.50	179.28±44.21
Mv_3(ml/min)	4127.25±1457.56	4124.71±1168.88
P_{E_3} (cmH_2O)	4.59±1.44	4.92±1.11
$\dot{V}_{E_3}$ (L/min)	20.28±3.50	20.63±1.91
C_{L_3} (ml/cmH_2O)	37.47±12.05	37.34±8.27
R_{A_3} (cm H_2O/L/sec)	13.67±4.12	14.44±3.53
WK/Kg_3(g.-m/kg)	0.06±0.025	0.06±0.014
WK/min/Kg_3 (g.-m/min/Kg)	1.44±0.574	1.38±0.375

Table 7. Age-Sex Group Means

PARAMETER	N=9	N=5	N=3	N=8	N=4	N=1
	YOUNG		ADULT		AGED	
	M	F	M	F	M	F
WT	15.05	14.27	11.48	15.26	10.73	11.82
HT RT_1	155.56	176.00	152.00	154.25	156.00	168.00
F_1(breaths/min)	23.56	25.20	19.33	21.38	21.50	17.00
V_{T1}(ml)	175.11	156.80	149.67	182.37	132.25	120.00
MV_1(ml/min)	4096.78	3768.00	2905.33	3876.38	2808.00	2040.00
$\dot{V}_{E1}$(L/min)	20.92	19.66	19.73	20.95	18.25	20.00
$\dot{V}_{I_1}$ (L/min)	13.27	11.76	11.67	13.28	10.38	10.00
P_{E1}(cmH_2O)	4.54	4.70	5.12	5.01	5.50	6.39
C_{L_1}(ml/cmH_2O)	39.36	34.76	30.93	36.38	25.57	18.77
R_{A_1} (cmH_2O/L/sec)	12.88	14.69	15.30	14.37	18.50	19.18
WK/Kg_1(g.-m/kg)	0.054	0.054	0.074	0.062	0.068	0.065
WK/min/Kg_1	1.253	1.169	1.720	1.333	1.491	1.102
F_2(breaths/min)	26.11	24.80	20.67	24.50	23.25	17.00
VT_2(ml)	176.44	152.00	168.67	172.75	138.50	120.00
MV_2(ml/min)	4617.78	3627.00	3341.33	4100.75	3225.50	2040.00
P_{O_2}	88.36	88.86	84.53	92.04	94.73	88.00
P_{CO_2}	46.27	40.42	50.03	41.66	42.22	45.80
pH	7.37	7.35	7.34	7.33	7.34	7.34
Hb(g/100ml)	14.49	12.98	14.20	13.67	13.22	14.10
PCV	33.83	32.10	35.90	37.58	34.52	36.20
F_3(breaths/min)	26.55	24.40	22.00	22.38	25.00	28.00
V_{T3}(ml)	179.44	165.00	152.00	194.62	135.25	128.00
M_{V_3}(ml/min)	4697.77	3994.00	3350.67	4274.00	3426.00	3584.00
P_{E_3}(cmH_2O)	4.24	4.55	4.62	4.91	5.33	6.80
$\dot{V}_{E_3}$ (L/min)	21.16	19.86	20.00	21.20	18.50	20.00
C_{L_3} (ml/cmH_2O)	43.12	36.94	36.08	39.91	25.81	18.82
R_{A_3} (cmH_2O/L/sec)	11.81	14.09	13.58	13.91	17.91	20.40
WK/Kg_3 (g.-m/kg)	0.051	0.053	0.066	0.064	0.069	0.074
WK/min/kg_3	1.321	1.248	1.431	1.370	1.726	2.062

Table 8. Matrix of Statistically Significant Coefficients of Correlation*

	WT	HR_1	F_1	V_{T_1}	MV_1	V_{E_1}	V_{I_1}	P_{E_1}	C_{L_1}	R_{A_1}	F_2	VT_2	MV_2	P_{O_2}	P_{CO_2}	pH
WT	1.00			0.69	0.71	0.49	0.77		0.40			0.55	0.58			
HR_1		1.00	0.38											-.43		
F_1		0.38	1.00		0.57						0.85		0.44			
V_{T_1}	0.69			1.00	0.69	0.66	0.80	0.48	0.50			0.87	0.56			
MV1	0.71		0.57	0.69	1.00	0.62	0.82				0.46	0.61	0.80		-.39	
V_{E_1}	0.49			0.65	0.62	1.00	0.77	0.46				0.55	0.43		-.40	
V_{I_1}	0.77			0.80	0.82	0.77	1.00	0.46				0.71	0.66		-.40	
P_{E_1}				0.48		0.46	0.46	1.00	-.50	0.75		0.40			-.38	
C_{L_1}	0.40			0.47				-.50	1.00	-.63		0.42	0.37			
R_{A_1}								0.75	-.63	1.00	-.38					
F_2			0.85		0.46					-.39	1.00		0.57			
VT_2	0.55	-.38		0.87	0.61	0.55	0.71	0.40	0.42			1.00	0.70			
MV_2	0.58		0.43	0.56	0.80	0.43	0.66		0.37		0.57	0.70	1.00	0.41	-.38	
P_{O_2}		-.43											0.41	1.00	-.64	
P_{CO_2}					-.39	-.40	-.40	-.39					-.38	-.64	1.00	-.50
pH															-.49	1.00

*$r \geq 0.35$; $p < 0.05$
$r \geq 0.43$; $p < 0.01$
$r \geq 0.52$; $p < 0.001$

Table 9. Means From Three Sample Periods

Parameter	Period 1	Period 2	Period 3
F (breaths/min)	22.33±5.63 *	24.17±6.11	24.46±5.32
V_T (ml)	163.90±38.05	163.07±43.39	170.73±48.67
MV (ml/min)	3623.67±1122.84[a]	3915.60±1371.17	4126.07±1308.19[a]
P_E (cmH_2O)	4.94±1.16	4.87±1.27	4.74±1.29
C_L (ml/cmH_2O)	34.43±7.41	35.81±8.16	37.41±10.38
R_A ($cmH_2O/L/sec$)	14.78±3.41	14.59±3.53	14.02±3.81
WK/Kg	0.06±0.02	0.06±0.02	0.06±0.02
WK/min/Kg	1.33±0.44	1.39±0.44	1.41±0.48

[a]Superscript indicates significant mean difference ($p \leq 0.05$).

*Mean value ±Standard Deviation

Heart Rate and Respiratory Rate

Analysis of variance tables for the cardiopulmonary parameters heart rate and respiratory rate are shown (Tables 10A & B and 11A & B). Age, sex, age by sex interaction and weight have no effect on either heart rate or resiratory rate. Further analyses, eliminating sex and age by sex interactions (Tables 10B and 11B) demonstrated that age and weight do not significantly effect heart rate and respiratory rate. Because the independent variables age and weight do not significantly effect the dependent variables heart rate and respiratory rates, graphical illustrations of these relationships are not necessary.

Table 10A ANALYSIS OF VARIANCE TABLE, REGRESSION COEFFICIENTS, AND STATISTICS OF FIT FOR DEPENDENT VARIABLE HEART RATE

SOURCE	DF	SUM OF SQUARES	MEAN SQUARE	F VALUE	PROB > F
Regression	6	22128.38045198	354.73007533	0.61421	0.7184
Error	23	13283.48621469	577.54287890		
Corrected Total	29	15411.86666667			

SOURCE	DF	PARTIAL SS	F VALUE	PROB > F
Age	2	748.73081268	0.64820	0.5336
Sex	1	498.90039770	0.86383	0.3623
Age*Sex	2	534.70143658	0.46291	0.6404
Wt	1	134.23600753	0.23243	0.6343

Table 10B

SOURCE	DF	SUM OF SQUARES	MEAN SQUARE	F VALUE	PROB > F
Regression	3	622.50323790	207.50107930	0.36479	0.7815
Error	26	14789.36342877	568.82167034		
Corrected Total	29	15411.86666667			

SOURCE	DF	PARTIAL SS	F VALUE	PROB > F
Age	2	501.17797941	0.44054	0.6537
Wt	1	98.09631149	0.17246	0.6813

Table 11A ANALYSIS OF VARIANCE TABLE, REGRESSION COEFFICIENTS, AND STATISTICS OF FIT FOR DEPENDENT VARIABLE RESPIRATION RATE

SOURCE	DF	SUM OF SQUARES	MEAN SQUARE	F VALUE	PROB > F
Regression	6	130.95340312	21.82556719	0.63727	0.7010
Error	23	787.71326355	34.24840267		
Corrected Total	29	918.66666667			

SOURCE	DF	PARTIAL SS	F VALUE	PROB > F
Age	2	93.16387063	1.36012	0.2760
Sex	1	1.15292302	0.03366	0.8560
Age*Sex	2	27.94649496	0.40800	0.6748
Wt	1	10.85062534	0.31682	0.5790

Table 11B

SOURCE	DF	SUM OF SQUARES	MEAN SQUARE	F VALUE	PROB > F
Regression	3	99.03907309	33.13002436	1.04723	0.3893
Error	26	819.62759357	31.52413821		
Corrected Total	29	918.66666667			

SOURCE	DF	PARTIAL SS	F VALUE	PROB > F
Age	2	69.98391712	1.11001	0.3455
Wt	1	12.92305578	0.40994	0.5276

Tidal Volume

Analysis of variance tables (Tables 12A & B and 13A & B) for tidal volume$_1$ (period 1) and tidal volume$_3$ (period 3) are shown. Age, sex, and age by sex interaction do not significantly influence an animal's tidal volume. The weight effect is statistically significant at the $p<0.0001$ level even before insignificant main effects (sex and age by sex interaction) are removed.

There were no significant differences between the mean tidal volumes of the three measurement periods (Table 9). As a result, tidal volumes for all dogs for each of the three measurement periods were grouped together. Figure 5 is a graphical illustration of tidal volumes vs. body weight in all dogs for all three periods. The correlation coefficient (r), regression equation, regression line, and five percent confidence intervals are shown. The correlation coefficient ($r = 0.7189$) is highly significant ($p<0.01$). The independent variable age was not shown to significantly effect tidal volume. Figure 6, a plot of tidal vs body weight for each of the age groups illustrates the insignificant age effects. The r values are all highly significant ($p<0.01$) but the slopes and intercepts of the regression lines for the three age groups are not significantly different.

Table 12A ANALYSIS OF VARIANCE TABLE, REGRESSION COEFFICIENTS, AND STATISTICS OF FIT FOR DEPENDENT VARIABLE TIDAL VOLUME$_1$

SOURCE	DF	SUM OF SQUARES	MEAN SQUARE	F VALUE	PROB > F
Regression	6	22659.19219166	3776.53203194	4.49227	0.0040
Error	23	19335.50780834	840.67425254		
Corrected Total	29	41994.70000000			

SOURCE	DF	PARTIAL SS	F VALUE	PROB > F
Age	2	1715.12165265	1.02009	0.3779
Sex	1	237.11994997	0.28206	0.6004
Age*Sex	2	842.94432072	0.50135	0.6174
Wt	1	12003.47274722	14.27839	0.0010

Table 12B

SOURCE	DF	SUM OF SQUARES	MEAN SQUARE	F VALUE	PROB > F
Regression	3	21573.85880907	7191.28626969	9.15601	0.0004
Error	26	20420.84119093	785.41696888		
Corrected Total	29	41994.70000000			

SOURCE	DF	PARTIAL SS	F VALUE	PROB > F
Age	2	1716.35400752	1.09264	0.3512
Wt	1	14450.11465323	18.39802	0.0002

Table 13A ANALYSIS OF VARIANCE TABLE, REGRESSION COEFFICIENTS, AND STATISTICS OF FIT FOR DEPENDENT VARIABLE TIDAL VOLUME$_3$

SOURCE	DF	SUM OF SQUARES	MEAN SQUARE	F VALUE	PROB > F
Regression	6	47812.04961860	7968.67493643	8.78120	0.0001
Error	23	20871.81704807	907.47030644		
Corrected Total	29	68683.86666667			

SOURCE	DF	PARTIAL SS	F VALUE	PROB > F
Age	2	1440.42813048	0.79365	0.5321
Sex	1	198.17159698	0.21838	0.6447
Age*Sex	2	333.35633856	0.18367	0.8344
Wt	1	34483.03017416	37.99907	0.0001

Table 13B

SOURCE	DF	SUM OF SQUARES	MEAN SQUARE	F VALUE	PROB > F
Regression	3	47363.28302120	15787.76100707	19.25284	0.0001
Error	26	21320.58364546	820.02244790		
Corrected Total	29	68683.86666667			

SOURCE	DF	PARTIAL SS	F VALUE	PROB > F
Age	2	1488.80267080	0.90778	0.5815
Wt	1	38711.07349740	47.20733	0.0001

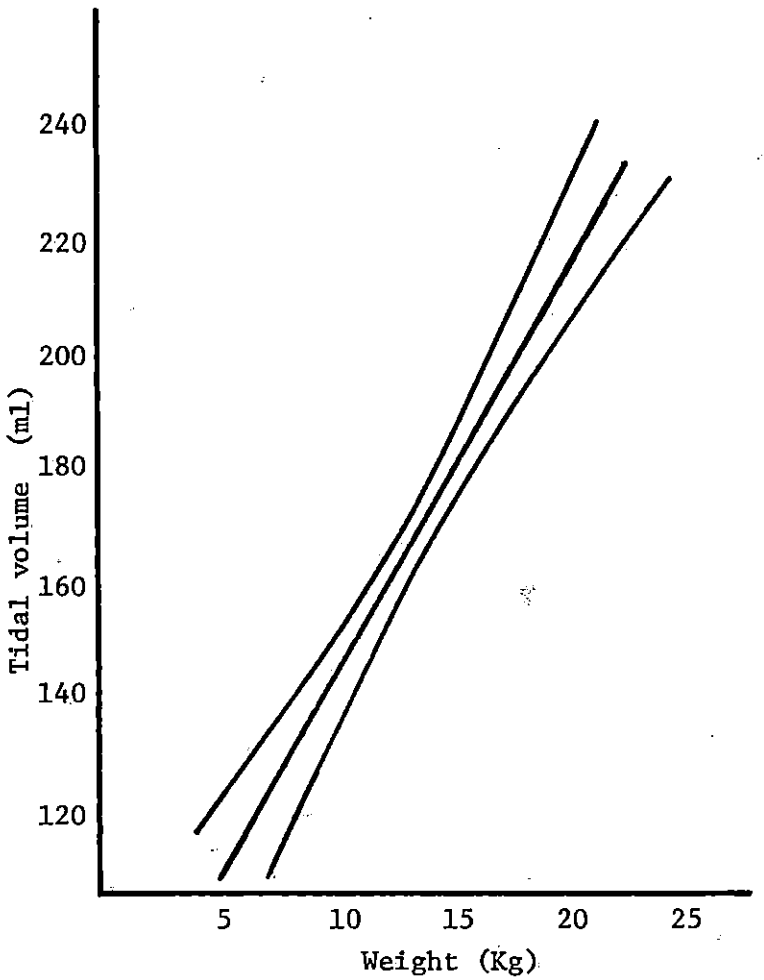


Figure 5. Tidal volume vs. body weight in all dogs.
r = 0.7189 Y = 50.99 + 8.23(Wt)

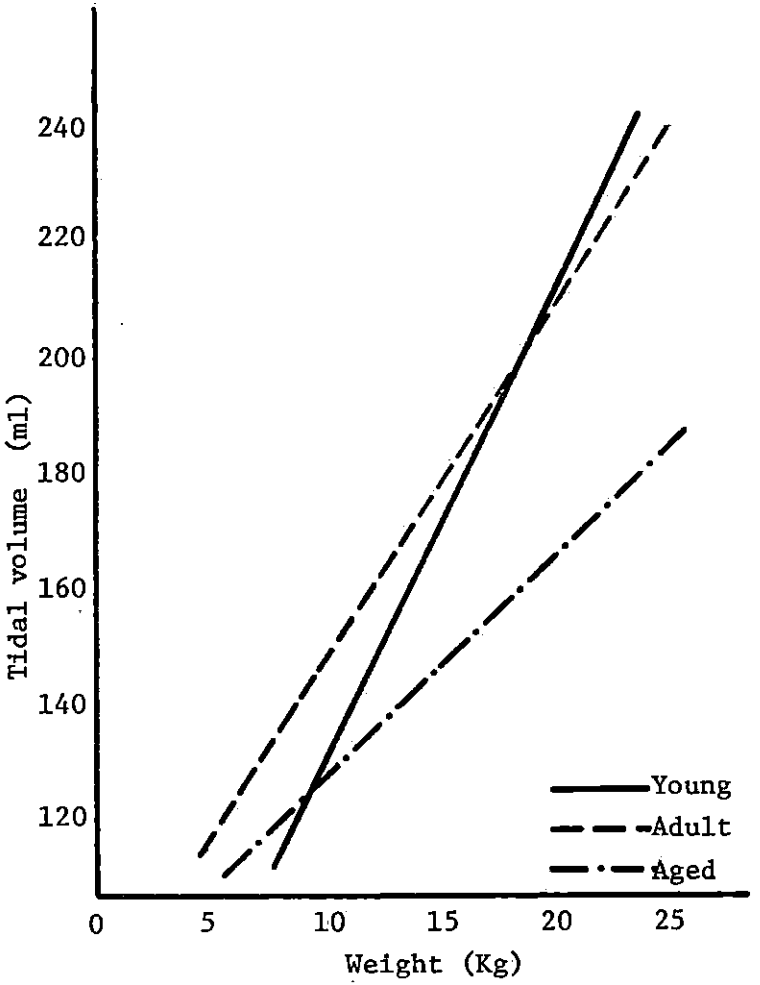


Figure 6. Tidal volume vs. body weight in each age group.
Young; r = 0.6249 Y = 46.31 + 0.39(Wt)
Adult; r = 0.5354 Y = 92.34 + 5.83(Wt)
Aged; r = 0.5786 Y = 90.81 + 3.83(Wt)

Minute Volume

Analysis of variance tables for minute volume$_1$ (Table 14A & B) and minute volume$_3$ (Table 15A & B) are shown. Body weight was found to be the only independent variable to significantly influence minute volume. The effect of weight on MV is highly significant ($p<0.0001$) in both periods analyzed (periods 1 and 3).

A comparison of minute volume means for the three measurement periods (Table 9) indicated that significant mean differences existed ($p<0.05$). Mean MV_1 was not different from MV_2 but did significantly differ from MV_3. This necessitated separate graphical treatment of the three treatment periods. Figure 7 illustrates minute volume vs body weight for all ages during Period 1. The r value of 0.6295 is highly significant ($p<0.01$). The regression equation, regression (best fit) line and confidence interval bands are demonstrated. Although ANOVA procedures did not reveal significant age effect on minute volume, Figure 8 illustrates minute volume$_1$ vs body weight in the three separate age groups. Only the r value for the young dogs ($r = 0.9045$) is statistically significant ($p<0.01$).

Figure 9 illustrates MV_3 vs body weight for all ages. The r value is highly significant ($p<0.01$). Figure 10 is a plot of MV_3 vs body weight for each age group. All three of the r values are highly significant ($p<0.01$) but the slopes and intercepts of the three regression lines are not significantly different illustrating that age does not significantly effect minute volume.

Table 14A ANALYSIS OF VARIANCE TABLE, REGRESSION COEFFICIENTS, AND STATISTICS OF FIT FOR DEPENDENT VARIABLE MINUTE VOLUME$_1$

SOURCE	DF	SUM OF SQUARES	MEAN SQUARE	F VALUE	PROB > F
Regression	6	20505100.78776580	3417516.79796097	4.89519	0.0026
Error	23	16057157.87890089	698137.29908265		
Corrected Total	29	36562258.66666668			

SOURCE	DF	PARTIAL SS	F VALUE	PROB > F
Age	2	1964222.32527330	1.40676	0.2646
Sex	1	362925.47894036	0.51985	0.4782
Age*Sex	2	927056.30066318	0.66395	0.5286
Wt	1	11158284.21832126	15.98294	0.0006

Table 14B

SOURCE	DF	SUM OF SQUARES	MEAN SQUARE	F VALUE	PROB > F
Regression	3	19476574.32858600	6492191.44286200	9.87944	0.0003
Error	26	17085684.33808068	657141.70531080		
Corrected Total	29	36562258.66666668			

SOURCE	DF	PARTIAL SS	F VALUE	PROB > F
Age	2	1295912.73478445	0.98602	0.6115
Wt	1	13006348.80347769	19.79230	0.0001

Table 15A ANALYSIS OF VARIANCE TABLE, REGRESSION COEFFICIENTS, AND STATISTICS OF FIT FOR DEPENDENT VARIABLE MINUTE VOLUME$_3$

SOURCE	DF	SUM OF SQUARES	MEAN SQUARE	F VALUE	PROB > F
Regression	6	29825522.98731323	4970920.49788554	5.77312	0.0011
Error	23	19804048.87935344	861045.60345015		
Corrected Total	29	49629571.86666667			

SOURCE	DF	PARTIAL SS	F VALUE	PROB > F
Age	2	246837.68871780	0.14334	0.8673
Sex	1	220758.01356546	0.25738	0.6174
Age*Sex	2	275276.89855051	0.15985	0.8537
Wt	1	22563613.34286875	26.20490	0.0001

Table 15B

SOURCE	DF	SUM OF SQUARES	MEAN SQUARE	F VALUE	PROB > F
Regression	3	28994882.93792764	9664960.97930921	12.17799	0.0001
Error	26	20634688.92873903	793641.88187458		
Corrected Total	29	49629571.86666667			

SOURCE	DF	PARTIAL SS	F VALUE	PROB > F
Age	2	5563433.55206763	0.35497	0.7093
Wt	1	25205087.33619602	31.75877	0.0001

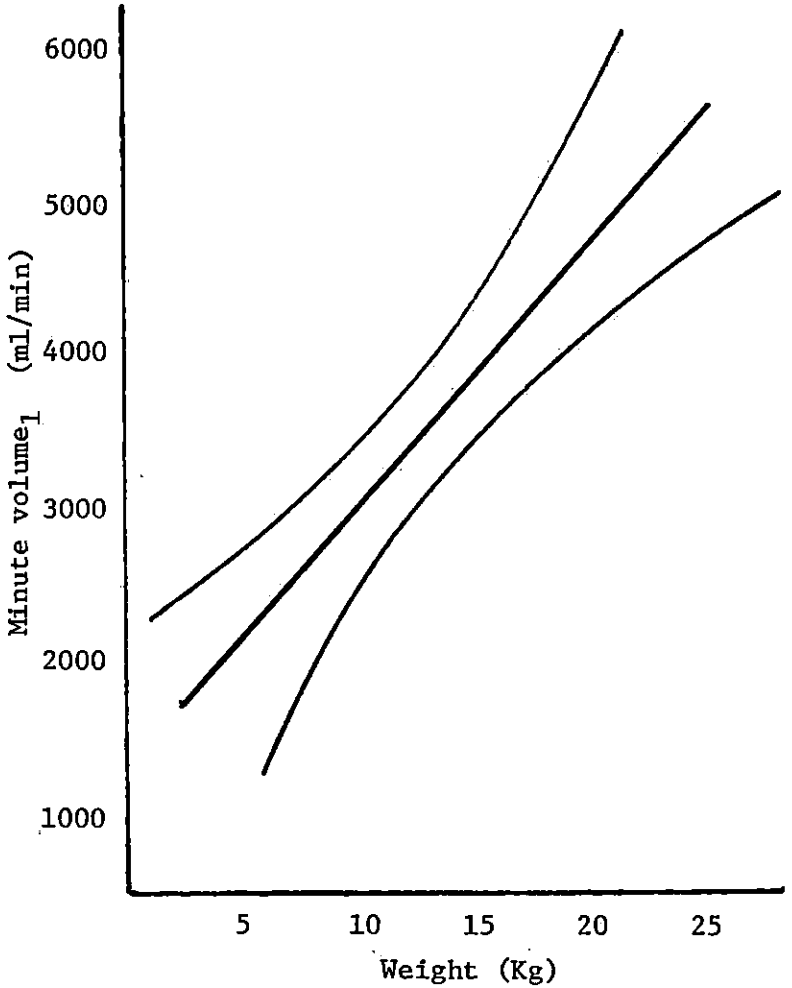


Figure 7. Minute volume$_1$ vs. body weight in all dogs.
r = 0.6295 Y = 559.28 + 212.65(Wt)

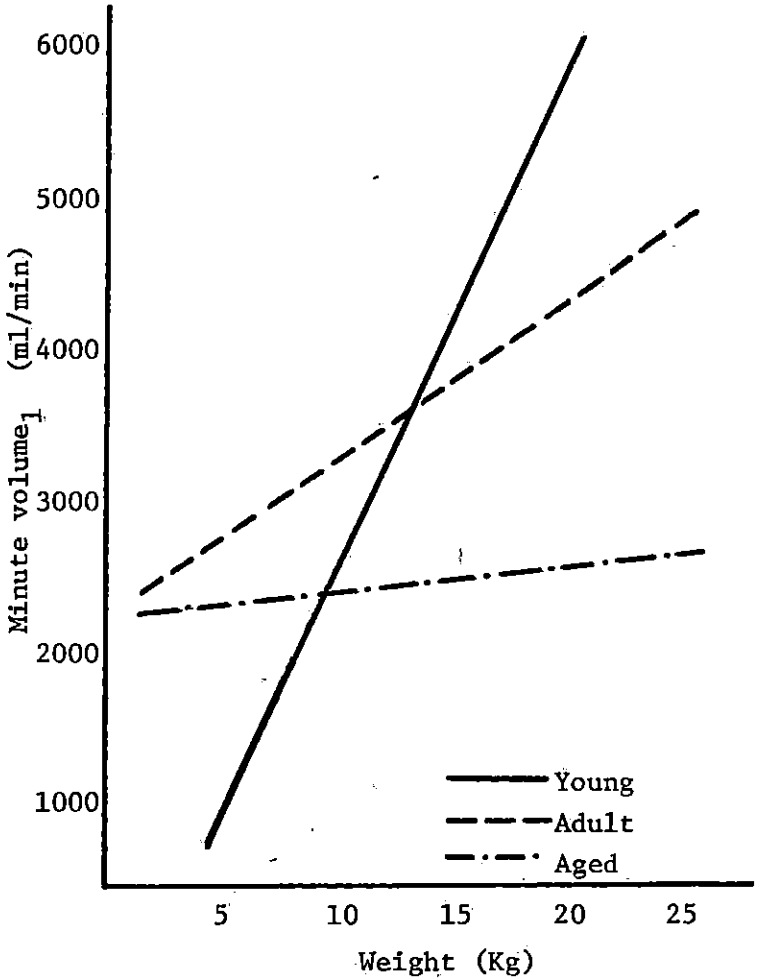


Figure 8. Minute volume$_1$ vs. body weight in each age group.
Young; r = 0.9045 Y =-759.98 + 320.91(Wt)
Adult; r = 0.4667 Y =2087.31 + 107.14(Wt)
Aged; r = 0.2190 Y =2916.29 - 23.94(Wt)

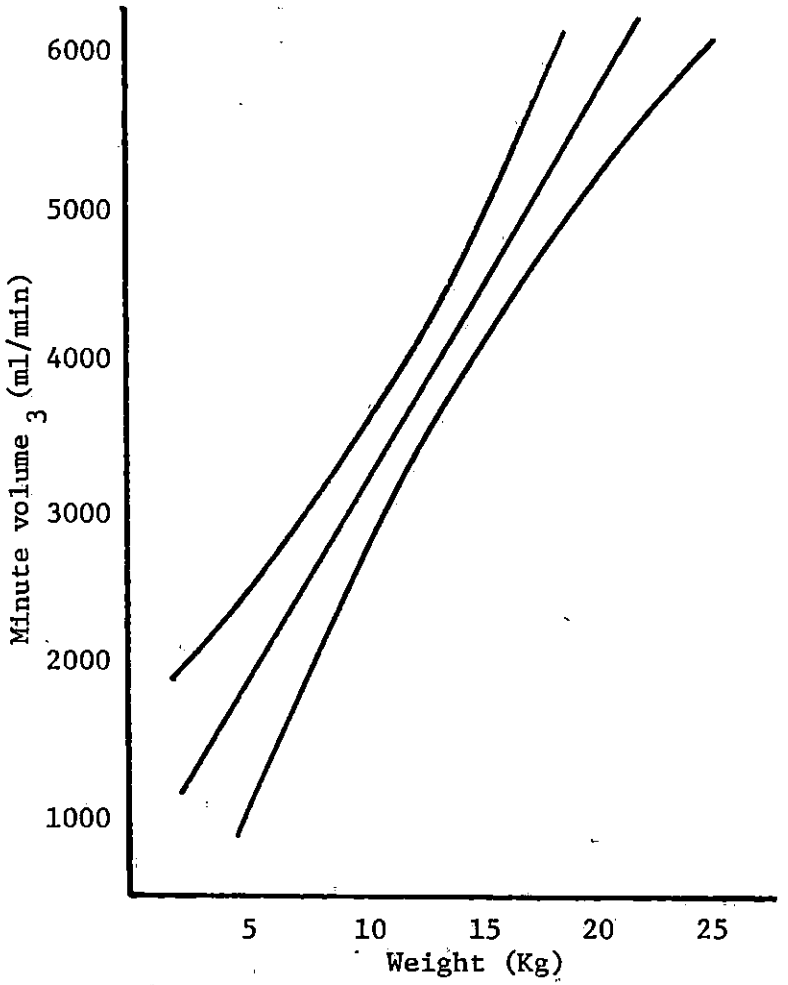


Figure 9. Minute volume$_3$ vs. body weight in all dogs.
r = 0.7568 Y = 540.44 + 257.28(Wt)

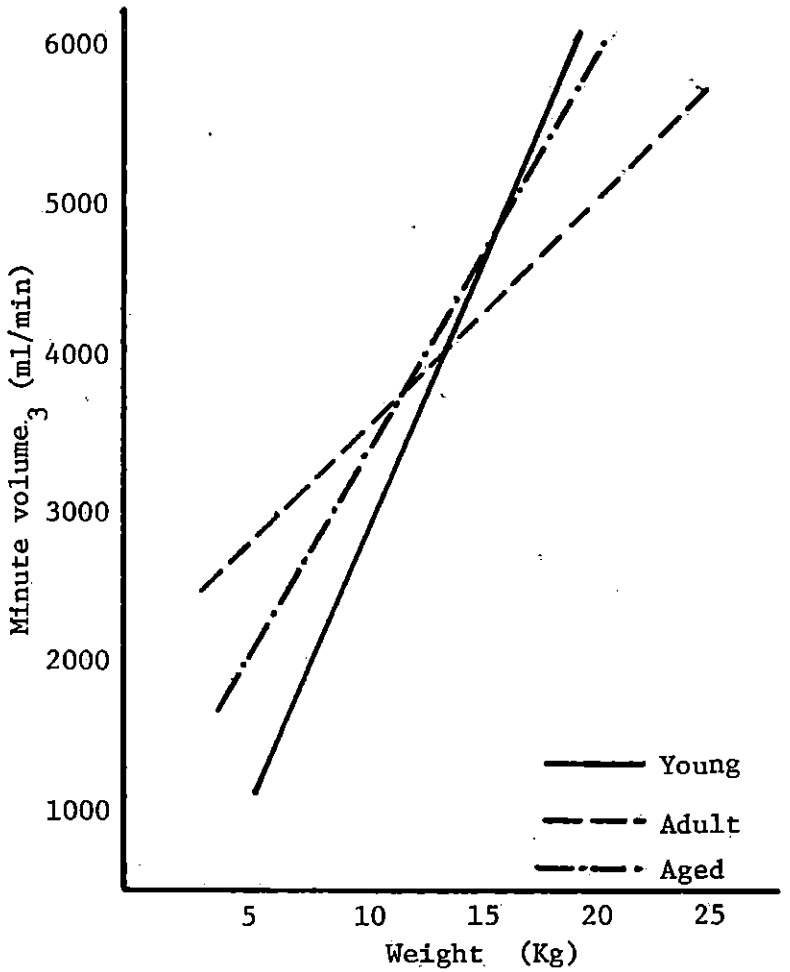


Figure 10. Minute volume$_3$ vs. body weight in each age group.
Young; r = 0.8111 Y =-901.39 + 362.11(Wt)
Adult; r = 0.6368 Y =1930.26 + 147.04(Wt)
Aged; r = 0.9383 Y = 655.33 + 255.23(Wt)

Inspiratory Velocity

Analysis of variance tables (Tables 16A and B) for the dependent variable inspiratory velocity are shown. Weight is the only independent variable with a significant effect on inspiratory velocity ($p<0.0001$).

Figure 11 is a graphical illustration of inspiratory velocity$_1$ vs body weight for all dogs. The r value of 0.7696 is highly significant $p<0.01$). The five percent confidence intervals demonstrate the little variability among observations. Figure 12 is a plot of V_{I_1} vs body weight for the three age groups. The r value for young dogs (0.8520) is highly significant ($p<0.01$) and the r value of r = 0.6929 for adult animals is also significant ($p<0.05$). Although the slope and intercept of the regression for young dogs appear quite different from the other two age group lines, it does not differ significantly.

Table 16A ANALYSIS OF VARIANCE TABLE, REGRESSION COEFFICIENTS, AND STATISTICS OF FIT FOR DEPENDENT VARIABLE INSPIRATORY VELOCITY$_1$

SOURCE	DF	SUM OF SQUARES	MEAN SQUARE	F VALUE	PROB > F
Regression	6	229.13585676	38.18930946	6.08557	0.0009
Error	23	144.33380991	6.27538304		
Corrected Total	29	373.46966667			

SOURCE	DF	PARTIAL SS	F VALUE	PROB > F
Age	2	4.42611685	0.35266	0.7112
Sex	1	5.37233763	0.85610	0.3644
Age*Sex	2	0.11867818	0.00946	0.9914
Wt	1	190.46735676	30.35151	0.0001

Table 16B

SOURCE	DF	SUM OF SQUARES	MEAN SQUARE	F VALUE	PROB > F
Regression	3	222.22240445	74.07413482	12.73364	0.0001
Error	26	151.24726221	5.81720239		
Corrected Total	29	373.46966667			

SOURCE	DF	PARTIAL SS	F VALUE	PROB > F
Age	2	1.57774590	0.13561	0.8738
Wt	1	196.60676376	33.79748	0.0001

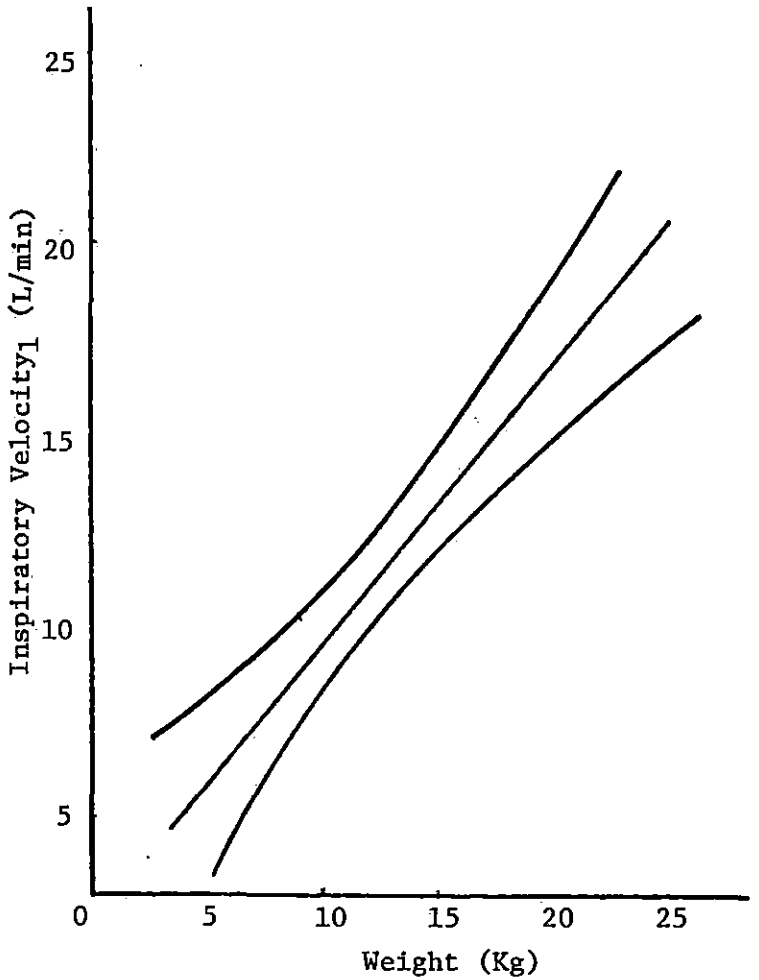


Figure 11. Inspiratory velocity$_1$ vs body weight in all dogs.
r = 0.7696 Y = 2.37 + 0.72(Wt)

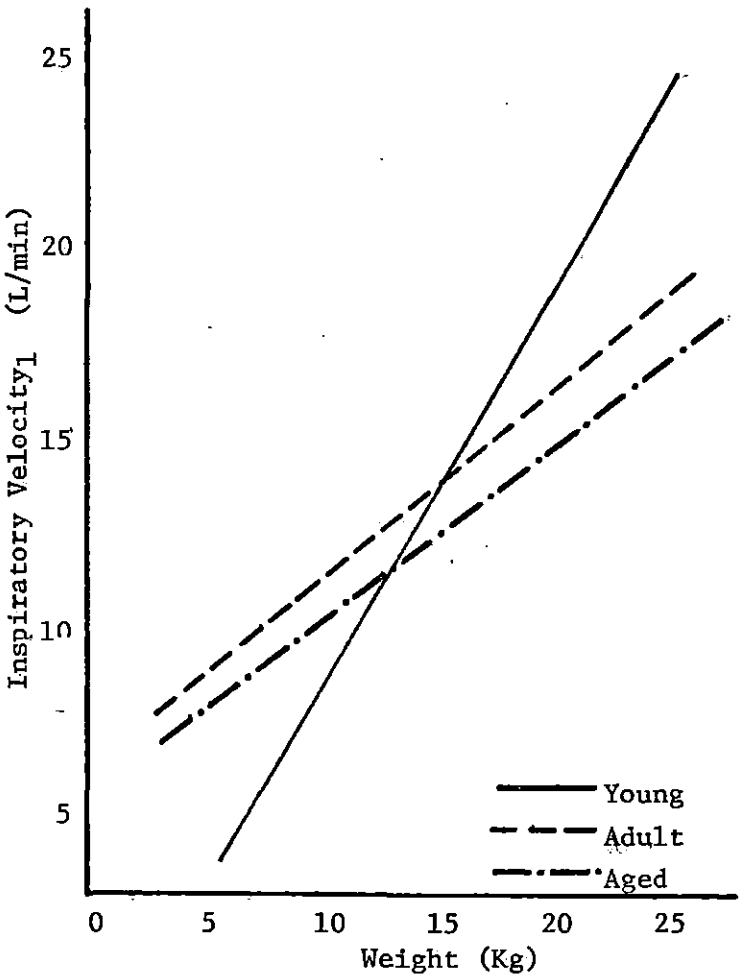


Figure 12. Inspiratory velocity$_1$ vs body weight in each age group.
Young; r = 0.8520 Y = -0.74 + 0.06(Wt)
Adult; r = 0.6929 Y = 5.76 + 0.50(Wt)
Aged; r = 0.5984 Y = 5.45 + 0.44(Wt)

Expiratory Velocity

Analysis of variance tables for the dependent variable expiratory velocity are shown (Tables 17A & B and 18A & B). The independent variables age, sex, and the first order interaction of age by sex do not influence the expiratory velocity of a dog. However, body weight does significantly effect expiratory velocity ($p < 0.05$).

Figure 13 is a graph of the expiratory velocity of all dogs for measurement periods 1 and 3 versus body weight. The correlation coefficient ($r = 0.4956$) is highly significant ($p < 0.01$). Figure 14 illustrates expiratory versus body weight for each of the age groups for the two measurement periods (period 1 and 3). The correlation coefficients for the yound dogs ($r = 0.5829$) and aged dogs ($r = 0.7659$) are highly significant ($p < 0.01$). Graphically, the slopes and intercepts of the regression lines for adult dogs appears to be different from the other two age groups. However, the correlation coefficient for the adult group is quite low ($r = 0.0731$). Therefore, the regression (best fit) line could actually be drawn anywhere on the graph. This does not permit comparison of this line with the other two age groups. As a result, the regression lines are not significantly different.

Table 17A ANALYSIS OF VARIANCE TABLE, REGRESSION COEFFICIENTS, AND STATISTICS OF FIT FOR DEPENDENT VARIABLE EXPIRATORY VELOCITY$_1$

SOURCE	DF	SUM OF SQUARES	MEAN SQUARE	F VALUE	PROB > F
Regression	6	64.11855167	10.68642528	1.45114	0.2382
Error	23	169.37611500	7.36417891		
Corrected Total	29	233.49466667			

SOURCE	DF	PARTIAL SS	F VALUE	PROB > F
Age	2	1.33867726	0.09089	0.9129
Sex	1	0.05763661	0.00783	0.9303
Age*Sex	2	3.91021444	0.26549	0.7722
Wt	1	37.56810722	5.10147	0.0337

Table 17B

SOURCE	DF	SUM OF SQUARES	MEAN SQUARE	F VALUE	PROB > F
Regression	3	59.36793658	19.78931219	2.95487	0.0502
Error	26	174.12673009	6.69718193		
Corrected Total	29	233.49466667			

SOURCE	DF	PARTIAL SS	F VALUE	PROB > F
Age	2	2.56999584	0.19187	0.8279
Wt	1	43.61820498	6.51292	0.0169

Table 18A ANALYSIS OF VARIANCE TABLE, REGRESSION COEFFICIENTS, AND STATISTICS OF FIT FOR DEPENDENT VARIABLE EXPIRATORY VELOCITY$_3$

SOURCE	DF	SUM OF SQUARES	MEAN SQUARE	F VALUE	PROB > F
Regression	6	65.42141924	10.90356987	1.49655	0.2231
Error	23	167.57324743	7.28579337		
Corrected Total	29	232.99466667			

SOURCE	DF	PARTIAL SS	F VALUE	PROB > F
Age	2	1.71502440	0.11770	0.8891
Sex	1	0.00012541	0.00002	0.9966
Age*Sex	2	3.35786941	0.23044	0.7982
Wt	1	38.53875257	5.28958	0.0309

Table 18B

SOURCE	DF	SUM OF SQUARES	MEAN SQUARE	F VALUE	PROB > F
Regression	2	60.89890667	20.29963556	3.06684	0.0448
Error	26	172.09576000	6.61906769		
Corrected Total	29	232.99466667			

SOURCE	DF	PARTIAL SS	F VALUE	PROB > F
Age	2	2.84464762	0.21488	0.8100
Wt	1	44.44605818	6.71485	0.0155

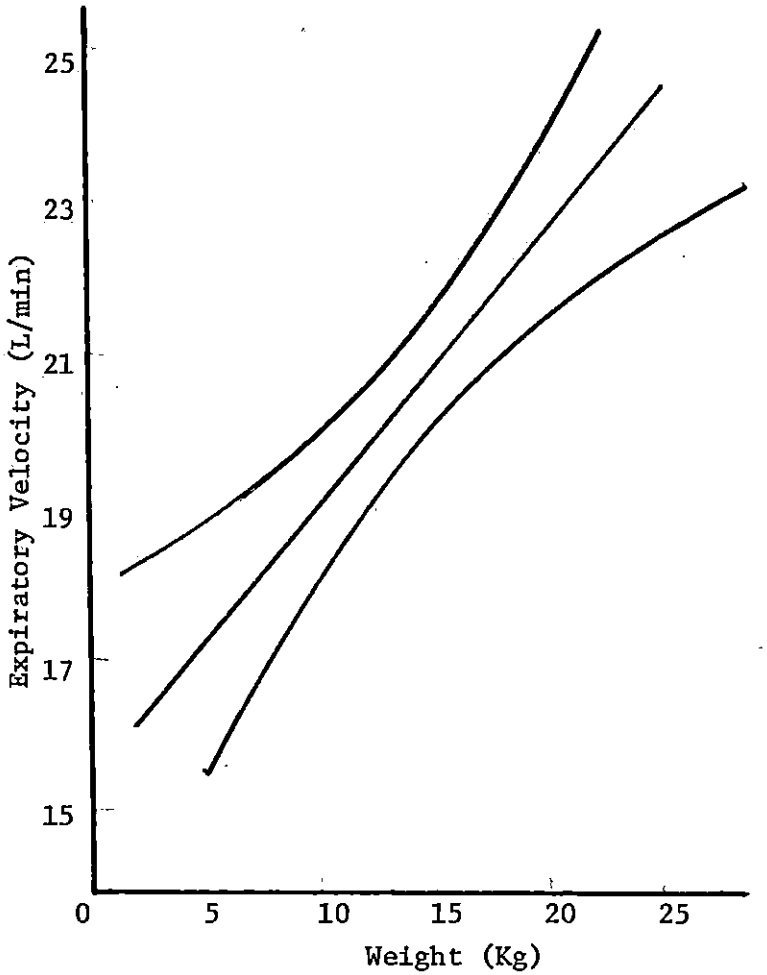


Figure 13. Expiratory velocity vs body weight for all dogs.
r = 0.4956 Y = 15.24 + 0.37(Wt)

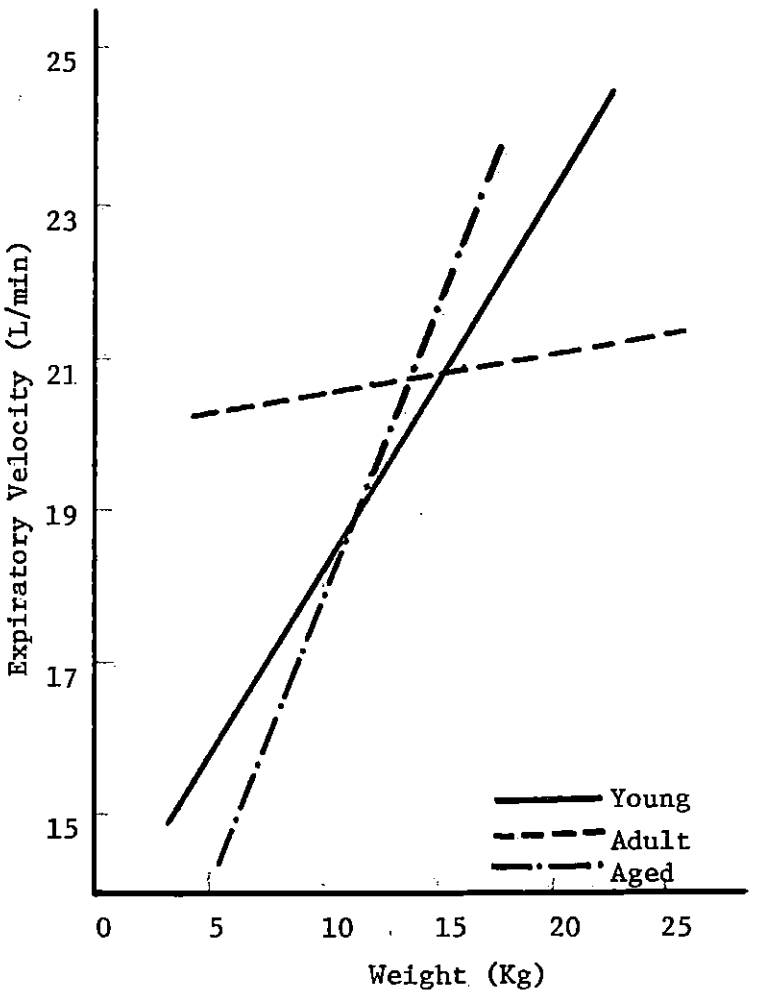


Figure 14. Expiratory velocity vs body weight for each age group.
Young; r = 0.5829 Y = 13.32 + 0.49(Wt)
Adult; r = 0.0731 Y = 20.17 + 0.04(Wt)
Aged; r = 0.7659 Y = 10.41 + 0.76(Wt)

Esophageal Pressure

The analysis of variance tables for the dependent variable esophageal pressure are shown in Table 19A & B and 20A & B. The independent variables age and weight are shown to significantly effect esophageal pressure ($p<0.05$). After removing the insignificant independent variables sex and age by sex interaction, age and weight have highly significant ($p<0.01$) on P_E (Table 20B).

Table 9 has shown that the three pressure means are not significantly different form each other. Therefore, Figure 15 represents a graph of esophageal pressure vs body weight for all dogs and all three measurement periods. The r value of 0.3164 is highly significant for the body weight and pressure correlation. Figure 16 is a graphical illustration of esophageal pressure vs body weight for each age group for the three testing periods. ANOVA procedures (Tables 19 & 20) have demonstrated significant age effects on pressure. However, graphically this relationship is not readily apparent. The r value for young dogs ($r = 0.5607$) is highly significant ($p<0.01$) and the correlation coefficient for the aged animals is also significant at the $p<0.05$ level. Because the correlation coefficient for adult dogs is not statistically significant, the regression line could actually be drawn anywhere on the graph, therefore, the slopes and intercepts of the three regression lines cannot be demonstrated to be significantly different.

Table 19A ANALYSIS OF VARIANCE TABLE, REGRESSION COEFFICIENTS, AND STATISTICS OF FIT FOR DEPENDENT VARIABLE ESOPHAGEAL PRESSURE$_1$

SOURCE	DF	SUM OF SQUARES	MEAN SQUARE	F VALUE	PROB > F
Regression	6	6.92929442	1.15488240	1.86784	0.1297
Error	23	14.22085225	0.61829792		
Corrected Total	29	21.15014667			

SOURCE	DF	PARTIAL SS	F VALUE	PROB > F
Age	2	4.46152405	3.60791	0.0423
Sex	1	0.02832517	0.04581	0.8324
Age*Sex	2	0.84566847	0.68387	0.5188
Wt	1	4.09576442	6.62426	0.0170

Table 19B

SOURCE	DF	SUM OF SQUARES	MEAN SQUARE	F VALUE	PROB > F
Regression	3	6.08256915	2.02752305	3.49861	0.0291
Error	26	15.06757752	0.57952221		
Corrected Total	29	21.15014667			

SOURCE	DF	PARTIAL SS	F VALUE	PROB > F
Age	2	4.49973573	3.88228	0.0326
Wt	1	3.64699910	6.29311	0.0187

Table 20A ANALYSIS OF VARIANCE TABLE, REGRESSION COEFFICIENTS, AND STATISTICS OF FIT FOR DEPENDENT VARIABLE ESOPHAGEAL PRESSURE$_3$

SOURCE	DF	SUM OF SQUARES	MEAN SQUARE	F VALUE	PROB > F
Regression	6	21.57727181	3.59621197	3.06441	0.0234
Error	23	26.99144819	1.17354123		
Corrected Total	29	48.56872000			

SOURCE	DF	PARTIAL SS	F VALUE	PROB > F
Age	2	12.88888252	5.49145	0.0112
Sex	1	0.78007072	0.66472	0.4233
Age*Sex	2	1.97114145	0.83983	0.5521
Wt	1	13.28555404	11.32091	0.0027

Table 20B

SOURCE	DF	SUM OF SQUARES	MEAN SQUARE	F VALUE	PROB > F
Regression	3	19.18177391	6.39392464	5.65700	0.0043
Error	26	29.38694609	1.13026716		
Corrected Total	29	48.56872000			

SOURCE	DF	PARTIAL SS	F VALUE	PROB > F
Age	2	12.73013472	5.63147	0.0093
Wt	1	13.12702482	11.61409	0.0022

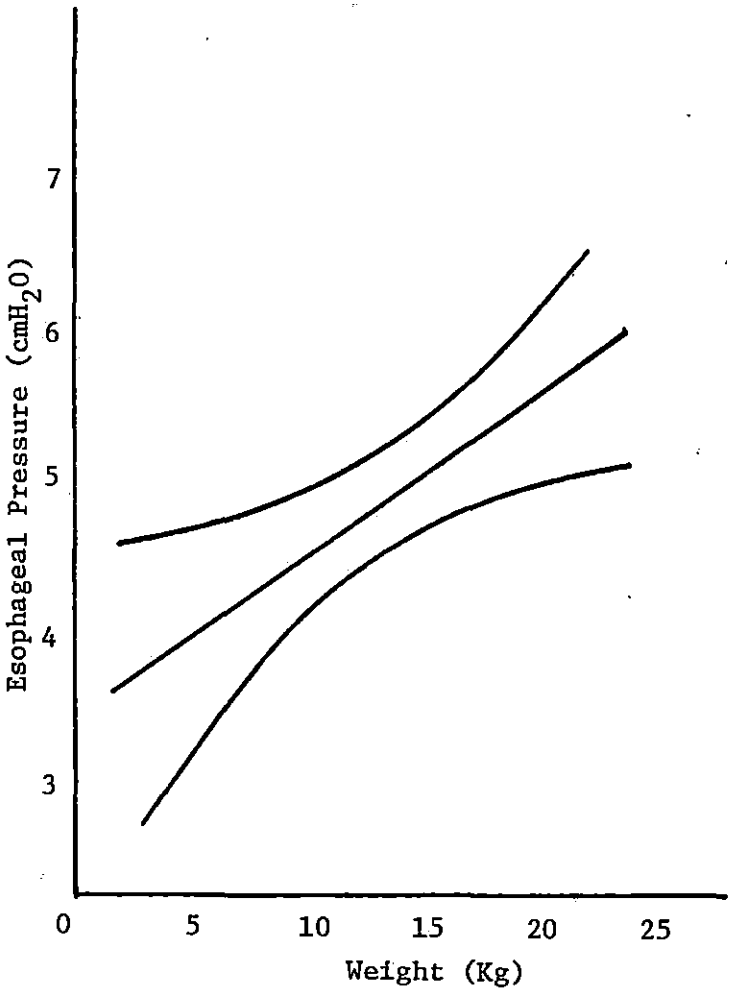


Figure 15. Esophageal pressure vs body weight in all dogs.
r = 0.3164 Y = 3.43 + 0.10(Wt)

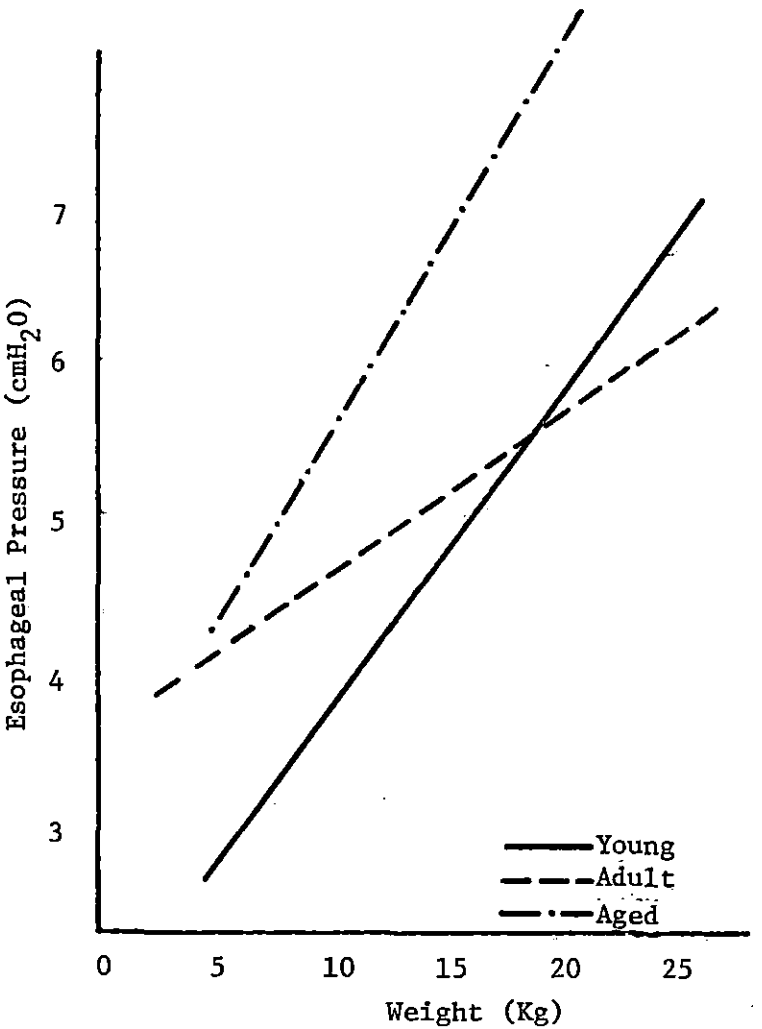


Figure 16. Esophageal Pressure vs body weight in each age group.
Young; r = 0.5609 Y = 1.59 + 0.19(Wt)
Adult; r = 0.3481 Y = 3.55 + 0.10(Wt)
Aged; r = 0.6711 Y = 3.08 + 0.23(Wt)

Lung Compliance

Analysis of variance tables for the dependent variable lung compliance are shown (Tables 21A & B and 22A & B). ANOVA procedures demonstrate that sex, age by sex interaction and weight do not significantly effect lung compliance. The independent variable age does significantly effect this parameter ($p<0.01$). This effect is expected since several investigators have reported lung compliance to be reduced in aged dogs.[81,111] However, the failure of weight to significantly influence compliance is surprising, especially since compliance has as components tidal volume and esophageal pressure which both have previously been shown to be significantly effected by body weight.

Figure 17 demonstrates the best fit regression line for lung compliance vs. body weight on all dogs for all three measurement periods. Although the r value (0.3927) is highly significant ($p<0.01$), this correlation coefficient is much less than reported by other investigators. With the absence of the strong correlation, it is anticipated that ANOVA procedures would be unable to find a significant weight effect on compliance.

Figure 18, a graph of body weight vs compliance for each age group, demonstrates that the regression lines for young and adult dogs run almost parallel. However, none of the r values for the individual age groups are significant. This is indicative of the variability within age groups, especially the aged group where the slope of the regression line is basically zero, making it imposssible to graphically illustrate the significant age effect.

Table 21A ANALYSIS OF VARIANCE TABLE, REGRESSION COEFFICIENTS, AND STATISTICS OF FIT FOR DEPENDENT VARIABLE $COMPLIANCE_1$

SOURCE	DF	SUM OF SQUARES	MEAN SQUARE	F VALUE	PROB > F
Regression	6	865.43124048	144.23854008	4.55933	0.0037
Error	23	727.62656552	31.63593763		
Corrected Total	29	1593.05780600			

SOURCE	DF	PARTIAL SS	F VALUE	PROB > F
Age	2	466.56204974	7.37392	0.0036
Sex	1	23.32379957	0.73726	0.3994
Age*Sex	2	123.47282320	1.95146	0.1634
Wt	1	20.11624085	0.63587	0.4334

Table 21B

SOURCE	DF	SUM OF SQUARES	MEAN SQUARE	F VALUE	PROB > F
Regression	3	723.15665428	241.05221809	7.20468	0.0014
Error	26	869.90115172	33.45773660		
Corrected Total	29	1593.05780600			

SOURCE	DF	PARTIAL SS	F VALUE	PROB > F
Age	2	475.88686808	7.11176	0.0037
Wt	1	47.36719935	1.41573	0.2449

Table 22A, ANALYSIS OF VARIANCE TABLE, REGRESSION COEFFICIENTS, AND STATISTICS OF FIT FOR DEPENDENT VARIABLE $COMPLIANCE_3$

SOURCE	DF	SUM OF SQUARES	MEAN SQUARE	F VALUE	PROB > F
Regression	6	1344.92500225	224.15416704	2.89717	0.0295
Error	23	1779.50861442	77.36993976		
Corrected Total	29	3124.43361667			

SOURCE	DF	PARTIAL SS	F VALUE	PROB > F
Age	2	610.79636539	3.94725	0.0327
Sex	1	66.09544438	0.85428	0.3649
Age*Sex	2	82.52183536	0.53329	0.5988
Wt	1	111.53853475	1.44163	0.2421

Table 22B

SOURCE	DF	SUM OF SQUARES	MEAN SQUARE	F VALUE	PROB > F
Regression	3	1187.84717981	395.94905994	5.31589	0.0057
Error	26	1936.58643685	74.48409373		
Corrected Total	29	3124.43361667			

SOURCE	DF	PARTIAL SS	F VALUE	PROB > F
Age	2	661.07732372	4.43771	0.0215
Wt	1	148.42532730	1.99271	0.1699

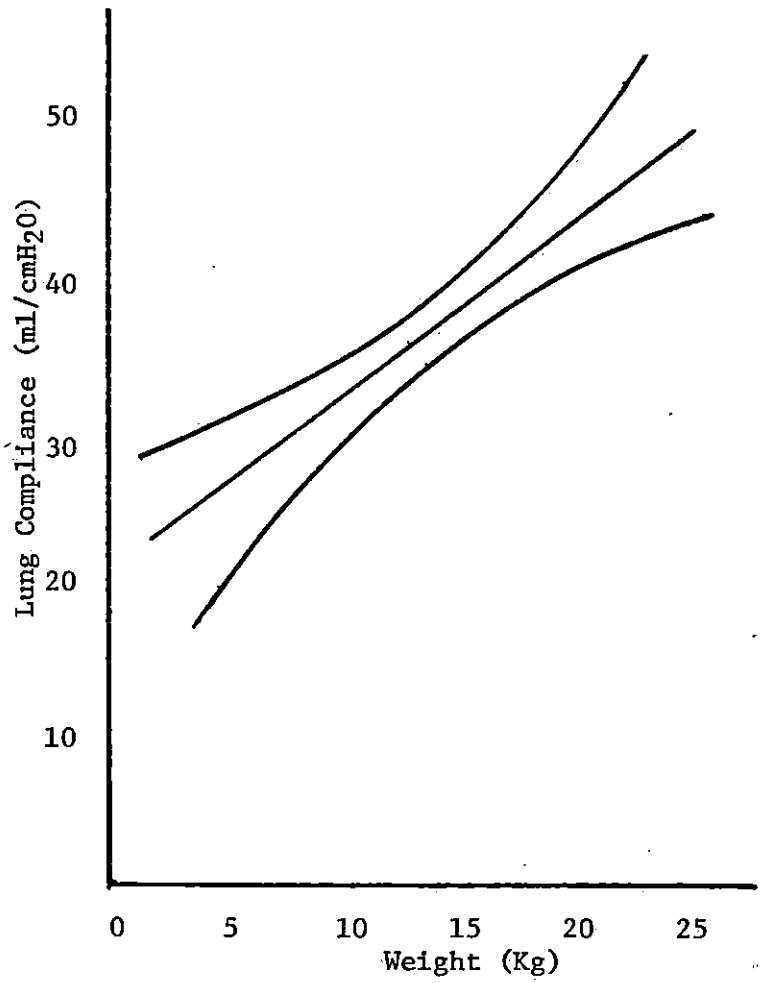


Figure 17. Lung compliance vs body weight in all dogs.
r = 0.3927 Y = 22.92 + 0.93(Wt)

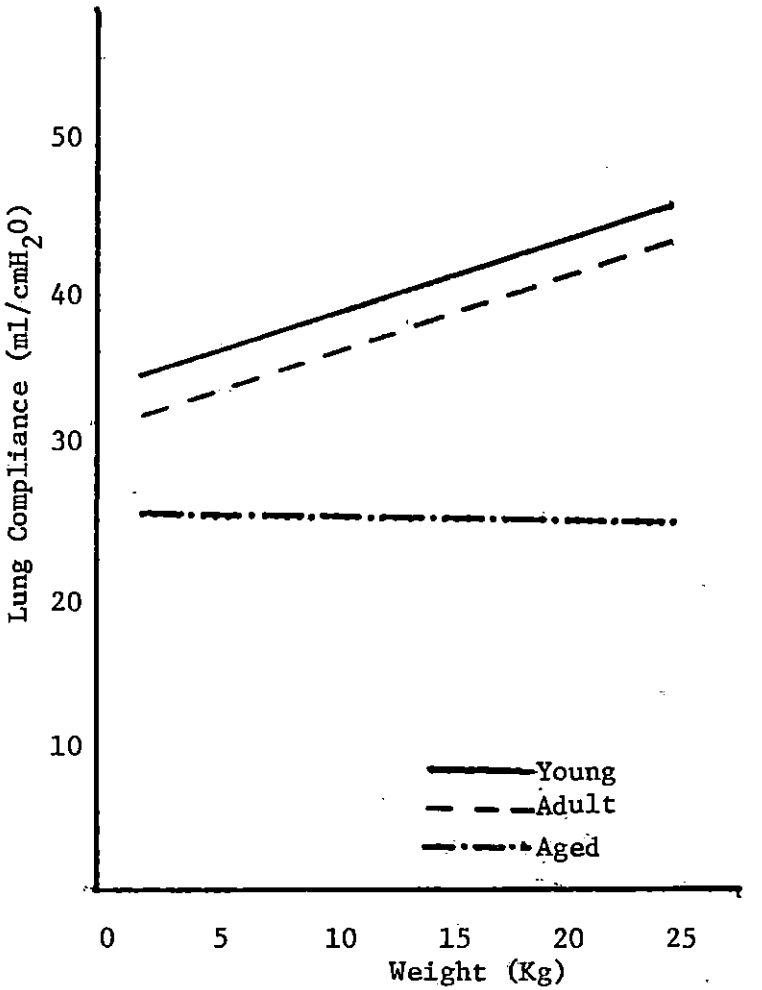


Figure 18. Lung compliance vs body weight for each age group.
Young; r = 0.2556 Y = 30.22 + 0.62(Wt)
Adult; r = 0.3153 Y = 29.07 + 0.54(Wt)
Aged; r =-0.0530 Y = 25.24 - 0.05(Wt)

Airway Resistance

Analysis of variance tables for the dependent variable airway resistance are presented (Tables 23A & B and 24A & B). The independent variables sex, age by sex interaction and weight do not significantly influence airway resistance in the dog. However, a highly significant relationship between age and airway resistance does exist. After sex and age by sex interaction effects were removed, age is found to have a highly significant effect on airway resistance ($p < 0.01$). The absence of body weight effect on resistance is vividly illustrated in Figure 19, a graph of body weight versus airway resistance for all dogs over the three measurement periods. The correlation coefficient is actually negative ($r = -0.0339$) as it is for aged dogs in Figure 20. In Figure 20 the correlation coefficients for young dogs ($r = 0.1081$), adult dogs ($r = 0.3904$), and aged dogs ($r = -0.0574$) are all insignificant. Although graphically (Figure 20) the differences in the regression lines for the three age groups appear to be different, the observation is not statistically substantiated since these regression (best fit) lines can actually be drawn anywhere on the graph. This figure does demonstrate that the airway resistance in aged animals is consistently higher than either young or adult dogs over the body weight distribution limits.

Table 23A ANALYSIS OF VARIANCE TABLE, REGRESSION COEFFICIENTS, AND STATISTICS OF FIT FOR DEPENDENT VARIABLE $RESISTANCE_1$

SOURCE	DF	SUM OF SQUARES	MEAN SQUARE	F VALUE	PROB > F
Regression	6	116.70272142	19.45045357	2.01313	0.1048
Error	23	222.22124795	9.66179339		
Corrected Total	29	338.92396937			

SOURCE	DF	PARTIAL SS	F VALUE	PROB > F
Age	2	72.63730205	3.75900	0.0377
Sex	1	0.43462409	0.04498	0.8339
Age*Sex	2	13.99009927	0.72399	0.5004
Wt	1	7.35143556	0.76088	0.3921

Table 23B

SOURCE	DF	SUM OF SQUARES	MEAN SQUARE	F VALUE	PROB > F
Regression	3	100.53129615	33.51043205	3.65477	0.0249
Error	26	238.39267322	9.16894897		
Corrected Total	29	338.92396937			

SOURCE	DF	PARTIAL SS	F VALUE	PROB > F
Age	2	97.76844474	5.33150	0.0114
Wt	1	3.94188332	0.42992	0.5178

Table 24A ANALYSIS OF VARIANCE TABLE, REGRESSION COEFFICIENTS, AND STATISTICS OF FIT FOR DEPENDENT VARIABLE $RESISTANCE_3$

SOURCE	DF	SUM OF SQUARES	MEAN SQUARE	F VALUE	PROB > F
Regression	6	171.41483678	28.56913946	2.62972	0.0429
Error	23	249.87120842	10.86396558		
Corrected Total	29	421.28604520			

SOURCE	DF	PARTIAL SS	F VALUE	PROB > F
Age	2	120.83080241	5.56106	0.0107
Sex	1	7.64835281	0.70401	0.4101
Age*Sex	2	13.03187415	0.59978	0.5619
Wt	1	25.74632926	2.36988	0.1373

Table 24B

SOURCE	DF	SUM OF SQUARES	MEAN SQUARE	F VALUE	PROB > F
Regression	3	146.78399190	48.92799730	4.63431	0.0101
Error	26	274.50205330	10.55777128		
Corrected Total	29	421.28604520			

SOURCE	DF	PARTIAL SS	F VALUE	PROB > F
Age	2	146.54015522	6.93992	0.0041
Wt	1	23.00829203	2.17928	0.1519

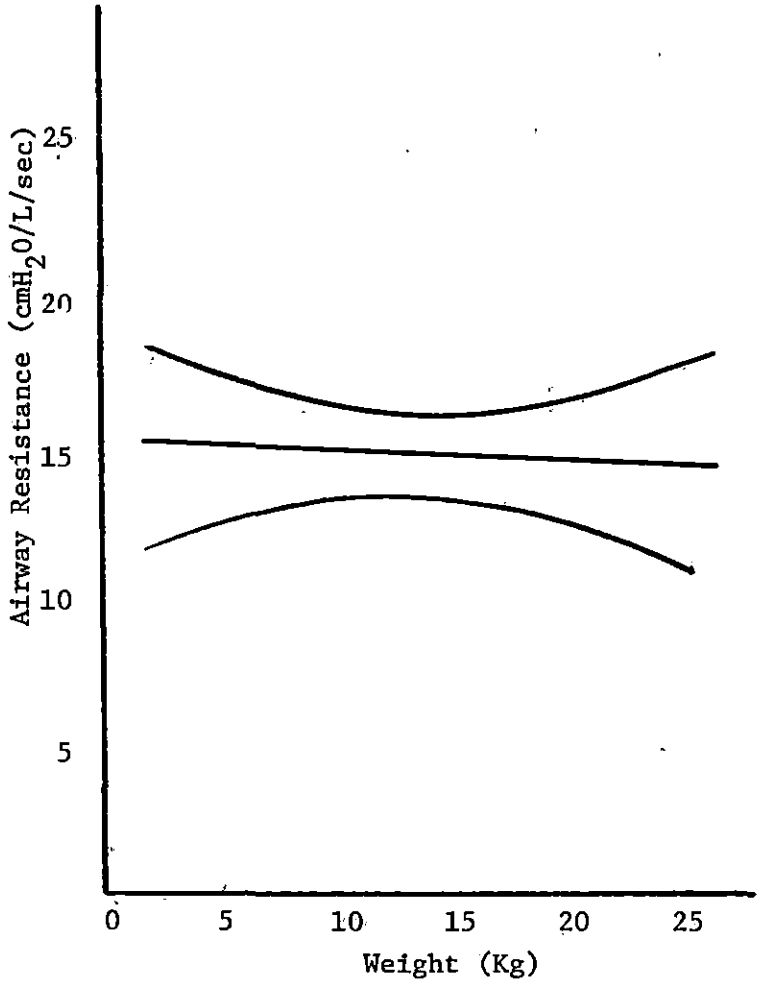


Figure 19. Airway Resistance vs body weight in all dogs.
r =-0.0339 Y = 14.84 - 0.03(Wt)

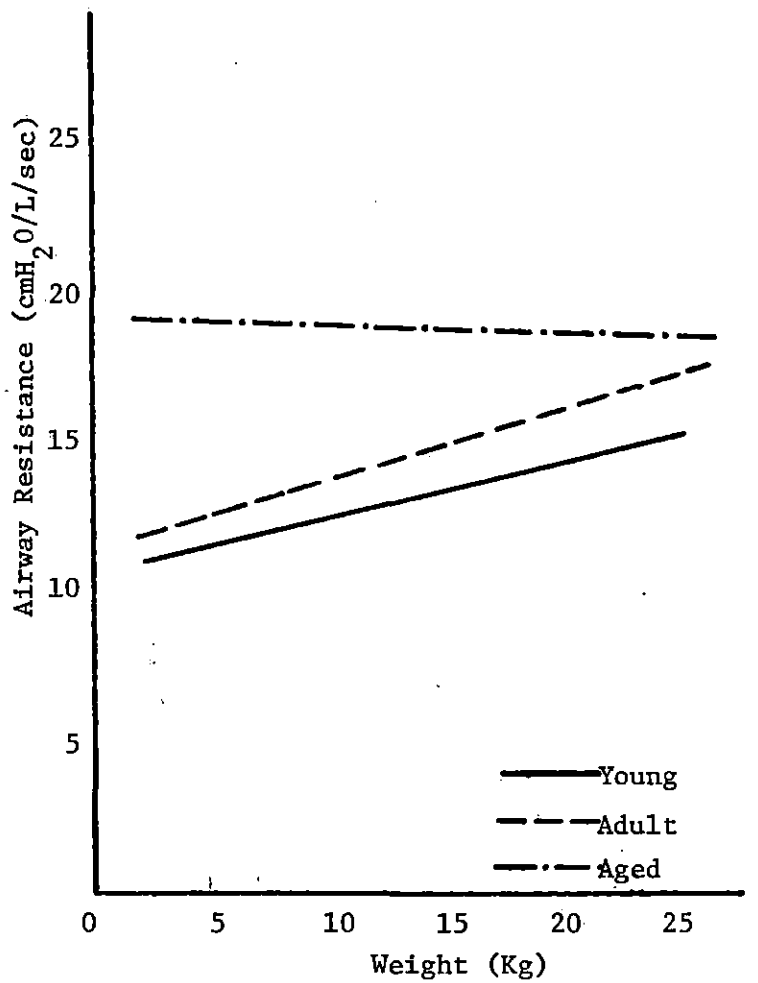


Figure 20. Airway Resistance vs body weight in each age group.
Young; r = 0.1081 Y = 10.69 + 0.17(Wt)
Adult; r = 0.3904 Y = 10.66 + 0.25(Wt)
Aged; r =-0.0574 Y = 19.32 - 0.07(Wt)

Respiratory Work

Analysis of variance procedures were not initiated for the mechanical parameter, respiratory work. Methods for calculating this parameter have been previously explained.

In the simple statistics section of the results, significant means differences ($p<0.05$)were found between the Wk/Kg_1 means. The young dogs values were significantly less than the other two groups.

Graphical illustrations (Figure 21) indicate that respiratory work is not influenced by the weight of the animal. The r value ($r = -0.0350$) substantiates this. In figure 22, the regression lines appear to be significantly different. However, even though the slopes and intercepts appear to be different, the r values are all insignificant, and as a result,statistically the lines are not different.

The other work parameter, Wk/min/Kg, was shown to also be age influenced. The aged dogs had significantly higher work values than the adult and young groups as shown in Table 5. Although this parameter is not graphically analyzed, correlation coefficients for Wk/min/Kg were significant ($p<0.05$) for the body weight and respiratory work relationship.

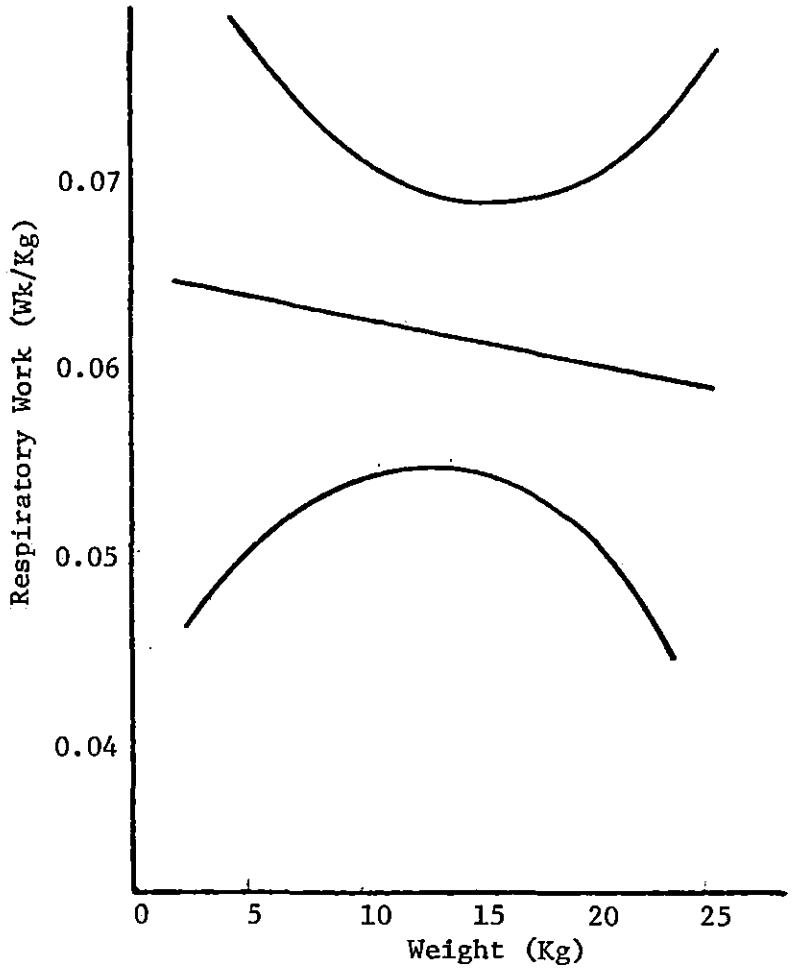


Figure 21. Respiratory work vs body weight in all dogs.
r = -0.0350 Y = 0.0626 + -0.0001(Wt)

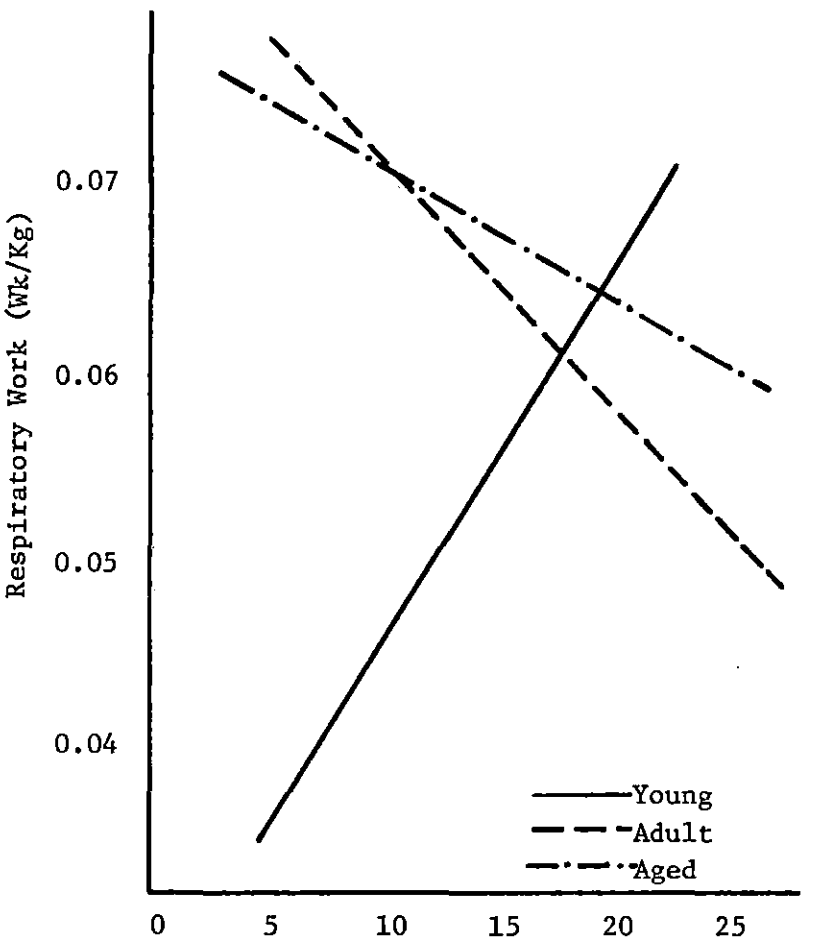


Figure 22. Respiratory Work vs body weight in each age group.
Young; r = 0.2411 Y = 0.02 + 0.002(Wt)
Adult; r =-0.2265 Y = 0.08 - 0.0001(Wt)
Aged; r =-0.1458 Y = 0.08 - 0.001(Wt)

Blood Gas Analysis

Femoral arterial blood samples were taken from 10 unanesthetized dogs. These serve as controls for comparisons of samples taken from dogs during the function measurement procedures. Respiratory rates, blood gas tensions, and pH are shown in the table below with means and standard deviations indicated. Further, the means and standard deviations for the experimental group is presented for comparison.

Table 25. Blood Gas Analysis in Control Group

Respiratory Rate	P_{O_2}	P_{CO_2}	pH
24	105.7	30.1	7.359
20	94.1	36.2	7.335
22	89.5	40.1	7.363
24	103.4	35.1	7.321
26	92.5	37.1	7.362
22	97.3	34.3	7.362
21	85.6	40.3	7.360
20	90.4	39.1	7.402
24	101.2	32.4	7.391
24	93.3	34.6	7.330
$\bar{x}$ = 22.70	95.30	35.93	7.350
S.D.= $\pm$0.63	$\pm$2.05	$\pm$1.05	$\pm$0.008
Blood Gas Analysis in Experimental Group			
$\bar{x}$ = 24.16	89.88	43.89	7.346
S.D.= $\pm$0.61	$\pm$9.20	$\pm$5.80	$\pm$0.054

Anova Result Summary

The following is a simple table indicating which independent variables significantly effect the various respiratory parameters. The X represents a significant effect.

Table 26. Analysis of Variance Summary Table

Parameter	Age	Sex	Weight
Respiratory Rate			
Heart Rate			
Tidal volume			X
Minute volume			X
Inspiratory velocity			X
Expiratory velocity			X
Esophageal pressure	X		X
Lung Compliance	X		
Airway Resistance	X		
pH			
P_{O_2}			
P_{CO_2}		X	

DISCUSSION

Introduction

The purpose of this investigation was to examine and evaluate the influences of sex, age and weight on respiratory function in the canine. Mean values, ranges, standard deviations, and significant correlations as well as the effects of each of the independent variables on respiratory function as determined by analysis of variance procedures have been presented.

The Respiratory Model

In the introduction of this paper, it was emphasized that prior to attempting a study of respiratory function, two major experimental design features must be considered. The first is that a respiratory model must be selected that will permit pulmonary function parameters to be measured that could be useful for eventual comparison with clinical values. It is desirable to obtain values that can be associated with an awake, normal dog and serve as base-line values for which to compare parameters of clinically ill, pulmonary disease dogs. The second consideration is that the design of the investigation must allow for an effective evaluation of the influences of age, sex and weight on function and permit appropriate statistical analysis.

Taking into account these two design considerations, it is apparent that the nature of the respiratory model dictates the state of the respiratory system of the animal at the time of function measurements, and this in turn determines how effectively the effects of age, sex and

weight on these pulmonary measurements can be evaluated.

It has been demonstrated that the respiratory system is probably the system most readily deranged by preanesthetic and anesthetic agents.[104,109,132] Three agents; Acepromazine, atropine, and Brevane were administered to each dog prior to function measurements. Because experimental design did not permit measurement of pulmonary function in normal awake dogs, it is necessary to use as controls function measurements obtained by other investigators utilizing similar methodology in unanesthetized dogs. In addition to comparisons with reported parameters, there are several cardiopulmonary parameters that were measured during the course of the current study that can serve as indicators of anesthetic influence.

Barbiturates, even in sedative dosages, have been shown to significantly influence the respiratory system.[74,119,127] Brevane, an ultrashort acting barbiturate, follows the pattern established for other barbiturates except that its action is of shorter duration; as the depth of anesthesia increases, respiratory minute volume changes from an initial increase during stage I to a definite decrease in stage III. This progressive decrease is attributed initially to a decreased respiratory frequency with adequate tidal volume, to an actual decrease in tidal volume in the surgical plane of stage III.[74,127] In the current investigation, the respiratory frequency dropped to low levels of 12 breaths/minute in several dogs shortly after administration of Brevane, but generally the initial frequency was in the range of 15-17 breaths/minute. This initial period of reduced frequency was quite transient

with rates returning to levels of 18-24 ($\bar{F}$ = 22) within three to four minutes after brevane administration. Tidal volume appeared adequate at this time and there was not a noticeable increase in tidal volume ascertained during the course of the three measurement periods.

A comparison of the means of the function parameters over the three measurement periods was shown previously (Table 9, page 70). No significant differences were shown to exist between mean frequency and tidal volume for each parameter over the three periods. In both cases there was a trend for an increase in frequency and tidal volume as the measurement periods progressed. However, the slight increase in both of these parameters is manifested by a significant increase in minute volume from period 1 to period 3 ($p<0.05$). Although this tends to indicate an initial respiratory depression was present in the model, comparisons with the values obtained by other investigators is necessary before any valid conclusions can be drawn.

Table 27 is a comparison of ventilation parameters reported by other investigators using techniques similar to this investigator. It is immediately apparent that two models are represented in the table; dogs anesthetized with barbiturates and unanesthetized dogs. The values from the present study included in the table are those measured during the initial period (period 1), within two to four minutes of administration of brevane. Frequencies in unanesthetized dogs range from 13 to 24[40,81,104,136] with a suggested breathing optimum of 22.[134] The mean frequency ($\bar{F}$ = 22) in the present study compares favorably with these reported parameters and is considerably higher than those reported

in anesthetized dogs.[21,50,94]

Over a wide range of body weights, dog lung volumes are proportional to body weight.[111] Although dividing lung volumes by body weight over such a small weight range is a questionable technique, an index of ventilation/Kg body weight is gained, crudely eliminating weight effects to facilitate comparison (Table 27).

Table 27. Comparison of Ventilation Parameters

Reference	Weight	Anesthesia	Frequency	Tidal volume	V_T/Kg	Minute volume	MV/Kg
Present	13.94	Brevane	22	164	11.72	3623	259.90
21	12.60	Pentobarb	21	144	11.42	3100	246.03
40	18.60	none	13	309	16.61	3878	208.49
50	19.10	Pentobarb	13	203	10.68	2819	144.15
81	9.10	none	20	186	20.43	3720	408.79
81	10.90	none	19	170	17.00	3230	296.33
94	--	Pentobarb	11	180	--	--	--
104	9.10	none	24	220	24.17	--	--
136	--	none	22	149	--	--	--

In dogs anesthetized with pentobarbital, the V_T/Kg range was 10 to 12 ml/Kg and in unanesthetized dogs the range was from 16 to 24 ml/Kg. The 11.72 ml/Kg observed in the present work falls into the range for anesthetized animals. However, to consider either frequency or tidal volume separately can lead to misinterpretations; minute volume is more representative of actual ventilation. When placed on a body weight basis, hypoventilation is apparent in some anesthetized models.[50] In the present study, the value of 259.90 ml/min/Kg is somewhat low compared

to the majority of the unanesthetized values but still signficant hypoventilation is not demonstrated. Further, if the mean minute volumes for the other two measurement periods (Period 2 and 3) were placed on a body weight basis, they would establish themselves well within the group of parameters obtained with unanesthetized models. Therefore, on the basis of volume comparisons, only slight respiratory depression is indicated in the present model.

This depression can further be assessed by blood gas analysis. Arterial blood gas tensions and pH when combined with alveolar ventilation has long been recognized as the best method of evaluating ventilation efficiency.[37] Values for blood gas tensions and pH obtained in this study can be compared to those of other investigators in Table 28.

Table 28. Arterial Blood Gas Tensions and pH

Reference	Anesthetic	P_{O_2}	P_{CO_2}	pH
Present	Brevane	89.87	43.89	7.346
Present	none	95.30	35.93	7.354
35	none	89.10	36.70	7.414
40	none	94.00	31.50	7.430
104	none	73.70	36.00	7.440
127	Pentobarb	71.10	53.00	7.250

There are few reports of blood gas analysis in anesthetized dogs. When compared to the unanesthetized values in the table, the P_{CO_2} in the present study is elevated. In the control group of animals run in this study (Tables 25 & 28) P_{CO_2} values were comparable to those reported in the awake animal.[35,40,105]

The elevated P_{CO_2} and the acidotic pH (7.346) appear to substantiate the respiratory acidosis that is characteristic of barbiturate anesthesia. Compared to values in the literature,[35,40,104] both the experimental and control groups in the present study are acidotic. However, previous blood gas analysis in this laboratory routinely produced values for pH in the 7.34-7.38 range in both unanesthetized and anesthetized dogs. The arterial pH is quite sensitive to sampling and storage effects,[105] but in this study suggested sampling procedures were carefully and consistently followed and determinations were routinely performed within 10 minutes of sampling. Sources of error in blood gas measurements have been reported to include; (1) characteristics of the polargraphic measuring system (especially the membrane neutralized to cover the electrode), (2) change in blood P_{O_2} prior to measurement, (3) and properties in the blood which might alter the measured tension.[110] However, the existence of these errors in the present study is slim. As as result, arterial blood gas tensions and pH measurements in this laboratory strongly suggest that the pH of the arterial blood is slightly more acidic than the 7.38-7.42 that is normally reported.[134] Further examination of this area is necessary.

To this point, arterial blood gas tension and pH parameters, as well as depressed minute/volume/Kg body weight, indicate that respiratory function is depressed. The amount of this depression is difficult to quantify, but it is important to be aware of the many physiological mechanisms that can be altered by this depression.

Hypoventilation is a common complication of general anesthesia.[132]

Brevane, like any general anesthetic, can depress the respiratory chemoreceptors and thus ventilation.[74,119,127,132] The ventilatory response to hypercarbia is depressed and varies in intensity with the anesthetic level. The depth of anesthesia in the present study produced a marginal acidosis, slightly elevated P_{CO_2} and slightly low P_{O_2} values. Although the arterial blood gas tensions are only slightly altered, this is indicative of gas exchange complications. The relatively normal minute volume makes it questionable if gas exchange disturbances can be totally attributed to decreased alveolar ventilation. Other considerations include increased venous admixture and changes in dead space.

The depressed arterial P_{O_2} can be in part attributed to an increase in venous admixture which commonly occurs during anesthesia. Although the mechanism remains unclear, venous admixture can result from "shunt-like" effects caused by perfusion of poorly ventilated alveoli or perfusion of alveoli where diffusion is impaired.[109] It has been suggested that ventilation to perfusion mismatching $(\dot{V}/\dot{Q})$ is a probable cause of increase venous admixture during anesthesia.[11,98] Finley et al. attributes spontaneous collapse of lung area as being responsible for poor gas exchange during anesthesia, resulting in increased venous admixture.[36]

In the present study, tidal volumes were lower than those reported in awake dogs.[40,81,104] Since minute ventilation was not significantly reduced as compared to reported values,[40,81,104] the dogs were breathing at normal frequencies but at a more shallow depth than would normally be expected. Low tidal volumes encourage airway closure which affects exchange either by creating poorly ventilated regions or by leading to cessation of ventilation if opening volume exceeds end-inspiratory

lung volume.[20,71] A significant decrease in right to left shunting has been reported in dogs mechanically ventilated with positive end-expiratory pressure,[109] apparently eliminating much of the venous admixture related to or caused by airway closure. Although "closing volume" is an attractive explanation for the altered gas exchange in this study, valid experimental proof for its contribution to hypoxemia is lacking.[109]

Piiper and associates, on the basis of experiments with anesthetized dogs, concluded that unequal distribution of diffusion to perfusion was the main factor involved in altered gas exchange during anesthesia.[108] Other workers have found that there are no significant changes in diffusion capacity in anesthetized dogs.[109] The possibility that CO and O_2 transfer may be carrier mediated in the human lung has been reported.[134] However, the role of facilitated transfer and anesthetic influences on this transfer in the dog has not been proposed.

Still other mechanisms that could be responsible for the altered arterial blood gas tensions in the study include an increase in alveolar dead space. Impaired elimination of CO_2 during anesthesia with an increase of arterial tension of 2-4 mmHg is reported.[109] The mechanisms underlying this change are related to an increase in alveolar dead space.[99] The anatomic dead space is also affected during anesthesia by preanesthetic agents and is significantly increased by atropine.[118] It is further altered by the position of the head and neck. In man an extended neck and protruded jaw can double the anatomic space but effects in canine have not been examined.

Mismatching of ventilation to perfusion can occur if pulmonary blood distribution does not match with the distribution of ventilation.

The bulk of the evidence suggests that regional distribution of pulmonary blood flow remains primarily gravity dependent during anesthesia.[109] The sternal position of the dogs in this study should encourage blood flow to be normally distributed, suggesting that intrapulmonary gas distribution changes would be responsible for mismatching of ventilation to perfusion. FRC measurements are necessary to determine distribution changes.

Functional residual capacity measurements are routinely performed in the canine, unfortunately, FRC was not determined in the present study. FRC is reduced during anesthesia in man in the recumbent position[37,109] and is decreased in the anesthetized dog.[32,39,40] Mechanisms are not clear, but it is suggested that a change in chest wall mechanics is responsible. Westbrook found a right shift of the chest-wall P-V curve shortly after induction of anesthesia, indicating changes in chest wall properties. Gas trapping has also been suggested for the change in FRC[109] as has the position of the patient during the actual measurement. Gillespie placed dogs in three different body positions and was unable to demonstrate significant differences in FRC in unanesthetized dogs but did demonstrate a significant decrease during anesthesia.[39] One can conclude that anesthesia apparently alters intrapulmonary gas distribution and that this can be partly explained by a decrease in FRC.

Respiratory mechanics are directly responsible for intrapulmonary gas distribution. It follows then that any altered distribution seen during anesthesia could be the result of changes in pulmonary mechanics. In the present study, lung mechanics, specifically lung compliance and airway resistance, were measured shortly after administration of

brevane until the dog began resisting measurement procedures. It is reported that these parameters are altered during anesthesia and can disturb an animal's ventilation and gas exchange efficiency.[39,40,132] If the three measurement periods are considered for dynamic lung compliance (Table 9, page 70), the three compliance means were not significantly different. However, there was a trend for an increase in C_L as the measurement periods progressed. Again, this increase is so small that it is necessary to compare the values of the present study with reported parameters in order to assess these measurements. Table 29 is a comparison of the present values with those reported in the literature.

Table 29. Reported Values for Dynamic Lung Compliance (DC_L) and Airway Resistance (R_A)

Reference	Weight	Anesthesia	DC_L	R_A
Present	13.94	Brevane	38	14.0
2	10-15	Pentobarb	51	-
10	9-16	Pentobarb	84	-
21	12.6	Pentobarb	40	-
31	5-13.8	none	46	-
40	18.6	none	97	1.3
81	6.6-13.6	none	53	13.0
83	-	none	75	8.6
104	9.1	none	48	10.4
130	-	Pentobarb	30-75	0.6-3.7
136	12.0	Pentobarb	38	14.0

The dynamic lung compliance value of 38 ml/cmH_2O in the present study is lower than reported values regardless of the anesthetic state of the dog. This strongly indicates that another mechanism other than anesthetic effects is responsible for this low value. This is discussed in more detail in the subsequent section.

Lung compliance does decrease during anesthesia.[31] This decrease starts shortly after induction with the largest portion of the decrease coming within the first 10 minutes after induction.[88] The mechanisms responsible for this decrease are for the most part not understood. Anesthetics or premedicants may have a direct pharmacological effect on lung compliance, possibly by constriction of alveolar ducts or respiratory bronchioles but this has never been demonstrated. However d- tubocurarine has been shown to decrease lung compliance, presumably by releasing histamine.[109] Airway closure may reduce lung compliance through the reduction in the number of distensible units accessible to ventilation, but again, this is only conjecture at this time.[109] Mead and Collier observed progressive atelectasis and a decreased lung compliance in dogs, observing atelectatic regions in the dependent lungs on post mortem following extended periods of anesthesia.[88] Further, it has been demonstrated that there is a disproportionately large reduction in lung compliance than in lung volume in anesthetized dogs.[15,77,88] This suggests that another mechanism, a change in surface tension in the lung unit may be contributing to the reduction in compliance. Possible causes include changes in lung air configurations,[109] high transpulmonary pressures that result in abnormal surface tension in the lungs, or direct effect of anesthetics on surfactant. Lipid soluble anesthetics, such

as halothane and chloroform, can change surfactant in excised, unperfused dog lungs.[109] The possibility of intravenous agents having a direct effect on surfactant has not been examined.

As a result, the low compliance values of the present work could be attributed to anesthetic effects, but the possible mechanisms involved could be any number of those discussed. Among these mechanisms, the depressed tidal volume of this model does allow for airway closure to play a role, but at this time, this phenomenon is only conjecture. Table 9 does indicate a gradual increase in compliance from induction. However, since it has been demonstrated that the major portion of the compliance reduction in anesthesia occurs during the initial minutes after induction, one would expect greater difference between mean compliance values from period 1 to period 3 if the compliance was initially reduced. The possibility that compliance was reduced for the duration of the testing periods is unlikely since the dogs were awake and alert for the final two measurements, certainly not in the stage of anesthesia where lung mechanics are normally altered.

The other mechanical parameter, airway resistance, is inversely related to lung volume and presumably this is also true of regional resistance in the lungs. Airway resistance increases during general anesthesia.[42,74,113,124,132] Whether this increase is due to altered lung volumes during anesthesia or due to a direct pharmacological action of the anesthetic and preanesthetic agents on bronchial or bronchiole diameter is not certain. Atropine, a common preanesthetic agent that was used in this study, decreases airway resistance in anesthetized dogs but this is not clinically noticeable.[128] The values

for airway resistance reported in the literature are quite variable. Only part of this variation can be attributed to the difference in anesthetized and non-anesthetized animals, the rest is attributed to different measurement procedures. The R_A of 14 $cmH_2O/L/sec$ in the present study is higher than any reported. Anesthetic influence could be responsible for a part of this, but this value does not appear different from those reported by Dubin[34] and others in unanesthetized dogs.[81,104] Different measurement techniques are believed responsible for the differences in resistance values.

Several times during the course of this discussion, the effects of preanesthetic agents on lung function has been mentioned. Acepromazine, a phenothiazine derivative, was found to be necessary to eliminate the tremors and excitement that accompanies brevane utilization, besides reducing the necessary dosage of barbiturate considerably. Although phenothiazine derivatives are notorious for hypotensive effects, no significant effects on pulmonary function are reported in dog with acepromazine.

Atropine was used in this study to reduce secretions of the respiratory tract and salivary glands and to inhibit effects of vagal stimulation on the cardiovascular and respiratory systems. Attempts to intubate dogs and application of the topical anesthetic to the laryngeal area was futile without having the animal atropinized. Therefore, the side effects of atropine on the cardiopulmonary system must be recognized. Atropine was quite effective in blocking the effects of the vagus on the sinoatrial node, for the mean heart rate shortly

after administration of atropine was 158 beats/minute. Atropine also decreases airway resistance through its action on bronchial and bronchiolar tone, and a similar mechanism explains its influence on dead space. Increases in dead space of 55% is reported by atropinization of dogs during spontaneous respiration.[118] Although acepromazine is also an autonomic depressant, its effects on dead space and resistance are not known.

The increase in dead space in the atropinized dog could possibly be the explanation of the mild respiratory acidosis present in the present model. Certainly this dead space increase contributes to altered gas exchange since alveolar ventilation = F (tidal volume - dead space). With minute volumes being moderately depressed, a significant increase in dead space could decrease effective alveolar ventilation just enough to cause a mild acidosis.

Regardless of the mechanisms responsible, the amount of respiratory depression due to anesthetic and preanesthetic agents cannot be quantified in this model. No matter what the extent of this depression, the respiratory system does not appear to be responding to these disturbances. This could either indicate that only slight, insignificant depression is present, or this could indicate that some of the system's ability to intricately respond to slight changes in blood gas tensions has been lost. Apparently, without simultaneous unanesthetized controls to compare, these questions cannot be answered.

Whatever the amount of depression, the primary concern in this study is to decide whether this depression affects the ability to evaluate

age, sex and weight influences on respiratory function.

In most domestic animals, no statistics are available demonstrating a sex or specific age relationship to barbiturate. The exceptions are the extremes, the very young and the very old, but dogs falling into these two groups were not used in the current study. The administration of a fixed dose of barbiturate on a body weight basis produces marked variation in response. Each animal's body has different proportions of body fat and muscular structure.[126]

One can conclude that the anesthetic and preanesthetic agents do confound the evaluation of age, sex and weight on function, but that this effect appears to affect all animals involved in a similar manner. Very few parameters for the 30 dogs are completely different from the mean indicating that all animals are in similar experimental conditions. Therefore, this model does lend itself to an examination of the effects of age, sex and weight on pulmonary function.

Age, Sex And Weight Effects

It is again convenient to separate the various parameters measured into three categories to facilitate discussion; (1) ventilation parameters, (2) lung mechanics, and (3) blood gas analysis.

Ventilation parameters; tidal volume, minute volume, and inspiratory and expiratory velocity are reported to be correlated to body weight.[30,48] The findings of the present study is in agreement in that all these parameters were found to be correlated to weight at the $p<0.0001$ level. ANOVA procedures examined the effects of the independent variables age, sex, weight and the first order interaction of age by sex on ventilation

parameters. The sex of the animal, animal age, and the age by sex interaction had no significant effect on ventilation parameters. Differences among dogs can solely be attributed to weight differences. Therefore, if nomograms of these parameters were made, the sex and the age of the dog would not have to be considered, only the weight of the dog must be known.

Flow velocities measured in this study are seldom discussed in the literature, however, inspiratory and expiratory durations have proven useful as screening devices in ventilation disturbances.[16,17] They have been successfully used in the physiological assessment of allergic asthma in dogs and monkeys.[94] In human pulmonary function testing, flow velocities are helpful when applied to flow volume studies and vital capacity maneuvers, but because these require voluntary breathing patterns, efforts to apply these tests to animals are without success.

The strong correlation ($p<0.0001$) that exists between weight and flow velocities is expected. Because frequency is not weight dependent, small and large dogs apparently breathe at the same frequency. Therefore if no pathology is present, inspiratory and expiratory durations would be roughly the same in all sizes of dogs meaning that the only way a large dog is able to move the greater tidal volume at the same frequency necessary for proper ventilation, is by increasing flow velocity.

The pulmonary mechanical parameters measured in this study, lung compliance, airway resistance, and respiratory work, can provide

a sensitive and reliable evaluation of the mechanical deficit present in pulmonary disease syndromes.[31,104] Compliance values for the thirty dogs average 35.88 ml/cmH_2O for the three periods. The values ranged from 18.77 to 66.17, but the standard deviation (8.00) indicates most of the values to fall between 27 and 42 ml/cmH_2O. These values were low compared to those reported in the literature (see Table 29). A definite decrease in lung compliance with anesthesia has been reported.[31,40] The compliance values that were recorded immediately after administration of brevane but not included in the first period measurements were little different from the mean compliance value for the first period. The increase in compliance with time from induction could be indicative of response to early depression, but this should not affect independent variable evaluation unless experimental treatment affected individual animals differently and this does not appear to be the case.

Compliance is shown to be a weight dependent variable. Dynamic lung compliance, the ratio of tidal volume to the change in pressure is quantitatively influenced by either changes in tidal volume or pressure. In this study, it was demonstrated that when the tidal volumes for the 30 dogs are placed on a body weight basis, the tidal volume is less than reported for awake dogs. This could be responsible for the lower compliances reported here but this is dubious since there was only a minor reduction in tidal volume. However, the pressure value is critical in calculating dynamic lung compliance. In this study, the intrapleural pressure changes were measured by an esophageal

balloon. This is a proven safe and effective method of estimating intrapleural pressure changes.[31,40,41,91,104] Some investigators use intraesophageal pressure changes directly in calculating lung compliance[31] while others measure the difference between the pleural cavity and the mouth which is defined as transpulmonary pressure.[17,21,40] Transpulmonary pressure changes are normally less in raw value than esophageal pressure changes and as a result, if tidal volume remains constant, those methods that calculate compliance using transpulmonary pressure will obtain higher values for lung compliance. This perhaps better explains the low compliance values recorded in this study than does depressing effects of anesthetic and preanesthetic agents.

However, the difference in methodology does not discourage an analysis of the three age groups and their lung compliance. Analysis of variance procedures indicate that the age of the animal has a significant effect on lung compliance. In the canine, a decrease in lung compliance is associated with increased age.[81,111,112] This relationship is further supported by comparisons of mean values for the three age groups. The mean compliance of the aged dogs (24.14) was found to be significantly lower ($p<0.05$) than the compliance means of the young (40.91) and adult (38.86) dogs. ANOVA procedures further indicated that sex and the age by sex interaction do not influence compliance. It is surprising that these analysis procedures do not find weight to be a significant effect. This finding certainly indicates that it is important to not only consider an animal's weight when comparing compliance values, but also one must consider the animal's age. Therefore, the typical nomograms that have been

constructed for compliance and body weight can be mis-leading. This study indicates that the age of the animal is in fact a more important determinant of lung compliance than is the animal's weight. For this reason, when nomograms are prepared, it is strongly recommended that age groups, however divided, be treated separately.

Airway resistance is the ratio of the change in esophageal pressure to the expiratory velocity. A mean value of 14.46 $cmH_2O/L/sec$ was found for the three testing periods. This value is high as compared to other reported R_A parameters.[40,81,104] Again, perhaps the method of measurement is more responsible for this elevated value than are anesthetic and preanesthetic effects. Using intraesophageal pressure changes instead of transpulmonary pressure will provide an increased calculated airway resistance if velocity remains constant. The influence of anesthetic agents should not be overlooked. Airway resistance is increased during general anesthesia in the dog.[109,123,132] Further, atropine has been shown to decrease airway resistance,[128,132] counteracting some of the resistance attributed to anesthesia. The use of the endotracheal tube system instead of the face mask or body chamber can alter resistance values, but the tube system, if appropriate sized endotracheal tubes are used, is actually a lower resistance system than the other two. Taking these factors into consideration, the method of measuring the pressure parameter seems responsible for the disparity that occurs between the present study and the literature. However, because all animals in the present study, regardless of age, sex or weight were all measured in the same manner, the effects of these independent variables on airway resistance can be evaluated.

Airway resistance, like dynamic lung compliance, is a parameter that is significantly influenced by age ($p<0.01$). Sex, age by sex interaction, and body weight have little effect on resistance in the dog. This contradicts the findings of Crosfill and Widdicombe who found that resistance was a weight dependent parameter.[21] Other investigators do not list airway resistance with the function parameters considered to be weight related.[113,136] Figures 19 and 20 lend graphical support to this conclusion since the slopes of the regression lines are essentially zero. However, when comparison of clinically ill animals with normal parameters is being done, the age of the animal is a necessary consideration.

The work of respiration is the final mechanical parameter that was analyzed. ANOVA procedures were not used for this variable, however, simple statistics and linear regression procedures work, as expressed in a Work/Kg basis, is not weight dependent. It should be emphasized that the values for work used in this study were not arrived at by integration of the pressure-volume curve. The Work/Kg is the product of tidal volume multiplied by esophageal pressure change and placed on a KG of body weight basis. Figure 22 indicates that an age effect is possibly present, but because of the very low correlation of coefficients, no statistical conclusions can be drawn. Simple statistical analysis of means indicate that work is age dependent. The older animals consistently had higher work values than the other two groups ($p<0.05$). There is a paucity of literature considering work as a possible parameter in evaluating disease conditions.

The final group of parameters, blood gas tension and pH, have been discussed in depth in regards to anesthetic and preanesthetic agent effects. ANOVA procedures revealed that none of the independent variables significantly influence these parameters. Mean comparisons did reveal a significant difference between male and female dogs. This difference cannot be explained.

Model Limitations

Anytime physiological procedures are used that do not have established classical foundations, experimental obstacles are initially encountered. The purpose of this study was to establish normal respiratory parameters in the canine and then to examine these parameters for the effects of age, sex and weight. A new respiratory model was selected; a tranquilized, atropinized, sedate animal was intubated and pulmonary function was measured. The model itself proved to be a confounding factor in that parameters recorded did not simulate values expected for normal, awake dogs. However, this model did not show the severe respiratory depression that other investigators routinely encountered when using anesthetized dogs. The respiratory frequencies that sometimes are reduced to 4-6 breaths/minute in studies[50] were avoided in this model. Frequency variability was minimal with sixty-eight percent of the dogs having a frequency between 17 and 27 breaths/minute.

Further, although the 30 observations compare favorably with the number used in other reports of normal parameters, many correlations were insignificant because of the inherent variability within the thirty dogs. Complicating factors contributing to this variability

include the fact that when selecting animals from an open colony, no control of breed was available and more importantly, little or no history on each dog was known. Ages and disease status were two crucial factors that were not known. Judging from teeth characteristics, the adult group was much closer in age to the young dogs with the mean age of the 30 dogs being around 3 years of age. This can partially explain why the adult dogs and young dogs seldom demonstrated significant differences for the various dependent variables.

The aged group, only 5 in number, consistently showed the most variability for each of the parameters, often times showing negative correlations where population trends were going in the other direction. Part of the statistical problems associated with the aged group could be eliminated by increasing the number of observations. Originally 36 dogs were involved in the experiment. Because of sampling problems or instrument problems, six dogs were dropped from the analysis keeping the parameters with equal numbers enhancing statistical testing. Of these six dogs dropped from the experiment, three were aged animals. All three demonstrated low compliances (mean compliance of 24.19) and high airway resistances (mean resistance 17.09). The addition of these dogs to the study could significantly influence the linear regression and ANOVA procedures. However, this may be a bit optimistic for several dogs within the aged group were very erratic in their response and provided so much variation that it is questionable if these dogs were in fact normal, healthy animals. Respiratory infections and canine distemper have been present in the open colony from time to time. Whether these dogs had suffered pulmonary pathology or had ever shown signs of

respiratory disease is not known.

One further complication was the fact that mixed breeds were used in this study. Other investigators use primarily beagles.[40,104] The possibility that breed differences could be a confounding factor in determining pulmonary function parameters should be considered. Thoracic cavity and chest wall features that some breeds possess could influence respiratory function, especially the mechanical measurements. This is still another area that needs further investigation.

The method of using esophageal pressure in computing lung compliance and resistance values is established, but this investigator feels that subsequent work should utilize transpulmonary pressure changes. The use of intraesophageal pressure for all animals in this study allows for age and sex group comparisons, but it does make comparisons with reported parameters in the literature difficult.

In several instances within this paper, the need for functional residual capacity measurements has been demonstrated. FRC is a diagnostic parameter that is significantly altered in emphysema, asthma, cystic fibrosis and other restrictive and obstructive diseases. Further, FRC measurements are necessary for calculating specific compliance, a ratio of dynamic lung compliance and FRC that has proven to be more indicative of altered mechanical function than is dynamic lung compliance alone.

One final limitation must be considered. This is not unique to the present repiratory model, but is present in all studies of respiratory function in animals; limitations of the functions tests themselves. Do the physiological tests applied to canine pulmonary function evaluation possess the sensitivity necessary to be of diagnostic value? Certain

investigators in the human pulmonary fields emphasize that even routine compliance measurements are of little diagnostic significance if they are not measured during voluntary breathing patterns.[17,18] Admittedly, dynamic lung compliance and airway resistance parameters are not sensitive indicators of peripheral airway pathology unless the disturbance is extensive. Hamlin and Smith studied respiratory function and measured airway resistance after introducing a 50% stenosis of the trachea and found that values for resistance did not differ significantly from normal, causing them to question the confidence they had placed in their mechanics measurements.[50] Although use of these function tests has not been reported in clinical conditions in evaluating naturally occurring disease, manipulative and induced disease studies indicate that measurements of ventilation parameters, pulmonary mechanics, and blood gas analysis can provide a sensitive and reliable evaluation of respiratory deficit in pulmonary disease and can facilitate clinical diagnosis and evaluation of therapy. Applications of pulmonary function tests in combinations, emphasizing interrelationships between the various parameters is essential in canine studies, especially since the voluntary breathing patterns necessary in the more sensitive tests, will never be realized.

CONCLUSION

The influence of age, sex and weight on pulmonary function in the sedate canine has been presented. The tranquilized, sedated, intubated respiratory model facilitated pulmonary function measurements without a severe compromise of the normal physiological state of the respiratory system.

Although the effects of the anesthetic and preanesthetic agents on respiratory function have been emphasized, their effects were unable to be quantified. However, it was determined that whatever respiratory depression was present in the model did not significantly interfere with the evaluation of the effects of the independent variables; age, sex, and weight on the various respiratory function parameters.

In this study, sex did not influence the animal's respiratory function. The first order interaction of age by sex also had no significant effect on any of the pulmonary measurements. The weight of the dog was found to significantly effect all respiratory parameters with the exception of airway resistance and lung compliance. The age of the animal was demonstrated to have a significant influence on esophageal pressure, dynamic lung compliance, and airway resistance. This effect makes it mandatory to consider age of the animal as well as his weight when evaluating selected respiratory parameters.

Although the model's immediate clinical applicability is questionable, it is an easy and efficient method of evaluating respiratory function.

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