

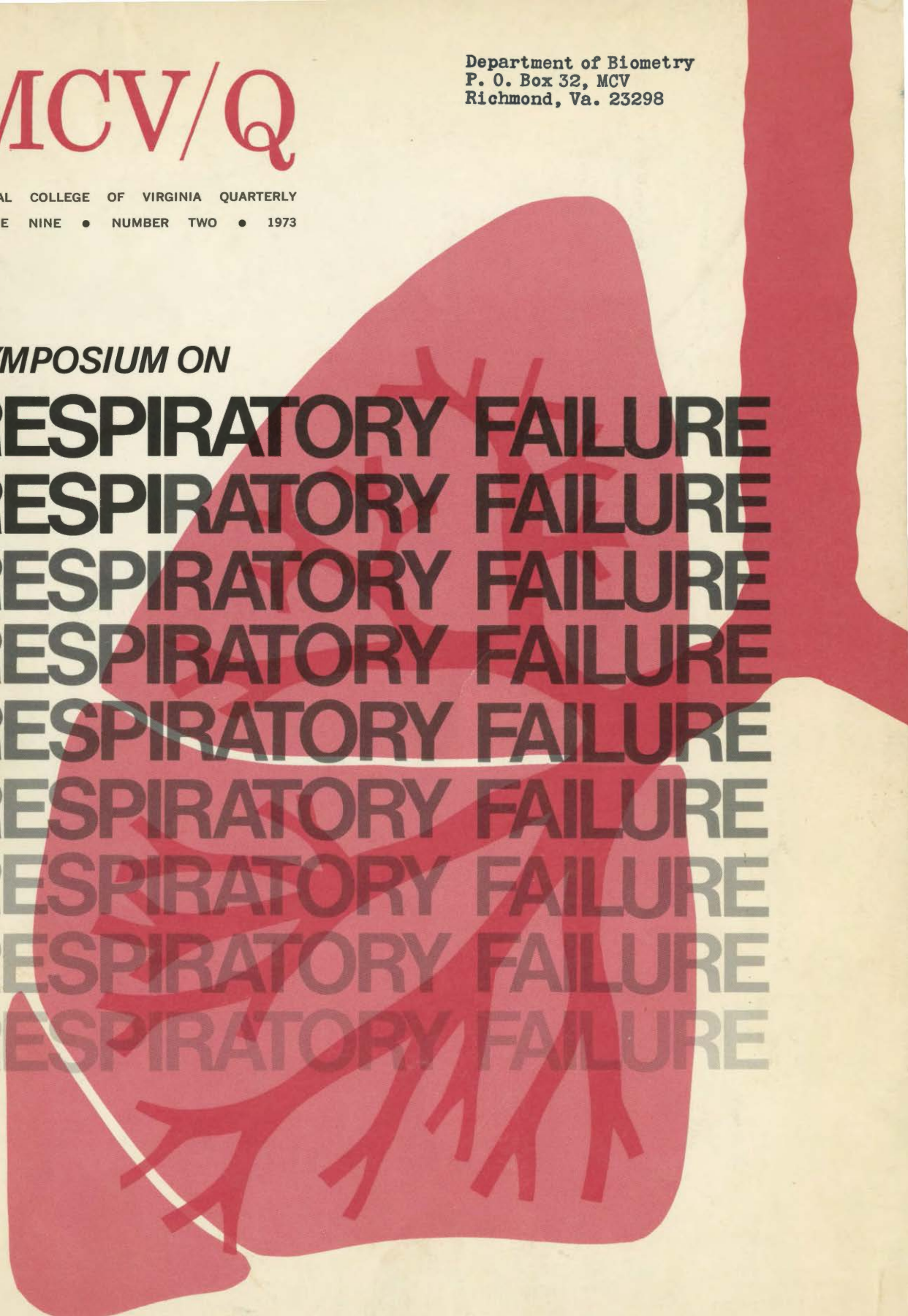
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Department of Biometry
P. O. Box 32, MCV
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MEDICAL COLLEGE OF VIRGINIA QUARTERLY
VOLUME NINE • NUMBER TWO • 1973

SYMPOSIUM ON

RESPIRATORY FAILURE
RESPIRATORY FAILURE
RESPIRATORY FAILURE
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RESPIRATORY FAILURE





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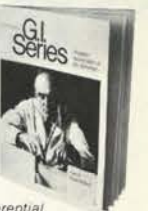
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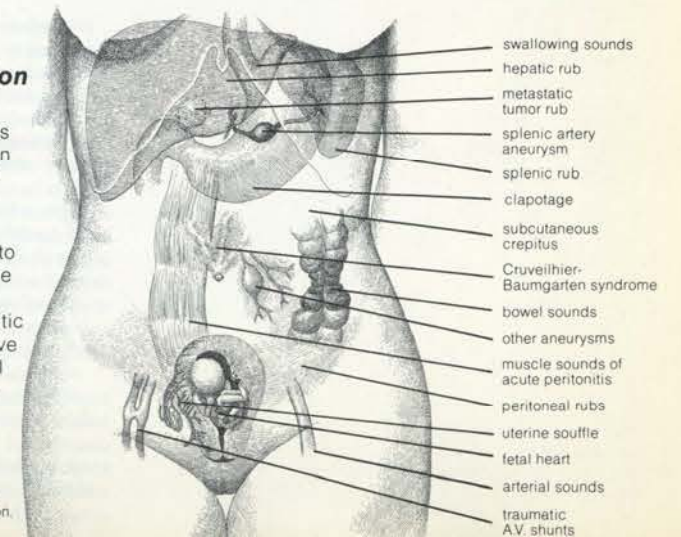
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Pointers on auscultation

"It is fair to say that the stethoscope is as important as any instrument for examination of the gastrointestinal tract."*

Sources of diagnostic noises to be considered during a routine abdominal auscultation. In addition to visceral-peristaltic activity, these sounds may have their origin in visceral-parietal friction as well as in vascular and muscular activities.



*Palmer, E.D.: Clinical Gastroenterology, ed. 2. New York, Hoeber Medical Division, Harper & Row, Publishers, 1973



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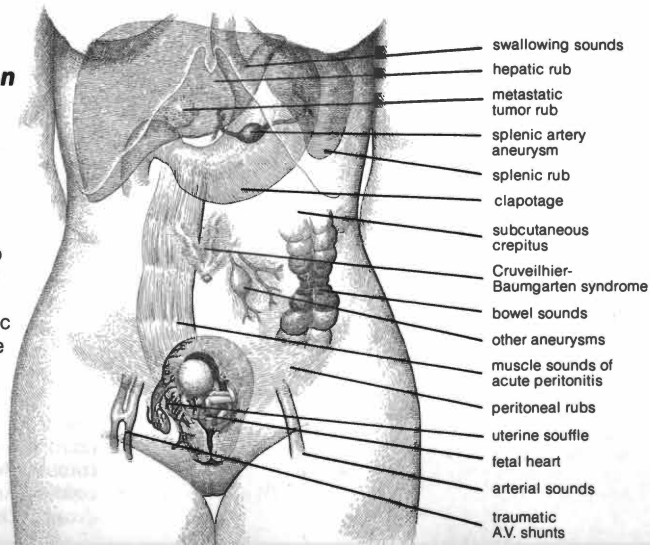
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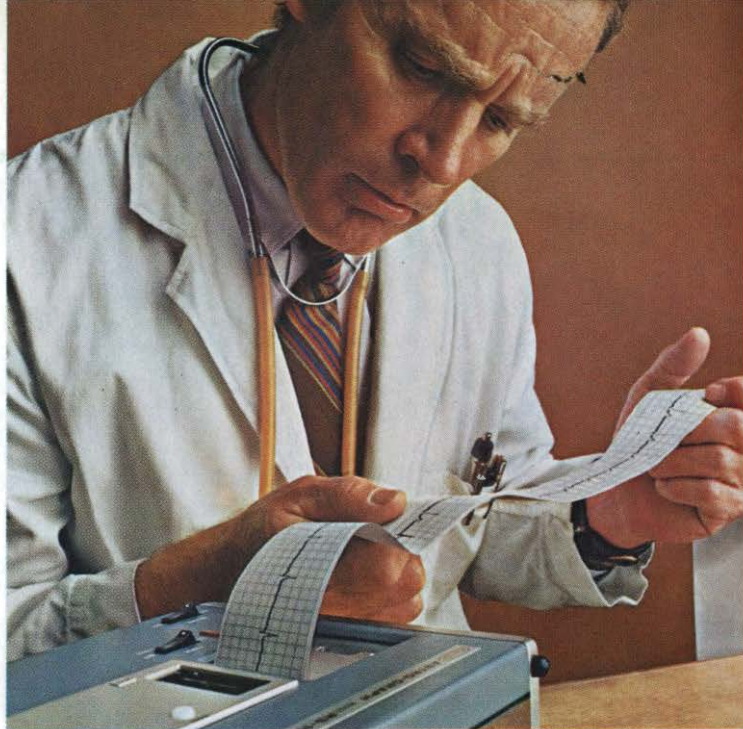
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When cardiac complaints occur in the absence of organic findings, underlying anxiety may be one factor



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Precautions: In the elderly and debilitated, and in children over six, limit to smallest effective dosage (initially 10 mg or less per day) to preclude ataxia or oversedation, increasing gradually as needed and tolerated. Not recommended in children under six. Though generally not recommended, if combination therapy with other psychotropics seems indicated, carefully consider individual pharmacologic effects, particularly in use of potentiating drugs such as MAO inhibitors and phenothiazines. Observe usual precautions

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An Introduction to the Third Annual Symposium on Respiratory Failure

The rapid development of knowledge, techniques, and equipment in the area of respiratory care has both greatly improved and complicated the care of the patient with respiratory failure. Due to this progress, the physician who has an intermittent opportunity to care for these types of patients is at a major disadvantage. Consequently, over the past three years the Departments of Medicine of the Schools of Medicine at the Medical College of Virginia and University of Virginia have held an annual symposium to provide the practicing physicians in the state with the opportunity to review the pathophysiology of respiratory failure and become aware of the more modern techniques, approaches, and available equipment for the management of acute respiratory failure. This publication will reach a considerably wider audience than had the opportunity to attend the symposium, and we hope it will extend our program to many other concerned physicians.

JAMES P. BAKER, M.D.

*Associate Professor of Medicine
Medical College of Virginia*

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Clinical Pathological Correlation of Chronic Obstructive Pulmonary Disease (COPD)*

ORHAN MUREN, M.D.

*Associate Professor of Medicine and Anesthesiology,
Medical College of Virginia, Health Sciences Division of
Virginia Commonwealth University, Richmond, Virginia*

The two most common forms of COPD, chronic bronchitis and pulmonary emphysema, will be briefly reviewed.

Etiology. The causes of COPD are not definitely known. However, there appears to be a statistically significant correlation between the incidence of COPD, cigarette smoking, and air pollution. This is especially true for chronic bronchitis. In some cases, genetic factors (α_1 - antitrypsin deficiency) may be responsible for development of COPD. This is called familial type of COPD or familial emphysema. Chronic irritation of the tracheobronchial tree is common to all cases of chronic bronchitis. Cigarette smoking appears to be the single most important factor in the development of chronic bronchitis. Heavy cigarette smokers appear to be affected to a greater extent than light smokers, and the symptoms are worse in patients who give a history of long cigarette smoking. However, not all cigarette smokers develop chronic bronchitis. Individual susceptibility may play a role in some people. The symptoms of smoking are greater if a person lives in a heavily polluted area and also if there is cold and damp weather.

The Incidence. It has been estimated that there are currently 15 million people suffering from COPD in the United States. The incidence of COPD is higher in industrial areas, especially among men who engage in dusty jobs, such as coal miners.

Mortality. In the United States in 1969, 35,000 died primarily from chronic bronchitis and pulmonary emphysema. In 65,000 cases chronic bronchitis

and pulmonary emphysema contributed to the demise of the patients. Since 1950, the death rate from emphysema has doubled every five years. The federal government pays more than \$200,000,000 annually to respiratory cripples.

Definition. Chronic bronchitis is a clinical syndrome which is characterized by productive cough on most days during at least three months a year for two or more successive years. There is chronic productive cough without known specific causes such as tuberculosis or chronic suppurative lung disease. It is more common in males.

There is excessive mucous production with hypertrophy and hyperplasia of the mucous secreting glands including the Goblet cells. Bronchial mucous glands are normally located in the bronchi which contain cartilage in their wall. Hypertrophy of the gland size can be measured as a gland to wall ratio, and this is called the Reid Index. In normal people over the age of four years, this falls below one-third. In children under the age of four years, the ratio is a little higher.

A high Reid Index is very suggestive of chronic bronchitis, but there is no close correlation between clinical chronic bronchitis and the degree of mucous gland hypertrophy and hyperplasia. There is also an overlap of the Reid Index between bronchitis and nonbronchitis.

Clinical and Functional Manifestations of Chronic Bronchitis. The cardinal manifestation of chronic bronchitis is productive cough. There is in general a history of 20–30 years of cigarette smoking. The disease in general has a slow onset. In the beginning, patients attribute the cough to cigarette smoking. The so-called "cigarette cough" is an early sign of

* Presented by Dr. Muren at the Symposium on Respiratory Failure, May 25, 1972, at Richmond, Virginia.

bronchitis. In many patients there is also an associated chronic sinusitis. The cough may disappear if smoking is stopped early enough.

The activity of cilia in the bronchial tree is inhibited by tobacco smoke. As a result of this, movement of mucous blanket is reduced significantly. The mucous glands and Goblet cells are stimulated and they produce more mucous. The result will be chronic cough and expectoration.

Excessive mucous production increases the tendency to infection which causes further hypersecretion. There develops a vicious cycle of excessive mucous secretion, infection, and more hypersecretion results. Tobacco smoke also causes bronchoconstriction which may aggravate the symptoms of bronchitis.

Normally the lower respiratory tract is essentially sterile. This is primarily due to cough reflexes, mucociliary, and alveolar macrophagic activity that eliminates bacteria or foreign particles that may have been inhaled during inspiration.

In chronic bronchitis many organisms can be isolated from the sputum which may be responsible for acute exacerbations. However, viruses probably are responsible to a great extent for the acute episodes in chronic bronchitis.

Following viral infections, as a result of damage to bronchial mucous, growth of bacteria may be encouraged. *Diplococcus pneumoniae* and *Hemophilus influenzae* appear to be important organisms; however, sometimes *Staphylococcus aureus* and the Friedlander's bacillus may be responsible for acute infection. Some patients trace the beginning of symptoms to some acute episode of infection such as bronchopneumonia.

In general there is fluctuation in the manifestations during the course of the disease. Symptoms become worse after exposure to cold, damp, or foggy weather or to irritants. However, during the end-stage of the disease the patients are, more or less, continuously symptomatic. Death secondary to pneumonia, congestive heart failure, or acute respiratory failure may occur 15 to 30 years after the beginning of symptoms. In a typical bronchitic, sputum is usually mucoid which becomes mucopurulent during acute bronchopulmonary infections.

Dyspnea may also occur during episodes of acute bronchoconstriction secondary to infections, irritants, and so forth. It may also indicate development complicating pulmonary emphysema. Intermittent wheezing may also be present.

Dyspnea, cough, and wheezing may awaken

the patient, and the picture may be confused with paroxysmal nocturnal dyspnea due to left-sided heart failure. But in bronchitis the symptoms are generally improved by expectoration of sputum. The body weight of these patients is generally normal or heavy.

Arterial gas abnormalities are quite common. Many patients have hypoxemia alone. CO_2 retention takes place late in the course of the disease or during acute episodes of bronchopulmonary infection.

When hypoxemia and respiratory acidosis are present, pulmonary hypertension develops which may result in cor pulmonale.

There is a high incidence of erythrocytosis resulting from hypoxemia. Many patients later in the course of the disease have florid appearance and cyanosis. Because of increased incidence of congestive heart failure and cyanosis, the patients are called "Blue Bloaters."

The amount of airway obstruction will influence the physical signs. In advanced stages, the thoracic cage is in the inspiratory position. There is kyphosis of the dorsal spine. The anteroposterior diameter of the chest increases. There is excessive use of accessory respiratory muscles. The degree of scalene muscle contraction may give an idea about the extent of airway obstruction. In general, the breath sounds are normal. Ronchi are present in most patients.

In the early stages of chronic bronchitis and pulmonary emphysema, there is a significant degree of involvement of the small airways. It should be emphasized that small airways (2 mm or less in diameter) are only responsible for approximately 15 to 20% of the total airway resistance; thus, marked increases in peripheral or small airways will not be detected by the conventional tests such as FEV_1 (forced expiratory volume in one second) or MMFR (maximum mid expiratory flow rate).

In the early stages of these conditions, frequency-dependent dynamic compliance studies and alveolar-arterial O_2 tension gradient, $A-a \text{ P}_{\text{O}_2}$, may detect pulmonary dysfunction. For clinical purposes, however, simple spirometric studies with measurements of FVC (forced vital capacity), FEV_1 , and MMFR are satisfactory.

Improvements in flow rates after administration of bronchodilating agents indicate the presence of partially reversible obstruction.

In established chronic bronchitis, there is over-expansion of the lungs with enlargement of

residual volume and FRC (functional residual capacity). VC (vital capacity) is either normal or decreased. The total lung capacity may be normal or increased. The ratio between FEV₁ and FVC, and the maximal mid expiratory flow rate are reduced.

Radiologic Findings. In simple or uncomplicated chronic bronchitis, the chest x-ray may be normal. There may be over-expansion of the lungs and the diaphragm may be depressed.

Some cases would show "tram lines" or parallel shadows and prominence of the lung markings mainly at the bases. Prominence of the main pulmonary artery may suggest pulmonary hypertension. Bronchograms may demonstrate tiny diverticulum-like shadows in the large bronchi. Irregularity of the caliber of segmental and subsegmental bronchi is frequently seen.

Pulmonary Emphysema. Pulmonary emphysema is accurately defined in morphologic terms only. It is defined by increase beyond normal in the size of air spaces distal to the terminal bronchioles, with destruction of the walls of these air spaces. It is a destructive process. There is reduction in elastic retractive force of the lungs.

The portion of the lung distal to the terminal bronchiole is called acinus, and it contains respiratory bronchioles, alveolar ducts, alveolar sacs, and alveoli. It is in this area that gas exchange takes place. For this reason, acinus is considered as the basic functioning unit of the lungs which is analogous to the nephron of the kidney.

In panacinar emphysema, there is involvement of the entire acinus. In centriacinar emphysema, only those alveoli near the center of the acinus are affected. The centriacinar type is more common in the upper two-thirds, and the panacinar is roughly uniform, commonly affecting the basal regions of the lungs.

Many patients have both types of emphysema together; however, centriacinar is much more common than panacinar and is in general associated with chronic bronchitis and chronic respiratory irritation. Dr. W. M. Thurlbeck found panacinar as often in women as men, while the centriacinar was more common in men.

Emphysema is more common in patients with bronchitis than in nonbronchitics. There is also a higher incidence of emphysema in patients with extensive bronchiectasis. This is also true in other chronic inflammatory diseases of the lungs, especially when both lungs are diffusely affected. On the

other hand, emphysema is rarely found in the post-mortem studies of the lungs of patients with bronchial asthma.

Clinical and Functional Manifestations. The main symptom of emphysema is dyspnea which has an insidious onset and becomes manifested on exertion. Dyspnea gradually increases, and in advanced stages, ordinary daily activities may induce severe shortness of breath.

Cough may be absent or insignificant during the early course of the disease. Episodes of severe dyspnea and wheezing may occur, usually during acute bronchopulmonary infections or after exposure to irritants. In general, the body weight is below normal, and loss of weight is common in emphysematous patients.

The anteroposterior diameter of the chest is increased. Breath sounds are distant. The heart sounds are frequently inaudible. They may be heard easily in the epigastric area. There is a higher incidence of peptic ulcer disease in patients with emphysema. The exact cause of this is unknown at the present time.

Airway resistance is increased especially during expiration. Static compliance of the lungs is greater than normal. However, frequency dependent compliance studies are generally abnormal. Residual volume, FRC, and TLC (total lung capacity) are frequently elevated. VC may be normal or reduced due to increased RV and FRC. There is obstruction to airflow. FEV₁, MMFR, and MVV (maximal voluntary ventilation) are diminished.

X-ray Findings. In mild pulmonary emphysema the chest x-ray may be normal. In some cases there is x-ray evidence of over-expansion of the lungs which is a nonspecific finding that is seen in cases of diffuse bronchial obstruction such as bronchial asthma and chronic bronchitis. If, in addition to over-expansion, there is marked reduction or absence of peripheral vascular markings associated with engorged hilar pulmonary vessels and blebs bullae, presence of underlying emphysema is almost certain. The heart shadow is usually long and narrow.

Arterial gas studies reveal only mild abnormalities at least during early stages of the disease. Patients attempt to maintain a relatively normal P_{O₂} and P_{CO₂}. Because of this, these patients are called "Pink Puffers." The incidence of cor pulmonale is less frequent in Pink Puffers as compared with Blue Bloaters.

There are two primary factors responsible for

TABLE 1.
MAIN MANIFESTATIONS OF PURE CHRONIC BRONCHITIS
OR PULMONARY EMPHYSEMA

	(Blue Bloater) Chronic Bronchitis	(Pink Puffer) Pulmonary Emphysema
Cough	++++	±
Dyspnea	±	++++
Body Weight	normal or heavy	thin
Arterial Gas Abnormalities	++++	+
Cor Pulmonale	++++	+(Terminally)
Erythrocytosis	++++	+
Breath Sounds	normal	diminished
±: Insignificant		
+: Increase		
++++: Significant increase		

the development of pulmonary hypertension in patients with COPD: 1) Functional or reversible factors due to hypoxemia and hypercapnia, 2) Irreversible factors due to loss or occlusion of pulmonary capillaries.

Functional factors are mainly responsible, and they play a major role in the production of pulmonary hypertension. Since there are in general more disturbed arterial gas tensions in bronchitis, incidence of pulmonary hypertension and cor pulmonale are higher in bronchitics.

In over 90% of the cases of COPD, patients have combined chronic bronchitis and pulmonary emphysema. Some of these patients have predominantly chronic bronchitis and some predominantly pulmonary emphysema. However, a very small percentage of these patients would only have either chronic bronchitis or pure pulmonary emphysema.

TABLE 2.
CAUSES OF ACUTE RESPIRATORY FAILURE IN COPD

1. Bronchopulmonary infections.
2. Heavy sedation and anesthesia.
3. Improper use of oxygen.
4. Pulmonary edema and congestion.
5. Thoracotomy, abdominal surgery.
6. Atelectasis or pneumothorax.
7. Dehydration.
8. Pulmonary embolism.
9. Severe episode of air pollution.

TABLE 3.
THE FINDINGS THAT MAY INDICATE POOR PROGNOSIS
IN COPD

1. Recent significant weight loss.
2. Persistent tachycardia at rest.
3. Presence of cor pulmonale.
4. FEV₁ less than 750 ml.
5. Persistent severe hypoxemia and hypercapnia.
6. Marked reduction in pulmonary diffusion capacity.

If manifestations due to pure chronic bronchitis or emphysema are appreciated, one may have some opinion as to symptoms and signs primarily related to either chronic bronchitis or pulmonary emphysema (Table 1). It has been shown that chronic bronchitis does not necessarily always lead to pulmonary emphysema nor does pulmonary emphysema always lead to chronic bronchitis.

Table 2 shows causes of acute respiratory failure in patients who have chronic respiratory failure with COPD. Finally, Table 3 shows factors that may indicate poor prognosis in patients with COPD.

Comment. There are currently 15 million people affected with COPD in the United States. It appears that once the disease is well established or advanced, the ultimate course cannot be altered significantly. Emphasis should be given upon prophylactic measures. Discouragement of cigarette smoking is probably the most important means to reduce the incidence of COPD.

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The Pathophysiology of Respiratory Failure in Chronic Obstructive Pulmonary Disease*

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The most important pathophysiologic aspects of chronic and acute obstructive pulmonary disease involve disturbances in ventilation with resulting derangement of gas exchange in the lung. There is considerable variability in the type of abnormality, the time of its appearance in relationship to the history of the disease, and in the progression of the abnormality in blood gases. The usual sequence, however, is the following: 1) In the earliest stages there is no blood gas abnormality at rest or with exercise, 2) With further progression of the disease the blood gas tensions are normal at rest but on exercise there is a significant decrease in arterial blood P_{O_2} , 3) In a more advanced stage there may be minimal re-

duction in arterial blood P_{O_2} at rest, while on exercise hypoxemia is accentuated and arterial blood P_{CO_2} rises, 4) In advanced COPD there is decrease in arterial blood P_{O_2} and increase in arterial blood P_{CO_2} at rest, with moderate or marked worsening of these changes on exercise.

Hypoxemia results from one or more of the following factors: disturbance in ventilation/perfusion relationships of lung, hypoventilation, and, to a degree, impaired diffusion. Hypercapnia results from alveolar hypoventilation. Ventilation/perfusion disturbances of the lung may occur because obstruction of bronchi and bronchioles is uneven, resulting in portions of the lung being hypoventilated and other parts being hyperventilated. The mechanism of obstruction can involve several of the following factors, all of which may be unevenly distributed in different areas of the

* Presented by Dr. Patterson at the Symposium on Respiratory Failure, May 25, 1972, at Richmond, Virginia.

lung: tenacious exudate in the bronchi and bronchioles; edema of the bronchial wall and bronchial or bronchiolar wall and mucosa; bronchiolar spasm; loss of the normal radial (outward) traction on the wall of the bronchi and bronchioles, owing to loss of the normal pattern of the pulmonary stroma through departmenting of the lung; and, finally, varying degrees of fibrotic obstruction of the airways. The loss of radial traction from departmenting of the lung, owing to breakdown of alveolar septae, is perhaps the least appreciated of these common mechanisms of obstruction. During expiration, the airways are normally held open, in part, by the outward pull of the various elements in the pulmonary stroma. When this outward pull is diminished or lost, and particularly when the other factors producing obstruction are operative, including loss of integrity of the bronchial and bronchiolar walls, some collapse or closure of the airways after the early phase of expiration is inevitable. As the chest becomes barreled and assumes the position of hyperinflation, the radial traction may be maintained to a greater degree than if the chest had retained its normal contour, although a price is paid in the form of a less efficient performance of the muscles of respiration, including the diaphragm. The accessory muscles of respiration, particularly the scalenes and less importantly the sternomastoids, the upper trapezius, and the pectoral muscles, assume increasing importance in the maintenance of ventilation, particularly in the upright position.

Blood leaving the alveolus, which is under-ventilated in relation to the amount of blood flow, thus has a low ventilation/perfusion ratio (low \dot{V}_A/\dot{Q}_C), both in the oxygen and carbon dioxide exchange. Blood leaving this alveolus will have a lowered oxygen tension and content and an elevated carbon dioxide tension and content. In contrast, certain alveoli are overventilated, since their airways are less obstructed and they feel the effects of the increased respiratory efforts which the patient commonly makes to overcome the overall increase in airway resistance. Blood leaving the hyperventilated alveolus with a high ventilation/perfusion ratio (high \dot{V}_A/\dot{Q}_C ratio) will have an oxygen tension slightly above normal. Owing to the fact that the oxygen dissociation curve is very flat at the arterial end of its normal range, very little additional oxygen content is gained by this increase in oxygen tension. Further-

more, oxygen is relatively insoluble, with only about 0.3 ml of oxygen normally dissolved in 100 ml of arterial blood. The gain in dissolved oxygen from the small increase in oxygen tension is almost negligible. On the other hand, much more carbon dioxide is in solution in the plasma and can be more readily moved under a given diffusion gradient. The CO_2 dissociation curve is steeper than the oxygen dissociation curve. As a result, the blood leaving the hyperventilated alveolus has lost much more carbon dioxide than it has gained oxygen. When these two blood streams, one from an underventilated alveolus and the other from an overventilated alveolus, are united, the stream with low oxygen content, mixing with the stream containing a minimally increased oxygen content, results in blood which has a reduced oxygen content and tension. On the other hand, the mixing of a stream with an elevated CO_2 content with one having a reduced CO_2 content can readily result in blood with normal or near normal carbon dioxide content and tension. Therefore, we commonly observe arterial hypoxia, first during exercise and later at rest, as the initial blood gas abnormality during the progression of chronic obstructive pulmonary disease. The elevation of carbon dioxide tension occurs later as alveolar hypoventilation becomes widespread with further deterioration of respiratory function.

Impairment of diffusion (the third major type of respiratory insufficiency) is usually not marked in COPD unless there is concomitant fibrosis of the lung. In the centrilobular type of emphysema, however, owing to dilatation of terminal airways, diffusion may be impaired because of the longer diffusion path ("distance barrier").

The heart is frequently secondarily involved in emphysema. This introduces another abnormality in the oxygen delivery system. Impairment of cardiac function results primarily from pulmonary hypertension which eventually leads to chronic cor pulmonale. The pulmonary hypertension is due to increased pulmonary vascular resistance which in turn is due to the following factors: 1) loss of vascular bed as a result of destruction of vascular channels, 2) increased intra-alveolar pressure compressing the blood vessels in the lung, 3) vasoconstriction due to the reduced P_{O_2} of the blood, primarily when acidosis is present. This last factor is at present thought to be an important reason for the development of pulmonary hyper-

tension in emphysema, but operates primarily when there is respiratory acidosis. Hypoxic constriction of pulmonary arteries and arterioles is relatively weak when the blood pH is normal. Cardiac function in emphysema may be further impaired as a result of direct harmful effects of the low P_{O_2} and high P_{CO_2} on cardiac muscle and also as a result of increased work of the heart in the high cardiac output stage of the disease. Impairment of cardiac function in emphysema may be more severe if there is associated coronary disease.

Chronic hypoxia of a severe degree in the later stages of chronic obstructive pulmonary disease brings about a deterioration of function of most organs of the body. A patient in late emphysema commonly loses weight, is depressed and often confused, and has little or no tolerance for exertion. Reduction of cardiac output with failure of the right heart further increases tissue hypoxia. The hypoxia does, however, stimulate two types of tissue rather late in the disease: the chemoreceptors of the aortic and carotid bodies (the function of the glomus pulmonale at the bifurcation of the pulmonary artery is still unclear), and the bone marrow. The chemoreceptor stimulation is important in offsetting the narcotic effects of high arterial carbon dioxide tension on the respiratory center complex in the brain stem. Therefore, too rapid or too large a reduction of the hypoxia without adequate respiratory assistance can reduce the drive to respiration and rapidly worsen the elevation of arterial CO_2 tension (hypercapnia).

Physiological Patient Management. In the application of physiology to patient care we seek to use previously accumulated knowledge of physiological processes and mechanisms to plan our therapy, with the aim of shifting abnormal processes and disease toward the normal. We also utilize the physiological approach in evaluating the effect of management in a given patient on a day to day, hour by hour, and, at times, moment to moment basis, as well as in evaluating our past performances so as to plan more effective therapeutic strategies for the future.

The application of cardiovascular and respiratory physiology to the management of a *specific* patient rests upon the adequacy of *quantitative* knowledge of physiological responses and mechanisms. If the information is not quantitative, effective "physiological" management may not be

possible. A difficult and ever present problem is the effective application of knowledge of physiological processes and mechanisms obtained from studies on other human beings and animals, both normal and ill, to the care of one particular patient; the physiological responses may differ in important respects, both qualitative and quantitative, from those described in the literature.

As an example of the need for quantitative information, we may cite the pulmonary vascular response to hypoxia. It is not enough to know that pulmonary vessels constrict on the influence of arterial hypoxia and that this constriction is greater during states of acidemia. One needs to know the quantitative relations between hypoxia and acidemia in the studies reported in the literature. From this information, an estimate can then be made of the probable magnitude of the pulmonary vasoconstriction in the patient under treatment, given the data on his arterial blood gas tensions and pH. Certain additional questions must be answered in order to plan effective therapy: Is the magnitude of this patient's hypoxia and of his acidemia by combined effect sufficient to produce a serious increase in pulmonary vascular resistance and an increase in the work load of the right heart? Are the hypoxia, the hypercapnia (if present), and the acidemia acting to impair the ability of the right heart to handle the increased work load? What other important factors, for example, coronary arterial or pulmonary vascular disease, are present and how do they interact with the blood gas and pH abnormalities? Is therapeutic intervention needed, and how urgently? What are the probable favorable and potentially unfavorable physiological effects of the therapeutic options?

If only rough and approximate answers to such questions can be given, which is commonly the case, then some means of continuous or frequent discontinuous monitoring of the physiological state of the patient must be available. Such monitoring can be instrumental, including biochemical, or human. The continuous human monitoring of the patient—the nurse at the bedside of a single patient—is becoming less and less common. The development of intensive care units, providing the nurse with physical proximity to more than one patient, makes possible effective visual and auditory monitoring of two, perhaps three, patients by one nurse. The more seriously

ill the patient, the smaller his physiological reserves and the greater the need for continuous or frequent discontinuous monitoring of basic functions. Such monitoring provides the essential feedback information required for precise adjustment of therapy to the physiological state of the patient and for the early detection and correction of errors in management.

A difficult challenge that must be met is the devising of means of continuous and discontinuous measurement of physiological processes in the individual patient that are sufficiently basic yet *practicable* to provide the data required for effective therapy. At present, variables commonly and readily monitored are: intravascular pressures, the electrocardiogram and the heart rate, the tidal volume and respiratory rate (although this last presents some problems), and rectal temperature. Continuous body weight recording can be done, but these recording scales are at present expensive. Frequent discontinuous information on the blood gas tensions and pH is, of course, readily obtained but continuous recording of these variables still presents problems. Continuous information on other functions, including cardiac output and oxygen delivery to the tissues, is clearly needed in many patients critically ill with cardiorespiratory disorders.

The need is particularly great in relation to the often rapidly changing clinical states of respiratory failure. This is not to say that in every case sophisticated instrumentation is required, or that it will provide all of the information needed for optimal management. Sensitive clinical observation remains essential. For example, the human face, particularly in the elderly in whom physiological reserves are low, is an exceedingly delicate indicator of favorable or unfavorable terms of physiological events. The greatest clinicians of the past, or of today, appear to have an intuitive feeling of the pathophysiology in the patient, even though they are not always able to articulate this feeling. The present day clinician should not abandon efforts to sharpen his own sensitivities toward the subtle summation of physiological processes that result in changes in the appearance of the patient's face, tone of voice, gesture, feel of tissue, in favor of excessive reliance on sophisticated instrumentation. These methods of study of the patient are complementary, not usually exclusive. One can safely predict that, for example, when continuous recording of arterial blood gas tensions, pH, and cardiac output become commonplace in the management of critically ill patients, these same measurements will make it possible to sharpen our bedside observations and the conclusions that we draw from them.

Arterial Blood Gases: Their Meaning and Interpretation*

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The measurement of arterial blood gases is essential in the management of respiratory failure and in the diagnostic assessment of the nature and severity of pulmonary disease. Adequate therapy for patients with acute respiratory insufficiency is often impossible without the information obtained from arterial blood gases. These studies must be readily available around the clock, including nights, weekends, and holidays and should not have to depend upon a technician called in from home. A ready knowledge of arterial blood gases in acute respiratory failure is just as important to good medical care as knowing the urine sugar and acetone in diabetic ketoacidosis or the blood count in an acute infection. In the practice of modern medicine, the lack of availability of arterial blood gases is unjustified and unacceptable. No hospital that maintains intensive care facilities or treats acutely ill patients can afford to be without blood gas equipment and properly trained personnel to provide accurate measurements.

The techniques for obtaining arterial blood samples are simple and can be done without difficulty by qualified laboratory technicians and nurses. A 10 cc glass syringe with a 20 or 22 gauge needle is flushed with aqueous heparin, and an arterial sample is obtained without air bubbles from a brachial, radial, or femoral artery. A glass syringe is preferable to one made of plastic be-

cause the glass plunger moves more freely and allows easy detection of arterial pulsation. After the puncture, the artery should be compressed by hand for no less than five minutes. If the blood gas analysis is not done immediately, the capped syringe should be placed in an iced container. Equipment for blood gas analysis is readily available and relatively easy to operate. The cost of basic equipment is approximately \$3,000. An arterial blood sample of 3-5 cc is sufficient for a complete study. Micromethods are also available for "arterialized" capillary blood obtained by puncture of a hyperemic ear or fingertip. Only arterial blood is of consistent value in detecting the gas exchange in the lungs. Venous blood is unreliable because it has already passed through the systemic capillaries where oxygen and carbon dioxide exchange occurs. It is also influenced by changes in tissue metabolism and regional changes in circulation.

Oxygen and carbon dioxide are both physically dissolved in blood, and each exerts a tension or pressure (P_{O_2} and P_{CO_2}) which, in the capillaries of the lung, is in equilibrium with the gas pressures within the alveoli. The oxygen tension in the alveoli is determined by the partial pressure of the oxygen in the atmosphere and averages slightly above 100 mm Hg at sea level. The carbon dioxide in the alveolar gas averages 40 mm Hg. It comes almost entirely from the blood and reflects tissue metabolism (fig. 1).

The arterial oxygen tension is normally 5 to 10 mm Hg lower than the alveolar oxygen tension, due to shunting of the unoxygenated blood into the left atrium from the bronchial veins and the Thebesian

* Presented by Dr. O'Donohue at the Symposium on Respiratory Failure, May 25, 1972, at Richmond, Virginia. Reprint requests to Walter J. O'Donohue, Jr., M.D., Box 862, Medical College of Virginia, Richmond, Virginia 23298.

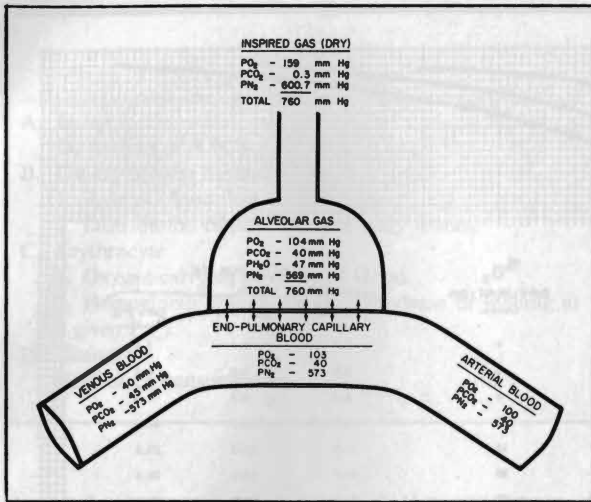


Fig. 1—Normal gas tensions in the inspired gas and blood.

veins of the heart. Alterations in the distribution of ventilation and perfusion within the lungs also contribute to this alveolar-arterial oxygen gradient. As demonstrated in figure 2, during normal tidal breathing, about four times more ventilation goes to the bases of the lungs than to the apices. Perfusion is also distributed regionally with about 18 times more blood going to the bases than to the apices. This unequal matching of ventilation to perfusion accounts for lower tensions of oxygen and higher tensions of carbon dioxide in the alveoli at the bases of the lungs, and it is responsible for part of the alveolar-arterial oxygen difference.

The alveolar surface of the lungs is about 70 to 90 square meters with the pulmonary capillary volume approximately 70 cc. Gas exchange occurs within about 0.3 of a second and because of the enormous efficiency and reserve of this system, arterial blood gases remain within normal limits even with strenuous exercise when disease is not present. The physically dissolved oxygen in the arterial blood accounts for only a small fraction of the total oxygen that is available to the tissues. Sixty times more oxygen is carried by the red blood cells than is physically dissolved in the plasma. Venous blood returning to the lungs is about 75% saturated with oxygen. By the time it has traveled about one-third the distance through the pulmonary capillary bed, the hemoglobin has become fully oxygenated, and oxygen tensions in the alveoli and capillaries have reached equilibrium. Each gram of hemoglobin is capable of carrying 1.39 cc oxygen when fully saturated. In normal individuals with 15 g

of hemoglobin the total oxygen content of arterial blood is about 20 cc per 100 ml of blood. Only 0.3 cc of oxygen is physically dissolved in each 100 ml of blood when the arterial P_{O₂} is 100 mm Hg.

Hemoglobin saturation is calculated from the oxyhemoglobin dissociation curve (fig. 3). At arterial oxygen tensions ranging from 60 to 100 mm Hg, the dissociation curve is relatively flat with hemoglobin saturation changing only 8% (90% to 98%). Arterial oxygen tensions below 60 mm Hg are not normally encountered during life, except at very high altitudes and in disease. In systemic capillaries where oxygen tensions are as low as 30 to 40 mm Hg, the hemoglobin dissociation curve becomes quite steep, and oxygen is readily released from the red blood cells. Changes in pH, P_{CO₂}, and temperature all favor the release of oxygen from hemoglobin in the tissues and increase oxygen uptake by the red blood cells in the lungs.

Although the arterial P_{O₂} is the most important blood gas indicator of oxygen transport, there are multiple factors that must be considered in the evaluation of tissue oxygen delivery. These include

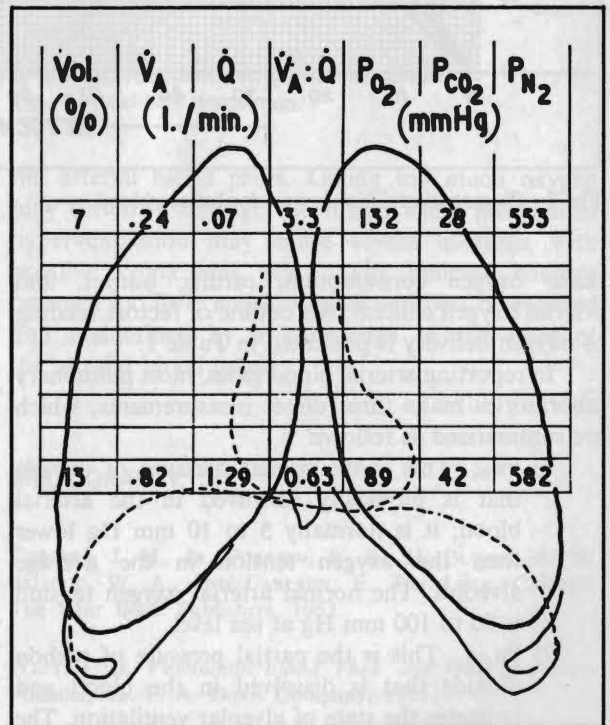


Fig. 2—Distribution of ventilation and perfusion in the lungs. (Reproduced by permission of J. B. West, F. A. Davis Co., and Blackwell Scientific Publications, Ltd. *Ventilation/Blood Flow and Gas Exchange*, p. 42, 1965.)

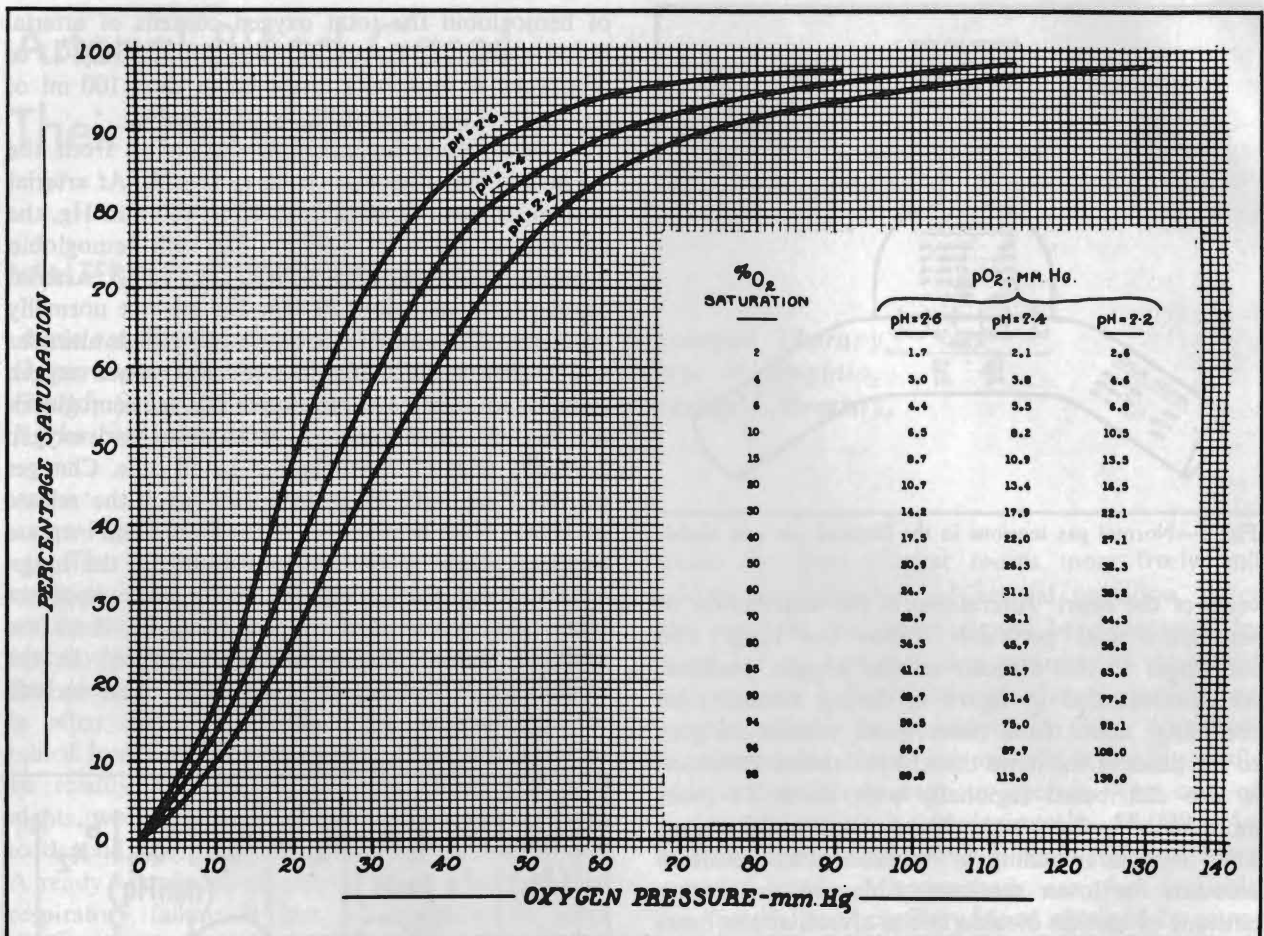


Fig. 3—Oxygen dissociation curves for human blood.

tissue oxygen consumption, cardiac output, and arterial oxygen content. An outline of factors relating to oxygen delivery is presented in Table 1.

In reporting arterial blood gases, most pulmonary laboratories make three direct measurements, which are summarized as follows:

- 1) Pa_{O₂}. This is the partial pressure of oxygen that is physically dissolved in the arterial blood; it is normally 5 to 10 mm Hg lower than the oxygen tension in the average alveolus. The normal arterial oxygen tension is 90 to 100 mm Hg at sea level.
- 2) Pa_{CO₂}. This is the partial pressure of carbon dioxide that is dissolved in the blood and indicates the state of alveolar ventilation. The normal arterial carbon dioxide tension is 36 to 44 mm Hg.
- 3) pH. This is an expression of the hydrogen ion concentration of the blood (negative

logarithm) and relates directly to the ratio of the concentrations of bicarbonate and CO₂ in the blood. The normal range is 7.36 to 7.44.

In addition to these three direct measurements there are other determinations which are based on calculations and are reported from nomograms. These are summarized as follows:

- 1) Oxygen saturation of hemoglobin. This indicates the capacity of hemoglobin to carry oxygen and is measured from the oxyhemoglobin dissociation curve using the Pa_{O₂} and the pH determinations. The normal range for arterial blood is 95 to 98%.
- 2) Plasma bicarbonate (HCO₃⁻). This is measured from a standard acid base nomogram using the Pa_{CO₂} and pH determinations. The normal range is 23 to 27 meq/liter (fig. 4).
- 3) Some laboratories report the base excess concentration. This is an expression of the

TABLE 1.
OXYGEN TRANSPORT

- | |
|---|
| A. Lungs |
| O ₂ loading of RBC's |
| B. Cardiovascular System |
| 1. Rate of blood flow. |
| 2. Distribution of flow between body tissues. |
| C. Erythrocyte |
| 1. Oxygen-carrying capacity of blood. |
| 2. Hemoglobin affinity for O ₂ (O ₂ release or loading at a given P _{O₂}). |
| D. Tissues |
| Rate of O ₂ consumption |

base excess in meq/liter, as relates to a normal value of 0 for blood with pH 7.40 and P_{CO₂} 40 mm Hg. Negative values indicate a base deficit or acid excess. The normal range is 0 plus or minus 2.3 meq/liter.

In the diagnostic evaluation of pulmonary disease, arterial blood gases provide a direct approach to ventilatory function since the primary purpose of the lungs is to oxygenate the blood and eliminate CO₂. Arterial blood gases are usually obtained at rest, following exercise, and after breathing 100% oxygen. This combination of studies provides considerable information in the evaluation of the nature and severity of respiratory disease. These data are much less influenced by patient cooperation and performance than many of the other tests performed in the pulmonary function laboratory.

In the management of patients with respiratory failure, it is frequently impossible to judge the level of alveolar ventilation or the adequacy of oxygenation by clinical evaluation alone. All of the signs and symptoms that suggest hypoxia or hypercapnia may be absent at times, and only by measurement of arterial blood gases can the physician assess the degree of respiratory impairment and render the appropriate therapy. Once active treatment has begun with oxygen or mechanical ventilation, it is important to evaluate the effectiveness of such therapy by measuring

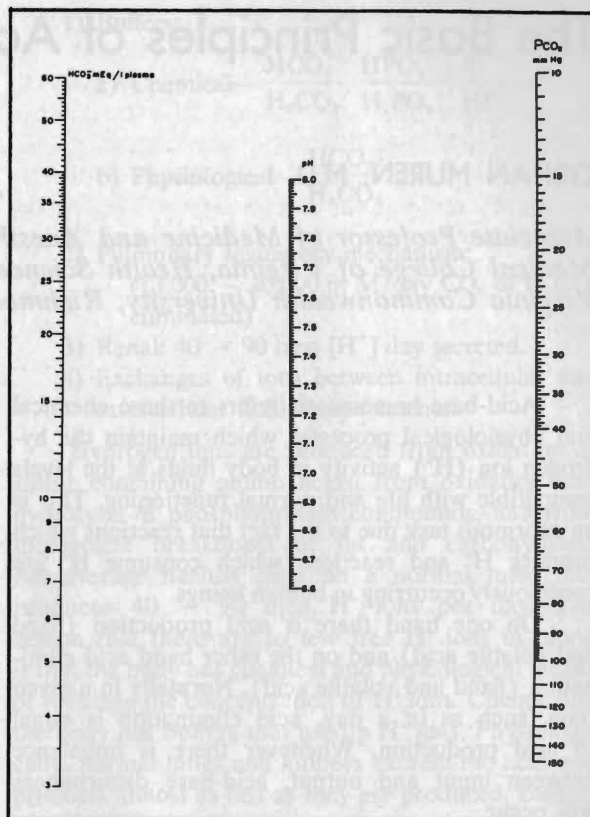


Fig. 4—Acid-base nomogram.

the arterial blood gases. Giving too much oxygen may seriously damage the lungs, while mechanical hyperventilation may cause severe alkalosis with possible coma and death. The delicate balance between too little and too much can best be reached and maintained by a knowledge of the state of the arterial blood gases.

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The Basic Principles of Acid-Base Regulation*

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Acid-base homeostasis refers to those chemical and physiological processes which maintain the hydrogen ion (H^+) activity in body fluids at the levels compatible with life and normal functioning. This is an enormous task due to the fact that reactions which produce H^+ and reactions which consume H^+ are continuously occurring in human beings.

On one hand there is acid production (fixed and volatile acid) and on the other hand acid elimination (fixed and volatile acid). Normally in a given time, such as in a day, acid elimination is equal to acid production. Whenever there is imbalance between input and output, acid-base disturbances will occur.

Many biochemical processes require optimum H^+ ion concentration. Changes in H^+ concentration markedly affect the catalytic activity of enzymes. Myocardial and muscular contraction, vascular tone, central nervous system, and so forth all require optimum H^+ ion concentrations to function properly. This is why the regulation of hydrogen ion concentration is so important.

The relationship between extra- and intracellular H^+ ion concentrations is still disputed because of differences in opinion concerning the measurements of intracellular pH. Intracellular pH has been found to be 5.9 to 7 depending upon the method used. Another problem in measurement of intracellular pH is the multicompartmental structure of most cells. It is believed that mitochondria, nuclei, and cell sap have different pH. As a result of this, intracellular pH is probably not homogeneous for a given cell. For these reasons extracellular fluid, especially arterial blood, is used to study the acid-base status of the patients.

In normal people, the concentration of H^+ is approximately 40 nanomoles (n moles) per liter of plasma. One nanomole equals 10^{-9} moles. However, it would be more correct to indicate the thermodynamic activities rather than the concentrations, the two being related as follows:

$$\frac{\text{activity}}{\text{concentration}} = \text{activity coefficient}$$

At infinite dilution the activity coefficient is equal to one. However, in concentrations in body fluids, it is much less than one. The pH meter electrode responds to hydrogen ion activity and not concentration. However, it is customary to work in concentrations, and values for the different equilibrium constants are adjusted accordingly, as indicated by a prime after a symbol such as K' .

Since concentration of H^+ ions in arterial blood is extremely small, the activity coefficient of H^+ ions may be assumed to be equal to one. Therefore, in this discussion the term H^+ ion concentration will be used interchangeably with H^+ ion activity.

The body maintains H^+ ion concentrations between 44 to 36 nanomoles per liter of plasma which correspond to a pH of 7.36 to 7.44. The most extreme pH that is compatible with life ranges between 6.8 and 7.8 which is equal to a ten-fold change in H^+ ion concentrations.

As can be seen, the body could tolerate four times an increase in H^+ ion concentrations and 2.5 times a decrease in H^+ ion concentrations, indicating better tolerance to acidosis than to alkalosis. These also indicate that H^+ ion regulation is not the most precise regulatory mechanism in the body. A similar change in potassium or sodium concentrations is usually fatal (Table 1).

Since modern chemical formulation of acids

* Presented by Dr. Muren at the Symposium on Respiratory Failure, May 27, 1972, at Richmond, Virginia.

TABLE 1.
SOME USEFUL COMPARISONS OF pH AND nEQ/L

	pH	nEq/L
"Neutral" Solution at 37° C	6.8	160
Severe Acidosis	6.9	125
Neutral Solution at 25° C	7.0	100
Normal Arterial Blood	7.4	40
Severe Alkalosis	7.8	16
	8.0	10
	9.0	1

and bases by Brønsted, acid-base regulation has been easier to understand. Brønsted defines an acid as any molecule capable of donating H^+ or a proton to a base, and a base as any compound that will accept a H^+ . HCl , H_3PO_4 , or H_2CO_3 are acids since they form H^+ ions in solution and can donate these protons to a base. HCO_3^- is considered a base, since it accepts H^+ ions and produces H_2CO_3 . Almost all protons (H^+) in aqueous solutions are reacted with H_2O to form hydrated ions such as H_3O^+ , called hydronium ions. It should be clear that what is meant by the concentration of H^+ in body fluids is hydronium ions or hydrated protons.

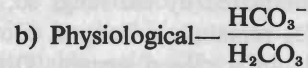
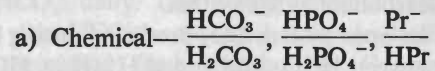
Since concentrations of free H^+ ions in plasma of human beings are very small, in 1909 Sorenson proposed the term of pH which he defined as the negative logarithm to the base 10 of H^+ ion concentration:

$$\begin{aligned} \text{pH} &= -\log (H^+) \\ H^+ &= 40 \times 10^{-9} \text{Eq/L} \\ \text{pH} &= -\log (40 \times 10^{-9}) \\ &= -\log 40 - \log 10^{-9} \\ &= -1.6 - (-9) \\ \text{pH} &= 7.4 \end{aligned}$$

Distilled water molecules at 25° C dissociate into very small amounts of H^+ ions and the same number of OH^- ions. The concentration of H^+ and OH^- is 10^{-7} Eq/L. Water is neutral and has a pH of 7.0. In normal plasma, there is a slight predominance of OH^- ions resulting in a pH of 7.40. Since the scale is logarithmic, a reduction of one pH unit indicates 10 times an increase in H^+ ion concentration.

The following are four primary mechanisms which regulate H^+ ion concentration or activity in the blood:

1) Buffers:



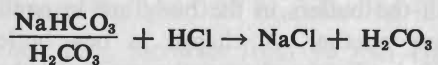
2) Pulmonary regulatory mechanism:

(13,000 – 20,000 m M/day CO_2 of H_2CO_3 eliminated)

3) Renal: 40 – 90 meq $[H^+]$ day secreted.

4) Exchanges of ions between intracellular and extracellular fluid compartments.

Hydrogen ions are produced from oxidation of sulfur containing amino acids, from oxidation and hydrolysis of phosphoprotein compounds, and from incomplete breakdown of fat and carbohydrate. An average healthy man on a normal meat diet produces 40 – 90 meq H^+ ions per day. The reason that there are so few free H^+ ions in blood is that the body has chemical and physiological means of reducing the concentration of H^+ ions. Chemically, the body has buffers that use up H^+ ions. Physiologically, normal lungs and kidneys excrete the acid end products almost as fast as they are produced. Buffers are substances that resist changes in pH when acids or bases are added to them. A typical example of a buffer is a weak acid (or a weak base) and its salt:



HCl will react with the sodium bicarbonate to form additional carbonic acid. Since carbonic acid is a weak acid, it is only partly ionized, and the above reaction decreases the concentration of free H^+ ions in solution. A bicarbonate buffer system functions as a chemical as well as a physiological buffer system. It is physiological because it works in an open system. The denominator of this buffer pair, CO_2 , is constantly being produced in the tissues and eliminated from the lungs almost as fast as it is formed.

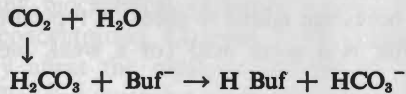
The body plays an important role in the regulation of H^+ ions by increasing or decreasing the elimination of CO_2 through the lungs. This is why a bicarbonate buffer system is very important. As a matter of fact, bicarbonate buffer is the most important buffer in the plasma, and approximately

50% of the entire buffering of whole blood resides in the bicarbonate buffer system.

In an open system CO_2 produced during the reaction between HCO_3^- and added H^+ ($\text{H}^+ + \text{HCO}_3^- \rightarrow \text{CO}_2 + \text{H}_2\text{O}$) is eliminated by the lungs so, physically, dissolved CO_2 remains unchanged. However, this is not possible in a closed system. Dissolved CO_2 will be increased. Since pH is determined by the ratio between HCO_3^- and dissolved CO_2 , in a closed system pH will be reduced to a greater extent than in an open system (Table 2).

In the red blood cells, the hemoglobin is the most important buffer. The other buffers of less significance in red blood cells are proteins and phosphate compounds. In the body H_2CO_3 can only be buffered by non-bicarbonate buffer systems which consist of hemoglobin, proteins, and phosphate buffers.

The buffer capacity of hemoglobin is far greater than that of plasma proteins. This is partly due to greater buffer value of hemoglobin and partly to greater quantity of hemoglobin in a given volume of blood as compared with plasma proteins. The conjugate base of non-bicarbonate buffer pairs is represented as Buf^- ; during the buffering of H_2CO_3 the following reaction takes place:



All the buffers in the body are in equilibrium with one another. A change in one buffer pair would immediately change the ratios in the other buffers. Since it is easy to study the bicarbonate system, this is used for the determination of H^+ ion concentration.

The bicarbonate buffer system is described as follows:

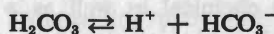


TABLE 2.

QUANTITATIVE RESPONSE OF CLOSED AND OPEN SYSTEMS TO ADDITION OF 10 MEQ/L OF STRONG ACID

$[\text{HCO}_3^-] = 24.0 \text{ meq/L}$	
$S \times P_{\text{CO}_2} = 1.2 \text{ m M/L}$	
+10 meq/L H^+	+10 meq/L H^+
$[\text{HCO}_3^-] = 14.0 \text{ meq/L}$	$[\text{HCO}_3^-] = 14.0 \text{ meq/L}$
$S \times P_{\text{CO}_2} = 11.2 \text{ m M/L}$	$S P_{\text{CO}_2} = 1.2 \text{ m M/L}$
Closed System	Open System

If V_1 is the rate of ionization of carbonic acid, it is related to the concentration of H_2CO_3 .

$$V_1 = K_1[\text{H}_2\text{CO}_3]$$

K_1 is the rate constant. The rate of opposite reaction, V_2 , is proportional to the product of the molar concentrations of H^+ and HCO_3^- :

$$V_2 = K_2[\text{H}^+][\text{HCO}_3^-]$$

At equilibrium, $V_1 = V_2$. Hence,

$$K_1[\text{H}_2\text{CO}_3] = K_2[\text{H}^+][\text{HCO}_3^-]$$

$$\frac{K_1}{K_2} = \frac{[\text{H}^+][\text{HCO}_3^-]}{[\text{H}_2\text{CO}_3]}$$

The ratio of the two rate constants must also be constant, and can be expressed as:

$$K = \frac{[\text{H}^+][\text{HCO}_3^-]}{[\text{H}_2\text{CO}_3]}$$

if solved for $[\text{H}^+]$:

$$[\text{H}^+] = K \frac{[\text{H}_2\text{CO}_3]}{[\text{HCO}_3^-]}$$

obtaining the negative logarithm of both sides:

$$-\log [\text{H}^+] = -\log K - \log \frac{[\text{H}_2\text{CO}_3]}{[\text{HCO}_3^-]}$$

$$\text{since } \text{pH} = -\log [\text{H}^+] \text{ and } -\log K = \text{pK}$$

$$\text{pH} = \text{pK} - \log \frac{[\text{H}_2\text{CO}_3]}{[\text{HCO}_3^-]} = \text{pK}' + \log \frac{[\text{HCO}_3^-]}{[\text{H}_2\text{CO}_3]}$$

The pK' for this system in blood is 6.1. This is the pH corresponding to half neutralization and the point of most efficient buffering. It represents the negative logarithm of the apparent first ionization constant of H_2CO_3 corrected for the ratio of CO_2 to H_2CO_3 . Replacing the human value for pK (6.1) expresses Henderson-Hasselbalch equation.

$$\text{pH} = 6.1 + \log \frac{[\text{HCO}_3^-]}{[\text{H}_2\text{CO}_3]}$$

Since the solubility constant of CO_2 is 0.03 total H_2CO_3 pool = $0.03 \times P_{\text{CO}_2}$, where p is the partial pressure of dissolved CO_2 . So final expression of Henderson-Hasselbalch formula would be:

$$\text{pH} = 6.1 + \log \frac{[\text{HCO}_3^-]}{P_{\text{CO}_2} \times 0.03}$$

As can be seen, the ratio between HCO_3^- and dissolved CO_2 determines the pH. Normally,

$$\text{pH} = 6.1 + \log \frac{24}{40 \times 0.03}$$

$$\text{pH} = 6.1 + \log \frac{24}{1.2}$$

$$\text{pH} = 6.1 + \log \frac{20}{1}$$

$$\text{pH} = 6.1 + 1.3 = 7.40$$

It should be emphasized that buffers are the first defense lines in any acid-base disturbance. They work within seconds; however, this effect is only temporary. Restoration of normal acid-base status depends upon the elimination of excess acid or base and restoration of buffers to normal levels.

The lungs react to acid-base disturbances within seconds to minutes by increased or decreased elimination of CO_2 . Renal compensatory mechanisms are slow; it may take five to seven days before efficient compensation can operate. Exchanges of ions between intracellular (ICC) and extracellular (ECC) fluid compartments also begin to operate fast; however, full equilibrium may take a few hours. For instance, in metabolic acidosis, intracellular K^+ moves into plasma and H^+ ions from plasma move into cells.

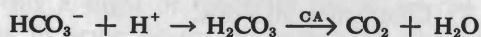
The Henderson-Hasselbalch equation:

$$\text{pH} = \text{pK}'_1 + \log \frac{[\text{HCO}_3^-]}{\text{P}_{\text{CO}_2} \times 0.03}$$

The numerator of this equation, HCO_3^- , is primarily under the influence of the kidneys and is the metabolic component. The denominator of this formula, P_{CO_2} , indicates the level of ventilation and is primarily under the influence of the lungs. This is considered a respiratory component.

$$\text{Blood pH} \propto \frac{[\text{metabolic component}]}{[\text{respiratory component}]}$$

Normally the kidneys reabsorb more than 4,000 meq of bicarbonate daily. Only less than 5 meq of bicarbonate is found in the urine per day. Approximately 85% to 90% of the filtered bicarbonate is reclaimed in the proximal tubule, and the rest is reabsorbed from the distal tubules. HCO_3^- is reabsorbed indirectly across the luminal tubular membrane. When NaHCO_3 is filtered, Na^+ is actively reabsorbed in exchange for H^+ formed within the tubule cells by the carbonic anhydrase catalyzed hydration of CO_2 . NaHCO_3 formed within the tubule cells is reabsorbed into peritubular blood. The secreted H^+ reacts with the HCO_3^- in the lumen of the tubule, and the following reaction takes place:



The CO_2 produced diffuses back into the cell and produces H_2CO_3 . The pH of the fluid leaving the proximal tubules is not significantly different from that of the initial glomerular filtrate.

This event conserves filtered HCO_3^- . However, in order to maintain normal H^+ ion concentration,

the kidneys must generate about 40 to 90 meq of new HCO_3^- daily. This newly generated HCO_3^- replaces the HCO_3^- consumed daily to buffer fixed acids produced from metabolism. Generation of HCO_3^- is performed by excretion of 40 to 90 meq of H^+ ion by the kidney as ammonium ions (NH_4^+) and titratable acids. The titratable acid represents buffer reaching the tubular urine by glomerular filtration; on the other hand, NH_3 buffer is produced by tubular cells.

The net quantity of acid eliminated in the urine is equal to titratable acid plus NH_4^+ , minus any small amount HCO_3^- that escapes into the urine. Normally, NH_4^+ is responsible for about two-thirds of the acid excreted, and titratable acid for the rest of the one-third.

Acid-Base Abnormalities. There are four simple or primary acid-base disturbances: respiratory acidosis and alkalosis, and metabolic acidosis and alkalosis. In addition, there are mixed or combined acid-base disturbances which indicate the presence of two independent acid-base abnormalities going on at the same time.

Respiratory Acidosis. This is characterized by a primary increase in P_{CO_2} , and it results when CO_2 production in the tissues exceeds the rate of its removal by the lungs. In acute hypercapnia, the body's defense mechanisms are very limited. The pH is always acidotic. Blood (H^+) increases linearly as P_{CO_2} increases.

$$[\text{H}^+] \text{ nano Eq/L} = 0.76 \text{ P}_{\text{CO}_2} \text{ mm Hg} + 9.3$$

When P_{CO_2} increases from 40 mm Hg to 80 mm Hg, plasma HCO_3^- increases only slightly (by < 3 meq/L). This small rise in plasma (HCO_3^-) is almost entirely due to non-bicarbonate buffers of blood, mainly hemoglobin.

In chronic respiratory acidosis, blood (H^+) is also a direct linear function of arterial P_{CO_2} , but the slope is less steep.

$$[\text{H}^+] \text{ nano Eq/L} = 0.24 \text{ P}_{\text{CO}_2} \text{ mm Hg} + 27.2$$

At any given arterial P_{CO_2} , plasma (HCO_3^-) is higher and blood (H^+) is lower in chronic hypercapnia than during acute hypercapnia. During hypercapnia, renal acid elimination (ammonium + titratable acid) increases, thus generating more new HCO_3^- . Increased generation and absorption of HCO_3^- from the kidneys may bring pH towards normal. It may take from 5 to 7 days before pH may come within normal range.

In chronic respiratory acidosis at a P_{CO_2} of

50 mm Hg, 75% of the patients may have pH values in the normal range. At a P_{CO_2} of 60 mm Hg, approximately 15% of the patients may have low normal pH values; at a P_{CO_2} of 70 mm Hg, less than 1% of the patients may have low normal pH values.

In summary, body buffers play a major role against acute hypercapnia; however, this buffering is limited. On the other hand, renal mechanisms play a major part against chronic hypercapnia, and pH may reach within low normal range.

Respiratory Alkalosis. This is characterized by a primary decrease in arterial P_{CO_2} . When CO_2 elimination by the lungs exceeds CO_2 production in the tissues, the result will be a lowering of arterial P_{CO_2} . During acute hypocapnia, blood (H^+) is again a linear function of arterial P_{CO_2} .

$$[H^+] \text{ nano Eq/L} = 0.74 P_{CO_2} + 10.4$$

During acute hyperventilation, the tendency for H^+ ion activity in the body fluids to decrease is somewhat opposed by buffers. Approximately one-third of the extracellular fluid HCO_3^- reduction seen *in vivo* with acute hyperventilation is due to blood buffers, mainly hemoglobin; the remaining two-thirds is due to tissue buffering. During acute hyperventilation, there is a slight increase in blood lactate and to a lesser degree, pyruvate; the role played by these organic acids in regard to the buffering is small. When P_{CO_2} falls acutely from 40 to 20 mm Hg plasma HCO_3^- falls, on the average, by 7.5 meq/L.

Chronic hypocapnia causes lowering of the renal HCO_3^- threshold and a retention of the chloride ion by the kidneys. Patients with chronic respiratory alkalosis do not appear to have increased lactate in the plasma. The pH tends to be slightly high but may be normal. In chronic respiratory alkalosis, low plasma HCO_3^- is associated with hyperchloremia. The same electrolyte composition is seen in patients with hyperchloremic metabolic acidosis. However, the pH tends to be high in chronic respiratory alkalosis and lowered in hyperchloremic metabolic acidosis.

Metabolic Acidosis. This is characterized by increased H^+ ion activity in the extracellular space due to increased concentration of fixed acids. There is primary reduction in plasma (HCO_3^-) concentration.

Decreased pH stimulates respiration, thus lowering arterial P_{CO_2} . If kidneys are normal, they secrete more H^+ into the final urine. There will be more complete titration of filtered phosphate. As the

duration of metabolic acidosis becomes longer, pulmonary compensation is reduced. This is probably due to the fatigue of the respiratory muscles secondary to the excessive work required. Arterial P_{CO_2} would have a tendency to rise toward normal. Kidneys increase renal acid secretion by increasing urinary NH_4^+ content. Provided acid loads are not excessive (>500 meq per day), renal acid secretion may reach acid production, hence increasing plasma HCO_3^- and, for a short time, exceed towards normal.

In simple metabolic acidosis, the ventilatory response is probably the most predictable. Predicted P_{CO_2} can be calculated by the following formula:

$$P_{CO_2} = 1.54 \times [HCO_3^-] + 8.36 \pm 1.1$$

If the P_{CO_2} is markedly lower than that predicted by the above equation, there is probably also a primary respiratory alkalosis. If measured P_{CO_2} is markedly higher than P_{CO_2} predicted by the above equation, then there is a complicated respiratory acidosis.

Metabolic Alkalosis. This is characterized by a primary increase in plasma bicarbonate concentration. This should not be confused with elevation of plasma (HCO_3^-) concentration secondary to chronic hypercapnia, which represents a renal compensatory mechanism for a primary respiratory dysfunction. Hypoventilation is a compensatory mechanism in metabolic alkalosis.

In general, respiratory compensation is poor. In most of the patients arterial P_{CO_2} rises by 5 mm Hg; however, in rare occasions P_{CO_2} may reach 60 or 65 mm Hg. An arterial P_{CO_2} higher than 65 mm Hg virtually always indicates primary respiratory acidosis rather than hypercapnia secondary to primary metabolic alkalosis.

The following are common causes of metabolic alkalosis:

- 1) Loss of acid (vomiting, gastric suction).
- 2) Excessive alkali administration.
- 3) Chloride depletion.
- 4) Post hypercapnic alkalosis.
- 5) Mineralocorticoid excess syndrome.
- 6) Severe potassium depletion.
- 7) Contraction alkalosis.

In clinical medicine, more than one factor is generally responsible for metabolic alkalosis, for instance in a patient with pyloric stenosis who has been vomiting. He is losing not only acid and potassium but he is also volume depleted.

Chloride depletion is an important and common

cause of metabolic alkalosis. Sodium is actively reabsorbed in renal tubules. Multiple factors influence how much sodium is reabsorbed, such as: effective plasma volume, aldosterone, filtration fraction, and so forth. The amounts of sodium reabsorbed as NaCl and in exchange for H^+ or K^+ depend mainly on the amount of chloride, the only permeant anion present in glomerular filtrate.

In chloride depletion, the amount of sodium reabsorbed in exchange for H^+ and K^+ increases. It should be remembered that for every meq of H^+ secreted into the urine, the same amount of HCO_3^- enters into the blood, either by indirect reabsorption of HCO_3^- or by generation of new HCO_3^- in the renal tubular cells. During this increased cation exchange, some potassium will also be lost. The result will be hypochloremic metabolic alkalosis. The serum potassium level may also be reduced. Diuretic induced metabolic alkalosis is primarily related to the chloride depletion and volume contraction. In these simple acid-base disturbances, the stimulus for compensation is the change in pH brought about by the primary change in P_{CO_2} or HCO_3^- .

Since abnormal pH is the stimulus, normal compensation should not over-correct or overcompensate. It should not even return pH to control levels; however, this does not mean that in simple acid-base abnormalities, normal pH cannot be observed. Since the normal pH range is 7.36-7.44, a slight acid-base disturbance, once compensated, might return pH to the normal limits.

A pH value opposite to that expected by the initial disturbance indicates a mixed acid-base disturbance. And again, if there is a marked disturbance in a primary acid-base disorder, there will be less likelihood of a normal pH. A normal pH in this instance strongly suggests the presence of a mixed acid-base disorder.

A lack of any compensatory response strongly suggests a mixed acid-base disorder. However, there are two exceptions: very little, if any, increase in plasma (HCO_3^-) occurs in acute respiratory acidosis, and only a slight or moderate rise in arterial P_{CO_2} occurs in acute or chronic metabolic alkalosis. It should be pointed out that pulmonary compensation in metabolic acidosis is reduced as metabolic acidosis continues, and renal compensation in hypercapnia becomes more efficient with time. Because of these last two points, the use of 95% confidence bands cannot truly reflect the expected

responses in acute and chronic acid-base disturbances.

From serum total CO_2 content alone, one cannot draw any definite conclusion. At least two unknown factors in the Henderson-Hasselbalch equation should be measured. The third can be calculated. For instance, in acute respiratory acidosis the total CO_2 content may be entirely normal. For example, a serum total CO_2 content of 24 meq/L in a patient may suggest normal acid-base status. The pH might be found to be 7.2 which is equal to $[H^+] = 40 + 23 = 63$ nano Eq/L. If one uses a rearranged Henderson's equation,

$$P_{CO_2} = \frac{[H^+][HCO_3^-]}{0.03 \times K}$$

$$K = 800$$

$[H^+]$ is given in nano Eq/L

$$P_{CO_2} = \frac{[H^+][HCO_3^-]}{24}$$

In the above example, P_{CO_2} will be:

$$P_{CO_2} = \frac{63 \times 24}{24} = 63$$

For intelligent interpretation of the acid-base status of the patients the following points should be checked:

1. Clinical information should include history and physical examination, medication taken, therapeutic measures undertaken such as assisted mechanical ventilation, limited salt intake, and so forth.
2. Routine serum electrolytes. It should be known that serum CO_2 content in m M/L represents almost entirely HCO_3^- . The total H_2CO_3 pool (H_2CO_3 and physically dissolved CO_2) is equal to $0.03 \times P_{CO_2}$.

P_{CO_2} and pH should be known. Anion gap or undetermined anion fraction should be calculated. This is normally less than 12 - 14 meq/L which represents phosphates, sulfates, anionic proteins, and organic anions normally present. It is measured by subtracting the sum of the plasma chloride and (HCO_3^-) concentrations from the plasma sodium concentration.

The following are causes of increased anion gap:

- 1) Azotemic renal failure.
- 2) Diabetic ketoacidosis.
- 3) Lactic acidosis.

- 4) Ingestion or administration of:
- a) methyl alcohol.
 - b) salicylate.
 - c) ethylene glycol.
 - d) paraldehyde.

In chronic azotemic renal failure alone anion gap seldom exceeds 20 meq/L. Undetermined anion fractions above 25 meq/L are usually observed only in salicylate, methanol, ethylene glycol poisoning, and lactic or diabetic ketoacidosis.

Serum potassium levels may be useful in predicting arterial pH. In acidosis, there is a tendency for serum potassium to rise unless there is underlying potassium depletion or acidosis was secondary to loss of $K HCO_3$ which occurs in diarrhea, acetazolamide (Diamox®) administration, and renal tubular acidosis.

Other laboratory findings such as blood sugar, BUN, urinalysis, liver function studies, and so forth should be examined for an explanation of acid-base disorder. For instance, in a patient with metabolic alkalosis, in the absence of diuretic administration, lack of urinary chloride is virtually diagnostic of metabolic alkalosis due to chloride depletion.

In summary, arterial gas studies including pH determinations can be vitally important in the diagnosis and management of patients with a va-

riety of serious medical problems. These studies should be interpreted in the light of clinical and other necessary laboratory findings.

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Non-Ventilator Management of Respiratory Failure: The Ventimask*

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The Problem—Acute Respiratory Failure in Chronic Obstructive Pulmonary Disease. In a recent review the authors comment on acute respiratory failure complicating chronic obstructive pulmonary disease. They state that because of the tolerance to chronic hypoxemia, the recurrent nature of the lung failure, and the increased number of complications during mechanical ventilation, “artificial ventilation is not indicated until all other attempts have failed to reverse hypoxemia without causing hypocapnia” (2).

This paper will detail the conservative management of acute respiratory failure in patients with chronic respiratory failure due to chronic bronchitis and emphysema. It is important to recognize that this is a very specific group of patients. They have had chronic hypoxia and hypercarbia for months or years preceding their current episode of acute respiratory failure. There occurs a further drop in arterial P_{O_2} ($P_{a_{O_2}}$) and usually a further rise in arterial P_{CO_2} ($P_{a_{CO_2}}$). The baseline arterial $P_{a_{O_2}}$, $P_{a_{CO_2}}$, and pH in such patients are usually as follows:

$$\begin{aligned} P_{a_{O_2}} &= 50 \text{ mm Hg} \\ P_{a_{CO_2}} &= 45 \text{ mm Hg} \\ \text{pH} &= 7.4 \end{aligned}$$

Because of infection, sedation, heart failure, associated asthma, and so forth, they usually pre-

sent to their physician with increasing dyspnea, cyanosis, disorientation, and commonly the following arterial gases and pH:

$$\begin{aligned} P_{a_{O_2}} &= 40 \text{ mm Hg} \\ P_{a_{CO_2}} &= 55 \text{ mm Hg} \\ \text{pH} &= 7.35 \end{aligned}$$

Remember that the statements in this paper *do not apply to asthma*, only to chronic bronchitis and emphysema.

The Therapeutic Goal. The physician must increase the $P_{a_{O_2}}$, “significantly” with “little increase” in $P_{a_{CO_2}}$, and “little decrease” in pH. While this stopgap measure keeps the patient alive, therapeutic efforts are directed toward complicating diseases responsible for the acute respiratory failure. An attempt will be made to define the vague term “significant decrease” in $P_{a_{O_2}}$, and “little decrease” in pH.

The Tool—The Ventimask.¹ Since this group of patients has had an elevated $P_{a_{CO_2}}$, for varying periods of time, ventilation is keyed to the low arterial oxygen, rather than to the CO_2 partial pressure. The usual methods of oxygen delivery, the nasal catheter and face mask, deliver 30% to 40% oxygen, enough to lethally depress ventilation.

The ventimask represents a method by which the physician can deliver low flow oxygen inexpensively and with safety. Because of the Venturi effect, the 100% oxygen that flows into the mask will entrain room air (21% O_2) through the side ports of the mask (fig. 1). Four liters of oxygen flow per minute is necessary to achieve the 24% O_2 concentration in the mask. However, further increases in flow will merely draw more 21% oxygen into the mask, and by clever engineering the oxygen concentration in the mask is therefore kept constant at 24%. The 28%

* Presented by Dr. Hunt at the Symposium on Respiratory Failure, May 26, 1972, at Richmond, Virginia.

¹ The ventimask can be obtained from The Bethlehem Corporation, 225 W. Second Street, Bethlehem, Pennsylvania.

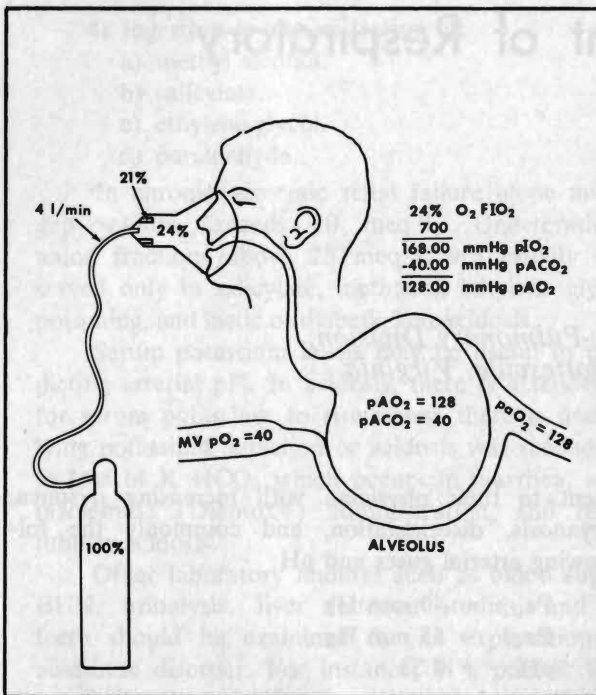


Fig. 1—The 24% ventimask.

ventimask is similar in all respects except that the final $F_{I_{O_2}}$ is 28%.

Guidelines for Arterial Gases.

Arterial Oxygen. When the $P_{a_{O_2}}$ falls below 50 mm Hg, pulmonary capillary vasoconstriction occurs, and pulmonary hypertension occurs or is accentuated. $P_{a_{O_2}}$, below 40 will decrease sodium and free water excretion and may depress ventilation. In this range (40 or below) digitalis intoxication is markedly accentuated and ventricular arrhythmias occur.

In practice then, the immediate goal of therapy should be to increase the $P_{a_{O_2}}$ from 30–40 mm Hg to the 45–55 mm Hg range. This frequently can be done with the 24% ventimask, remembering that an increase in inspired oxygen concentration ($F_{I_{O_2}}$) from 21% (room air) to 24% is really 3% of an atmosphere (760 mm Hg) or approximately 21 mm Hg. Since in patients with chronic bronchitis and emphysema ventilation is usually reduced to many alveoli, the alveolar O_2 ($P_{a_{O_2}}$) of 128 mm Hg (as in fig. 1) is usually reduced so that the increase in $P_{a_{O_2}}$ is more like 10 mm Hg than 21 mm Hg.

But it is very important to note that this 10 mm Hg change in $P_{a_{O_2}}$ is on the steep portion of the oxyhemoglobin dissociation curve (fig. 2) and will

actually nearly double the oxygen delivered at the tissue level.

Guidelines for $P_{a_{CO_2}}$ and pH. Except for its narcotic properties, $P_{a_{CO_2}}$ elevation *per se* is probably not important but may be used as a guide to oxygen delivery. If the 24% ventimask therapy results in a 10 mm Hg increase in $P_{a_{O_2}}$, and at the same time elevates the $P_{a_{CO_2}}$, greater than 5 mm Hg, further increase in oxygen concentration should not be attempted. If the $P_{a_{CO_2}}$ remains the same or is reduced then one can safely go on to a 28% ventimask and another 4% (28 mm Hg) increase in $F_{I_{O_2}}$. A $P_{a_{CO_2}}$, greater than 65 mm Hg may decrease salt and free water excretion, but this can usually be overcome with the use of diuretics (Lasix® not ethacrynic acid).

The pH, however, is critical. Many vital enzyme systems do not work as the pH falls below 7.2, and hydrogen ion elevation will also cause pulmonary capillary vasoconstriction.

If the pH can be kept between 7.3 and 7.4 and does not remain consistently below 7.2, and if the patient remains conscious and *able to cough*, then conservative therapy should be continued.

General Measures. Dr. E. J. M. Campbell has said, “controlled oxygen therapy plus ineffectual nursing is better than uncontrolled oxygen plus ineffectual nursing only because the patient gets into less trouble” (1). The most important factor immediately is nursing care.

The patient should be:

1. In a chair, not flat in bed.
2. In a lighted room or corridor for the first 24 hours for observation and stimulation.

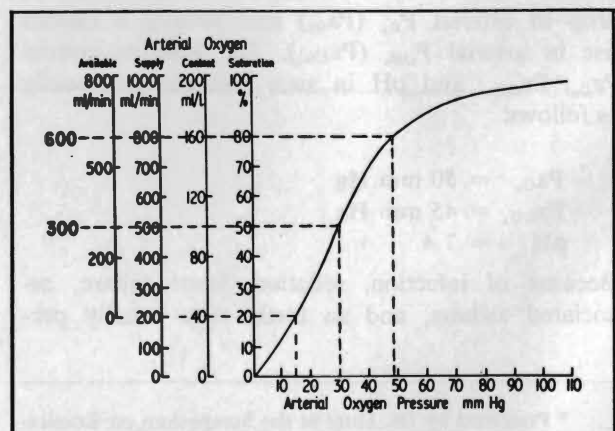


Fig. 2—Increase in $P_{a_{O_2}}$ on 24% ventimask. “Available” means available at the tissue level (modified after Campbell).

3. Receiving chest physiotherapy each hour from the floor nurse or relatives or at least encouraged to cough and breathe deeply every 15 minutes.
4. Encouraged to use a pressure regulated IPPB machine (Bird or Bennett) five minutes out of every 30 or 60 minutes (without Isuprel®). This is for "stir-up," cough, and stimulation not specifically for ventilation.

Specific Therapy. In general, there is no "specific therapy" for chronic bronchitis and emphysema, so that complications or associated diseases must be diligently searched for and vigorously treated if present. One must not blindly and mindlessly treat each patient with chronic bronchitis and emphysema with digitalis, antibiotics, diuretics, steroids, and broncholytic agents.

Mucolytics. There are none that are effective. Acetyl cysteine (Mycomyst®) may actually aggravate any bronchospasm that may be present. Robitussin® should be reserved for your grandmother who has a "tickle in her throat."

Look for and treat:

1. *Left ventricular failure.* This is most easily diagnosed by an upright chest x-ray showing pulmonary venous engorgement in the upper lobes or Kerley B lines (fig. 3). Obvious pulmonary edema, whether unilateral or mild, should be suspected and searched for. Treat vigorously with Lasix® and replace K losses with KCl not K-Triplex. Digoxin should be used judiciously. The right ventricle will respond to digitalis, but toxicity may occur at half the usual digoxin level when the Pa_{O_2} is below 50 mm Hg.

2. *Asthma.* Eosinophils in the blood or on Hansel stain² of the sputum suggest a diagnosis of asthma. Suspect this diagnosis if the patient does not smoke, is under 50, or has a childhood history of asthma. If asthma is not present, Isuprel® can accentuate hypoxemia and in the already hypoxemic individual, aminophylline, adrenalin, and ephedrine may cause dangerous arrhythmias. In the patient with chronic bronchitis and emphysema in respiratory failure without prior evidence of a good response, certainly Isuprel® and prob-

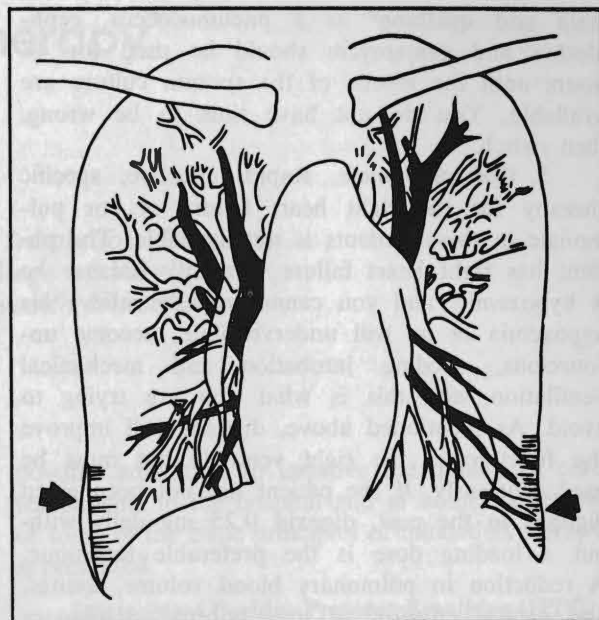


Fig. 3—The arrows indicate the position of Kerley B lines. The pulmonary veins are shown in black.

ably the other bronchodilator drugs are contraindicated.

Steroid therapy (prednisone 40–60 mg daily) in patients with associated asthma may be life saving. An intermediate PPD should be done on every patient on admission prior to the institution of steroids and, if positive, isoniazid therapy should be considered, depending on the duration of the steroid therapy and the appearance of the chest x-ray.

3. *Infection.* The sputum should be observed, stained (both Gram and Hansel), and cultured if grossly purulent. Infrequently, grossly purulent sputum can be due to the presence of eosinophils alone. Usually acute purulent bronchitis is the cause. The most common pathogens found are the pneumococcus or hemophilus influenza. Since probably 10% of all strains of streptococcus pneumoniae are resistant to tetracycline, ampicillin 2 g daily is the treatment of choice (unless penicillin sensitivity is present).

4. *Pneumonia:* A chest x-ray must be obtained. The use of a stethoscope alone in the examination of the emphysematous chest is grossly inadequate. The presence of pneumonia in the patient with acute respiratory failure constitutes a medical emergency. Unless the overwhelmingly predominant organism can be identified by gram

² Hansel stain may be obtained from Lide Laboratories, 6828 Oakland Avenue, St. Louis, Mo. 63139—\$7.50 for 8 ounces.

stain and quellung³ as a pneumococcus, cephalothin and gentamycin should be used for 48 hours until the results of the sputum culture are available. You do not have time to be wrong, then switch.

5. *Cor pulmonale*. Rapid, effective, specific therapy for the right heart failure of cor pulmonale in these patients is not available. The patient has right heart failure primarily because he is hypoxemic, and you cannot rapidly relieve his hypoxemia or he will underventilate, become unconscious, needing intubation and mechanical ventilation, and this is what you are trying to avoid. As mentioned above, digitalis will improve the function of the right ventricle but must be used cautiously. If the patient has not been given digitalis in the past, digoxin 0.25 mg daily without a loading dose is the preferable technique. A reduction in pulmonary blood volume, ascites, and pleural effusion all may improve pulmonary function so that aggressive diuretic therapy may be indicated. Ethacrynic acid may produce underventilation and should be avoided. Currently Lasix[®] is the drug of choice. *Thoracentesis may produce a lethal pneumothorax and should be avoided unless a massive effusion is present*. There is no evidence that phlebotomy is an effective method of therapy under these circumstances.

Sedation. If over sedation with morphine or pentazocine is suspected, naloxone (narcane) is specific therapy and can be given without risk of further sedation. If other drugs (Valium[®], meprobamate, and so forth) are known to have been primarily responsible for the respiratory depression, then it becomes even more imperative that vigorous attempts be made to keep the patient awake for the first 24 hours of therapy. It should be noted here that it is self-defeating to keep patients awake continuously for more than 24 hours. At the end of that time, alternating naps with arousal every 30 minutes to one hour becomes necessary.

³ Quellung reagent may be obtained as "Omniserum" from Statens Serum Institute, Artillerivej 5, DK-2300, Copenhagen S, Denmark.

When to Intubate. Reduced consciousness and an inability to cough are the major indications for intubation and ventilation. Inability to achieve an arterial Pa_o, greater than 30 mm Hg or maintain a pH greater than 7.2 after 24 hours of therapy are relative indications for intubation. But, one should never act precipitously on a single number obtained from the laboratory that does not fit the clinical course that has been observed.

Emergency tracheostomy should never be done without prior intubation. Ideally a period of mechanical ventilation with achievement of good oxygenation and reversal of the respiratory acidosis should be accomplished prior to tracheostomy.

Summary. Low flow oxygen therapy should be given a trial in all conscious patients presenting with acute respiratory failure due to chronic bronchitis and emphysema. The tolerance of these patients to hypoxemia and hypercarbia make this means of therapy possible. The ventimask is an effective, inexpensive method of administering low flow oxygen, with the added attraction that the oxygen concentration cannot be inadvertently increased. Nursing care and aggressive therapy of complicating or associated medical problems are the key to successful management.

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(A more complete bibliography may be obtained by writing Dr. William Hunt.)

Principles of Inhalation Therapy*

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With the increasing complexity of ventilatory equipment and the rapid development of new techniques for respiratory care, it has become progressively more difficult for the average physician to keep pace with clinical and technical advancements. The management of acute respiratory failure is now a demanding art which requires a broad knowledge of cardiopulmonary physiology and sophistication in the use of complicated equipment. Careful attention to detail is often the critical factor that determines survival. The mortality from acute respiratory failure has been substantially reduced in respiratory intensive care units where there are well trained teams of physicians, nurses, and technicians to manage patients during life-threatening episodes of ventilatory failure (6).

In many hospitals such facilities and specialized teams do not exist. The busy physician often finds that he has neither the time nor technical skill to provide optimum patient care. Valuable assistance can be provided by medical personnel, such as inhalation therapists, who have been trained in respiratory physiology, principles of good patient care, and the proper application of mechanical devices to aid in the management of respiratory disease. With the continuing shortage of physicians and nurses trained in pulmonary disease, the inhalation therapists can be expected to assume a larger role in the care of respiratory patients. The practicing physician must be aware of the services available and be able to utilize these to the best

possible advantage to improve the quality of care for patients in the hospital and at home. A review of some of the basic principles of inhalation therapy is presented.

Intermittent Positive Pressure Breathing (IPPB).

Intermittent positive pressure breathing is commonly employed in the treatment of atelectasis, bronchitis, and pneumonia and may be useful for the prevention of postoperative respiratory complications. Its effectiveness in these areas is a subject of considerable controversy and any beneficial effects appear to be related more to the technique of administration than to any other single factor (1). The routine use of IPPB without adequate patient instruction and without a well trained person to administer therapy appears to be of little benefit (5). Long-term home treatment with IPPB in patients with chronic obstructive lung disease has failed to demonstrate measurable improvement, as indicated by arterial blood gases and pulmonary function testing; yet many of these patients feel that IPPB helps them to raise secretions, breathe more easily, and live more comfortable lives (3). Aerosol bronchodilators may be delivered very effectively by IPPB equipment. These agents are of benefit in reducing bronchoconstriction and aid in the removal of secretions. IPPB is also indicated in the management of acute pulmonary edema with severe hypoxemia.

Aerosol Therapy. Aerosol therapy is of considerable importance in helping to facilitate removal of abnormal secretions. Accumulation of thick, tenacious secretions represents one of the most important reversible factors in acute and chronic respiratory disease. The terms "aerosol" and "mist" imply that water or a liquid substance is delivered as small particles suspended in air. Water particles

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are generally unstable and are deposited primarily in the upper airways. Ultrasonic nebulizers deliver a high-density mist with relatively small particles. They are effective in thinning secretions in the upper airway but may be poorly tolerated by some patients and are potentially hazardous with prolonged continuous use (4). Mist tents are commonly used in pediatrics for the management of pneumonia, bronchiolitis, and cystic fibrosis. Heated aerosols from reservoir nebulizers are often helpful for removal of secretions in patients with bronchitis, asthma, and acute respiratory failure. Induced sputum specimens may also be obtained for diagnostic studies. When gas is heated, more water may be transported in the gaseous state, significantly increasing the humidity. Careful attention to the principles of humidification is important in mechanical ventilation and frequently may mean the difference between success and failure in the management of patients with endotracheal tubes and tracheostomies.

Oxygen Therapy. Many of the physiologic alterations present in acute respiratory failure occur as a result of hypoxia. Oxygen is therefore one of the most important drugs used in managing this disease. Like any other drug, it must be ordered and administered with care, and its effects must be observed carefully. Oxygen transport to the tissues depends upon multiple factors, including cardiac output, arterial oxygen content, and metabolic requirements. All of these factors have to be considered for safe and intelligent administration of oxygen therapy. Excessive oxygen may result in damage to the lungs or depression of ventilation in patients with respiratory failure and hypercapnia. In the treatment of patients with acute ventilatory failure, the proper administration of oxygen may mean the difference between successful conservative management or failure of such therapy with endotracheal intubation or tracheostomy necessary for survival. The inhalation therapist may provide assistance in all areas of oxygen therapy.

Respiratory Monitoring. Patients in respiratory failure need careful monitoring, regardless of whether they are being managed conservatively or with mechanical ventilatory support. Clinical evaluation of the patient by a trained observer is essential with administration of bronchodilators, oxygen, mechanical ventilation, or other forms of therapy that may result in cardiac or respiratory alterations. Bedside spirometry can aid in determining changes in lung

volumes and minute ventilation. Portable oxygen and carbon dioxide analyzers are valuable for monitoring inspired and expired gas mixtures. Evaluation of lung mechanics, particularly when patients are on respirators, can detect significant changes in airway resistance and lung compliance. Arterial blood gases are the ultimate laboratory guide to therapy and must be available at all times to adequately manage patients with acute respiratory failure.

Mechanical Ventilation. The indications for mechanical ventilation are frequently based on a combination of clinical observations and physiologic changes which can be measured at the bedside with equipment that is readily available and familiar to the inhalation therapist (2). Once mechanical ventilation has been instituted, continuous observation is necessary and adjustments in therapy must be made, as indicated by arterial blood gases and clinical response. Advances in the design of ventilators and in techniques of ventilation have resulted in increased survival and less morbidity for patients requiring artificial ventilation. Continuous positive pressure ventilation has proved to be of considerable value in managing the adult respiratory distress syndrome and acute pulmonary edema when severe hypoxemia is present. With such therapy the effects on venous return, cardiac output, and oxygen delivery must be known and fully appreciated. Careful physiologic evaluation is necessary to determine when the patient is ready for weaning from the respirator and to follow his progress during the weaning period. Improper weaning often results in rapid deterioration of the patient and reversal of much that has been previously accomplished by good respiratory care.

Home Care. Home care is often neglected in the comprehensive medical management of patients with respiratory disease. The respiratory equipment and techniques for home care must be individualized for each patient, depending upon his disease and needs. Often simple and inexpensive equipment will give results equal to or better than more expensive and complicated devices. Instruction in cleaning and maintaining respiratory equipment at home is best given by persons who constantly concern themselves with these problems. Discharge from the hospital is sometimes dependent upon the ability of the family to render appropriate respiratory care at home. Some families are able to manage extremely complicated situations when good training and su-

supervision are provided by interested respiratory nurses and inhalation therapists. Home visits are often necessary to assure that the best possible care is given and to assist with problems that may be unrecognized by the patient, family, and physician. Frequently the practicing physician has neither the time nor awareness for the many technical and mechanical aspects of home care. Techniques for chest physiotherapy should be taught to the patient and family when indicated, and continued instruction and supervision are necessary for maximum effectiveness of this therapy. The multiple problems of outpatient care are best handled by a team of respiratory specialists, but when such a team is not available, much can be accomplished with the aid of the well trained inhalation therapist of today.

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How to Get Patients On and Off Respirators*

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This title implies that one has already decided that one's patient needs to be artificially ventilated, that is, that he is in respiratory failure. How does one diagnose respiratory failure? Much of what I have to say in this regard is in terms of arbitrary limits, values, and guidelines. Since these guidelines are arbitrary, there may exist legitimate grounds for differences of opinion about some of them. However, we have found these guidelines to be quite helpful, and experience would indicate that they are reasonable.

Let us first define what we are talking about. Respiratory insufficiency, which is the first step in the departure from normal pulmonary function, is the failure to maintain normal blood gases without persistent tachypnea, cough, or both. Hence, it can be seen that a patient may be in respiratory insufficiency and still have normal blood gases, that is, a patient in severe status asthma may be maintaining essentially normal blood gases but only with the expenditure of considerable effort and energy manifest as tachypnea and dyspnea. When the patient is inspiring room air normal blood gases are a P_{O_2} of 90 to 95 mm of mercury, a P_{CO_2} of 40 mm of mercury, and a pH of 7.4. Mixed venous blood, as it is taken from the pulmonary artery under normal circumstances, contains a P_{O_2} of 40 mm of mercury, a P_{CO_2} of 46 mm of mercury, and a pH of approximately 7.38 to 7.39. Thus it can be seen that while venous blood may give a fairly accurate representation of the patient's acid-base balance, it is of virtually no use in determining the state of oxygenation. The main function of the lungs is to convert venous blood into arterial blood, and in order to evaluate this function one must look at the finished product, not the raw material. Respiratory insuffi-

ciency can be said to have progressed to a state of respiratory failure when the P_{O_2} is below 50 mm of mercury or the P_{CO_2} is above 50 mm of mercury, at which time the pH may or may not still be near normal. Depending upon the etiology of the respiratory failure, some patients may need the institution of artificial ventilation at this point; others may not. Regardless of the etiology of the respiratory failure, when the P_{O_2} remains below 50 or the P_{CO_2} remains above 50 in conjunction with an arterial pH at or below 7.25, mechanical ventilation is indicated. There may be a few exceptions to this degree of ventilatory impairment, but they are few indeed. In this outline, one can see a summary of the indications for respiratory support, which are: a respiratory rate of greater than 35 per minute, a vital capacity of less than 10 to 15 ml per kg of body weight, an alveolar-arterial oxygen tension gradient of greater than 400 mm of mercury (an arterial P_{O_2} of less than 200 mm of mercury on 100% oxygen), a dead space to tidal volume ratio of greater than 60%, and an arterial carbon dioxide tension in excess of 60 mm of mercury, except in the case of patients with chronic hypercapnia.

It is arterial oxygen tension or P_{O_2} that we speak of and that we think about, but in actuality, the thing that we are concerned about is the delivery of an adequate amount of oxygen to the tissues, a determination which is not directly or easily measurable. However, if by means of the oxyhemoglobin dissociation curve, one relates arterial oxygen tension to oxygen saturation and in turn relates oxygen saturation into total oxygen content, implying a normal oxygen carrying capacity, such as an hematocrit of 35% or better, and if one can then derive at least indirect evidence of an adequate cardiac output, one can then assume that oxygen delivery to the tissues is adequate. The point to be made here is to stress the fact that an adequate arterial oxygen tension may indeed exist in the

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presence of a grossly inadequate oxygen supply to the tissue, such as with either severe anemia or an inadequate cardiac output, or both. The arterial oxygen tension is what we measure, but with few exceptions it is not the arterial oxygen tension *per se* in which we are interested. Arterial oxygen saturation is quite satisfactory even down to an arterial oxygen tension of 60 mm of mercury, and indeed hemoglobin does not reach 50% saturation until a P_{O_2} of approximately 26 mm of mercury is reached.

We can therefore summarize the following factors as indications for immediate intubation and ventilation:

1. A consistently rising arterial carbon dioxide tension.
2. A pH at or below 7.25.
3. A previously alert patient who becomes somnolent and unresponsive.
4. An alveolar-arterial oxygen tension gradient on 100% oxygen of 400 mm of mercury or more.
5. A respiratory rate of above 35 per minute or more.
6. A tidal volume of less than 3 to 4 ml per kg.
7. A vital capacity of less than 10 ml per kg.

How do we measure an alveolar-arterial oxygen tension gradient? This is no more than the alveolar oxygen tension minus the arterial oxygen tension measured in millimeters of mercury. This measurement is accomplished by giving the patient 100% oxygen to breathe for a minimum of 15 minutes. In some patients with severe degrees of shunting due to pneumonia or pulmonary edema and the like, as much as 30 minutes of 100% oxygen breathing may be required to completely denitrogenate the lung because of severe ventilation/perfusion inequalities. At the end of this arbitrary 15 to 30 minutes of 100% oxygen breathing, one then measures the atmospheric pressure and draws a blood gas sample. The arterial carbon dioxide tension can be assumed to completely equilibrate with the alveolar carbon dioxide tension, and this, plus the alveolar water vapor tension, determined as a function of body temperature, is subtracted from atmospheric pressure. The difference must be the alveolar oxygen tension since one can assume that the oxygen breathing for 15 to 30 minutes has completely eliminated all alveolar nitrogen. When this maneuver is performed upon healthy patients, one

will find an arterial oxygen tension of between 575 to 600 mm of mercury, implying a shunt of about 3% of the cardiac output, which is the normal anatomic shunt. The alveolar-arterial oxygen tension gradient, or the $A-aDO_2$, can therefore be said to be 75 to 100 mm of mercury on 100% oxygen and 5 to 10 mm of mercury on 21% oxygen, that is, room air. Both of these $A-aDO_2$'s imply a difference in oxygen content or oxygen saturation of precisely the same amount, that is, 3% of the cardiac output. The difference in the numerical values of the two calculations is due to the shape of the oxyhemoglobin dissociation curve.

The initial steps in instituting mechanical ventilation in most, but not all patients, are:

1. Produce a tidal volume of approximately 12 to 15 ml per kg, realizing that in the great majority of patients in respiratory failure it is necessary to achieve an initial tidal volume of approximately 2 times that of normal, in order to compensate for the ventilation/perfusion inequalities present. (This would be excessive in patients with chronic obstructive pulmonary disease).
2. A cycling rate of approximately 12 to 15 times per minute.
3. An inspired oxygen concentration of FI_{O_2} of 100%.
4. Mechanical dead space may be added at this time if it is anticipated that such large tidal volumes will produce an abnormally low level of arterial carbon dioxide tension.
5. Sedation is often necessary especially at the outset of mechanical ventilation.
6. Arterial blood gases should be done after approximately 15 minutes of ventilation with these settings in order to determine the future needs and appropriate settings of the ventilator. Since the patient was started on 100% oxygen, the first set of blood gases will allow one to calculate the $A-aDO_2$ on 100% oxygen. This value can then be put into the following formula in order to calculate the minimal desired inspired oxygen concentration:

$$\text{Desired } FI_{O_2} = \frac{(A-aDO_2) + 100 \text{ mm Hg}}{P \text{ atmos.}} \times 100$$

In this fashion one determines the least amount of oxygen that will adequately saturate the patient's hemoglobin without running undue risk of pulmonary oxygen toxicity; one is using oxygen as a drug.

Next one must be prepared to look at certain parameters of the cardiovascular and respiratory systems to note the response to therapy. Among these observations are:

1. The electrocardiograph oscilloscope should be used in patients with arrhythmias, congestive heart failure, those critically ill or hemodynamically unstable.
2. Intra-arterial pressures may need to be measured when cuff pressures are unobtainable or unreliable.
3. Central venous pressure measurements are of value in determining the effective circulating blood volume and when myocardial efficiency is in question.
4. The FI_{O_2} should be measured at least daily or when altering oxygenation parameters.
5. The tidal volume, respiratory rate, and minute volume of ventilation should be measured while the patient is on the ventilator approximately every 1 to 4 hours.
6. When the patient is breathing spontaneously, the tidal volume, respiratory rate, and, in conscious patients, the vital capacity should be measured every 1 to 4 hours.
7. The $A-aDO_2$ on 100% oxygen should be measured at least daily or as necessary.
8. The VD/VT ratio—the dead space to tidal volume ratio—should be measured daily or as necessary.

What is the dead space to tidal volume ratio, and how is it measured? The VD/VT ratio is that percentage of tidal volume which is wasted in the total of the anatomic dead space and the alveolar dead space, that is, areas of lung parenchyma which are ventilated but not perfused, or at least ventilated in excess of the amount of perfusion present. This value in normal patients is 30%. The observation is performed by dividing the difference between alveolar and mixed expired carbon dioxide tensions by alveolar carbon dioxide tension.

$$VD/VT = \frac{(P_{ACO_2}) - (P_{\bar{E}CO_2})}{(P_{ACO_2})}$$

As the ratio increases, it means that the patient's ventilation/perfusion inequalities are increasing and that he is wasting more and more of each tidal volume in ventilating areas of the airway and lung which are not perfused and which therefore contribute nothing to the exchange of gas. As the VD/VT ratio increases, one must increase his minute ven-

tilation to higher and higher levels in order to maintain a normal carbon dioxide tension of 40 mm of mercury. At VD/VT ratios above 60%, the curve begins to rise in an exponential fashion, and above this level of dysfunction patients can no longer breathe enough volume to maintain normal carbon dioxide tensions, and respiratory acidosis begins to occur. The VD/VT ratio can be measured both on and off the ventilator, but measurements made while the patient is being ventilated tend to run slightly higher than those when he is breathing spontaneously, especially during high inspiratory flow rates.

Nursing routines are important for physicians to know and understand for one reason only. If the nurse is unaware of the problems attendant to the management of respiratory failure, no one other than the physician can make her knowledgeable in this respect. The physician must know what he wants in order to tell the nurse what to do and what not to do. I do not wish to under-emphasize the importance of intelligent physician care in the management of such patients; nonetheless, the successful treatment of respiratory failure is largely a nursing venture. If nursing care is less than optimal, patients are unlikely to survive regardless of the degree of sophistication and intelligence of their physicians.

The following nursing routines are therefore recommended:

1. The patient is *NEVER* left unattended. (This is virtually impossible except in an ICU setting.)
2. Sterile technique in airway care and suctioning is of utmost importance in order to prevent iatrogenic contamination and infection.
3. Endotracheal and tracheostomy tube cuffs should be pre-stretched or of the soft cuff design to avoid tracheal trauma.
4. Daily weights must be obtained and recorded.
5. Intake and output must be accurately recorded daily.
6. The arterial pressure, pulse rate, temperature, and central venous pressure are recorded at intervals.
7. The patient's position in bed should be changed hourly while he is awake or hourly around the clock if comatose.
8. Attention should be directed to the care of the skin of the dependent parts. Heels,

knees, and elbows should be padded if deemed appropriate.

9. Chest physiotherapy should be coordinated with position change, airway suctioning, and IPPB treatments, if utilized. The frequency of this is to be determined according to the severity of the disease.
10. All joints in comatose or paralyzed patients should be put through a passive full range of motion daily.
11. The color and approximate quantity of tracheal aspirate are recorded.
12. An extra sterile tracheostomy tube and cuff of the appropriate size are kept at the bedside at all times.
13. Water condensing in ventilatory tubing is drained each hour.
14. The humidifier is checked and refilled every 8 hours or more often if necessary. The volume of water required to do so is recorded. This is done in an aseptic fashion.
15. Oxygen lines and flow meters are checked hourly to be sure that they are properly connected and functioning as ordered.
16. The house officer is notified immediately in case of a change in the level of consciousness or the occurrence of tachycardia, hypotension, confusion, agitation, tarry stools, or arrhythmias.

Appropriate laboratory studies during the maintenance of artificial ventilation include:

1. A chest x-ray is taken initially, following airway placement or change, daily to every 3 days, frequency to be determined by the severity of the disease.
2. The hematocrit is determined daily.
3. All stools are examined for occult blood.
4. Electrolytes, BUN, creatinine, sugar, total protein, and albumin are measured initially and as necessary.
5. The white blood count and differential are determined initially and as necessary.
6. Tracheal aspirate obtained with sterile technique for Gram stain smear, culture, and sensitivities is accomplished initially and every 3 to 5 days as necessary.

The inability to maintain good nutrition is one of the primary problems faced by patients suffering from long-term respiratory failure. The average patient on intravenous maintenance fluids alone can maintain his own state of caloric need for only

approximately two days by means of glycogenolysis. After this the patient must utilize his own protein stores, thereby developing negative nitrogen balance. When the patient is taking nothing by mouth maintenance fluids should total 40 to 45 ml per kg per day of which one-third can be dextrose 5% in normal saline or dextrose 5% in lactated Ringer's solution, and the other two-thirds dextrose 5% in water. These figures must be adjusted upward for fever, for abnormal fluid loss, or in the presence of hypovolemia. They should be adjusted downward appropriately for patients in congestive heart failure, or those with limited renal function. Their content must be adjusted for electrolyte abnormalities. The average adult, when taking nothing by mouth, and on maintenance fluids only, should lose approximately $\frac{1}{2}$ kg per day. Intake and output and daily weights must be carefully observed to make sure that this weight loss is taking place. Patients who are alert and cooperative, who exhibit normal gastrointestinal integrity, and who have audible bowel sounds, can and should eat. Patients who are comatose or paralyzed but with normal gastrointestinal integrity should have a high protein, high carbohydrate diet per nasogastric tube or gastrostomy. Patients with compromised gastrointestinal integrity lasting more than one week should receive parenteral hyperalimentation. The serum albumin should be kept above 2.0 g%, preferably above 3.0 g% in order to avoid the complication of pulmonary extravascular fluid sequestration. Starving patients cannot effectively breathe indefinitely. Successful weaning from prolonged controlled ventilation requires positive nitrogen balance.

Prolonged ventilatory support is attended by various complications which need to be anticipated and prevented if at all possible. Included in this list are the following:

1. The lowest inspired oxygen concentration possible should be used in order to prevent the adverse effects of pulmonary oxygen toxicity.
2. Sterile airway care is the hallmark of the prevention of iatrogenic pulmonary infection.
3. Soft cuffs or intermittently deflated cuffs on endotracheal and tracheostomy tubes should be used in order to prevent damage to the tracheal mucosa.
4. Prophylactic antibiotics should not be given routinely. Antibiotics should not be used

merely in the presence of positive airway cultures, but reserved for those cases where actual pulmonary or other infection exists.

5. Diuretics and serum albumin should be used as necessary for the management of interstitial pulmonary edema.
6. Anemia is not well treated with oxygen. Anemia should be corrected by the administration of additional red cells.
7. Patients who are persistently hyperventilated and thus rendered hypocapnic tend to lose potassium in the urine, and if digitalized at the same time, tend to develop arrhythmias.
8. Hypotension occurring during artificial ventilation is often due to hypovolemia.
9. Patients in chronic respiratory failure with preexistent hypercapnia should not be vigorously hyperventilated, as this form of treatment may produce dangerous degrees of metabolic alkalosis.
10. In patients with the adult respiratory distress syndrome, fluids and crystalloids should be restricted.
11. In patients with large shunts and an alveolar-arterial oxygen tension gradient in excess of 500 mm of mercury, the use of positive end expiratory pressure (PEEP) should be considered.
12. When hyperventilation and PEEP fail to lower the alveolar-arterial oxygen tension gradient, oxygen consumption must be decreased by use of morphine, curare and/or hypothermia.
13. When administered through an artificial airway, all inspired gas must be warmed and humidified appropriately.
14. Following long periods of parenteral nutrition, the resumption of oral intake must be preceded by some attempt to determine that the patient is capable of swallowing without aspirating.
15. The appearance of sudden tachypnea, cyanosis, hypotension, or arrhythmia should lead to the suspected diagnosis of either pulmonary embolism or pneumothorax.

Getting a patient off a ventilator implies that he has survived his bout of respiratory failure and is approaching that point at which he no longer needs respiratory support. When ideally ventilated

and oxygenated on a ventilator, patients may indeed appear clinically well and yet be totally unable to maintain adequate spontaneous ventilation once the ventilator is discontinued. Some appraisal must therefore be made of the patient's ability to oxygenate, to eliminate carbon dioxide, and to mechanically move air in and out of his chest for an appropriate period of time in order to insure that he can breathe spontaneously. The attempt to discontinue mechanical ventilation without obtaining this information previously may result in an otherwise "unexpected cardiac arrest." The requirements for weaning include the following 8 points:

1. The etiology of the respiratory failure must be sufficiently reversed.
2. The alveolar-arterial oxygen tension gradient on 100% oxygen must be below 350 mm of mercury.
3. The dead space to tidal volume ratio must be below 0.6.
4. The tidal volume must be above 3 ml per kg.
5. The vital capacity must be above 8 to 10 ml per kg to commence the weaning process. It must be better than 15 to 20 ml per kg to complete the weaning process.
6. The patient must be in positive nitrogen balance if he has been in negative nitrogen balance for any longer than one week previously.
7. The spontaneous respiratory rate in adults must remain below 35 per minute.
8. The hematocrit must be at least above 30%, preferably 35%.

The technique in weaning may be one of several. The following technique has been successful for us. The patient must have met the requirements for weaning already delineated.

1. The patient is in the sitting or semi-sitting position.
2. The ventilator is disconnected.
3. With the tracheostomy or endotracheal tube cuff still inflated, the tidal volume, rate, minute ventilation, and vital capacity are measured and recorded.
4. The cuff is deflated and 100% oxygen is administered for a period of 5, 10, or 15 minutes depending upon how long one expects the patient to be able to breathe spontaneously and to do so adequately.
5. At the end of this time an arterial sample

- of blood is drawn to be analyzed for P_{O_2} , P_{CO_2} , and pH.
6. The artificial airway cuff is re-inflated, and the previously mentioned ventilatory functions are remeasured and recorded.
 7. The patient is then reconnected to the ventilator.
 8. On the basis of the blood gas analysis and the ventilation studies, one then determines the duration of subsequent spontaneous trials at ventilation and the appropriate inspired oxygen concentration to be used during those spontaneous trials.
 9. The patient should progress to continuous spontaneous ventilation for one entire day before the same is attempted during sleep at night.
 10. After 24 continuous hours of spontaneous ventilation with acceptable blood gases, acceptable ventilatory function, and the patient not being excessively tired, he can be considered weaned from the ventilator.
 11. A higher inspired oxygen concentration should be utilized when the patient is breathing spontaneously than that which is used on the ventilator during the weaning process.

12. Assisted ventilation may be substituted for controlled ventilation during the weaning process if considered necessary.

In closing, I would like to remind you that the experience of an episode of ventilatory failure with the vigorous and sometimes heroic treatment that is required for successful management, and the stresses that go along with a stay in an average intensive care unit, are poorly tolerated by most patients. In addition to intelligent and sophisticated medical care and dedicated nursing care, these patients need compassion and respect for the fact that they are human beings undergoing a period of extreme stress. They will not only survive but they will survive as much more grateful patients if we all can remember to treat them as individuals with a disease rather than as disease entities alone. With this in mind, I would commend to you the following admonition which, I think, is said as beautifully as it can be said: "From inability to let well alone; from too much zeal for the new and contempt for what is old; from putting knowledge before wisdom, science before art, and cleverness before common sense; from treating patients as cases, and from making the cure of the disease more grievous than the endurance of the same; Good Lord deliver us."

Complications of Mechanical Ventilation*

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With increasing utilization of mechanical ventilation during the past decade or so, complications related to its use have also increased. Ventilators are primarily indicated when acceptable safe levels of oxygenation and ventilation cannot be maintained by other means.

The goal of assisted mechanical ventilation should be to improve arterial oxygen, CO₂ tensions, and pH to acceptable safe levels compatible with life or normal functioning.

The following are the complications which may occur during assisted mechanical ventilation:

- 1) Reduced venous return and cardiac output.
- 2) Complications related to endotracheal tubes and tracheostomies.
- 3) Atelectasis.
- 4) Infection.
- 5) Oxygen toxicity.
- 6) Acid-base, fluid, and electrolyte disturbances.
- 7) Gastrointestinal problems.
- 8) Technical and mechanical problems.
- 9) Emotional stress.
- 10) Miscellaneous: cardiac arrhythmias, pulmonary emboli, pneumothorax, and so forth.

Reduced venous return and cardiac output are commonly observed in patients with significant volume depletion. It is important that blood pressure and urine output should be checked at regular intervals. A central venous pressure catheter may need to be inserted for proper fluid replacements. The two other common causes of decreased venous return are prolonged severe hy-

poxemia and impaired sympathetic nervous system activity.

Normal people can compensate for the decreased venous return by a reflex increase in venous tone and pressure provided: 1) mean airway pressure does not go above approximately 15 mm Hg, 2) effective blood volume is adequate, 3) sympathetic nervous system function is unimpaired. If any one or a combination of any of the above factors is not met, mechanical ventilation results in decreased cardiac output and lowering of arterial blood pressure.

Proper adjustments in ventilators to reduce the mean intrathoracic pressure may need to be performed to improve decreased venous return. In this respect, volume cycled respirators are probably advantageous over pressure cycled respirators.

Negative pressure during exhalation may occasionally be used to improve venous return to the heart. However, this is somewhat contraindicated in patients with chronic obstructive pulmonary disease. It may cause closure of airways leading to clinical or subclinical atelectasis.

The following complications are related to endotracheal intubation and tracheostomies:

- 1) Tube in right main bronchus which causes massive atelectasis of the left lung. If not recognized this usually causes rapid deterioration of pulmonary function.
- 2) Dislodgement, kinking of the tube, obstruction by secretions, laryngeal edema and damage, herniation of cuff over end of the tube.
- 3) Complications related to tracheostomy: bleeding, infection, necrosis, tracheal stenosis, erosion of vessels, obstruction, and tracheoesophageal fistula.

* Presented by Dr. Muren at the Symposium on Respiratory Failure, May 26, 1972, at Richmond, Virginia.

The incidence of atelectasis is increased especially in patients requiring prolonged assisted mechanical ventilation. The administration of high concentrations of O_2 in inspired air causes further increase in the incidence of atelectasis.

Adequate humidification of the inspired gas, chest physiotherapy, proper suction, and hydration are essential in prevention and treatment of atelectasis. Bronchoscopy should be performed if atelectasis does not improve with conservative measures.

Atelectasis may be first manifested by decreasing compliance and increased alveolar-arterial O_2 pressure gradient.

To prevent atelectasis, a proper breathing pattern to obtain optimum ventilation should be maintained. Intermittent sighing is also an important therapeutic measure to prevent atelectasis. Inflation hold and continuous positive pressure ventilation are additional steps that may be used in prevention and treatment of this problem.

As to O_2 toxicity, two factors are primarily responsible for O_2 toxicity in the lungs: 1) high O_2 tension in inspired air, 2) prolonged exposure to high inspired O_2 tension. Patients may be at risk of developing O_2 toxicity if they are given inspired air containing 50% or greater O_2 concentration for prolonged time. There seems to be an individual susceptibility. As a general rule, just enough O_2 concentration in the inspired air should be given to maintain a safe and adequate level of oxygen tension in the arterial blood for a given patient.

It should be noted that most pressure cycled ventilators administer higher O_2 concentrations than one may think. On the air dilute setting, these ventilators usually deliver somewhere between 60 to 95% O_2 in inspired air.

This is prevented by running the ventilator with compressed air and bleeding 1 to 3 L of O_2 into the system. By measuring inspired O_2 concentration, proper adjustments should be made to administer the desired O_2 concentrations in the inspired air.

Infection, especially with gram negative organisms, may be a dangerous problem. Nebulizers, humidifiers, and tubes with warm, humid inspired gases may be a source of a good culture media for many gram negative organisms.

The respiratory tubing should be changed at least once daily and sterilized before it is used again. No respirator should be used for another

patient unless proper sterilization techniques have been utilized.

Acid-base, fluid, and electrolyte disturbances: one of the common iatrogenic complications of assisted mechanical ventilation is post-hypercapnic metabolic alkalosis. This is observed in patients with chronic respiratory acidosis. As a result of rapid lowering of P_{CO_2} , pH may become alkalotic, since HCO_3 cannot be lowered significantly under these circumstances.

Severe alkalosis can cause confusion, convulsions, coma, and even death. To prevent this, arterial pH should be monitored, and increased P_{CO_2} should be reduced gradually in chronic hypercapnia.

Marked hyperventilation with severe respiratory alkalosis alone can cause tetani with symptoms and signs related to it. And again, arterial gas tensions and pH need to be monitored to prevent this problem.

Some patients on prolonged assisted mechanical ventilation may develop fluid retention and even pulmonary congestion and edema, primarily interstitial type.

Another complication of mechanical ventilation is the development of inappropriate ADH-like electrolyte abnormality in some patients. This appears to be related to stimulation of ADH through thoracic volume chemoreceptors by positive pressure breathing. Therefore, patients should be weighed and electrolytes should be checked repeatedly.

Gastrointestinal complications consist of acute gastrointestinal bleeding, acute gastric dilation, ileus, and chronic aspiration during assisted ventilation. The physician should always consider these problems, and if they occur, proper steps must be taken.

Technical and mechanical problems arise quite often. A physician or inhalation therapist should be prepared to cope with a respirator in case it becomes disconnected from the patient or malfunctions or in case the tube becomes obstructed. These complications can be disastrous for the patient within a few minutes. The ventilatory and O_2 requirements of these patients change quite often, so necessary adjustments must be made accordingly.

Emotional problems quite often arise from the inability to talk and communicate properly with people. Sincere understanding of the patient's problem and taking time to explain to the patient

what is being done is extremely important in stabilizing the patient's emotional status. In general, patients receiving intensive respiratory care have a tendency to develop many cardiopulmonary problems such as pulmonary emboli, cardiac arrhythmias, digitalis intoxication, and so forth. Other complications of assisted ventilation are pneumothorax and mediastinal emphysema, which may cause further deterioration of the pulmonary function; these must always be considered whenever pulmonary function of the patient becomes worse.

Lastly, weaning the patient from ventilation may be a problem. The following guidelines are somewhat useful in deciding when to start weaning a patient:

- 1) Tidal volume should approach 5 to 6 ml/kg and vital capacity exceeds 10 ml/kg.
- 2) Alveolar-arterial O₂ pressure gradient should be less than 300 mm Hg on 100% breathing.
- 3) The ratio between dead space and tidal volume (VD/VT) should be less than 50%.
- 4) Inspiratory negative pressure should be more than 20 cm H₂O negative pressure.

Weaning is in general complete when vital capacity reaches 20 ml/kg. It should be noted that many patients may require additional O₂ for some days or for weeks after weaning.

Proper humidification must be provided when the patient is off the ventilator. Frequent short periods of spontaneous ventilation, that is, five to ten minutes per hour, should be attempted. As the patient's tolerance increases, time off the respirator is frequently increased. Vital signs, general appearance of the patient, and arterial gas studies are examined during these periods. The patient should not be allowed to sleep without assisted ventilation until he has tolerated three to four hour periods of spontaneous breathing during the day.

During the weaning period, emotional support is extremely important. A patient who can communicate can get better emotional support. We insert a plastic tracheostomy tube which can be plugged to permit the patient to talk during the period of weaning. This has been very useful during this critical period.

In conclusion, it must be recognized that properly trained physicians, nurses, and inhalation therapists are necessary for the care of acutely and critically ill patients with major pulmonary problems, to prevent and treat complications. Team work is essential for the proper management of those patients who require assisted mechanical ventilation.

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Recognition of the Asthmatic Component of Respiratory Failure*

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Definitions. In this discussion we shall understand each other better if we define two important terms first. They are "respiratory failure" and "asthma." It is not too difficult to define respiratory failure. Asthma is much more of a problem. The word has been used since the time of Hippocrates; yet contemporary authors do not agree on what it means.

Respiratory Failure. The "50-50 rule" is easy to remember and very satisfactory. Respiratory failure is present when the arterial blood P_{O_2} is less than 50 mm Hg, or the P_{CO_2} is greater than 50 mm Hg.

Asthma. We shall consider definitions from two recent books and from the American Thoracic Society. Bates, Macklem, and Christie (1) insist that asthma "denotes a condition of usually intermittent episodes of bronchospasm, with symptom free periods, in a subject with a history or a family history of an allergic condition." They also recognize that some patients with chronic bronchitis develop such severe bronchospasm during exacerbations of infection that their symptoms appear similar to spasmodic asthma. This definition is too restrictive. Also, if we consider only patients with evidence of allergy or infection we shall seldom have a problem of recognizing asthma, and such patients rarely develop severe respiratory failure.

Dr. Swineford (4) has a very simple definition: "Asthma is a complex pulmonary syndrome characterized by wheezing." Many of us find this definition too broad in that it includes conditions with fixed or localized airway obstruction unresponsive to any treatment.

The American Thoracic Society's (2) definition has been widely accepted. "Asthma is a disease characterized by an increased responsiveness of the trachea and bronchi to various stimuli and manifested by a widespread narrowing of the airways that changes in severity either spontaneously or as a result of therapy." This is a more satisfactory definition because it recognizes that the difficulty is due to a generalized airway obstruction that may respond to treatment.

We cannot insist on strict adherence to any definition because we are considering the asthmatic component in respiratory failure. Few patients with pure asthma will develop dangerous respiratory failure. We are chiefly concerned with individuals who have one of the acute or chronic lung diseases but who also have an element of generalized reversible bronchial constriction. When there is an asthmatic component, if it is recognized early, treatment should prevent the development of respiratory failure. If it is recognized at any time, treatment should prevent the death of the patient.

Causes of Respiratory Failure. There are a number of diseases that may cause respiratory failure and may also be confused with or complicated by asthma. The common ones are: chronic bronchitis and emphysema, pulmonary fibrosis, pneumonia, infectious bronchitis, pulmonary edema, pulmonary embolism, carcinoma or other lung tumor, and foreign body in the bronchus. Whenever a physician is dealing with patients manifesting any of these conditions he should think of and look for evidences of asthma.

Recognition of Asthma. An asthmatic component is usually easily recognized if considered. The history, physical examination, chest roent-

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genogram, blood and sputum examination for eosinophils (3), and pulmonary function studies may be helpful.

The history is important. A story of hay fever, a family history of allergic disease, seasonal symptoms and previous relief from the use of epinephrine, isoproterenol, xanthine, or steroids suggest asthma.

The physical examination is often not helpful since wheezing is common in so many patients with airway obstruction. However, pale, moist, swollen nasal membranes and inspiratory wheezing suggest asthma.

Likewise, the chest roentgenogram is often not helpful. However, if the lungs look almost normal, the heart is of normal size and shape, and the signs of heart failure are missing, asthma becomes an important consideration.

The sputum and blood examination is of critical importance. Blood eosinophilia suggests asthma. Sputum eosinophilia is the single most important sign of asthma and is a strong indication that steroid treatment will lead to improvement. For proper study the sputum should be fresh. The physician should separate out strands of thick mucus or a bronchial cast, spread the material on a slide, and stain it with Hansel stain¹. Even small clumps in which most of the cells are eosinophils are significant. The higher the percentage of eosinophils the more likely that asthma is contributing to the symptoms.

In the presence of respiratory failure it is usually not possible to do ventilatory tests or diffusion studies. If there is a record of a recent good CO diffusion or a good response to isoproterenol, asthma deserves serious consideration. Blood gas measurements are essential for the proper management of any patient with respiratory failure.

Treatment. If respiratory failure is of short duration and if there is an asthmatic component treatment with isoproterenol by nebulizer, subcutaneous epinephrine or IV, aminophylline may be effective. All of these drugs may contribute to ventricular irregularity and should be used cautiously in patients with coronary artery disease.

In most patients steroids will be needed and effective. Prednisolone or prednisone is commonly used. If a patient with respiratory failure has used steroids in the past, if there is convincing evidence that asthma is present, if he is obese, if the asthma began in middle life or later, or if the arterial blood P_{O_2} is falling or the P_{CO_2} is rising in spite of treatment, steroid treatment should be started promptly and used aggressively (5). The ideal dose is not known. Fifty to 100 mg of prednisone or prednisolone every two hours until improvement begins is a reasonable dose. In respiratory failure due to asthma the presence of tuberculosis or other infection, diabetes, heart failure, or hypertension do not contraindicate the use of steroids. Other forms of treatment such as the use of assisted ventilation, antibiotics, or treatment of heart failure should be used as needed.

Summary. Respiratory failure from various causes is occasionally associated with or confused with asthma. Therefore, asthma should be considered and looked for in all patients with respiratory failure. Sputum eosinophilia when present is the most important indication that asthma may be important. Steroids used early and aggressively are usually indicated and effective.

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Management of Severe Asthma*

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In this summary of therapy for severe asthma there is no mention of etiologic factors. The author presumes that if infection is the primary factor in the progression to severe asthma that this will be recognized and appropriately treated. A chest x-ray must be an initial laboratory study for the recognition of pneumonia or complicating pneumothorax. However, unlike respiratory failure due to emphysema, here the specific therapy of the altered pulmonary physiology is of paramount importance. Attention to the inciting factors is of minimal therapeutic benefit once infection can be ruled out. After the patient can breathe comfortably again the role of allergy can be investigated. Premature investigation of emotional factors can be a lethal therapeutic error in the ill asthmatic.

The treatment of asthma at the University of Virginia Hospital can be divided into three rather specific periods (Table 1).

Mystery Period. Until 1962 arterial blood gas and pH measurement were not routinely available as a clinical tool in our laboratories. Most patients with severe asthma did well with our routine management. Other patients who looked the same might die suddenly with no major change in their clinical course. The mystery revolved around our inability to judge precisely who had life threatening asthma and who did not.

Measurement and Aggression 1962-1968. (Table 2). As soon as arterial puncture became a routine procedure the mystery cleared somewhat. Many patients with severe asthma were found to our surprise to have severe hypoxemia and hypercarbia. It is presumed that the prior mystery deaths were most likely due to respiratory failure with CO₂ narcosis or hypoxemia-induced fatal ar-

rhythmias. These patients were recognized usually late in their disease. Immediate tracheostomy was done; many were hyperventilated with a volume controlled ventilator into frightening states of alkalosis, and the hospitalization was prolonged for two to three weeks. The patients did not die from asthma, however, and survived their respiratory care (3).

Measurement and Intensive Care. Employing the lessons learned from our middle period, since 1968 our management of severe asthma has changed (Table 3). In the period 1965-1967, 10 patients with severe asthma were ventilated following tracheostomy and all survived. From 1968 to 1971 there were 299 admissions of asthmatics to the University of Virginia Hospital. Of these patients, 50 were judged to be in status asthma, and 36 had a P_{CO₂} greater than 45 mm Hg. Despite the serious nature of their disease, only 8 patients were intubated, 6 were briefly ventilated, and only 1 patient needed a tracheostomy. No deaths occurred (4).

Common Errors in Management. (Table 4). A review of patients previously reported with tracheostomy and our current series since 1968 revealed the same errors in management with the difference being one of degree.

Steroids. In the prior series, two patients received no steroids at all prior to tracheostomy. In our current patient group, several who were intubated received steroids late in their clinical course and in small amounts.

Sedation. The use of sedation continues to be an identifiable factor probably responsible for the deterioration and intubation in at least half of the patients intubated since 1968. Valium® and other tranquilizers are replacing the barbiturates as major offenders. Sedatives have no place in the management of severe asthma.

* Presented by Dr. Hunt at the Symposium on Respiratory Failure, May 26, 1972, at Richmond, Virginia.

TABLE 1.
MANAGEMENT OF SEVERE ASTHMA
University of Virginia Hospital

Mystery Period—Until 1962
Measurement and Aggression 1962–1968
Measurement and Intensive Care 1968–Present

Oxygen. The indiscriminate use of high flow oxygen is not as devastating to the asthmatic in acute respiratory failure as to the patient with chronic bronchitis and emphysema. An attempt should be made to keep the arterial oxygen in the physiologic range (70–110 mm Hg) which generally means the use of no more than 28–35% oxygen.

Nursing Position. Classically, the patient with asthma is immediately put flat in bed, and, to make sure he stays there, intravenous fluids are begun apparently to facilitate rapid drug administration. Like the patient with emphysema, the asthmatic is much more comfortable breathing in a chair. IV fluids should be replaced with oral medication usually within 24–48 hours except in unusual circumstances. This can be of immense psychological benefit as well as prevent painful phlebitis.

Tracheostomy. From our current experience and that of others (2), tracheostomy should rarely be necessary in the management of asthma. The morbidity associated with the procedure itself and the prolongation of hospital care, coupled with the short clinical course of aggressively treated asthma, all make nasotracheal tube intubation the procedure of choice when respiratory failure supervenes.

Patients at Risk. Who are the patients who are in the most danger of progression to respiratory failure? The same group (Table 5) appears in every series.

TABLE 2.
MEASUREMENT AND AGGRESSION 1962–1968

Arterial Gas Measurements Begun in 1962
Usually Obtained Late in Course
Serious Nature of Disease Recognized
Usually Immediate Tracheostomy
Frequently Hyperventilated
Two to Three Week Hospitalization

TABLE 3.
MEASUREMENT AND INTENSIVE CARE 1968–PRESENT

Arterial Gas Measurement Early in Suspicious Cases
Review of Prior Medication Imperative
Uncomplicated Asthma—Low P_{O_2} —Low P_{CO_2}
Severe Asthma—Normal P_{CO_2} , a Grave Prognostic Sign

How to Evaluate Severity of Asthma.

Prior Medications. A patient who is in marked respiratory distress with asthma, and who has taken only a few tablets in the prior 24 hours, is in a different prognostic category than the patient with the same degree of airway obstruction who has tried Tedral[®], aminophylline suppositories, and 20 mg of prednisone two hours before. An assessment of prior therapy then enables you to plan current therapy and escalate from theophylline, ephedrine and adrenaline, to high dose steroid therapy and hopefully avoid respiratory failure and intubation.

Arterial Blood Gases. The major initial defect in asthma is hypoxemia, as large areas of the lung that have excellent perfusion get progressively less ventilation, shunting poorly oxygenated blood into the arterial circulation. Initially, the asthmatic in respiratory distress can easily overventilate the uninvolved areas of the lung lowering arterial CO_2 (P_{aCO_2}). The classical arterial gases of the dyspneic, but non-fatigued asthmatic, are a low P_{aO_2} (50–60 mm Hg) and a low P_{aCO_2} (20–30 mm Hg). As the patient tires, is sedated, gets worse, and is restrained in bed, he will begin to move less air, and underventilation will begin with the P_{aCO_2} approaching normal. This is a *grave* prognostic sign.

If the arterial oxygen rises as the P_{CO_2} rises and the patient is more comfortable, all is well. If the arterial oxygen falls and the P_{CO_2} approaches normal, you should immediately escalate your therapy (Table 6).

TABLE 4.
COMMON ERRORS IN MANAGEMENT

Too Little Steroids Too Late
Sedation
High Flow Oxygen
Patient Put in Bed
Tracheostomy

TABLE 5.
PATIENTS AT RISK

Tired
Old
Fat
Chronic Bronchitis and Emphysema
Heart Disease

Escalation of Drug Therapy.

Combination Tablets and Isuprel®. Most patients with asthma who present to the physician with a severe episode have already tried regular therapy with one of the phenobarbital, theophylline, or ephedrine combinations such as Tedral® or Quadrinal®. They have generally used, and at times have overused, an Isuprel® preparation. These drugs then have little place in the management of the severe asthmatic. It is important, however, to obtain specific historical facts about their use in planning therapy. A patient who has had little or no prior medication can be expected to respond more rapidly to less medication.

One investigator has found that patients with severe asthma are specifically unresponsive to Isuprel®, so that response to Isuprel® was a measure not only of the severity of the disease, but also an index of the patient's response to other therapy, primarily steroids. More and more Isuprel® is then used by the worsening patient with less and less results. At times the Isuprel® has been shown to have been responsible for increasing the asthma and may actually cause hypoxemia.

Epinephrine and Aminophyllin. The response to 0.3 cc of epinephrine subcutaneously can at times be magical and should always be tried. The effect occurs within minutes and may last an hour. If no results are obtained after three doses

repeated at 15 minute intervals, a response will usually not be obtained. The response to IV aminophyllin may be equally as rapid and last for hours, frequently as long as six. The dose must be large—500 mg for an adult—and must be given over 15–45 minutes, not over hours in a large bottle of fluids. Two methods are equally acceptable:

1. 500 mg (a 20 cc ampule) given intravenously by syringe, over a 10 minute period. This is excellent if you have the time.
2. 500 mg in 250 cc glucose and water given by IV drip over a 30–60 minute period may be equally effective.

Decisions. Only the consultant the next morning has the benefit of the clearly outlined flow sheet documenting blood gases, clinical state, and time of the therapeutic maneuvers. In actual practice, the patient arrives in respiratory distress, arterial gases are obtained, and the above medications are given—epinephrine X2 followed by 500 mg of IV aminophyllin. This takes approximately one or one and one-half hours. The initial blood gases become known to the physician about half way through this therapy. He usually waits until 15–20 minutes after the aminophyllin is given and repeats the arterial gases and pH.

Initial Gases. If the P_{aCO_2} is below 50 mm Hg, supplemental oxygen is begun (24 or 28% ventimask). If the P_{aCO_2} is greater than 40 mm Hg and the patient has not obtained evident clinical improvement from his initial therapy, 250 mg of hydrocortisone is given intravenously in addition to the other drugs previously described.

Second Arterial Gases. These results have usually been obtained at a time when full therapeutic benefits will have occurred from epinephrine and aminophyllin therapy. A lack of clinical response by the patient and a lack of significant reduction in P_{aCO_2} , dictates that *aggressive steroid therapy should be begun*. If the P_{aCO_2} has dropped into the 30 mm Hg range, therapy with aminophyllin and epinephrine can be continued and a maintenance drug such as Tedral® SA begun at an appropriate time.

Steroid Therapy.

General Considerations. There is no reason to give hydrocortisone except for the initial dosage. There is theoretical evidence that the therapeutic effect of hydrocortisone should be more rapid

TABLE 6.
BOTH STATES MAY BE ASSOCIATED WITH REDUCTION
IN WHEEZING AND A QUIET PATIENT

P_{O_2} —60	→	P_{O_2} —50	WORRY! ACT!
P_{CO_2} —30		P_{CO_2} —40	
pH—7.48		pH—7.4	
↓			
P_{O_2} —70			
P_{CO_2} —40			
pH—7.40			REJOICE!

than prednisolone, but there is little data. I am in agreement with Sheehy *et al.* that airway resistance is reduced by steroids "in several hours" (4). This has been shown to be true by the studies of Pinkerton and Van Meter (1).

This brings up the practical consideration that by the time one decides to escalate to steroid therapy one must wait one to two hours for therapeutic effect. One must then give steroids *one or two hours before they are needed*. This is why 250 mg of hydrocortisone is given if the initial gases indicate even slight CO₂ retention instead of awaiting the second set two hours later. Pinkerton and Van Meter (1) could show little difference in the dose response curves of oral and IV steroids. However, in a seriously ill patient who may vomit, the intravenous method is preferable.

Dosage Schedule. As long as the patient is in respiratory distress and the PaCO₂ is 44 mm Hg or above, prednisolone 50 mg should be given every two hours. If the PaCO₂ continues to rise, the dosage should be increased to 100 mg every one to two hours.

Pediatric Dosage. In severe asthma (as defined under "Initial Gases") 7 mg/kg of hydrocortisone should be given as an initial stat dose. Another 7 mg/kg of hydrocortisone may be given during the next 24 hours in divided doses. As is true in adults, there is little specific data to direct prednisone therapy in children within narrow dosage guidelines.

Mucolytic Agents. Hydration with appropriate intravenous fluids and aggressive therapy of asthma are the only two mucolytic techniques of proven benefit. Glyceryl guacolate (Robitussin®) is of proven uselessness and acetylcysteine (Mucomyst®) will provoke asthma. Humidified air can be added to the ventimask if the patient is a mouth breather, but humidity and heat are usually no problem as long as the nose is still in the circuit.

Intubation and Ventilation.

Indications for Intubation. A rising PaCO₂, above 60 mm Hg, a pH below 7.2, increasing fatigue, increasing somnolence with inability to cough despite the therapy as outlined above are indications for intubation and ventilation.

General Considerations. The use of the cuffed nasotracheal tube has revolutionized the respiratory care of severe asthma. Only in unusual circumstances should tracheostomy have to be done

for asthma. Once nasotracheal intubation is accomplished and the patient is being artificially ventilated, *aggressive therapy must be continued*. Unlike the patient with chronic bronchitis and emphysema, the patient with asthma responds quickly and fairly predictably to therapy (primarily corticosteroids) and can be weaned from the ventilator in 24 to 72 hours. The unfortunate tendency is for the physician to relax following intubation of the patient. Unless the appropriate therapy is continued, weaning from the ventilator can be prolonged by a relapse which increases the possibility that tracheostomy will need to be done.

Plan of Action. The physician should presume that with appropriate therapy and barring serious complications, the patient can be extubated within 48 hours. The first twelve hours that the patient is on the ventilator should *not* be complicated by premature weaning procedures. The fatigued patient should be allowed to rest. His ability to cycle with the ventilator should be enhanced with diazepam (Valium®) or if this is not immediately effective, with 5 to 10 mg of intravenous morphine (given every one to four hours as needed). Obviously the patient cannot be simultaneously sedated for control of ventilation and weaned from the ventilator, although this is frequently tried with disastrous results. Prednisone 100 mg every two hours should be continued during this most important phase of therapy.

Choice of Ventilator. The tendency of a nasotracheal tube to leak, coupled with the extremely high airway pressures (30–60 cm H₂O) necessary to ventilate asthmatics, makes pressure cycled ventilators (Bird or Bennett) poor choices. A volume controlled ventilator such as the Bennett MA-1 or the Emerson postoperative ventilator is usually necessary for effective ventilation of these noncompliant lungs. The MA-1 enables the respiratory care personnel to easily monitor tidal volumes and oxygen percentage of inspired air (FI_{O₂}). Both machines will intermittently and automatically hyperinflate the patient's lungs to reduce atelectasis. Both are dependable machines.

Complications. All of the legion of complications incident to intubation and mechanical ventilation of course can occur. The excellent prognosis for return to normal in these patients should make their recognition and reversal all the more important. Several complications however are more peculiar to the asthmatic.

Pneumothorax. In the pediatric patient, the

extremely high airway pressures needed for ventilation make this a common complication. Insertion of a chest tube with adequate seal is imperative to prevent a tension pneumothorax. This is a rare complication in adults.

Overventilation with Alkalosis. The very nature of the disease makes this complication potentially common and severe. The patient with severe, reversible airway obstruction is connected to an efficient ventilator, and aggressive appropriate therapy is given. Success in therapy will almost always result in hyperventilation, unless blood gases are monitored frequently as the patient improves and the minute ventilation reduced.

Cardiovascular Collapse as Mechanical Ventilation is Begun. This is more common in the patient with emphysema since the high airway pressures are transmitted more readily to the heart through abnormal lung tissue hindering right heart filling. The asthmatic has some protection due to the normal lung parenchyma. However, the combination of high inspiratory airway pressures, hypovolemia, and a short expiration time may rapidly reduce cardiac output even in the asthmatic. The physician must prolong expiration as much as possible relative to inspiratory time, reduce tidal volumes even if CO_2 cannot be lowered initially, and immediately correct the hypovolemic state.

Weaning. Improvement can be judged by a return of the Pa_{CO_2} to normal (30–40 mm Hg) and a reduction in the percentage of oxygen necessary to maintain Pa_{O_2} within a physiologic range (70–100 mm Hg). Reduction in airway obstruction can be monitored by following the “effective compliance” (tidal volume divided by airway pressure expressed as liters/cm H_2O).

If at the end of 12 hours, blood gases and pH are normal and the effective compliance has doubled, sedation should be discontinued and the patient's ventilatory capabilities measured, using a Wright Respirometer. If it can be determined that the tidal volume is greater than 5 cc/kg and the vital capacity greater than 10 cc/kg, a period of time off the ventilator should be monitored with blood gas measurements (arterial puncture 15–30 minutes off ventilator with patient receiving humidified 28–30% O_2 by means of a Briggs T-piece). If the patient is able to maintain a normal or reduced Pa_{CO_2} , extubation should be considered. Alternately this procedure

is repeated every 12 hours or at even shorter intervals depending upon the observed rate of improvement.

Preparing for Discharge. The exciting part of the therapy is now over, and the tendency toward management errors increases. If the reason for the onset of the severe episode of asthma is known and has been corrected (infection, exposure to irritant fumes, resolved psychic trauma) then the steroid dosage can be quickly reduced to 100–200 mg of prednisone given as a single daily dose, then every other day, and finally discharge of the patient on 10 or 20 mg of prednisone every other day. If the cause of the asthma remains unknown, caution will have to be exercised in the rapid reduction of steroids.

Two major facts should be borne in mind: 1) Even large amounts of prednisone (50–100 mg) given as a single early morning dose may be taken by the patient for up to 30 days without significant adrenal suppression. 2) Alternate day prednisone therapy, again a single early morning dose, can be given with little danger of side effects and may be continued for months.

Summary. The successful management of severe asthma involves recognition and aggressive appropriate therapy, with rapid escalation to steroid therapy as soon as indicated. Intubation with a nasotracheal tube and ventilation with a volume controlled mechanical ventilator should be an available option in therapy. Tracheostomy need rarely be done since most patients can be extubated within 72 hours.

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Ambulatory Care for Emphysema and Chronic Bronchitis*

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The immense problem of chronic airway obstruction (CAO)—emphysema and chronic bronchitis—which has now reached epidemic proportions, presents to the practitioner of medicine an increasing number of suffering persons asking for care. These patients are dyspneic, anxious, bewildered by their predicament, sometimes demanding and frightened about prospects for future comfortable life.

Although there has been a tremendous upsurge of interest in the field of respiratory care, and a growing number of nebulizers, humidifiers, physical therapy techniques and drugs, all of the answers on emphysema care are not in. We must admit as physicians that although we are absolutely sure that we save many lives in the organized intensive respiratory care unit in the case of acute respiratory failure (3, 13), no study has thus far convinced the critics of respiratory care that the natural course of CAO is altered from the standpoint of survival. Nonetheless, today's patients cannot wait for all the answers. They flock to hospitals, clinics, and physicians' offices, seeking some relief of their symptoms, some hope for improvement in their status and for prolonged survival. It is therefore mandatory for all physicians interested in chest medicine and interested in their sick patients, to provide some form of service for

the growing crowd of puffers and coughers—both pink and blue.

This communication defines a practical clinic and outpatient treatment regimen that is applicable for most individuals suffering severe CAO with disability.

Ambulatory Care Program.

Patient Education. The management of any chronic disease must be based upon a high level of patient indoctrination and education. This has been the reason for success in large measures in diabetes mellitus management where for years, the sufferer has been instructed in nutrition, activity, insulin dosage, self-management, evaluation of glycosuria and proper clothing, leading to the development of an adjustment to the burdens of disease designed for a maximum of serenity in daily life. It does not take a great deal of talent, although it does take time, to describe the airways, the lungs, the circulation and to explain what is wrong in the emphysema-chronic bronchitis spectrum. The office nurse or clinic nurse, once properly trained herself, is a superb individual to assume the responsibility for this task. Patients receive an in-depth discussion of general care with reinforcement in specific instructions guided by the physician's explicit prescription. These sessions are supplemented by a simple treatment manual (17) designed to give the patient material for serious reading which will reinforce the personal instruction and probably develop new questions for the nurses on revisits. We not only teach the patients about their disease process, but what physicians, nurses, and therapists are trying to do in their therapeutic endeavors. We stress the specific facets in man-

* Presented by Dr. Petty at the Symposium on Respiratory Failure, May 26, 1972, at Richmond, Virginia. Reprinted with permission from *Chest*, Volume 58, pp. 441-448, October, 1970. Supported in part by USPHS Contract #108-66-227, Chronic Respiratory Diseases Control Program. Reprint requests to Thomas L. Petty, M.D., 4200 East Ninth Avenue, Denver, Colorado 80220.

agement listed below with details stressed for each individual patient.

Bronchial Hygiene. Much of therapy must be directed at the bronchial element of disease. In many cases we are dealing with the bronchospasm, mucosal edema, retained secretions, and impaired mucociliary clearance. Each patient must learn an effective method of bronchial hygiene to be used each day. Fundamental, of course, is the absolute cessation of smoking. This is best handled in a nursing session where the threat of a physician and his authority is less traumatic to the patient.

In specific therapy, individuals are taught to inhale a bronchodilator aerosol followed by moisture, followed by expulsive coughing on a systematic basis at least twice daily. One of the sympathomimetic amines is inhaled for a period of at least ten deep breaths and a duration of, at times, up to ten minutes. Isoetharine with phenylephrine or racemic epinephrine or isoproterenol is used for this purpose. Aerosolized bronchodilators are delivered by a variety of devices, including a simple hand bulb nebulizer which does require some patient coordination and strength, the newly available pump driven nebulizers¹ or simple hand held IPPB devices which have recently been provided for the practitioner² (fig. 1). Ordinarily the drug is diluted with equal amounts of water with individual adjustments based upon side effects and apparent clinical efficacy. Bronchodilators relieve muscular spasm, combat mucosal edema, and probably stimulate mucociliary clearance (8, 10). The use of bronchodilator drugs must become an art with final judgment on the absolute details of therapy, a joint effort between patient and physician, a matter which obviously requires a great trust and orientation on the part of both.

Following the bronchodilator administration, inhaled moisture is the next step. This may be done by simple steaming devices, that is, a nursery humidifier, tea kettle, facial sauna and in some cases a more advanced nebulizer including an ultrasonic nebulizer. The choice of device is a matter of judgment based upon the ability to thin and raise secretions. It should be said and emphasized that general hydration in the form of adequate water intake is fundamental in maintaining ade-



Fig. 1—Hand held IPPB device suitable for hospital or home use. It is used in the home with compressor pump and has pressure flow characteristics similar to conventional ventilators.

quate mucociliary clearance. The purpose of the moisture, of course, is to help thin secretions, which also facilitates mucociliary clearance. After approximately ten minutes of moisture inhalation, expulsive forceful coughing helps clear retained secretions. If these endeavors are insufficient, simple postural drainage techniques over pillows in bed often help the situation (18, 19). At times pummeling, or so-called clapping, is useful in removing secretions (fig. 2). This is usually taught the spouse by the physical therapist.



Fig. 2—Technique of percussion taught by physiotherapist. This often aids mucociliary clearance.

¹ Maxi-Myst pump driven nebulizer, Mead Johnson Co., Evansville, Indiana.

² Hand-E-Vent, Ohio Medical Products, Madison, Wisconsin.

Breathing retraining stressing abdominal-diaphragmatic control, allowing the abdomen to protrude during inspiration, followed by forceful abdominal contractions during expiration, probably helps empty the lung and improves the efficiency of breathing (1, 2, 11). These maneuvers with exhalation against pursed lips, have been learned by many individuals who suffer dyspnea and who learn that this is a means of relief of symptoms. In a clinical study the pursed-lip maneuver has been shown to reduce the oxygen ventilation equivalent, reduce alveolar-arterial oxygen difference and the necessary minute ventilation for a given level of arterial oxygen tension (12). Therefore the pursed-lip breathing maneuver enhances oxygen transport or at least is a more efficient breathing technique. This should be taught to all patients or at least tried in patients who are well indoctrinated in modern methods of emphysema care.

Physical reconditioning in the form of simple daily exercises with increasing goals from the standpoint of more activity, has been shown to greatly improve exercise ability (6, 22). Most patients can be taught to participate in comfortable exercise on an increasing basis in spite of the fact that their level of chronic airway obstruction may not change a great deal in response to therapy (20). Nonetheless, this training is an important activity for it provides increased facility for daily living. Most patients with chronic airway obstruction find dyspnea on exertion their most disabling symptom and any improvement in comfortable mobility can be translated into a better life. Figure 3 demonstrates the measured improved walk tolerance at various rates and grades for an individual trained daily for the first week and every other day for the second week as part of a rehabilitation program. No measurable change in ventilatory function or blood gases (arterial) were observed during this brief training period³.

Oxygen. The clinical benefit of ambulatory oxygen therapy has been repeatedly demonstrated (9, 15). In brief, oxygen is valuable for the hypoxemic bronchitic person who is markedly disabled and suffers from heart failure. Oxygen has been shown to reduce the level of pulmonary hypertension by reducing pulmonary arteriolar resistance and also helps combat the secondary poly-

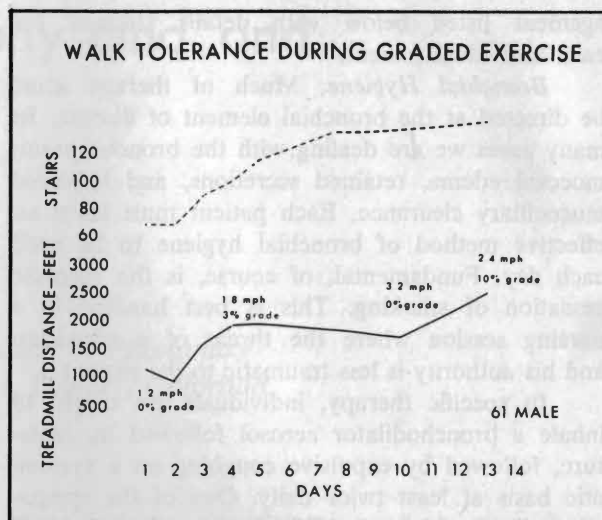


Fig. 3—Improved walk tolerance at increasing rate and grade following daily training for two weeks.

cythemia of the bronchitic hypoxemic state (9). The development of a home based portable oxygen system has made the use of continuous ambulatory oxygen a reality. Figures 4 and 5 demonstrate the apparatus in common use today. The lower canister contains a liquid oxygen supply which usually suffices for three to four days. This canister is capable of filling a smaller device which now provides three to six hours of oxygen therapy. The duration is a function of rate of oxygen administration controlled by a flow rate mechanism on the device. Ambulatory oxygen provides for additional mobility. Experience with these devices for over four years has proved the efficacy and safety in over 200 patients with profound hypoxemia who cannot gain mobility by any other means.

Pharmacologic Therapy. The weight of current evidence suggests that the immediate use of antibiotics for specific episodes of bronchitis manifested by increasing cough, leukocytosis, elevated temperature, and purulent appearing sputum is effective in reducing the duration of symptoms and fever. Since the most common invading bacterial organisms after the original insult, which may be viral, appear to be *D. pneumonia* and *H. influenza*, the rather empiric use of ampicillin or tetracycline seems advisable. Ampicillin is usually given in doses of 4 g daily the first two days followed by 2 g daily for three or four days. Tetracycline is usually given in 2 g doses daily the first two days

³ MVV 31 L; FEV₁ 0.91 L.



Fig. 4—Linde oxygen walker system. Lower container has approximately 3½ days oxygen supply. This can be used directly or used to fill the 7.5 pound canister which the patient uses for ambulatory oxygen therapy.

followed by 1 g daily for the duration of therapy, which usually covers five to seven days. Many patients with CAO are provided with a supply of antibiotics for home use to be instituted at first signs of a deep chest infection. It is also wise, however, from the standpoint of communication and further advice, to have these individuals contact their physician at the time of institution of these drugs.

Digitalis and diuretic drugs are useful in the management of cor pulmonale with heart failure. These drugs, however, are fraught with the difficulty of arrhythmia, but the weight of evidence in recent years indicates that an improved hemodynamic state can be achieved with digitalizing doses of cardiac glycosides along with the use of diuretics if adequate correction of hypoxemia is employed to provide adequate oxygenation of the myocardium and to control the reactive pul-



Fig. 5—Patient carrying Linde oxygen walker system. Depending upon flow, three to five hours supply is available.

monary hypertension associated with the hypoxic state (15).

The corticosteroid drugs are definitely useful in some patients with chronic airway obstruction. Indications for their use include the bronchitic patient with marked cough, expectoration, and repeated bouts of wheezing or choking spells superimposed upon the chronic symptom complex. Often these individuals have significant changes in their expiratory flow parameters as they are observed serially. Generally, prednisone 30 mg daily for the first five days, followed by a dose of 15 mg daily for the next five days, followed by a low maintenance dose of 5 to 10 mg, with decisions for further therapy guided by measurements of expiratory flow in the form of forced expiratory volume in one second (FEV₁) or maximum mid-expiratory flow (MMEF). A certain number of patients with apparent chronic irreversible airway obstruction actually have a reversible component of disease if observed carefully under steroid therapy (14).

Oral bronchodilators may be useful in an occasional patient. The only harm of the ephedrine-containing drugs aminophylline, amytal, and ephedrine HCl (Amesec®), theophylline, phenobarbital, ephedrine HCl (Tedral®), and so forth, is occasional urinary tract obstruction. Although

these drugs are not very effective, they are frequently used by patients for reasons good or bad. Soluble xanthines in the form of oxtriphylline (Brondecon®) or choline theophyllinate (Chole-dyl®) may also prove useful in some patients.

The expectorants such as saturated solution potassium iodide and guaiacolate have not been proved by critical study to be effective in patients within this spectrum. Nonetheless, they may be used for apparent symptomatic benefit for short periods but should not be an agent of prolonged use. Polyvalent influenza vaccine should be given each fall for whatever protection is afforded.

Occupational Therapy, Hobbies, and Change of Life Style. If life is to be worthwhile for the emphysema-bronchitis patient, it has to have meaning. The details of therapy enumerated above should not be excessively demanding from the standpoint of time and should be applied in a systematic manner to allow patients to lead a happy and hopefully productive life. A number of patients can be returned to work. Return to work, of course, has to do with many factors and is basically based upon the energy requirement of the job, the patient's physiologic resources, and the patient's personal motivation to maintain a gainful status (16). Certainly the provision of ambulatory oxygen therapy is a great aid for some patients (15, 16). Additional oxygen provides for additional activity and improvement in work capacity while on the job.

For those not so fortunate, occupational therapy in the form of hobbies is tremendously important. Many patients have a longing or desire to paint, write, garden, golf, or simply walk around a bit. This should be encouraged by the total application of the program described above.

Effectiveness of Today's Ambulatory Care Program. Although this is difficult to assess with cool scientific certainty, because no clinical care program ever is totally controlled, a number of statements can be made based upon contemporary knowledge about the effectiveness of organized care for CAO.

Symptomatic Improvement. Most patients seek medical care because of adverse symptoms. There is no question that the development of comprehensive care programs has greatly improved the patients subjective feeling of well being. For example, Table 1 shows the patients' clinical assessment at one and two years following entry into the comprehensive rehabilitation program

TABLE 1.

SUBJECTIVE ANALYSIS OF SYMPTOMS

	One Year	%	Two Years	%
Worse	17	13	18	21
Same	36	28	27	32
Better	76	59	39	47

which has been described in this report. The vast majority of patients remain clinically better or at least the same up to two years and in many cases longer.

The application of care principles described above can be assessed by a reduction in hospital needs. A small group of patients requiring hospitalization for respiratory causes was selected, and the need for hospitalization following entry into a comprehensive care program was compared to the patients' prior hospital needs. In brief, Table 2 shows that the total number of patients requiring hospitalizations was reduced, the total number of hospital days was reduced, and the average stay per patient reduced over a one year period compared to the patient's previous performance. It must be admitted that the clinic and outpatient nature of the program emphasized independent existence in order to minimize hospital needs. This makes absolutely no difference, however, and the facts speak for themselves, that is, 326 hospital days saved in this small group of patients. One has only to multiply the number of hospital days saved by the average cost of hospitalization today to gain a quick assessment of a tangible economic saving provided by ambulatory care methods.

Return to work in an aging population is not common (16). Nonetheless, certain individuals

TABLE 2.

REDUCTION IN HOSPITAL DAYS DURING FIRST YEAR OF PROGRAM COMPARED WITH PREVIOUS YEAR*

	Year Before Entry	First Year of Program
Total hospital days	868	542
Number of patients hospitalized (from group)	34	25
Average hospitalized patients	25.5 ± 39.8	21.7 ± 30.2

* Previously reported (20).

can return to gainful employment and, in some, this may represent a striking improvement over past performance. Most individuals who can return to work or at least maintain their level of gainful employment are rewarded by a continued sense of pride over their productive state.

Physiologic Changes. One hundred and eighty-two patients were evaluated for CAO and entered into the comprehensive care program which is re-

ported here. They were selected on the basis of having irreversible airway obstruction with *expected* pulmonary function deterioration with age (4, 5, 6, 7, 9, 11, 12, 14, 15, 16, 20, 21, 22). The overall physiologic changes in our series suggest that the expected pulmonary function deterioration is retarded. For example, patients at risk for one and two years are the subjects of Tables 3 and 4⁴. It

⁴ Symbols explained in Tables 3 and 4.

TABLE 3.
COMPARISONS: PRELIMINARY VERSUS ONE YEAR

	Preliminary			One Year		
	Mean	SD	No.	Mean	SD	P
VC	2.66	.80	120	2.63	.81	
FEV ₁	1.00	.39	120	.95	.49	
MMF	.44	.23	120	.41	.31	
MVV	38.5	51.1	118	37.3	19.4	
All Patients						
pH	7.40	.04	109	7.40	.04	
P _{CO₂}	40.2	8.3	108	43.6	11.7	.0002
P _{O₂}	57.2	8.2	95	60.1	11.5	.025
O ₂ sat.	87.5	6.3	109	88.8	5.8	.05
Dist. walked*	609.8	570.0	91	1280.3	862.6	<.0001
Stairs	42.3	23.5	77	68.3	32.4	<.0001
Work on stairs	581.6	304.0	59	874.8	438.6	<.0001
Non O₂ Patients						
pH	7.40	.04	73	7.40	.04	
P _{CO₂}	38.8	7.4	73	39.4	6.0	
P _{O₂}	59.0	7.4	67	61.2	9.1	.05
O ₂ sat.	88.8	4.7	73	90.0	4.1	.02
Work	626.0	323.5	44	956.1	457.1	<.0001
Dist. walked*	671.5	616.6	67	1449.1	906.9	<.0001
Stairs	49.7	20.9	52	76.2	28.6	<.0001
O₂ Patients						
pH	7.40	.04	36	7.38	.04	.01
P _{CO₂}	43.0	9.2	35	52.5	15.2	<.0001
P _{O₂}	53.1	8.7	28	57.4	15.7	
O ₂ sat.	84.8	8.1	36	86.4	7.9	
Work	451.3	192.3	15	636.1	273.2	.025
Dist. walked*	437.5	370.9	24	809.2	487.1	.01
Stairs	36.7	18.3	16	54.6	28.6	.01

- VC —Vital capacity (liters)
- FEV₁ —Forced expiratory volume (liters/second)
- MMF —Maximal mid expiratory flow (liters/second)
- MVV —Maximal voluntary ventilation (liters/minute)
- pH —Expression of hydrogen ion concentration (Negative Lung Volume)
- P_{CO₂} —Carbon dioxide tension in arterial blood
- P_{O₂} —Oxygen tension in arterial blood
- O₂ sat. —Oxygen saturation in arterial blood
- Distance walked—On treadmill (various increasing rates and grades)
- Stairs —Number walked until dyspneic
- Work —Kilogram meters vertical work on stairs

* Various increasing rates and grades.

TABLE 4.
COMPARISONS: PRELIMINARY VERSUS TWO YEAR

	Preliminary			Two Year		
	Mean	SD	No.	Mean	SD	P
VC	2.73	.80	78	2.65	.89	
FEV ₁	1.04	.42	78	1.00	.58	
MMF	.46	.24	78	.43	.40	
MVV	41.7	15.6	78	38.5	23.2	
All Patients						
pH	7.40	.04	73	7.40	.04	
P _{CO₂}	39.0	7.3	73	41.9	9.0	.002
P _{O₂}	58.7	8.3	63	61.4	11.1	
O ₂ sat.	88.2	5.9	72	89.3	5.1	
Work	612.8	358.4	29	939.6	608.1	.0001
Dist. walked*	789.7	557.5	41	1276.8	794.3	.001
Stairs	45.1	24.9	34	73.6	38.3	.0001
Non O ₂ Patients						
pH	7.40	.04	52	7.41	.04	
P _{CO₂}	37.4	5.6	52	38.9	5.3	
P _{O₂}	60.0	7.8	49	60.2	8.0	
O ₂ sat.	89.3	4.6	52	89.6	4.0	
Work	663.0	366.8	24	1064.2	593.2	.0001
Dist. walked*	773.5	578.2	31	1429.4	801.8	.0002
Stairs	50.3	24.1	25	79.6	36.8	.0001
O ₂ Patients						
pH	7.40	.05	21	7.40	.03	
P _{CO₂}	43.1	9.2	21	49.2	11.8	.01
P _{O₂}	54.5	9.1	14	65.4	18.2	.025
O ₂ sat.	85.5	7.8	20	88.4	7.3	
Work	371.7	194.8	5	341.7	159.0	
Dist. walked*	839.7	513.1	10	803.6	576.7	
Stairs	39.3	15.7	7	50.0	43.1	

VC —Vital capacity (liters)
 FEV₁ —Forced expiratory volume (liters/second)
 MMF —Maximal mid expiratory flow (liters/second)
 MVV —Maximal voluntary ventilation (liters/minute)
 pH —Expression of hydrogen ion concentration (Negative Lung Volume)
 P_{CO₂} —Carbon dioxide tension in arterial blood
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 O₂ sat. —Oxygen saturation in arterial blood
 Distance walked—On treadmill (various increasing rates and grades)
 Stairs —Number walked until dyspneic
 Work —Kilogram meters vertical work
 * Various increasing rates and grades.

is apparent that ventilatory function abnormalities do not change significantly. Oxygen tension and saturation are significantly increased at one year. Carbon dioxide rises occur only in the oxygen patients, but not to an important degree since pH remains normal (compensated).

It is probably most noteworthy that in spite

of the fact that the patients essentially remain about the same from a physiologic standpoint, they have not deteriorated at the expected rate. Moreover, it may be quite important that increased exercise tolerance is sustained for periods up to two years.

Mortality. Within a 3.5 year period, 56 pa-

TABLE 5.
MORTALITY DATA

Months	At Risk	Dead	Cum Mor %	Surv Rate %
0-6	179	8	4.5	95.5
6-12	169	9	9.6	90.4
12-18	158	10	15.5	84.5
18-24	139	12	23.2	76.8
24-30	111	12	32.6	67.4
30-36	74	1	33.8	66.2

tients have died (mean survival 1.4 years). This is expressed in life table form by year in Table 5. An analysis of death indicates that at any point in time, early deaths are related to the poorest pulmonary function measurements at time of entry into the program. The most common cause of death is combined cardiac and respiratory failure. No claim is currently made that the mortality rate is decreased except in the case of acute respiratory insufficiency. Nonetheless, our population, averaging 61 years with an FEV₁ of 0.94 liters on entry, represents a most adverse population from the standpoint of age and loss of pulmonary function. Clearly patients with less severe forms of disease will have a better prognosis (5, 21).

Summary. An ambulatory care comprehensive program for emphysema and chronic bronchitis has been described. The basic modalities of therapy are patient education, bronchial hygiene using simple home techniques, breathing retraining, physical reconditioning, oxygen, and ancillary chemotherapeutic agents. The application of these principles in care provides great symptomatic benefit, improved exercise tolerance, and a reduction in hospital needs. A reduction in the progressive pulmonary function deterioration which is expected in this disease spectrum has been observed up to two years.

In view of the immense number of patients with CAO, suffering and disabled, the application of outpatient care programs on a nationwide basis will help to reduce the overall social and economic impact of this disease complex.

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Trauma Resulting in Respiratory Failure*

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Respiratory failure may occur secondary to thoracic trauma. Several important conditions develop as a result of chest injuries and may occur singly, or in combination, in patients with injuries from any cause. Unrecognized and therefore without proper management, the results are necessarily poor. If recognized and their mode of production is understood, treatment may be simple. These conditions are:

- 1) Retention of bronchial secretions with inadequate pulmonary aeration caused by:
 - a. Severe chest wall pain
 - b. Abnormal mobility of the chest wall
 - c. Pulmonary contusion
 - d. Depression of the cough reflex, through
 1. Unconsciousness
 2. Excessive opiates
- 2) Open chest wall with "sucking wound" phenomenon
- 3) Flail chest wall
- 4) Pneumothorax, simple or tension
- 5) Hemothorax
- 6) Hemopneumothorax
- 7) Ruptured diaphragm
- 8) Ruptured bronchus
- 9) Non-pulmonary injuries causing marked ventilation problems

Ribs are the most frequently injured structures in the chest area and must be taken into consideration with nearly all thoracic trauma cases.

The presence or absence of preexisting pulmonary disease and the extent of injury will govern the amount of difficulty encountered after chest injury. A small injury may cause marked derangement of pulmonary function in the patient

having preexisting chronic pulmonary disease. Since adequate treatment of these conditions will correct the resulting cardio-respiratory disturbances and thereby aid in resuscitation of the patient, each condition will be discussed in some detail.

Chest wall pain may have serious consequences in injuries which otherwise would be of no great importance. Pain may effectively immobilize the chest wall, thereby making cough ineffectual. This results in retention of tracheobronchial secretions and/or aspirated material. The accumulation of such material in the bronchi interferes with pulmonary ventilation and leads to atelectasis and perhaps even to suppurative pneumonia. If inadequately treated, such patients may actually go on to asphyxiation. Recognition of such a situation is not difficult. Cough is ineffectual and auscultation reveals moist rales and/or rhonchi widely distributed over both lungs. Dyspnea and cyanosis may develop.

Treatment is directed toward relief of the chest wall pain and cleaning the airway of secretions. Adhesive strapping is inadvisable since it leads to poor ventilation, retained secretions, atelectasis, and pneumonia. Mild analgesics or cautious administration of narcotics is helpful. Voluntary, periodic cough and breathing exercises should be encouraged and advised. Added to these is the routine use of intermittent positive pressure breathing apparatus to assist full lung ventilation. Frequent position change will aid the normal drainage of the bronchi.

Patients with retained secretions should have immediate and repeated aspiration by nasotracheal catheter (fig. 1). Tracheal suction is easily done, and physicians treating patients with thoracic injuries must familiarize themselves with its technique. Using a fairly stiff, slightly curved,

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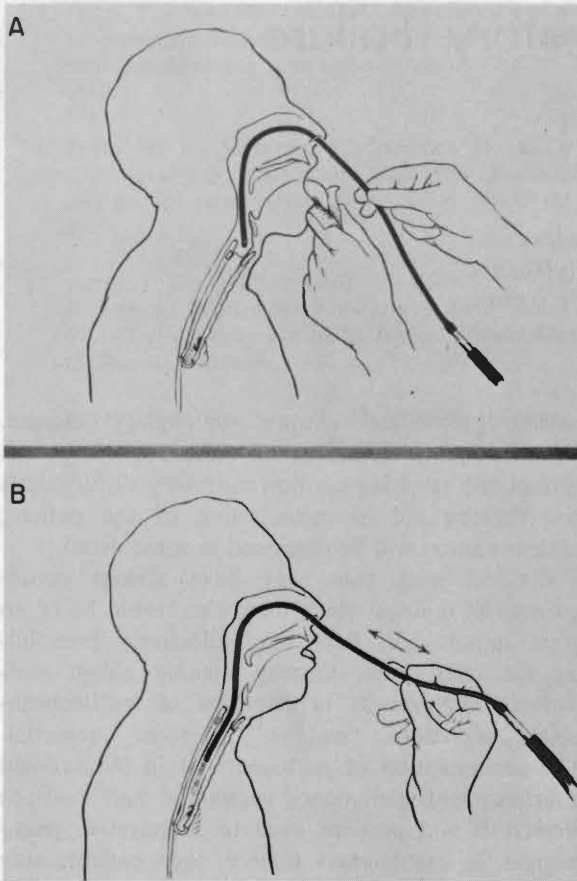


Fig. 1—A. Illustration of nasotracheal suction as an effective stimulus to cough. B. Suction is applied to the catheter for removal of resultant secretions.

catheter (#16-18 French), the patient is placed in the sitting or semi-sitting position with the back supported and the head and neck dorsally extended. The lubricated catheter is quickly passed through the nose into the pharynx without suction attached. The patient is instructed to take a deep breath and during inspiration the catheter is passed into the trachea. Success is signified by violent coughing and hoarseness. Suction is applied intermittently as the catheter is passed into the tracheobronchial tree.

In some patients effective aspiration can be accomplished only by means of the bronchoscope.

Oxygen is administered as an aid to these measures used to clean the airway of secretions but cannot serve as a substitute.

It should be stressed that opiates must be used with particular care in patients with exces-

sive bronchial secretions, especially in those who have difficulty in evacuating these secretions. Opiates reduce the cough reflex and slow or stop cilia action. They also slow or prevent patient activity, thus promoting stasis.

The importance of an open, adequate airway cannot be overemphasized. The temporary use of an orotracheal or nasotracheal tube (up to 72 hours) may be necessary and advisable in the early management of chest trauma cases. In patients with serious cervical or facial injury, or in any condition where suction or bronchoscopy is not feasible, or where excessive irritation has been produced by gas or smoke, it is advisable to perform a tracheostomy so that catheter aspiration can be adequately accomplished.

Open chest injuries produce profound disturbances in intrathoracic physiology. Because of the opening in the chest wall, negative intrapleural pressure is replaced by atmospheric pressure. A number of factors determine the severity of the effects on cardio-respiratory physiology, the most

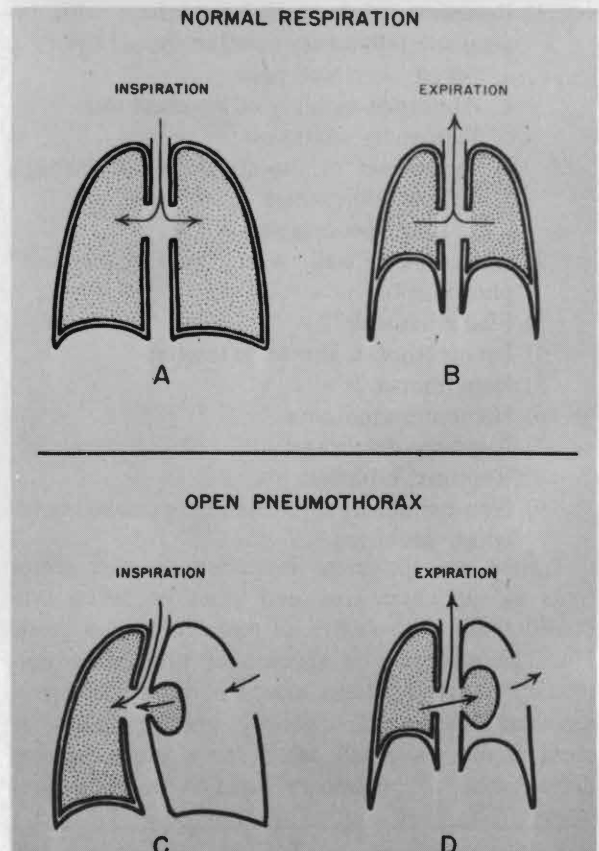


Fig. 2—Diagram of adverse effects of open pneumothorax.

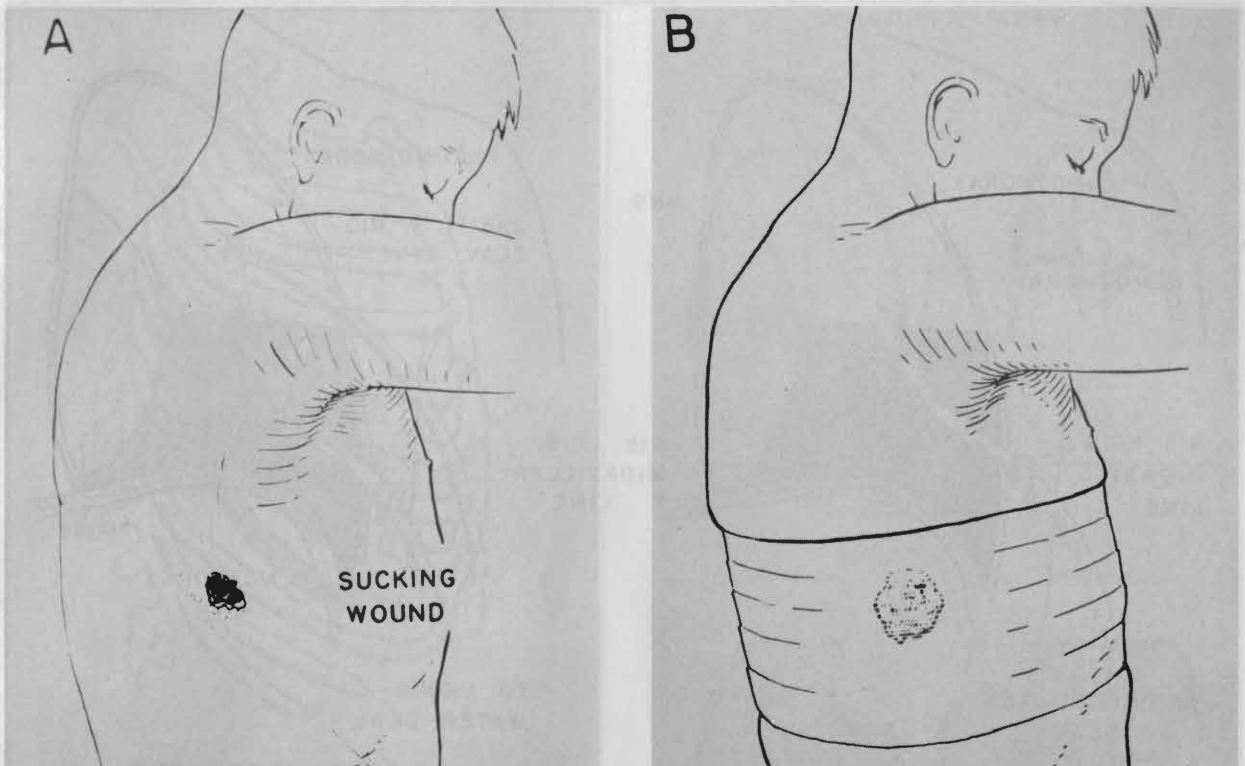


Fig. 3—A. Open thoracic wound. B. Emergency closure to stop sucking of air into pleural space.

important being the size of the opening in the chest wall. Small openings are, in general, tolerated better than large ones. If the size of the opening approaches or exceeds the size of the trachea, the patient may get into serious difficulty. Other important factors are the type of wound and the mobility of the mediastinum. If the wound allows air to enter the pleural space but does not permit it to escape, the patient's condition deteriorates more rapidly. Since the mediastinum is usually quite mobile, open pneumothorax generally leads to a shift of the mediastinum to the opposite side with compression of the contralateral lung as well as the lung on the side of injury. The swing of the mediastinum with each respiratory cycle causes poor air exchange and also interferes with the return of venous blood to the heart (fig. 2).

Open wounds must be effectively closed as soon as possible. As an emergency measure, a simple occlusive dressing of vaseline gauze is adequate (fig. 3). When the patient has been removed to a location where facilities are adequate, the wound is debrided and an airtight,

pleuro-muscular closure is done. A large catheter is inserted through an intercostal space into the pleural cavity and is connected to a water-seal arrangement (figs. 4 and 5).

If one or more ribs are broken in two or

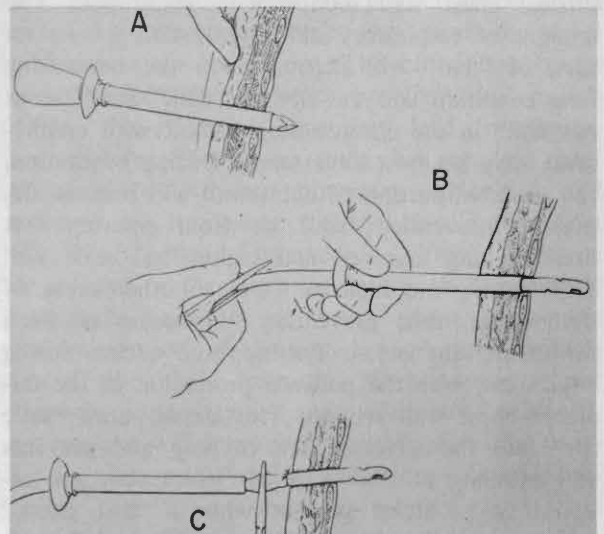


Fig. 4—Trochar method of inserting chest drainage tube.

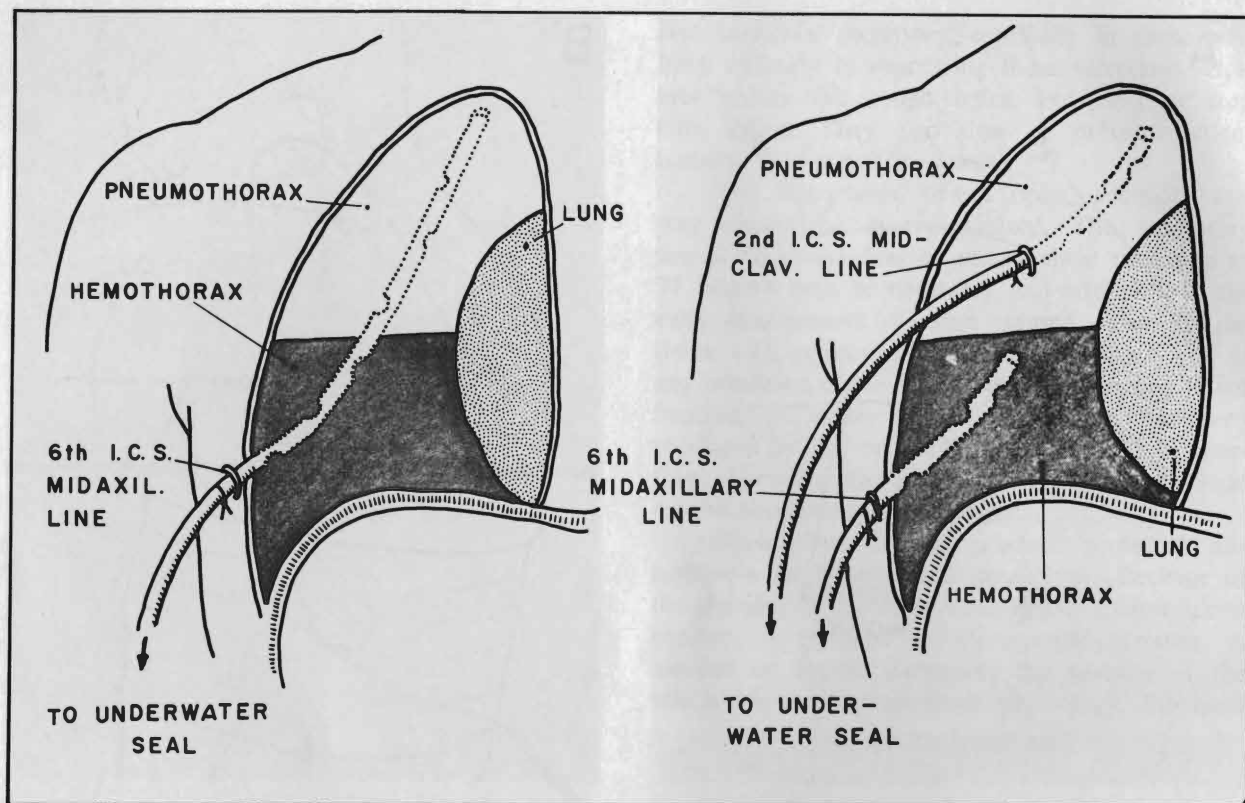


Fig. 5—Single tube and double tube drainage of air and fluid from the pleural space.

more places (fig. 6), the stability of the chest wall is interfered with and a "flail chest wall" results (fig. 7). This "flail" area results in paradoxical chest wall motion with respiration. The amount of respiratory difficulty resulting from an area of "flail" will depend upon the preexisting lung condition and the size of "flail." Small areas of "flail" in the chronic lung patient with emphysema may be most devastating. During inspiration, the unstable portion of chest wall will become depressed preventing fresh air from entering that area of lung involved and expressing "stale air" (low in O_2 and high in CO_2) to other areas of both lungs, thus preventing full access of fresh air to all lung areas. The opposite occurs during expiration, with the outward protrusion of the unstable chest wall section. This draws more "stale air" into the affected area of lung and prevents full exhaling of the "stale air." Not only are respiratory problems present with a "flail chest," but the swinging back and forth of a virgin mediastinum alters and slows blood flow into the right

side of the heart, in some cases bringing about shock due to poor inflow to the heart and thus poor outflow from the left ventricle. Paradoxical chest wall motion may be temporarily managed with a bulky dressing to stop paradoxical motion but is most effectively treated by tracheostomy and assisted ventilation with an intermittent positive pressure apparatus (figs. 8, 9, and 10).

Pneumothorax resulting from injury to the lung parenchyma allows escape of air through the visceral pleura into the pleural space and may cause severe, sudden respiratory distress. Traumatic collapse of lung is far more significant in bringing about respiratory failure in the individual with preexisting lung disease than in the healthy individual with no previous lung disease. This air should be promptly removed by the insertion of an intercostal drainage tube and connection to underwater suction drainage (fig. 11). In the post-traumatic patient, aspiration of pneumothorax which is greater than 15 to 20% is generally not satisfactory because it is not as com-

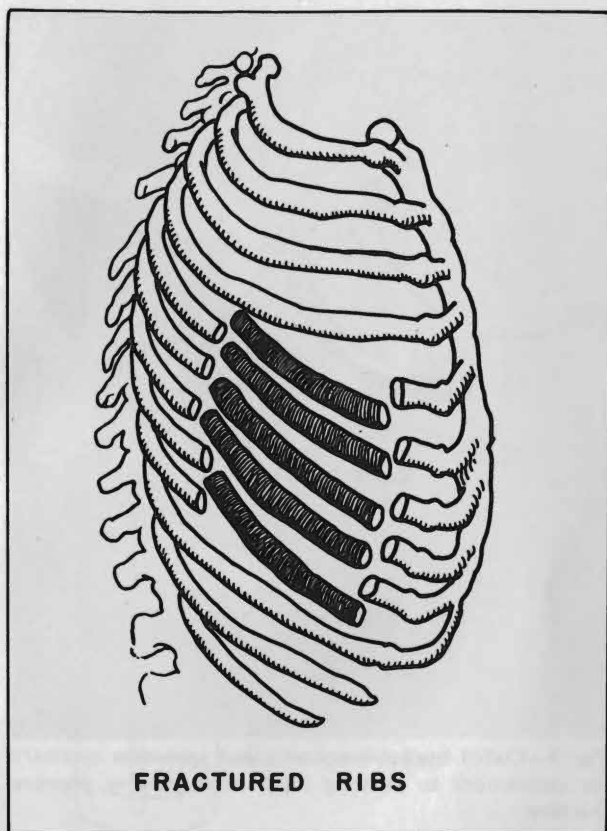


Fig. 6—Illustration of unstable section of chest wall due to multiple rib fractures.

plete, continuous, or efficient as the insertion of a tube for 24 to 72 hours. If the pneumothorax is bilateral, immediate prompt attention to the re-expansion of the lungs is essential. Tension pneumothorax results when a ball valve type of injury to the lung parenchyma occurs. Air can readily escape into the pleural space but not pass back and forth through the opening. Thus, positive pressure is built up in the side of injury such that there is total collapse of the ipsilateral lung, widening of the intercostal spaces, depression of the diaphragm, and displacement of the mediastinum causing further embarrassment to the more normal contralateral lung. Immediate relief of this tension is essential to prevent respiratory failure. Temporary benefit can be achieved using a large bore needle until the chest tube is assembled and inserted. Not only are the respiratory effects of tension pneumothorax most devastating but so are the circulatory effects with torsion of the great veins in the mediastinum diminishing flow of blood to the right heart and thus influencing out-

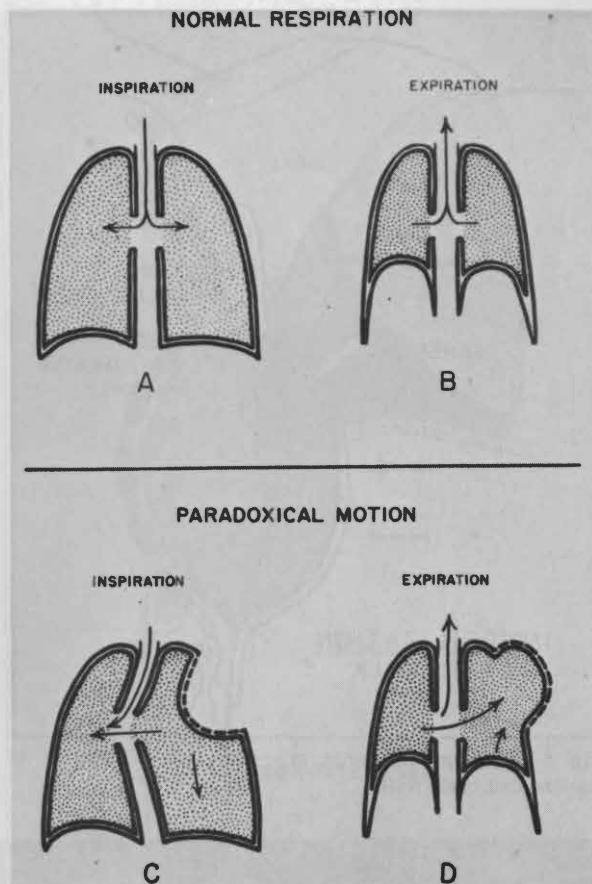


Fig. 7—Diagram showing effect flail chest wall.

flow from the left ventricle and shock because of poor output.

Loss of blood into the pleural space giving rise to a hemothorax may also cause the same problem as pneumothorax. The blood loss brings about peripheral circulatory problems, but in addition, the collapsed lung may lead to respiratory failure. The blood must be removed continuously to prevent pulmonary difficulties and replaced by transfusion for the circulatory effect (fig. 12). If blood loss exceeds 1,500 to 2,000 cc in an hour or two after the injury, thoracotomy is frequently necessary to bring about hemostasis and prevention of continued respiratory difficulties. If the blood from the pleural space is not properly, adequately, and efficiently removed, a coagulum will form over the collapsed lung causing its entrapment and possible need for decortication (fig. 13). Therefore, prompt removal is important for the immediate as well as long-term respiratory benefit.

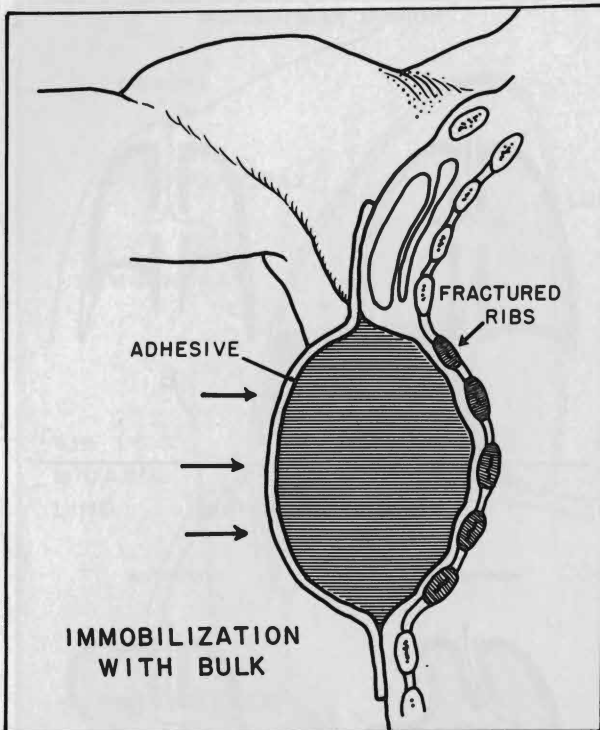


Fig. 8—Diagram of temporary bulky chest dressing to stabilize flail chest wall.

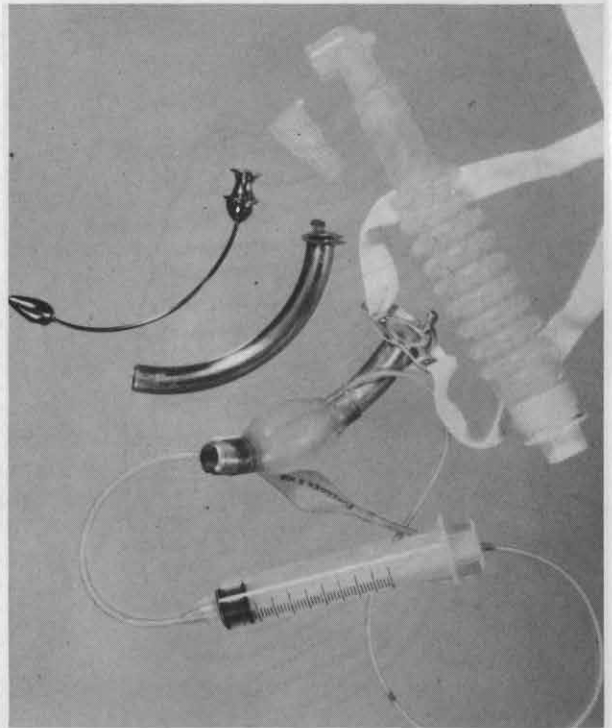


Fig. 9—Cuffed tracheostomy tube and apparatus necessary for connections to assisting intermittent positive pressure machine.



Fig. 10—Patients with face mask and tracheostomy attachments using intermittent positive pressure machines.

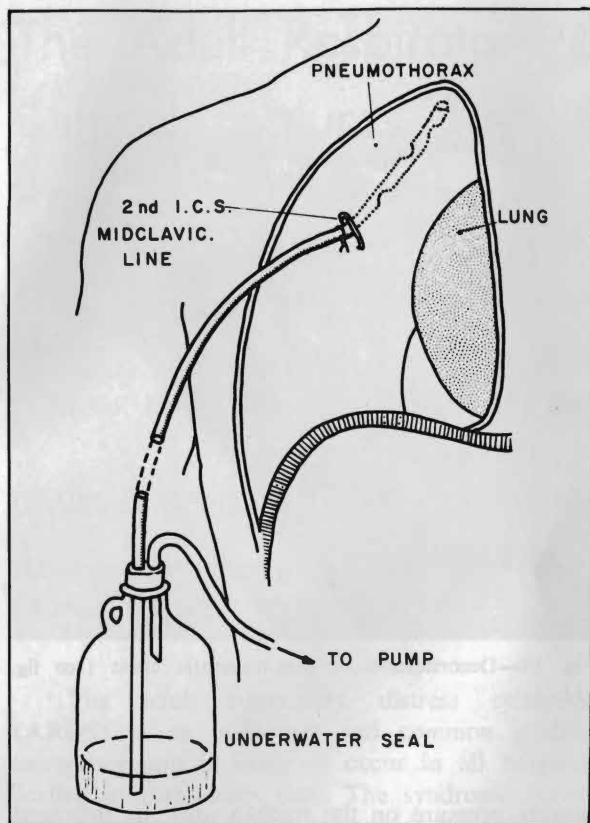


Fig. 11—Chest tube inserted for drainage pneumothorax.

Patients with massive trauma may have a ruptured bronchus. Such injury leads to extravasation of air into the mediastinum and pleural space with marked dyspnea and hemoptysis. The presence of mediastinal, pleural, and subcutaneous air in a patient with hemoptysis at the time of massive injury strongly suggests the possibility of a ruptured bronchus. Prompt diagnosis and repair is essential. The diagnosis can be made by bronchoscopy, and this examination should be done promptly after the suspicion of the possibility of such an injury. Once the diagnosis has been made, prompt operative exposure and closure of the defect is essential.

Massive blunt trauma may rupture the diaphragm. The left diaphragm tends to rupture far more frequently than the right. Under these circumstances, intestinal contents from the positive pressure peritoneal cavity are forced into the negative pressure pleural space bringing about collapse of the ipsilateral lung tissue and shift of the

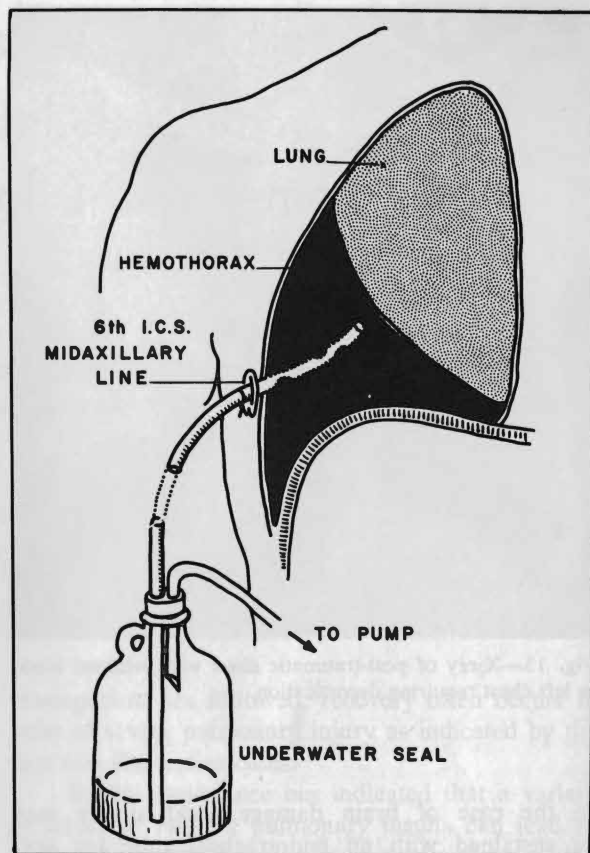


Fig. 12—Chest tube inserted for drainage hemothorax.

mediastinum and heart to the opposite side. The amount of respiratory embarrassment is proportional to the amount of peritoneal contents in the pleural space and the antecedent lung condition. Prompt recognition of this problem is essential, and operative repair must be carried out promptly if the ruptured diaphragm leads to respiratory embarrassment.

Non-pulmonary injuries may effect the lung itself. Of great importance in this area is the presence in the orthopedic injury of possible fat emboli to the lungs. If such a diagnosis is made, pulmonary assistance is essential to the maintenance of the patient after injury even with support from tracheostomy and positive pressure breathing apparatus. Other areas distant from the lung which may give severe respiratory embarrassment are spinal cord injuries which will effect diaphragm and intercostal action. Severe brain damage may so effect the respiratory activity that the patient's problems will be mainly in the area of the lung.

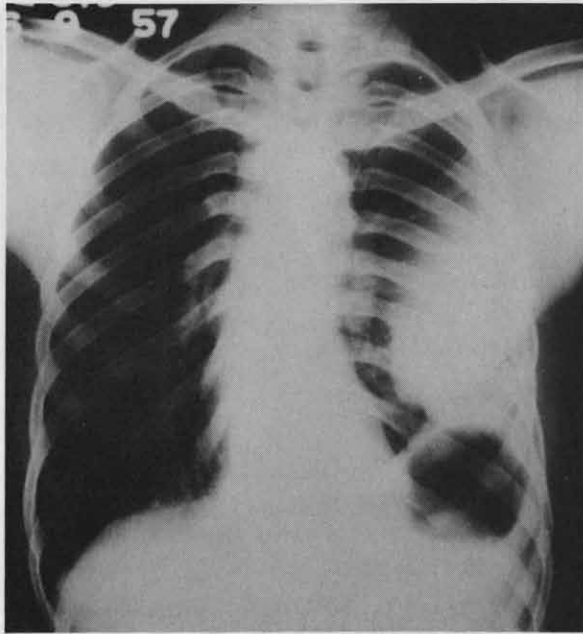


Fig. 13—X-ray of post-traumatic chest with retained blood in left chest requiring decortication.

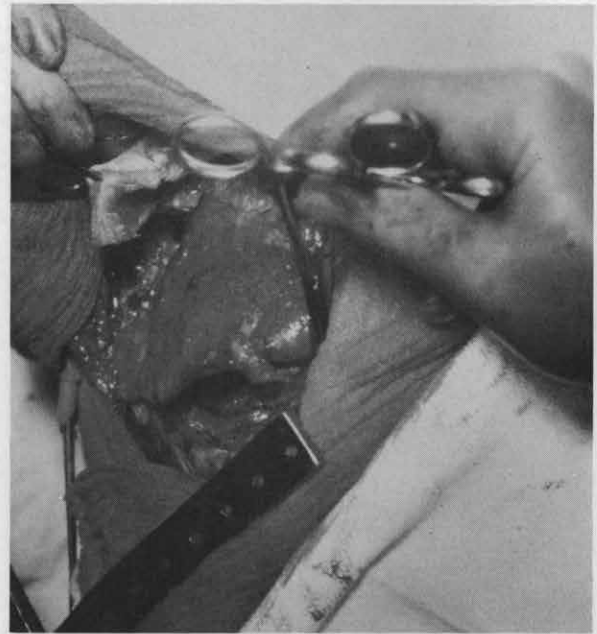


Fig. 14—Decortication of post-traumatic chest (see fig. 13).

In the case of brain damage good airway may be sustained with an endotracheal tube for several days and then replaced with tracheostomy. Facial, jaw or sinus injuries may so crowd the upper respiratory passages that tracheostomy is essential to prevent asphyxia. Severe neck injuries

causing pressure on the trachea must be managed carefully to provide for an adequate, continuous airway. Extensive injuries immobilizing the patient in bed for long periods of time must be carefully observed in order to prevent atelectasis, pneumonia, and respiratory failure.

The Adult Respiratory Distress Syndrome: Clinical Features, Factors Influencing Prognosis and Principles of Management*

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The adult respiratory distress syndrome (ARDS) is an important and common medical emergency and is likely to occur in all hospitals dealing in respiratory care. The syndrome occurs from a variety of diffuse pulmonary injuries which are either direct or indirect attacks on the lung parenchyma. Once lung damage occurs, exudation of fluid and loss of surfactant activity leads to impaired gas exchange and reduced pulmonary compliance. The syndrome presents clinically as marked respiratory distress, tachypnea, cyanosis, refractory hypoxemia, high inflation pressure requirements during ventilatory support, diffuse alveolar infiltrates on chest roentgenograms and postmortem pulmonary congestion, hyperemia and hyaline membrane formation. Principles of management include adequate support of oxygen transport, ventilation, and circulation employing volume respirators with positive end-expiratory pressure (PEEP). During the support phase, further pulmonary injury in terms of fluid overload, oxygen toxicity, or infection, must be prevented or treated. When these principles of

management are followed, recovery often occurs in spite of severe pulmonary injury as indicated by the first two illustrative cases.

Recent experience has indicated that a variety of direct or indirect pulmonary insults can lead to a clinical picture of marked respiratory distress, diffuse pulmonary infiltration on x-ray examination, impaired effective pulmonary compliance, marked impairment in oxygen transport¹ in spite of ventilatory assistance, pulmonary congestion, and hyaline membrane formation (1). This clinical picture, which arises from unrelated pulmonary insults, has been termed the adult respiratory distress syndrome (ARDS) (1). The response of the lung to a variety of pulmonary insults has been the subject of a recent conference sponsored by the National Academy of Sciences. It is apparent on reviewing the conference proceedings that this clinical syndrome is encountered frequently in both civilian and military hospitals (9).

This report redescribes the adult respiratory distress syndrome and discusses factors which in-

* Presented by Dr. Petty at the Symposium on Respiratory Failure, May 25, 1972, at Richmond, Virginia. Reprinted with permission from *Chest*, Volume 60, pp. 233-239, September, 1971. Reprint requests to Thomas L. Petty, M.D., 4200 East Ninth, Denver, Colorado 80220.

¹ Impaired oxygen transport is defined as an increased inspired-arteriolar oxygen tension difference (similar to increased alveolar-arterial tension difference). Normally this is approximately 50 mm Hg (difference between inspired and arterial tensions with an adequate alveolar ventilation for CO₂).

fluence prognosis and presents principles of management.

The Clinical Syndrome. Patients with this syndrome suddenly develop marked tachypnea, dyspnea, and cyanosis which is refractory not only to nasal oxygen but also to intermittent positive pressure breathing (1, 2). Chest x-ray films show diffuse alveolar infiltration, usually with a normal cardiac silhouette (see x-ray films of three illustrative cases). The difference between inspired and arterial oxygen tensions is markedly increased (1, 2) (often 200 to 500 mm Hg) representing a large right to left shunt (20). It must be stressed that the original injury leading to this problem may be direct chest trauma, indirect trauma such as shock associated with abdominal wounds, ruptured spleen, drug ingestions, massive aspiration pneumonia, and acute pancreatitis with shock (1). Similar clinical entities include the syndrome of prolonged cardiopulmonary bypass (4), congestive atelectasis (6), viral pneumonia (17), and massive fat embolism (3).

In addition, this clinical syndrome has been equated with oxygen toxicity (16) or use of a ventilator *per se*, and the unfortunate term "respirator lung" has been added to the already confusing literature concerning the subject (7).

In spite of marked pulmonary damage and impaired oxygen transport, however, modern management has proved to be effective in certain patients². Fatalities are usually a result of septic com-

² See illustrative case examples. Our total series will be the subject of a subsequent report.

plications including pneumonia with gram-negative organisms, lung abscess, and occasional septicemia. The outcome is dependent upon the nature and degree of the original pulmonary injury and the presence or absence of further superimposed pulmonary damage (1, 2).

Case Reports. The following three illustrative cases represent two basic types of clinical response which may occur, that is, rapid resolution with recovery or progressive pulmonary insufficiency leading to interstitial fibrosis and death.

Case 1. The patient, a 21-year-old student, became ill following a bout of heavy drinking which led to unconsciousness after he attempted to prepare some food by cooking on a gas stove. The patient later awakened in a smoke filled room and vomited. He became extremely short of breath with a cough productive of reddish purulent sputum. Because of progressive difficulty with breathing, the patient entered the emergency room. No industrial exposure was reported by relatives. On examination the patient was in marked respiratory distress with tachypnea, cyanosis, and moderate supraclavicular retractions. His pulse was 110, respirations 38, temperature 38.8°C, and blood pressure 103/70. The chest was symmetrical and moist coarse rales were heard throughout both lung fields with some decrease in breath sounds. The results of cardiac examination were normal. The chest x-ray picture revealed diffuse bilateral infiltrates (fig. 1). (Note that in each figure factors of oxygen administration, that is, nasal O₂ liter flow or oxygen tension on a ventilator—P_iO₂,—are compared to simul-

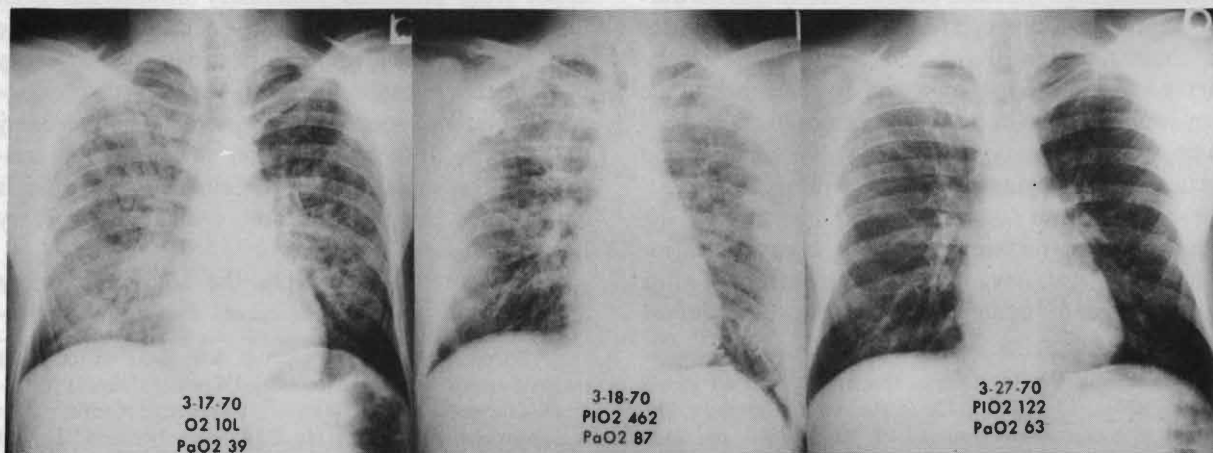


Fig. 1 (left)—Chest roentgenograms on admission. Note oxygen liter flow with concomitant arterial oxygen tensions (Case 1). Fig. 2 (center)—X-ray clearing on second hospital day. High inspired oxygen tension (462) required for adequate arterial oxygenation (Case 1). Fig. 3 (right)—Further x-ray clearing and near normal oxygen transport (Case 1).

taneous arterial oxygen tensions— $P_{a_{O_2}}$). The difference between $P_{I_{O_2}}$ and $P_{a_{O_2}}$ is an index of impaired gas transport across the lung (10) (see Discussion). Initial arterial analyses revealed $P_{a_{O_2}}$ 33 mm; carbon dioxide tension ($P_{a_{CO_2}}$) 35 mm and pH 7.435, breathing air (Table 1). With 10 liters of nasal oxygen the $P_{a_{O_2}}$ increased only to 38.5. The hematocrit was 52%,³ white cell count was 21,000.

The clinical impression was smoke inhalation and possible aspiration pneumonia. In view of the profound hypoxemia which was refractory to nasal oxygen, an endotracheal tube was placed and a tracheostomy performed. With 80% inspired oxygen fraction the $P_{a_{O_2}}$ increased to 88 mm Hg (Table 1). On the next day $P_{a_{O_2}}$ was 87 with 80% inspired oxygen fraction. The x-ray picture showed slight clearing (fig. 2). With 10 cm positive end-expiratory pressure (PEEP) $P_{a_{O_2}}$ elevated to 119⁴ (Table 1). This allowed the inspired oxygen fraction to be reduced to 70% providing a $P_{a_{O_2}}$ of 85 and later in the afternoon 104, indicating improved oxygen transport (Table 1). In addition to the ventilatory management, the patient also received nafcillin, 8 g daily, hydrocortisone 600 mg intravenously daily, and kanamycin 500 mg twice daily in view of the possibility of aspiration pneumonia. On the following day, the patient's $P_{a_{O_2}}$ was 92 with an inspired fraction of 60% via the ventilator. Rapid clearing of the pulmonary infiltrates occurred by the third hospital day and the patient made an uneventful recovery (data in Table 1 indicates marked improvement in the $P_{I_{O_2}}$ - $P_{a_{O_2}}$ difference which became nearly normal on March 27, 1970; figure 3: normal $P_{a_{O_2}}$ is 65 to 75 mm Hg).

Comment. This case represents diffuse pulmonary injury from smoke inhalation and aspiration of gastric contents. Corticosteroid drugs are generally considered desirable to combat the chemical pneumonitis from aspiration of gastrointestinal content (12) and are also considered useful in smoke inhalation. The antibiotics were used in the belief that some bacterial infection may have been present. Following initial refractory cyanosis, the patient could be adequately oxygenated with a high oxygen fraction (70%) and positive end-expiratory pressure on exhalation (see Discussion). An uneventful recovery

³ Upper normal for Denver although in this case this value may be representative of some degree of hemoconcentration.

⁴ Ohio 560 Respirator, Ohio Medical Products, Madison, Wisconsin.

TABLE 1.
INSPIRED AND ARTERIAL BLOOD GAS TENSIONS
DURING MANAGEMENT (CASE 1)

	Admission	3 Hr*	24 Hr*	2 Days*	7 Days
Oxygen	10 L	80%	80%	60%	20.9%
$P_{I_{O_2}}$		460	462	353	121
$P_{a_{O_2}}$	39	88	119	92	59
$P_{a_{CO_2}}$	35	38	40	38	37

* Ventilatory assistance with PEEP—See text.

followed and the patient remains well five months after the original pulmonary insult.

Case 2. Patient 2, a 34-year-old white woman, was admitted via the emergency room with a history of ingestion of an unknown quantity of phenobarbital and chlordiazepoxide along with tablets composed of aspirin and phenacetin some 30 hours before admission. The patient had vomited and aspirated according to her husband. She had a history of drug overdosage on two occasions in the past.

On physical examination she was found to be semi-stuporous and deeply cyanosed. Her blood pressure was 110/70, temperature 38.2°C, respirations 30 and labored. Examination of the chest revealed scattered bilateral rales in both axillary areas. Cardiac examination was normal. No edema was present. Chest x-ray picture (fig. 4) revealed extensive bilateral pulmonary infiltrates. Initial blood gas values revealed $P_{a_{O_2}}$ (on air) 34.5, $P_{a_{CO_2}}$ 23.5, pH 7.51; with 10 liters of oxygen (Table 2), $P_{a_{O_2}}$ 40, $P_{a_{CO_2}}$ 23, pH 7.49.

In addition, hematocrit was 32%, white cell count 21,300 with 95% polymorphonuclear leukocytes, BUN 13 mg% and creatinine 1.3%. The patient was managed in the intensive care unit following tracheostomy with a volume cycled ventilator and initially required oxygen fractions of 80% to

TABLE 2.
INSPIRED AND ARTERIAL BLOOD GAS TENSIONS
DURING MANAGEMENT (CASE 2)

	Admission	1 Hr*	3 Hr*	2 Days	4 Days	7 Days
Oxygen	10 L	100%	80%	50%	30%	20.9%
$P_{I_{O_2}}$		585	468	294	176	121
$P_{a_{O_2}}$	40	70	116	159	92	75
$P_{a_{CO_2}}$	23	33	37	30	26	30

* Ventilatory Assistance with PEEP—See text.

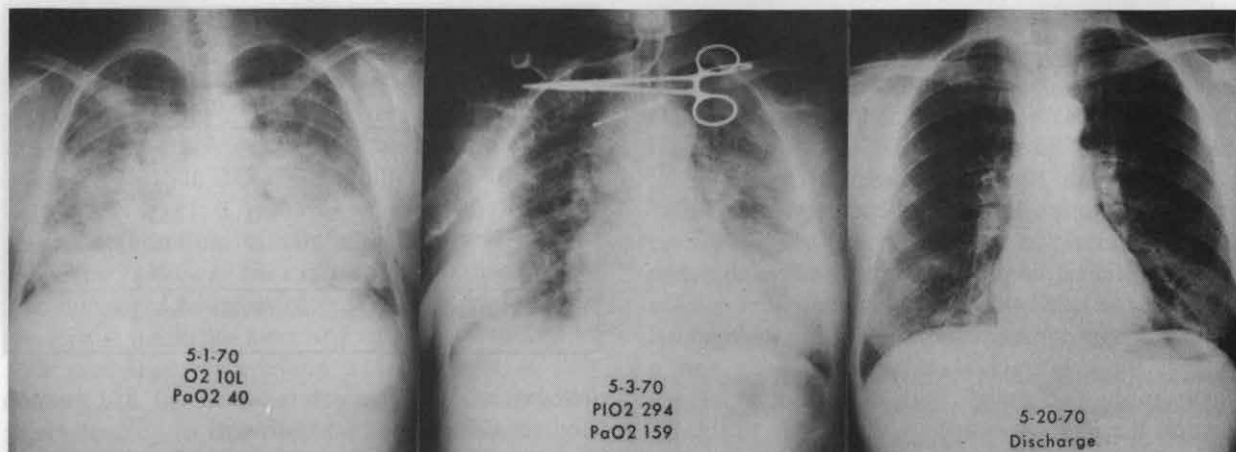


Fig. 4 (left)—Bilateral pulmonary infiltration on admission. Severe hypoxemia— Pa_{O_2} , 40 in spite of 10 L nasal oxygen flow (Case 2). Fig. 5 (center)—Clearing pulmonary infiltrate and evidence of improved oxygen transport ($\text{P}_{\text{I}_{\text{O}_2}}$, 294; Pa_{O_2} , 159) (Case 2). Fig. 6 (right)—Normal chest x-ray on discharge (Case 2).

100% to effect an adequate arterial oxygen tension (Table 2). In addition, she received intravenous hydrocortisone 100 mg three times daily; cephalosporin and kanamycin were given for presumed aspiration pneumonia. Her temperature elevated to 39.2°C on the first hospital day. On the second hospital day elevated arterial oxygen tensions were produced by an oxygen fraction of 50% ($\text{P}_{\text{I}_{\text{O}_2}}$, 294—Table 2), and the oxygen fraction was lowered to 30%. Marked improvement was noted upon x-ray examination along with improved oxygen transport (fig. 5). Thereafter an uneventful recovery occurred over the next four days. The ventilator was discontinued on the fifth hospital day, and the patient made further progress and was discharged on the 20th hospital day (fig. 6).

Comment. Factors of pulmonary injury included aspiration of gastric contents following drug ingestion. The diffuse pulmonary damage presented the picture of pulmonary edema. A longer period of impaired oxygen transport was present than in case 1, and at times 100% oxygen was needed to effect an adequate arterial oxygen tension. Evidence of improved gas transport occurred, and a complete recovery was achieved nonetheless.

Case 3. This patient, a 34-year-old man, was transferred to Colorado General Hospital by air evacuation from a resort community. The patient had been found comatose on the floor of his rooming house, having vomited and was hospitalized in a local hospital with extensive bronchopneumonia

as well as numerous rib fractures from unexplained chest trauma. Numerous bruises of the chest were found. A tracheostomy was performed and *Staphylococcus aureus*, coagulase positive was isolated from the sputum. The patient was initially managed in the community with a pressure cycled respirator on oxygen, which presumably provided high oxygen fractions (10). It was also believed, by a careful scrutiny of input and output records, that fluid overload had occurred. The patient was managed with furosemide which produced a brisk diuresis. Because of a worsening chest x-ray picture, high fever, and difficulty providing adequate arterial oxygenation, the patient was transferred to Colorado General Hospital seven days after admission to the community hospital. On admission, the patient was alert and cooperative and followed commands well. His blood pressure 150/85, pulse 120, temperature 40°C , respirations controlled at 20. Chest examination revealed coarse rhonchi and scattered rales throughout. No cardiac abnormalities were present. A cardiac gallop rhythm was not observed. The chest x-ray film (fig. 7) showed diffuse bilateral alveolar infiltration.

Initial arterial blood gases (Table 3) on the respirator revealed Pa_{O_2} , 49, produced by an inspired oxygen fraction of 70% (simultaneously Pa_{O_2} , 32, pH 7.42). With use of 10 cm positive end-expiratory pressure by artificial ventilator, the pulmonary oxygen transport improved as evidenced by Pa_{O_2} , 72, 24 hours later at the same inspired oxygen fraction (70%). These values are representative of numerous

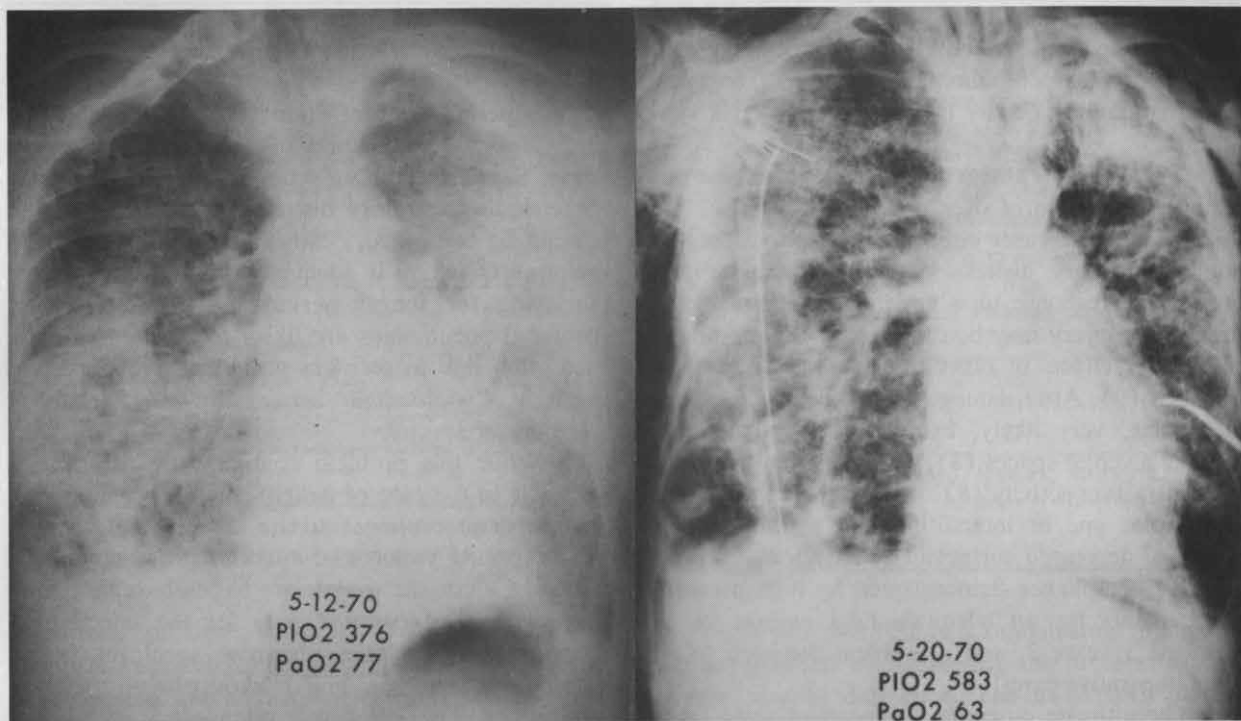


Fig. 7 (left)—Massive bilateral pulmonary infiltrations on admission with severe impairment in oxygen transport (PI_{O_2} , 376; Pa_{O_2} , 77) (Case 3). Fig. 8 (right)—Terminal chest x-ray film shows diffuse pulmonary fibrosis and evidence of right-sided pneumothorax and tube placement.

gas tensions and fractions observed throughout the day. Arterial oxygen tensions as high as 86 were initially achieved.

Antibiotics were continued (ampicillin and kanamycin) and large doses of corticosteroid drugs were given (see Discussion). Strict avoidance of fluid overload was practiced. In spite of continued respiratory support, a severe impairment of oxygen transport across the lung remained, and on the fifth hospital day, or 12 days after the original pulmonary injury, 65% inspired oxygen fraction was

still required to provide a Pa_{O_2} of 77 mm Hg in spite of positive end-expiratory pressure (Table 3).

The chest x-ray film (fig. 8) did not show resolution, and just before death, 100% oxygen was required to provide an acceptable Pa_{O_2} of 63. The patient died following a pneumothorax (fig. 8).

Comment. The original injury was pneumonia, presumably bacterial, but also aspiration pneumonia was a possibility. Further injury may have been high oxygen ventilation in the original hospital as well as fluid overload (see Discussion).

At no time in our institution did excessive arterial oxygenation occur, and all efforts were made to minimize the inspired oxygen tension that would still provide adequate arterial oxygenation. Nonetheless, the patient's course was one of progressive pulmonary infiltration, increasing pressure requirements on the ventilator (up to 75 cm inflation pressure⁵) for a tidal volume of 700 ml (effective compliance 9 ml per centimeter normal; 40 to 60 ml per centimeter). Permission for postmortem exami-

TABLE 3.
INSPIRED AND ARTERIAL BLOOD GAS TENSIONS
DURING MANAGEMENT (CASE 3)

	Admission	24 Hr*	5 Days*	12 Days*
Oxygen	70%	70%	65%	100%
PI_{O_2}	405	404	376	583
Pa_{O_2}	49	72	77	63
Pa_{CO_2}	37	38	44	46

* Ventilatory Assistance with PEEP—See text.

⁵ Ohio 560 Respirator, Ohio Medical Products, Madison, Wisconsin.

nation was not obtained. The x-ray picture and markedly reduced effective compliance suggested the development of pulmonary fibrosis, a response which commonly occurs in fatal forms of this syndrome.

Theories of Pathogenesis. It appears from our clinical experience of over 40 cases, as well as the three illustrative cases cited in this report, that the adult respiratory distress syndrome is basically a nonspecific response to a variety of pulmonary injuries. The injury may be direct chest trauma or the pulmonary effects of other injurious agents as well as shock (9). After damage to the alveolar capillary membrane, very likely, exudation of fluid occurs into the alveolar spaces (8). This causes interference with surfactant activity (8). It is likely a combination of alveolar and/or interstitial fluid as well as the effects of decreased surfactant activity leads to poor effective compliance demonstrated by high pressure requirements for an adequate tidal volume as illustrated by case 3, and a problem common to all three illustrative cases.

The ultimate outcome is dependent upon three factors: a) the degree of original injury, b) the effectiveness of respiratory support and c) the prevention of further pulmonary injury. The majority of patients can be adequately supported by the use of constant volume ventilators through use of the controls described below. It is likely that fluid overload may compound the problem. Once the alveolar capillary barrier is injured, and vascular integrity lost, expansion of the circulating blood volume may allow outpouring of fluid into alveolar spaces with resulting pulmonary edema and impairment in oxygen transport.

An additional contributing factor in the development of progressive stiff lungs is the possibility of oxygen toxicity (11, 19). All of the facts on oxygen toxicity are not known at the present time; however, the weight of evidence suggests that long-term exposures of oxygen in fractions higher than 40% to 50% in certain cases, may be harmful (11, 19). On the other hand, our experience, as well as that of others, has shown that in states of profound hypoxemia, 100% oxygen inspired fraction may be required for periods of several days with recovery. Questions remain concerning the nature of the damaging effects of high oxygen and whether this is a function of alveolar or arterial oxygen tension. Recent evidence suggests that at atmospheric pressures high alveolar oxygen tensions are potentially

damaging (15). In principle, one should minimize the inhaled oxygen fraction as much as possible (see below).

Superimposed infection represents a common and serious complication of acute respiratory distress. Sepsis from burn wounds or peritonitis may precipitate respiratory distress, and if the infection cannot be controlled, death may occur even though respiratory failure is adequately treated. In patients surviving for longer periods of time, secondary bacterial pneumonias are likely to occur, and these are often due to resistant gram-negative organisms such as *Pseudomonas aeruginosa* and *Klebsiella-Aerobacter* species.

While this problem continues to be a major obstacle in the care of patients, it can be minimized by proper precautions and use of antibiotics. Careful and repeated cultures of sputum, urine, stool, and wounds alert the physician to early changes in flora and provide sound data for the selection of appropriate antibiotics. Narrow spectrum highly specific antibiotics are preferred over broad spectrum antibiotics. The latter will often eradicate normal flora and allow secondary invasion of highly resistant organisms. Attempts at isolation of these patients are of little value since the organisms causing pulmonary infection are almost always of endogenous origin from another infected site.

Principles of Management. Principles of management are listed in Table 4. Management includes support of ventilation and gas exchange, minimizing further pulmonary damage, and ancillary therapeutic maneuvers.

We have learned that high tidal volume ventilation with both inspiratory plateau and positive end-expiratory pressure (PEEP) improves oxygen transport across the lung (see figure 9 for pressure wave form of inspiratory plateau and PEEP compared

TABLE 4.
MANAGEMENT PRINCIPLES IN ARDS

1. Prevent alveolar collapse and maintain oxygenation
 - a. Tracheostomy
 - b. Volume respirator
 - c. Oxygen control
 - d. Positive end-expiratory pressure (PEEP)
2. Prevent further injury
 - a. Oxygen control
 - b. Fluid restriction
 - c. Antibiotics for specific infections
 - d. Corticosteroid drugs

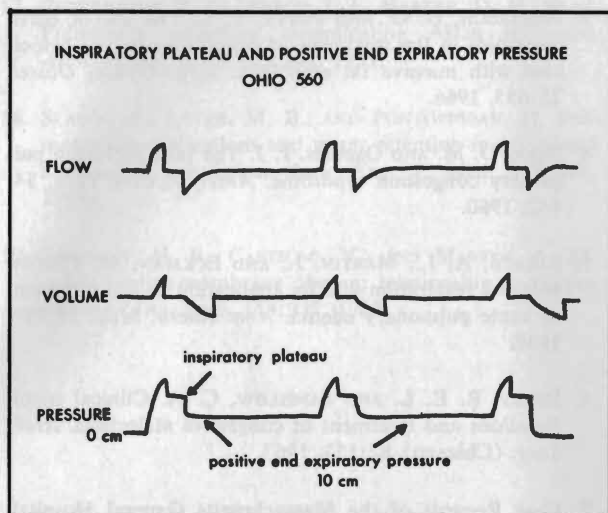


Fig. 9—Modified pressure wave forms showing inspiratory plateau and positive end-expiratory pressure (arrows).

to normal pressure wave form, figure 10). The effects of inspiratory plateau and positive end-expiratory pressure are additive in certain patients; this is demonstrated in Table 5.

Our clinical (1, 2) and laboratory experience

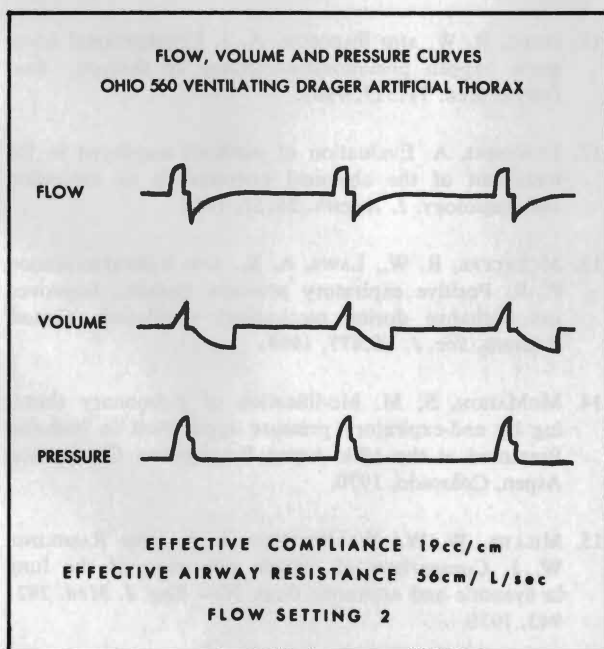


Fig. 10—Flow and pressure wave forms using Ohio 560 ventilator and artificial thorax. Note square wave form (flow); volume signal electrically integrated from flow signal. Inspiratory flow wave oriented upward and expiratory flow wave downward.

TABLE 5.
ADULT RESPIRATORY DISTRESS SYNDROME
(IMPROVED OXYGEN TRANSPORT WITH INSPIRATORY
PRESSURE* AND POSITIVE END-EXPIRATORY
PRESSURE—PEEP)

44-year-old man—multiple trauma, liver laceration 40 units whole blood, 8 liters Ringer's lactate

	2 P.M. in OR	4 P.M. Vol Resp 1000 ml TV	4:30 P.M. + Insp Plateau 2 sec	5 P.M. + Insp Hold Positive End-exp Plateau 10 cm
PrO ₂	570	345	345	345
PaO ₂	81	82	101	151
PaCO ₂	27	25	23	25

* Courtesy of D. Boyd Bigelow, M.D., Chief of Respiratory Diseases, St. Anthony's Hospital, Denver, Colorado.

(20) indicates that PEEP⁶ is fundamental in improving oxygenation by decreasing the alveolar arterial oxygen tension difference. The inspiratory plateau may have similar value, but this has provided a lesser improvement in oxygenation than PEEP in our recent experience. This ventilator capability is only available as a standard feature on one machine in common use today⁷.

PEEP will allow improved oxygen transport of lower inspired oxygen fractions on most occasions (1, 2). It is likely that the use of high pressure constant volume ventilation, inspiratory plateau, and end-expiratory pressure all provide local tamponade of circulation to areas of poor ventilation, and these techniques maintain alveolar stability by preventing alveolar collapse on expiration (8, 14). It is clear that PEEP increases the functional residual capacity and reduces right to left shunting (13, 14, 20). End-expiratory pressures of 5 to 15 cm H₂O are used, and in clinical situations no apparent adverse effect on venous return and cardiac output can be noticed. It is likely that this small back pressure is dissipated across the stiffened lung and therefore is not "felt" in the pulmonary circulation (20).

⁶ PEEP has also been termed CPPB (continuous positive pressure breathing) in earlier reports. We now believe CPPB is a confusing term since this designation was first advanced to refer to breathing against a fixed pressure head, and did not originally refer to both positive inspiratory and expiratory pressures by a ventilator (5).

⁷ Ohio 560 Respirator, Ohio Medical Products, Madison, Wisconsin.

In addition, the possibility of fluid overload should be minimized by recognizing the tendency toward fluid retention during artificial ventilation and the possibility of transudation of fluid into alveolar spaces in the face of an expanded circulatory volume (18).

Clinical experience indicates the use of corticosteroid drugs is highly beneficial in patients with the adult respiratory distress syndrome. Evidence supporting the use of corticosteroid drugs is based both on theoretic considerations and clinical observations. Corticosteroid drugs are known to combat the effect of fat found in the lungs in the respiratory distress syndrome associated with massive trauma (9). Corticosteroids have been shown to be effective both clinically and in laboratory models of fat embolism (3, 21). Also, evidence that corticosteroid drugs inhibit adherence of leukocytes to the pulmonary vascular bed in hemorrhagic shock has recently been presented (22). Adherent leukocytes may cause pulmonary damage by the release of proteolytic enzymes. Finally, corticosteroids may enhance the secretion of surfactant, which is invariably absent in lungs with the adult respiratory distress syndrome (1) and which is needed to maintain alveolar stability (8).

Specific pulmonary and other infections must be managed with appropriate antibiotics. We believe corticosteroids are effective in aspiration pneumonia probably by correcting the inflammatory effects of acid gastric juices on the lung (12). Penicillin is effective against mouth organisms and is probably the antibiotic of choice. Kanamycin is effective against a broad spectrum of gram-negative organisms.

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Bedside Assessment of Left Ventricular Function in the Respiratory Intensive Care Unit*

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The measurement of the central venous pressure is a widely used technique for gaining information concerning the relationship of the blood volume as it relates to cardiac function. This concept has been widely popularized, and the central venous pressure measurement is extremely useful; however, it has too frequently been thought to be a direct measurement of cardiac function.

The normal value of the central venous pressure is 6 to 12 cm of water as measured vertically from the midaxillary line, preferably with the patient in a supine position. The tip of the catheter, if properly placed, is either in the superior vena cava or the right atrium. The pressure measured is obviously the mean value of the pressure in that particular vascular compartment. If we are to use the central venous pressure as a measurement of left heart function, we are really interested in the relationship of the superior vena cava or right atrial pressure to the left ventricular end diastolic pressure or the pulmonary capillary wedge pressure.

It is known that the mean right atrial pressure does not always accurately predict the mean left atrial pressure, and it is in reality the left atrial pressure that constitutes the filling pressure for the left ventricle and is the more important measurement. It is known that acute left ventricular failure may give rise to increased pulmonary capillary wedge pressure with pulmonary edema in the presence of a normal central venous pressure.

The cardiac output is partially determined by

the amount of fluid that is available to the cardiac pump. Obviously, if only a small amount of fluid is placed into the pump, it follows that only a small amount of fluid can be ejected. It has been found that the central venous pressure measurement gives a good indication of the peripheral venous capacity and the state of the blood volume. If there is a low central venous pressure or low mean right atrial pressure, it generally indicates underfilling of the peripheral circulation which gives rise to a lowered cardiac output. An elevation of the central venous pressure usually indicates a full peripheral circulation, and this should lead to an increased cardiac output. An elevation of the central pressure in the presence of a normal to reduced peripheral volume generally indicates either a decrease in pump efficiency or an increased resistance to flow through the pulmonary vasculature.

The indications for monitoring the central venous pressure are:

- 1) Shock: In hypovolemic shock the central venous pressure is an invaluable guide to effective fluid replacement. The measurement of the CVP often provides the means by which we are able to wean patients off vasopressors after restoring adequate blood volume. In septic shock, there is frequently reduced blood volume as well as impaired cardiac efficiency. The central venous pressure measurement enables us to give the patient an adequate or optimal blood volume, and if this does not restore adequate blood pressure, we then add Isuprel® or massive steroids to increase pump efficiency and to dilate the peripheral vascular beds. In cardiac shock the monitoring of

* Presented by Dr. Parker at the Symposium on Respiratory Failure, May 27, 1972, at Richmond, Virginia.

central venous pressure has lesser value than hypovolemic or septic shock. It has been shown that elevation of the central venous pressure may be a relatively late sign of cardiac failure.

2) To monitor fluid therapy in patients with cardio-respiratory disorders: Patients with histories of congestive heart failure or chronic obstructive pulmonary disease are at relatively greater risk when exposed to the hazards of trauma, major surgery, or prolonged illness with protracted vomiting or blood loss. One of the primary reasons for this much greater risk is the difficulty in optimally replacing the blood volume without overloading the circulation and causing diminution in cardiac function or interstitial edema, thus reducing pulmonary function.

3) Acute renal failure: In the presence of acute renal failure it is essential to rule out hypovolemia as a cause. This is a completely reversible cause, but it must be discovered and treated early in order to avoid acute tubular necrosis. Whenever there is any doubt as to the adequacy of the peripheral vascular volume in the presence of acute renal failure, the central venous pressure should be measured and monitored in an effort to eliminate pre-renal factors as a cause of the renal failure.

The physician who is asked to see a patient with an elevated central venous pressure and a cardio-respiratory problem has to consider many factors. Pulmonary hypertension, that is, a pressure in the pulmonary artery greater than 35/15 mm Hg, can cause elevation of the central venous pressure.

As you look at the causes of pulmonary hypertension (Table 1) and note the variety of disorders and the variety of treatments that would be necessary, it is obvious that the mean right atrial pressure may at times be insufficient physiological data to enable us to arrive at a correct diagnosis.

Bedside clinicians have been measuring the pulmonary capillary wedge pressure for years by listening for the presence of fine inspiratory rales at the bases of the lungs which indicate the presence of pulmonary edema. It is known that rales and pulmonary edema do not occur unless the wedge pressure has approached 25 mm Hg. However, it must be kept in mind that pulmonary edema or pulmonary congestion may exist on a basis of a pulmonary disease giving rales in the lung bases that may be indistinguishable from those rales heard in congestive heart failure, in which

TABLE 1.
PULMONARY HYPERTENSION
(Greater than 35/15 mm Hg)

1. Elevation of pulmonary capillary pressure and/or left atrial pressure.
 - a. Increased volume, fluid overload.
 - b. Elevated left ventricular end diastolic pressure.
 - c. Mitral valvular disease.
 - d. Obstruction proximal to the mitral valve.
2. Decrease in total cross sectional area of the pulmonary vascular bed.
 - a. Pulmonary emboli.
 - b. Medial hypertrophy of small arterioles.
 - c. Functional reduction of the pulmonary vascular bed due to hypoxia and/or acidosis.
3. Increase in pulmonary arterial blood flow with left to right shunts.

case the pulmonary capillary wedge pressure may be normal or may even be reduced. Therefore, it is obvious that a means for determining the pulmonary capillary wedge pressure at the bedside would be useful in the management of the more difficult cardio-respiratory problems. Formal cardiac catheterization is certainly of great help; however, it is frequently difficult to have use of the cardiac catheterization facilities on an emergency basis, and it is frequently very difficult to transport the patient from the intensive care unit to the cardiac catheterization laboratory. Bedside right heart catheterization is now a practical procedure using the recently perfected Swan-Ganz catheter.

The Swan-Ganz balloon tipped catheter is a number 5 French double lumen catheter with a small balloon at its tip that can be inflated with 0.8 cc of air or carbon dioxide. The Swan-Ganz catheter can be inserted into the vein either percutaneously through a 12 gauge needle or via a cutdown, and is advanced to the right atrium much as a central venous pressure catheter is inserted. When the pressure tracing curves, typical of the catheter with its tip in the thoracic cage, are seen, the balloon is inflated. The catheter is carried by the current of blood and quickly passes through the right ventricle into the pulmonary artery. In the original report concerning this catheter, the average time for passage from the right atrium to the pulmonary artery was 35 seconds, and the ease of passage has been borne out by our use of the catheter in the respiratory intensive care unit.

Once the catheter is in the pulmonary artery, the balloon is left blown up, and it is then slowly advanced to the wedge position at which time the pressure contour will damp considerably. At this point, the balloon is deflated and the catheter is advanced approximately another two to three centimeters. The tip now lies in a small peripheral pulmonary artery, and with the balloon down we can measure the pulmonary artery pressure. When the balloon is inflated the pulmonary artery pressures are damped, and the pressure recording then is essentially that of the pulmonary capillary wedge pressure. This procedure does not require the use of fluoroscopy and can be done quite safely if the pressure pulse contours and the electrocardiogram are monitored. It has been determined that the pulmonary capillary wedge pressures as determined by the Swan-Ganz catheter, when compared with simultaneous direct left atrial pressure measurements, have been approximately equal. There have been no serious cardiac arrhythmias reported as yet with the Swan-Ganz catheter. There appear to be fewer cardiac arrhythmias when using the Swan-Ganz catheter than there are when using the regular cardiac catheter under direct fluoroscopic control. The explanation for this probably lies in the fact that the tip of the catheter is cushioned by the balloon. Other complications would be those pursuant to any indwelling catheter left in position for a prolonged period of time.

I would like to describe several cases in which the Swan-Ganz catheter and bedside measurement of pulmonary capillary wedge pressure were invaluable in helping us to direct therapy. The first case is that of a 59-year-old man who was referred to the Medical College of Virginia due to severe dyspnea. He had been hospitalized approximately two weeks prior to his admission because of congestive heart failure and chronic obstructive pulmonary disease. He had been treated with digoxin, diuretics, and bronchodilators with improvement. Following his discharge his condition deteriorated and he developed a cough with purulent sputum and was transferred to MCV where he arrived with severe tachypnea and cyanosis. His past history revealed admission to MCV three years previously with congestive heart failure, atrial flutter, and chronic obstructive pulmonary disease. With cardioversion, digoxin, and the care of the lung disease, he had improved and no specific cardiac diagnosis was made. On physical examination on admission, his temperature was 100.8°, his pulse was

106, his respiratory rate was 36, his blood pressure was 120/80, and there was neck vein distention at 40°. Chest examination revealed that his lungs were hyperresonant to percussion, that there was an increased anterior-posterior diameter, and that there were bilateral diffuse wet fine inspiratory rales. Examination of the heart revealed a grade III holosystolic murmur maximal at the xiphoid radiating to the axilla. There was an S-3 gallop and there was a question of an opening snap. His liver was enlarged and was somewhat tender. The extremities showed 1+ pitting edema. The arterial blood gases on room air on admission showed a P_{O_2} of 29, P_{CO_2} of 75, pH of 7.22, with a bicarbonate of 29. Following treatment with a 24% ventimask the P_{O_2} rose to 45, the P_{CO_2} slightly improved at 70, the pH was improved at 7.31, and the bicarbonate was 34. It was felt initially that the elevation of his neck veins and his obvious cor pulmonale could be explained almost exclusively by chronic obstructive pulmonary disease. However, his chest x-ray revealed cardiomegaly, and there was a hazy pulmonary infiltrate with increased blood flow to the apices. This led to speculation that there was something present other than chronic obstructive pulmonary disease. A Swan-Ganz catheter was inserted, and it was found that his pulmonary artery pressure was 75/37 with a mean pressure of 42, and his wedge pressure had a mean of 20. The wedge pressure remained elevated even after his arterial blood gases were improved. This provided sufficient stimulus to get a formal cardiac catheterization. Significant mitral stenosis was found and mitral commissurotomy was performed. The patient has done quite well following this operation.

The second case involved a 23-year-old man admitted due to a progressively worsening cough productive of bloody, foamy sputum. He had first noted the cough six weeks prior to admission and had received Lincocin® with slight improvement. However, he later became worse and began to cough up bloody sputum and was referred to MCV. He delayed his admission one week and became much worse and was admitted *in extremis*. Physical examination showed blood pressure was 94/60, pulse was 120, respiratory rate was 40, and temperature was 102°. The patient was acutely ill, sitting straight up in bed, and was exceedingly short of breath. He had palpable cervical axillary and inguinal nodes. The neck veins were distended, and he was coughing up a foamy, pink sputum which was thought to be characteristic of pulmonary edema. He had rales throughout his

lung fields and an enlarged tender liver. Review of his chest x-rays showed a widespread pulmonary infiltrate, and there was a question as to whether his cardiac silhouette had enlarged. Blood gases showed that the P_{O_2} was 42, the P_{CO_2} was 29, and the pH was 7.38 with a bicarbonate of 16. The initial diagnosis was pulmonary edema with cause unknown. In this particular case, we were unable on clinical grounds to adequately determine whether this was pulmonary edema on the basis of lung disease or pulmonary edema on the basis of cardiac disease. He was transferred to the respiratory intensive care unit and a Swan-Ganz was passed; this showed that the pulmonary artery pressure was 45/35 mm Hg, and the pulmonary capillary wedge pressure was quite low at 0 to 5 mm Hg. This information led to an open lung biopsy which revealed noncaseating granulomas and an interstitial pneumonia. He was treated with isoniazide, streptomycin, ethambutal, and solu-medrol. He was ventilated with a volume respirator via a tracheostomy performed at the time of lung biopsy. Over the next week his pulmonary congestion rapidly cleared and his blood gases returned to normal. This case demonstrates quite graphically that pulmonary edema is not necessarily on a cardiac basis and it may be difficult, if not impossible, to tell at the bedside which is the primary physiological disturbance.

The third case in which the Swan-Ganz catheter was helpful concerns that of a young man who was brought to our emergency room unconscious with pinpoint pupils and irregular slow respirations. He was immediately intubated, placed on a respirator, and given 10 mg of nalline intravenously. He became more responsive and was coughing up foamy sputum. His blood gases on admission revealed a P_{O_2} of 35, a P_{CO_2} of 70, and a pH of 6.94 with a bicarbonate of 14. The chest x-ray showed diffuse pulmonary edema with a normal cardiac silhouette. The patient at this time had a Swan-Ganz catheterization performed and revealed a low pulmonary capillary wedge pressure. This finding allowed us to push fluids to increase his blood pressure, even in the presence of pulmonary edema. He was continued on the ventilator, and over the next 18 hours he was able to be extubated; within three days he was completely normal. At that time cardiac consultation was ob-

tained and it was felt that there was no cardiac basis for the pulmonary edema. We were unable to elicit a positive history of heroin or other drug abuse.

In summary, central venous pressure measurement has greatly extended our ability to care for severely ill patients with cardiopulmonary disorders and difficult fluid balance problems. However, the central venous pressure measurement is essentially a measurement of the mean right atrial pressure. It may not be a reliable indicator of the mean left atrial pressure, which is essentially the filling pressure of the left ventricle that determines the cardiac output and the blood pressure. There is now available, and in use at this institution, a bedside method for determination of the pulmonary artery and pulmonary capillary wedge pressures. In selected cases, the data obtained with this catheter have been of great aid in management of the patient. The ease and safety of the procedure seems to be well documented and should make it accepted both by the doctor and the patient.

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The Respiratory Intensive Care Unit*

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Each hospital which accepts the responsibility of providing total patient care must establish an area capable of providing care for patients with acute respiratory failure. This does not necessarily have to be a respiratory intensive care unit but may well be an area within a general intensive care unit. The reasons for a designated area are that nursing service personnel, who are a most important portion of the intensive care team, must be adequately trained and experienced with the equipment which is becoming more sophisticated and complicated. The nursing care techniques are those techniques of good nursing care and should be learned by any intensive care unit nurse. Additionally, paramedical personnel need to be trained to provide the type of care that is of great importance in the delivery of acute intensive care to this very ill group of patients. A respiratory intensive care unit was established at the Medical College of Virginia in 1967. This was initially done at the request and with the support of the Federal Public Health system and has been continued by the hospital following the discontinuation of grant support. The unit functions as a patient care area; a teaching laboratory for house staff, nurses, and medical students; and a clinical research laboratory to study the techniques of respiratory care and the pathophysiologic processes which occur in patients with respiratory failure. The unit has lent itself well to these areas while performing its primary purpose, that is, providing superior patient care for patients with acute respiratory failure.

This unit functions within the Department of Medicine and as a regular rotation for the second year medical residents and for the straight medical

interns. Each of these groups of house officers spends one month in rotation on this service. In addition there are medical students and house officers who elect to spend time on this service available most of the time. The nursing service has been trained by the attending physicians in addition to the senior nurses, and it has a continuing program of review and training of respiratory care skills. With this approach, in addition to having a physical facility designed for respiratory intensive care, the following patient care statistics have been generated.

There have been a total of 629 admissions of 503 patients to the respiratory intensive care unit from October, 1967 through October, 1971. Table 1 shows the multiple types of illnesses treated which resulted in respiratory failure. Approximately one-third of these patients have chronic obstructive pulmonary disease and the others a myriad of problems which have resulted in respiratory failure.

Table 2 demonstrates the average bed occupancy bed-day stay and the source of these admissions. Table 3 demonstrates the same information for the group of patients with chronic obstructive pulmonary disease. There was a slightly longer stay for a patient who had chronic pulmonary disease, but other than this, there is no major difference in these two patient populations.

The definition of respiratory failure varies with investigators, however based upon a certain level of arterial oxygen and carbon dioxide. Table 4 contains the values seen in our patients. There were only four patients who had a P_{CO_2} of less than 60 in this group of patients with chronic obstructive pulmonary disease; thus we are effectively dealing with a group of people who meet the criteria for respiratory failure in most series. It can also be seen that there was considerable improvement in the blood gases at the time of discharge from the hospital.

* Presented by Dr. Baker at the Symposium on Respiratory Failure, May 25, 1972, at Richmond, Virginia.

TABLE 1.
RESPIRATORY INTENSIVE CARE UNIT MCV
1967-1971

Diagnosis	No. Adms.	Percent
Total Admissions	629	
Total Patients	503	
COPD	203	32.3
Pneumonia (complicated)	78	12.4
Drug Overdose	46	7.4
Postoperative Complication	40	6.4
Asthma	33	5.2
Muscular Dystrophy	24	3.8
Kyphoscoliosis	22	3.5
Chest Trauma	21	3.3
Guillain-Barré	21	3.3
Pulmonary Fibrosis	13	2.1
TOTAL:		80%
Others (2% or less)		
Pulmonary Emboli	Cystic Fibrosis	
Multiple Trauma	Polymyositis	
Respiratory Arrest	Drug Reaction	
Myasthenia Gravis	Bronchiolitis	
Laryngotracheal Obstruction	Myxedema	
Tetanus	Mediastinal Abscess	
Burns & Smoke Inhalation	Reyes Disease	
Pulmonary Malignancy	Massive Hemoptysis	
Meningitis & Encephalitis	Gunshot Wounds	
C.V.A.	Fat Emboli	
Obesity Hypoventilation	Pulmonary Hemosiderosis	
Post Partum Respiratory Failure	Cardiac Disease with Ventilatory Failure	
TOTAL:		20%

The approach to the management of respiratory failure is properly divided into two phases, conservative and complicated. Approximately 80% of patients who have acute respiratory failure with chronic obstructive lung disease should be able to be

TABLE 2.
RESPIRATORY INTENSIVE CARE UNIT MCV
Acute Respiratory Failure from All Causes
(1967-1971)

Total admissions	629
Number of patients	503
Average bed occupancy	72%
Average bed stay	10 days
Direct admissions	55%
Transfer admissions	45%
126 readmissions of 43 patients	

TABLE 3.
RESPIRATORY INTENSIVE CARE UNIT MCV
Acute Respiratory Failure with COPD
(1967-1971)

Total admissions	203
Number of patients	131
Average bed stay	12.3 days
Average hospital stay after transfer from RICU (1967-1970)	7.8 days
Direct admissions	60%
Transfer admissions	40%
72 readmissions of 28 patients	

managed with conservative or low-flow oxygen type therapy as has been described elsewhere in the symposium. Our respiratory unit sees a skewed population of patients, that is, those patients who are refractory to or who have failed with conservative management elsewhere in the hospital; thus, our patient population demonstrates an unusually large percentage of patients who require assisted ventilation. Table 5 demonstrates this fact as well as our results of low-flow oxygen therapy in the respiratory unit. The errors in oxygen therapy occurred early in our experience and consisted basically of giving patients more oxygen than necessary for management of their problem. Approximately one-third of the patients had a tracheostomy at the time of admission. Some of these are patients with chronic tracheostomies and are readmissions to the respiratory unit. Others had required tracheostomy for management prior to transfer to the respiratory intensive care unit.

It has been interesting to us to evaluate the results of our statistics from the mortality of patients within the respiratory unit (Table 6). A year prior

TABLE 4.
ACUTE RESPIRATORY FAILURE
CHRONIC OBSTRUCTIVE PULMONARY DISEASE
(1967-1970)

Arterial Pa _{CO₂}	
Before Definitive Therapy	Discharge
73 ± 16 mm Hg	47 ± 8 mm Hg
Arterial Pa _{O₂}	
Admission	Discharge
36 ± 9 mm Hg	59 ± 11 mm Hg

TABLE 5.
OXYGEN THERAPY IN PATIENTS WITH COPD
(1967-1970)
152 Admissions

Controlled oxygen therapy		
Attempts	Success	Failure
83	19 (23%)	64 (77%)
A. Reason for failure of low-flow O ₂		Admissions
Clinical worsening with conservative management		47
Intubation to facilitate management		12
Errors in O ₂ therapy		5
B. Management after failure of low-flow O ₂		
Intubation (subsequent tracheostomy in 24)		36
Tracheostomy		28

to the development of the respiratory intensive care unit, approximately 62 patients were seen in consultation by the attending staff, who subsequently have run the respiratory intensive care unit. Of these there were 27 in-hospital deaths or a mortality of 43.5%. During the four years of operation of the respiratory intensive care unit, there has been a mortality of less than 10%. In the patients with chronic obstructive pulmonary disease, there was a mortality of less than 90% over the four years. This is compared in Table 7 to the mortality of patients admitted to the Medical College of Virginia hospitals with chronic obstructive pulmonary disease and a P_{CO₂} above 59 mm of mercury during the year prior to opening of the respiratory intensive care unit. As can be seen, there was reduction in mortality in this group of patients, which is a roughly comparable group to the people managed within the respiratory unit of from 47 to 8.9%.

The cause of death of patients within the respiratory unit is listed in Table 8. Of major importance here, one must note that sepsis was responsible for 18 of the 60 deaths. This is generally complicated

TABLE 6.
MORTALITY IN PATIENTS WITH ACUTE
RESPIRATORY FAILURE

	Admissions	Deaths	Mortality
One year prior to RICU	62	27	43.5%
4 years RICU (1967-1971)	611*	60	9.8%

* 18 patients excluded because of brain death on admission

TABLE 7.
MORTALITY IN PATIENTS WITH ACUTE RESPIRATORY
FAILURE AND COPD

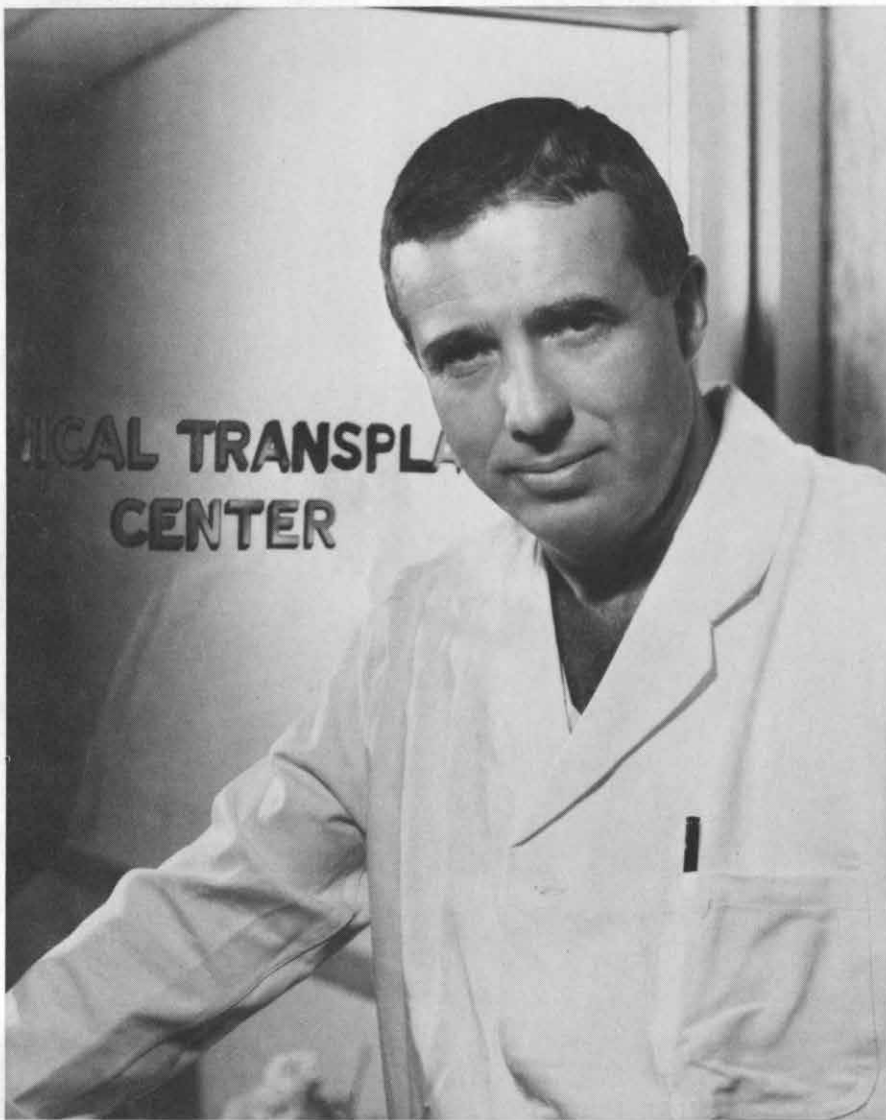
	Admissions	Deaths	Mortality
1. One year prior to RICU Patients with COPD and Pa _{CO₂} , 60 mm Hg or greater	45	21	47%
2. Four years RICU (1967-1971)	203	18	8.9%

sepsis of gram negative etiology and indicates that pulmonary infection is a major cause of death in patients with respiratory failure. The cardiovascular failure is a complex of etiologies involving acute cardiac standstill or ventricular tachycardia as well as central and peripheral cardiovascular failure with unresponsive hypotension.

As is indicated in the foregoing paragraphs and tables, the respiratory intensive care unit at the Medical College of Virginia provides, in addition to an outstanding patient care service, the opportunity for a large number of our house officers, medical students, graduate nurses, and nursing students to become familiar with the techniques and equipment available for the management of acute respiratory failure. The application of these techniques has led to a remarkable reduction in the mortality in this group of very ill patients. These techniques are explained by others and are included in this symposium and may be applied to any hospital.

TABLE 8.
RICU DEATHS
(1967-1971)

Cause	Number
Cardiovascular failure	25
Sepsis	18
Ventilatory failure	5
Technical problems with artificial airways	3
Bleeding abnormalities	3
Myocardial infarction	2
Renal failure	2
Hepatic failure	1
Pulmonary emboli	1
TOTAL:	60



In Memoriam

DAVID M. HUME, M.D.

October 21, 1917—May 19, 1973

**Professor and Chairman, Department of Surgery
Medical College of Virginia, Health Sciences Division of
Virginia Commonwealth University, Richmond, Virginia**





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Though Talwin® Tablets can be compared to codeine in analgesic efficacy, Talwin is not subject to narcotic controls. For patients who require potent analgesia for prolonged periods, Talwin can provide consistent, long-range relief, with fewer of the consequences you've come to expect with narcotic analgesics.

- **Comparable to codeine in analgesic efficacy:** one 50 mg. Talwin Tablet appears equivalent in analgesic effect to 60 mg. (1 gr.) of codeine. Onset of significant analgesia usually occurs within 15 to 30 minutes. Analgesia is usually maintained for 3 hours or longer.

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- **Not subject to narcotic controls:** convenient to prescribe—day or night—even by phone.

- **Generally well tolerated by most patients:** infrequently cause decrease in blood pressure or tachycardia; rarely cause respiratory depression or urinary retention; seldom cause diarrhea or constipation. If dizziness, lightheadedness, nausea or vomiting are encountered, these effects may decrease or disappear after the first few doses. (See last page of this advertisement for a complete discussion of Adverse Reactions and a Brief Summary of other Prescribing Information.)

50 mg. Tablets

Talwin[®]
brand of
pentazocine (as hydrochloride)

in moderate to severe pain

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in moderate to severe pain





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in chronic pain: continued
relief without risk of tolerance

Talwin® Tablets brand of pentazocine (as hydrochloride) Analgesic for Oral Use—Brief Summary

Indications: For the relief of moderate to severe pain.

Contraindication: Talwin should not be administered to patients who are hypersensitive to it.

Warnings: Drug Dependence. There have been instances of psychological and physical dependence on parenteral Talwin in patients with a history of drug abuse and, rarely, in patients without such a history. Abrupt discontinuance following the extended use of parenteral Talwin has resulted in withdrawal symptoms. There have been a few reports of dependence and of withdrawal symptoms with orally administered Talwin. Patients with a history of drug dependence should be under close supervision while receiving Talwin orally.

In prescribing Talwin for chronic use, the physician should take precautions to avoid increases in dose by the patient and to prevent the use of the drug in anticipation of pain rather than for the relief of pain. **Head Injury and Increased Intracranial Pressure.** The respiratory depressant effects of Talwin and its potential for elevating cerebrospinal fluid pressure may be markedly exaggerated in the presence of head injury, other intracranial lesions, or a preexisting increase in intracranial pressure. Furthermore, Talwin can produce effects which may obscure the clinical course of patients with head injuries. In such patients, Talwin must be used with extreme caution and only if its use is deemed essential.

Usage in Pregnancy. Safe use of Talwin during pregnancy (other than labor) has not been established. Animal reproduction studies have not demonstrated teratogenic or embryotoxic effects. However, Talwin should be administered to pregnant patients (other than labor) only when, in the judgment of the physician, the potential benefits outweigh the possible hazards. Patients receiving Talwin during labor have experienced no adverse effects other than those that occur with commonly used analgesics. Talwin should be used with caution in women delivering premature infants.

Acute CNS Manifestations. Patients receiving therapeutic doses of Talwin have experienced, in rare instances, hallucinations (usually visual), disorientation, and confusion which have cleared spontaneously within a period of hours. The mechanism of this reaction is not known. Such patients should be very closely observed and vital signs checked. If the drug is reinstated it should be done with caution since the acute CNS manifestations may recur.

Usage in Children. Because clinical experience in children under 12 years of age is limited, administration of Talwin in this age group is not recommended.

Ambulatory Patients. Since sedation, dizziness, and occasional euphoria have been noted, ambulatory patients should be warned not to operate machinery, drive cars, or unnecessarily expose themselves to hazards.

Precautions: Certain Respiratory Conditions. Although respiratory depression has rarely been reported after oral administration of Talwin, the drug should be administered with caution to patients with respiratory depression from any cause, severe bronchial asthma and other obstructive respiratory conditions, or cyanosis.

Impaired Renal or Hepatic Function. Decreased metabolism of the drug by the liver in extensive liver disease may predispose to accentuation of side effects. Although laboratory tests have not indicated that Talwin causes or increases renal or hepatic impairment, the drug should be administered with caution to patients with such impairment.

Myocardial Infarction. As with all drugs, Talwin should be used with caution in patients with myocardial infarction who have nausea or vomiting.

Biliary Surgery. Until further experience is gained with the effects of Talwin on the sphincter of Oddi, the drug should be used with caution in patients about to undergo surgery of the biliary tract.

Patients Receiving Narcotics. Talwin is a mild narcotic antagonist. Some patients previously given narcotics, including methadone for the daily treatment of narcotic dependence, have experienced mild withdrawal symptoms after receiving Talwin.

CNS Effect. Caution should be used when Talwin is administered to patients prone to seizures; seizures have occurred in a few such patients in association with the use of Talwin although no cause and effect relationship has been established.

Adverse Reactions: Reactions reported after oral administration of Talwin include **gastrointestinal:** nausea, vomiting; infrequently constipation; and rarely abdominal distress, anorexia, diarrhea. **CNS effects:** dizziness, lightheadedness, sedation, euphoria, headache; infrequently weakness, disturbed dreams, insomnia, syncope, visual blurring and focusing difficulty, hallucinations (see **Acute CNS Manifestations** under **WARNINGS**); and rarely tremor, irritability, excitement, tinnitus. **Autonomic:** sweating; infrequently flushing; and rarely chills. **Allergic:** infrequently rash; and rarely urticaria, edema of the face. **Cardiovascular:** infrequently decrease in blood pressure, tachycardia. **Other:** rarely respiratory depression, urinary retention.

Dosage and Administration: Adults. The usual initial adult dose is 1 tablet (50 mg.) every three or four hours. This may be increased to 2 tablets (100 mg.) when needed. Total daily dosage should not exceed 600 mg.

When antiinflammatory or antipyretic effects are desired in addition to analgesia, aspirin can be administered concomitantly with Talwin.

Children Under 12 Years of Age. Since clinical experience in children under 12 years of age is limited, administration of Talwin in this age group is not recommended.

Duration of Therapy. Patients with chronic pain who have received Talwin orally for prolonged periods have not experienced withdrawal symptoms even when administration was abruptly discontinued (see **WARNINGS**). No tolerance to the analgesic effect has been observed. Laboratory tests of blood and urine and of liver and kidney function have revealed no significant abnormalities after prolonged administration of Talwin.

Overdosage: Manifestations. Clinical experience with Talwin overdosage has been insufficient to define the signs of this condition.

Treatment. Oxygen, intravenous fluids, vasopressors, and other supportive measures should be employed as indicated. Assisted or controlled ventilation should also be considered. Although nalorphine and levallorphan are not effective antidotes for respiratory depression due to overdosage or unusual sensitivity to Talwin, parenteral naloxone (Narcan®, available through Endo Laboratories) is a specific and effective antagonist.

Talwin is not subject to narcotic controls.

How Supplied: Tablets, peach color, scored. Each tablet contains Talwin (brand of pentazocine) as hydrochloride equivalent to 50 mg. base. Bottles of 100.

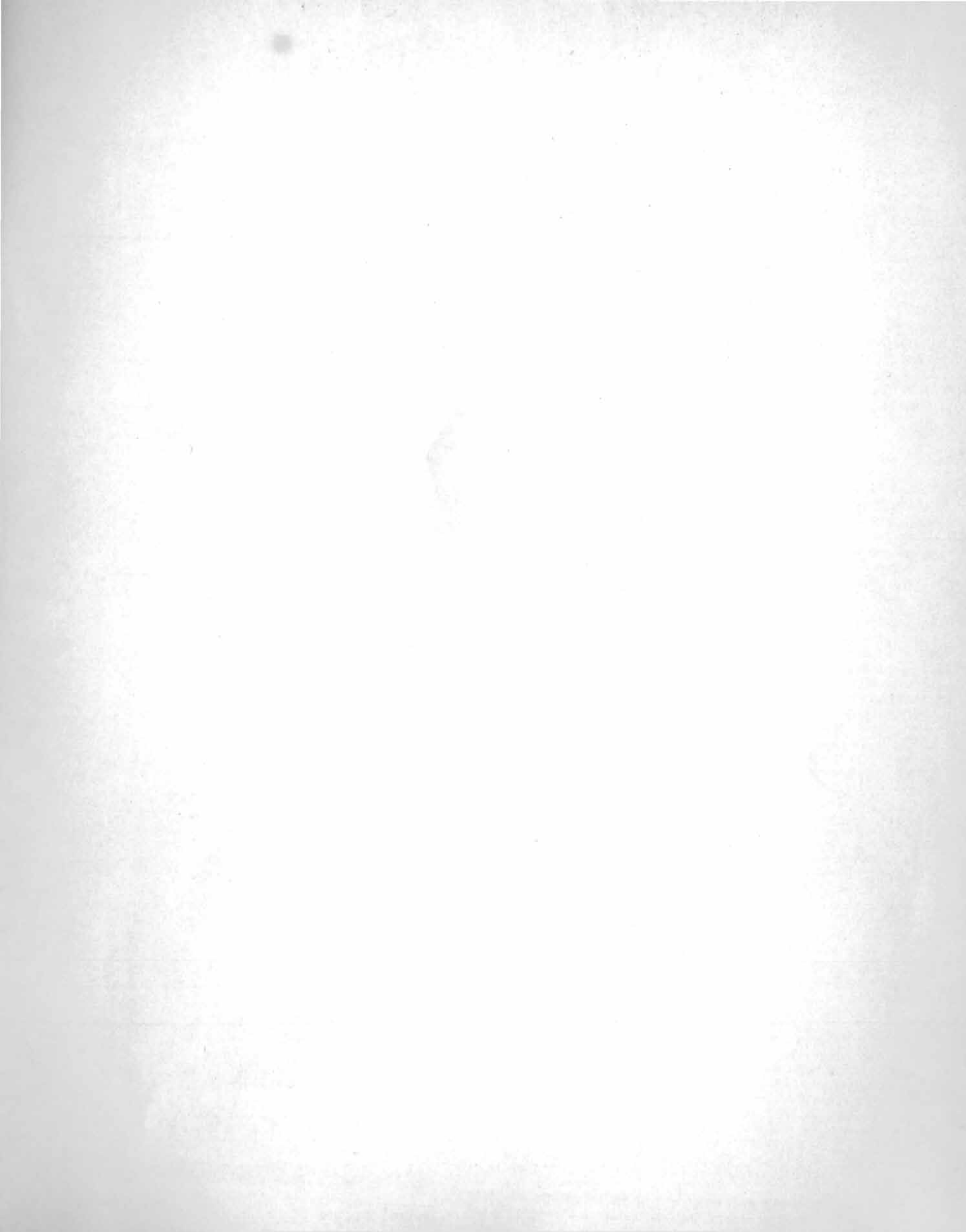
50 mg. Tablets

Talwin®
brand of
pentazocine (as hydrochloride)

in moderate to severe pain

Winthrop Winthrop Laboratories, New York, N.Y. 10016

(100714)



Before prescribing, please consult complete product information, a summary of which follows:

Indications: Tension and anxiety states, somatic complaints which are concomitants of emotional factors; psychoneurotic states manifested by tension, anxiety, apprehension, fatigue, depressive symptoms or agitation; symptomatic relief of acute agitation, tremor, delirium tremens and hallucinosis due to acute alcohol withdrawal; adjunctively in skeletal muscle spasm due to reflex spasm to local pathology, spasticity caused by upper motor neuron disorders, athetosis, stiff-man syndrome, convulsive disorders (not for sole therapy).

Contraindicated: Known hypersensitivity to the drug. Children under 6 months of age. Acute narrow angle glaucoma; may be used in patients with open angle glaucoma who are receiving appropriate therapy.

Warnings: Not of value in psychotic patients. Caution against hazardous occupations requiring complete mental alertness. When used adjunctively in convulsive disorders, possibility of increase in frequency and/or severity of grand mal seizures may require increased dosage of standard anticonvulsant medication; abrupt withdrawal may be associated with temporary increase in frequency and/or severity of seizures. Advise against simultaneous ingestion of alcohol and other CNS depressants. Withdrawal symptoms (similar to those with barbiturates and alcohol) have occurred following abrupt discontinuance (convulsions, tremor, abdominal and muscle cramps, vomiting and sweating). Keep addiction-prone individuals under careful surveillance because of their predisposition to habituation and dependence. In pregnancy, lactation or women of childbearing age, weigh potential benefit against possible hazard.

Precautions: If combined with other psychotropics or anticonvulsants, consider carefully pharmacology of agents employed; drugs such as phenothiazines, narcotics, barbiturates, MAO inhibitors and other antidepressants may potentiate its action. Usual precautions indicated in patients severely depressed, or with latent depression, or with suicidal tendencies. Observe usual precautions in impaired renal or hepatic function. Limit dosage to smallest effective amount in elderly and debilitated to preclude ataxia or oversedation.

Side Effects: Drowsiness, confusion, diplopia, hypotension, changes in libido, nausea, fatigue, depression, dysarthria, jaundice, skin rash, ataxia, constipation, headache, incontinence, changes in salivation, slurred speech, tremor, vertigo, urinary retention, blurred vision. Paradoxical reactions such as acute hyperexcited states, anxiety, hallucinations, increased muscle spasticity, insomnia, rage, sleep disturbances, stimulation have been reported; should these occur, discontinue drug. Isolated reports of neutropenia, jaundice; periodic blood counts and liver function tests advisable during long-term therapy.

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