A STUDY OF CHRONIC PULMONARY EMPHYSEMA

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by

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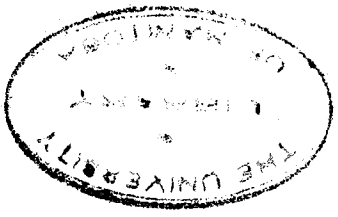

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PART 1

A REVIEW OF THE PATHO-PHYSIOLOGY OF PULMONARY EMPHYSEMA

INTRODUCTION

Derived from the Greek word meaning inflation, emphysema is a disease in which there is permanent over-distension of the lung alveoli. A decreased elasticity of the pulmonary tissues produces a progressive and incapacitating disorder in which there are marked disturbances of lung function. Various theories have been developed to explain emphysema but the etiology is still obscure. Much attention has been directed to the functional disturbances which result. These have been given special emphasis in this review as they form the basis of the study reported in Part II of this thesis.

PATHOGENESIS

Laennec (1) in a thesis which has yet to be superceded, suggests that emphysema could be entirely explained by mechanical factors. He felt that all emphysema began as a catarrh of the bronchi leading to partial bronchial obstruction during both inspiration and expiration. The time-honored belief, also dating from Laennec, that glass blowers, musicians who play wind instruments and men engaged in heavy manual labor are more prone to develop emphysema than individuals not engaged in such occupations is not as certain as many would imply and has been seriously questioned (2). The basis of this hypothesis would appear to be that the repeated building up of a high positive

pressure in the lungs will eventually result in damage to alveoli and distension of the lungs. It is difficult to visualize how this procedure, no matter how often repeated, will result in damage to alveolar walls since one would expect that any increased stress would be taken up by the expiratory muscles which are creating the increase in intra-pulmonary pressure. It is possible that this increased stress on the expiratory muscles might eventually lead to some weakness, and because of this result in a disproportion between inspiration and expiration, with eventual distension of the lung and secondary loss of elasticity.

Loeschke (3) concluded that the disease may be brought about by various factors such as spinal deformity particularly kyphosis, while Hofbauer (4) suggested that the fixed chest of emphysema is due to overaction of the inspiratory muscles. Other suggested causes of emphysema have included strenuous exercise, degenerative changes in the lungs and visceral pleura, pulmonary arteritis, arteriosclerosis of the lung and inflammatory lesions in the lungs. Low barometric pressure has also been considered as a causative factor, and Prinzmetal (5) has subjected rats to a low barometric pressure and noted great lung inflation. The condition has also been seen to develop during anaphylactic shock in the guinea pig (6).

However, emphysema is most often associated with and follows asthma, paroxysmal attacks of broncho-constriction, and bronchial infection of long standing. Harris and Chillingworth (7) and others (8,9,10) produced emphysema in animals by partially obstructing respiration. It has been shown to follow partial obstruction to expiration alone more

consistently than partial obstruction to either inspiration alone or both. Brill et al. (11) showed that bronchoconstricting drugs caused a more negative pleural pressure and an increase in size of the chest. It has been shown in patients suffering from asthmatic attacks that the intrapleural pressure is more negative than before or after the paroxysm (5), and that the pulmonary distension slowly decreases after an attack (12).

There are a number of cases of emphysema without history or demonstrable signs of bronchial obstruction. Some of these are probably caused by deformities of the spine, such as kyphosis. Another group includes the familial cases which may develop in childhood and also the infantile type where the etiology has been attributed to a congenital defect in elastic tissue element of the lung.

Thus considerable controversy exists not only as to the etiology of emphysema but also as to the mechanism of its development. The failure of the emphysematous lung to collapse when the chest is opened at post-mortem as well as the appearance of atrophied stroma have suggested that the elastic tissue element of the lung is at fault. Some investigators have suggested that the elastic tissue is atrophied or broken, others that it is congenitally defective, and still others that it is merely stretched and not diminished. Detailed studies of pulmonary elasticity at post-mortem by measuring the force required to inflate and deflate the lung have given conflicting results in emphysema (13, 14, 15), and the significance of post-mortem measurements has been

seriously questioned. The pleural pressure has been shown to fluctuate around atmospheric pressure in emphysema (16, 17, 18, 19) and similar changes have been demonstrated in experimental emphysema (20). This has led to the suggestion that the elasticity of the lungs may be lost at a comparatively early stage of this disease (20).

Proctor et al (21) have recently pointed out that there is an increased viscous resistance in emphysema, and Mellroy and Christie (22) demonstrated on postmortem lungs that this was due to changes in the lungs and not to bronchial obstruction. They have suggested that what has been called loss of elasticity in the past is largely an increase in tissue viscous resistance. This increase in tissue viscous resistance does not however mean there is no loss of elasticity. Christie (17) and others (16, 18, 19) have conclusively demonstrated that a definite loss of elasticity does occur so that the pleural pressure fluctuates around atmospheric pressure.

It would appear that the loss of elasticity in pulmonary emphysema results either as the basic defect in this disease or secondary to other lesions elsewhere, be it in the bronchi, spine, respiratory muscles, or ribs. Christie (23) believes that the major factor in the development is bronchial obstruction, due to either bronchial oedema, secretions, muscular constriction or congestion, which leads to increased respiratory resistance. He states that as emphysema develops in man there is at first an increased negative intrapleural pressure during inspiration and a more positive intrapleural pressure during expiration. However though this is true of bronchial asthma it has never been

demonstrated in emphysema. Instead a pleural pressure which is fluctuating around atmospheric pressure has been repeatedly demonstrated. He has also stated that the mechanism of coughing, building up of a high positive pulmonary pressure followed by its sudden release, will increase the stress and strain on alveolar walls, particularly in the chronic bronchitic, in time producing the degenerative changes and loss of elasticity characteristic of emphysema. It is difficult to visualize how the tussive force produced by the expiratory muscles can result in any damage to alveolar walls since the pressure on either side of the alveolar wall should be equal. It is possible however that in the presence of bronchospasm, the repeated deep inspirations preceeding the cough may be followed by inefficient expiration due to the relative weakness of the expiratory muscles and bronchial constriction. The increased stress and strain, if any present, is on the expiratory muscles and this might add to the relative weakness of the muscles for expiration.

In those cases which develop as a result of bronchial obstruction pulmonary distension results due to the relative weakness of the expiratory muscles. If this distension persists over a long period of time or is repeated over and over again a loss of retractile power or the loss of pulmonary elasticity will result. An irreversible emphysema will now develop. The intrapleural pressure being around atmospheric pressure, the chest will assume an inspiratory position with diminished excursion of the chest cage and diaphragm with associated alterations in lung volumes.

PATHOLOGY

At postmortem the most apparent finding is voluminous lungs which do not collapse. The heart is obscured by overlying dilated lung margins. The pleural surfaces are stretched, smooth and shiny and adhesions are common. Bullae due to vesicular emphysema within the lung, and blebs caused by rupture of alveoli immediately beneath the pleura with separation of the pleura from contiguous alveolar walls are present most extensively at the lung apices and along the margins. Pressure on a bulla will cause it to empty into a bronchus and collapse while pressure on a bleb will only cause it to shift position. Localization of emphysema to one lung and even to one lobe can occur.

Microscopic examination reveals thin alveolar walls and dilated, stretched and even ruptured alveoli. In the early stages the position of the dilated alveoli is along the main bronchi and the superior surfaces of the interlobular septa. The lung lobule or air-sac becomes distorted and sometimes distended (24,6). As the alveolar walls become thin and disappear, the air sacs may lose their honeycomb structure and so be deprived of supporting framework. Loss of elastic tissue may be demonstrated by elastic tissue stains. The air sacs of a lobule may be fused together with no definite uniformity of shape in contrast to the normal grape-like appearance. As emphysema progresses there is gradual obliteration of the pulmonary vascular bed and the capillaries are often narrowed and occluded.

The terminal bronchioles and alveolar ducts are dilated and funnel-shaped so that air no longer enters the atrium as a jet (24). The lumen of the bronchi show various changes. The smaller bronchi may be dilated and produce a picture resembling cylindrical bronchiectasis, or they may be obliterated by chronic inflammatory tissue. The state of the medium and large bronchi is very variable and depends on the degree of associated bronchitis. Bronchial muscle hypertrophy and narrowing have been found on some occasions and atrophy and dilation on another.

The lesion extends throughout the lung although dilation of air sacs is most conspicuous at the periphery. Characteristic changes outside the lung have been described. The visceral pleura is thin, flimsy and atrophic. There is usually a moderate degree of kyphosis, involving all the thoracic vertebrae. The vertebral cartilage may be thin and compressed anteriorly and there may be lipping. The ribs are widely spaced and run horizontally or become elongated and less elastic (6).

Though the lungs in emphysema as a whole contain more air than they would normally at the end of expiration, this never amounts to more than the increase in size of a normal individual's lungs when he takes a breath of moderate depth (17, 24). At postmortem these lungs seem to be greatly enlarged because they do not collapse and the gross overdistension seen microscopically is due chiefly to destruction of alveolar walls and fusion of air spaces.

Thus it can be seen that what is called emphysema is really a syndrome which can result from a variety of causes and in which the pathologic findings are very variable. These

findings more often than not show no correlation with the severity of the clinical manifestations. Therefore in recent years greater emphasis has been placed on the evaluation of the physiologic disturbances resulting from emphysema. Baldwin et al (25) divided patients into four different groups, and judged the severity of the disease by the arterial blood desaturation, the presence or absence of carbon dioxide retention at rest and after exercise, and by the development of right heart failure. Although they found an increased residual volume total lung capacity ratio in most of the patients, the mean ratio was around 50% in all groups despite the fact that their patients varied from moderate to very severe emphysema. Also some of the most disabled patients had almost normal ratios while some of the mildest cases had the highest residual volume.

Though good correlation between the severity of clinical manifestations and physiological measurements is still not attainable, much has been learned in recent years about the physiologic disturbances resulting from emphysema. These may be dealt with from the standpoint of 1) the mechanics of respiration, 2) lung volumes 3) the distribution of air and blood in the lungs and gas exchange and 4) the role of carbon dioxide and anoxia in the regulation of respiration.

MECHANICS OF RESPIRATION

One of the prime causes of impaired function in emphysema is the loss or fragmentation of pulmonary elastic tissues. In the normal resting position of the chest, the forces

of the chest wall tending to expand the lung are in equilibrium with the elastic forces of the lung which tend to deflate it. As the loss of elasticity in emphysema progresses, the lungs exert a reduced traction on the chest wall so that the resting position resembles that of a moderate inspiration. Furthermore, the reduction of lung elasticity results in an insufficient storage of elastic energy during inspiration to meet the needs of expiration, so that the lungs can no longer deflate by the normal process of passive elastic recoil but have to be compressed by active expiratory effort.

The diaphragm, which is a muscle of inspiration is gradually displaced downward by the increased intrathoracic pressure as the intrapleural pressure rises to about atmospheric pressure. There is subsequent impairment of contractility so that its action becomes more and more limited. The position of extreme contraction may be reached where the diaphragm can no longer function. This downward displacement might possibly be prevented by increasing the intra-abdominal pressure, using the abdominal muscles, but the abdomen in emphysema is apt to be relaxed and pendulous.

The ribs separate and the levators of the ribs are distorted and impaired in obstructive emphysema (6). The intercostal muscles which are concerned with moderate inspiration are unable to perform their proper function. Since the chest is already expanded when inspiration begins the accessory muscles have to be used to expand the chest further. The pectorals particularly are brought into play and these raise the front of the chest in a

'heaving manner'. As they expand the chest the diaphragm may even ascend paradoxically. Also, since expiration now requires active muscular effort, assistance from the accessory muscles of expiration is again required. Incoordination of the muscles of respiration is not uncommon in this disease (26), the accessory muscles of inspiration sometimes remaining contracted even after expiration has begun.

LUNG VOLUMES

As a result of the chronic hyperinflation the total lung volume may become slightly larger than normal, but most striking is the increase in residual air and midcapacity, a reflection of the characteristic inability of the lungs to empty. There is a corresponding decrease in the vital capacity. Definite deviations in size, shape and expansion of the chest give rise to the increased antero-posterior diameter and the barrel-shaped chest. Since the retractile power of the lungs is reduced, the lung distends until the traction of the thoracic wall in the resting position is in equilibrium with the pleural pressure. The level of the functional residual capacity or end of normal expiration thus increases until the pleural pressure approaches atmospheric pressure.

However, these changes in lung volumes are determined by static measurements and do not reflect the true changes which may be present. Although an elevation of the ratio of residual volume to total lung capacity is present in almost every case of emphysema there is only a fair correlation between this ratio and the

clinical severity of the disease. Alterations in lung volumes are the result of bronchial and elastic tissue factors and constitute only a part of the picture. There may be great variations in the functional residual capacity in the same patient within a short period of time especially when there have been exacerbations of bronchospasm or bronchitis. The presence of blebs, bullae and air cysts which communicate poorly or not at all with the tracheobronchial tree are inaccessible to physiologic measurement. Thus in some cases the obviously hyperinflated chest may be found to have a very reduced total lung capacity.

An important concomitant of the disturbances in mechanics of breathing and the alterations in lung volumes is reduction in breathing reserve. The breathing reserve is the difference between the ventilation and the maximum breathing capacity. The onset of dyspnea seems to some extent to depend on the relationship of the ventilation under the conditions being studied to the maximum breathing capacity or what the chest bellows is capable of doing (27). Dyspnea in emphysematous subjects has been claimed to be due chiefly to reduction in the maximum breathing capacity and is usually experienced when the breathing reserve is less than 60-70% of the maximum breathing capacity.

DISTRIBUTION OF AIR AND BLOOD IN THE LUNGS AND GAS EXCHANGE

In the normal subject about 1/3 to 1/4 of the inspired air does not pass beyond the anatomical dead space and therefore takes no significant part in gas exchange. Efficient distribution of inspired air to all alveolar spaces depends largely on even

distribution of expansion in the lung which in turn depends on the fact that the elasticity of the healthy lung is nearly uniform. With loss of elasticity the expanding force is no longer distributed equally and equal expansion in different parts of the lung does not occur, the emphysematous lung distending in parts but not in others when stretched. This leads to an exceedingly uneven and inefficient distribution of inspired air. Cournand et al (28, 29) showed that the alveolar nitrogen was abnormally high in emphysema after seven minutes of quiet oxygen breathing, and attributed this to inefficient ventilation of many alveoli and air spaces. Many other investigators (30, 31, 32, 33, 34, 35, 36, 37) have demonstrated gross impairment of mixing in emphysematous subjects.

The blood supply to alveoli is also equally distributed in the normal individual. It has not been demonstrated directly that there is uneven distribution of blood in emphysema but recently developed injection studies of the pulmonary blood vessels and haemodynamic studies of pulmonary circulation during rest and exercise suggest that circulation as well as air distribution is uneven in the emphysematous lung (38).

Imbalance in alveolar ventilation-perfusion relationships is a characteristic feature in emphysema and a major cause of defective gas exchange (38, 39, 40, 41, 42). Damaged alveoli which owing to capillary destruction have a relatively small amount of blood flowing through them, are probably overventilated at the expense of alveoli which are relatively normal. This ventilation of underperfused lung tissue means that an

abnormally large proportion of inspired air takes no part in the removal of carbon dioxide or oxygenation of the blood and will thus have the same effect as an increased dead space. The blood that perfuses these poorly vascularized, over-ventilated alveoli becomes fully oxygenated and probably excessively depleted of carbon dioxide but the quantity of blood flow is so small that the total gas exchange in these alveoli is slight and a greater than normal burden falls on other alveoli. Adequate carbon dioxide elimination in the presence of excessive ventilation of underperfused alveoli only occurs when the normally perfused alveoli are hyperventilated (43). Larger ventilatory volumes will thus be necessary for any additional effort and this extra demand on the patient will be difficult to deal with in the presence of a reduced ventilatory capacity.

Perfusion of alveoli that are poorly ventilated results in arterial anoxia as well as a tendency towards carbon dioxide retention because not enough oxygen is added or carbon dioxide removed from these alveoli. Carbon dioxide retention may not occur if sufficient hyperventilation of remaining well ventilated, well perfused alveoli occurs, but arterial anoxia cannot be corrected to any significant degree by hyperventilation of normal alveoli.

The capacity of oxygen to diffuse across the alveolar capillary membrane is also often found to be reduced in emphysema when measured by the Riley method (41). By analysis of the alveolar-arterial oxygen pressure gradient at two levels of inspired oxygen concentration the diffusion characteristics

of the lung is estimated. The reduced oxygen diffusing capacity in emphysema is probably due to a reduction in the size of the total pulmonary vascular bed (43).

The ventilatory capacity determines in large measure the adequacy of the mechanisms which serve to compensate for the disordered pulmonary gas exchange. In the early stages of the disease the ability of the lungs to eliminate carbon dioxide probably becomes inefficient only when the demands for gaseous exchange are increased by exercise. Under these circumstances the elevated carbon dioxide tension and increased acidity of the blood tend to make the patient dyspneic (44). As the disease progresses gaseous exchange may become insufficient even when the patient is at rest and the oxygen saturation in severe cases may fall as low as 60 or 70%.

THE ROLE OF CARBON DIOXIDE AND ANOXIA IN THE REGULATION OF RESPIRATION

It has been shown that the emphysematous subject does not respond to the inhalation of carbon dioxide by the normal increase in ventilation (45, 46, 47). Cases of emphysema with impairment of hemo-respiratory exchange may have developed some acclimatization to higher pressures of carbon dioxide but they are unable to hyperventilate voluntarily and lower their arterial pCO_2 (47, 48). Hurtado et all (49, 50) have demonstrated an inability to increase the pulmonary ventilation during exercise.

If, due to the ventilatory disability, there is a lag in carbon dioxide excretion on each occasion that these patients exercise there will be a tendency for the partial pressure of

carbon dioxide to rise. If this is increasingly buffered a compensated gaseous acidosis will result. The increased buffering will cause less increase in H ion concentration and the respiratory stimulation by a fixed amount of carbon dioxide will be diminished.

Under certain circumstances excessive levels of carbon dioxide have a narcotic action and actually depress ventilation (51, 52). The inhalation of 10.4% CO2 for 3-4 minutes has resulted in stupor in normal men (53), while slightly higher levels have been used as an anaesthetic agent (54). The possibility of acclimatization of the respiratory center to high carbon dioxide tensions has been suggested (55). Schafer (56) has observed adaptation to a carbon dioxide environment in normal subjects and noted a diminution of sensitivity of the respiratory center, while Otis (57) noted an elevated pCO2 and diminished response to carbon dioxide after exposure to 3% CO2 for 3 days. Changes in respiratory response to carbon dioxide after normal subjects had been overbreathed in a body respirator have been demonstrated (58). It has therefore been postulated that the respiratory mechanism adopts itself to prolonged disturbances of pCO2 level by changes in the sensitivity of the respiratory center of such a degree as to restore a normal response to the abnormal carbon dioxide tension.

A likely factor in the retention of carbon dioxide in patients with pulmonary emphysema is the presence of bronchiolar obstruction due either to bronchospasm or the presence of thick viscid bronchial secretions. Proctor et al (21) have simulated

the pneumotachographic pattern of emphysema by introducing an obstruction to respiration in normal subjects. Davies, Haldane and Priestley (59, 60) and others (61, 62, 63, 64) have demonstrated anoxia and a rise in alveolar carbon dioxide tension during the period of obstructive dyspnea.

The added insult of anoxia plays an important role in these patients. In the normal individual respiration is primarily under the control of the medullary respiratory center. The activity of this center is controlled by the carbon dioxide tension and pH of the arterial blood. A rise in CO_2 tension or a fall in pH results in immediate stimulation of this center to increase the minute ventilation and blow off excess carbon dioxide. In contrast, the peripheral chemoreceptors in the carotid and aortic bodies are relatively insensitive to changes in arterial pH or carbon dioxide tension, but are remarkably sensitive to any lowering of arterial oxygen tension which will cause a prompt increase in pulmonary ventilation.

When the medullary respiratory center loses its ability to respond to excessive levels of carbon dioxide in emphysema there will be a diminution in the pulmonary ventilation. This will result in a fall of arterial oxygen tension and subsequent stimulation of the peripheral chemoreceptors. These centers now become the principal regulators of the respiratory drive and anoxia the primary stimulus (46). When the arterial oxygen saturation is raised by the administration of oxygen the peripheral chemoreceptors are no longer stimulated and a diminution in pulmonary minute ventilation will take place.

Mosso (65) first described a depression of respiration during the administration of oxygen to animals anesthetized with morphine and chloral. Under certain conditions of respiratory depression oxygen administration may further depress respiration and even lead to apnea and respiratory failure (66).

The pulmonary ventilation often decreases during the administration of oxygen to patients with pulmonary and cardiac disease (67, 68, 69, 70, 71, 72). A rise in arterial carbon dioxide was shown to take place as a result of oxygen therapy in cases with impaired diffusion of oxygen by Barach (73) and Richards and Barach (74). In their cases compensatory retention of base and elimination of chlorides generally though not always accompanied respiratory acidosis. Since then respiratory acidosis with irrational and comatose states as a consequence of oxygen therapy have been reported by Donald (75), Comroe et al (76) and others. Davies and MacKinnon (77) observed that breathing oxygen caused a rise in cerebro-spinal fluid pressure in cor pulmonale and Simpson (78) showed that the inhalation of carbon dioxide did the same. He also pointed out that some patients with advanced emphysema have papilloedema though the mechanism of its development is uncertain. Barach et al have stated that a program of graded increase of oxygen administration will prevent the ill effects of oxygen by allowing the body to compensate for the gradual accumulation of carbon dioxide, thus preventing the development of acidosis (72, 73, 79, 80).

SUMMARY

Chronic pulmonary emphysema results in marked disturbances in the mechanics of respiration, lung volume measurements,

the distribution of air and blood in the lungs and gas exchange, and regulation of respiration. As the disease is difficult to prevent and the etiology ill understood, attention in recent years has been directed towards correcting the functional disturbances that result in pulmonary emphysema, namely the problem of respiratory acidosis. It is the management of this problem which will be dealt with in the study to be reported.

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PART II

THE EFFECT OF MECHANICAL EXSUFFLATION ON RESPIRATORY GAS EXCHANGE IN PULMONARY EMPHYSEMA

INTRODUCTION

An elevated arterial carbon dioxide tension is not infrequently found in patients with pulmonary emphysema. Donald and Christie (1) and Wilson et al (2) have shown that such patients are unable to lower their arterial pCO_2 significantly by voluntary hyperventilation. This mechanical defect in the control of blood carbon dioxide tension makes these patients particularly susceptible to the development of respiratory acidosis. An associated event is a depression of the ventilatory response to increases of carbon dioxide tension so that anoxic stimulation of the carotid and aortic bodies becomes the prime stimulus for breathing (3). When oxygen therapy is instituted in an attempt to alleviate the anoxia, the obviously distressed cyanotic patient may become almost apneic, drowsy and even comatose. This poses a difficult therapeutic problem.

The immediate object of the therapy in such patients is to provide an adequate lung ventilation which will overcome the anoxia and increase the elimination of carbon dioxide. Often some mechanical aid to respiration is urgently required. Electrophrenic respiration (4,5) and mechanical respirators using intermittent positive pressure breathing applied to the upper airway (6) or as applied in the conventional tank respirator (7,8) have been recommended as an adjunct to therapy in respiratory acidosis. As the exsufflator attachment to the tank respirator has been shown to effectively reverse disturbed

alveolar gases resulting from obstructed breathing (9) it was of interest to determine its effect in pulmonary emphysema.

The purpose of this paper is to present the effect of the mechanical exsufflator on respiratory gas exchange in chronic pulmonary emphysema, to compare its effect to that of the conventional tank respirator, and to describe their combined use in the treatment of a severely ill emphysematous patient who developed respiratory acidosis.

METHODS

Mechanical exsufflation, devised as a means of eliminating bronchial secretions in patients with an ineffective cough (10, 11) is accomplished in a conventional tank respirator by producing a negative intratank pressure of 40 mm.Hg. for inflation of the lungs, and, by means of a swiftly opening butterfly valve, returning the intratank pressure to atmospheric in 0.06 seconds. Expiration therefore, in contrast to that in other forms of intermittent pressure breathing, is not impeded except for the initial 0.06 seconds. Expiratory volume flow rates measuring 60% of the rates obtained during maximally vigorous coughs in normal subjects have been attained by this procedure (12).

In the present study the exsufflator was cycled 9 times a minute. The inspiratory pressure was built up over a 2 second period, thus allowing 4.6 seconds for expiration. The observations on the effect of the conventional tank respirator were made using an Emerson respirator cycled 17 times a minute with a pressure range of -20 to +8cm. water, the time of inspiration and expiration being approximately equal. Each patient was instructed to 'breathe with' the apparatus being used.

Studies were made on 13 cases of chronic pulmonary emphysema in whom retention of carbon dioxide due to impaired pulmonary ventilation was suspected. In order to

obtain a resting level all reclined in a conventional tank respirator for 30 minutes before any experiment was begun. The exsufflator was attached to the respirator so that either apparatus could be used and followed immediately by the other.

In order to determine the effect of these procedures and of the administration of oxygen, pulmonary ventilation was measured on a Benedict-Roth respirometer. Arterial blood samples were drawn by means of an indwelling Cournand needle and the Van Slyke-Neill technique was used for the determination of their oxygen content and capacity and carbon dioxide content (3). The arterial pH was determined by glass electrode at 37°C. without exposure to air on a Beckman pH meter and the carbon dioxide tension was derived by the Henderson-Hasselbach equation.

RESULTS

In four patients with emphysema the effect of the exsufflator was compared to that of the conventional tank respirator. In case 1, 30 minutes of exsufflation were followed immediately by 60 minutes of respirator treatment. This procedure was reversed in case 2 and broken into two parts in cases 3 and 4, the patients receiving exsufflation for 30 minutes one day and respirator treatment for 60 minutes the next.

The effect of these two procedures on minute volume, arterial pH, carbon dioxide tension, and oxygen saturation is shown in Fig. 1. The exsufflator resulted in an appreciable rise in pH, a rise in oxygen saturation averaging 4.6% and a fall in carbon dioxide tension averaging 10 mm.Hg. while the respirator produced only a slight effect on these measurements. It is seen that the minute ventilation was practically unchanged from the resting control level during respirator therapy while the exsufflator increased the average minute volume by 4 liters per minute or by 55%. The tidal volume, unchanged by the respirator, was increased to three times that of the control when exsufflation was applied(Table 1.).

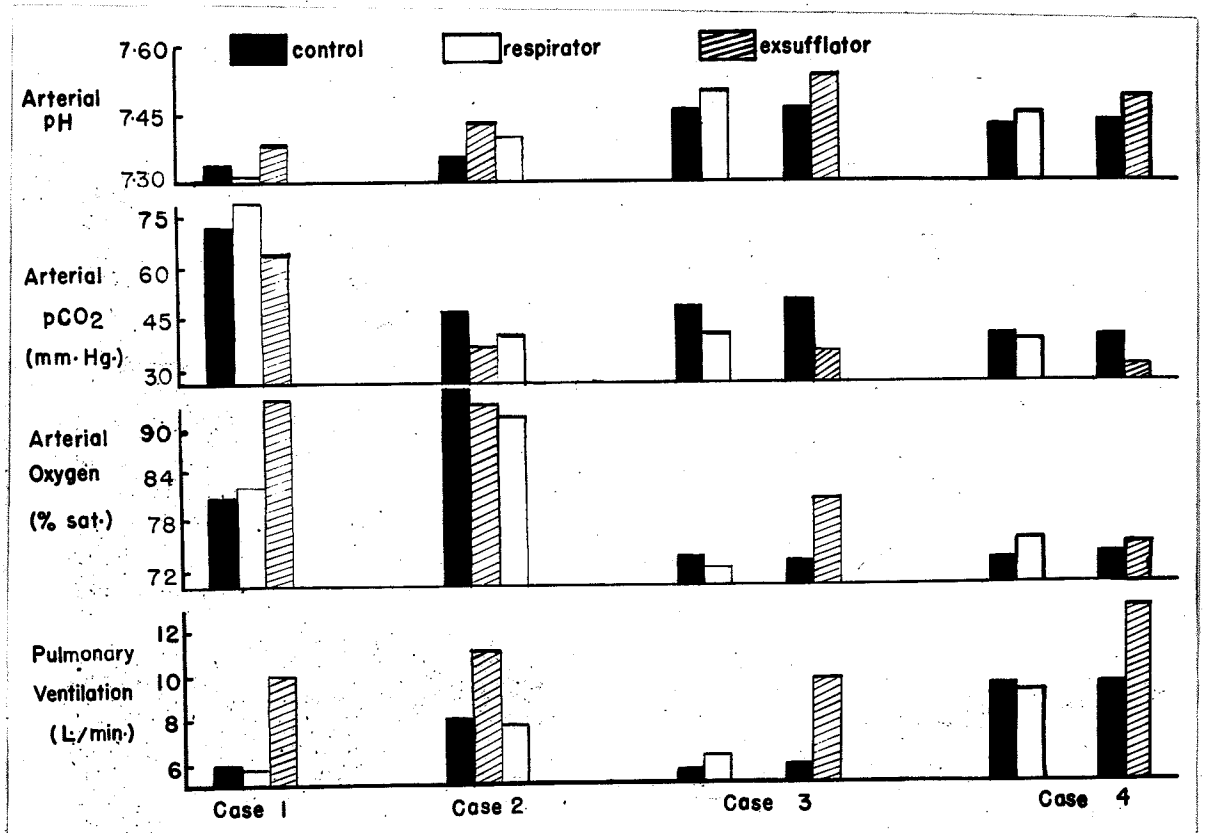
Respiratory acidosis was produced in eight patients with emphysema by the administration of 100% oxygen by mask. Cases 5 and 6 received oxygen for 60 and 30 minutes respectively and were treated with the exsufflator immediately following cessation of oxygen therapy. The exsufflator was applied for

Table 1.

The Effect of the Respirator and Exsufflator on Tidal Volume

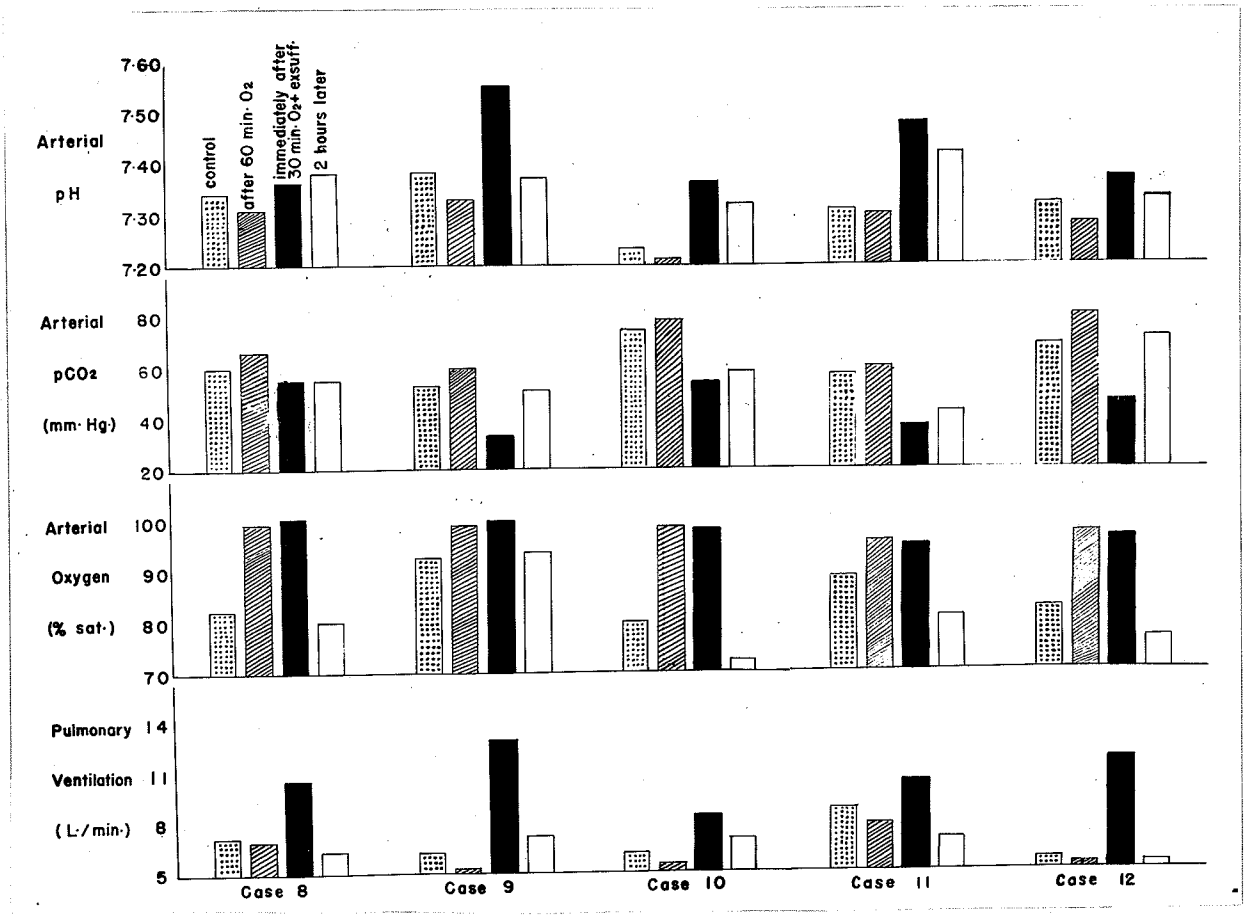
Case No.	Control ml.	Respirator ml.	Exsufflator ml.
1	360	312	1133
2	473	467	1400
3	312	369	1075
4	588	569	1700

Fig. 1.



A comparison of the physiological effects of the respirator and exsufflator in emphysema.

Fig. 2. Respiratory gases before and after exsufflation in 5 patients with emphysema made acidotic with oxygen therapy.



30 minutes in Case 5 and 15 minutes in Case 6. Cases 7-12 received oxygen for 90 minutes and exsufflation for the last 30 minutes of administration.

In all eight cases oxygen caused a rise in arterial carbon dioxide tension and a fall in arterial pH. Table 11 shows that in cases 5 and 6 exsufflation promptly reversed these changes, the values being shifted towards normal. The reversal of acid-base disturbance when exsufflation was applied in case 7, despite the continued administration of 100% oxygen is illustrated in Table 111.

Determinations of ventilation and blood gases were also made 2 hours after the experiment in cases 8-12. Fig. 2 shows that in 3 out of 5 cases the pH remained elevated and the pCO_2 was maintained at a lower level 2 hours after the period of exsufflation, but that the oxygen saturation fell to below the control value in 4 out of 5 cases.

The usefulness of the exsufflator in the treatment of a patient with severe emphysema who developed a marked respiratory acidosis was demonstrated in the following case:

Case 13 (A.M.) - A 53 year old white man, was admitted to the hospital on July 5, 1952, complaining of severe dyspnea of seven months duration. He had been in good health until January, 1952, when he developed tightness in his chest, dyspnea and cough with expectoration of green sputum. Despite penicillin therapy these symptoms

increased in severity and he required admission to hospital for a short time in February and again in March. He was found to have pulmonary emphysema with bronchopneumonia and possibly an early cor pulmonale. Vital capacity was 2.0 liters. He improved markedly when penicillin, aureomycin and digitalis were administered and phlebotomy performed and was discharged from the hospital. On June 15 his dyspnea increased and by July 4, 1952, his symptoms had become very severe. He was then given continuous oxygen by mask at 6-7 liters per minute. Drowsiness was noted and he was taken to hospital.

On admission he was drowsy, cyanotic and extremely dyspneic. The jugular veins were distended. Chest was barrel-shaped and movement was limited bilaterally. Hyperresonance, distant breath sounds and bilateral scattered ronchi were present. Blood pressure was 140/85. The liver was palpable one and one-half finger breadths below the costal margin. There was pitting edema of both ankles and slight clubbing of the fingers. Haemoglobin was 15.5 gms.%, red blood cells 7.8 million, per cmm., hematocrit 55% and white blood cells 11,600 per cmm. Vital capacity was 1.6 liters. The chest film revealed bullous emphysema with some right ventricular enlargement. EKG showed right axis deviation.

On July 7 further oxygen was administered and he became almost apneic. The arterial pH was 7.31 and the carbon dioxide tension 84 mm.Hg. He was placed in a tank respirator and also received exsufflation for 1/2 hour every 2 hours. A comparison of the effect of the respirator and exsufflator on tidal volume and minute ventilation is shown in Table IV. He was treated by the combined use of the respirator and exsufflator and oxygen by nasal catheter at 1-3 liters/min. until July 10, 1952. The improvements in arterial pH and carbon dioxide tension are shown in Table V. By July 20th he was up and about, though limited in activity, and discharged from hospital.

Table 11.

The Effect of Exsufflation on Acid-Base Disturbance Produced by Oxygen Therapy in Pulmonary Emphysema.

Case No.	State	Minute Volume (L/min.)	Arterial pH	Arterial pCO_2 (mm.Hg.)
	Rest	7.65	7.38	46
5	O_2 60 min.	6.90	7.33	52
	Exsuff. 30 min.	9.90	7.42	39
	Rest	9.46	7.35	64
6	O_2 30 min.	6.85	7.30	77
	Exsuff. 15 min.	12.74	7.36	57

Table 111.

The Effect of Exsufflation During Continuous Oxygen Therapy in a Patient with Emphysema.

State	Minute Volume (L./min.)	Oxygen Saturation %	Arterial pH	Arterial pCO_2 (mm.Hg.)
Resting	6.8	92.8	7.44	44
Oxygen 60 min.	5.9	98.1	7.36	55
Oxygen and Exsufflation	9.2	99.0	7.42	43

Table IV.

The Effect of the Respirator and Exsufflator on Tidal Volume and Minute Ventilation (Case 13).

	Tidal Volume (ml.)	Minute Volume (L./min.)
Control	286	5.2
Respirator	278	4.7
Exsufflator	545	5.8

Table V.

The Effect of Therapy on Arterial Blood Estimations
(Case 13)

Date	Arterial pH	Arterial pCO_2 (mm.Hg.)	Comment
7/7/52	7.31	84	prior to therapy
7/8/52	7.43	67)	during therapy
7/9/52	7.39	66)	
7/11/52	7.38	63	day after cessation of therapy
7/15/52	7.40	64	out of bed, limited activity.

DISCUSSION

The results reported above indicate that the exsufflator is superior to the conventional respirator in managing the acid-base disturbance associated with respiratory acidosis in pulmonary emphysema. This might be explained by the ability of the exsufflator both to overcome obstruction to breathing (9) and to ventilate the alveoli more effectively.

The presence of bronchiolar obstruction due to either spasm or thick viscid secretions in the bronchi is probably a considerable factor in the development of anoxia and carbon dioxide retention in severe emphysema. The exsufflator has been shown to result in a marked elimination of secretions in many cases of emphysema (13). This effect could thus play a large role in the shift towards normal of the arterial blood gases and pH.

In the cases treated in the conventional respirator the tidal volume and minute ventilation did not change appreciably from that present during unassisted respiration. However, a consistently marked increase in tidal volume occurred during the period of exsufflation. The increase in arterial oxygen saturation and fall in carbon dioxide tension despite a respiratory rate of only nine times a minute is due to the threefold increase in tidal volume resulting in a more effective alveolar ventilation. Case 13 demonstrates that despite only a slight increase in minute

ventilation, the marked increase in tidal air produced beneficial results.

No post-exsufflater period of apnea was observed despite the fact that the stimulus of anoxia was removed. It seems possible that the sensitivity of the respiratory mechanisms was at least partially restored by the changes in gas tension induced by the exsufflator. It is also noteworthy that in cases 8, 10 and 11 the O_2 saturation at 2 hours was below the original control level while the CO_2 tension and pH were maintained at closer to normal values. This anomolous effect on arterial O_2 and CO_2 levels was presumably due to an increased ventilation of normal alveoli occurring at the expense of ventilation of malfunctioning parts of the lung.

It is concluded that exsufflation is a helpful adjunct in the handling of the problem presented by retention of carbon dioxide in a patient with severe pulmonary emphysema. During exsufflation, oxygen may be administered to such patients, thereby relieving the consequences of severe anoxia without inducing respiratory acidosis. However, as a sequel to the maintenance of a lowered arterial pCO_2 the arterial blood may become more anoxic following cessation of therapy.

SUMMARY

In four cases of pulmonary emphysema 30 minutes of therapy with the exsufflator resulted in an increased minute ventilation and beneficial effect on arterial pH, carbon dioxide tension and oxygen saturation. Respirator therapy for 60 minutes resulted in no appreciable change.

Uncompensated respiratory acidosis was produced in eight cases of emphysema by the administration of oxygen. The acid-base disturbance was effectively treated by a short period of exsufflation. In 3 of 5 cases the low level of CO_2 was maintained after 2 hours while the oxygen saturation fell below the control level. The beneficial effect of the use of the exsufflator in the treatment of a patient with emphysema who developed respiratory acidosis was demonstrated.

The decisive increase in tidal air and minute ventilation with the rapid effect on pulmonary gas exchange during exsufflation appears to be a valuable adjunct to therapy in respiratory acidosis.

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