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The Altered Configuration of the Chronically Hyperinflated Thorax

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THE ALTERED CONFIGURATION OF THE CHRONICALLY HYPERINFLATED THORAX

by

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VITA

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CHAPTER I.

INTRODUCTION

Chronic hyperinflation of the human thorax occurs most often as a result of chronic obstructive pulmonary disease (COPD), with the primary event being an increase in lung volume due to a loss of lung elastic recoil. In response, the thorax[1] enlarges to maintain the ability to develop adequate negative pleural pressures to produce inspiration. To increase thoracic volume, the thorax must reposition one or both of its two basic components, the rib cage and diaphragm. This results in alterations of the length and position of the respiratory muscles which can significantly affect their function. Generalized shortening of the inspiratory muscles places them at a suboptimal position on their force-length curve (Kim et al., 1976). This is reflected in the decreased maximal inspiratory pressures observed with acute and chronic hyper-inflation (Rahn et al., 1946; Sharp et al., 1968). With hyperinflation, 3the normal parallel arrangement of the costal and crural components of

[1] For the purpose of this thesis, the "thorax" will be considered as defined in the Gould Medical Dictionary : The portion of the trunk above the diaphragm and below the neck. The framework of bones and soft tissues bounded by the diaphragm below; the ribs and sternum in front; the ribs and thoracic portion of the vertebral column behind; above, by structures in the lower part of the neck. For operational purposes it can be thought of as two components, the rib cage and the diaphragm.

the diaphragm can change into a series relationship (Macklem et al., 1983). The resulting series mechanical linkage is unable to generate the equivalent force as the normal parallel arrangement and therefore is less able to tolerate heavy loads. If the radius of curvature of the diaphragm is increased, the diaphragmatic tension required to produce the same amount of transdiaphragmatic pressure is increased (Sharp, 1983). Extreme hyperinflation has been suggested to result in both external and internal layers of intercostal muscles functioning as primarily expiratory muscles due to the altered position of the rib cage (Macklem, 1984). Global effects of hyperinflation include an increased oxygen cost of breathing for both normals with acute hyperinflation (Collett and Engel, 1986) and in COPD patients (Rochester, 1984). Acute hyperinflation has also been shown to increase diaphragmatic fatigability in animals (Farkas and Roussos, 1984). These types of altered respiratory mechanics are felt to account for part of the respiratory dysfunction observed in subjects with COPD (Macklem, 1980).

The literature contains numerous investigations of a variety of aspects of chronic thoracic hyperinflation. In general, these studies examine individual aspects of the thorax or view the thorax in a more global perspective. These studies have resulted in our current concept of thoracic hyperinflation, which as implied by the literature, is a progressive elevation of the rib cage and lowering of the diaphragm. Without solid evidence, these studies suggest that changes occur in the rib cage and diaphragm in a progressive, simultaneous manner and to similar degrees, dependent on the extent of hyperinflation. This concept lacks specific details of the alterations of the components of

the thorax in reference to each other or to fixed structures (i.e. the spine). Overall, the effects of chronic hyperinflation on the position and movement of thoracic components and respiratory muscles are not clearly understood.

The working hypothesis of this thesis is that the pathologic alterations in configuration and movement of the thorax are not simple and uniform progressions of rib cage elevation and diaphragm lowering. Rather, chronically hyperinflated subjects are projected to have wide variability in the alterations of these two components of the thorax. Thus, in some subjects for example, the rib cage could be elevated predominantly, while in others diaphragmatic lowering would predominate. Many intermediate combinations would also be possible. Different rib cage-diaphragm configurations in chronic hyperinflation could result in different respiratory muscles being affected in subjects with chronic hyperinflation. Given the different mechanical and electrophysiologic properties of the various respiratory muscles (Sharp and Hyatt, 1986), different patterns of adaptation could produce physiologically different thoracic mechanics in subjects having similar degrees of hyperinflation. Because COPD subjects are frequently categorized both clinically and experimentally by the extent of hyperinflation, the results of this thesis may improve the understanding and interpretation of both clinical and experimental observations of subjects with COPD.

Therefore, the purpose of this thesis is to characterize the alterations of the human thorax occurring in chronic hyperinflation. It is anticipated that the results will improve the understanding of the altered thoracic mechanics which occur in this common pulmonary disease state.

CHAPTER II.

LITERATURE REVIEW

Current concepts on the alterations occurring in the thorax with chronic hyperinflation developed from initial observations made at the beginning of this century. Three major methods of investigations of this subject have been utilized. The oldest method utilized roentgenography to view the rib cage and diaphragm. These roentgenographic studies combined with clinical criteria, pathologic examination of the lung and/or pulmonary function testing, were the primary method of investigation until the late 1960's. Physiologic studies followed, utilizing methods which closely examine respiratory pressures, volumes, movement and muscle activity. This type of study continues to be used today in evaluation of subjects with chronic hyperinflation. Recently, animal models of chronic hyperinflation have been developed, providing an insight into this process which was previously unavailable.

A. Radiographic Studies

1. Early period

Following Roentgen's description of the use of X-ray to study human structures in 1895, Thomas Edison produced fluoroscopy machines in the U.S. the following year. This resulted in numerous generalized radio-

graphic descriptions of subjects with emphysema, consisting of hyperlucent lungs and low, flat, less mobile diaphragms (as outlined in a historical review by Hawes, 1987). In 1917 Hoover outlined the function of the respiratory muscles as he had determined from numerous animal studies and human observations, explaining and resolving the controversy about the function of the diaphragm being an inspiratory or expiratory muscle. His fluoroscopic observations of subjects in whom "...the entire lung is emphysematous to a sufficient degree..." led to the description of Hoover's sign, the abnormal inspiratory narrowing of the costal margins (Hoover, 1920). Described over 65 years ago, this clinical sign continues to be utilized by physicians today as one indication of advanced hyperinflation. Kerley (1936) used radiography to study a large number of subjects with emphysema and "over-extension" of the lung. He noted more transverse-appearing ribs, widened intercostal spaces, very low diaphragms, and increased transverse and antero-posterior (A-P) diameters. Hypertrophy of the pectoralis major and scalene muscles were also visible radiographically in many of these subjects. These were very generalized findings with a great deal of variability between subjects. For example, some subjects with advanced emphysema maintained normal diaphragm movements, and in some, the appearance of accessory muscle hypertrophy was observed quite early or very late in the course of emphysema. Despite the variability of these signs of emphysema, Kerley felt the component of diaphragm lowering and flattening was the predominant factor in the mechanical dysfunction of these subjects.

The concept of diaphragm lowering and flattening as the principal mechanical defect resulted in the development of a variety of devices designed to reposition the diaphragm (Alexander and Kountz, 1934; Gordon, 1934). These devices primarily produced abdominal compression to elevate the diaphragm towards a more normal position. This idea, combined with the clinical observation of patients gaining relief by assuming positions which compress the abdomen (leaning forward in the sitting posture, squatting on the haunches, tightening the belt) produced initial enthusiasm for the various devices. Herxheimer's review (1948) of the scant anecdotal benefit of the abdominal compression devices marked the end of investigations in this direction. Despite being unable to produce beneficial effects in subjects with severe emphysema, this type of study reinforced the concept of diaphragmatic dysfunction being the primary defect in these subjects. Utilizing fluoroscopic screening (1940's state of the art technique examining movement of thoracic components) of 18 subjects with moderate to severe emphysema, the level of the diaphragmatic dome at full inspiration and expiration was determined (Grossmann and Herxheimer, 1948). Initially measured as the distance above the iliac crests, the diaphragm level was then "normalized" for subject height by dividing it by the distance between the tuber ischii and the acromion process. Unfortunately, this method utilized a moving structure which is closely related to the rib cage (acromion process) to normalize the level of the diaphragm. Therefore, if the rib cage was markedly elevated, the acromion process would also be elevated resulting in a falsely lowered normalized diaphragm level. Nonetheless, the diaphragm level in emphysema was

reported by Grossmann and Herxheimer to be significantly lower than in normals at full inspiration, and at full expiration appeared to be just below the level recorded in normals at full inspiration.

One of the last studies of the early roentgenographic period examined 20 subjects with moderate or severe emphysema and 20 control subjects (Knott and Christie, 1951). Four physicians examined postero-anterior (P-A) and lateral chest X-rays performed at total lung capacity (TLC) and residual volume (RV). The purpose was to identify the subjects utilizing classic radiographic signs of emphysema and hyper-inflation without knowledge of clinical status. They were able to correctly classify most subjects when given all 4 X-rays to view. When using only full inspiration films (the most common type of chest radiograph), only 75% of the emphysema subjects and 40% of controls were correctly classified. The authors noted the marked variability in the occurrence of the classic radiographic signs of emphysema. Specifically noted was that the diaphragmatic movement (TLC vs. RV) was greater than 3 cm in three emphysema subjects and less than 3 cm in seven normal controls. In addition, horizontal ribs and widened rib spaces were observed in subjects of each group.

The aforementioned studies focused on detailed radiographic technique including; controlling for magnification and the distance from the X-ray source to the patient and film, and the use of numerous X-ray exposures or lengthy fluoroscopic exposures to observe the thorax as its volume changed. However, there were numerous drawbacks to studies of this period. The diagnosis and quantification of emphysema in these studies were very vague and a significant source of potential error. As

an example, one study classified the subjects as having moderate to severe emphysema if the subjects had breathlessness, cough, and bronchial spasm and were "...severely handicapped in their physical ability, although not bedridden." (Grossmann and Herxheimer, 1948). Vital capacity was usually measured and was typically reduced in the severe emphysema groups, but asthmatics could not be excluded and the extent of hyperinflation was unknown. Subjects were not randomly chosen and frequently reports consisted of general subjective observations of selected patients. Little attempt was made to evaluate the rib cage, and the height of the diaphragm was rarely recorded in reference to a fixed skeletal structure alone.

2. Modern radiographic period

The lack of specificity and sensitivity of the classic radiographic findings of emphysema resulted in a search for a different approach in the investigation of the emphysema. This change is reflected in the literature beginning in the early 1960's. Studies began to be directed toward correlating the radiographic exam with the pathologic analysis of lung tissue. In 1962 Laws and Heard retrospectively reviewed the P-A and lateral chest X-rays of over 100 subjects with lung disease in whom post mortem examination of the lung was performed. The focus of their study was to detect correlative radiographic and pathologic findings of emphysema. Unfortunately, results consisted of only six example cases and generalized comments. However, their observations are relevant to this thesis. The classic findings of elevated horizontal ribs and low flat diaphragms (well-known

signs of hyperinflation) were not always associated with emphysema and variability of these findings was a common feature. The variability may have been related to the fact that radiographs were only performed at TLC and that asthmatics were not excluded. However, it is possible the variability of their findings may reflect the variability of the alterations in the thorax with chronic hyperinflation.

Similar radiologic-pathologic studies examined in detail the pathologic changes of lung tissue, while structural thoracic analysis became less detailed and more subjective (Reid and Millard, 1964; Simon, 1964). Further investigations along these lines focused on examining lung parenchyma with no attention to the rib cage, and a minimal assessment of diaphragmatic level (Nicklaus et al., 1966; Sutinen et al., 1966). A review article by Pugatch (1983) summarized the radiology of emphysema up to that time. The focus was on the radiologic detection of pathologic changes of emphysema in the lung parenchyma, disregarding the structural changes of the thorax in emphysema. These changes in the lung consisted of abnormal enlargement of the air spaces distal to the terminal nonrespiratory bronchioles, accompanied by destructive changes of alveolar walls. Radiologic-pathologic studies emphasized the radiologic examination of the lung parenchyma, not the thorax. In summary, analysis of the structural thoracic changes associated with emphysema and hyperinflation were overlooked, but a few general observations (i.e. low diaphragms) continued to be reported in the literature of this period. Thus, this type of study served only to reinforce previous generalized concepts of the thoracic alterations of chronic hyperinflation.

More recent radiologic studies do address the issue of thoracic changes of hyperinflation. The commonly held belief of increased A-P thoracic diameter in subjects with emphysema and hyperinflation was specifically examined (Kilburn and Asmundsson, 1969). Maximum A-P diameter was determined by two methods including external caliper measurement of the chest at TLC and RV and radiographic measurement using the lateral chest X-ray performed at TLC alone. Twenty-five subjects with documented chronic hyperinflation were compared to 22 controls. No difference in the A-P diameters at TLC by either method could be demonstrated between normals and subjects with COPD. This study is important because TLC measurements represent the maximum A-P dimension of the rib cage and because TLC is the volume at which the majority of clinical chest X-rays are performed. Soft tissue changes in the abdomen (i.e. decreased abdominal girth in emphysema secondary to weight loss) produced an increased ratio of chest A-P diameter to abdominal A-P diameter, resulting in the appearance of a relatively increased A-P chest diameter in the hyperinflated subjects. These findings support the concept of minimal or no rib cage elevation in chronic hyperinflation beyond the maximum observed in normals (at TLC).

Simon et al. (1973) compared P-A and lateral full inspiration chest radiographs with pulmonary function tests (PFTs) of 101 subjects with COPD, and found a lower diaphragm to be associated with an increased TLC (measured by plethysmography), but many patients with large TLCs had a normal position and contour of the diaphragm. In a similar study which included a control group it was found that the lower diaphragm was highly specific for hyperinflation, but lacked in sensitivity for

hyperinflation (Burki and Krumpelman, 1980). It is important to consider major limitations of these two studies. First, both studies used the anterior aspect of the 7th rib as a reference point for diaphragmatic height. The use of an acutely (during inspiration) and/or chronically (in the case of chronic rib cage elevation) moving reference point, imposes variable error in diaphragm height measurement. Secondly, performing the chest X-ray in the P-A view requires the subject to lean forward against the X-ray film cassette, producing variable tilt of the thorax and a variable limit on the movement of the anterior aspect of the rib cage during full inspiration. Thirdly, without including expiratory films, the range of movement of the thoracic components cannot be assessed. Finally, these studies made no attempt to evaluate the rib cage position.

One study examining the radiographic evidence of thoracic hyperinflation found that it did not correlate with the prognosis of the patients with COPD (Kok-Jensen and Ebbehoj, 1977). However, the radiologic changes of an enlarged heart and dilatation of the pulmonary artery (changes associated with pulmonary vascular hypertension) were associated with a reduced survival. These results may reflect the variability of thoracic structural changes in chronic hyperinflation, and the well-recognized association of a poor prognosis of patients with pulmonary vascular hypertension (Nocturnal Oxygen Therapy Trial Group, 1980).

Goddard et al. (1982) utilized computerized tomography (state of the art radiographic technique at that time) performed at full inspiration in the supine position to complement the full inspiratory and

expiratory P-A and lateral chest X-ray measurements. This study of 53 patients with COPD included PFTs and an age-matched control group. The authors primarily examined the lung parenchyma and only superficially investigated the diaphragm, disregarding the rib cage completely. Nonetheless, they reported the diaphragm being lower in subjects with COPD compared to normal subjects.

Sharp et. al. (1986) performed a roentgenographic study of the rib cage and diaphragm in normal and emphysematous subjects. The study included 10 normals and 12 COPD subjects, and utilized only the lateral radiograph. The acute angle formed by the 4th through 7th ribs and the diaphragm height were measured at TLC, functional residual capacity (FRC), and RV. This study revealed a tendency for the rib cage (determined by rib angle alone) to be elevated in COPD compared to older normals at all lung volumes. The diaphragm level in the COPD subjects was significantly lower than normal only at RV. Utilizing intercostal muscle data obtained at autopsy, the authors found that despite the rib cage changes, the intercostal muscle in COPD was not significantly altered from its normal operating length. The study was limited by the small number of subjects, the number of assessments of rib cage position ("rib angle" alone) and because it examined only lateral radiographs.

After reviewing the radiographic studies involving thoracic hyperinflation, a few points become clear. Original observations of the thorax revealed the diaphragm to be lower and the rib cage to be elevated with increased dimensions. These were only descriptive observations of selected subjects and were not examined in a carefully controlled manner. These early studies formed the basis for the

physician's concept of thoracic changes which occur with hyperinflation from emphysema. This early period was followed by a number of studies which closely examined the lung parenchyma but in which little attention was paid to the structure of the thorax. Finally, a few studies attempted to evaluate thoracic changes associated with hyperinflation using PFTs to determine the extent of disease. While these moved closer to correctly addressing the issue of thoracic changes, they were flawed in many respects as noted.

In summary, while radiographic study could be extremely useful in providing details of rib cage and diaphragm position and movement, no study has answered the question of how the thorax is altered in chronic hyperinflation. In addition, modern radiographic studies have reinforced concepts about the thoracic alteration in chronic hyperinflation first developed at the turn of the century.

B. Physiologic Studies

Physiologic studies of subjects with COPD began in the late 1960's. Utilizing methods to examine respiratory flows, pressures, and volumes together with thoracic motion and muscle activity via electromyogram (EMG), investigators gained insight into thoracic mechanics of chronic hyperinflation. While this allowed better assessment of thoracic movement, the position of thoracic structures (especially in reference to a fixed structure) was very difficult to determine.

One of the earliest physiologic studies to suggest a structural/mechanical alteration in the hyperinflated thorax was by Sharp et al. (1968). Previous work had demonstrated a reduced thoracic compliance in

subjects with COPD (similar to the compliance observed in the normal thorax approaching TLC). The decreased compliance was felt to contribute to ventilatory insufficiency of COPD subjects. Sharp questioned previous work regarding the ability of a dyspneic patient to fully relax his respiratory muscles and thereby obtain the true compliance measurement of the thorax. To resolve the issue about compliance of the thorax in chronic hyperinflation, compliance was measured following neuromuscular blockade. With neuromuscular blockade, they observed that the lungs and thorax of COPD subjects maintained normal compliance at greatly increased lung and thoracic volumes. They also found that while paralyzed, passive inflation to physiologic inflation pressures, resulted in lung volumes exceeding the maximum inspiratory capacity (IC) measured while awake and spontaneously breathing. In 11 of 12 subjects this volume ranged from 0.5 to 2.0 liters above IC and did not correlate with the extent of hyperinflation or obstruction. The authors concluded that an important defect in these subjects was inspiratory muscle disability, impairing the ability to actively inspire to the same maximum lung capacity that was measured while paralysed. The authors could not determine which component of the thorax (i.e. diaphragm vs. rib cage) was responsible for this. An important consideration in this study is dynamic hyperinflation which may have been unknowingly reduced with general anesthesia and passive deflation towards a lower FRC. This may have lowered the FRC greatly; and if unrecognized, it could produce compliance curves falsely elevated (do to an error in the volume recorded), producing results similar to those in the study. Also an unrecognized fall in FRC during paralysis below the FRC measured while

conscious, could explain the large difference between conscious and paralyzed inspiratory capacity measurements.

Many physiologic studies analyzed rib cage and diaphragmatic movements utilizing the method of Konno and Mead (1967). While this method directly measures movement of the chest and abdominal wall, it reflects movement of the diaphragm and rib cage, respectively. From this type of study, one can make inferences about abnormalities of the components of the thorax in subjects with COPD and hyperinflation. Ashutosh et al. (1975) found 13 of 30 COPD subjects (43%) had asynchronous respiratory patterns in which the abdomen suddenly moved inward near the end of inspiration, returning outward at variable times during expiration. Information is not provided regarding the TLC of these patients, but based on the spirometry data supplied, the asynchronous subjects had more severe airway obstruction. Therefore, subjects with asynchronous movement probably had greater lung volumes. After ruling out double contractions of the diaphragm, the authors offered one speculative explanation for the asynchronous pattern. They proposed that, with asynchronous movement, a low flat diaphragm is ineffective and that inspiration is primarily via the rib cage. Near the end of inspiration, rib cage elevation is further accentuated by straightening the spine thereby causing inward movement of the abdomen. Their study raised the possibility that variability in the alteration of the components of the thorax (increased rib cage volume versus lowering the diaphragm) was responsible for producing asynchrony in nearly one half of this group of subjects. The unresolved issue is whether the asynchronous pattern represents advanced hyperinflation in which the

diaphragm was lower and dysfunctional combined with rib cage elevation or whether the asynchronous pattern occurred in subjects with less hyperinflation but in whom the thorax was altered primarily by diaphragm flattening with maintenance of normal rib cage position.

Sharp et al. (1977) found that 13 of 30 COPD subjects (43%) had paradoxical abdominal motion defined as an inward movement of the abdomen coincident with outward rib cage motion during inspiration. Inspiratory ascent of the diaphragm was confirmed in three of five of the patients studied radiographically. The extent of hyperinflation did not correlate with the presence or absence of the paradoxical pattern. Three subjects with paradoxical patterns demonstrated obvious accessory muscle use, and measurement of abdominal wall muscle EMG failed to account for inward abdominal motion during inspiration as an explanation. Because paradox did not correlate with advanced hyperinflation, it was concluded that paradox represented malfunction of the diaphragm. Alternatively, paradoxical motion could occur with modest hyperinflation, in subjects who have preferentially lowered the diaphragm to an ineffectual position maintaining a normal rib cage position and movement as well as in subjects with advanced hyperinflation with low diaphragms and elevated rib cage.

In a related study by the same group, 7 of 17 COPD subjects (41%) with inspiratory paradox showed striking relief of dyspnea and resolution of inspiratory paradox in the leaning forward position (Sharp et al., 1980). As a group, these 7 patients had greater lung volumes, although there was overlap with those who did not have paradoxical thoracic motion. In addition, the cross sectional area of the rib cage

and abdomen (measured with magnetometers) at FRC tended to be larger in the subjects with paradoxical motion although not statistically significant. As these 7 subjects gained relief from dyspnea (by sitting leaning forward), they exhibited a decrease in accessory muscle activity. Based on patterns of gastric and esophageal pressures, the diaphragm in these 7 subjects appears to contribute a lesser share (compared to rib cage muscles via esophageal pressures) of the tidal pleural pressure change during paradoxical pattern of breathing. As in the previous study (Sharp et. al. 1977), because of the overlap of lung volumes between those with and without paradox, paradox may have occurred in subjects in whom diaphragm was predominantly lowered, sparing the rib cage and as well, in those subjects with advanced hyperinflation who had low ineffectual diaphragms and elevated rib cages.

Six subjects with severe COPD and hyperinflation, and 8 normal subjects were studied more invasively by Druz and Sharp (1981). Four of the 6 COPD patients had pronounced postural relief of dyspnea in the supine or leaning forward seated positions. All 6 COPD subjects had a marked decrease in the tidal change in transdiaphragmatic pressure (delta P_{di}) in the standing and seated upright positions (as opposed to no change in delta P_{di} in normals) which was associated with increasing accessory muscle activity. This occurred in the face of increasing rising diaphragmatic EMG activity in 4 of the 6 COPD subjects. The two COPD subjects without rises in diaphragmatic EMG had less of a fall in P_{di} than the other COPD subjects. These two COPD subjects may have had increased rib cage elevation (compared to the other 4 COPD subjects), thereby protecting the diaphragm from descending as far, resulting in

the ability to develop a greater P_{di} compared to the other 4 COPD subjects. Without knowing the movements and positions of the rib cage and diaphragm in these subjects, this hypothesis cannot be tested.

Sackner et al. (1984a and 1984b) analyzed the respiratory pattern of hyperinflated subjects with COPD. Using loop analysis of the X-Y plot of rib cage versus abdominal excursions, the authors determined that a degree of respiratory paradox occurred variably in COPD, independent of the severity of lung disease. The COPD subjects had a greater extent of paradox than normals by this method of analysis, but 7 of 10 (70%) had more than half of their tidal volume contribution from abdominal movement when supine which is similar to normals. In summary, indexes of rib cage and abdominal respiratory paradox varied significantly and overlapped with normals. The findings that paradox was independent of the extent of lung disease and that hyperinflated subjects had rib cage and/or abdominal movement similar to normal are consistent with variability in the patterns of alteration of the rib cage and diaphragm in chronic hyperinflation.

Using rib cage magnetometers, Gilmartin and Gibson (1984) found paradoxical respiratory motion in 35 of 40 COPD subjects (88%) seated upright. This was unrelated to the degree of hyperinflation or estimates of diaphragm length or diaphragm configuration obtained from chest X-rays at TLC. This raised the possibility that paradoxical respiratory motion is not necessarily a result of advanced hyperinflation, but that other factors such as the pattern of alteration of the thoracic components may result in respiratory paradox.

Dodd et al. (1984) performed upright bicycle exercise and detailed pressure-volume assessment of 7 subjects with COPD and extreme hyperinflation (mean TLC of 154% predicted). All subjects acutely hyperinflated with exercise and doubled their minute ventilation by doubling their breathing frequency while maintaining a constant tidal volume. Consequently, mean inspiratory and expiratory flows were substantially increased and mean end-expiratory lung volume increased by over 600 mL per patient. In most subjects this occurred via marked elevation (followed by limited movement) of the rib cage coupled with phasic abdominal wall contractions allowing improved position and function of the diaphragm. During exercise, the end-expiratory dimensions of the abdomen (and therefore volume displaced by the diaphragm) were less than that at rest. Therefore, the rib cage at end-expiration was required to incorporate all of the volume (over 600 mL) of exercise-induced acute hyperinflation plus the volume which the abdomen was decreased by at end-expiration. The diaphragm (i.e. abdominal displacement) then provided the majority of the tidal volume change of the thorax during exercise in these subjects. This required elevation of the rib cage maintained throughout the respiratory cycle, maintaining the acute hyperinflation of exercise in these subjects. Thoracic volume alterations during exercise in these subjects are distinctly different from that in normals. The normal response to exercise is a slight decrease or no change in end-expiratory lung volume with a majority of the tidal volume occurring via rib cage movement (Henke et al., 1988). The response to exercise in these COPD subjects depended on marked tonic elevation of the rib cage. While this paper does not quantify the

absolute elevation of the rib cage, it does point out the importance of acute rib cage elevation and the potential limitations resulting from impairment or reduced ability of the rib cage to acutely elevate at times of increased ventilation.

A recent study examined diaphragm length and its relationship to lung volumes and maximum inspiratory and expiratory pressures in COPD (Rochester and Braun, 1985). While there was a modest correlation between diaphragm length and inspiratory pressure generation, diaphragm length varied by over 75% between subjects, for the same lung volume. The variability in diaphragm length in subjects at the same lung volume may imply variability of which component of the thorax is altered to contain the increased lung volume of hyperinflation. Further analysis of the data determining the change in diaphragmatic length over a change in volume (including vital capacity) may clarify which component of the thorax was predominantly altered.

C. Animal Studies

Animal models of emphysema have been developed over the last few years which provide insight into the thoracic changes that occur in humans with chronic hyperinflation. In a rat model of elastase-induced emphysema, the diaphragm length was found to be shortened as a result of hyperinflation which developed (Farkas and Roussos, 1982). However, for the same degree of hyperinflation there was up to 50% difference in the measured length of the diaphragm. While there was no assessment of the rib cage, the variability in diaphragm length could be due to variability of alterations in the rib cage in chronic hyperinflation.

The elastase-induced hamster model was carefully studied in regard to both rib cage and diaphragmatic alterations (Thomas et al., 1986; Oliven et al., 1986). The chest wall compliance curve was shifted upward and to the left, reminiscent of work by Sharp et al. (1968) in humans with emphysema. The structure of the rib cage was substantially altered in the emphysematous hamster. The A-P, transverse and rostral-caudal dimensions of the thorax and its circumference significantly increased in the emphysematous animals compared to controls. In addition, the rib and sternal length had grown to 140% of control. Diaphragmatic adaptation (perhaps by sarcomere reabsorption) appeared to have occurred, because the Pdi at high lung volumes in the emphysematous animals was significantly greater than in controls at similar lung volumes. However, the maximal transdiaphragmatic pressure in the emphysematous animals was greatly diminished. No attempt was made to correlate rib cage changes with the diaphragm alterations. The mean FRC of the emphysematous hamsters in these two studies was 183% and 239% of the control groups. Comparing these data to human data is difficult because of growth in the rib cage components occurring in hamsters given elastase at approximately 2 months of age, and the jointed, highly flexible rib cage of the hamster. Nonetheless, these studies point out the potential adaptability of the thorax in chronic hyperinflation and correlate with previous work demonstrating sarcomere reabsorption of the diaphragm in emphysematous rats (Farkas and Roussos, 1983).

In summary, the literature to date does not specifically and directly address the question of how the thorax is structurally altered in chronic hyperinflation. The general concept of diaphragmatic lowering and rib cage elevation occurring together as hyperinflation progresses is a result of many observations over the last 90 years. Numerous studies have generated data which imply or suggest that significant variability occurs in the alterations of the chronically hyperinflated thorax. The clinical course of hyperinflated emphysematous subjects is extremely variable and does not correlate well with any one factor. Despite such variability, these patients are frequently categorized clinically and for investigational purposes by only a few criteria such as extent of hyperinflation or degree of obstruction. Therefore, the purpose of this thesis is to determine how the human thorax is structurally altered in chronic hyperinflation.

CHAPTER III.

METHODS

The study consisted of radiographic examination of the configuration and movement of the rib cage and diaphragm of volunteer subjects. It was performed at Hines V.A. hospital under the direction of Dr. John T. Sharp and was approved by the Investigational Review Board. All subjects gave informed consent prior to investigation.

A. Experimental Groups

Twenty-two subjects with COPD and severe hyperinflation and obstruction (mean TLC = 136% predicted and mean forced expiratory volume in 1 second (FEV_1/FVC) = 37%) were studied. These subjects were collected from screening of the male patients at Hines V.A. Hospital and Clinics. Selection criteria consisted of the following: 1) airway obstruction based on an FEV_1/FVC less than 75%; 2) hyperinflation, consisting of a TLC greater than 120% predicted; 3) the clinical diagnosis of COPD; 5) age greater than 40 years. Exclusion criteria included: obesity (greater than 115% of ideal body weight), skeletal deformities (clinical evidence of kyphoscoliosis or moderate to severe arthritis), previous history of thoracic surgery and gross abnormalities on a routine chest X-ray (other than findings consistent with COPD).

The pulmonary function testing consisted of spirometry and lung volumes (by plethysmography). PFTs and radiographs were performed while the patient was clinically stable.

Ten normal non-smoking male subjects over the age of 40 years formed the control group. These subjects had completely normal pulmonary function tests and chest X-rays as well as the absence of obesity, skeletal deformities, or a previous history of thoracic surgery. They were obtained from the same general population as the COPD subjects. Clinical characteristics and PFTs of both groups of subjects are displayed in Table 1.

B. Radiographic Technique

Antero-posterior and left lateral upright standing chest radiographs were produced using a radiography and fluoroscopy unit model number G1050F (Picker International Corporation). The tube focal point was 6 feet from the radiograph cassette and the initial settings were 75 kilovolts, 300 milliamps, and an exposure time of 0.25 seconds. These settings were minimally varied to provide adequate visualization of the bony structures. A backboard fixture 6.5 feet high, 12 inches wide, firmly anchored perpendicular to a base plate and with a 1 by 1 inch strip of aluminum angle stock over its entire length (to provide a radiopaque vertical reference) was placed in front of the radiograph cassette. Subjects stood in front of the backboard with head, shoulders, buttocks, calves and heels firmly against the board. The backboard fixture was secured in front of and parallel to the radiograph cassette for the A-P radiograph and in front of and perpendicular to the

TABLE 1

CLINICAL CHARACTERISTICS

	n (#)	Age (years)	Height (inches)	Weight (pounds)
Normal subjects	10	62 ± 6	69 ± 2	166 ± 22
COPD subjects	22	64 ± 5	68 ± 3	156 + 34

PULMONARY FUNCTIONS

	TLC	FEV_1	FVC	FEV_1/FVC RATIO
	(Percent of predicted values)			(%)
Normal subjects	104 ± 6	105 ± 10	107 ± 7	74 ± 4
COPD subjects	136 ± 12	34 ± 12	71 ± 10	37 ± 10

Values are mean ± SD

radiograph cassette for the left lateral radiograph. The subject's arms were held in front of and at right angles to the longitudinal axis of the body. The X-ray beam was centered on the xiphoid level in the mid-sternum (A-P view) or at the xiphoid level in the mid-hemithorax (lateral view). Divergence of the X-ray beam causes magnification of structures displayed on the radiograph. Magnification increases with the distance away from the center of the beam and the distance in front of the radiograph film. The magnification of thoracic structure with an X-ray source 72 inches from the radiograph is 10% to 15% maximally. This was similar among all subjects and the thoracic structures examined were less than 20 centimeters from the radiograph. For these reasons, corrections for magnification were not made. A-P and lateral radiographs were performed in this manner at TLC, FRC and RV. Subjects were instructed on how to maintain an open glottis during the X-ray and were observed through leaded glass during the X-ray exposure to insure compliance. This was found in prior studies to be critically important to obtain maximal rib cage dimensions (Sharp et al.,1986).

C. Rib Cage Analysis

The first method of rib cage analysis was measurement of rib width (RW), which was the maximum inside diameter of the third, seventh and ninth pairs of ribs, visualized on the A-P radiograph (Fig. 1a). The measurement of the RW examines the "bucket handle" motion of the rib cage which is the cranial-caudal/abduction-adduction movement of the lateral aspects of the rib cage. These were chosen to represent the upper, middle and lower pairs of ribs.

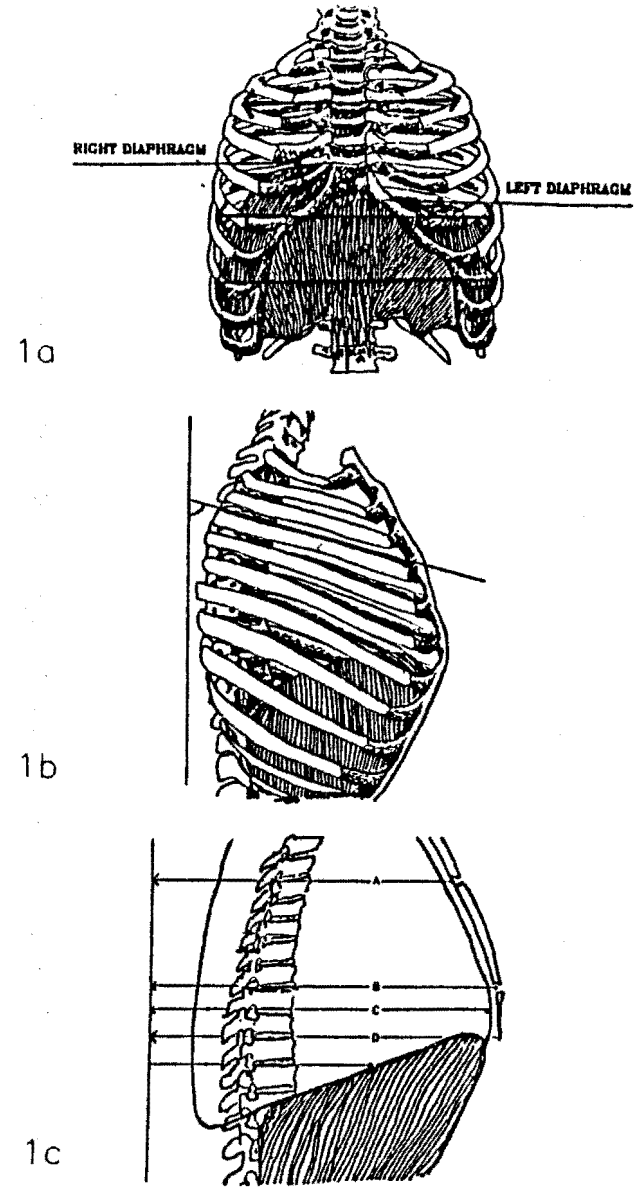

Figure 1. Methods of Analysis.

Figure 1a represents the A-P radiograph and the method of determining the rib width and diaphragm height. Figure 1b represents the lateral radiograph and the method of determining the rib angle. Figure 1c represents the lateral radiograph with the method of determining the A-P diameter and diaphragm height. See text for details.

The second method of rib cage analysis was measurement of the rib angle (RA), which examines the "pump handle" motion of the rib cage. Classically, this has been considered the cranial-caudal movement of the anterior aspect of the rib cage. RA was determined as shown in figure 1b, using the left-sided ribs on the left lateral radiograph, which were identified using the standard radiographic methods (Austin, 1984). Two vertical lines were drawn on the radiograph at one-third and two-thirds of the maximum A-P distance from sternum to radiopaque vertical reference marker. The two points formed by the intersection of the vertical lines with the superior border of a rib created the rib line. Rib lines were constructed along the superior borders of ribs 4 through 7. These ribs were chosen from prior experience as the only four ribs consistently well visualized in both normals and subjects with lung disease. The RA was the acute angle formed by the vertical reference line and the rib line. As the rib cage was elevated, RA increased; as the rib cage was lowered, RA decreased.

The third rib cage analysis was the measurement of A-P diameter on the lateral radiograph. This measurement also indicates "pump handle" motion, because the anatomy of costal vertebral junction results in cranial-caudal movement of the anterior rib cage producing anterior-posterior movement of the anterior aspect of the rib cage. Because assessment of A-P thoracic diameter in the literature is mostly subjective and lacking an established method of analysis, four methods (A,B,C,and D) were used to determine A-P diameter. These consisted of identifying 4 points on the radiograph as shown in figure 1c: Point A was the junction of the manubrium and body of the sternum, Point B was

the junction of the body and xiphoid process of the sternum, Point C was the anterior most visible bony point on the sternum, and Point D was the anterior most visible air space. Points A and B were chosen because they represent consistently visible skeletal structures. Points C and D were selected because they represent the most prominent anterior aspects of the lateral radiograph which a subjective viewer may use in assessment of A-P diameter. The perpendicular distance from the radiopaque vertical reference line to points A, B, C and D was then measured yeilding the A-P diameter for each of these 4 methods.

D. Diaphragm Analysis

The height of the diaphragm was determined in both the A-P and lateral radiographs. The position of each hemidiaphragm was determined in the A-P radiograph in reference to the thoracic and lumbar vertebral column. The vertebral column was numbered by assigning the superior aspect of the first thoracic vertebral body the value of 0 vertebral units. Each subsequent vertebral body was given a value of 0.8 vertebral units and its adjacent interspace a value of 0.2 vertebral units. Numbering was continued to the inferior aspect of the second lumbar vertebral body which had the value of 13.8 vertebral units (Fig. 1c). This method was chosen to provide a relatively fixed reference for the diaphragm which could also be used for comparison to other subjects. On the A-P radiographs the level of the diaphragm at the mid-hemithorax was chosen for determination of the level of each hemidiaphragm. A line perpendicular to the vertebral column was drawn through the mid-hemidiaphragm point, and was used to determine the height of the hemidiaphragm

in reference to the vertebral column (Fig. 1a). For example, a hemidiaphragm which was at the level of the middle of the ninth thoracic vertebra would be recorded as having a level of 8.4 vertebral units.

A similar method was used in the lateral radiograph to determine the height of the diaphragm as displayed in Figure 1c. The A-P midpoint of the left hemidiaphragm was determined and the level of this point was determined in reference to the vertebral column as noted above for the A-P radiograph.

E. Data Analysis

The raw data consisted of RA, RW, A-P diameter and diaphragm level performed at the three volumes TLC, FRC, and RV. The difference of measurements at TLC and RV was considered the change across vital capacity for each of the variables studied. In addition to reporting the raw data for the difference between TLC and RV, the COPD data were also analyzed as corrected for vital capacity. To correct for vital capacity, the raw difference of the TLC and RV measurements (RW, RA, A-P diameter and diaphragm height) was divided by the percent of predicted vital capacity for each COPD subject. Because of the varied vital capacities in the COPD subjects (48 to 95 percent predicted), this correction normalized the change in position observed over vital capacity for the different volumes of vital capacity observed in the COPD subjects. This was not done with the normal subjects, as by selection criteria they had normal vital capacities. With this correction, the change in position over vital capacity could be compared for a similar change in volume between the COPD and normal subjects. Mean

values and standard errors were calculated and are reported unless otherwise stated. Rib cage measurements (continuous data) were analyzed using Student's t-test to compare the findings of the COPD subjects to normals. The diaphragm measurements (nominal data) were analyzed using the nonparametric Mann-Whitney U test in a similar fashion. A one-way analysis of variance (ANOVA) test was used to compare the change over vital capacity, where three groups existed (i.e. when COPD data was corrected for vital capacity). P values less than 0.05 were considered significant.

CHAPTER IV.

RESULTS

The following results demonstrate that in chronic hyperinflation associated with COPD, the rib cage is not significantly different than that of normals with respect to position and change in position across vital capacity. Rather it is the diaphragm in chronic hyperinflation which is significantly altered, with a lower position and decreased change in position across vital capacity.

A. Position of the Thoracic Components

1. Rib cage measurements

The rib width at TLC, FRC and RV are shown in Figure 2. This reveals the striking similarity of the RW between the chronically hyperinflated and normal groups. The largest mean difference between these two groups was less than 1.0 cm.

The rib angles at TLC, FRC and RV are displayed in Figure 3. Note that the COPD values are similar to normal. The rib angle declines from rib 4 to rib 7 at each volume in both groups.

The A-P diameter is displayed in Figure 4. Note the marked similarity between the two groups at all lung volumes. The largest mean diff-

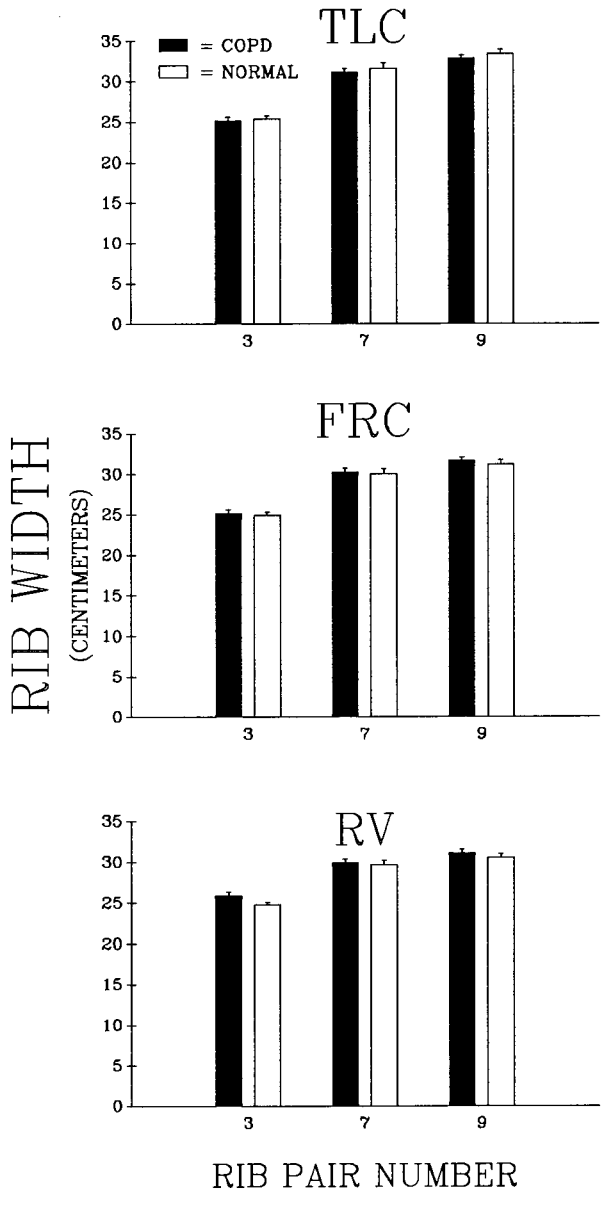

Figure 2. Rib Width.

Rib width in centimeters for rib pairs 3, 7, and 9 at TLC, FRC and RV. The rib width is essentially the same in the normal and COPD groups for each lung volume ($p > 0.05$). Values are mean $\pm$ SEM. N = 10 for normals and N = 22 for COPD.

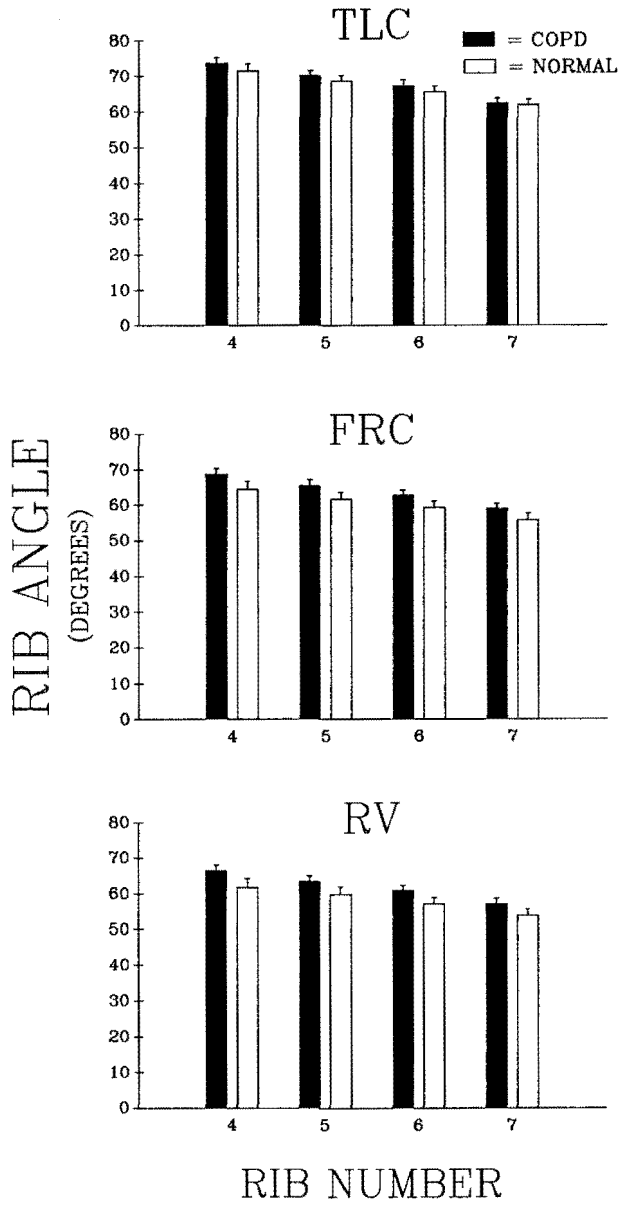

Figure 3. Rib Angle.

Rib angle in degrees for ribs 4, 5, 6, and 7 at TLC, FRC and RV. There is no difference between the normal and COPD rib angles for ribs 4 through 7 at TLC, FRC and RV ($p > 0.05$). Values are mean $\pm$ SEM. N = 10 for normals and N = 22 for COPD.

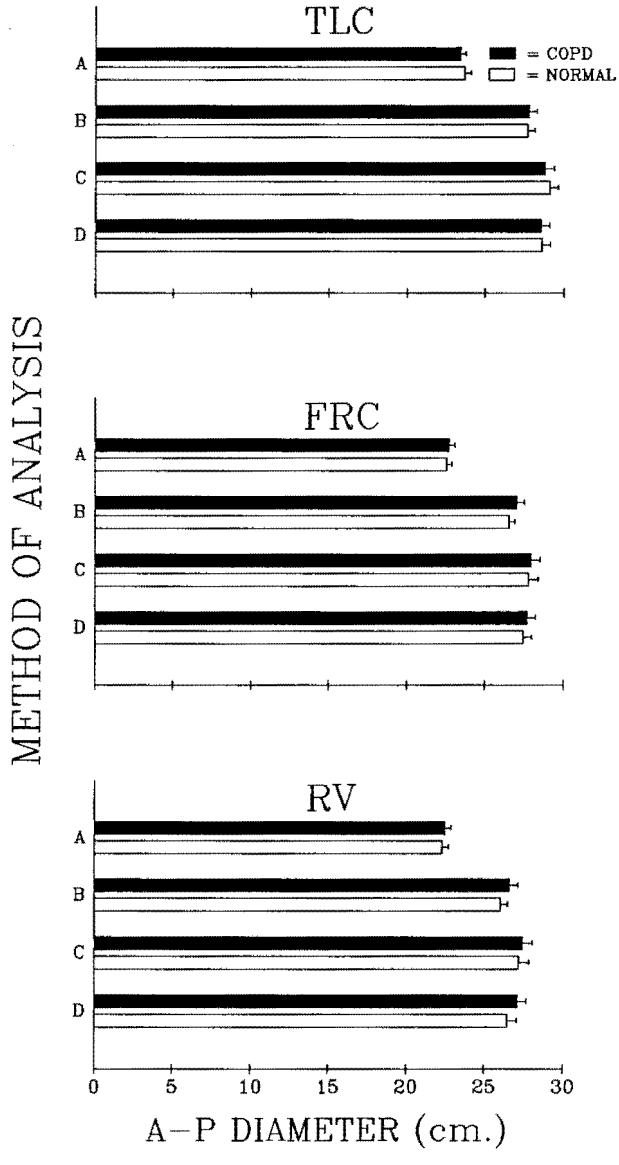

Figure 4. Rib Cage A-P Diameter.

The A-P diameter of the rib cage in centimeters at TLC, FRC and RV. There is no difference between the COPD and normal A-P diameters at all lung volumes ($p > 0.05$). Values are mean $\pm$ SEM. N = 10 for normals and N = 22 for COPD. Methods A, B, C and D as described in figure 1c.

erence is less than 1.0 centimeter. This is comparable to the similarity between the COPD subjects and normals for both RW and RA as noted above.

2. Diaphragm measurements

The relationship of the right and left hemidiaphragms determined in the A-P radiograph at the respective volumes for each group is displayed in Figure 5. Note the tendency for the right diaphragm to be higher than the left diaphragm. To condense the data, the mean of the right and left diaphragm of each subject was calculated and reported as the average diaphragm height as shown in Figure 6. At each volume the COPD diaphragm is significantly lower compared to normal. The highest level of the COPD diaphragm (at RV) is even less than that of the normal diaphragm at its lowest level (at TLC).

The level of the diaphragm as determined in the lateral radiograph is displayed in Figure 7. As seen in the A-P view (Fig. 6), the level of the diaphragm in COPD is significantly lower than normal at all lung volumes. The highest level of the COPD diaphragm (at RV) is lower than that of the normal diaphragm at its lowest level (at TLC).

B. Change in Position of the Thoracic Components Across Vital Capacity

1. Rib cage

The change of the rib width across vital capacity is illustrated in Figure 8. The third pair of ribs has minimal change in width across vital capacity. The seventh and ninth rib pairs however do have a much greater change in width across vital capacity. The change in rib

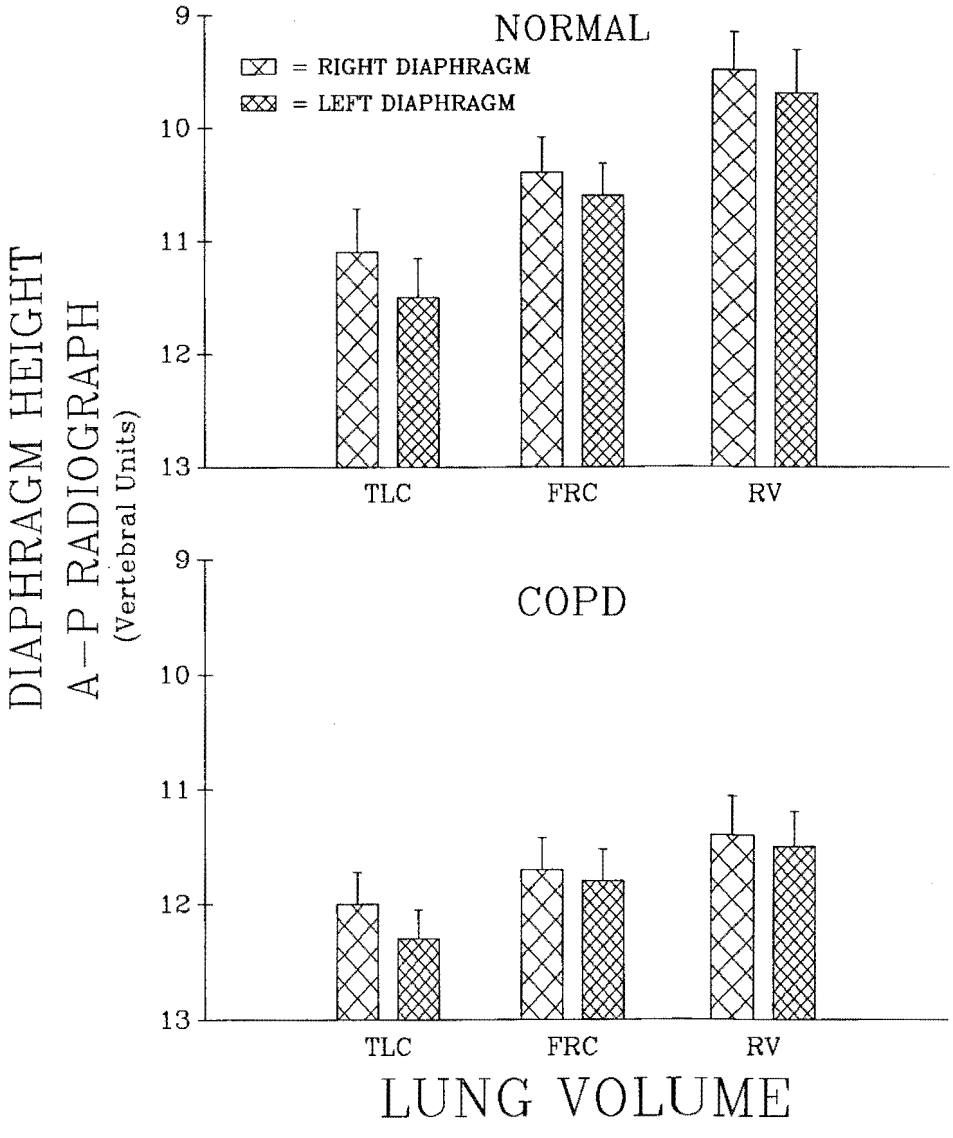

Figure 5. Diaphragm Height in A-P Radiograph.

The right and left diaphragm levels for each group. There is no difference between right and left diaphragm levels ($p > 0.05$). Values are mean $\pm$ SEM. N = 10 for normals and N = 22 for COPD.

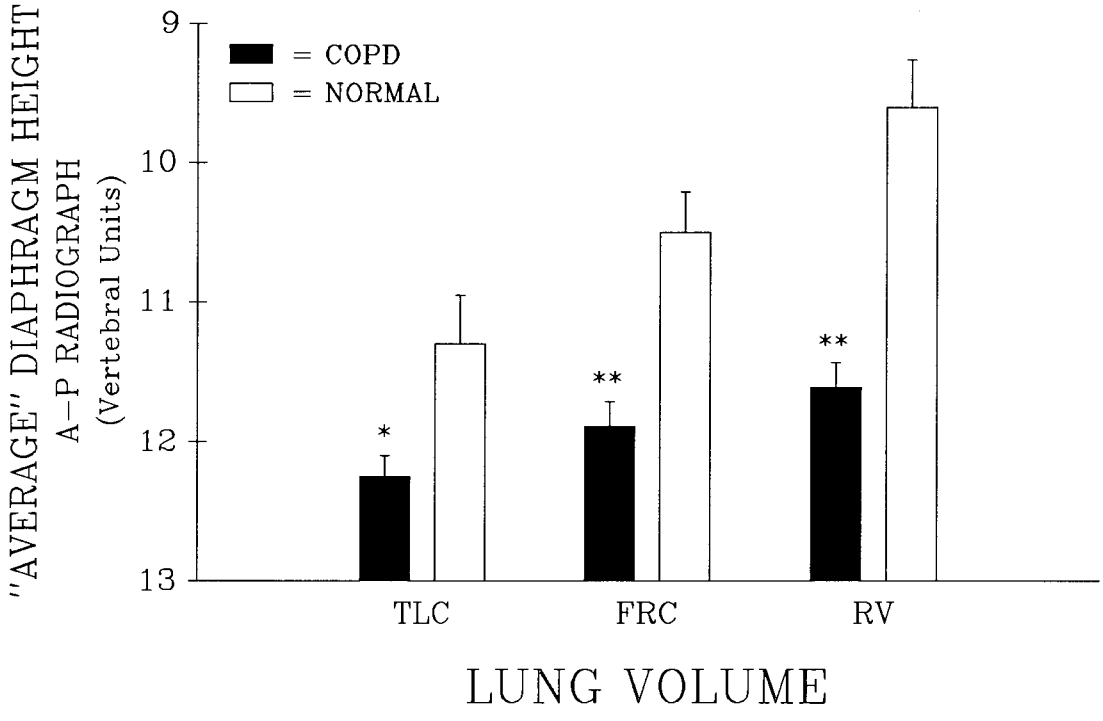

Figure 6. Average Diaphragm Height in A-P Radiograph.

Average diaphragm level in the A-P radiograph at TLC, FRC and RV. In marked contrast to the results of the rib angle and rib width, the diaphragm height was significantly lower in the COPD group at all volumes. Values are mean ± SEM. N = 10 for normals and N = 22 for COPD. * = $p < 0.05$, ** = $p < 0.01$.

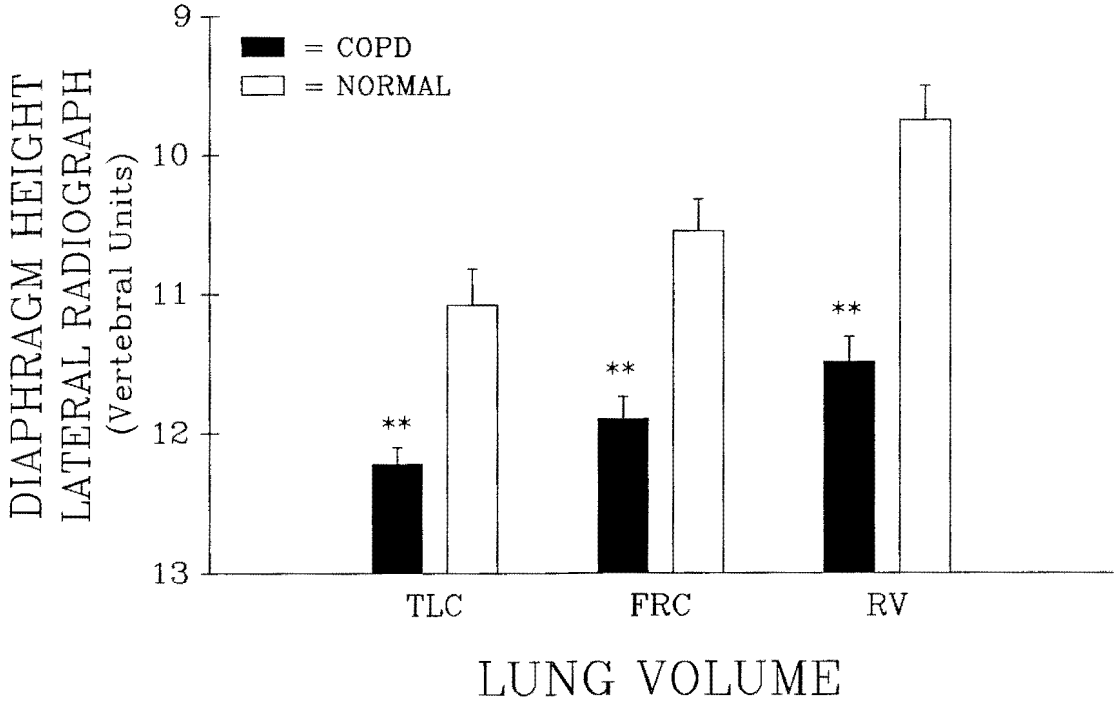

Figure 7. Diaphragm Height in Lateral Radiograph.

Diaphragm height in the lateral radiograph at TLC, FRC and RV. Note how much lower the COPD diaphragm is compared to normal, at all lung volumes. These findings are similar to those of the diaphragm height in the A-P view. Values are mean ± SEM. N = 10 for normals and N = 22 for COPD. ** = $p < 0.01$.

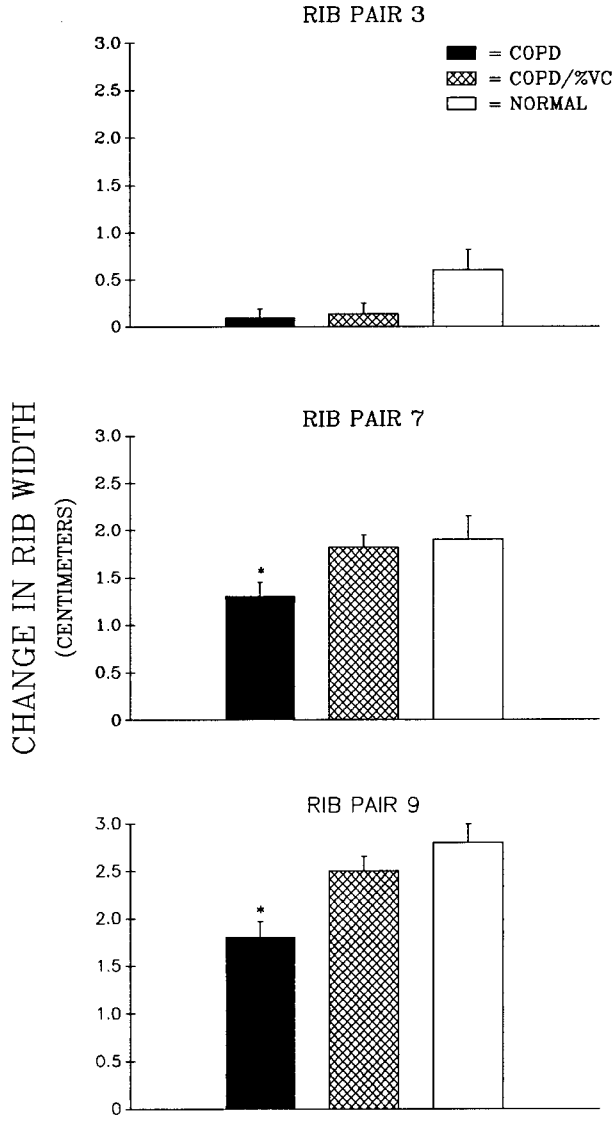

Figure 8. Change in Rib Width.

Change in rib width for rib pairs 3, 7, and 9 (TLC - RV). The change in rib width in the COPD group becomes no different from normal when corrected for the diminished vital capacity of the COPD group. Values are mean ± SEM. N = 10 for normals and N = 22 for COPD. * = $p < 0.05$.

width (uncorrected) is greater in normals than in COPD subjects. However, when corrected for the reduced vital capacity of subjects in the COPD group, the change in rib width is no different between normal and COPD subjects.

Figure 9 illustrates the change of rib angle across vital capacity (or the difference between TLC and RV values). This was obtained using the average of the rib angles 4, 5, 6, and 7 for each subject at TLC and RV. The value for the COPD group is not significantly different from the normal group.

The change in the A-P diameter is shown in Figure 10. There is no significant difference between any of the groups by any of the four methods. When the COPD data is corrected for the vital capacity the mean values become virtually identical to the normal data.

2. Diaphragm

Figure 11 displays the change in diaphragm height across vital capacity as determined in the A-P radiograph and Figure 12 displays the similar data as determined in the lateral radiograph. The change in diaphragm height (in both A-P and lateral radiographs) is significantly less in the uncorrected COPD group, and when corrected for vital capacity, it remains significantly less than normal.

C. Comparison of Rib Cage Versus Diaphragm Position Across Vital Capacity

Figure 13 plots the position of the rib cage (represented by the average values of the rib angle) as a function of diaphragm position

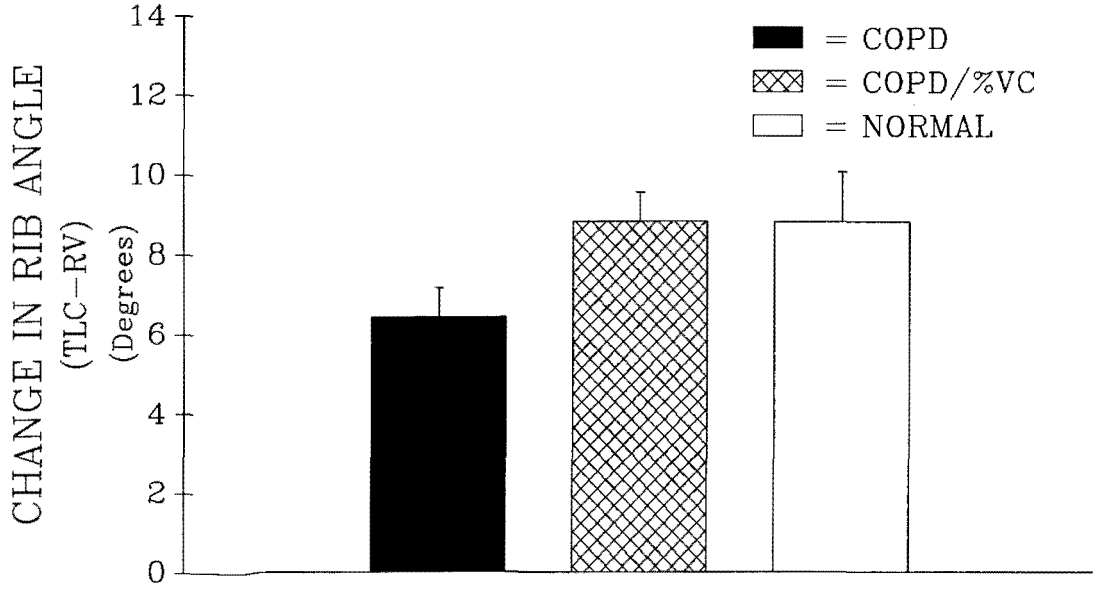

Figure 9. Change in Rib Angle.

Change in rib angle from RV to TLC. The difference between normal and uncorrected COPD values does not reach statistical significance ($p = 0.08$). When the COPD values are corrected for the diminished vital capacity in that group the resultant change in rib angle is indistinguishable from normal. Values are mean $\pm$ SEM. N = 10 for normals and N = 22 for COPD.

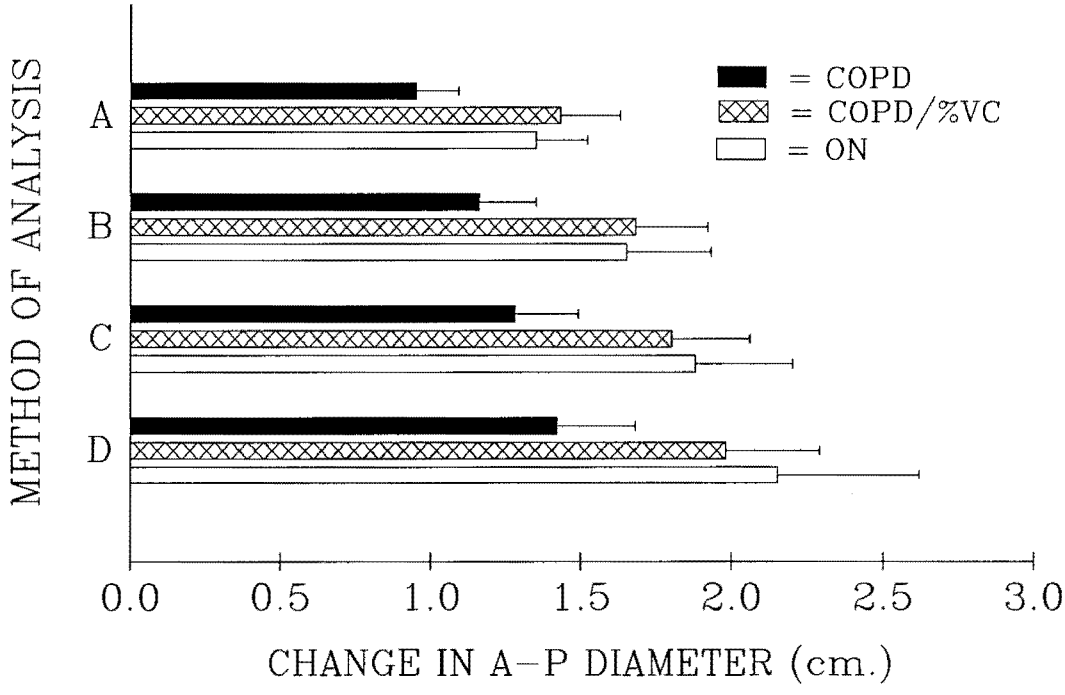

Figure 10. Change in Rib Cage A-P Diameter.

Change in rib cage A-P diameter from RV to TLC. There was no difference between any of the three groups ($p > 0.05$). Values are mean $\pm$ SEM. N = 10 for normals and N = 22 for COPD. Methods A, B, C and D as described in figure 1c.

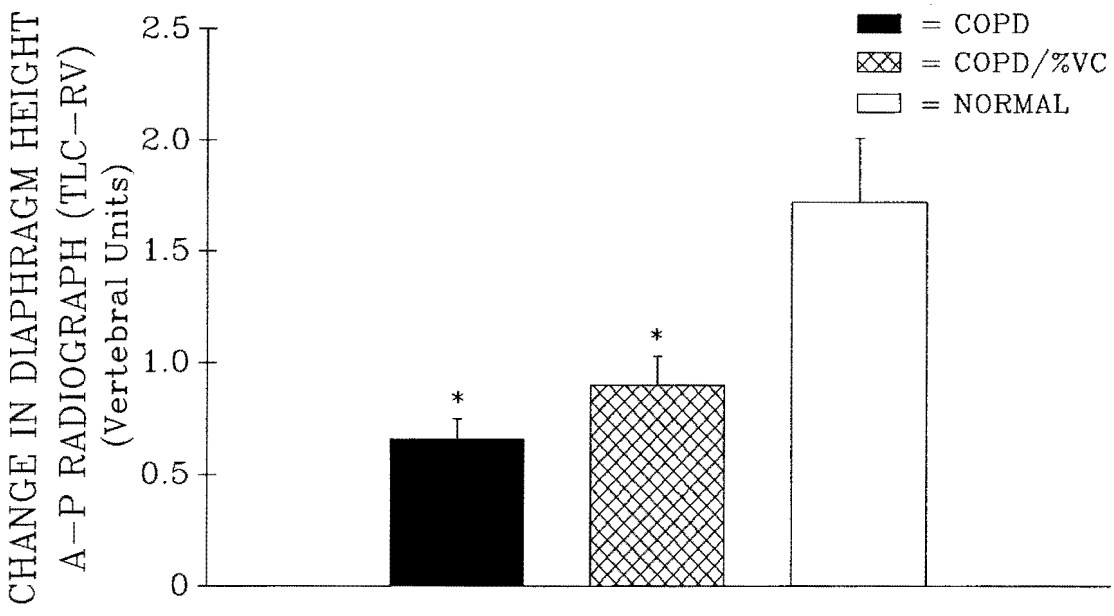

Figure 11. Change in Diaphragm Height in the A-P Radiograph.

Change in diaphragm height (TLC - RV). Even with the correction for vital capacity, the change in diaphragm height is significantly less in the COPD group than normal. Values are mean ± SEM. N = 10 for normals and N = 22 for COPD. * = $p < 0.05$.

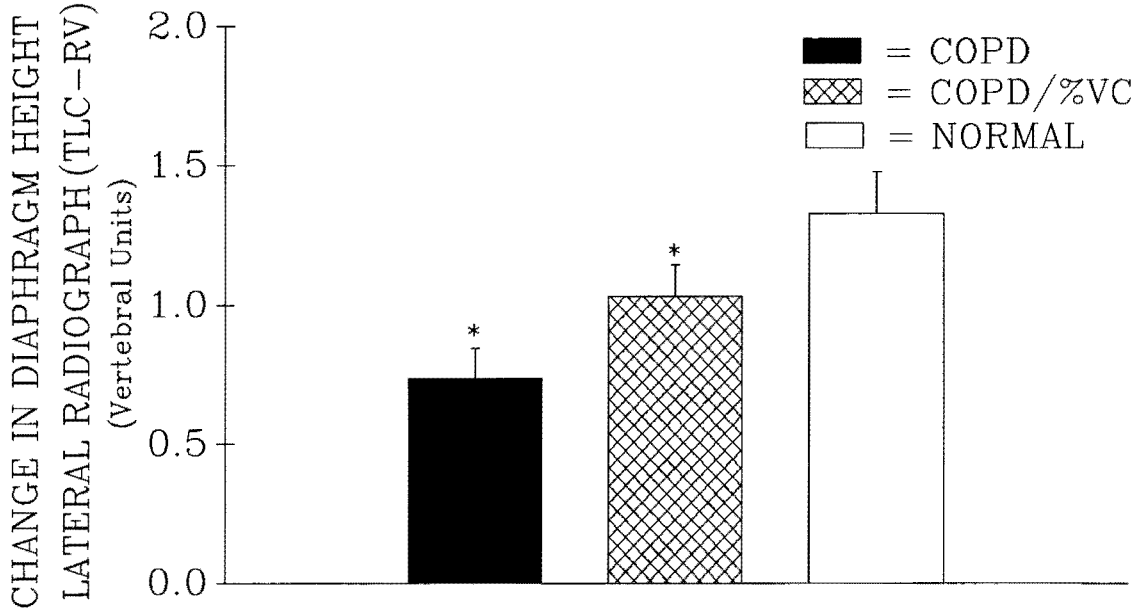

Figure 12. Change in Diaphragm Height in the Lateral Radiograph.

Change in diaphragm height in the lateral radiograph from RV to TLC. Even with the correction for vital capacity, the change in diaphragm height is significantly less in the COPD group than in normals. Values are mean $\pm$ SEM. N = 10 for normals and N = 22 for COPD. * = $p < 0.05$.

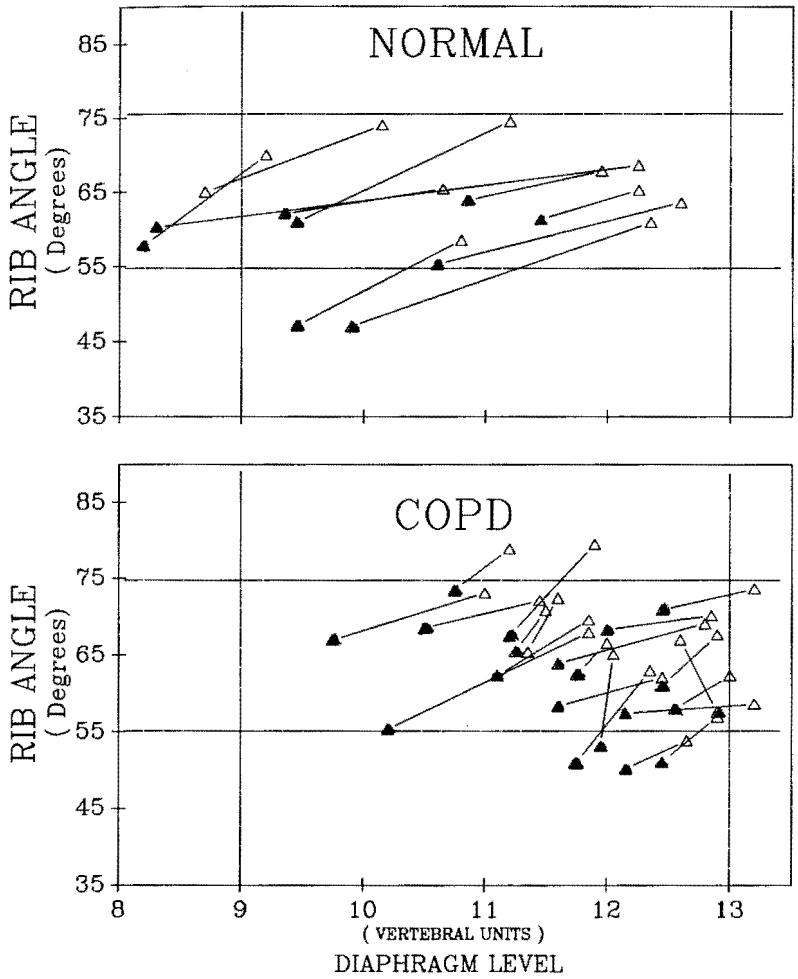

Figure 13. Comparison of Rib Cage Versus Diaphragm Position Across Vital Capacity.

RV values of rib angle and diaphragm height (closed triangles) connected to TLC values of rib angle and diaphragm height (open triangles) for each subject. Note the similarity of the rib angles for the two groups, but that the diaphragm levels in COPD are shifted to the right (lower) in comparison to the normal group. N = 10 for normals and N = 22 for COPD. Horizontal and vertical lines added for comparison only.

(determined on the A-P radiograph) for all subjects. The closed triangles represent the values at RV and the open triangles the values at TLC. The slope of the line which connects the RV values to the TLC values represents the change in the position of the rib cage relative to the change in the position of the diaphragm over vital capacity. This figure demonstrates the similarity of the range of rib angles in both groups, in contrast to the range of diaphragm levels, which for the COPD group is shifted to the right (lower).

Table 2 displays the mean slope of the change in rib angle versus the change in the diaphragm level across vital capacity for the normal and COPD subjects. The mean slope of the normal subjects is less then the COPD subjects (5.7 vs. 13.7 degrees per vertebral unit res-pectively). This represents the greater relative contribution of the rib cage in movement across vital capacity in the COPD subjects compared to normal subjects. This is not due to a greater absolute movement of the rib cage in COPD, but to the limited movement of the diaphragm in COPD. The 95% confidence limits for the slopes of normal subjects were calculated to arbitrarily create high, middle and low slope categories to further compare the slopes of the normal subjects to those of the COPD subjects. As seen in Table 2, the majority of COPD subjects fall into the high slope category. This demonstrates that in the majority of the COPD subjects there is more change in the rib cage position than diaphragm height over vital capacity, compared to normals ($p < 0.05$ by Chi square analysis).

Table 2

Comparison of Rib Cage Versus Diaphragm Position Across Vital Capacity
Change in Rib Angle / Change in Diaphragm Height
(slope = degrees / vertebral units)

	MEAN ± SEM	RANGE	HIGH	MIDDLE	LOW
Normal	5.7 ± 1.0	2.1 to 12.2	2	5	3
COPD	13.7 ± 5.5	1.1 to 120.0*	13	5	4

* In addition 1 subject had paradoxical motion of the diaphragm with a slope of -31.3. High represents slopes greater then the 95% confidence limits for the normal group. Middle represents slopes within the 95% confidence limits for the normal group. Low represents slopes less then the 95% confidence limits for the normal group.

CHAPTER V.

DISCUSSION

A. Altered Thoracic Configuration in Chronic Hyperinflation

The results demonstrate that rib cage configuration is not altered in chronic hyperinflation. The rib widths, rib angles and A-P diameters at all lung volumes were not different in the chronically hyperinflated COPD subjects compared to normal subjects (Figs. 2, 3 and 4). The nearly identical rib angle and rib width at TLC imply a maximal limit of the elevation of the rib cage, which is not exceeded in chronic hyperinflation. The change in rib cage (RW, RA and A-P diameter) over vital capacity was the same in COPD as in normals (Figs. 8, 9 and 10). These findings agree with work of Kilburn and Asmundsson (1969) who found that the thoracic A-P diameters at full inspiration for 25 hyperinflated emphysema patients were not different from 22 normal control subjects.

The diaphragm height of COPD subjects was significantly lower at all lung volumes and displayed a reduced range of motion over vital capacity in the COPD group compared to normals (Figs. 6, 7, 11, and 12). The highest level of the diaphragm in COPD subjects (RV level) only approached the lowest level of the diaphragm in normals (TLC level). Thus, the thorax in chronic hyperinflation is characterized by a lowered diaphragm with maintenance of a normal rib cage position. The change in

diaphragm height across vital capacity is reduced, while normal rib cage change in position across vital capacity is maintained.

The change in rib cage position versus change in diaphragm position over vital capacity (Fig. 13) provides an overall summary view of the data. The diaphragm in the COPD group is greatly displaced to the right (lower), while the range of rib angles is very similar between the two groups. When compared to normals, the majority of COPD subjects had a greater change in the position of the rib cage (relative to the change in the diaphragm across vital capacity). This is not surprising since the diaphragm was lower and changed position less in these subjects.

Positioning of the subjects is important to consider. The subjects stood erect, firmly against a backboard at the time of X-ray exposure. This was done to standardize the position of the subject and limit variation between subjects. The erect position utilized in the study may have been different from normal posture for some of the subjects and could have contributed to the altered relationship of the change in position of the rib cage to the diaphragm. For instance, a subject who normally assumes a mildly kyphotic posture would undergo passive elevation of his rib cage by assuming the study position, and therefore limit further rib cage elevation. Also, degenerative joint disease could limit the mobility of the costovertebral junctions although subjects who demonstrated clinical evidence of kyphoscoliosis or moderate to severe arthritis were eliminated from study. Although the study posture may be different than an individual subject's normal posture, the study posture was constant between subjects within a group, and between groups.

It is important to compare these results to that of Sharp et. al. (1986) in which it is implied that the COPD rib cage was elevated at all lung volumes, compared to older normals. The rib angle of older normals in their study was very similar to that found in this study, as was the change in rib angle over vital capacity (for both COPD and older normals). The major difference from Sharp et. al. (1986) was that the rib angle in COPD subjects was reported as approximately 5 degrees higher (at all lung volumes) than in the current work. In diaphragm assessment, Sharp et. al. (1986) found the COPD diaphragm levels to be slightly higher, and the older normal diaphragm levels to be slightly lower than those in this thesis. As a result Sharp et. al. (1986) found the COPD diaphragm to be lower than older normal diaphragm only at RV. The change in diaphragm level in their study was nearly identical to the data in this thesis. In summary, the key differences in the work by Sharp et. al. (1986) are that the COPD rib cage appeared to operate at a higher range of rib angle (but with the same change from TLC to RV) and that the COPD diaphragm was only lower than older normal at RV (but with the same change from TLC to RV).

Four main distinctions exist between these results and Sharp et. al. (1986). First, the number of COPD subjects in this work is nearly double that of Sharp et. al. (1986). Secondly, in regard to the rib angles, the method of Sharp et. al. used "the best straight line drawn by eye along the top edge of each rib" whereas the current method utilizes a line produced by the intersection of the superior border of the rib and two vertical lines, drawn by dividing the thorax into equal thirds. The method of determining the rib angle utilized in this thesis

reduces the subjectivity of drawing the "best straight line", and could explain some of the differences in rib angle reported in these two studies. Thirdly, the method of determining the level of the diaphragm by the Sharp study is different than in this work. For example, Sharp used the level of the highest point in the diaphragmatic dome to determine the level of the diaphragm. In the lateral view, the highest point of the diaphragm is often the most anterior aspect especially at increased lung volumes and especially in COPD. Therefore, utilizing the highest level of the diaphragm may result in higher and possibly different points of the diaphragm being referenced, producing both inter- and intra-subject variations in diaphragm measurements. The current work utilized the mid-hemidiaphragm in both A-P and lateral radiographs to reduce the chance of such error. Finally, the current work examined the thorax in both A-P and lateral views, including two methods to assess "pump handle" motion, one method to assess "bucket handle" motion and two methods of determining the level of the diaphragm.

The altered relative change in position of the rib cage and diaphragm across vital capacity (displayed in figure 13) may not directly reflect the altered volume contributions or energy cost of breathing of the rib cage or diaphragm in COPD. This is especially true for the diaphragm, where at lower levels it may lose its area of apposition resulting in less volume change per unit distance the midpoint descends. In addition, with a lower and flatter position, the radius of curvature of the diaphragm can increase, resulting in the diaphragm being required to generate greater tension to produce the same degree of P_{di} as compared

to a diaphragm in the normal position and curvature. The degree of P_{di} developed is proportional to the volume change produced by the diaphragm. As a result, the tension (and therefore the energy requirement) of the diaphragm in COPD to generate vital capacity may be greatly increased.

These findings are compatible with the findings that thoracic compliance is normal in COPD subjects as described by Sharp et al. (1968). They are also compatible with the work of Rochester and Braun (1985) who reported that the maximal inspiratory pressures COPD subjects produce were directly related to the diaphragm length, and inversely related to the degree of hyperinflation.

The normal rib cage position and normal change in position across vital capacity combined with a lower diaphragm with decreased change in position, differs greatly from the long-held concept of the barrel chest, elevated rib cage, increased A-P diameter and other classic signs of hyperinflation. This can be resolved to some extent when the method of observation in this study is considered.

Study subjects were carefully instructed, coached and observed to attain TLC and RV with an open glottis. This method assures achieving the maximal limits of position of the rib cage. Routine radiologic studies are often performed at TLC with minimal instruction or observation and no attempt to maintain an open glottis. This results in a submaximal achievement of TLC. The closed glottis permits relaxation of the respiratory muscles with the rib cage recoiling towards its relaxation position, decreasing the rib angle and displacing the diaphragm downward. In the COPD subjects, the extent to which the rib cage falls

may be limited by the lower depressed diaphragm. Normal subjects may have a higher diaphragm at full inspiration and may have a greater fall in the rib cage and diaphragm with closure of the glottis. Therefore, standard radiologic technique may produce the appearance of rib cage elevation in the COPD subjects in comparison to normals.

Another aspect to consider is that the subjects were all studied while stable. Many subjects with COPD are examined by clinicians during exacerbations of obstructive lung disease during which they are acutely hyperinflated in addition to their chronic hyperinflation. The volume of acute hyperinflation may be contained within the rib cage (as observed with exercise) as the diaphragm has already been lowered by the increased volume of the chronic hyperinflation. Subjects may increase the volume of the rib cage during periods of acute hyperinflation at which time they may have elevated rib cage position at FRC and RV (TLC continuing to represent the absolute limit of rib cage position).

Increased retrosternal airspace is one of the radiologic findings frequently associated with hyperinflation which may produce a false perception of increased A-P diameter (Burki and Krumpleman, 1980). The increased distance between the sternum and aorta on the lateral chest radiograph may give the viewer the impression of increased A-P diameter.

Finally, the perception an elevated rib cage position can result from an altered relationship of the chest to abdominal dimensions as reported by Kilburn and Asmundsson (1969). They found no difference in the dimensions of the rib cage in COPD but that the COPD subjects had smaller abdominal dimensions than the normals. The ratio of chest to abdominal dimension was greater in the COPD subjects creating the

illusion of increased size of the rib cage.

B. Mechanisms of the Pattern of Adaptation in COPD

The following is speculation on the mechanism of how the alteration of the human thorax in chronic hyperinflation occurs. From the data presented, chronic hyperinflation results primarily in diaphragm lowering without significant elevation of the rib cage. A proposed model of this development is as follows. In normal subjects in the upright position, the forces returning the rib cage to its normal FRC position (and therefore normal FRC length of intercostal and accessory muscles) are lung recoil and gravity. The rib cage has no primary forces opposing these. The primary force to return the diaphragm to its normal FRC length and position is the inward recoil of the lung and only at times (such as with exercise or other causes of increased ventilation), active abdominal pressure resulting from abdominal muscle activity. The diaphragm has gravity acting as a primary force opposing the return of the diaphragm to the normal FRC position, acting through abdominal hydrostatic forces pulling downward on the diaphragm. As COPD and chronic hyperinflation develop, a primary defect is loss of elastic recoil of the lung. This results in the loss of the major force returning the diaphragm to its normal FRC position. The rib cage is also affected by loss of recoil but continues to have gravity acting upon it, to return it to its normal resting FRC position. In addition, Macklem (1984) suggests that the intercostal muscles are exclusively expiratory at high lung volumes (i.e. elevated rib cage). These factors may limit elevation of the rib cage beyond the range observed in

normals. This would result in tension being maintained on the inspiratory muscles of the rib cage (maintaining a normal functional length), while the diaphragm would undergo a loss of tension. This loss of tension in the diaphragm resulting from the loss of lung recoil may permit the mechanism of sarcomere reabsorption, which was shown to occur in animal models of chronic hyperinflation (Farkas and Roussos, 1982). Sarcomere reabsorption results in a decrease in optimal length of the diaphragm and may allow the diaphragm to continue to develop inspiratory pressures at higher thoracic volumes. This speculative mechanism of thoracic alterations in response to chronic hyperinflation would continue to occur with the diaphragm being primarily altered and rib cage unchanged.

C. Implications

The findings presented in this thesis imply that the rib cage, and therefore the intercostal and accessory respiratory muscles, may continue to function normally in chronic hyperinflation. During normal breathing and especially in acute hyperinflation superimposed on chronic hyperinflation, inspiratory rib cage muscles may supply a tremendous portion of the work of breathing required during acute hyperinflation because of the limitations imposed on the diaphragm. This is an important concept in the evaluation of exercise, the understanding of dyspnea, respiratory muscle function and training, and in the evaluation of drug therapy in COPD.

1. Exercise and the development of dyspnea

Exercise or other demands for increased minute ventilation ($\dot{V}_E$) in COPD subjects with chronic hyperinflation requires the addition of acute hyperinflation increasing end-expiratory lung volumes (Oliven et al. 1985). This differs from normals, in whom the end-expiratory lung volume decreases slightly during exercise (Henke et al. 1988). The higher end-expiratory lung volume in COPD is necessary to increase the mean expiratory flow rate, which is otherwise fixed by airway obstruction. This acute increase in thoracic volume produced by the rib cage and the diaphragm is maintained near the resting end-expiratory position (Dodd et al., 1984; Macklem, 1984). These observations are compatible with the results presented in this thesis, in that the rib cage in chronic hyperinflation maintains the ability to function significantly and increase its dimensions similar to the rib cage of normals.

Increasing $\dot{V}_E$ is frequently related to the development of respiratory muscle fatigue and the sensation of dyspnea. Ventilation at increased lung volumes causes decreased respiratory muscle efficiency and increases oxygen cost of breathing (Collett and Engle, 1986). Such changes may be related to the development of respiratory muscle fatigue in the chronically hyperinflated subjects who have significantly lower diaphragms at their stable baseline. Accompanying the lower diaphragm observed in the subjects with chronic hyperinflation can be a change from a parallel to series arrangement of the costal and crural components of the diaphragm. This can further diminish the ability to produce the needed force to generate increased $\dot{V}_E$ (Macklem et al., 1983). In addition, the lower diaphragm may have an increased radius of

curvature requiring a greater tension development to generate the required transdiaphragmatic pressure (Sharp 1983). While human diaphragmatic fatigue has been examined and defined (Bellmare and Grassino, 1982), the limitation of respiration due to dyspnea does not always occur in association with diaphragmatic fatigue (Grassino et al., 1984). Grassino et al. showed that only 1 of 9 COPD subjects (11%) had diaphragmatic fatigue when maximum tolerable dyspnea occurred with cycle ergometry. The alterations in the thorax presented in this thesis suggest that because the diaphragm is the primary thoracic component altered in COPD, the muscles of the rib cage may play a greater role then previously recognized during periods of increased $\dot{V}_E$ in COPD. A lowered diaphragm, as observed in the COPD subjects in this study may be markedly dysfunctional and inefficient in producing P_{di}. The rib cage muscles may then be required to provide a major contribution (and greater energy requirements compared to normal) to the development of negative inspiratory pressure for ventilation. There may be unrecognized fatigue of the accessory or intercostal muscles which are functioning to maintain rib cage elevation during increased $\dot{V}_E$. Investigation of accessory muscle fatigue in COPD/chronic hyperinflation may be very rewarding, as the accessory muscles could provide an accessible indicator of respiratory muscle fatigue or status, which was previously limited to the diaphragm. The important role of the accessory muscles in elevation of the rib cage during periods of increased $\dot{V}_E$ could explain some of the sensation of dyspnea. El-Manshawi et al. (1986) proposed that the perception of respiratory muscle effort is a conscious awareness of the intensity of outgoing motor commands by corollary

discharge within the central nervous system (CNS). The sensation of dyspnea in the chronically hyperinflated COPD subject may be related to a combination of markedly increased CNS output to the diaphragm (because of the inefficiency of the low flat diaphragm to generate pressure) and increased output to the accessory and intercostal muscles (because they are providing a greater contribution to ventilation than in normals).

Since the rib cage may play a much greater role in COPD subjects, processes which effect the rib cage could be critical. Joint disease (i.e. degenerative joint disease or arthritis) would greatly impair a COPD subject. Figure 13 and Table 2 reveal four COPD subjects in whom the rib cage changes position little from RV to TLC. Subjects such as these may have a much greater limitation to exercise or other demands for increased ventilation. These may also be the subjects who develop positive end-expiratory abdominal pressure, to utilize in inspiration by sudden release at the onset of inspiration.

2. Respiratory muscle function and training

Respiratory muscle training has frequently produced varied responses in COPD subjects (Sharp, 1985). The potential importance of the accessory muscles in the COPD subjects may be a reason for observation and investigation of the accessory muscles during respiratory muscle training and in evaluating the response to training. This concept is also applicable to the evaluation of subjects being weaned from mechanical ventilation. Swartz and Marino (1985) examined nine failed trials of weaning from mechanical ventilation. They observed <u>no</u> decrease in transdiaphragmatic pressure development during weaning and concluded

that weaning failure was not due to the failure of the diaphragm as a pressure generator. Accessory muscles may have played an unrecognized role in the weaning failure and may indicate the value of studying these muscles during weaning of COPD patients from mechanical ventilation.

3. Pharmacologic implications

The effects of drugs on respiratory muscle function and ventilation may also need to be reconsidered in light of the results of this thesis. While aminophylline has been shown to improve diaphragmatic contractility and the recovery from fatigue (Aubier et al., 1981), its influence on increased ventilation in COPD is minimal (Belman et al. 1985). A study of the response to theophylline in severe hyperinflated COPD subjects yielded interesting results (Kongragunta et al. 1988). The authors observed incapacitating dyspnea without diaphragmatic fatigue during cycle exercise and severe dyspnea with diaphragmatic fatigue during inspiratory resistive breathing. Data from Aubier et al. (1986, 1987) showed that digoxin enhanced diaphragmatic contractility in man and dog but had no effect on the sartorius muscle of dogs, and may also lack affect on the accessory muscles.

One interpretation of the above is that there is a differential effect of drugs (such as theophylline or digoxin) on the diaphragm versus the accessory or intercostal muscles, due to inherent differences of these muscle groups. Mechanical and electrical property data of the intercostal and accessory muscles is limited compared to the vast data available on the diaphragm (Sharp and Hyatt, 1986). Therefore, further investigation of the pharmacologic responses of the intercostal and

accessory muscles in comparison to the diaphragm may be very rewarding in interpreting results of clinical pharmacologic studies involving COPD subjects. New information about these muscles combined with future studies of the role of the rib cage in ventilation in COPD subjects will improve the understanding of the mechanics of breathing in chronic hyperinflation.

CHAPTER VI.

CONCLUSIONS

1. Rib cage dimensions in chronic hyperinflation are not significantly increased as compared to normal.
2. The change in the position of the rib cage (from TLC to RV) in chronic hyperinflation is not significantly different as compared to normal subjects.
3. The diaphragm in chronic hyperinflation is significantly lower and has a decreased change in position from TLC to RV as compared to normal.
4. The rib cage and associated muscles may play a greater role in producing ventilation in COPD subjects than in normals.
5. Understanding the importance of the rib cage and accessory muscles in the ventilation of hyperinflated subjects may provide new insights into the understanding of the pathophysiology of COPD.

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