WORK OF BREATHING

Part I. A review of the literature.

Part II. The oxygen cost and the efficiency of the respiratory system in hypoxia and in congestive heart failure.

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PART I. WORK OF BREATHING

A Review of the Literature

In order to move air into and out of the lungs, work must be done to overcome the various resistances involved in respiratory movements. These various resistances may be considered the algebraic sum of three different components; a) the resistance involved in acceleration of the system, that is, inertia; b) the non-elastic resistances and, c) the elastic resistances.

Mead (1) in his review of the mechanical properties of lungs, states, "To speak of elastic, flow resistive and inertial terms is to imply knowledge as to the responsible physical properties. This is probably justified for the inertial term, since mass inertia is the only likely possibility in this instance. On the other hand, it is not justified for the 'elastic' term. It is safe to say that elasticity of tissues accounts for part of the elastic term, but it is also certain that other properties, e. g. the force of gravity on the abdominal contents and of surface tension in the alveolar lining, which are not elastic in nature, contribute".

INERTIA

Since the system is almost continuously accelerating or decelerating, inertia should be considered as a resistance to be

overcome. The calculations of Rohrer (2) however, indicate that the force required for acceleration must be ordinarily very small, and is in general, considered negligible. Dean and Visscher (3), using a pump as an artificial respirator, found the magnitude of the inertia effect in moving air was very small, probably because of the small masses involved, and it amounted to a maximum pressure of less than 0.5 mm. of water at the maximum respiratory frequencies and pump volumes that they used. Mead (4) also has shown that inertia is a negligible factor up to respiratory rates of 100 per minute.

TOTAL NON-ELASTIC RESISTANCE

This can be further divided into two significant components; a) the tissue viscous resistance due to friction within tissues that move during respiration, such as the rib cage, the diaphragm and structures in the thoracic and abdominal cavities. It is dependent upon the velocity of motion and is therefore related to the rapidity or quickness of breathing. b) resistance to air flow along the tracheo-bronchial tree which depends upon the number, length and cross sectional area of the tubes conducting air into the lungs. It is also dependent upon the rate and the nature of the air flow which may be laminar or turbulent. The pressure required to produce laminar flow is proportional to the volume flow (V) times a constant

(K_1) which is related to the viscosity of the gas; it is independent of the density of the gas. For turbulent flow, the pressure required is proportional to the square of the volume flow (V^2) times another constant (K_2) which is related to the density of the gas; it is independent of the viscosity of the gas.

There is some discrepancy in the literature as to whether non-elastic resistance differs during inspiration and expiration. Some of this discrepancy may be explained on the variety of methods used, and the differences in respiratory rates and tidal volumes of the subjects being studied. Otis and Proctor (8), using an interrupted flow technique, and Mead and Whittenberger (9) using esophageal pressures and an electrically integrated pneumotachometer, could find no significant difference in non-elastic resistance between expiration and inspiration except at high rates when resistance was higher during expiration (9). Fry et al (7) using esophageal pressures, pneumotachographic recordings, and Attinger et al (10) using almost the same technique, found that non-elastic resistance was higher during expiration than during inspiration. This is in agreement with the early work of Neergard and Wirz (11).

Non-elastic resistance is dependent on the lung volume at which respiratory movements occur. Resistance is higher the

lower the lung volume; that is, more pressure is required to produce flow when the lung volume is below the functional residual capacity (7,8,9,12). Fry et al (7) have offered a possible explanation on the basis that the terminal bronchioles being unsupported by cartilaginous structures are dependent on intra-thoracic pressure and therefore, when lung volume is increased during inspiration, the bronchioles are surrounded by a greater negative pressure and their diameters increase, thus exerting less resistance to flow.

Non-elastic resistance is also affected by body position, the resistance being higher in the supine position than in the sitting position (10,12).

AIRWAY RESISTANCE

Fenn (5) in discussing the theoretical concepts of resistance to airflow, reviewed the work done by Rohrer (2) in 1915. Rohrer's was rather a laborious and painstaking study which involved detailed anatomical measurements of the tracheo-bronchial tree on post-mortem human lung preparations. He calculated the cumulative resistance to airflow in the entire system using his anatomical measurements, Poiseuille's law and theories of turbulence. Rohrer concluded that in a single airway the flow of air was predominately laminar. The pressure drop required for a given velocity of flow could be expressed by Poiseuille's law, i.e.

$P = \frac{8lvn}{981r^2}$ where P is pressure in cm. H_2O

v is velocity in cm./sec.

r is the radius in mm.

l is length in cm.

n is the viscosity

When the velocity exceeds a critical value, the flow becomes turbulent and the pressure drop varies as V^n where 'n' has a value of 1.7 to 2.0. The critical velocity in cm./sec. for turbulent flow was theorized to be $\frac{1290n}{d\rho}$ where n is viscosity, ρ is the density and d is diameter in mm. He concluded that in a given airway there was little likelihood of exceeding the critical velocity except perhaps briefly, during a cough. Gaensler et al (6) however, during studies in bronchospirometry concerning critical velocity, found that Rohrer's original hypothesis concerning critical velocity was erroneous and that turbulence is encountered even at flow rates as low as 5 litres/min., particularly in the smaller diameter airways. Rohrer was aware of turbulence occurring whenever air flow changed direction rapidly, as in the nasopharynx, or at the dichotomous branchings of the airways. His study produced an equation to represent the pressure required to overcome air flow resistance:

$P = 0.79V - 0.801\ V^2$ P in cm./H_2O

v in l./sec.

The first term represents laminar resistance and the second turbulent resistance at particular points in the airway.

Fry et al (7) in 1954, in a mathematical analysis of their data on non-elastic resistance, reasoned on purely physical grounds that at least part of the pressure flow relationship in pulmonary ventilation must be expressible by a polynomial:

$$P = (R_1 u Q) + (R_2 d Q^2) + f^{Q}_{(\text{tissue})}$$

where P is the total pressure drop required

u is the viscosity

d is the density

and f is the flow

The first term, the linear coefficient represents laminar flow, the second term, the quadratic coefficient represents turbulent flow. The functional notation f^{Q} (tissue) represents tissue viscous resistance and the nature of this term is totally unknown.

Various attempts have been made to measure airway resistance as a separate component of total non-elastic resistance. Since airway resistance is the ratio of alveolar pressure during flow to airflow, airway resistance alone could be measured if there were a method for determining alveolar pressure during flow.

Earlier investigators (8) used an interrupted flow technique for determining airway resistance alone. The theory was

that when flow of air is interrupted during inspiration, the flow record goes to zero and the pressure at the mouth falls to a value which is nearly equal to the low pressure existing in the relatively large volume of alveolar air at that instant. The change in pressure at the mouth indicates, therefore, the pressure gradient required to cause airflow at the velocity recorded immediately prior to the interruption. Mead and Whittenberger (13) evaluated the interrupted flow technique and concluded that it was not really just a measure of airway resistance, but rather a measure of total resistance. The basic hypothesis of the interrupted technique is that the alveolar pressure does not change appreciably in the interval after interruption before equilibrium is established in the system. Mead and Whittenberger (13) claimed that this is a false assumption and that 18 milliseconds is probably a conservative estimate of the time it would take alveolar pressure to change more than 50% of the way towards its new level following interruption. The pressure equilibrated at the mouth would then approximate the sume of the pre-existing respiratory tract and tissue resistive pressure drops, and with the measured flow prior to interruption would yield a measure of total lung resistance rather than just airway resistance. Bayliss and Robertson (14) artificially inflating cat's lungs, found that airway resistance constituted approximately 5% of the total lung

resistance, but they made no mention of the flow rates at which they were working.

Dubois et al (15) developed a body plethysmographic method for determining alveolar pressure during air flow and found that mean airway resistance was 1.5 cm. H_2O/l./sec. at a flow of one l./sec. It must be mentioned that this was for mouth breathing only and the subjects had to carry out their respiratory movements in a panting manner due to artefact produced by ordinary tidal volumes.

TISSUE VISCOUS RESISTANCE

The importance of this component of non-elastic resistance is at some variance, probably due to the variety of methods used to determine it as a separate entity.

Otis, Fenn and Rahn (16) in their studies on trained subjects in a Drinker respirator, found that tissue viscous resistance probably was a small portion of the total resistance.

Other attempts to determine, separately, this component of non-elastic resistance have been based on the assumption that the breathing of gases of different viscosities and densities should only alter the airway resistance and not the tissue viscous resistance. By extrapolation back to the resistance which would be present if the viscosity and density of the inhaled gas were zero, the pressure required to overcome tissue viscous resistance could be calculated.

Bayliss and Robertson (14) ventilated isolated animal lungs with gases of different density and viscosity and they calculated that the tissue viscous resistance was about 15% of the total pulmonary resistance. McIlroy and Christie (17) studying human lungs at post mortem, concluded that tissue viscous resistance was a major factor in the resistance to movement of the lungs under the circumstances of their experiment. Fry et al (7) found that the third term of their polynomial, that is, the term representing tissue viscous resistance, showed no significant change when using gases of different density and viscosity, and concluded that tissue viscous resistance was a negligible quantity.

McIlroy, Mead, Selverstone and Radford (18) criticized the work of previous investigators, using different gas mixture technique, because they did not use gases of equal kinematic viscosity. They explained the meaning of this term and the rationale of its use in the following manner: Reynolds had shown that the tendency to turbulent flow could be expressed by a dimensionless number, since called Reynolds' number, which was proportional to the product of the linear flow velocity, the radius of the flow channel and density of the fluid and inversely proportional to the viscosity of the fluid. In the respiratory tract the distribution of turbulence at a given flow rate will be the same for gases of various viscosity and density only

if Reynolds' number at all points is unchanged. For this to be true the ratio of viscosity to density, that is, the kinematic viscosity must be kept constant. For gases of equal kinematic viscosity, the pressure drop necessary to produce a given flow rate through any gas flow resistance, will change proportionately with the density of the gas flowing. This fact makes it possible to examine the tissue viscous resistance by measuring the resistive pressure difference at a given flow rate while breathing gas mixtures of equal kinematic viscosity but with known differences in density and viscosity and extrapolating to conditions of zero density and viscosity. By using different gas mixtures at different rates of flow, the mean value for tissue viscous resistance was 0.6 cm. H_2O/l./sec. or about 30 to 40% of the total respiratory resistance in quietly breathing normal adult males. The work of Fry et al (7) introduces conflicting results, however, as they did use gases of equal kinematic viscosity and as stated above, found that tissue viscous resistance was a negligible quantity.

An additional method for determining tissue viscous resistance has been used by Marshall and Dubois (19). They measured simultaneously the pressure required to overcome total non-elastic resistance, using esophageal pressure and the pressure required to overcome airway resistance by a body plethysmograph.

By simple subtraction, the pressure necessary to overcome tissue viscous resistance was determined. The total non-elastic resistance was 1.20 cm. H_2O/l./sec., airway resistance was 0.99 cm. H_2O/l./sec. and tissue viscous resistance was 0.21 cm. H_2O/l./sec. or approximately 18% of the total.

ELASTIC RESISTANCE

Elasticity is a property of matter that causes it to return to its resting shape after having been distorted by some external force. The tissues of the lung and chest wall are said to possess this property of elasticity. The slope of the line that results from plotting the external force, i.e. pressure, against the increase in volume serves as a measure of the stiffness or distensibility of the lung and chest wall. This is referred to as the compliance of the system and is defined as the volume change per unit pressure change, being expressed in litres/cm. H_2O. The lower the compliance, the less distensible is the system. Inherent in most studies on compliance is the assumption that the pressure volume relationship is linear. Actually the plotting of this relationship when determined by inflating a collapsed lung to rather high volumes, assumes a sigmoid shaped curve (20). However, most clinical studies are carried out with tidal volumes within the linear portion of the pressure-volume curve.

It should be pointed out that the complete pressure-volume cycle is not purely elastic in nature but exhibits hysteresis (21,22,23,24). This has been defined by Landowne and Stacy (25) as the failure of a system to follow identical paths of response upon application of and withdrawal of a forcing agent. The result of this failure to retrace the same path on withdrawal as on application, is the formation of a hysteresis loop.

Recent investigations suggest that this phenomenon of hysteresis is due to surface tension factors at the gas-tissue interface (1,21,23,24). This is based on the observation that little or no hysteresis is evident when lungs are inflated with saline rather than air (23) or when the airway is pre-treated with non-ionic detergents such as Tween 80 (20,21).

Surface tension factors are not just involved in the production of hysteresis but actually account for about one half of the total elastic behaviour of the lung (21,24). Pierce et al (24) commented that the precise role of the elastic fibres is not completely defined, but they felt that they were not essential for normal elastic performance on inflation with air. This conclusion was based on their observation that elastase treated lung preparations exhibited normal pressure volume relationships on inflation with air. There is also some evidence that normal lungs contain a

surface stabilizing substance (21) that prevents alveolar collapse due to surface forces. Apparently this substance is not present in infants dying with severe atelectasis neonatorum (21,26). Since surface tension seems to play such an important role in the so-called elastic properties of the lung, it might be emphasized that lung compliance studies are not really a measure of true elastic resistance, but rather a measure of lung distensibility.

The compliance of the lung or chest wall can be determined separately by knowing the volume change associated with the pressure difference across each separately. Changes in pleural or intrathoracic pressure can be measured directly or approximated by esophageal pressure change. The use of esophageal pressure as an estimation of pleural pressure has been a subject of considerable investigation. Cherniack et al (27) observed extreme variability between esophageal and pleural pressure in subjects in the recumbent position. On the other hand, Mead and Gaensler (28) in studying subjects in the erect position, observed much less variation. They also felt that in the supine position, the esophagus was compressed by mediastinal structures. In addition, there may not be a single value for intra-pleural pressure when the lungs are in natural motion (29). Mead has summarized the problem regarding the pressures at the surface of the lungs by stating "the best data avail-

able suggest that these differences are small over much of the outer surface, but there is need for more information on this point and on the general question of the distribution of forces and their pressure equivalent in the lungs". He also stated that in human subjects in the upright position, the esophageal pressure appears to be as good as directly measured pleural pressure.

LUNG COMPLIANCE

McIlroy (30) gives the range for lung compliance in normal adult males as 0.14 - 0.33 l./cm. H_2O, and for females 0.09 - 0.18 l./cm. H_2O. Two other terms, the elastance and the index of elastic resistance are also used to describe the distensibility of the lung. They are simply the reciprocal of compliance and they describe the pressure required to produce a given volume change. Otis, Rahn and Fenn (31) give a value for normal subjects of 0.5 cm. H_2O per 100 cc. volume change. Fry et al (7) were in agreement, stating a figure of 0.43 cm. H_2O.

Since many factors affect the distensibility of the lung, even in normal subjects, no single number will adequately describe the elastic properties of the lung. As mentioned previously, the sigmoid shape of the pressure volume curve necessitates the mentioning of the tidal volumes used in the measurement of compliance. Lung volume is another variable, as the lung becomes more dis-

tensible at higher lung volumes (32). This has been explained by the theory that the elastic properties of a three-dimensional structure, such as the lung, are more correctly expressed by the modulus of elasticity (11), i.e.:

$$\text{mod. el} = \frac{P_{EL}}{\frac{\Delta V_L}{V_L}} = \frac{V_L}{C}$$

Where ΔP_{EL} is the elastic pressure difference for a given volume change ΔV_L

V_L is the initial lung volume, and

C is the compliance. It follows from this that if the modulus of elasticity is to remain constant, the compliance must increase with increasing lung volume. Attinger and Segal (32) propose that the elastic properties of the lung are due to the elastic fibres in the alveolar walls and that the total elastic force of the lung depends upon the number of ventilated alveoli. A small lung consists of less alveoli than a larger lung, and therefore requires a greater pressure gradient for a given volume change. The previously mentioned work of Pierce et al (24) which places some doubt on the role of the elastic fibres in lung distensibility, perhaps invalidates the theory of Attinger and Segal (32). The dependence of compliance on lung volume may be due to surface tension factors because once an alveolus or group of alveoli become relatively

airless it requires large pressures to re-inflate them, and it has been demonstrated that the pressures necessary to re-inflate 'closed off' alveoli with saline are considerably less than the pressures required for re-inflation by air (23). Clements et al (33) have suggested that when the alveoli are extended, tissue forces predominate, while at moderate to small volumes, surface forces predominate. This would seem to indicate that at high lung volumes, the surface factors are minimized and thus, the lung is more distensible. In addition to these observations on lung volumes, animal (34, 35) and human experiments (36) have shown that the lung is more distensible if it has been previously 'stretched' by near maximal inflations.

Changes in surface forces and decreased lung volume may be partially responsible for the observation that elastic resistance is higher in the supine position than in the erect position (10, 12). It has also been suggested that with the adoption of the supine position, there is an increase in thoracic blood volume and this causes the lung to be less distensible (10).

Another variable involved in the measurement of compliance is the respiratory frequency and this will be discussed in the following section.

STATIC AND FUNCTIONAL COMPLIANCE

Two types of lung compliance have been described by Otis et al (37), the static compliance and the dynamic or functional compliance. Static compliance expresses the true compliance of the lungs as a whole and is determined as the pressure change per unit volume change when air flow is interrupted long enough to allow equilibration of intra-thoracic pressure. Functional or dynamic compliance is that determined during spontaneous breathing, as the pressure change per unit volume change between points of zero air flow (usually end of inspiration and end of expiration). Since in the normal lung equilibration of intra-thoracic pressure is essentially instantaneous, there is no difference between static and functional compliance. In the presence of unequal ventilation, however, intra-thoracic pressure is not yet equilibrated during the brief time of zero air flow in spontaneous breathing and the functional compliance is lower than the static compliance (38). In this situation, the functional compliance decreases even more with increasing respiratory rate (37, 38) and may be explained by the effects of a non-uniformly distributed non-elastic resistance (39). At slower respiratory rates, the non-elastic resistance factor is minimal and all areas of the lung take part in ventilation and compliance will be high. At faster respiratory rates, the portions of

the lung with low non-elastic resistance will be over-distended and the measured compliance will be low (39).

CHEST WALL COMPLIANCE

While the compliance of the lung may be studied with relative ease in the spontaneously breathing subject, that of the chest wall is more difficult to measure. Ferris et al (40) estimated chest wall compliance by measuring total respiratory and lung compliance in a supposedly 'relaxed' normal subject ventilated by a respirator. The obvious drawback of this method is that it requires an extremely well-trained subject. Butler and Smith (41) estimated chest wall compliance in anesthetized subjects under the influence of muscle relaxants. It is unlikely that their results are directly applicable to the conscious, spontaneously breathing subject. Heaf and Prime (42) and later Naimark and Cherniack (43), measured total respiratory, chest wall and lung compliance in spontaneously breathing subjects by slightly different techniques. The results of Naimark and Cherniack were that total respiratory compliance was 0.110 l./cm. H_2O, lung compliance 0.283 l./cm. H_2O, and chest wall 0.224 l./cm. H_2O. These results are similar to those of Heaf and Prime (42).

In summary, the various resistances involved in the act of breathing have been discussed. Their relative roles and factors

affecting their measurement, and some of the controversy about each of them has been pointed out. The following sections will discuss the association of the resistances involved in pulmonary mechanics and the work of breathing and how these are altered in heart disease.

TOTAL MECHANICAL WORK

Total mechanical work, that is work done on the thorax and abdomen as well as on the lungs and gas, has been measured using two different techniques. The first is to have the respiratory muscles completely relaxed or paralyzed and have breathing effected by a pump, such as a Drinker respirator, or an intermittent positive pressure resuscitator. The differential pressure between the mouth and the outside of the body, plotted against volume changes gives a pressure-volume loop from which an estimate of the total mechanical work can be calculated. Otis, Fenn and Rahn (16) found in a relaxed normal subject in a Drinker respirator with a 500 cc. tidal volume at a frequency of 15 per minute, the total mechanical work was 0.315 kgM/min. With 950 cc. tidals and at the same frequency, the work rose to 0.945 kgM/min. Sixty-three percent of the total work in inspiration was used in overcoming elastic forces, 29% in overcoming airway resistance, and 8% in deforming tissues, but these are all dependent on the pattern of breathing. Campbell (44) claims that the true values may be somewhat greater than those

found by this method because it is unlikely that a conscious subject can relax his respiratory muscles completely. The inspiratory muscles probably assisted the respirator and decreased the pressure difference between the cabinet and the mouth.

OXYGEN COST

The other technique of determining total mechanical work is to measure the total energy cost of breathing. The general procedure is to measure the oxygen consumption first with the subject at rest and then with ventilation increased, either voluntarily or by stimulation with carbon dioxide. The latter may be accomplished by breathing gas mixtures with varying lengths of dead space. Provided there is no other reason for an increase in oxygen consumption, the excess consumption during increased ventilation can be attributed to the metabolism of the respiratory muscles. By extrapolation, the oxygen consumption of the respiratory muscles during quiet breathing can be obtained, and by measuring the oxygen consumption at various levels of ventilation, an oxygen cost curve can be obtained.

Although Murray (45) found that there was no difference in the oxygen cost when hyperventilation was induced voluntarily or by the addition of carbon dioxide to the inspired gas, the earlier investigators (46,47) had agreed that voluntary hyperventilation required a greater oxygen consumption than the equivalent ventilation stimu-

lated by carbon dioxide. Liljestrand (46) believed that voluntary hyperventilation was more costly because it was less natural and was carried out by a less efficient mechanical action of the muscles, that is, there were more extraneous movements. Other authors argue that the higher cost of voluntary hyperventilation is related to an effect that the lowered alveolar and arterial pCO_2 have on the respiratory muscles such that they use more oxygen for a given amount of ventilation when the arterial pCO_2 is low than when it is high. Michaelis (47) et al controlled the alveolar pCO_2 during voluntary hyperventilation by the addition of various concentrations of carbon dioxide to the inspired air and found that for a similar amount of hyperventilation, the oxygen requirement was higher, the lower the alveolar pCO_2. This is in the German literature and possible explanation of the mechanism may or may not have been given, and also it is unknown whether they actually measured alveolar pCO_2.

Liljestrand (46) in 1918, and Nielsen (48) in 1936, were among the first to determine oxygen cost and they estimated the oxygen cost of quiet breathing in normal subjects to be about 0.5 ml./O_2/litre of ventilation. Cherniack (49) increased ventilation in normal subjects by the addition of dead spaces and found the oxygen cost of increased ventilation to be a mean value of 1.16 ml./l. with ventilations not exceeding 30 l./min.

Investigators who have measured the oxygen requirements for breathing over a considerable range of ventilations have noted that the relationship between energy requirement and ventilation is not a straight line, but a curve of ever increasing slope. Cournand et al (50) by having their subjects increase their ventilation voluntarily and adding carbon dioxide to the inspired air to prevent carbon dioxide unloading, showed that in normal subjects when ventilation was 25 l./min. above resting, the oxygen cost was 1 ml./l. and when the ventilation was 50 l./min. above resting the cost was 2 ml./l., and at 80 l./min. above resting the cost was 3.2 ml./l. They also showed that at the same ventilation there was a larger oxygen uptake at a respiratory rate of 20 than at a respiratory rate of 30. They did not mention what the normally adopted respiratory rate of their subjects was.

Nielsen (48) found that at a ventilation of 10 l./min. the oxygen cost was about 1 ml. of oxygen/litre of ventilation, but at 50 l./min. it was about 2 ml./l. Otis and McKerrow (53) found that at maximal levels of voluntary hyperventilation (200-270 l./min.) the oxygen cost was 3 - 8 ml./l.

An important implication of the increasing steepness of the oxygen cost curve is that for any subject there is a critical level of pulmonary ventilation above which the respiratory muscles use all the additional oxygen provided by further increase in ventilation

and the arterial oxygen tension consequently falls. Otis calculated this critical level of ventilation to be about 140 l./min. in young normal subjects. In diseases which cause an increase of the mechanical work of breathing, this critical level may be as low as 20 l./min. Even at lower ventilation rates, the high proportion of the total oxygen consumption required by the respiratory muscles greatly decreases that available to the rest of the body and hence contributes significantly to the limitation of exercise tolerance.

Bartlett et al (52) measured oxygen cost in two normal subjects at different respiratory rates. They confirmed that the oxygen cost curve was one of ever increasing slope. The oxygen cost at low ventilations increases with increasing respiratory rates. This was determined by the angle at which the extrapolation of the oxygen cost curve approached the O axis. They explained this by the fact that at higher rates the increased air flow and acceleration must be accompanied by increased airway and tissue components of non-elastic work. They claimed that it follows that when the same pulmonary minute volume is accomplished at several breathing rates, the non-elastic work must increase with increasing frequency. This finding is contrary to that found by Cournand et al (50), who compared rates of 20 and 30 per minute, but Bartlett et al were comparing rates of 23, 41 and 98 per minute. The latter

rate of 98 per minute can hardly be considered of any physiological significance and their conclusions are based on extrapolated data. Another very obvious criticism of their work is that they used three different methods to attain their different respiratory rates.

The oxygen cost of hyperventilation is a way of measuring total energy expenditure of the respiratory muscles, but Campbell, Cherniack and Westlake (54) have described a method of measuring mechanical work in terms of kilogram metres, using the oxygen cost curve. It is an indirect method by which the efficiency of the respiratory system is determined by measuring the change in oxygen consumption associated with the addition of known inspiratory resistances. The efficiency measured in this way has been shown to be constant over a wide range of added work loads and it is assumed that the efficiency is the same at rest with no extra loads. Mechanical work during quiet breathing in normal subjects is 0.8 to 3.0 kgM/min. and it is of interest that with this method, the total mechanical work at rest in patients with emphysema is no different than the normals. Another assumption in this technique of measuring total mechanical work, is that the oxygen cost curve maintains the same slope at ventilations below the resting level.

Cournand et al (50) studied one patient with mitral stenosis and clinical evidence of pulmonary congestion and found that the oxygen cost was higher than normal, that is, for a ventilation 15 l/min. above resting the oxygen cost was 3.2 ml/l. McGregor and Becklake (51) on the

other hand, found that the oxygen cost in patients with congestive heart failure was no different from normal. However, their values for the normal oxygen cost of breathing were higher than those reported by most investigators (46, 48, 49, 50, 54).

MECHANICAL WORK DONE ON THE LUNG

Measurement of the mechanical work done on the lung during breathing requires the simultaneous measurement of the pressures exerted on the lung and the volumes displaced. When such measurements of pressure and volume changes are plotted against each other for a complete breathing cycle, a pressure volume loop is obtained. The mechanical work done on the lungs per minute can be determined from this pressure volume loop when the respiratory rate is known. This includes the work done to overcome elastic resistance of the lung, inspiratory non-elastic resistance and expiratory non-elastic resistance if it occurs. Various investigators have studied normal subjects but only those studies involving both normal subjects and patients with heart disease will be presented.

Marshall, McIlroy and Christie (55) measuring intra-esophageal pressures with a balloon in the esophagus and volume changes with an electrically integrated pneumotachograph, found the work done on the lung to be increased in patients with mitral stenosis. At rest they obtained values of 0.39 - 1.77 kgM/min.

compared to their normal values of 0.19 - 0.46 kgM/min. On exercise the work done rose much more abruptly than in the normals and this was attributed to an increase in lung rigidity due to congestion. They also noted that when normal subjects were supine, the work done on the lung increased but there was little alteration in the elastic resistance. On the other hand, patients with orthopnoea when lying flat, showed a much more marked increase in mechanical work and noticeable increase in elastic resistance. Hayward and Knott (56) measured the coefficient of elastic resistance and work done on the lung in 30 patients with mitral stenosis and tried to correlate the degree of lung rigidity with the grade of clinical disability. They confirmed that the lungs in mitral stenosis were less distensible than normal at rest, and this further decreased on exercise, whereas normal subjects actually increased their lung distensibility on exercise. There was no correlation between the coefficient of elastic resistance and the degree of clinical disability. The work done on the lung at rest was in the same range in all four clinical grades - 0.21 - 1.77 kgM/min - as compared to the previously mentioned normal values of 0.19 - 0.46 kgM/min. Four out of five patients studied after successful valvotomy showed a decrease in lung rigidity at rest and failed to show the increase in rigidity on exercise which they manifested pre-operatively.

They also stated that exercise sufficient to cause dyspnea caused the rate of work to reach the same level as pre-operatively. This is not so alarming, as McIlroy et al (55) noted that both normals and patients with mitral stenosis experienced dyspnea when 2 - 3 kgM/min. was the work being done on the lung. The important factor is the degree of exercise which will cause this amount of mechanical work to be done, and in this respect the patients of Hayward and Knott showed improvement post-operatively.

Cherniack, Cuddy and Armstrong (12) have also shown that the index of elastic resistance is higher than normal in patients with congestive heart failure (12.47 cm. H_2O/l. compared to 5.4 cm. H_2O/l.) and on assuming the supine position, the elastic resistance increased in both groups. When sitting, viscous resistance, expressed as cm./H_2O to produce a flow of 30 l./min. was also higher in the patients with congestive heart failure. The values rose in both groups on lying flat, but was most marked in the patients with heart failure. In the normals, the increased viscous resistance in the supine position was spread uniformly over the respiratory cycle but in patients with congestive heart failure, the increase was particularly marked in early inspiration and late expiration. In the sitting position, the work done on the lung against both viscous and elastic resistances, was greater for the

cardiac than the normal subject. Similarly, total work on the lung was higher - 119.3 kg. cm./min. - compared to 47.8 cm./min. On assuming the supine position the total work done on the lung increased in both groups and was most marked in the patients with congestive heart failure. The work of breathing in the supine cardiac patients was approximately 25% greater than when sitting and this difference was attributed to the difference in the work done against viscous resistance.

Sharp et al (57) found that the lung compliance was decreased in pulmonary edema, quoting a mean value of 0.037 l./cm. H_2O for eight patients. Airway resistance was approximately three to four times the accepted normal value and when they plotted resistance against time in four patients they found that inspiratory resistance was highest early in inspiration in all cases, the peak resistance occurring in the first 0.1 to 0.2 seconds of inspiration.

On the other hand, Brown et al (58) have shown that not all patients with heart disease had increased resistance to airflow and the pressure-flow diagrams showed considerable overlapping between normals and patients. They concluded that exertional dyspnea was most closely related to a reduction in vital capacity and altered elastic properties of the lung, but that increased resistance to air flow plays an important role in dyspnea of cardiac

asthma. Bondurant et al (59) artificially produced pulmonary vascular engorgement in normal subjects by use of inflated G suits and immersing the subjects in water. They found that lung compliance decreased in both situations. Their evidence of pulmonary vascular engorgement was based on increase in thoracic radioactivity using I^{-131} tagged albumin and an increase in the density of the chest x-ray.

Many investigators have found a relationship between vital capacity and elastic forces of the lung and suggest that the reduction in vital capacity in patients with heart disease is a result of an alteration in the elastic properties of the lung. Many theories have been postulated as to the mechanism of decreased lung distensibility and diminution of vital capacity and resulting increased work done on the lung in heart disease.

One theory is that an increase in pulmonary blood volume would encroach upon the alveolar spaces and animal experiments (52) have shown that an increased pulmonary blood volume leads to an alteration in the elastic properties of the lung. However, the reduction in compliance cannot be accounted for completely by simple replacement of alveolar volume, as it has been shown in dogs that a decrease in compliance of 70% is accompanied by a reduction in total and ventilated pulmonary gas volumes of only

20 to 32% respectively (64). Also pulmonary blood volume, while it may be raised in some forms of left ventricular failure, is not so in mitral stenosis (60) in which condition the compliance of the lung is decreased.

von Basch (61) postulated that there was an increase in the rigidity of lung tissue as a result of an increased pulmonary capillary pressure. However, it has been shown that there is no clear relationship between compliance and pulmonary capillary pressure or pulmonary artery pressure (62).

A theory that has been proposed to account for the decreased compliance in pulmonary edema, is that the alveoli of the non-dependent portions of the lung that are not surrounded by edema fluid, become overdistended because they are exposed to an increased negative pressure. This overdistension of alveoli forces them to operate over a less compliant portion of their pressure volume curve. If this were true, then one might expect the functional residual capacity in congestive heart failure to be at least normal, if not increased, whereas in fact, it is decreased (63). Also one would then expect the lung compliance in chronic pulmonary emphysema to be decreased and this is not so (38).

It has been suggested that in pulmonary edema that either the composition or the geometry of the distending elements

of the lung are altered in such a way as to render the lung less compliant. Some investigators have indicated that alveolar surface forces play a more dominant role in determining lung compliance in the presence of pulmonary edema (65). Brown (66), however, has suggested that the surface properties of edema fluid are much the same as the normal alveolar surface, but if this fluid was geometrically arranged as bubbles, the radii of which were smaller than the parent alveolus, the resulting compliance would be that of alveoli with radii equal to those of the bubbles. Assuming that both an alveolus and its contained bubbles are portions of spheres, the volume of such a unit is approximately equal to $\frac{4\Pi r^3}{3}$. If one considers only surface compliance, Laplace's law states that transmural pressure is directly proportional to surface tension and is inversely proportional to the first power of the radius, $P = \frac{2T}{r}$. Thus V/P or compliance equals $\frac{4\Pi r^3}{3}$ divided by $\frac{2T}{r}$ or $\frac{2\Pi r^4}{3T}$. By application of differential calculus, it may be shown that the slope of the volume pressure curve $\frac{dV}{dP}$ as well as the compliance V/P varies directly as the fourth power of the radius and inversely as the surface tension. Thus, halving the radius would decrease the compliance sixteenfold, while doubling the surface tension would only halve the compliance. If this mathematical analysis is applicable to the situation in the alveoli during pulmonary edema,

then it may be concluded that the geometrical arrangement of edema fluid, rather than any change in surface tension properties, is the important factor responsible for the reduction in compliance (57).

If most alveoli had edema fluid at their mouths, then with inspiratory expansion the lung compliance would be low at the beginning of inflation of the bubbles and would rise as their radii increased. This affect is apparently characteristic of pulmonary edema as suggested by Clements (67), and shown by the work of Whittenberger and Affeldt (68) who have described an alinear pressure volume relationship of lungs and thorax in pulmonary edema with the compliance being lowest in early inspiration.

The increase in airway resistance is perhaps not as difficult to explain as is the decreased compliance for the presence of edema, which could account for a great deal of this resistance if one considers the resistance to flow in a tube to be inversely proportional to the fourth power of its radius. Also foam and secretions, present in the airways, may increase turbulent resistance (57). However, the resistance being highest in early inspiration (12, 57), is not as readily explained. It must be pointed out that the value for resistance is usually based on a calculation that assumes that the pressure volume curve is linear within the range of tidal volumes used. However, as has been suggested, this

linear relationship may not exist and this would tend to make the calculation of the early inspiratory resistance an overestimation. If, on the other hand, the resistance is actually highest during early inspiration, it requires explanation. Cherniack, Cuddy and Armstrong (12) suggest that the high resistance at low lung volumes, such as exists in early inspiration and late expiration, is due to narrowing of the air passages in this state. As the lungs expand, these passages would be opened, lowering the resistance to air flow. Patients with congestive heart failure are most apt to show this phenomenon, as congestion and edema are obstructing the air passage. This concept may partially explain the fact that even in the sitting position the viscous resistance is higher in cardiac patients, as the functional residual capacity and total lung capacity are reduced in patients with congestive heart failure.

Another possible explanation of the apparent high resistance early in inspiration is the concept of critical opening pressures of terminal lung units, as Burton (69) has described in blood vessels. If the presence of edema fluid disturbed the balance of forces about the respiratory bronchioles and alveolar ducts, causing them to close off, fewer expandible alveoli would be available and compliance would be lowest and airway resistance highest in early inspiration.

SUMMARY

The respiratory resistances and the mechanical work of breathing in normal subjects and in patients with heart disease, have been discussed. It is rather evident that the majority of the investigators who have studied patients with heart disease have been concerned with the mechanical work done on the lung alone. The following section will present data on the total energy expenditure, that is, the oxygen cost of breathing in patients with congestive heart failure as well as in normal subjects breathing a hypoxic gas mixture. Oxygen cost has been found to be elevated in chronic obstructive pulmonary emphysema (70) and in obesity (71, 72). Since hypoxia is common to both conditions it is possible that the oxygen cost which will be shown to be raised in patients with congestive heart failure and in normal subjects breathing a hypoxic gas mixture, is due to tissue hypoxia.

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PART II. THE OXYGEN COST AND THE EFFICIENCY OF THE RESPIRATORY SYSTEM IN HYPOXIA AND IN CONGESTIVE HEART FAILURE

A. Introduction

The oxygen cost of an increase in ventilation is high and the efficiency of the respiratory system is low in such disease states as chronic obstructive pulmonary emphysema (1) and obesity (2,3). Since hypoxia is common to both conditions, it is possible that the high oxygen cost and low efficiency are a result of tissue hypoxia because of either arterial hypoxemia or reduced blood flow.

It was therefore of interest to determine whether the oxygen consumption and efficiency of the respiratory system were altered in other conditions in which hypoxia was present. This paper reports measurements of the oxygen cost of an increased ventilation and the efficiency with which added inspiratory work loads were handled in; 1) normal subjects breathing hypoxic gas mixtures and, 2) patients with congestive heart failure.

B. Methods

Nine normal subjects and 20 patients with cardiac disease and clinical evidence of congestive heart failure were studied. Their physical characteristics and measurements of ventilatory function are

presented in Table I. The clinical grading of the patients with congestive heart failure was based on the severity of the dyspnea as suggested by the New York Heart Association (4).

Arterial gas tensions were measured by a modification of (5) the technique of Riley, Proemmel and Franke (6). The vital capacity, maximum mid-expiratory flow rate and maximum breathing capacity, were measured with a 9 litre Collins spirometer from which the carbon dioxide adsorber and valves had been removed, and a high speed rotating drum incorporated. The maximum of at least three trials was recorded. Predicted values were obtained from Baldwin et al (7) and Leuallen and Fowler (8).

The oxygen cost of increased ventilation was measured by a closed circuit technique employing a modification (1) of the method of Campbell, Westlake and Cherniack (9). This essentially consists of measuring the oxygen consumption and minute ventilation at rest, before and after measurements at two different levels of increased ventilation produced by the introduction of various lengths of dead space. The value used for the resting oxygen consumption in the calculation of the oxygen cost of increased ventilation was the lower of the two resting determinations since it was felt that this was a better representation of the resting state. The subjects were in a fasting state and had been resting comfortably for at least one half

hour before the study. The subjects breathed into and out of the spirometer system for eight to ten minutes prior to any measurements. Records of oxygen consumption and ventilation were then obtained for four to eight minutes at each level of ventilation. Ten minutes rest was allowed between measurements at different states.

The efficiency for handling added inspiratory work loads was determined by measuring the additional oxygen consumption associated with breathing through a known inspiratory resistance in the form of a metal tube which projected down under a water seal (9). The inability to handle the added inspiratory resistance precluded the determination of efficiency in six patients with congestive heart failure.

The total mechanical work of breathing per litre of ventilation at rest was calculated from the product of the efficiency and the energy equivalent of the oxygen cost of breathing per litre of ventilation at rest and expressed in kilogram-meters per litre of ventilation.

The normal subjects were studied while breathing 100% oxygen and a hypoxic gas mixture of 10 - 12% oxygen in nitrogen. An ear oximeter was used as a monitor in order to insure the stability of the arterial oxygen saturation during the hypoxic studies. The oxygen saturations ranged from 55 - 85% during hypoxic studies.

Some of the patients with congestive heart failure were

studied while breathing 100% oxygen and the others were studied breathing room air. Table II presents the values obtained for the oxygen cost and efficiency in two normal subjects and one patient with congestive heart failure who were studied twice, once while breathing room air, and on the other occasion, while breathing 100% oxygen. It will be seen that in these three subjects, similar values were obtained utilizing either room air or 100% oxygen.

C. Results

Hypoxia

Table III presents the values obtained for the oxygen cost of increased ventilation, the efficiency with which added inspiratory work loads were handled and the total mechanical work of breathing in nine normal subjects, while breathing 100% oxygen and the hypoxic gas mixture. The measurements were made over the same range of ventilation during inhalation of either 100% oxygen or the hypoxic gas mixture. Resting ventilation increased slightly while breathing the hypoxic gas mixture. It will be seen that the oxygen cost of increased ventilation rose ($p < .01$), while breathing the hypoxic gas mixture. This increase was apparently due to a decrease in the efficiency with which added inspiratory work loads were handled ($p < .01$) for there was no change in the total mechanical work of breathing ($p > 0.2$). These findings could not be attributed to a change in respiratory patt-

ern as there was no consistent change while breathing the hypoxic gas mixture.

In order to insure that the rise in oxygen cost was related to the hypoxia rather than the inhalation of carbon dioxide which was inherent in the closed circuit technique, the oxygen cost of increased ventilation was measured during voluntary hyperventilation in two of the normal subjects while breathing room air and the hypoxic gas mixture using the open circuit technique of Cournand et al (10). The respiratory rates selected were those at which the subject had breathed during the studies with the closed circuit technique. The end-tidal carbon dioxide tension was monitored continuously with an infra-red carbon dioxide analyzer, sufficient carbon dioxide being added to the inspired gas to maintain a normal end-tidal pCO_2 throughout the periods of hyperventilation. In Table IV the results obtained with both the open and closed circuit techniques are compared. In each subject the closed circuit technique was used on two occasions and the open circuit technique on four occasions. It can be seen that hypoxia led to an increase in oxygen cost during both voluntary hyperventilation and carbon dioxide induced hypercapnea. This indicates that the rise in oxygen cost of increased ventilation during hypoxia which was demonstrated with the closed circuit technique was not due to the associated hypercapnea. It can also be seen that the values for

the oxygen cost of increased ventilation were higher when the ventilation was increased voluntarily. This is in agreement with other investigators as reported by Otis (11).

Congestive Heart Failure

The oxygen cost of increased ventilation in 20 patients with congestive heart failure is presented in Figure 1. The range of values obtained in the nine normal subjects is also shown. The measurements were made over the same range of ventilation in the normal subjects and the patients with congestive heart failure. The resting inspiratory rate was generally higher in the patients with congestive heart failure but showed similar changes with increased ventilation, the respiratory rate rising five to six breaths per minute. It is seen that the oxygen cost of increased ventilation was higher than normal ($p < .01$) in the patients with congestive heart failure.

In 14 patients with congestive heart failure, the mean efficiency for handling added inspiratory work loads was 2.83% (range 0.86 - 5.10%) which was lower than normal ($p < .01$). On the other hand the mean value for mechanical work of breathing in these 14 patients was 0.166 kg. M/l. (range .050-.416 kg. M/l.) which was no different than normal ($p > 0.2$).

D. Discussion

The data presented indicate that the oxygen cost of increased ventilation was high in patients with congestive heart failure and in normal subjects who were breathing a hypoxic gas mixture. The oxygen cost of breathing at resting ventilation is likely similarly elevated.

The high oxygen cost found in the patients with congestive heart failure is in agreement with the data of Cournand et al (10) who studied one patient with mitral stenosis and clinical evidence of congestive heart failure, but differs from that of McGregor and Becklake (12) who found that the oxygen cost in patients with congestive heart failure was not increased above normal. However, the values for the normal oxygen cost of breathing in the latter study were higher than those reported by most investigators (1,2,9,10,13,14).

The high oxygen cost of breathing in hypoxia and in congestive heart failure may be attributed to either an increase in total mechanical work done or a less efficient respiratory system, or both. Table III demonstrates that the rise in oxygen cost which developed when the normal subjects breathed a hypoxic gas mixture was due to a fall in the efficiency of the respiratory system, rather than a change in total mechanical work done.

Since elastic resistance and mechanical work done on the

lungs are increased in patients with congestive heart failure (15, 16, 17, 18), it is surprising that the total respiratory mechanical work done was not increased in the present series of patients with congestive heart failure. However, calculation of the total mechanical work of breathing was dependent on the estimated efficiency for handling added inspiratory work loads. The added work load was derived from the knowledge of the minute ventilation and the depth of the water seal through which the subjects inspired. Since the added inspiratory resistance may have led to pulmonary congestion and thereby increased the elastic resistance of the lungs, the additional work load may have been underestimated. In this way, the efficiency of the respiratory system would also have been underestimated.

In order to determine whether the elastic resistance of the lungs was altered during measurements of efficiency, the compliance of the lungs was determined by measuring simultaneous changes in esophageal pressure and tidal volume, at rest, at different levels of ventilation and when added inspiratory work was imposed, in two normal subjects and in two patients with heart failure. The mean of ten breaths was calculated for each of these situations. Table V shows that in the two normal subjects, the lung compliance was unaltered at approximately equivalent respiratory rates and minute ventilations when inspiratory work was added. In the two patients with congestive

heart failure, however, the lung compliance decreased when the inspiratory resistance was added. This suggests that in the patients with congestive heart failure the additional work done was actually greater than that used for the calculation of efficiency, so that the actual efficiency was underestimated. It follows that the calculated values for total mechanical work of breathing were also underestimated.

Although the efficiency data are difficult to interpret in the patients with congestive heart failure, it is nevertheless possible that the efficiency of the respiratory system is decreased in congestive heart failure, and that this inefficiency may be partly responsible for the high oxygen cost of breathing. A high oxygen cost has been found in other disease states in which hypoxia was present, such as chronic obstructive pulmonary emphysema (1) and obesity (2,3). The present paper demonstrates that the oxygen cost of breathing was high in two other situations in which hypoxia was present, namely congestive heart failure and normal subjects breathing a hypoxic gas mixture. Since arterial hypoxemia was not a consistent finding in the patients with congestive heart failure, it is suggested that the high oxygen cost of breathing in this situation was the result of tissue hypoxia due to inadequate blood flow.

E. Conclusions

1. The oxygen cost of increased ventilation and the "efficiency of the respiratory system" were measured in nine normal subjects and 20 patients with cardiac disease and clinical evidence of congestive heart failure.
2. The oxygen cost of increased ventilation rose and the efficiency of the respiratory system fell in normal subjects when they breathed a hypoxic gas mixture.
3. The oxygen cost of increased ventilation was high and "the efficiency of the respiratory system" was low in patients with cardiac disease and clinical evidence of congestive heart failure. It is suggested that the "added work" and the efficiency may be underestimated in this condition.
4. The presence of hypoxia results in a rise of the oxygen cost of increased ventilation and a fall in "the efficiency of the respiratory system".

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TABLE I

PHYSICAL CHARACTERISTICS AND PULMONARY FUNCTION OF NORMALS AND PATIENTS WITH CONGESTIVE HEART FAILURE

Subj. (No.)	Age (yr.)	Sex	B.S.A. m^2	Diagnosis	Clinical Grade	V. C. (ml.)	V. C. (%Pred.)	M. B. C. (l./min.)	M. B. C. (%Pred.)	M.M.F (l./sec.)	Arterial pO_2 (mm.Hg.)	Arterial pCO_2 (mm.Hg.)
1.*	22	M	1.78	normal		4650	118	183	142	4.78		
2.*	35	M	1.95	normal		4410	110	120	102	3.29		
3.*	22	F	1.56	normal		3420	107	96	99	2.60		
4.*	22	M	1.70	normal		4210	98	143	108	4.79		
5.*	29	F	1.55	normal		3180	109	123	138	2.43		
6.*	21	M	2.04	normal		5500	123	201	146	4.46		
7.*	20	M	1.73	normal		5430	135	177	139	3.93		
8.*	31	M	2.00	normal		6160	137	219	168	5.12		
9.*	22	M	2.05	normal		6124	122	222	155	6.80		
10.	29	M	2.10	rheumatic	i	5140	112	109	82	2.73	80	36
11.*	17	M	1.88	rheumatic	i	5140	120	146	100	4.97	93	40
12.	55	M	1.77	hypertensive	ii	3780	111	110	120	3.30	94	36
13.	49	F	1.68	rheumatic	ii	3450	129	68	82	1.15		
14.	33	M	1.91	rheumatic	ii	3870	90	98	79	2.18	95	36
15.*	37	F	1.62	rheumatic	ii	4200	139	125	138	2.37	95	40
16.	53	M	1.74	hypertensive	iii	3465	92	93	92	1.32	75	35
17.	59	M	1.97	hypertensive	iii							
18.	55	F	1.34	myxoma	iii	2140	91	73	100	1.76	85	41
19.*	60	M	1.85	arterio-sclerotic	iii						81	28
20.*	30	M	1.68	rheumatic	iii							
21.	44	M	1.92	rheumatic	iv	4750	113	134	116	4.86	84	40
22.	47	F	1.60	rheumatic	iv						81	38
23.	70	F	1.66	arterio-sclerotic	iv	2085	84	43	52	2.99	80	29
24.	52	F	1.44	rheumatic	iv	1342	43	40	45	1.37		
25.	78	M	1.49	arterio-sclerotic	iv	2360	81	28	42	0.43		
26.	62	F	1.33	rheumatic	iv							
27.*	83	M	1.67	arterio-sclerotic	iv						101	55
28.*	75	M	1.55	hypertensive	iv						73	44

TABLE II

THE O_2 COST AND EFFICIENCY BREATHING ROOM AIR AND 100% OXYGEN

Subj.	Diagnosis	O_2 Cost (ml./l.) 100% O_2	O_2 Cost (ml./l.) Room Air	Efficiency (%) 100% O_2	Efficiency (%) Room Air
1	normal	0.69	0.73	10.1	8.8
2	normal	1.16	1.14	10.7	9.8
18	atrial myxoma	1.85	1.48	1.28	1.82

TABLE III

THE EFFECT OF HYPOXIA ON THE O_2 COST, EFFICIENCY, AND TOTAL MECHANICAL WORK IN NORMAL SUBJECTS

Subject	O_2 Cost (ml. /l.)		Efficiency (%)		Total Mechanical Work (kg. m./l.)	
	100% O_2	Hypoxia	100% O_2	Hypoxia	100%	Hypoxia
1.	0.69	2.31	10.1	2.7	0.146	0.133
2.	1.16	2.25	10.7	4.3	0.258	0.203
3.	1.28	2.59	7.8	4.2	0.141	0.099
4.	1.32	3.24	10.0	4.0	0.277	0.272
5.	1.19	2.44	6.4	3.2	0.160	0.164
6.	0.60	3.31	8.1	2.4	0.102	0.167
7.	0.89	3.03	6.3	4.0	0.118	0.255
8.	1.12	2.25	6.0	2.1	0.210	0.228
9.	1.26	3.86	12.0	4.0	0.318	0.324
Mean	1.05	2.81	8.6	3.4	0.194	0.196
S. D.	$\pm$0.27	$\pm$0.58	$\pm$ 2.16	$\pm$0.85	$\pm$0.077	$\pm$0.072
P	< .01		< .01		> 0.2	

TABLE IV

THE OXYGEN COST OF INCREASED VENTILATION USING THE OPEN AND CLOSED CIRCUIT TECHNIQUES

OXYGEN COST OF INCREASED VENTILATION
(ml. /l.)

Subject	Closed Circuit Method		Open Circuit Method	
	Room Air	Hypoxia	Room Air	Hypoxia
1.	0.87	2.43	2.01	2.71
	0.73	2.20	1.74	2.51
			1.75	2.81
			1.89	2.97
2.	1.14	2.30	1.92	2.82
	1.07	2.19	1.71	3.09
			1.87	2.95
			1.96	2.96

TABLE V

THE EFFECT OF ADDED INSPIRATORY WORK ON THE COMPLIANCE OF THE LUNGS

Subject No.	Condition	Ventilation (l./min.)	Respiratory Frequency	Compliance (l./cm. H_2O)
Normal 8	rest	7.65	11.5	.234
	increased ventilation a)	11.85	11	.252
	increased ventilation b)	18.75	13	.225
	work	11.08	10	.241
10	rest	7.56	11.5	.244
	increased ventilation a)	11.2	12.5	.295
	increased ventilation b)	18.7	14.5	.340
	work	14.4	14.5	.280
C. H. F. 28	rest	9.77	22.5	.098
	increased ventilation	19.02	25	.095
	work	9.78	22.5	.074
29	rest	9.57	17.5	.059
	increased ventilation a)	19.87	25	.045
	increased ventilation b)	21.95	23	.043
	work	20.5	25	.038

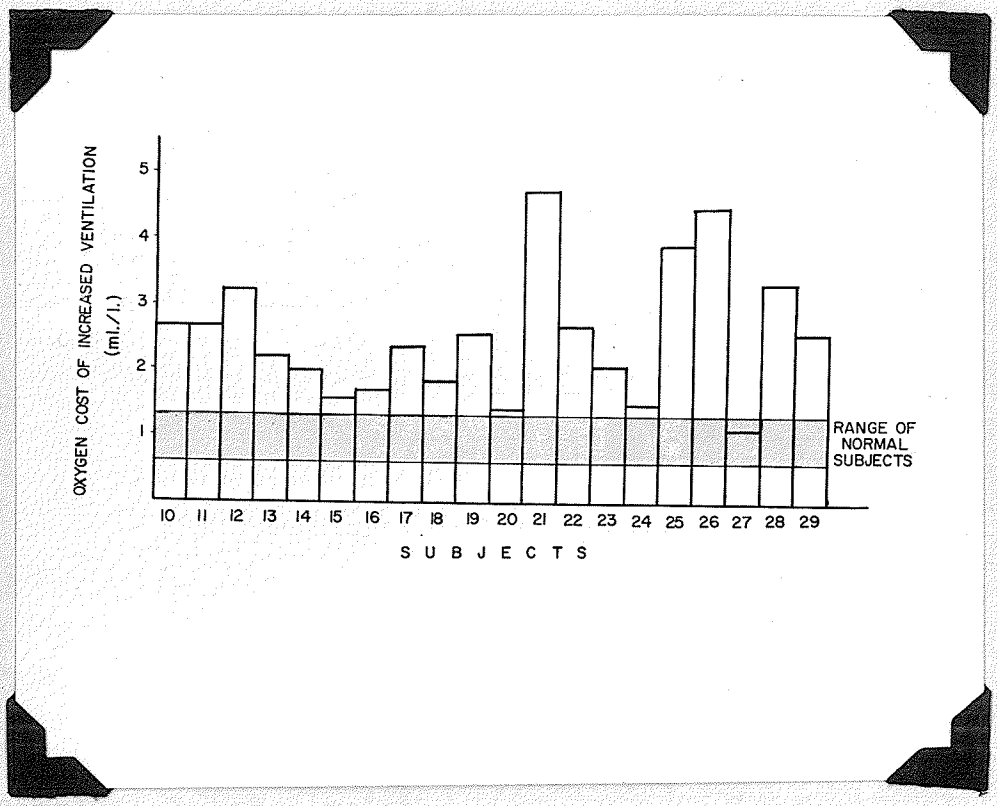

Figure 1. The oxygen cost of increased ventilation in 20 patients with congestive heart failure. The range of values found in nine normal subjects is also shown.