The Treatment of Chronic Cor Pulmonale

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MODERN concepts of therapy in chronic cor pulmonale, or heart disease secondary to lung disease, have developed largely as a result of increased knowledge of the physiologic disturbances in pulmonary function which give rise to the circulatory sequelae in these diseases. Since the cardiocirculatory complications spring from the underlying pulmonary dysfunction, therapy, if it is to be successful, must be directed at the former as well as at the latter. The older pessimistic attitude concerning therapy in these patients resulted from attacking exclusively or primarily the cardiac insufficiency to the neglect of the parent entity, pulmonary insufficiency. All too often a cyanotic patient with dyspnea and cough, some abnormality in x-ray films of the lungs, and right heart failure is diagnosed as having chronic cor pulmonale without further effort at clarification of the nature of the underlying pulmonary disease. The treatment of chronic cor pulmonale must include an attack upon the pulmonary insufficiency, and treatment of the latter can only be fruitful if the nature and extent of the lung disease and its consequences are known.

Hence one can say that treatment of chronic cor pulmonale really begins with a correct diagnosis of the lung disease causing it. Prognosis of the ultimate outcome is also dependent upon accurate diagnosis. One cannot outline the same therapy for a patient with pulmonary fibrosis as for one with pulmonary emphysema as far as improvement of pulmonary function is concerned. On the other hand the treatment of right heart failure consists of much the same regimen in both cases.

Although there are many forms of lung disease which can secondarily compromise the circulation and produce chronic cor pulmonale, the commonest include chronic obstructive pulmonary emphysema, different types of pulmonary fibrosis, and granulomatous lesions which may eventually result in fibrosis. However, right heart enlargement, with or without cardiac failure, the essential characteristic of chronic cor pulmonale, is uncommonly associated with uncomplicated pulmonary tuberculosis, bronchiectasis or bacterial pneumonia. The circulatory complications associated with kyphoscoliosis are probably related to an accompanying emphysema in most instances, although no extensive study of the circulation in this group of patients is available. Finally, we shall not concern ourselves here with the rarer types of chronic pulmonary hypertension such as those due to pulmonary emboli or secondary to pulmonary metastases.

It is evident, then, that the treatment of chronic cor pulmonale usually involves the treatment of pulmonary fibrosis or emphysema. One cannot stress too emphatically that the presence of one disease, for example, emphysema, does not automatically imply the coexistence of the other. The tendency to write down pulmonary fibrosis and emphysema as a
diagnosis is to be depleted unless both conditions are shown by objective measurements to be present. This is particularly important in setting up a regimen of therapy for these patients and in understanding the mechanisms whereby the cardiocirculatory complications develop in each case.

**Chronic Cor Pulmonale Due to Chronic Pulmonary Emphysema**

Chronic pulmonary emphysema is the commonest cause of chronic cor pulmonale, and hence its pathophysiology, including the circulatory complications, will be reviewed briefly as a background for the discussion of treatment.

There are three fundamental disturbances in pulmonary function in chronic pulmonary emphysema: (1) there is gross impedance to air flow in and out of the lungs, (2) the air is unevenly distributed to the alveoli, and (3) the blood returning to the lungs is similarly unevenly distributed to the alveoli.1-3 At the present time we cannot attack the latter dysfunction therapeutically. Means are available, however, which permit us to remedy the first two abnormalities.

The inadequate air flow is caused not only by loss of elasticity of the lung tissue, but also by bronchiolar spasm and mucosal edema, and by obstruction resulting from secretions and exudates. Vaporized bronchodilators are often quite effective in alleviating the symptoms due to bronchial obstruction. This can be readily demonstrated by the improvement in the maximum ventilatory capacity, which so frequently follows the inhalation of these drugs. In our experience the best results are obtained with certain of these drugs if they are used systematically, and not just when the patient is in distress. Five to eight drops of the undiluted bronchodilator solution are vaporized at each treatment and inhalation of this amount should take place over a 10- to 20-minute period. Such a preparation as Vaponefrin, can be inhaled three or four times a day using a manually operated nebulizer and will usually produce bronchodilator effects without tachycardia or tremor. However, it has been amply demonstrated that bronchodilator drugs can be better disseminated if a positive pressure apparatus is used in conjunction with the nebulizer.4 Bothering secretions and exudates so often encountered in the patient with emphysema, generally result from either acute or chronic pulmonary infections, and may be combated by the intensive use of antibiotics given in a variety of ways. In these patients one cannot ignore what might ordinarily be considered to be a trivial respiratory infection, because the patients do not tolerate well any further encroachment upon their pulmonary reserve. The loss of even a small area of functioning lung tissue as a result of bronchial or pulmonary infection, may be sufficient to precipitate severe pulmonary insufficiency.

The majority of patients with emphysema, however, do not present only simple ventilatory insufficiency. At some time in their disease more severe ventilatory dysfunction, coupled with gross disturbance in distribution of air and blood to the alveoli, leads to alterations in gas exchange, with resulting anoxia and hypercapnia. In some individuals, anoxia with or without carbon dioxide retention is only seen with acute pulmonary infections and subsides with the alleviation of the infection. In others, of course, the disease process itself is more advanced or is associated with frequent and severe attacks of bronchiolar spasm; hence anoxia and hypercapnia of varying degree are constantly present. It is when anoxia and hypercapnia become a dominant feature of emphysema that the circulatory complications may appear, i.e., pulmonary hypertension, hypervolemia with polycythemia and right heart failure.

**Management of Acute Exacerbations of Cardiopulmonary Insufficiency**

Unfortunately many of the patients with chronic pulmonary emphysema and cor pulmonale are not seen by a physician until heart failure is present. Then one is faced with a most difficult therapeutic problem, namely, the management of the patient with advanced pulmonary emphysema who enters the hospital acutely ill, intensely cyanotic, coughing ineffectively, bringing up with difficulty thick tenacious sputum. Sometimes somnolent, usually restless, he is often unable to cooperate. The
cerebral manifestations of anoxia may even reach a stage of paranoia and disorientation. This patient requires constant and expert medical attention. He cannot be given a nebulizer with brief instructions as to its use and left to medicate himself. Bronchoscopy and postural drainage usually are impractical because of the precarious state of the patient. He can, however, often bring up sputum if urged constantly.

Generally this type of treatment is insufficient and oxygen must be supplied. In a certain group of these subjects whose interference with gas exchange has produced anoxia without hypercapnia, this is not hazardous and administration of oxygen by mask, tent or nasal catheter rapidly alleviates the symptoms and signs of oxygen want. In others, however, where alveolar hypoventilation is marked and carbon dioxide retention is present in addition to anoxia, the respiratory response to carbon dioxide is known to be diminished and anoxia, operating through the carotid body chemoreceptors, remains the primary stimulus to breathing. The increase in arterial blood oxygen tension following oxygen therapy results in a further marked reduction in alveolar ventilation and hence a further rise in carbon dioxide tension and bicarbonate levels in the blood. Eventually the carbon dioxide retention may lead to narcosis and even death. Thus in all emphysematous patients one should always determine the carbon dioxide content of the arterial blood before starting oxygen therapy, and if there is hypercapnia, employ some mechanical means to maintain adequate alveolar ventilation while oxygen is being supplied.

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 air. Furthermore it has not been found necessary to utilize helium-oxygen mixtures to achieve adequate oxygenation. During the acute episodes of cardiac and pulmonary insufficiency the patient should use these mechanical ventilatory aids as much as 18 to 20 hours a day. The use of vaporized bronchodilators makes these aids more effective. As the patient improves—and this can best be gauged by frequent determinations of the arterial blood oxygen saturation and carbon dioxide content—the periods of unassisted breathing can be increased. It generally requires 10 days to 2 weeks of intensive treatment to achieve a state in which the respiratory aids are no longer essential. 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, codeine and barbiturates is contraindicated and if used in some subjects may be fatal. If sedation is absolutely necessary, chloral hydrate or paraldehyde can be administered.

So far the discussion has centered around the treatment of the pulmonary insufficiency in these patients with emphysema and cor pulmonale. Emphasis has been placed upon relief of anoxia and carbon dioxide retention because they set into motion the cycle of events which precipitate and perpetuate cardiac failure. The anatomic restriction of the pulmonary vascular bed is, of itself, generally not sufficient to produce anything but minimal pulmonary hypertension at rest in the emphysematous patient. When anoxia and hypercapnia appear there evolves the classic picture of cor pulmonale: severe pulmonary hypertension, polycythemia, high cardiac output and ultimately right heart failure.

The specific cardiac therapy of the patient in failure with chronic 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. One must remember that one cannot rely solely on the heart rate as an index of full digitalization in these patients, as they 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 run resting ventricular rates of 90 to 100, and if digitalis dosage is increased to combat this rapid rate, intoxication may result. Arrhythmias are very rare in patients with pure chronic cor pulmonale. Their occurrence strongly suggests the coexistence of another type of heart disease. Hydrothorax due to heart failure is rarely seen in uncomplicated cor pulmonale and if pleural effusion is found, one must consider an additional diagnosis such as empyema due to a pneumonia, or hemorrhagic effusion due to pulmonary infarction. In the presence of pleural fluid in an emphysematous subject one must weigh the possible improvement in lung function, after thoracentesis, against the real danger of inducing a pneumothorax by this procedure.

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 towards the satisfaction of tissue oxygen needs in the presence of anoxia, as they are in normal man. Therefore, it is imperative to reduce blood flow and blood volume by means of phlebotomies. The diagnosis of this secondary polycythemia, which is characterized by hypochromic red blood cells, can best be made clinically by a measurement of the hematocrit. Determinations of hemoglobin content alone will be misleading as this value may be within normal range when the hematocrit is high.

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 cc. to 500 cc. at each phlebotomy, and the use of a vacuum bottle makes the withdrawal of this very viscid fluid fairly easy. Serial measurements of the hematocrit and hemoglobin will indicate the total amount of blood which must be removed to return the hematocrit 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 two to three days.

The patient in full-blown acute cardiac and pulmonary insufficiency represents a real challenge to both physician and nurse. Constant attention is needed to urge effective cough. Steam inhalation and sputum liquefiers such as potassium iodide or terpin hydrate may be used. Adequate fluid intake and particularly an adequate caloric intake must be almost forced on these somnolent patients who may even doze off with their mouths full of food. Infinite patience may be necessary in handling the cerebral aberrations of which they may bitterly complain, particularly during a restless night time. It is well known that these individuals may suddenly, almost unaccountably, take a turn for the worse in a few minutes time; it is best, therefore, to have a physician visit their bedside every two or three hours during the first few days, particularly if they are using a respirator. Obviously the nurse must be carefully trained in handling such patients and particularly in the use of the mechanical ventilatory aids.

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 the 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. A recent case of cor pulmonale who died in severe right heart failure illustrates this point. The patient was admitted
in marked cardiac and pulmonary insufficiency with all the evidence, clinical and physiologic, of severe obstructive pulmonary emphysema. This lesion, in addition to a superimposed pneumonia, was considered to be the basis of his disability. Despite the intensive use of all the measures stressed above, cardiac failure was not relieved. Three other unusual features were present. He had recurrent and large amounts of right chest fluid, a complication rarely seen in pure chronic cor pulmonale secondary to emphysema; he became icteric a few days before death; and cardiac catheterization shortly after admission revealed an extraordinary elevation of pulmonary artery pressures, 115/48 with a mean of 72 mm. Hg, values not encountered in our laboratory in a patient with cor pulmonale and only emphysema. The pulmonary artery pressures suggested the presence of severe anatomic curtailment of the pulmonary vascular bed, and the appearance of icterus terminally suggested pulmonary infarction. This was confirmed by necropsy which revealed multiple large pulmonary emboli, both old and new, in addition to the pulmonary emphysema.

**Maintenance Therapy**

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 carbon dioxide content, associated, if possible, with a determination of arterial pH, so that carbon dioxide tension can also be calculated. If the emphysematous patient with cor pulmonale is doing well, there are only minor fluctuations in arterial blood oxygen saturation and carbon dioxide content as determined at rest under basal conditions. The frequency with which these determinations need to be made depends upon many factors and in our experience may vary from every two to six 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 per cent; the carbon dioxide tension generally lies in the range of 45 to 55 mm. Hg when the patient is well controlled. Variations in carbon dioxide tension are much smaller than variations in arterial oxygen saturation and hence a change of 5 mm. Hg or more in this measurement in the individual patient is highly significant. 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 which 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. These individuals, who are already using Vaponefrin by nebulizer regularly three times a day, are advised to use it every four hours. Antibiotics are used vigorously even if the subject is afebrile. The improvement following antibiotics is often so satisfactory that one is led to believe that there is an important element of hidden bronchial or pulmonary infection present. 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.

One can anticipate that the use of mechanical respirators may become a part of the maintenance therapy of these individuals, in order to promote better alveolar ventilation and hence better respiratory gas exchange. Preliminary trials show this to be a feasible and effective procedure if used three to four hours a day, but it is at present limited by the ex-
pense of the equipment. Abdominal belts, breathing exercises, and pneumoperitoneum have been reported to be of benefit in certain cases, particularly those with inadequate diaphragmatic motion.9

In treating pulmonary insufficiency in these patients with chronic cor pulmonale, emphasis has been placed upon the various therapeutic means which promote better gas exchange, inasmuch as cardiac complications in large measure spring from anoxia and hypercapnia. It has been shown that anoxia and hypercapnia stimulate polycythemia and that the latter frequently appears or suddenly increases just prior to heart failure. This represents an important clue to success in the management of the patient with cor pulmonale. If repeated measurements of the hematocrit show an increasing red cell mass, phlebotomies are performed as indicated. Obviously the hematocrit 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 bimonthly to biannually—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 cautious attitude is dictated by the fact that even though these subjects may now have normal pulmonary artery pressures at rest they will have a rise in pulmonary artery pressure on exertion and hence may experience some right heart strain. However, it is not our custom to institute digitalization in patients with emphysema who have never shown any evidence of heart failure. One must also remember that cough and dyspnea are symptoms of pulmonary and not cardiac dysfunction in these patients, and hence are not indications for mercurial diuretics in the absence of right heart failure.

Following the progress of the pulmonary disease, in this instance emphysema, by means of serial chest x-ray films is not often helpful except in the diagnosis of complicating pulmonar}
tion in the number of the functioning vessels. In either event pulmonary hypertension will be present whether blood flow is normal or reduced.

In silicosis it has long been known that the pulmonary dysfunction may remain one of ventilatory insufficiency without arterial anoxia for long periods of time.\(^{11,12}\) Whether pulmonary hypertension is frequent in these patients is not yet known, but it can be present without producing changes in the heart size or configuration of the electrocardiogram.\(^7\) How well this pulmonary hypertension is tolerated, that is, how soon right heart failure will follow, if ever it appears in this group, is unknown. The few patients studied in congestive failure due to silicosis alone appear to have a low cardiac output even in the presence of anoxia and polycythemia, in contrast to the cor pulmonale due to emphysema. Anoxia is seldom severe in silicosis unless the disease is far-advanced or unless there coexists with the pneumoconiosis its frequent complication, chronic obstructive emphysema. When both diseases are present either may dominate the functional status and hence circulatory changes due to either or both may occur.

Although little is known of the circulatory complications in silicosis not associated with emphysema, the picture is a little clearer in that group of rarer diseases which produce pulmonary lesions located in the pulmonary alveolar-capillary membrane and which are characterized by difficulty of oxygen diffusion. The term “syndrome of alveolar-capillary block” has been proposed for this group of diseases which include various granulomas of the lung (due to exposure to beryllium, Böeck’s sarcoïd, and of undetermined origin), scleroderma, and the diffuse reticular pulmonary fibroses.\(^{13}\) It has been shown that in these patients the cardiac output is elevated and that mild pulmonary hypertension, due to anatomic restriction of the vascular bed and not to anoxia, is common at rest, increases with exertion, and in some instances may even be progressive. This latter feature is in sharp contrast to the pulmonary hypertension of the patient with emphysema and cor pulmonale, in whom the pulmonary hypertension, which is related to anoxia, is reversible and may be kept minimal by good treatment. Hence in the patient presenting this syndrome the anatomic lesion is the fixed and dominant factor and the compromising of the right heart—at first minimal, later in the disease severe—is irreversible.

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 will improve the cardiac output\(^6\) and should be administered and maintained. Polycythemia is not a frequent complication but if present should be relieved. Obviously attention to pulmonary infection is of great importance. The use of oxygen by the usual clinical means is satisfactory as long as there is no complicating pulmonary emphysema with its dangerous hypercapnia. When emphysema develops, as it often does,\(^{12,14,15}\) one should suspect that much of the patient’s cardiopulmonary disability relates to this disease, and vigorous therapy, as outlined above, should be directed at its sequellae. Indeed, in several patients with silicosis followed in our clinic almost all the circulatory complications were found to be secondary to emphysema and consequently the patients were relieved of heart failure and have been maintained free of it for long periods of time.

There is as yet little direct therapy for the primary pulmonary disease in patients with some form of fibrosis. Attention to secondary pulmonary infection is obviously important.\(^{16}\) 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 patients with pneumoconiosis this appears at present to be the only rational therapeutic program, meager and pessimistic though it be. In the granulomas the use of cortisone and corticotropin (ACTH) 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 which results from hormonal treatment. Many patients with this type of progressive pulmonary disease frequently die of pulmonary insufficiency before chronic cor pulmonale has developed. It has been our experience that once the latter is seen, the patients progress to terminal heart failure in weeks or months.

To summarize, the prognosis in a patient with chronic cor pulmonale due to some form of pulmonary fibrosis or granulomas may be poor as compared with the subject with pulmonary emphysema as his primary disease.

**Summary**

In this presentation stress has been laid upon the concept that the treatment, as well as the prognosis of chronic cor pulmonale depend upon the underlying pulmonary disease. It has long been known that the chief causes of chronic cor pulmonale are chronic obstructive pulmonary emphysema and various forms of fibrosis, particularly the pneumoconioses. An understanding of the difference between these diseases, both as to their pulmonary dysfunction and their circulatory complications, is crucial to success in therapy. Management of the patient with chronic pulmonary emphysema and cor pulmonale is quite different from that of the subject with fibrosis and right heart involvement.

In emphysema, we are fortunately able to reverse two features of the pulmonary insufficiency, anoxia and carbon dioxide retention, which are of paramount importance in producing the salient circulatory complications, that is pulmonary hypertension, hypervolemia, right heart failure. By vigorously combatting anoxia and hypercapnia, it is possible to reverse these circulatory abnormalities and prevent their recurrence. If the premonitory signs of increasing anoxia and hypervolemia are heeded and proper therapy instituted, it may even be possible to prevent an initial episode of heart failure in the emphysematous subject.

Unfortunately, little as yet is known about the circulation in the pulmonary fibroses. In patients with pulmonary fibrosis as well as those with granulomas of the lung it would appear that the anatomic pulmonary lesion is chiefly responsible for the pulmonary hypertension, in contradistinction to the patients with emphysema. Inasmuch as the anatomic lesions are for the most part irreversible, so is the pulmonary hypertension. This has limited our therapeutic approach in this form of chronic cor pulmonale to rigorous restriction of physical activity directed at minimizing exacerbations of pulmonary hypertension.

While emphasis has been placed upon the difference in management of the patient with emphysema or fibrosis and cor pulmonale, nonetheless it should be remembered that in any individual patient these two conditions may coexist. In that event, intensive therapy directed at the sequellea of emphysema may be very rewarding.

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