THE LUNG MECHANICS IN EMPHYSEMA:

A COMPARATIVE STUDY IN PATIENTS WITH AND WITHOUT CHRONIC RESPIRATORY FAILURE

by

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ABSTRACT

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The lung mechanics in emphysema: A comparative study in patients with and without chronic respiratory failure.

A comparative study, emphasizing lung mechanics, was made of the clinical and functional pattern in two groups of emphysematous patients; 8 with and 11 without chronic respiratory failure. Loss of lung elasticity appeared to be the most prominent mechanical abnormality in the group with normal arterial blood gases. Airway obstruction due to expiratory check valving was less marked than in the hypercapnic group where it seemed to be the major difficulty, impairment of lung elasticity being a secondary feature. These and other demonstrated differences, suggested that qualitatively different disease processes were represented in the two groups, possibly centrilobular emphysema in the hypercapnic group as opposed to diffuse emphysema in the group with normal blood gases. In addition, the findings suggested that the chief mechanism producing chronic hypercapnia in emphysema is an inability to compensate for distributional defects by increasing ventilation, due to mechanical restriction of the respiratory bellows.

PREFACE

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I. INTRODUCTION

1. The Variability in Manifestations of Emphysema

The original observations by Laennec on the subject of pulmonary emphysema, which he introduced as "an exaggeration of the normal condition of the viscus", involving "a dilatation of the air cells" (25), have been, in part, confirmed and considerably amplified by subsequent studies. The condition, nevertheless, still presents many problems, not the least of which are the absence of a satisfactory definition (14), and considerable uncertainty with regard to the pathogenesis (38).

Various factors underlie these problems, including a difficulty in correlating the clinical, functional and pathological manifestations (13,35) and the fact that patients are generally seen only in the advanced stages of the disorder and there is, consequently, ignorance concerning the incipient phases. However, as was suggested at a recent Ciba Foundation symposium on emphysema (14), the chief difficulty may be the fact that one is dealing not with a single, uniform disease entity but with several different disease processes, the outlines of which have not yet been precisely defined.

Variations which have been noted in the picture presented by individuals with emphysema, some of which suggest more than merely quantitative differences, lend support to the latter idea. For example, Ogilvie (35), by dividing patients with respect to the mode of onset, into one group with a long standing preceding history of chronic bronchitis

and another group without a bronchitic history, was able to demonstrate among other things, a strikingly more severe impairment of diffusion in the second group. He suggested that these clinical and functional dissimilarities might be based on differences in the underlying pathology, the patients with severe diffusion defects having the centrilobular destructive type of emphysema as opposed to simple overdistension in the other group.

Another such variation, and one which forms the subject of the present investigation, centers about the ability of patients with emphysema to compensate for the tendency to impaired gas exchange, with hypoxemia and hypercapnia, which results from such functional defects as non uniform ventilation-perfusion relationships. As a consequence of this variation, emphysematous patients can be divided into two groups: I - those presenting a picture of marked ventilatory insufficiency but with relatively normal arterial blood gas levels and without right heart failure except transiently, during exacerbations, or terminally; II - individuals in whom alveolar hypoventilation, hypoxemia, hypercapnia and cardiac insufficiency are prominent features throughout much of the course of their illness.

Such a differentiation of patients with emphysema is suggested by the findings of Baldwin et al. (3) in a large group of emphysematous patients and was formulated by Richards (38). In the former study two main groups emerged after clinical, radiological, functional and, in some cases, pathological assessment. One group (Type I, "Uncomplicated Pulmonary Insufficiency") had severe ventilatory impairment but was, for the most part, free of heart failure and blood gas abnormalities, when present, were of

a mild degree. The second and smaller group (Type II, "Combined Cardiopulmonary Insufficiency"), separated from the others by the presence of chronic congestive heart failure, or cardiomegaly on chest films, had, at the same time, marked blood gas abnormalities, including hypoxemia and hypercapnia, complained of drowsiness and manifested polycythemia, which was absent in the first group.

The first group of patients, with uncomplicated pulmonary insufficiency, was further subdivided into three progressively more severe varieties of the same pattern, on the basis of blood gas levels after exercise. It is of interest to the present study to detail the findings in this group of patients. Physical examination and chest x-rays revealed hyperinflation of the chest which was confirmed by the demonstration of increased residual air accompanied by reduced vital capacity and normal or slightly elevated total lung capacity. Maximum breathing capacity was decreased and mixing efficiency impaired, with progressively more severe disturbance in this function from sub group 1 to sub group 3. All subgroups displayed hyperventilation at rest and on exercise, except for subgroup 3, where the exercise ventilation was seen to be below normal. Finally, sub group 3 showed a mild degree of hypoxemia and hypercapnia both at rest and on exercise.

The authors' interpretation of the foregoing functional pattern was that these patients were in general, able to compensate for abnormalities of gas and blood distribution by hyperventilation except for sub group 3, where the severity of the distributional abnormality, in addition to the marked degree of mechanical restriction of the chest and lungs, impaired compensation.

Functional findings in the other major group with combined cardiopulmonary insufficiency were of a somewhat different pattern. The total lung capacity was lower, as was the residual capacity. Maximum breathing capacity and mixing efficiency were of the same order as in the uncomplicated type of emphysema but hyperventilation was absent at rest and there was marked hypoventilation on exercise. The authors felt that these findings showed a lesser degree of emphysema in this group as well as depressed responsiveness of the respiratory center to the stimulus of carbon dioxide.

In cases of Type I emphysema which were followed for varying periods, a tendency for a slow progression from sub group 1 to sub group 3 was noted but none moved into Type II emphysema, that is, developed chronic congestive heart failure.

Some difference was also present pathologically between the two major groups of patients. Cases of Type I emphysema revealed well marked diffuse emphysematous changes. In cases of Type II emphysema, morbid anatomical changes were variable. Some patients showed marked emphysematous changes, whereas others, despite severe clinical and functional abnormalities, displayed little in the way of gross emphysema.

In Richards' classification of emphysema (38), the type of emphysema associated with chronic bronchitis is divided into one group comprising subgroups 1 and 2 of Baldwin et al., without prominent blood gas abnormality or heart failure, and a second group, a "syndrome of alveolar hypoventilation", with chronic or recurrent hypoxemia, hypercapnia and heart failure. Though he feels that respiratory center de-

pression plays a part in the difficulties of this second group, he believes that the main problem is a profoundly disturbed ventilation-perfusion relationship such that ninety percent of the lung by volume is underventilated, with a failure of the "hypoxic reflex" to close off blood flow to nonventilated regions. In the other group of patients there is sufficient ventilation of perfused alveoli to maintain blood gases at relatively normal levels.

2. The Problem of Chronic Hypercapnia in Emphysema

The presence of chronic hypercapnia, generally associated with hypoxemia, polycythemia and heart failure, in some emphysematous patients has, in fact, not yet been satisfactorily explained and poses a problem which has engaged the attention of other investigators. Fishman et al. (17) analyzed the subject in the following way. The fundamental physiologic aberration in emphysema is a disturbance of ventilation - perfusion relationships, which is equivalent to an increase in dead space ventilation and in venous admixture. This is compensated for by an increase in minute ventilation which requires increased activity on the part of the respiratory center and the ability of the chest bellows to respond to the increased ventilatory drive.

Some patients with emphysema respond to the addition of carbon dioxide to the inspired air with only a slight increase in ventilation and these are the ones who show chronic carbon dioxide retention. This impaired responsiveness to carbon dioxide might be due to 1) reduction of the maximum ventilatory capacity, 2) increased buffering capacity of

the arterial blood and 3) depressed sensitivity of the respiratory center to carbon dioxide. Comparative studies in normal subjects and in emphysematous patients with and without carbon dioxide retention led these investigators to favor the concept that respiratory center depression was responsible for the hypoventilation of chronically hypercapnic patients. They based their conclusions on these findings: 1- chronically hypercapnic emphysematous patients showed a much reduced ventilatory response to carbon dioxide when compared with eucapnic patients or normals; 2- the response to carbon dioxide in the hypercapnic patients was well below their ventilatory responses both on exercise and in the performance of maximum voluntary ventilation; 3- a carbonic anhydrase inhibitor, administered over a twelve month period to hypercapnic patients, lowered the alkali reserve to normal levels but did not at the same time improve the ventilatory response to carbon dioxide breathing.

Among possible explanations advanced for the presence of central depression in emphysema were hypoxic damage to the respiratory center and prolonged hypercarbia.

Other investigators have, on the other hand, favored the idea that mechanical restriction and the increased work of breathing are responsible for the inadequate ventilation of hypercapnic emphysematous patients, as well as for the impaired responsiveness to carbon dioxide. Richards et al., (36) attempted to separate the part played by the central and neuromuscular apparatus from that of the chest bellows and lung in ventilation, by using the oxygen cost of breathing to measure the former and minute ventilation to assess the latter. In response to

carbon dioxide added to the inspired air, hypercapnic emphysematous patients showed a reduced ventilatory response when compared with normal subjects but the increment in the oxygen cost of breathing with increasing arterial PCO_2 was the same in both groups. The conclusion was, therefore, that mechanical factors played an important part in reducing the ventilatory response to carbon dioxide. Similar conclusions were suggested by the findings of Cherniack and Snidal (11) who demonstrated a correlation between maximum breathing capacity and maximum ventilatory response to carbon dioxide in both emphysematous patients and in normals breathing through added resistances. Furthermore, carbon dioxide stimulus-response curves (the ratio of alveolar ventilation with added carbon dioxide to resting alveolar ventilation plotted aginst increasing percentages of carbon dioxide added to the inspired air) showed a lower slope in emphysematous patients and in normals breathing through added resistances compared with normals breathing without added resistances. Finally, bronchodilators improved the response to carbon dioxide in hypercapnic patients.

To conclude this review of some of the approaches to the problem of carbon dioxide retention in emphysema, it might finally be pointed out that one aspect which seems to have been neglected, is the role, if any, of proprioceptive reflexes, mediated by stretch receptors in the lungs or chest wall, in producing ventilatory changes. Recent investigations (9,42) it is true have tended to discount the part played by the Hering-Breuer reflexes in modifying the breathing pattern in man. Nevertheless, Campbell (9) in a study of the effect of "threshold loads" on breathing has suggested the presence of an alternate reflex mechanism, not mediated

by the vagi, through which the activity of the respiratory muscles could be adjusted to mechanical changes. Furthermore, the hyperventilation observed in pulmonary fibrosis and other states associated with increased stiffness of the lungs has been ascribed to increased activity of stretch receptors (37,44). It seems, then, possible that the hypoventilation seen in some cases of emphysema could be correlated with changes in activity of stretch reflexes, resulting from alterations in lung mechanics, for example, increased compliance leading to decreased stretch.

3. The Purpose of the Present Investigation

The foregoing has suggested the need for a comparative study emphasizing lung mechanics in emphysematous patients with and without chronic respiratory failure. The present investigation which is such a study has two main objectives. Firstly it will try to confirm and more precisely define the differences between these two groups of patients. The study by Baldwin et al., already referred to, which outlined some of these differences, omitted, it should be noted, comparisons of lung mechanics as well as of diffusing capacity. Secondly, it will attempt to furnish, by means of alterations in lung mechanics, a convincing explanation of the differing ability in the two groups to compensate for functional changes tending to produce hypoxemia and hypercapnia. Such an explanation is, as has already been indicated, thus far lacking.

II. HISTORICAL REVIEW OF MECHANICAL STUDIES IN EMPHYSEMA

The importance of mechanical factors, particularly airway obstruction in emphysema, was recognized by Laennec who felt that the most usual cause of the disease was a severe and extensive "dry catarrh" resulting in obstruction of the smaller bronchi by "pearly sputa" or by swelling of their membranes. Trapping of air in the lungs by the bronchial obstruction was conceived of as a consequence of the normal imbalance between a strong inspiratory apparatus and a weak expiratory mechanism. Mention was made, furthermore, of the possibility of loss of elasticity, in explaining the 'pillow of down' sensation imparted by the emphysematous lung (25).

Quantitative evidence of increased flow resistance in emphysema was, however, not obtained until more than one hundred years later by Neergard and Wirz (34). Rohrer's principles of analysis and measurements of airflow and pleural pressure or, alternately, the lateral pressure at the mouth during occlusion of the airway, were used to determine alveolar pressure. This was demonstrated to be raised to three or four times that seen in normals, at the same flow rate, in one patient with chronic bronchial asthma and "slight emphysema". The same type of increase in alveolar pressure was evident in a second patient identified as having chronic bronchial asthma alone. This study is, of course, of importance chiefly for its introduction of a method of analysis of the mechanics of airflow rather than for a conclusive demonstration of the presence of increased flow resistance in emphysema.

Christie, in 1934 (12), pointed out that though indirect evidence suggested a loss of elasticity in emphysema, proof of such a loss and quantitative measurements of lung elasticity in the disease were lacking. He attempted to supply both with a study of intrapleural pressure and tidal volume, simultaneously recorded, in two cases of emphysema. The normal lung studied in this fashion was felt to possess "perfect elasticity" since the degree of distension was proportional to the change in intrapleural pressure so that when the change in intrapleural pressure per 100 cc. of distension was plotted against total distension of the lung a horizontal line was obtained. In advanced emphysema, by contrast, a complete loss of elasticity was postulated, chiefly on the basis of the loss of proportionality between the degree of distension and the change in pleural pressure. Plotting of the pleural pressure change per 100 cc. of distension against total lung distension, in the same way as before, yielded a logarithmic curve "characteristic of a non elastic body in which the same force can produce different degrees of distension". It has been noted by subsequent investigators (31,39) that the pressure-volume measurements in this pioneer study do not clearly differentiate between static and kinetic forces and the lung elasticity determined from these measurements probably includes an element of flow resistance.

Dayman (16) discounted Laennec's explanation of the expiratory difficulty in emphysema as being due to weaker expiratory forces, pointing out that greater force can, in fact, be exerted against a mercury column by expiratory effort, than by inspiratory effort. Measurements of lung tension and pulmonary pressure, derived from simultaneous air-flow and pleural pressure tracings in a group of eleven subjects,

including five normals and four with advanced emphysema, led him to suggest instead an expiratory check valve mechanism, potential in health, operational in emphysema. In normal expiration, the distending effect of lung tension on the walls of the airways is reduced by the drop between pulmonary and intra canalicular pressure, that is, in transmural pressure across the bronchial wall, and bronchial narrowing results. A decline in lung tension as the lung deflates, also promotes bronchial narrowing. This tendency toward expiratory bronchial narrowing is converted, in emphysema, into an actual valvular obstruction as a result of the presence of intrinsic obstruction of the airway, which increases the pulmonary pressure-intracanalicular pressure gradient, as well as by the reduction or loss of lung elasticity, leading to lack of support for the bronchioles and permitting their collapse in expiration. Such a mechanism was felt to be responsible for the findings on mechanical study of emphysematous patients. Reasonably good rates of airflow were present in inspiration, despite a higher than normal degree of airway resistance. In expiration, especially on forced expiration, good initial rates of airflow were followed by a sudden decrease in rate, in spite of sustained positive pleural pressure and in association with a drop in lung tension to zero levels. Post-mortem examination of gelatin-filled lungs suggested to Dayman that the pathological basis of check valving in emphysema was, in part, the breakdown of lung parenchyma, resulting in a loss of elastic support for the bronchioles.

His findings with regard to lung elasticity were similar to those of Christie, already referred to. In normal subjects there was a direct proportion between lung size and lung tension. In emphysematous patients,

on the other hand, a non linear relationship between lung size and lung tension was present. The maximum lung tension was not above 10 cm. of H_2O in the four cases examined. These findings suggested to this investigator a decrease rather than a complete loss of elasticity. He felt that the decline in lung tension was due to breakdown of lung parenchyma rather than to a primary defect in lung elasticity.

In a post-mortem investigation of emphysematous lungs, McIlroy and Christie (29) found an increase in viscous resistance to ventilation as measured by the ratio of tidal volume at a slow rate of ventilation in a plethysmograph to that obtained at a rapid rate, the pressure change being the same in both cases. The fact that the index of viscous resistance observed on hydrogen was greater than that predicted from the reduced viscosity of hydrogen as compared with air, was taken to indicate that the increase in viscous resistance was due chiefly to an increase in tissue viscosity, rather than to airway obstruction. Though reduced tracheal pressures recorded on opening the chest suggested a decrease in lung elasticity, it was felt that most of the "loss of elasticity" described in previous studies in emphysema, was due to an increase in tissue viscous resistance.

Stead et al. (39) reinvestigated the elastic properties of the lungs in normal subjects and in emphysematous patients, using intraesophageal pressures to assess intrathoracic pressure and momentary interruptions of the air stream to produce static conditions. The static pressure-volume relationship was found to have a curvilinear shape in both normals and emphysematous subjects with the preservation of a

functional relationship between pressure and volume in emphysema. Measurement of the slope of the pressure volume curve in the tidal volume range (where it was approximately linear), in terms of pressure change per 100 cc. of volume change, demonstrated a higher value, indicating a stiffer lung, in emphysema. On the other hand, intraesophageal gauge pressure at the functional residual capacity level was significantly lower than normal in emphysema and the entire pressure-volume curve was shifted upwards. The conclusion of these investigators was that the emphysematous lung retains some retractive force but "the functional relationship of this retractive force to change in lung distension is altered."

Fry et al. (21) studied the kinetic forces involved in ventilation by means of pressure-flow curves constructed from pneumotachygraphic and esophageal pressure tracings obtained before and during interruption of the air stream in normal subjects and in emphysematous patients. A comparison of pressure-flow curves obtained during the breathing of argon-oxygen mixtures with such curves obtained during air breathing left the conclusion that tissue viscous resistance was a negligible factor in both normals and in patients with emphysema. A increase in flow resistance in both inspiration and expiration was again demonstrated in emphysema. In addition, the expiratory portion of isovolume pressure-flow curves displayed, in emphysema, an increased tendency to "bend" and form flow peaks which could not be exceeded despite an increase in pressure. This effect increased as the lung deflated, flow maxima being reached at progressively lower levels of flow. These flow peaks would appear to be the equivalent of Dayman's "check valve"

mechanism, being explained as the consequence of bronchiolar collapse promoted by decreased lung retractive force and increased intra alveolar pressures producing positive intrathoracic pressures.

Assessing lung elasticity in terms of compliance, the volume change per unit of pressure change, Mead et al. (31) demonstrated an increase above normal levels in lung compliance in emphysematous patients when this was measured under static conditions, for example during airway interruption. However, compliance determined during quiet breathing from the volume and pressure changes between instants of zero flow was found to be somewhat less than normal and, in addition, a progressive fall in compliance was noted with increases in respiratory rate. No such drop was evident in normals. This variation in compliance with breathing frequency in emphysema was explained by the authors as being due to an unequal distribution of flow resistive properties (a non uniform distribution of elastic properties might also play a part) throughout the lung such that more and more of the airflow is deviated to unobstructed portions of the lung as the respiratory rate increases. The consequence is that the portion of the lung participating in ventilation becomes smaller and smaller, leading to a fall in the measured compliance.

Cherniack's studies of lung mechanics in a group of eighteen patients with emphysema (10) confirmed the findings of Mead et al. with regard to the variation in compliance with respiratory rate and the increase in static compliance, at least in patients presenting without signs of right sided heart failure. In six of the group presenting with congestive heart failure, however, the pattern of mechanical abnormalities

differed from that of the other patients. "Static" compliance (that is, in this study, compliance measured at breathing frequencies below resting levels) was lower than normal and the "functional" compliance (compliance measured at the resting respiratory rate) fell to lower levels than in the other group of patients. The coefficients of viscous resistance were much higher than in the group of patients without congestive heart failure. Finally, the work of breathing, including total, elastic and viscous components, was highest in this group of emphysematous patients. Cherniack felt that these differences could, possibly, be explained by the presence of fibrosis and pulmonary vascular congestion in these patients.

In summary, it is evident that there is no unanimity concerning the abnormalities of lung mechanics in emphysema. Previous studies are most in agreement as to the presence of increased flow resistance and as to the mechanism underlying this, the part played by expiratory check valving and bronchiolar collapse being emphasized. It should be noted, however, that at least one study (McIlroy and Christie) discounts the importance of airway narrowing in the increased flow resistance and suggests, instead, that an increase in tissue viscous resistance is responsible. There has been more disparity in the results obtained by different investigators from studies of lung elasticity in emphysema. A decrease in lung elasticity, complete loss of this property and increased stiffness of the lungs have all been demonstrated. This variation in findings is undoubtedly, in part, due to a difference in the methods used in the studies. For example the dependence of lung compliance or elastance in emphysema on the respiratory frequency and the time available for equi-

libration of pressures seems to have been clearly shown and it is apparent that different results will be obtained under static as opposed to dynamic conditions of measurement.

In addition, it seems possible that some of the variability in results is due to an actual variation in the type of mechanical abnormalities to be found in emphysematous patients. Except for Cherniack's study, previous investigations of lung mechanics in emphysema have not concerned themselves with such a possibility and it will be further explored in the present study.

III. METHODS

1. Subjects

The subjects of the study were nineteen male patients with emphysema selected from the wards and out-patient clinics of the Queen Mary Veterans' Hospital to which they had come for treatment of chronic chest disease. Most patients first came to attention because of the clinical picture they presented. A few were selected on the basis of routine pulmonary function studies. Criteria for the diagnosis of emphysema and for inclusion in the study were the following: 1- a history of chronic exertional dyspnea with or without asthmatic episodes, cough and sputum, not attributable to primary heart disease or to primary fibrotic or granulomatous disease of the lungs; 2- radiological evidence suggesting emphysema, particularly signs of vascular attenuation or obliteration involving both lungs in full-field mid-section tomograms of the chest; 3- a combination of abnormalities on ordinary pulmonary function tests, including evidence of hyperinflation manifested as an increase in residual volume with or without an accompanying increase in functional residual capacity above predicted values, evidence of airway obstruction suggested by a reduction in the 3/4 second forced expiratory volume (F.E.V. .75) below predicted values and reduction in the steady state carbon monoxide diffusing capacity below predicted values.

Where congestive heart failure or an acute exacerbation of symptoms was present, the studies of lung function, to be outlined subsequently, were delayed until compensation had been achieved or the acute symptoms

had subsided. Except in one case (E.D., Table II) patients having radiological evidence of extensive pulmonary fibrosis were excluded. In view of the age group studied (range 46 to 73 years), it was unavoidable that associated conditions, ischemic heart disease, diabetes mellitus, etc., were present but when these were of such severity as to relegate the emphysematous condition to a secondary place, patients so afflicted were excluded from the study. The tests performed, particularly the mechanical studies, demanded a great deal of cooperation from these generally markedly disabled patients and a few test failures resulted. It should finally be emphasized that in each case studied, one was dealing with an advanced emphysematous condition with a long history of illness and with repeated admissions to hospital for treatment of resulting symptoms. Details of the clinical picture and of the physical characteristics of individual patients are given in Tables I and II.

The subjects chosen for study were divided into two groups, a) those with relatively normal arterial blood gas levels (Group I) and b) those with chronic carbon dioxide retention (Group II), on the basis of arterial blood gas studies of oxygen saturation, pH, $PaCO_2$ and bicarbonate, repeated in most cases at weekly or longer intervals so as to clearly define the trend in each patient. In one case (W.S., Table IV), the patient did not return for repeat studies and he was allocated to Group I on the basis of one study showing a $PaCO_2$ of 47 mm. Hg.and an oxygen saturation of 94.5%. References to Tables IV and V will reveal that arterial blood gas values fluctuated considerably. However, where the $PaCO_2$ did not rise above 54 mm. Hg. and did not persist above 50 mm. Hg., particularly in conjunction with an arterial oxygen saturation of 90% or

above, the patient was assigned to Group I (in most cases in this group the $PaCO_2$ was below 50 mm. Hg.). Where the arterial PCO_2 remained, in general, at or above 55 mm. Hg., the patient was assigned to Group II. It is evident from the foregoing that the term "normal" arterial blood gases is, in this study, a relative one and, further, that Group II consists of patients with well marked arterial blood gas abnormalities, including hypercapnia and usually hypoxemia. There were eleven patients in Group I and eight patients in Group II.

2. Procedures

A history of illness with attention to the onset, type and course of respiratory and cardiovascular symptoms and with note of any family or early history of chest or allergic diseases, as well as of occupational factors and smoking, was obtained from each patient and was supplemented from the usually extensive hospital files. Examination of the chest and cardiovascular system was also performed.

Where these were not already available hemoglobin and hematocrit determinations, plain posteroanterior and lateral chest films as well as full-field mid-section chest tomograms were obtained for each patient.

Routine pulmonary function studies performed in every patient included measurements of vital capacity, residual volume and functional residual capacity, total lung capacity, mixing efficiency, the 3/4 second forced expiratory volume, the steady state resting carbon monoxide diffusing capacity and arterial blood gas studies (values for the diffusing capacity in one patient, P.D., Table IV, have been mislaid). The functional

residual capacity and mixing efficiency were determined by the helium dilution method described by Bates and Christie (4) and Bates et al.(6). Vital capacity and its subdivisions were determined during the breathing of oxygen in a six liter C.F. Palmer spirometer. Residual volume was obtained by subtracting the expiratory reserve volume from the functional residual capacity and total lung capacity was determined from the sum of residual volume and vital capacity. The diffusing capacity was determined by the steady state method with end tidal sampling of alveolar carbon monoxide described by Bates et al.(5). The forced expiratory volume was analyzed from the tracing of a forced expiration after a maximal inspiration, performed into a light spirometer made of Perspex. The volume expired in the first three quarters of a second multiplied by forty gives one the F.E.V. .75 which is, in effect, an indirect maximum breathing capacity (6). Arterial PCO_2, pH and bicarbonate were determined by the Astrup technique (1,2). Arterial oxygen saturation was determined on a Beckman spectrophotometer (33) as well as, in a few cases, with the Van Slyke-Neill method (40). Arterial blood was drawn from the brachial and femoral arteries with the patient recumbent. It should be mentioned that where these tests (of lung volume, diffusing capacity, mixing efficiency and F.E.V. .75) had already been performed they were not repeated at the time of the mechanical studies so that there was, in some cases, a lapse of several months between the two sets of studies. That no great error results from such an approach is suggested by the study of Becklake et al. (7), in which it is shown that repeated pulmonary function studies in emphysema show little change over considerable periods.

The predicted values for the subdivision of lung volume and for F.E.V. .75 were obtained from the regression formulae of Goldman and Becklake (22), with a correction of -15% in the case of the F.E.V. .75 to permit the formula for this to be used at sea level (6). Predicted values for diffusing capacity were derived from the formula presented by Bates et al. (6).

Resting and exercise minute ventilation were measured on room air in a 150 liter Tissot spirometer into which the subjects breathed through a two-way, low resistance flap valve. The average resting minute ventilation for a six minute period of breathing was determined after the subjects had rested in a semi-recumbent position in a garden chair for thirty minutes (15). Tests of exercise ventilation were performed on a treadmill at a speed of one-half mile an hour for all patients but with the slope varied according to the weight of the patient so that the product of speed, slope and weight, or, in other words, the work performed was kept constant at approximately 55 kg.-meters per minute. The test lasted six minutes with expired air being collected during the last two minutes and again an average figure for minute ventilation was calculated. Figures for ventilation were corrected to BTPS and expressed as liters per minute per square meter of body surface area.

The lung mechanics were assessed with modifications of methods and equipment described by Stead et al. (39) and Frank et al. (19), from simultaneous recordings of transpulmonary pressure, air flow and lung volume changes. Transpulmonary pressure was taken to be the difference between lateral mouth pressure, determined by a pressure tap in the mouth

piece and intraesophageal pressure, determined by a latex balloon 15 cm. in length attached to a 105 cm. polyethylene catheter (20,30) and inserted into the lower esophagus. Both pressure sources were attached to a differential pressure transducer (Sanborn 267B) which was calibrated against a water column. The balloon and catheter were passed through the nose after a small amount of pontocaine anesthesia to the nose and pharynx. Positioning of the balloon was obtained by passing it into the stomach, withdrawing until negative pressure fluctuations on inspiration were obtained and then withdrawing a further 15 cm. Alternately, a length of catheter, measured from the tip, equal to the distance from ear lobe to xiphisternum (approximately 40 cm.) was introduced. Prior to recording, a small amount of air, no more than 3.3 cc. in the balloons used in the study, was injected into the balloon.

Air flow was measured with a pneumotachygraph of the type decribed by Lilly (27) connected to a Statham strain gauge (PM. 97, 0.05 psid.). Calibration of the pneumotachygraph with a rotameter revealed that it was non linear above 3 liters per second of flow but it should be noted that none of the patients attained this level.

Volume changes were measured in a Stead Wells spirometer (41), to the wheel of which a potentiometer was attached. The amplified and recorded signal derived from the latter was calibrated against volume changes recorded on the kymograph of the spirometer.

The output of the two transducers and the potentiometer was amplified and recorded by a Sanborn 67-1200 four-channel recorder.

Static and dynamic measurements were performed with separate mouthpiece assemblies. For static measurements a solenoid valve was inserted between the spirometer tubing and the mouthpiece. 2.5 second closures of this valve were activated by an electrical timing device operated by a hand switch. The pneumotachygraph was not used in static measurements and the patient breathed through only one arm of the spirometer circuit.

The arrangement of equipment is illustrated in Fig. 1.

All measurements were performed in the sitting position at least one hour after meals. The following tests were done.

1. Static Compliance

After a short period of quiet breathing to obtain a baseline end expiratory level (taken to be the functional residual capacity level), interruptions of air flow were made with the solenoid valve, starting at the end expiratory level and continuing during the ensuing inspiration. The patient was instructed to delay further inspiration during the closure of the valve. The same procedure was attempted during the subsequent expiration but was achieved in only a few patients. In addition it was not usually possible to carry the patient to the point of maximal inspiration and the static pressure at the latter point was determined separately. After a period of quiet breathing, the subject was instructed to take in as deep a breath as possible and to continue trying to breathe in so as to maintain the pressure level static for at least two seconds. Duplicate determinations of both interrupted breathing and maximal inspiratory pressure were made.

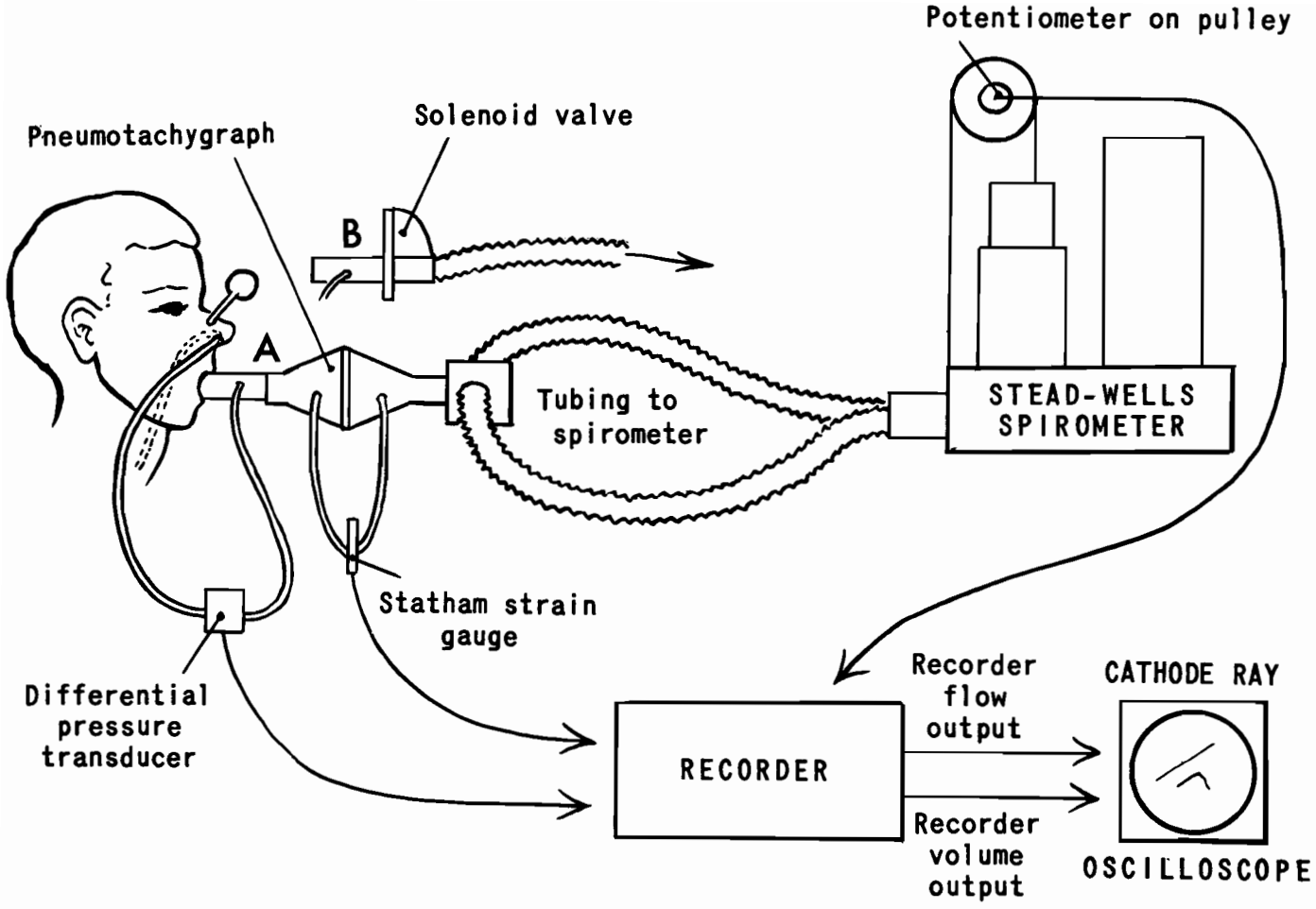

Fig. 1 Diagram of apparatus used in mechanical studies.
A. Mouthpiece assembly for dynamic studies.
B. Mouthpiece assembly for static studies.

The static transpulmonary pressures so obtained were plotted against the appropriate volume changes (added to the previously determined functional residual capacity) to obtain a "compliance" curve. Measurements of the slope of this curve in the tidal volume range (where it was invariably a straight line) were made and calculated as a percentage of the value predicted from the formula of Frank et al.(18). Measurements of overall compliance (31) were determined from the ratio of absolute lung volume at the maximum inspiratory level to the pressure at this point. Compliance measurements were expressed in liters per cm. of water pressure.

2. Dynamic compliance and Flow resistance

Recordings of transpulmonary pressure, change in lung volume and airflow were made while the patient breathed for approximately fifteen breaths into the spirometer through the pneumotachygraph. Records were taken at two respiratory frequencies: 1) the resting level and 2) moderate hyperventilation. Dynamic compliance was measured from the ratio of change in volume to the change in transpulmonary pressure between the instants of zero flow at the extremes of inspiration and expiration (19,34) and represented the average of ten breaths.

Flow resistance was calculated separately for inspiration and expiration by the method illustrated in Fig. 2. Verticals drawn upwards from the flow tracing indicated the points of zero flow on both the volume and transpulmonary pressure tracings. Straight lines were then drawn between the points of zero flow on both the volume and pressure tracings. It will be noted that the straight line on the volume record intersects

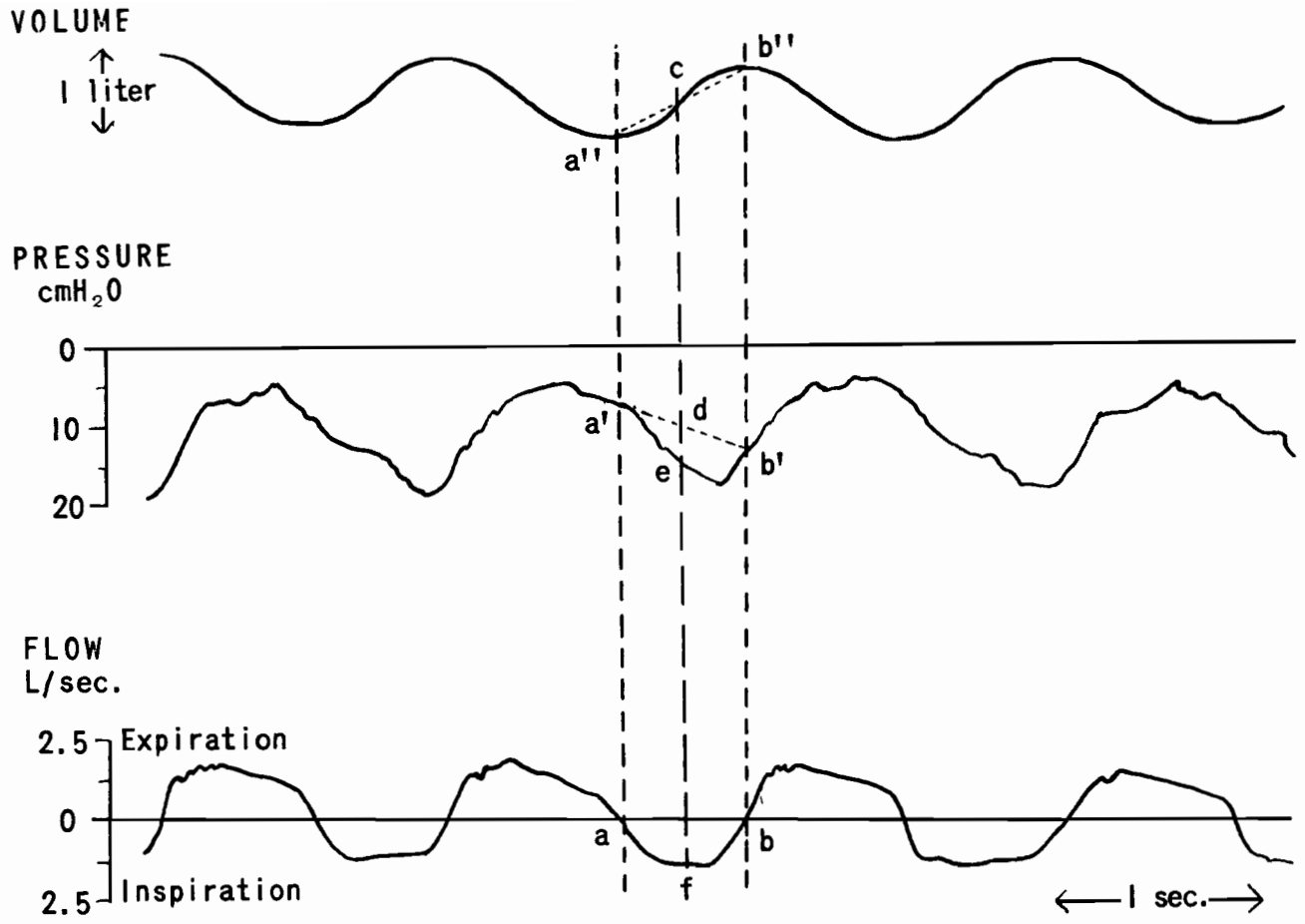

Fig. 2 Method used to determine airway resistance. a, b - points of zero flow on flow tracing. a'b' - straight line drawn through points of zero flow on pressure tracing. a"b" - straight line drawn through points of zero flow on volume tracing. cdef - vertical extended downwards from intersection of a"b" with inspiratory portion of volume tracing. d - indicates level of lung elastic pressure at this point in the respiratory cycle, de - equals flow resistive pressure and f is the appropriate rate of airflow. Airway resistance for inspiration is then equal to de/f. The same procedure is followed for the determination of expiratory airway resistance.

the sigmoid shaped inspiratory portion of the volume tracing. Since lung elastic pressure varies directly with volume change, lung elastic pressure will at this point in the respiratory cycle also fall on a straight line drawn between the points of zero flow on the pressure record. Consequently, a vertical extended downwards from the point of intersection on the volume record indicates the level of lung elastic pressure at this point as well as the difference between this and the total transpulmonary pressure, which is equal to the flow resistive pressure. The same vertical indicates, on the flow tracing, the appropriate flow rate. Flow resistance, which is the ratio of flow resistive pressure to flow rate and is expressed as cm. of H_2O per liter per second, was determined in this way for both inspiration and expiration. The figures presented are the average for ten breaths.

3. The Flow-Volume Curve

This determination has been introduced as a valuable method of assessing the physical properties of the lower airways and the method used was essentially that of Hyatt et al.(24). The esophageal balloon was not needed for this part of the study and was removed. The outputs of the flow and volume amplifiers were directly coupled to the Y and X axes respectively of a long persistence cathode-ray oscilloscope. Tracings of oscilloscopic patterns were at first made with grease pencil on the removable plastic grid of the oscilloscope and then were transferred onto tracing paper. The patient breathed into the spirometer through the pneumotachygraph. He was first instructed to breathe quietly so that a tracing of a tidal breath could be obtained. Subsequently, he was asked to exhale at first with maximum effort and speed and then, with lesser

degrees of effort after maximal inspirations. A peak flow-volume curve was obtained by these manoeuvers. The slope of this was measured and was expressed in terms of liters per second per liter. It should be mentioned that in some cases, the initial part of the curve had a concave shape and the slope given for such subjects is that of the lower part of the curve which was approximately linear.

The resistance of the spirometer circuit was determined by measuring the pressure drop between the mouthpiece and the inside of the spirometer while a subject breathed through the mouthpiece assembly containing the pneumotachygraph. For the purpose of determining pressures inside the spirometer, a plastic catheter was inserted into the bell of the latter through a connecting tube introduced into one arm of the spirometer circuit. Resistances determined in this fashion were relatively low, 0.37 cm. of H_2O per liter per second at 0.5 liters per second of flow and .54 cm. of H_2O per liter per second at 2 liters per second of flow. It was assumed that there was no significant phase lag between the flow and pressure recording systems. Phase lag between the pressure and volume recording systems was roughly assessed by recording mouthpiece gauge pressure and volume while a subject inspired or expired against the closed solenoid valve. Opening of the valve produced a sudden change on the volume record together with a sudden pressure change. The average lag measured between the points of onset of the volume and pressure changes was 0.034 seconds which would also appear to be minor in degree.

Where the significance of the difference between means has been assessed in this study, the p value was obtained through use of the t-test

for uncorrelated means. The coefficient of correlation, where this was determined, was obtained with the product-moment correlation test.

IV. RESULTS

Symbols and abbreviations used in the tables.

VC	Vital Capacity
RV	Residual volume
FRC	Functional residual capacity
TLC	Total lung capacity
RV/TLC	Ratio of residual volume to total lung capacity
$F.E.V._{.75}$	3/4 second forced expiratory volume
D_LCO	Diffusing capacity for carbon monoxide
$PaCO_2$	Partial pressure of carbon dioxide in arterial blood
SaO_2	Saturation of hemoglobin with oxygen in arterial blood
C_L	Lung compliance
F-V Curve	Flow-volume curve
Hct.	Hematocrit
B.S.A.	Body surface area
Ht.	Height
Wt.	Weight
M^2	Square meter
L.	Liter
% pred.	Percent of predicted value

1. Clinical Data

Clinical information in individual patients together with a tabular summary of this, with means where applicable, is presented in Tables I-III. It should be noted that the duration of illness was measured from the time of onset of any chronic respiratory symptoms and includes the period with chronic cough alone, where this preceded exertional dyspnea. There was no significant difference between the mean duration of illness in the two groups. In addition, the mean ages appear comparable. However, when these two pairs of means are considered together it is apparent that the illness resulting in chronic hypercapnia began at a somewhat earlier time in life, 29.5 years on the average compared with 37.5 years in Group I. Another item of interest is the lower average weight in Group II, with the same average height in both groups.

The type of onset of illness differed somewhat in the two groups. In Group I, eight had a typical "chronic bronchitic" history, chronic cough with or without episodes of asthmatic dyspnea preceding the onset of exertional dyspnea. In two patients the exertional dyspnea was present from the start and in one patient there was a history of seasonal episodes of paroxysmal wheezing dyspnea suggesting bronchial asthma, prior to the onset of exertional dyspnea. In Group II, on the other hand, only four of the eight patients had an initial bronchitic history, the other four complaining of exertional dyspnea from the start.

Physical examination proved to be of no value for comparative purposes. Both groups showed, on examination of the chest, similar

TABLE I Clinical Data in Individual Patients - Group I

Group I	Age	B.S.A. M^2	Ht. cm.	Wt. kg.	Clinical Course	Duration of illness-yr.	Congestive failure	Acute CO_2 narcosis	Years off work	Cigarettes per day	Evidence of Allergy	Physical Examination	Tomograms	HCT %	E.C.G. changes
D.M.	57	1.49	158	50	Chronic cough '46. Exertional dyspnea '57. Rt. hemiplegia '43 & '55.	16	0	0	0	30	0	Inc. AP diam. Poor movt. Diffuse exp. rhonchi.	+ + / + +	45	Normal
T.B.	52	1.62	168	55	Intermittent cough, wheezing '34. Persistent '43. Exertional dyspnea '58.	28	0	0	1½	20	Eosinophilia	Inc. AP diam. Poor movt. Diffuse insp.& exp. rhonchi	+ / + +	44	Normal
S.D.	63	1.65	157	64	Cough, wheezing, dyspnea spring-fall '28-'51. Then yr. round symptoms and exertional dyspnea.	34	0	0	11	10	History bronchial asthma.	Inc. AP diam. Fair movt. Diffuse rhonchi.	+ + / + +	46	Clockwise rotation.
G.F.	57	2.00	176	82	Winter bronchitis age 5-12. Chronic cough '42. Exertional dyspnea '55 after cholecystectomy.	20	0	0	0	20	Hay fever in family. 6-8% eosinophilia + skin test dust, ragweed.	Inc. AP diam. Poor movt. Rhonchi only on forced exp. Poor air entry.	+ / +	51	Normal
W.S.	46	1.58	160	55	Recurring cough, wheezing dyspnea '42 -'49. Then persistent symptoms & exert. dyspnea.	20	0	0	3	20	+ skin test tree pollen. dust, ragweed tobacco.	Inc. AP diam. Poor movt. Diffuse insp. & exp. rhonchi. Poor air entry.	+ / + +	45	Normal
S.C.	73	1.63	170	55	Chest symptoms after 'flu' '43. Gradually inc. cough, sputum exertional dyspnea.	19	0	0	13	20	0	Inc. AP diam. Poor movt. No rhonchi. Poor air entry.	+ + / + +	41	Dig. effect
D.L.	46	1.51	158	51	Cough '43-'54. Then exertional dyspnea	19	0	0	5	6	0	Inc. AP diam. Fairly free movt. Diffuse rhonchi.	/ + +	45	Normal
G.C.	69	1.71	168	62	Cough '16. History TB'31. Exertional dyspnea '47. 4 bouts spont. Px. Signs C.H.F. during 1 of these.	46	+	0	31	12	0	Barrel chest. Poor movt. Diffuse rhonchi. Good air entry.	+ + / + +	48	Dig. effect Transient P pulmonale
A.C.	67	1.48	165	45	Chronic cough '42. Exertional dyspnea '60. TB. pleurisy (rt) '55.	20	0	0	8	20	0	Small chest. Poor movt. No rhonchi. Good air entry.	/ + +	40	Tall P 2,3. aVF suggest. rt. auric. enlargement.
P.L.	70	1.71	168	62	Onset symptoms after chest cold '56. Exert. dyspnea, asthma. Ankle swelling 2 yrs. Mild diabetes.	6	+	0	6	0	Persistent eosinophilia 5-10%. + skin test bact. feathers.	Inc. AP diam. Poor movt. Diffuse insp. & exp. rhonchi.	+ / + +	47	Sinus tach. vert. heart. clockwise rot. P pulmonale
I.G.	58	1.62	168	54	Chronic cough '45. Exertional dyspnea after partial gastrect. for bleeding duodenal ulcer '53.	17	0	0	9	30	0	Normal size chest. Good movt. Diffuse exp. rhonchi Poor air entry.	+ + / + +	45	Vert. heart. clockwise rotat. P pulmonale

TABLE II Clinical Data in Individual Patients - Group II

Group II	Age	B.S.A. M^2	Ht. cm.	Wt. kg.	Clinical Course	Duration of illness-yr.	Congestive failure	Acute CO_2 narcosis	Years off work	Cigarettes per day	Evidence of Allergy	Physical Examination	Tomograms	HCT %	E.C.G. changes
C.C.	56	1.70	163	65	Recurring cough, wheezing '40. Exert. dyspnea '42. Tracheost. & mech. vent. for acute CO_2 narcosis '62.	22	0	+	0	30	0	Inc. AP diam. Poor movt. No rhonchi.	+ + / + +	58	Vert. heart. Peaked P 2.3, aVF
E.D.	48	2.04	176	87	Chronic cough, exertional dyspnea '42 Appear. C.H.F. '58. Comatose on O_2 & after morphia. Acute CO_2 narcosis '61.	20	+	+	0	15	0	Inc. AP diam. Poor movt. Diffuse exp. rhonchi. Basal rales.	+ + / + +	58	RAD prominent P 2.3, aVF V_1-V_2. Rt. vent. enlarge.
E.B.	51	1.49	155	52	Chronic cough, wheezing, exertional dyspnea '41.	21	0	0	0	10	0	Inc. AP diam. Poor movt. Diffuse exp. rhonchi.	+ / + +	51	Vent. heart. clockwise rotat.
L.P.	63	1.68	164	63	Onset cough, sputum, exert. dyspnea '42. First appearance (rt) heart failure '60.	20	+	0	5	5	0	Normal size chest. Poor movt. Diffuse exp. rhonchi	+ +	56	Clockwise rot. P pulm. Cor pulm. & myocard. ischemia
J.L.	64	1.69	155	70	Chronic cough '19. Exert. dyspnea '42. Recurrent C.H.F. '60. Myocard. infarct. '57 & '58. Acute CO_2 narcosis '61.	43	+	+	7	20	0	Normal size chest. Poor movt. Diffuse exp. rhonchi	+ +	67	RAD P pulmonale
R.F.	46	1.86	177	68	Pneumonia 3x childhood. Chronic cough, asthma '42. Subtotal gastrect. '61 for peptic ulcer. Exertional dyspnea after spont. Px. '61.	20	0	0	3	10	0	Barrel chest. Fair movt. Diffuse exp. rhonchi. Good air entry.	+ +	38	RAD. clockwise rotat. P pulmonale.
A.L.	65	1.62	161	59	Cough '18 after 'flu' & pneumonia. Exertional dyspnea '48. Ankle swelling '60.	44	0	0	4	20	0	Barrel chest. Poor movt. Diffuse rhonchi. Good air entry.	+ +	47	QS V_2 & V_3. Old ant. infarct.
L.M.	60	1.83	175	68	Chronic cough '35. Exert. dyspnea '42. C.H.F. '60. Drowsiness after O_2.	27	+	0	11	?	0	Inc. AP diam. Diffuse rhonchi on forced exp.	+ + / + +	57	P pulmonale 2,3. aVF

TABLE III

Summary and Comparison of Clinical Data in Groups I and II

	GROUP I	GROUP II	P
Number of patients	11	8	
Mean Age - Years	59.8	56.6	
Mean B.S.A.-M^2	1.63	1.73	
Mean Ht. - cm.	165.09	165.75	
Mean Wt. - Kg.	57.70	66.50	
Mean duration of illness - Years	22.27	27.12	N.S.
Number still at work	2	3	
Mean years off work (others)	9.7	6	
Mean cigarettes per day	17	15.7	
Number $\bar{c}$ possible occupational factors	4	1	
Number $\bar{c}$ allergic phenomena	5	0	
Number $\bar{c}$ acute CO_2 narcosis	0	3	
Number $\bar{c}$ congestive heart failure	2	4	
Number $\bar{c}$ ECG suggesting cor pulmonale	3	6	
Number $\bar{c}$ enlarged pulmonary conus or cardiomegaly on x-ray	3	5	
Mean hematocrit - %	45.18	54.00	
Tomograms			
Diffuse disease	5	3	
3 lobes	2	1	
2 lobes	4	4	

combinations of increases in chest size, hyperresonance, limited expansion, diminished air entry and diffuse rhonchi on expiration and inspiration. From the point of view of diagnosis in emphysema, the most constant physical signs would appear to be limitation of expansion and the presence of expiratory rhonchi or diminished air entry.

It will be evident from Tables I-III that the incidence of polycythemia, radiographic and electrocardiographic evidence of cor pulmonale and signs of heart failure, is highest in the hypercapnic and hypoxemic group. This is not surprising in view of previous work which has demonstrated a correlation between anoxia and, to a lesser extent, hypercapnia, and factors leading to right ventricular hypertrophy and failure, including pulmonary hypertension, increases in red cell and total blood volume and in cardiac output (23). The higher incidence of cor pulmonale in the hypercapnic group taken together with the presence of episodes of acute carbon dioxide narcosis only in this latter group, indicates a more malignant form of emphysema. This conclusion seems justifiable despite the fact that no difference in the severity of dyspnea or cough could be demonstrated and despite the fact also that a higher proportion of patients were still at work in Group II.

Possible differences in etiological factors were sought in an analysis of smoking habits as well as of the relative incidence of occupational contact with respiratory irritants, and allergic phenomena in the two groups. With such small numbers of patients, of course, the significance of this type of analysis will be quite limited. There was no difference between the two groups in terms of average number of cigarettes smoked per day. On the other hand occupational factors and allergic phenomena were more prominent in group I. Three patients in

this latter group had worked as house painters and felt that their symptoms were aggravated by their work, especially when they had to do "spray" painting and neglected to wear a mask. One additional patient in this group had worked as a bricklayer, described this as a very dusty job and felt that it increased his symptoms. One patient in Group II had been employed as a painter. "Allergic phenomena" in this study include a history of seasonal asthma in one patient, eosinophilia in three patients, otherwise unexplained and associated with positive skin tests in two, and positive skin sensitivity alone in one patient. All were members of Group I.

An attempt, finally, was made to describe the extent of the emphysematous process by means of the distribution of vascular changes, attenuation or obliteration, on tomograms of the chest. For convenience, the chest was reduced to four lobes with the right middle lobe being included with the right upper lobe. The vascular involvement is indicated diagrammatically in Tables I and II where the four quadrants represent the respective four "lobes" of the lung and the plus signs indicate involved areas. A tendency toward more diffuse disease is perhaps present in Group I but the difference in distribution of vascular changes is certainly not striking.

2. Routine Pulmonary Function Tests

The results of routine pulmonary function testing in individual patients are presented in Tables IV and V with means for the groups and p values for the differences between the means in Table VI. The results of arterial blood gas studies have already been discussed under methods.

TABLE IV Results of Routine Pulmonary Function Studies in Individual Patients - Group I

Group I	Date	$PaCO_2$	pH	HCO_3	SaO_2	Date	VC L.	% Pred.	RV L.	% Pred	FRC L.	% Pred	TLC L.	% Pred	RV TLC %	Mixing Eff. %	$FEV_{.75}$ L/min	% Pred	D_L CO cc/min/mm Hg	% Pred	Date	Ventilation L/min/M^2 Rest.	Exer.
D.M.	9-61	40	7.39	22		29- 8-61	1.92	62	3.39	191	4.00	133	5 31	110	63.8	41.5	41	57	7.53	52	15-11-61	7.2	13.2
	1-11-61	37	7.43	23.5	98.6																		
T.B.	25-10-60				94.2	22- 8-60	2.45	62	4.44	228	4.97	138	6.89	117	64.6	29.5	32	35	8.86	54	23- 1-62	6.9	15.7
	11- 1-61				90.8																		
	18- 1-61	45	7.36	24																			
	29- 8-61	47	7.31	22																			
S.D.	1- 9-61	49	7.36	26		8- 9-61	2.73	88	4.05	219	4.67	178	6.78	146	59.8	45	52	71	10.2	83	2- 2-62	4.4	11.1
	13- 9-61	48	7.36	25	82																		
G.F.	7- 2-62	53	7.36	27.5	95.4	23- 2-62	2.95	70	3.50	153	4.38	122	6.45	98	54.3	32.5	42	40	8.53	55	23- 2-62	6.1	14.2
	28- 2-62	54	7.35	27.5	95.5																		
	7- 3-62	47	7.36	25	95																		
	4- 4-62	50	7.38	27.5	96.9																		
W.S.	28- 2-62	47	7.40	27	94.5	22- 2-62	1.54	44	3.69	226	3.69	119	5.23	101	70.6	40.75	24	25	9.33	53	27- 2-62	5.1	16.8
S.C.	23-11-60				92.8	10-11-60	2.87	86	4.16	176	4.97	134	7.03	122	59.1	37	47	78	5.47	51	28- 2-62	8.9	18.7
	9- 3-61	44	7.35	24																			
	5- 9-61	45	7.35	23																			
D.L.	7- 3-62	47	7.33	23.5	96.4	8- 3-62	1.68	49	3.78	233	3.91	129	5.46	108	69.2	48.4	32	36			8- 3-62	6.6	12.2
	14- 3-62	44	7.37	24	97.7																		
G.C.	7- 3-62	47	7.42	28.5	94.3	9- 3-62	2.02	61	3.21	140	3.72	106	5.23	92	61.4	42	21	31	5.32	47	22- 3-62	5.0	9.8
	28- 3-62	46	7.44	29.5																			
A.C.	5- 4-62	45	7.40	26		9- 3-62	2.22	71	2.59	120	3.34	92	4.81	90	53.8	30	24	46	7.42	64	16- 4-62	9.7	18.9
	18- 4-62	44	7.38	24.5	95.6																		
P.L.	16- 5-62	51	7.42	31	96.75	18- 5-62	2.33	70	3.02	134	3.76	107	5.35	94	53.8	15	21	32	6.24	56	22- 5-62	6.7	12.5
	23- 5-62	50	7.43	31	95.9																		
	30- 5-62	46	7.46	31	90.75																		
	6- 6-62	45	7.46	30	93.1																		
I.G.	1-11-61	50	7.40	29		12- 6-62	2.97	80	4.12	197	5.15	141	7.09	121	58.1	22	32	41	9.20	64	8- 6-62	5.9	10
	6- 6-62	41	7.40	24	97.6																		
	13- 6-62	47	7.38	26	96.9																		

TABLE V Results of Routine Pulmonary Function Studies in Individual Patients - Group II

Group II	Date	$PaCO_2$	pH	HCO_3	SaO_2	Date	VC L.	% Pred.	RV L.	% Pred	FRC L.	% Pred	TLC L.	% Pred	RV TLC %	Mixing Eff. %	$FEV_{.75}$ L/min	% Pred	$D_L CO$ cc/min/mm Hg	% Pred.	Date	Ventilation L/min/M^2 Rest.	Exer.
C.C.	30- 1-61				85	3-10-61	1.88	54	3.67	195	3.85	126	5.55	104	66.1	31	20	23	7.87	53	21-12-61	6.4	12.6
	12- 9-61	64	7.31	29																			
	27- 9-61	64	7.31	29	80																		
	21-12-61	57	7.36	30	89.5																		
E.D.	13- 9-61	82	7.28	34	78	14- 9-61	1.69	38	2.79	133	3.05	87	4.48	67	62.3	27.8	31	25	6.39	36	11- 1-62	3.5	10.5
	26- 1-62	75	7.40	42	83.4																		
	29- 1-62	61	7.35	31	91																		
E.B.	13- 9-61	59	7.31	27	81	17-11-60	1.98	64	3.76	238	4.52	163	5.74	122	65.5	34.2	28	36	7.23	34	9- 1-62	6.9	13
	19- 9-61	59	7.32	28																			
	12- 3-62	60	7.33	29	99.1																		
L.P.	29- 8-58				82	5- 7-61	1.65	50	2.99	147	3.13	98	4.64	86	64	28.7	19	25	6.34	45	13- 2-62	4.1	8.8
	7- 6-61	72	7.28	30																			
	14- 6-61				86																		
	31- 1-62	59	7.38	32	86.5																		
	23- 2-62	75	7.30	33	82																		
J.L.	9- 2-61	62	7.36	32		29- 9-61	1.08	40	1.95	108	2.03	72	3.03	67	64	33	27	38	4.90	41	12- 2-62	4.4	8.5
	27- 9-61	76	7.31	34	82.8																		
	25-10-61	70	7.35	35	85																		
	17- 1-62	61	7.35	31	96																		
R.F.	11- 1-62	50	7.41	29	99.1	7- 2-62	2.14	46	3.38	160	3.42	87	5.52	80	61.3	24.4	32	28	8.94	47	13- 2-62	5.2	10.9
	14- 2-62	60	7.36	31	93.3																		
	21- 2-62	55	7.34	27	94																		
	7- 3-62	49	7.40	28	91																		
	30- 5-62	57	7.35	29	95.4																		
A.L.	8- 9-61	60	7.30	27	89	11- 5-61	1.78	65	3.92	199	3.98	133	5.70	110	68	33	39	57	8.34	70	19- 3-62	5.6	17.1
	12- 9-61	59	7.31	27																			
	18- 9-61	55	7.33	27																			
	19- 3-62	55	7.35	28	94.6																		
L.M.	17- 4-62	71	7.38	38	85.1	27- 4-62	1.93	47	2.97	127	3.49	91	4.90	76	60.6	33	31	35	5.37	37	1- 5-62	6.2	13
	2- 5-62	56	7.42	33	96.85																		

TABLE VI

Comparison of Mean Values for Routine Pulmonary Function Studies in Groups I and II

MEANS	GROUP I	GROUP II	P
$PaCO_2$ - mm Hg.	46.50	62.30	
SaO_2 - %	94.53	88.56	
VC - liters	2.33	1.76	
- % predicted	67.54	50.50	<.01
RV - liters	3.63	3.17	
- % predicted	183.00	163.37	N.S.
FRC - liters	4.23	3.43	
- % predicted	127.18	107.12	N.S.
TLC - liters	5.96	4.94	
- % predicted	109.	89.	<.05
RV/TLC- %	60.7	63.9	
Mixing Efficiency - %	34.87	30.63	
$F.E.V._{.75}$ - liters/min.	33.40	28.30	
- % predicted	44.72	33.37	N.S.
D_LCO - cc/min./mm. Hg.	7.81	6.92	
- % predicted	57.90	43.37	<.05
Resting Ventilation - $L/min/M^2$	6.59	5.28	<.1
Exercise Ventilation - $L/min/M^2$	13.91	11.80	N.S.

With regard to the remaining results, it should be noted that both groups displayed the type of abnormalities to be expected in emphysema. Vital capacity was reduced below predicted, residual volume and, in many cases, functional residual capacity were increased above predicted normal levels. Mixing efficiency was impaired, the forced expiratory volume was low and diffusing capacity was below predicted levels in both groups. When the two groups were compared, however, certain differences emerged. The mean values for the subdivisions of lung volume all tended to be lower in Group II, though only the differences between the means for vital capacity and total lung capacity were statistically significant. The mean total lung capacity was, in the case of Group I, moderately elevated above predicted normal levels and was, in contrast, below predicted levels in Group II, this difference being significant. Little difference was discovered between the figures for mean mixing efficiency in the two groups. The mean value for forced expiratory volume was lower in the hypercapnic group but the difference was not statistically significant. Mean diffusing capacity was significantly lower in Group II.

The measurements of resting and exercise ventilation were also performed on a group of ten subjects in the middle age range, without chest disease, who were being treated for a variety of minor conditions, diabetes, lumbar disc disease and the like. The average age was 48.5 years with a range of 44 to 64 years. The mean resting ventilation was 4.4 liters per minute per square meter of body surface area with a range of 2.7 to 5.6 liters/minute/M^2. The mean exercise ventilation was 10.3 liters per minute per square meter of body surface area with a range of 6.5 to 14.1 liters/minute/M^2. When the mean figures for the emphysematous

patients were contrasted with these figures it is evident that the latter tended to hyperventilate both at rest and on exercise. The degree of this hyperventilation was, however, lower in Group II than in Group I. A good deal of overlapping between the two groups will be noted if the individual figures for ventilation are examined (Tables IV and V) though the most pronounced examples of hyperventilation were to be found in Group I and the lowest figures for ventilation, with values within the normal range, occurred in Group II. Though the differences between the mean values for exercise ventilation were not statistically significant, the differences between the means in the case of resting ventilation approached the .05 level ($t = 1.93$ d.f. = 17) and could be considered significant.

3. Lung Mechanics

The results of mechanical studies in individual patients are presented in Table VII, with means for the two groups in Table VIII. In Table IX, firstly, the overall picture of lung mechanics in emphysema obtained by combining results for the two groups, is compared with results obtained by the use of similar techniques in a group of six normal subjects. The latter were very kindly furnished by Drs. M.R. Becklake and P.T. Macklem of the Joint Cardiorespiratory Service of the Royal Victoria Hospital (8). It can be seen that static compliance, whether measured in the tidal volume range or at the maximum inspiratory position, as "overall compliance", is elevated in emphysema. Dynamic compliance, measured during quiet breathing is, on the other hand, below normal levels. A further drop becomes evident with hyperventilation. It should be noted

TABLE VII Results of Mechanical Studies in Individual Patients - Groups I and II

Group	Date	STATIC C_L L/cm H_2O					DYNAMIC C_L L/cm H_2O				AIRWAY RESISTANCE QUIET RESP. cm H_2O/L/Sec			AIRWAY RESISTANCE HYPERVENTILATION cm H_2O/L/Sec			Slope of F-V Curve L/sec/L
		Tidal Vol Observed	Range % Pred	Max. Insp. Press.	Overall C_L	Shape of Compliance Curve	Resp Freq	Quiet Freq.	Resp Freq	Hyper Vent.	Resp. Freq.	Insp.	Exp.	Resp. Freq.	Insp.	Exp.	
Group I																	
D.M.	15- 1-62	.125	105	-16	.340	Concave	16	.115	39	.184	16	8.11	11.01	39	10.65	11.31	.94
T.B.	17- 1-62	.250	164	- 9.5	.356	Straight	16	.170	36	.288	16	7.87	9.68	36	9.39	12.08	.61
S.D.	24- 1-62	.131	113	-14	.443	Straight	14	.177	20	.186	14	11.12	9.46	20	10.23	9.25	.92
G.F.	1- 2-62	.375	209	-11	.579	Straight	16	.206	34	.155	16	8.61	9.60	34	6.18	5.42	.60
W.S.	26- 2-62	.128	102	-14.5	.345	Concave	18	.099	44	.086	18	13.59	20.80	44	14.60	18.36	.52
S.C.	28- 2-62	.387	245	-11	.627	Convex	14	.336	42	.194	14	7.16	6.79	42	6.85	8.23	1.36
D.L.	9- 3-62	.206	177	-15	.378	Convex	16	.165	24	.164	16	7.04	9.60	24	8.19	9.10	.68
G.C.	21- 3-62	.200	133	-16	.342	Straight	12	.151	34	.091	12	11.27	15.50	34	11.96	19.12	.39
A.C.	11- 4-62	.237	169	- 8	.590	Straight	16	.189	39	.155	16	5.08	6.38	39	6.17	9.37	1.2
P.L.	18- 5-62	.225	149	- 9	.577	Concave	20	.243			20	5.96	7.49				1.14
I.G.	7- 6-62	.250	165	-16	.426	Convex	16	.094	42	.037	16	16.06	22.65	42	17.25	22.70	.64
Group II																	
C.C.	20-12-61	.140	104	-16	.312	Straight	14	.114	24	.069	14	11.85	17.46	24	13.68	17.69	.38
E.D.	4- 1-62	.112	62	-13	.307	Straight	18	.067	24	.083	18	12.41	13.43	24	12.61	11.23	.84
E.B.	8- 1-62	.250	236	-15	.416	Straight	20	.122	64	.050	20	8.68	11.00	64	13.81	26.91	.57
L.P.	26- 1-62	.250	179	- 9	.229	Concave	20	.088	33	.094	20	20.26	29.33	33	18.18	21.18	.20
J.L.	5- 2-62	.196	181	-12	.277	Convex	18	.125	36	.092	18	8.10	7.78	36	9.61	10.06	.80
R.F.	12- 2-62	.237	129	-18	.286	Convex	18	.147	45	.096	18	8.12	11.58	45	9.44	10.81	.60
A.L.	19- 3-62	.228	179	-14.75	.379	Convex	16	.111	27	.117	16	7.04	9.61	27	8.28	10.54	.80
L.M.	30- 4-62	.318	181	-17	.329	Convex	18	.145	33	.161	18	10.40	13.98	33	11.46	16.15	.58

TABLE VIII

Comparison of Mean Values for Lung Mechanics in Groups I and II

MEANS		GROUP I	GROUP II	P
Static Compliance				
Tidal Volume Range - L/cm.H_2O		.228	.216	N.S.
	- % predicted	156.37	157.36	
Overall Compliance - L/cm.H_2O		.454	.316	<.01
Number with Normal C_L Curve		3	4	
Number with Straight C_L Curve		5	3	
Number with Concave C_L Curve		3	1	
Dynamic Compliance - L/cm.H_2O				
Resting (av. frequency)		.176(15.8)	.114(17.7)	<.05
Hyperventilation (av.frequency)		.154(35.4)	.095(35.7)	<.05
Airway Resistance - cm.H_2O/L./sec.				
Quiet Breathing:	Inspiratory	9.26	10.85	
	Expiratory	11.72	13.64	
Hyperventilation:	Inspiratory	10.12	12.13	N.S.
	Expiratory	12.49	15.57	N.S.
F-V Curve				
Slope: L./sec./L.		.818	.596	N.S.
Number $\bar{c}$ Tidal breath on F-V Curve		3	7	
Number $\bar{c}$ Tidal breath below F-V Curve		8	1	
Number $\bar{c}$ Linear F-V Relationship		8	2	
Number $\bar{c}$ Curvilinear F-V Relationship		3	6	

TABLE IX

Mean values, ranges and standard deviations for lung mechanics in combined group of 19 emphysematous patients compared with group of 6 normal subjects.

		STATIC C_L L/cm H_2O		Respiratory Rate	DYNAMIC COMPLIANCE L/cm H_2O	AIRWAY RESISTANCE cm H_2O/L/sec.		SLOPE OF F-V CURVE L/sec/L
	NO.	Tidal Volume Range	Overall Compliance			(average airway resistance)		
Normal	6							
Mean		.193	.178	14	.189	1.7		2.25
Range		.104-.260	.118-.206		.110-.273	1-2.2		2-2.9
S.D.		±.066	±.036		±.034	±1.1		±.34
Emphysema	19					Inspiratory	Expiratory	
Mean		.223	.396	16.63	.150	9.93	12.53	.724
Range		.112-.387	.229-.627		.067-.336	5.08-20.26	6.38-24.33	
S.D.		±.071	±.109		±.055	±3.63	±5.19	±.028

that the method used to calculate airway resistance in the normal subjects was different from that used in the emphysematous patients. Nevertheless it is clear that there is a marked increase in airway resistance in emphysema, particularly in expiration. The reduced slope of the flow-volume curve confirms the airway impediment.

Aside from this general picture of the abnormalities in lung mechanics, certain differences were discovered when the results in the two groups of emphysematous patients were compared. Static compliance measured in the tidal volume range was almost the same in the two groups, but when measured at the point of maximal inflation as overall compliance, it was found to be significantly lower in Group II.

Since it has been pointed out that no single figure adequately describes the elastic properties of the lungs (32), the shape of the static pressure-volume curves obtained in the two groups were also examined. In general three types of pressure-volume curves were obtained, a convex curve which is the normal relationship (19,39), a straight-line curve and, in a few patients, a curve with an upward concavity indicating an increase in lung compliance as lung volume increases, the same type of relationship as was demonstrated by Christie in his early study (12). These three types of curves are illustrated in Fig. 3. The more marked involvement of lung elasticity in Group I suggested by the mean figures for overall compliance was confirmed by the types of curves obtained in this group. Eight out of eleven patients had abnormal curves, either straight or concave, in Group I as compared with only half of the patients in Group II with abnormal curves (Table VIII).

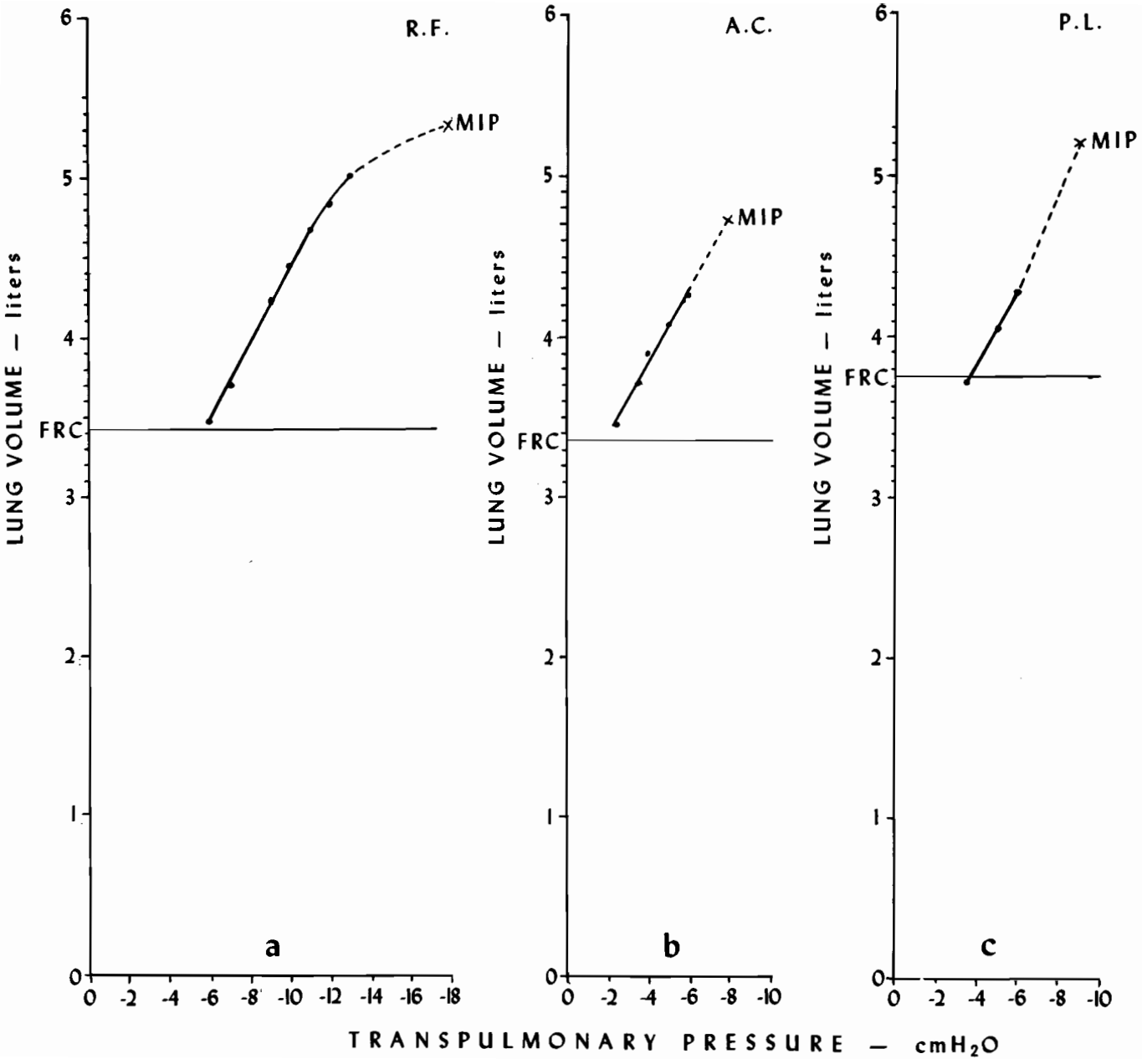

Fig. 3

Types of static pressure-volume curves obtained in emphysema.
MIP - maximum inspiratory point.

a. R.F., Group II - shows normal convexity of upper portion of curve, linear pressure-volume relationship in tidal volume range.
b. A.C., Group I - linear pressure volume relationship throughout full range of inspiration.
c. D.L., Group I - linear pressure volume relationship in tidal volume range, becoming concave towards maximum inspiratory position.

Mean dynamic compliance was similarly higher both during quiet breathing and on hyperventilation in Group I, these differences being significant. These means mask the fact that some patients (e.g. D.M. and T.B., Table VII) actually showed a considerable increase in dynamic compliance on hyperventilation, the explanation for which is not clear.

Mean inspiratory and expiratory resistance values were found to be slightly higher during resting breathing in Group II. This difference became somewhat more marked during hyperventilation but was, even then, not found to be statistically significant. It is of interest that at least three patients in Group I (S.C., A.C. and P.L., Table VII) displayed values for inspiratory and expiratory resistance only slightly above the range of resistance values found in elderly normal patients by Frank et al.(19).

The mean slope of the flow-volume curve was lower in the hypercapnic group of patients but the difference between the means of the two groups was not significant. Just as with the static pressure-volume relationship, the use of one figure to describe the peak flow-volume relationship is of questionable value for comparative purposes since some patients displayed a curvilinear flow-volume relationship. This curved type of flow-volume plot (Fig. 4b) with an exponential initial drop in maximal flow as volume decreased, suggested the operation of a check valve mechanism and bronchial collapse and was more frequent in Group II. Six of the eight patients in the latter group had curved as opposed to straight line flow-volume plots, whereas in Group I only three of the eleven patients had curved flow-volume plots, the other eight showing a linear relationship (Fig. 4a). In addition, in seven of the eight hypercapnic

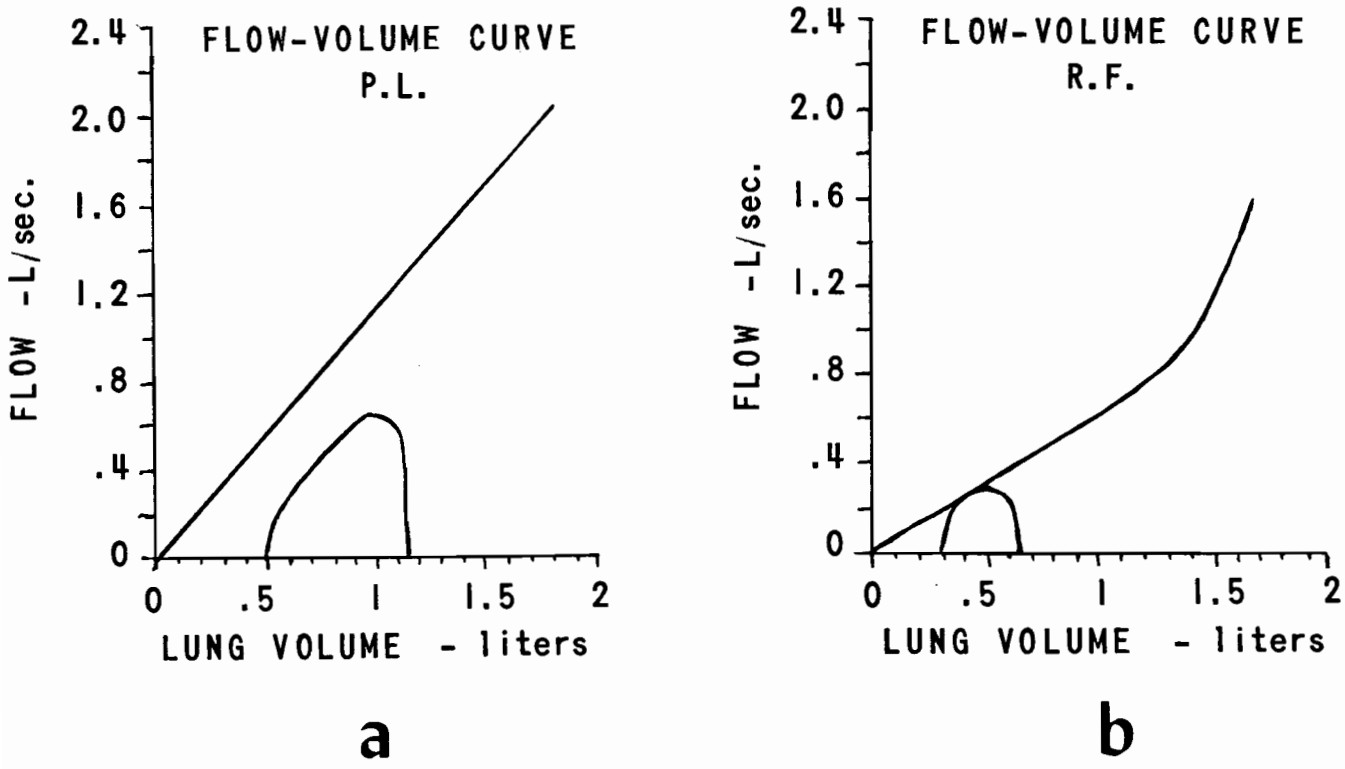

Fig. 4 Examples of typical expiratory peak flow-volume curves in Groups I and II, traced from oscilloscopic patterns. Lung volume is measured from residual volume.

a. P.L., Group I - linear flow-volume relationship with tidal breath falling below the curve.

b. R.F., Group II - curvilinear flow-volume relationship with tidal breath inpinging on the curve.

patients, the resting tidal breath was seen to impinge directly on the peak flow-volume curve (Fig. 4b) suggesting a markedly limited ability to increase ventilation. This phenomenon was observed in only three of the Group I patients, the tidal breath falling below the peak flow curve in the others.

The foregoing suggests that the hypercapnic group has in fact much more marked airway difficulty than the group with normal blood gases, despite the lack of significance found for the differences between the mean resistance values and between the mean values for slope of the flow-volume curve.

V. DISCUSSION OF RESULTS

Though a certain degree of overlap is evident from the results obtained, nevertheless some major differences between the two groups of patients have, it would seem, been demonstrated. The group with normal blood gases shows a much more marked loss of lung elasticity, evidenced by the higher mean overall compliance and the loss of the normal convexity of the static compliance curve in a majority of the cases. It has been suggested that the normal static pressure-volume curve is dependent on the interplay of two factors, the tension exerted by the alveolar surface and the elastic properties of pulmonary tissues (32). Tissue forces are said to be dominant at the higher lung volumes and would appear to be responsible for the convexity of the upper portion of the pressure-volume curve. On this basis the loss of the convexity in emphysema might be attributed to an impairment or loss of tissue elastic forces.

On the other hand, on the evidence of the different types of flow-volume curves, together with the small and admittedly not statistically significant differences in airway resistance, airway difficulties and check valving appear to be much less prominent in Group I than they are in Group II. Here loss of elasticity appears to be a secondary feature, with airway obstruction due to check valving, as suggested by the "collapsing" type of flow volume curve, being the major difficulty. Since it has been suggested that expiratory check valving is in part a result of decreased lung elasticity (16,21), it is surprising to find this mechanism to be more prominent in the group with lower compliance. This leads to

the speculation that there may be an increase of bronchial compliance in the hypercapnic group of patients.

In addition to these differences in lung mechanics, it is possible to distinguish between the two groups to some extent in other aspects of pulmonary function. The mean lung volumes, particularly the vital capacity and total lung capacity, are lower in Group II. It is true that differences between the two groups with respect to residual volume and functional residual capacity are not significant but the fact that these volumes are lower rather than higher in the hypercapnic group is, in itself, of some importance. If Group II is simply a more advanced stage of Group I, a more marked degree of hyperinflation would have been expected in the former group. It might in any case be pointed out that the larger lung volumes found in Group I could be explained by the higher levels of compliance found in these patients.

It has been recognized that the diffusing capacity as determined by the steady state carbon monoxide method does not distinguish between distributional defects and actual impairment of the alveolar-capillary membrane itself (28). The significantly lower mean diffusing capacity in Group II may consequently reflect only a more marked non uniformity of ventilation in this group. However, the mean values for mixing efficiency show little difference between the two groups and this suggests the possibility that there is more damage to the alveolar-capillary membrane in the hypercapnic group of patients.

The mean values for resting and exercise ventilation are lower in Group II but only those for resting ventilation can be considered signi-

ficantly different. The explanation of this difference between resting and exercise values is not clear. The limited significance of the variations in ventilation between the two groups may be due to the limitations of the techniques used for measurement but, more probably is the result of an overlap consequent on there being more than one mechanism underlying the development of chronic carbon dioxide retention in emphysema.

There are finally at least two features of interest in the clinical data obtained from the two groups of patients. One is that despite the presence of a more severe form of emphysema in Group II, the duration of illness in this group is not significantly different from the other group. In addition, the type of onset is somewhat different in the hypercapnic group suggesting, as does the first point, that one is, perhaps, not dealing simply with a difference in degree.

The results obtained in the two groups of patients in the present study are similar to those obtained by Baldwin et al., with respect to ordinary pulmonary function tests and to those obtained by Cherniack, with respect to lung mechanics (3,10). There is a suggestion that qualitatively different disease processes are represented in the two groups of emphysematous subjects. Cherniack suggested that the lower compliance values in his group of patients with heart failure were due to the presence of pulmonary fibrosis and pulmonary vascular congestion in these patients. On the other hand the hypercapnic patients in the present study were not, at least clinically, in congestive failure and only one patient displayed radiological evidence of extensive fibrosis. It is therefore difficult

to explain the lower compliance in this group on the basis of these factors. A better explanation perhaps, is that in the hypercapnic patients, the disease tends to be localized to, or around, the airways, leaving the lung parenchyma and lung compliance relatively intact. It is of interest in the latter connection that, in the study of Baldwin et al., some of the patients with combined cardiopulmonary insufficiency had at autopsy little in the way of gross emphysema (3). In contrast, it is possible to visualize the pathology in Group I as being more peripheral in localization, with involvement of lung elasticity as the chief, and perhaps as a primary feature.

Such a distribution of pathology, more centrally for the hypercapnic group and more peripherally for the group with normal blood gases, is similar to that found by Leopold and Gough in centrilobular as opposed to diffuse emphysema (26). It is of interest also that right ventricular hypertrophy was discovered by these authors to be much more common in centrilobular emphysema, as is of course the case with the hypercapnic group in the present study. The same investigators, furthermore, pointed to a possible pathological basis for check valving, found in the present study to be more common in the hypercapnic group, in centrilobular emphysema where destruction of inter alveolar septae leaves the supplying bronchiole unsupported. Ogilvie's suggestion that the lower diffusing capacity in one of his two groups of emphysematous patients might be due to the presence of the destructive parenchymal changes of centrilobular emphysema in these patients, is interesting in view of the significantly lower mean diffusing capacity in the hypercapnic group of patients. Wyatt finally, has suggested that the total lung capacity is lower in centri-

lobular emphysema than in "panlobular" emphysema, though he feels that right ventricular hypertrophy is more common in the latter disorder (43). Such considerations prompt the speculation that the chronically hypercapnic group of patients is composed largely of individuals with centrilobular emphysema as opposed to diffuse emphysema in the group with relatively normal blood gases.

With regard to the problem of the mechanism producing chronic hypercapnia in emphysema, as already suggested, the overlap between the groups in terms of values for minute ventilation indicates that more than one such mechanism is operative. For example, patient A.L. in the hypercapnic group (Table V) was found to be in chronic respiratory failure despite pronounced hyperventilation, at least on exercise. Such a state of affairs can only be explained by the presence of a marked distributional defect for which it is impossible to compensate by an increase in ventilation. However, the mechanical differences between the two groups, taken in conjunction with lower mean values for ventilation in Group II and the comparability of the mean values for mixing efficiency in the two groups, suggest that the chief mechanism producing chronic hypercapnia in emphysema is an inability to increase ventilation as a result of mechanical restriction of the respiratory bellows. Implied of course in such an explanation is the presence of a tendency to impaired gas exchange resulting from an imbalance between ventilation and perfusion which is, as indicated in the introduction, a basic feature in emphysema.

In patients in Group I, any airway obstruction is apparently compensated for by an increase in compliance and thus less work performed against elastic resistance to breathing. In Group II, relatively greater

airway difficulties are associated with a stiffer lung, both indicating a relatively greater total work of breathing than in Group I and a much more restricted ability to increase ventilation. Such a hypothesis is supported by significant positive correlations obtained between overall compliance and resting ventilation ($r = +.682$, $p < .01$), between overall compliance and exercise ventilation ($r = +.593$, $p < .01$), and between the slope of the flow-volume curve and resting and exercise ventilation ($r = +.554$, $p < .02$; $r = +.496$, $p < .05$). These correlations are illustrated in the scattergraphs (Fig. 5).

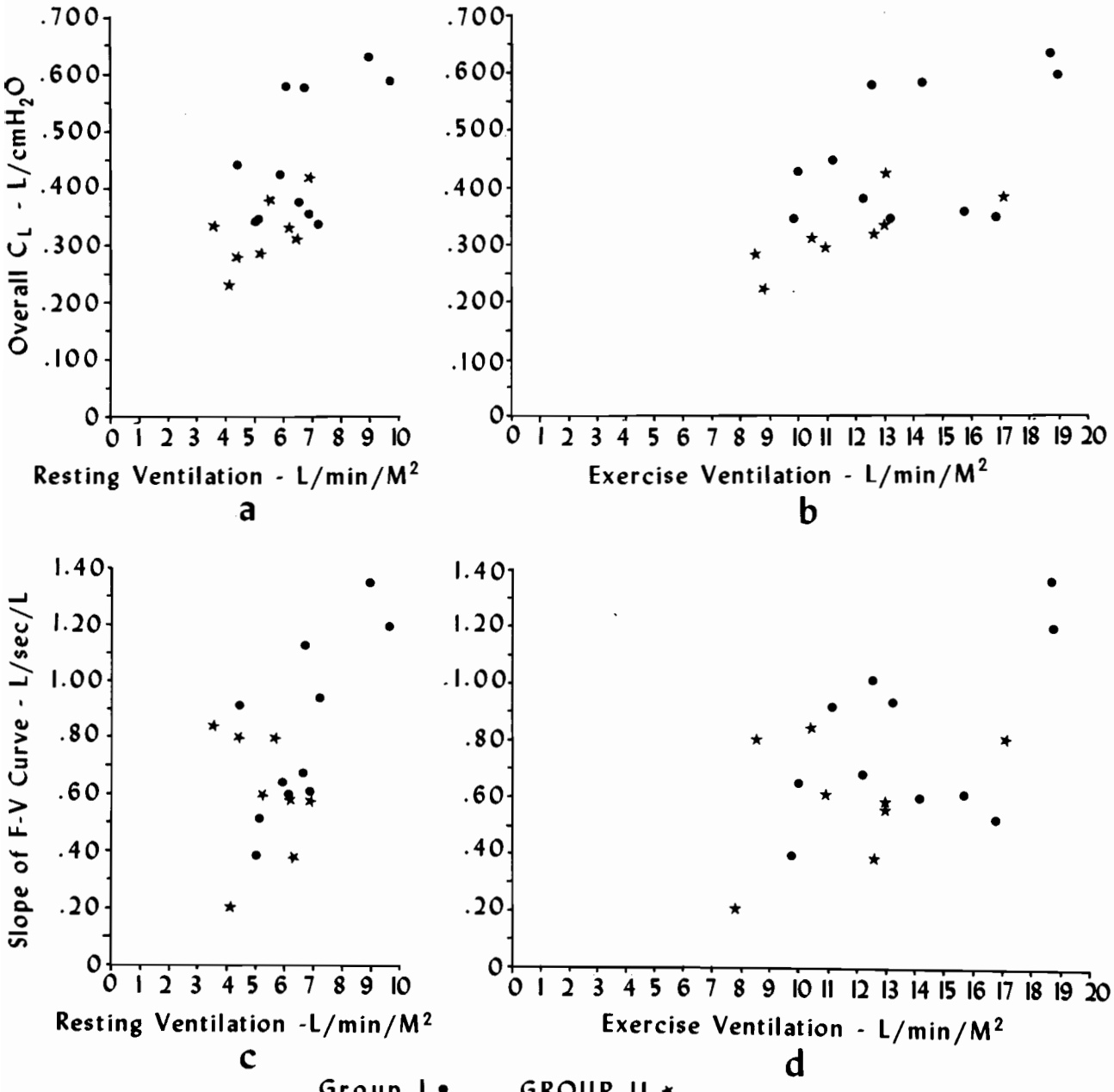

Fig. 5

Relationship between mechanical factors and ventilation.

a. Overall compliance plotted against resting ventilation. ($r=+.682$ $p<.01$)

b. Overall compliance plotted against exercise ventilation. ($r=+.595$ $p<.01$)

c. Slope of flow-volume curve plotted against resting ventilation. ($r=+.554$ $p<.02$)

d. Slope of flow-volume curve plotted against exercise ventilation. ($r=+.496$ $p<.05$)

VI. SUMMARY

1. The results of a comparative study of the clinical picture and pulmonary function, emphasizing lung mechanics, in emphysematous patients, with and without chronic respiratory failure, have been presented. The group studied included eleven patients with relatively normal arterial blood gases and eight patients with well marked chronic hypercapnia and hypoxemia.

2. Higher mean overall compliance values and a loss, in the majority of patients, of the normal convexity of the static pressure-volume curve suggested a much more marked loss of elasticity in the group of patients with normal blood gases. Airway obstruction was, on the other hand, less marked in this group than in the group with chronic hypercapnia. Here airway difficulties due to check valving in expiration seemed to be the major problem with impairment of lung elasticity a secondary feature.

3. These differences in lung mechanics were associated with differences in other aspects of pulmonary function. The hypercapnic group was found to have smaller lung volumes, at least with regard to vital capacity and total lung capacity, a lower mean diffusing capacity and lower values for resting minute ventilation. Mean values for exercise ventilation were also lower in this group than in the group with normal arterial blood gases but the difference was not statistically significant. On the other hand, mean values for mixing efficiency were comparable in the two groups.

4. From the clinical standpoint, despite the fact that the duration

of illness was not significantly different in the two groups, a more severe form of emphysema was present in the hypercapnic group, as is attested by a higher incidence of signs of cor pulmonale and congestive failure and of episodes of acute carbon dioxide narcosis. In addition, the type of onset of illness was different in the two groups with the typical picture of chronic bronchitis preceding exertional dyspnea being more common in the group with normal blood gases.

5. The clinical and functional differences brought out in this study suggested that qualitatively different disease processes are represented in the two groups of emphysematous patients. It was speculated that the underlying pathology in the hypercapnic type of emphysema might be centrilobular emphysema as opposed to diffuse emphysema in the group with normal blood gases.

6. The results suggested that the chief mechanism underlying chronic hypercapnia in emphysema is an inability to increase ventilation, due to mechanical restriction of the respiratory bellows, leading in turn to an inability to compensate for non uniformity of ventilation-perfusion ratios. In certain patients, however, who were found to be in respiratory failure despite an evident ability to augment ventilation, it would appear that distributional defects are so marked that they cannot be compensated for by an increase in ventilation.

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