A Clinical Consideration of Cor Pulmonale

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Definition

The term cor pulmonale is generally used to define the cardiac complications of certain forms of lung disease. From knowledge gathered in the recent past, it is apparent that a number of disease processes that attack pulmonary function in a variety of ways can produce circulatory embarrassment. The mechanisms by which they do so may be fundamentally different and indeed the lungs themselves need not be directly involved. The terms cor pulmonale or pulmonary heart disease are far from ideal, since they imply cardiac disorders secondary only to pulmonary parenchymal disease, whereas the name should be more inclusive and encompass cardiac abnormalities stemming from any form of pulmonary dysfunction. It is therefore suggested that the name cor pulmonale always be coupled with the responsible etiologic agent; for example, cor pulmonale due to chronic obstructive pulmonary emphysema, due to multiple pulmonary emboli (acute or chronic), due to exogenous obesity, due to berylliosis, due to poliomyelitis, etc. Inasmuch as many of the circulatory abnormalities and the cardiac enlargement itself may be reversible in some of these instances, it seems wise to eliminate the terms acute, subacute, or chronic as applied to these circulatory complications and use them solely in relationship to the respiratory illness. Cor pulmonale would then be diagnosed only when evidences of right ventricular enlargement or failure are, or have been, shown to be present. Physiologic complications, such as anoxia, hypercapnia, polycythemia, pulmonary hypertension, could also be included in the formulation of the diagnosis. The format of the New York Heart Association lends itself admirably to this purpose. The functional and therapeutic classification would be determined not only by the state of the circulation but also by the state of the pulmonary function. The formal declaration would thus represent a complete description of the cardiopulmonary status of the patient. This diagnostic expression could even be used to indicate potential cor pulmonale before such a complication occurred. A few examples are given below.

Etiologic: Cor pulmonale due to chronic pulmonary emphysema.
Anatomic: Enlarged heart (right ventricle), enlarged pulmonary artery.
Physiologic: Pulmonary hypertension, anoxia, hypercapnia, secondary polycythemia, normal sinus rhythm, cardiac insufficiency.

Functional and Therapeutic: IV-D.
When such a patient has been adequately treated his diagnosis might appear as:
Etiologic: Cor pulmonale due to chronic pulmonary emphysema.
Anatomic: —
Physiologic: Anoxia, normal sinus rhythm.
Functional and Therapeutic: II-C.

Another example follows:
Etiologic: Cor pulmonale due to pulmonary emboli, multiple, recurrent.
Anatomic: Enlarged heart (right ventricle), enlarged pulmonary artery.
Physiologic: Pulmonary hypertension, normal sinus rhythm.
Functional and Therapeutic: III-C.

The crux of the definition of cor pulmonale given above lies in the demonstration of cardiac enlargement or failure in association with a disease process known to attack primarily the lungs or some aspect of the act of
breathing and in so doing to compromise right ventricular function. It is clear that the presence of pulmonary artery hypertension per se does not constitute evidence of cor pulmonale. Indeed, there are many conditions that produce pulmonary hypertension, e.g., congenital heart disease, mitral stenosis, left ventricular failure, in which the basic abnormality is not a disturbance of pulmonary function. Therefore these cardiac states should not be included under the heading of cor pulmonale. Furthermore, it is now certain that all pulmonary disorders which induce mild or even moderate pulmonary hypertension do not necessarily go on to the complication of right heart involvement. The right ventricle has great adaptability and pulmonary artery pressure elevation alone may not, ipso facto, precipitate a disturbance in its function. An analogous situation obtains in the relationship of systemic hypertension to changes in the left ventricle.

Mechanisms

There are 2 basic mechanisms that lead to cor pulmonale: (1) alveolar hypoventilation* with moderate or severe anoxia and hypercapnia leading to pulmonary vasoconstriction, hypervolemia, and increased cardiac output, or (2) anatomic curtailment of the pulmonary vascular bed or a combination of these factors. Alveolar hypoventilation may result from lesions that involve the nervous system, the chest cage, or the bronchopulmonary apparatus. Central nervous system lesions that lead to depression of the respiratory center and right heart failure are rare and one hears of these in single case reports.1 Spinal cord lesions, peripheral polyneuritides as well as the muscular dystrophies may also lead to alveolar hypoventilation when the muscles of respiration are involved. Structural deformities of the chest cage due to kyphoscoliosis2 or surgery may disturb ventilation sufficiently to induce severe alterations in gas exchange and hence produce circulatory complications. The mechanisms of breathing in such patients, however, are rarely faulty enough of themselves to produce profound hypoxia and hypercapnia. These disturbances in gas exchange are more likely to appear when the breathing difficulties are associated with some other disease such as emphysema, bronchitis, or pneumonia. Although the mechanisms responsible for the hypoventilation associated with exogenous obesity3 are not fully understood, the primary disease is not of the lung parenchyma itself. In many of these instances of alveolar hypoventilation the lung parenchyma and vasculature may be virtually normal and the train of circulatory complications stems entirely from the disorders of gas exchange. Although there is some lung distention and even parenchymal destruction in patients who develop circulatory abnormalities with the disorders of bronchopulmonary function known as emphysema, alveolar hypoventilation is also the primary agent and not an anatomic reduction of the vascular bed. This is evident from the facts that the disturbances of the circulation are reversible and that pathologic examination indicates that widespread destruction of the vasculature is not characteristic of such lungs. Although most instances of cor pulmonale are seen in adults, children may also suffer from this disease. The excessive and thickened bronchial secretions produced in patients with cystic fibrosis of the pancreas may lead to severe alveolar hypoventilation. Acute diffuse bronchiolitis in children may also result in marked interference with ventilation and gas exchange, and hence in cardiac failure.

Anatomic curtailment of the pulmonary vascular bed as the primary cause of cor pulmonale is rare. This is so because there are very few diseases that attack the vascular bed

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*Alveolar hypoventilation is used in this paper as a simple term to characterize a somewhat complex type of disturbance in ventilation perfusion relationships and does not imply generalized or uniform under-ventilation of alveoli. Actually some alveoli may be poorly ventilated, others well ventilated, and still others hyperventilated; but perfusion to these areas is not correspondingly affected and indeed may be well maintained regardless of how the alveoli are ventilated. Hence if a large area of the lung is poorly ventilated but well perfused the net result is a disturbance in gas exchange.
so extensively as to reduce its area to a critical degree. It should be remembered that removal of one lung does not lead to right heart failure. Hence lesions that induce cor pulmonale solely by a reduction in the capacity of the pulmonary vascular bed must eliminate more than 50 per cent of this area. Among those that may do so are multiple or massive pulmonary embolization, the pulmonary arteritides, and certain of the pulmonary fibroses, particularly those producing the syndrome of alveolar-capillary block. It is difficult to classify the entity known as primary pulmonary hypertension, since so often the final examination in these subjects suggests that they were victims of multiple pulmonary emboli. Silicosis is one of the more frequently encountered fibrotic diseases associated with cor pulmonale. It has been assumed that these fibrotic lesions induce pulmonary hypertension and thence right heart failure. Closer inspection has indicated, however, that it is the patient with combined silicosis and emphysema who more usually develops circulatory disease. Moreover, it has been shown that the circulatory complications can be reversible as the anoxic secondary to alveolar hypoventilation lessens; this strongly suggests that anatomic lesions may not be the chief offenders and that the emphysema is at the root of the difficulties.

Cor pulmonale is not seen as a result of uncomplicated bronchiectasis, lung abscess, or pneumonia. Of course, if any of these diseases is accompanied by emphysema or any other cause of anoxia, right heart failure may follow. Similarly, uncomplicated pulmonary tuberculosis does not produce cor pulmonale even with extensive destruction of the parenchyma, although in some few cases mild pulmonary hypertension at rest or during exercise does exist. However, in the presence of abnormal chest mechanics due either to marked pleural fibrosis or to the results of chest surgery, ventilatory insufficiency in these tuberculous subjects may progress to an anoxic phase and then right heart involvement may occur.

Specific Disease Processes Responsible for Cor Pulmonale

Diseases That Produce Alveolar Hypoventilation and Cor Pulmonale

Emphysema

Chronic pulmonary emphysema is by far the commonest cause of cor pulmonale. On the other hand, not every patient with emphysema develops circulatory abnormality. This is well illustrated by the statistics collected by Dr. Anne L. Davis in the Emphysema Clinic of the First (Columbia) Division at Bellevue Hospital. Of 114 patients who were followed regularly in this clinic and are known well, not only clinically, but also from the point of view of pulmonary function, only 23 (20 per cent) have, or have had, a diagnosis of cor pulmonale. In an additional 5 subjects this diagnosis is being entertained but is as yet not confirmed. The sex incidence is striking. Of the 114 patients in this clinic, only 9 are female and, of these 9, 2 have cor pulmonale. Thus in this small but well-studied group, emphysema is much commoner in men, (92 per cent of this clinic population) but cor pulmonale occurs in 20 to 23 per cent of emphysematous patients regardless of sex.

The incidence of cor pulmonale in a general cardiac population is difficult to ascertain. In Sheffield, England, and in Belgrade, Yugoslavia, 25 and 16 per cent of cardiac patients in heart failure were found to have cor pulmonale. In Buenos Aires 3.3 per cent of general admissions to a cardiac clinic were so designated.

A most interesting example of the importance of cor pulmonale due to emphysema in another part of the world, namely New Delhi, India, is found in the statistics provided by Padmavati. In a 5-year survey (1950-1955) she found an incidence of cor pulmonale in the hospital admissions of 16.6 per cent of all cardiac cases, in contrast to 39.1 per cent for rheumatic and 11.3 per cent for degenerative heart disease. There were a larger number of women in this group as compared to western figures, as well as a number of adolescents, suggesting that this was in a sense a family ill-
ness. This group was made up of farmers and housewives. Padmavati suggested that the emphysema and bronchial disorders that predominate as the pulmonary causes of the heart condition are largely the consequence of desperate poverty and poor housing conditions. Many of these individuals in one family live in 1 or 2 rooms that have no ventilation and are filled with smoke from cow-dung fires. In addition, cotton spinning is also done in this room and the women are thus exposed to the respiratory tract irritation produced by fine cotton fluff.

It is essential to determine the common denominator in patients with emphysema who develop cor pulmonale. It is now well recognized that cor pulmonale will appear only in those subjects who have hypoxia and hypercapnia as a result of severe alveolar-respiratory insufficiency. This alveolar hypoventilation stems from bronchiolar obstruction, decreased lung elasticity, and fixation of the chest cage, which combine to interfere with gas distribution to the lungs. When arterial oxygen saturation at rest falls below 80 to 85 per cent and carbon dioxide tension rises, then one finds disturbances in the circulation and one or more of the following appear: a rising cardiac output, pulmonary hypertension, and an elevated hematocrit level. Although the exact mechanisms whereby anoxia elicits these changes are not fully known, there seems little doubt that it is the chief offender and with its relief comes a restoration to normal of the circulatory function. Thus the reversibility of the abnormal circulatory findings confirms the basic role of anoxia and minimizes the influence of the anatomic changes of the vascular bed.

 Destruction of the lung vasculature is not an important factor in inducing the circulatory complications in emphysema because it is not extensive. This is evident from inspection of these lungs by x-ray and at necropsy. On x-ray these patients do not necessarily show large bullae, blebs, and cysts and indeed may show none of these. Figure 1 illustrates the roentgenograms in one such patient. This par-

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**Figure 1**

X-rays of a 63-year-old man (W.W.) with emphysema and cor pulmonale. When in full-blown cardiopulmonary failure the x-ray (left) showed extensive pulmonary infection and cardiomegaly. Right ventricular pressures were 46/7. On recovery 2 3/4 months later (right) the lungs showed much less infiltration, no obvious blebs or bullae, and there was a decrease in heart size. The right ventricular pressures were 25/2. This chest film remained unchanged until his death from pneumococcus meningitis, 19 months after his first admission. The heart showed dilatation of the right ventricle but no hypertrophy.
ticular subject died of pneumococcal meningitis a number of months after these x-rays were taken. Necropsy examination of his lungs showed that he had emphysema (fig. 2), but the lung destruction was not marked and indeed large areas were free of alveolar disruption. The striking findings were evidences of bronchitis, bronchiolitis, and bronchopneumonia. Although it is true that the curtailment of the vascular bed seen in emphysema is not the sole, or even an important factor in the production of pulmonary hypertension, it may play a contributing role when the patient is under such stress as exercise or hypoxia.

The clinical picture of the emphysematous subject who develops cor pulmonale is a fairly distinct one. These individuals are usually in the fourth to the sixth decade when first seen and often give a history of chronic cough, bouts of bronchitis, and mild dyspnea on exertion, which becomes severe when associated with respiratory infections. Paroxysmal nocturnal dyspnea is commonly encountered in these patients but, unlike that of the subject with left ventricular failure or mitral stenosis, is relieved by cough if it is productive of sputum. Weight loss of a considerable degree may occur. These evidences of pulmonary disease may have been present from 5 to 10 years. Only very rarely does one encounter a patient with a history of bronchial or allergic asthma and cor pulmonale. In the past 13 years at Bellevue Hospital we have only found 1 such patient. Many patients state that their physicians told them they had asthma, but this began in their forties or fifties. It is likely that the evidences of obstructive breathing which these patients showed was termed "asthma" by their physicians. However, obstructive breathing is not peculiar or particular to bronchial asthma—it is also a major manifestation of emphysema.

To return to the patients' histories, despite cough and dyspnea they were able to continue their usual activities until a very bad "cold" or a "severe bout of bronchitis" or "pneumonia" precipitated extreme dyspnea, restlessness or somnolence, and ankle edema. Occasionally severe emotional tension will precipitate a period of marked bronchospasm and anoxia. Evidences of circulatory embarrassment are usually manifest only shortly before admission. Thus 2 salient traits characterize the history in such persons. First, the symptoms of their pulmonary disease were present for a considerable although variable period of time before cardiac disability was apparent. Second, their pulmonary disease was not rapidly or continuously progressive; rather it was marked by periods of remission. Unfortunately there is no symptom which marks the onset of the early circulatory complications of emphysema, and all too often it is not until hepatomegaly and edema are present that our attention is directed to the circulation. It is now known that a rising cardiac output, pulmonary hypertension, and an elevated hematocrit value antedate the manifestations of congestive failure and are all well correlated with the level of arterial oxy-
gen saturation. A change in arterial blood gases should raise the suspicion that circulatory complications may develop. The onset of a bronchitic or pneumonic infection, a frequent event in such cases, may be the cause of deterioration in gas exchange. Minor increases in heart size as seen on serial films or a rising hematocrit level would confirm such a suspicion. Most of the patients with overt cor pulmonale due to emphysema have hypercapnia and moderate to severe anoxia (saturation less than 80 per cent). One must remember, however, that the resting level of arterial oxygen saturation alone is not an absolute criterion of impending circulatory dysfunction as levels as low as 60 per cent can be found without it. It is probable that the duration of the hypoxic and hypercapnic state, the rapidity of its onset, its severity, as well as the physical activity engaged in by the patient, determine whether or not circulatory complications appear. A patient whose arterial oxygen saturation suddenly drops to a low level (e.g. 60 per cent) but who is confined to bed and vigorously treated may escape circulatory sequelae in large measure because his severe hypoxic state is transient. On the other hand the working man, unaware of the precarious situation may progress into them fairly rapidly. It is true that his saturation at rest may be above 80 per cent but on exertion it may fall to much lower levels.

On physical examination of the patient with cor pulmonale due to emphysema one finds a dyspneic, tachypneic, orthopneic, and cyanotic patient who is coughing ineffectively and bringing up thick, tenacious sputum with difficulty. His eyes may be froglike, protuberant, injected, and chemotic. The neck veins are engorged and fill from below. It should be remembered that the neck veins of many patients with emphysema but without heart failure are distended as a consequence of the marked changes in intrapleural pressure. Retrograde filling will distinguish the ones with an elevated venous pressure. The chest resembles a rectangle more than any other shape because the manubrium is raised upward and forward, and there is rounding or "buffalo hump" in the back. The patient uses the accessory muscles of respiration. The authors have never seen Cheyne-Stokes breathing in cor pulmonale in the presence of carbon dioxide retention. The lungs are filled with wheezes, rhonchi, and rales unless bronchospasm is extreme, in which case the chest is remarkably quiet and breath sounds are almost inaudible. Hydrothorax does not appear in this form of right heart failure. If pleural fluid is present, another cause such as pulmonary infarction or infection should be sought. The heart is enlarged, the rhythm is regular and rapid, and the pulmonic second sound may be equal to or greater than the aortic second sound. A systolic murmur may be heard over the pulmonic or apical areas. A gallop is often present over the ensiform. The liver is enlarged but ascites of any magnitude is not present. In congestive failure the extremities may or may not show considerable edema. This type of edema should not be confused with that due to peripheral circulatory stasis, which is a very common finding in the patient with severe pulmonary insufficiency not in cardiac failure who, bedridden because of dyspnea, sits constantly with his legs over the side of the bed. The fingers rarely show unequivocal clubbing although cyanosis may be marked.

The x-rays of the chest reveal low diaphragm, increase in intercostal spaces, and enlarged hearts. The cardiac enlargement may be quite marked, but is confined to the pulmonary arteries, right ventricle, and right atrium (fig. 1). One occasionally sees a patient in the fullblown congested state whose heart size appears to be within normal limits. However, the small vertical heart of the emphysematous patient on dilatation may not be very large and it is only by comparison with previous films that cardiomegaly can be defined. If this information is not available, cardiomegaly may only be apparent after recovery from failure, when the heart returns to its previous small size. The marked changes in heart size as the patient goes in and out of cardiac failure and the rapidity with which this may happen (fig. 3) lead one to believe that dila-
Serial x-ray films of a 57-year-old man (A.F.) with emphysema and cor pulmonale. He was admitted 11/4/58 with a 3-week history of increasing dyspnea and edema (see upper left). He was allowed ambulation in hospital, was given antibiotics and periods on a Bennett respirator but was not digitalized. By 11/18/58 the heart size had greatly increased (upper right) and a pulmonic systolic murmur and a right ventricular gallop appeared. He was digitalized and put on bedrest. Film taken 11/26/58 (lower left) shows a smaller heart and by 12/18/58 when he was no longer in failure, the heart size was normal (lower right). A comparison of the first and last films illustrates that the former actually depicted some cardiomegaly even though the cardiothoracic index was quite normal.
tation, rather than hypertrophy, is the major cause of cardiac enlargement. This observation has pathologic confirmation (fig. 1).

The electrocardiographic findings in cor pulmonale secondary to emphysema are variable, and the record may be quite normal. Right axis deviation, however, is a common finding in emphysematous persons, whether or not they have cardiac disease, and therefore is not an aid in making the cardiac diagnosis. In some patients there may be incomplete or complete right bundle-branch block, and in a relatively modest number the tracing shows the pattern of right ventricular hypertrophy. One should not refrain from making the clinical diagnosis of cor pulmonale because of the presence of left axis deviation, as occasionally a horizontal electrocardiographic position is present. Prolongation of the P-R and Q-T intervals is not encountered. The T waves in the right V leads are sometimes of considerable importance in defining right ventricular disturbances. The T waves may become negative during an acute anoxic period when the right heart enlarges, just as is well known to occur in acute pulmonary hypertension due to pulmonary emboli. Later, with improvement, they may become normal again. Chronic arrhythmias are not a part of the picture but acute anoxic periods even in the absence of heart failure will produce paroxysmal arrhythmias. These disappear with improvement in the anoxic state. Atrial or nodal arrhythmias and even ventricular premature contractions occurring in coupled rhythm may be seen in the phase of acute, recent, or severe cardiorespiratory failure. Indeed, the authors have now seen 7 patients with cor pulmonale due to emphysema who entered the hospital with atrial flutter and this arrhythmia persisted until anoxia was relieved; in some cases this required a number of days. Atrial fibrillation with rapid ventricular rate has also been seen as a result of marked overmedication with vaporized bronchodilators. On the other hand, a long-standing arrhythmia suggests a diagnosis in addition to, or instead of, cor pulmonale.

A word must be added about the rate in normal sinus rhythm in these emphysematous subjects. When they are moderately anoxic, and because of this, they tend to have ventricular rates of 90 to 100. When cardiac failure supervenes, this rate rises even higher and when either severe cardiac or severe respiratory distress is present, sinus rhythm may be extremely rapid; the fastest rate in sinus tachycardia seen by the authors was 215 beats per minute at a time when dyspnea was severe but there was no cardiac abnormality. Overuse of bronchodilator drugs is a common cause of persistent sinus tachycardia. An increase in heart rate should also alert one to an episode of increased anoxia in the emphysematous patient but it should also suggest the possibility of gastrointestinal bleeding. Peptic ulcers occur frequently in the emphysematous subject and may be asymptomatic unless hemorrhage is occurring. If bleeding is ruled out and cardiac failure is absent, an increasing sinus tachycardia will often indicate a serious prognostic sign of advanced pulmonary insufficiency.

Certain tests are of value in confirming the clinical impression of cor pulmonale due to emphysema and in following the course of these subjects. The levels of arterial blood oxygen and arterial carbon dioxide are of primary interest. These respiratory gases give a fairly close estimation of pulmonary insufficiency and, indirectly, of the circulatory changes. The hematocrit level affords direct information about an increased red cell mass and in addition, if elevated, suggests that a hypoxic state has been present for a considerable period of time. Determination of hemoglobin alone is not satisfactory because these red cells although large are hypochromic. Although ultimately one tries to evaluate pulmonary function as completely as possible, measurements of lung volumes and maximal breathing capacity are not always feasible in the state of acute cardiorespiratory failure and must await the subject’s recovery.

One might wonder somewhat at the authors’ emphasis upon the blood gas determinations in

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judging cardiac function rather than upon a hemodynamic evaluation such as the measurement of peripheral venous pressure. This pressure in the emphysematous chest, as determined at the bedside, is almost invariably too low. This error stems from inaccurate estimation of the atrial level in the thorax and the use of the very low frequency saline manometer.

The disturbances in cardiopulmonary function in cor pulmonale have been thoroughly explored in recent years. The hemodynamic alterations are of great physiologic interest but are not necessary information in making the clinical diagnosis. An understanding of them, however, is very helpful in directing the course of therapy. The cardiac output although it can be elevated is not always so. The elevation in pulmonary artery pressures covers a wide range but very high systolic pressures (over 100 mm. Hg) are not encountered. Indeed, heart failure may be seen when pressures are only moderately increased. Right ventricular diastolic hypertension is the rule in right heart failure. Both the red cell mass and the plasma volume are above normal, the former usually being the more augmented of the two, and hence one often finds an elevated hematocrit value. There is a decrease in all these circulatory measurements on relief of the severe anoxia and heart failure. The level of blood flow, even if it is not above normal, will be lower on recovery as compared to that found in the congestive episode. Although the circulatory abnormalities can be returned to a virtually normal state at rest, one must be aware of the response of the emphysematous subject to exercise. As shown in figure 4, these individuals with emphysema, even if they have never been in heart failure, may develop a considerable pulmonary hypertension on exercise and the arterial saturation may fall below 85 per cent. Those patients who have recovered from failure may also have a normal increase in blood flow but develop considerable pulmonary hypertension and a rise in right ventricular diastolic pressure. A more severe degree of hypoxia will also appear. Thus the 3 stimuli that lead to the reappearance of the congested state may be present during exercise although absent at rest; these stimuli are hypoxia, pulmonary hypertension, and the elevated ventricular diastolic pressure. The last may well be related to salt and water retention.

In these patients with emphysema therapeutic efforts are directed at treatment, not only of the heart failure, but also of the results of pulmonary dysfunction, anoxia, and hypercapnia. Although hypercapnia is a constant finding in those patients with emphysema and cor pulmonale. Each of the columns is represented by an actual study in an individual patient. CCP, chronic cor pulmonale; RVF, right ventricular failure; Hi, high; N, normal; R, rest; Ex., exercise. With emphysema alone (column 2) the patient can increase his cardiac output in a normal fashion whether or not pulmonary hypertension is present at rest or during this exercise. The rise in blood flow will raise pulmonary artery pressures (PAp) but if the right ventricle can tolerate this response its diastolic or filling pressure (RVD) does not exceed normal during the exertion. If the right ventricular filling pressure does rise during exercise (a in column 3) even though blood flow increases normally or is eu kinetic, an abnormal cardiac phase is present and physiologically this is probably where cor pulmonale begins. When diastolic ventricular pressure is elevated at rest (column 4), a more advanced cardiac phase exists but, in spite of this, blood flow may still rise adequately. The final phases are shown in columns 5 and 6; the right ventricle can no longer increase its output normally and is hypokinetic or cannot increase it at all above the resting level (akineti c).

Figure 4

Schema of the response to exercise in emphysema with and without cor pulmonale. Each of the columns is represented by an actual study in an individual patient. CCP, chronic cor pulmonale; RVF, right ventricular failure; Hi, high; N, normal; R, rest; Ex., exercise. With emphysema alone (column 2) the patient can increase his cardiac output in a normal fashion whether or not pulmonary hypertension is present at rest or during this exercise. The rise in blood flow will raise pulmonary artery pressures (PAp) but if the right ventricle can tolerate this response its diastolic or filling pressure (RVD) does not exceed normal during the exertion. If the right ventricular filling pressure does rise during exercise (a in column 3) even though blood flow increases normally or is eu kinetic, an abnormal cardiac phase is present and physiologically this is probably where cor pulmonale begins. When diastolic ventricular pressure is elevated at rest (column 4), a more advanced cardiac phase exists but, in spite of this, blood flow may still rise adequately. The final phases are shown in columns 5 and 6; the right ventricle can no longer increase its output normally and is hypokinetic or cannot increase it at all above the resting level (akineti c).
semia who develop circulatory complications, there is little evidence to indicate that hypercapnia itself produces them. Carbon dioxide retention, however, is in part responsible for the cerebral symptoms that these patients may display, particularly somnolence and coma.\textsuperscript{17} Restlessness, irritability, and paranoia may also be related to abnormalities of gas exchange. The mental status of these subjects in acute cardiorespiratory failure may interfere with therapy. The apprehension, distrust of personnel, and irritability which they display can only be overcome by constant supervision and reassurance by nurse and physician. It is well for the physician to advise the nursing staff that the disagreeable personality these subjects demonstrate is due largely to anoxia and is a major manifestation of their disease.

The importance of bed rest cannot be overemphasized, since it has been shown that the arterial blood oxygen saturation, already low at rest, becomes much lower on exertion and may even fall to 45 per cent in this type of emphysematous subject. Adequate fluid intake and particularly an adequate calorie intake must be almost forced on these weak or somnolent patients.

It is because bronchospasm and bronchopulmonary infections are of paramount importance in the interference with gas exchange that attack on these must be vigorous and, if possible, early. Vaporized bronchodilators used with or without a positive-pressure apparatus are often quite effective in alleviating bronchospasm and mucosal edema. The advantage of the aerosols now in use is that small doses are effective and without side reactions. Three or 4 drops of these preparations diluted with an equal volume of water or saline and given every 4 hours represent a sufficient dosage. It is rare to find a patient who requires more than 7 drops of these drugs per treatment, and the authors have never seen a tolerance develop even after years of usage. When larger amounts are used or intervals between administration are shorter than 4 hours, then tachycardia, tremors, or hyperexcitability follow. Swallowing of even small amounts of these drugs may produce severe epigastric pain. Aminophylline by suppository or slow infusion is often effective in relieving extreme bronchospasm.

The patients who reach the critical state of cor pulmonale with failure almost invariably have infection of the bronchopulmonary tree. The detection of such an infection may rest entirely on symptoms of increasing dyspnea, cough, and change in the quantity or quality of the sputum. There may however be no detectable change in the physical signs in the chest, and x-rays often fail to demonstrate a diffuse lobular pneumonia. Fever and leukocytosis are more often than not absent. Bacteriologic examination of the sputum usually reveals several organisms each of which could be the responsible agent (hemophilus influenzae, pneumococcus, staphylococcus aureus, and gram-negative enteric bacilli) but no one predominates.\textsuperscript{19} Because of the difficulty in defining the exact identity of the infective agent (and a viral etiology has not been excluded\textsuperscript{20}), these infections are handled much as one would a pneumonia of unknown etiology. The authors have been impressed by the fact that if infection is not attacked directly and intensively, little progress is made in alleviating the cardiopulmonary distress. Antibiotics are used in every case as one cannot ignore what might ordinarily be considered a trivial respiratory infection because the patients do not tolerate well any further encroachments on their pulmonary reserve. The loss of even a small area of functioning lung tissue as a result of infection may be sufficient to precipitate severe pulmonary insufficiency. Clearing of the air passages of secretions and exudates is vital. If the patient can cough he should be regularly encouraged to do so. Not infrequently the sputum is so thick and tenacious that steam inhalation and tracheal suction must be employed. In individuals with marked obstruction due to bronchial plugs bronchoscopy may be life saving. Because of the patient’s dyspnea and weakness postural drainage is not feasible. We have not found it necessary to use tracheotomy in our cases, and indeed have been discouraged from its employ-
Table 1

Studies of Arterial Blood Gases as Influenced by the Bennett Respirator or Pneumatic Balance Resuscitator (PBR) in Two Subjects with Emphysema

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...ment because of the complications that arise from its presence. Potassium iodide and other expectorants are not very helpful.

Frequently the above measures will improve ventilation sufficiently so that a more effective gas exchange ensues. If this is not the case, oxygen must be supplied. The hazards of administering this gas in high concentration to patients with hypercapnia are well known, and it must be given with assisted respiration by means of a respiratory aid. While it is true that low concentrations of oxygen can be given intermittently unaided by a mechanical respirator without inducing coma, the carbon dioxide tension of the arterial blood rises to precarious levels and unfortunately the patient cannot be persuaded to discontinue this form of oxygen therapy.

A number of respirators are available which can be employed as mechanical aids to ventilation. Although each of these operates in a somewhat different fashion, the ultimate aim of all is to improve alveolar ventilation in such a way that not only is more oxygen conveyed to the alveoli but also carbon dioxide is more effectively eliminated. With some of these aids, ventilation may be improved to such an extent on room air that adequate oxygenation occurs even without the use of high oxygen mixtures in the inspired gas. In the presence of carbon dioxide retention any respirator that depends upon the subject's initiating the cycling mechanism by voluntary inspiration should not be used with concentrations of oxygen higher than 30 to 40 per cent, as one faces the same hazard that occurs in oxygen therapy with unassisted respiration. Under these circumstances, if the patient becomes rapidly saturated with oxygen during the first few breaths, the stimulus to breathing is diminished. Studies of the effects of the respiratory aids on blood gases have confirmed the clinical impression of their value. The rise in arterial saturation and decrease in carbon dioxide tension, however, may be quickly dissipated (table 1) once the respirator is removed from the patient. Prolonged use of the aid, 6 to 20 hours per day, and for periods of no shorter than 45 to 60 minutes on each occasion, will eliminate the fluctuations in levels of anoxia and promote significant lowering of carbon dioxide values. The tank respirators are a boon in handling the semicomatous subject or one whose apprehension precludes covering his face with a mask. Any desired oxygen concentration can be used with these tank respirators. The constant presence of an understanding medical attendant is better than any sedation in securing the cooperation of the sufferer when using any of these respirators.

So far the discussion has centered around the treatment of the pulmonary insufficiency. The specific cardiac therapy of the patient in failure with cor pulmonale is the same as would be used in heart failure due to other forms of heart disease, that is, adequate digitalization, low-salt diet and, when necessary, mercurial diuretics or chlorothiazide. One must remember that one cannot rely solely on the heart rate as an index of full digitalization, as the patients tend to have rapid heart rates, not only because of failure, but also as a result of anoxia. Even when heart failure is not present, they tend to have resting ventricular rates of 90 to 100, and, if digitalis dosage is increased to combat this rapid rate, intoxication may result.
The polycythemic state of these patients is disadvantageous because it promotes an increased venous return to a failing right ventricle and also plays a role in maintaining and exaggerating pulmonary hypertension. In these patients, when the lesser circulation becomes abnormal, an increased blood flow and polycythemia cannot be considered as advantageous homeostatic responses directed toward the satisfaction of tissue oxygen needs in the presence of anoxia, as they are in normal man. Therefore, it is helpful to reduce blood flow and blood volume by means of phlebotomies. Phlebotomies should be performed judiciously, particularly in the acutely ill patient. Indeed, most of the preceding therapies should be instituted prior to blood letting. The volume of venous blood removed may vary from 300 ml. to 500 ml. at each phlebotomy, and the use of a vacuum bottle makes the withdrawal of this viscous fluid fairly easy. Serial measurements of the hematocrit and hemoglobin will indicate the amount of blood that must be removed to return the hematocrit value to 45 to 50 per cent without reducing the hemoglobin below 12 Gm. In this connection, it is important to emphasize that phlebotomies should not be done more often than every 2 or 3 days. Repeated phlebotomies initially may have little effect on the elevated hematocrit value until a considerable volume has been withdrawn.

The dangers of sedation in subjects with cardiorespiratory failure due to emphysema are well known. Since every effort is being made to improve ventilation and to clear the respiratory passages of secretions in the presence of a poor cough mechanism, it is obvious that the use of morphine, meperidine, and codeine are contraindicated. Barbiturates and tranquilizers have also proved deleterious. If sedation is absolutely necessary, chloral hydrate can be administered. The chest pain ascribed by some to pulmonary hypertension has not been encountered in our patients. The low chest and high epigastric pain, we have noted, was the consequence of either chronic or severe cough or peptic ulcer, so that analgesics mentioned above have not been required. A word of warning must be added here about the use of nitroglycerin in these anoxic subjects. This drug, a powerful peripheral vasodilator, when coupled with another systemic vasodilator such as hypoxia, can produce profound peripheral vascular collapse.

The use of steroids has been advised but in our experience the complications, namely gastrointestinal bleeding and fluid retention, following theretofrom have been more serious than the benefits to pulmonary function said to accrue.

If pursued unremittingly, all these measures will result in improved pulmonary function, reduction in and even abolition of pulmonary hypertension at rest, and relief of right heart failure. In fact, it has been our experience in recent years that the problem of heart failure per se can almost invariably be resolved in these subjects. The pulmonary insufficiency, however, remains as the important and sometimes fatal disability. When heart failure persists despite the measures discussed above, one should reconsider the diagnosis, as it is unlikely that emphysema alone is the primary cause of the difficulties.

Once the patient has recovered from the acute episode of cardiopulmonary insufficiency, all efforts are directed at maintaining him free of circulatory complications and in as optimal a state of pulmonary function as is possible with modern methods. These patients should be followed regularly and at frequent intervals, even when they are doing well, not only for appraisal by the usual clinical means, but also for evaluation by certain simple physiologic measurements.

One can obtain essential information concerning pulmonary function from analysis of the arterial blood for its oxygen saturation and the carbon dioxide content, associated, if possible, with a determination of the arterial pH, so that carbon dioxide tension can also be calculated. If the emphysematous patient with cor pulmonale is well controlled, there are only minor fluctuations in arterial blood oxygen saturation and carbon dioxide content. The frequency with which these determinations need to be made depends upon many
factors, and in our experience may vary from 1 to 3 months, depending upon the severity of the individual patient’s disease and the occurrence of complications. The oxygen saturation may vary as much as 10 per cent on repeated monthly samplings but is usually found to be above 80 to 85 per cent if the patient is doing well; the carbon dioxide tension generally lies in the range of 45 to 55 mm. Hg when the patient is well controlled. It is necessary to obtain such data because it is often difficult to demonstrate changes in the patient’s condition by clinical examination alone. The acute respiratory infection is apparent to patient and physician alike, but there may be a clinically imperceptible and gradual change that is uncovered only by serial laboratory determinations. The cause of this gradual decline in pulmonary function is not always clearly demonstrable, but frequently it is reversible by an intensification of the therapeutic pulmonary regime.

Advice concerning the physical activities to be engaged in by these patients must be given on an individual basis. The persisting dyspnea and fatigue limit exertion but the patient should be encouraged to operate at least up to that limit. Since the arterial saturation may fall considerably on exercise in some of these cases, sudden or strenuous exertion is best avoided. Airplane travel may be hazardous unless the cabin is adequately pressurized.

Vaporized bronchodilators are used systematically 3 or 4 times a day. The inhalations should be taken until the prescribed volume of fluid has been dispensed; this generally requires 10 to 15 minutes. A few puffs of the medication are inadequate. Those fortunate individuals who possess a respiratory aid and use it regularly 2 to 4 hours every day have been maintained in a far better state of alveolar ventilation than prior to its use. Smoking must be discouraged, and on numerous occasions renunciation of this habit has made a striking change in the patient’s clinical state.

The course of the patient with emphysema is in large measure determined by the frequency of bronchopulmonary infections. These infections may not only precipitate acute cardiopulmonary failure but often, because of their poor resolution, destroy areas of functioning lung tissue. Obviously intensive treatment by antibiotics of even a seemingly minor infection is mandatory. It is not necessary to use a different antibiotic at the time of each new infective episode, and if one drug is repeatedly successful there seems little reason to try a different agent. Whether or not prophylactic therapy will abolish some of these recurrent infections is not yet settled, nor is the relative value of continuous or intermittent programs or the effectiveness of various drugs. A preliminary study conducted at Bellevue Hospital by Davis and associates indicates that although prophylaxis changed the flora in the sputum and even reduced the number of lower respiratory tract infections in the treated group, the infection rate was still so high in this group that the effect of the drugs was considered minimal.

If repeated measurements of the hematocrit level show an increasing red cell mass, phlebotomies are performed as indicated. Obviously the hematocrit level may be measured from the arterial blood sample drawn for blood gas analysis, but venous blood, if properly drawn (that is, without use of tourniquets) will suffice. In the patient who must be repeatedly phlebotomized—and this may vary from bi-monthly to biennially—iron-containing foods should not be withheld, as this will not depress red cell formation effectively and serves only to increase the hypochromia.

The patients who have been in cardiac failure are maintained on digitalis preparations. This attitude is dictated by the fact that on numerous occasions patients who had this drug stopped for one reason or another have returned with evidences of heart failure. The physiologic reason for this may depend on the fact that even though these subjects may have normal pulmonary artery pressures at rest they will develop pulmonary hypertension and anoxia on exertion. However, it is not our custom to institute digitalization in patients with emphysema who have never shown any evidence of heart failure. One must always remember that cough and dys-
pneum. are symptoms of pulmonary and not cardiac dysfunction in these patients, and hence are not indications for digitalis or mercurial diuretics in the absence of right heart failure.

Following the progress of the emphysema by means of serial chest x-ray films is not often helpful except in the diagnosis of complicating pulmonary infections. Repeated measurements of heart size, however, are useful, since it has been shown that the heart diminishes in size once heart failure is relieved. Similarly, an increase in heart size in these patients suggests the onset of heart failure even though the clinical manifestations of peripheral congestion may not yet be present.

Diamox is another useful adjunct. It not only acts as a diuretic but it may also promote elimination of carbon dioxide. Inasmuch as this drug produces a metabolic acidosis, it should be discontinued in the patient with acute respiratory insufficiency because of the danger of increasing acidosis. However, in those patients who are improving as a result of the other measures mentioned but who nonetheless continue to show hypcapnia it is often successful in lowering carbon dioxide tension.

Silicosis

The appearance of cardiac complications secondary to pneumoconiosis has been noted predominantly in silicotic and anthracosilicotic subjects. Silicosis can be divided into "simple" (or nodular) silicosis and "complicated" silicosis (massive fibrosis or pseudotumoral form). This subdivision is useful when cardiovascular complications are considered. Right heart enlargement is infrequently seen with simple pneumoconiosis23 unless there is coexisting emphysema.4, 5 However, cor pulmonale is a frequent accompaniment of complicated silicosis.4, 23 Lavenne4 found that 40 per cent of miners with anthracosilicosis have right ventricular hypertrophy on autopsy. Furthermore the statistics he reported from Gough’s service, based on 358 autopsies of Welsh coalminers with pneumoconiosis, indicate that right heart failure was a more frequent cause of death (23.7 per cent) than tuberculosis (13.7 per cent). Since therapy of tuberculosis has made such strides in recent years, it is obvious that cor pulmonale will soon far outstrip tuberculosis as the major complication in silicosis.

The pathogenesis of right heart enlargement, with or without failure, secondary to silicosis is still being investigated and therefore no definitive outline of this phenomenon can be given. Physiologic studies are underway at present24 that should elucidate the problem in the same way as has been done in the pathogenesis of cor pulmonale due to emphysema alone. It has been assumed that in silicosis, as in other lung diseases producing cor pulmonale, pulmonary artery hypertension represents the major physiologic cause for the right heart enlargement and eventual failure. The inciting mechanisms for this hypertension may include not only a pathologic encroachment on, and destruction of, the pulmonary vasculature by the fibrosis (particularly the lesions seen in complicated silicosis25, 26) but also the physiologic effects of anoxia. The solution of the problem is greatly complicated by the fact that silicosis is very frequently accompanied by pulmonary emphysema. This is not only the perifocal type involving the lung tissue surrounding the silicotic and anthracotic nodules, but also the bronchitic type, which in itself is the commonest cause of cor pulmonale. Bullous areas and pulmonary as well as bronchiolar infections, all of which may impair respiratory gas exchange, are also frequent complications. Lavenne,4 whose exhaustive monograph is our most adequate appraisal of cor pulmonale due to pneumoconiosis to date, reports on the detailed pathologic findings in 100 cases dying in right heart failure. There were 79 cases of complicated (massive fibrosis) silicosis, of whom all but 5 had obstructive emphysema. There were 16 cases of simple silicosis, all of whom had considerable obstructive as well as perifocal emphysema; and the remaining 5 cases had advanced obstructive emphysema as their main lesion associated with a few coal nodules and a little perifocal emphysema. Thus, of this series of 100 cases with fatal

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right heart failure due to pneumoconiosis, 95 had obstructive emphysema. Finally, in a small series of silicotic patients studied by us obstructive emphysema always played a significant role in the pathophysiology whenever cor pulmonale was present.

These observations raise a very important point: does cor pulmonale occur in the silicotic subject who has no emphysema? The answer is not definitely known, but the implications are that it must be rare. If this is so, the circulatory complications in silicosis may be greatly if not entirely the result of the disturbances secondary to the alveolar hypoventilation of emphysema.

It may well be that the vascular lesions described in the conglomerate (pseudotumoral) complicated forms of silicosis are such as to produce this fixed type of pulmonary hypertension but this has not been shown as yet. Furthermore, Lavenne has noted the relief of right heart failure in these patients following treatment, suggesting that there may be some measure of reversibility even in such a severely altered pulmonary vasculature. He observed that these bouts of failure almost always followed acute respiratory infections and that the silicosis in these cases was accompanied by emphysema, so that anoxia again may be the more important mechanism.

It is probable that in the silicotic subject both mechanisms for the production of cor pulmonale—anatomic lesions and anoxia—coexist in varying proportions, and their importance in any single case depends on the relative extent of the vascular lesions and the obstructive emphysema.

From what has been said it seems apparent that one diagnoses the presence of cor pulmonale in the silicotic subject in much the same manner as one does in the emphysematous patient. Moreover, the success of therapy will depend on the ability to alleviate anoxia. The therapies described for the management of emphysema are applicable here.

Neuromuscular Diseases

Central nervous system lesions that lead to depression of the respiratory center as well as the lesions of poliomyelitis, Guillain-Barré disease, myotonic dystrophy, and other myopathic diseases—may result in alveolar hypoventilation and cor pulmonale because the muscles of respiration are not properly stimulated or are themselves too weak to perform their function adequately. The lungs themselves are normal. Treatment consists almost exclusively of combating intercurrent pulmonary infection and maintaining adequate ventilation by use of respirators. The prognosis in these circumstances rests with the progress of the primary disease although the heart failure may be reversible.

Structural Deformities of the Chest Cage

Kyphoscoliosis and surgical alterations of the chest cage may disturb the mechanics of breathing to such a severe degree that hypoventilation with anoxia and hypercapnia appear and circulatory disturbances follow. This however is a rare eventuality; it is much commoner for these subjects with chest deformity to develop the respiratory gas and circulatory alterations because of either recurrent bronchopulmonary infections or an accompanying emphysema. The treatment again revolves around provision of adequate gas exchange by means of respirators and attack upon the infections. Both positive-pressure and tank respirators have been used successfully in these patients. Vaporized bronchodilator drugs are not always effective and, if this is demonstrated, it is wise to discontinue them. Obviously it may be extremely difficult to delineate heart size in such chests.

Obesity

In certain fat people circulatory disturbances can appear in association with alveolar hypoventilation. Although the ultimate mechanisms are not well understood it is agreed that the excess fat plays a large role. This is best demonstrated by the fact that weight loss initiates a reversal of the syndrome. The lungs themselves appear normal but there may be increased need for gas exchange as well as increased resistance to ventilation as a result of the masses of fat. Whether, in addition, there must also exist a disturbance in
respiratory control centers in the central nervous system remains to be proved.

Cystic Fibrosis of the Pancreas

In this disease of children, the bronchial and bronchiolar obstruction due to viscid secretions and infections produces a picture similar to that seen in the adult with obstructive or bronchitic emphysema, and therapy is much the same in both groups. Efforts to thin the secretion by enzymatic agents may be successful.

Bronchiolitis

This other common cause of cor pulmonale in children in the western hemisphere is usually an acute respiratory illness without antecedent symptomatology. It is a diffuse inflammatory reaction associated with intense bronchospasm which can rapidly initiate alveolar hypoventilation. With treatment of bronchospasm and infection, the patient may have no further cardiopulmonary dysfunction.

Diseases That Produce Cor Pulmonale by Reduction of the Pulmonary Vascular Bed

This type of cor pulmonale, in contrast to that seen with alveolar hypoventilation, develops in the late stages of the diseases that cause it and is characterized by pulmonary hypertension, which so far has appeared to be irreversible.

Multiple Pulmonary Emboli

Although this is considered a rare cause of cor pulmonale, cases are being encountered in increasing number as a result of more careful attention to diagnosis. The site of origin of the emboli is usually in the pelvic or leg veins. There is a higher incidence in women than in men. In women one almost always finds a history of pregnancy, either at term or interrupted by abortion, or pelvic inflammatory disease prior to the onset of symptoms. In men the prostatic plexus or leg veins are noted as the source of the emboli. Embolization may be recurrent over several years with resultant obliteration or narrowing of many of the smaller vessels. The chronicity is indicated by pathologic specimens in which evidences of sclerosis, recanalization, and recent emboli can be found in the same microscopic section. These vascular occlusions seldom cause pulmonary infarcts that can be detected clinically. In some instances it may be impossible to distinguish such lesions from those due to the pulmonary arteritides with intravascular thromboses unless the lungs are only a part of a generalized vascular disease. In these patients with longstanding pulmonary hypertension, right ventricular hypertrophy is often quite marked in contrast to subjects with emphysema, in whom only dilatation or minor hypertrophy may be seen.

The onset of this illness may be difficult to determine. Complaints of sudden bouts of dyspnea occasionally associated with chest pain and sometimes accompanied by minor hemoptysis may be elicited for several years before evidences of right heart enlargement appear. The source of the emboli may not be readily apparent. Frequently the x-ray and electrocardiogram reveal no abnormalities during the early phase of the illness. Because of the paucity of objective findings early in the disease, these patients are often designated as psychoneurotics, especially since weakness and fatigue are prominent symptoms at this point. Ultimately one is confronted with a dyspneic patient with large pulmonary arteries and right heart enlargement in whom cyanosis may not be marked. The electrocardiogram at first indicates right ventricular change by inversion of the right precordial T waves but eventually most of these individuals show the characteristics of right ventricular hypertrophy. When right heart failure appears it is usually intractable and marks the onset of the phase of rapid deterioration. The ensiform gallop is a reliable physical sign of heart failure. The total course of this disease may last 5 to 10 years, although, in general, heart failure appears late. Except for treatment of heart failure, therapy is almost nonexistent, since the illness is rarely diagnosed until it is far advanced. Hence the efficacy of anticoagulants is not known. If the diagnosis is made prior to extensive destruction of the bed, ligation of the offending veins or even the inferior vena cava can be life saving. Drug
therapy directed at the hypertension, so far has been unsuccessful.

Tests of cardiopulmonary function may help to confirm the clinical diagnosis. There are marked hyperventilation and a low carbon dioxide tension of the arterial blood. At the stage of heart failure there is usually arterial oxygen unsaturation that may be as low as 80 per cent at rest, falling markedly on exercise. The unsaturation probably springs from a combination of changes, namely, a reduction in the diffusing surface of the pulmonary vascular bed and the development of intravascular pulmonary shunts. Some increase in hematocrit and hemoglobin may be present. These patients may have the highest pulmonary artery pressures found in cor pulmonale and their cardiac output is usually low. The hypertension is probably the major determinant of the cardiac involvement since the anoxia is seldom severe and blood volume is only slightly abnormal.

Syndrome of Alveolar-Capillary Block

Under this general heading come the diseases that produce lesions in the alveolar-capillary membrane and that are characterized by difficulty of oxygen diffusion. These include berylliosis, Boeck's sarcoid, scleroderma, and certain granulomatous lesions and reticular fibroses of undetermined etiology. These patients offer some interesting contrasts to those patients with cor pulmonale due to emphysema. The respiratory illness is usually short, unremitting, progressive and associated with an extraordinary tachypnea and little cyanosis. There is no obstructive breathing, and the lungs may be clear on physical examination or may show widespread rales. In some of these patients death from the rapidly worsening pulmonary insufficiency may occur before evidences of cardiac insufficiency appear. In those who do develop heart failure, it is irreversible and very often a terminal event. This is quite different from patients with emphysema in whom heart failure may occur at any time in the course of the disease when severe acute anoxia supervenes and in whom heart failure may be completely reversible and preventable. It is of interest that the authors have heard a basal diastolic murmur of pulmonic incompetence only in patients with irreversible pulmonary hypertension, i.e., those with fibrosis or embolization. The findings on chest x-ray depend of course on the nature of the pulmonary disease. If the hilar and paramediastinal areas are markedly fibrotic, the definition of cardiomegaly may be difficult. The electrocardiographic alterations are the same as those seen in cases of multiple emboli and are the expression of progressive right heart hypertrophy. In these subjects with difficulty in diffusion due to thickness of the alveolar capillary membrane or a reduction in its area, studies of cardiopulmonary function will indicate the defect. The resting arterial saturation is only slightly, or at most moderately, decreased, and carbon dioxide levels are not elevated and may even be diminished when hyperventilation is severe. Pulmonary hypertension and right heart enlargement may be present before even moderate anoxia appears at rest, therefore it seems likely that anatomic lesions are primarily responsible for the developments of cardiac complications. Of course as the lung disease progresses and severe anoxia occurs, either at the end stage or because of a complicating pulmonary infection or focal emphysema, its effects are superimposed. Heart failure is usually not seen until severe anoxia is present at rest. In contrast to patients with multiple emboli, these subjects have a high resting cardiac output but it is not on a hypervolemic basis, as polycythemia occurs uncommonly, except in the terminal phase. The exact stimulus for this hyperkinetic flow is unknown.

It is obvious then that therapy in cardiac failure due to chronic pulmonary fibrosis or pulmonary granulomas, with their irreversible pulmonary hypertension, cannot be expected to be as beneficial or successful as in cor pulmonale due to emphysema. Nevertheless digitalis may reverse evidences of failure and should be administered and maintained. Polycythemia is not a frequent com-

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plication but if present should be relieved. Attention to pulmonary infection is of great importance. The use of oxygen by the usual clinical means is satisfactory and is to be encouraged as long as there is no complicating pulmonary emphysema with its dangerous hypercapnia.

There is as yet little direct therapy for the primary pulmonary disease in these patients. It is reasonable to suggest that until better circulatory studies are available in all forms of pulmonary fibrosis physical exertion should be curtailed, as it is only by maintaining as low a level of pulmonary artery pressures as possible that right heart strain can be minimized. In the granulomas the use of steroids has offered some hope of limiting the cellular proliferation causing the syndrome of alveolar-capillary block. However, it is not always possible to control the degree of pulmonary fibrosis that results from hormonal treatment.

**Chronic Pulmonary Diseases Seen in Association with Certain Forms of Organic Heart Disease**

Chronic pulmonary diseases capable of producing circulatory abnormalities may occur along with organic heart disease. Usually, however, when these two disease entities coexist the patient does not present with the classical picture of cor pulmonale. Even if the nature of the pulmonary disease (and this is most frequently some form of emphysema) is identified by studies of pulmonary function, it is probably advisable to avoid the diagnosis of cor pulmonale. The reasons for this are the following: (1) the clinical course and prognosis are almost always dominated by the organic heart disease; (2) therapy must take both diseases into consideration and the results will depend upon the stage of the organic heart disease; (3) disturbances in gas exchange in these combined states are rarely as severe as in patients with uncomplicated cor pulmonale. Since anoxia is seldom marked (below 80 to 85 per cent), one is uncertain if the circulatory complications produced by anoxia are present. These patients with organic heart disease develop evidences of congestive failure with minor degrees of unsaturation. Indeed the levels of anoxia at which failure is seen are those one would be gratified to be able to maintain in patients with uncomplicated cor pulmonale. On the other hand, this level of unsaturation probably acts in a deleterious fashion upon the primarily disturbed ventricular myocardium. The fact that the patient with cor pulmonale develops heart failure at much lower levels of saturation than does the one with organic heart disease suggests that in the former the integrity of the myocardium has been fairly well preserved. One does not usually see marked hypercapnia in spite of severe emphysema in the presence of organic heart disease. This probably stems from the hyperventilation these individuals demonstrate when in the congestive state.

The presence of an enlarged left ventricle or left atrium precludes making the solitary diagnosis of cor pulmonale. Conversely, there is practically no form of acquired organic heart disease that results in isolated enlargement of the right heart and pulmonary arteries. Pure mitral stenosis, if it is hemodynamically important enough to produce right cardiomegaly, is usually accompanied by some left atrial abnormality.

A few comments should be added concerning therapy in patients with organic heart disease and chronic pulmonary disease. The minimal degree of carbon dioxide retention in the majority of these cases is reassuring in considering oxygen therapy and permits the use of high oxygen concentrations without risk of narcosis. The presence of arteriosclerotic heart disease warrants caution in the use of sympathomimetic bronchodilators as tachycardia and angina may be complications of these drugs. Aminophylline administered by suppository or infusion is often a satisfactory substitute. If bronchospasm and bronchial infection are severe, one should not hesitate to use mechanical respirators. The type of respirator that requires the dyspneic subject to initiate the inspiratory cycle may prove intolerable in those with primary heart
disease. If one supplies an apparatus with a very low opening or inspiratory pressure, as well as a very high rate of instantaneous flow, the respirator is acceptable. The tank type of respirator can also be used.

Summary and Conclusions
A number of different forms of pulmonary dysfunction are now recognized as causing cor pulmonale, and the disease processes acting as etiologic agents are numerous and variable. There are however only 2 basic patho-physiologic mechanisms that compromise the heart, and upon knowledge of these depends successful therapy.

Summario e Conclusiones in Interlingua
Es recognosce in nostre dies que un numero de differente formas de dysfunction pulmonar pot eser le causa de corde pulmonal e que le processos patho-logic fungente como agentes etiologic es numerose e variabile. Tamen, il existe solmente 2 mechanismos patho-physiologic fundamental que affice le corde, e le cognoscenciu de istos es le pre-condition de succeso therapeutique.

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