Pathogenesis and Treatment of Respiratory Failure

ROBERT F. JOHNSTON, M.D.
Division of Pulmonary Disease,
Hahnemann Medical College and Hospital,
Philadelphia, PA 19102

ABSTRACT

It is now recognized that acute respiratory failure, defined in terms of low arterial oxygen tension and/or CO₂ retention, is usually a reversible syndrome. This is particularly true when respiratory failure occurs as a consequence of impaired ventilation secondary to central nervous system depression. The early recognition of respiratory failure by widespread utilization of arterial blood gas determination and the application of a systematic scheme of treatment has been responsible for salvaging over 75 percent of these patients. Proper management of these patients does require application of a number of laboratory measurements, the most valuable of which has been arterial blood gas determination.

Introduction

Acute respiratory failure is defined as an acute worsening of pulmonary function manifested by abnormalities in the blood gases, i.e., by arterial hypoxemia and/or carbon dioxide retention and respiratory acidosis. It has been our practice to make a diagnosis of acute respiratory failure when the arterial oxygen tension (PO₂) is less than 50 mm Hg and/or the arterial carbon dioxide tension (PCO₂) is greater than 50 mm Hg. Sometimes it is mistakenly concluded that respiratory failure must be a manifestation of intrinsic lung disease. It is true that advanced lung disease does frequently lead to respiratory failure but, in many cases, the syndrome occurs without evidence of pre-existing lung disease. For example, 22 or 44 percent of 50 consecutive admissions to our respiratory unit had no known lung disease. There are some similarities and quite marked differences between respiratory failure occurring with and without lung disease. Respiratory failure occurring secondary to advanced lung disease is most frequently characterized by severe arterial hypoxemia. This is usually due to widespread ventilation perfusion abnormalities in the lung, i.e., areas of the lung which are continuing to be perfused but which are being inadequately ventilated. These areas with low V/Q (ventilation/perfusion) ratios cause significant quantities of unoxygenated or poorly oxygenated blood to be returned to the left side of the heart after passing through the lungs. Characteristically, patients with advanced lung disease will also have a normal or increased measured minute ventilation; they frequently have normal or decreased arterial PCO₂ levels indicating adequate alveolar
ventilation. The major problem is that venti-
latory efficiency and gas exchange mech-
isms, especially for oxygen, are badly
deranged by the advanced disease.

By contrast, respiratory failure can be
produced in patients with perfectly normal
lungs if the ventilatory mechanism is dis-
turbed. This most commonly is the result
depression of the medullary respiratory
center by drugs. Other abnormalities in the
central nervous system, abnormalities in
the respiratory muscles, abnormalities of
the pleural space or major airway obstruc-
tion can all produce decreased ventilation
leading to respiratory failure. The charac-
teristic findings in this type of respiratory
failure are decrease in measured minute
ventilation, significant elevation of the ar-
terial PCO2 and development of respira-
tory acidosis. Hypoxemia does develop in
these instances but it is not as prominent
as it is in respiratory failure occurring with
severe intrinsic lung disease. In this type
of respiratory failure, the elevation of the
PCO2 and the reduction in the arterial
oxygen tension tend to be approximately
of equal magnitude. In our respiratory care
unit, although the causes of respiratory
failure vary from time to time, the most
frequent single cause is central nervous
system depression owing to drug overdose.5
It is important to realize that respiratory
failure does occur in the presence of nor-
mal lungs because this type of failure may
be completely reversible if the diagnosis is
made promptly and if therapy is appro-
priate.

Diagnosis

The diagnosis of respiratory failure is
made by the demonstration of significant
arterial hypoxemia and/or hypercarbia.
Certain clinical features can suggest the
presence of respiratory failure. These in-
clude cyanosis and hypoventilation. How-
ever, more subtle findings may be the only
indication that respiratory failure is pres-
et, e.g., bizarre or inappropriate behavior
in a patient, particularly after surgery,
should suggest the possibility of cerebral
hypoxia. The presence of persistent tachy-
cardia, sweating and systolic hypertension
also may indicate hypoxemia. These find-
ings are thought to be secondary to the
release of catecholamines. Patients seen in
the emergency room with unexplained
coma may be suffering from respiratory
failure. Clearly, when patients have ad-
vanced pulmonary disease the possibility
that respiratory failure may occur is usually
considered. The development of simple
techniques to obtain arterial blood,7 and
the ready availability of analyzers which
will accurately measure pH, oxygen and
carbon dioxide tension, have made it com-
paratively easy to recognize these severe
degrees of pulmonary insufficiency which
have been defined as respiratory failure.

The causes of carbon dioxide retention
are decreased effective alveolar ventilation
and ventilation-perfusion abnormalities.13
On the other hand, arterial hypoxemia can
be produced by a number of mechanisms
including hypoventilation, inspiration of
air with a PO2 less than 149 mm Hg, the
presence of significant ventilation-perfusion
abnormalities, (the presence of areas of
lungs which are still being perfused, al-
though they are being poorly ventilated),
the presence of significant right to left
shunting of blood either through the lung
or through an anatomic defect elsewhere
and, in rare cases, actual impairment of
diffusion of oxygen across the alveolar-
capillary membrane. It appears that this
latter defect rarely produces hypoxemia at
rest. However, during exercise it may be a
cause of arterial hypoxemia of a significant
degree. Low cardiac output can also pro-
duce a significant decrease in the arterial
PO2 if significant right to left shunting is
present or if there are significant abnor-
malities in the lung allowing blood to bypass
functioning alveoli. As the cardiac output
drops, the oxygen tension of the blood in the pulmonary artery may drop quite markedly. The remixing of venous blood with a low oxygen tension which has passed through the lungs without being oxygenated will significantly lower the arterial $PO_2$ if the quantity of shunted blood is substantial.\(^8\)

**Treatment**

The techniques of treating respiratory failure are somewhat complex, but the concepts involved are quite simple. Basically, two things are attempted in the management of patients with respiratory failure. These are the maintenance of adequate oxygenation and the improvement of pulmonary function.

**Oxygenation**

Adequate oxygenation can usually be obtained by the administration of continuous oxygen by nasal cannula, nasal catheter or, in some instances, by the use of a face mask. Although it is difficult to be arbitrary about what level of arterial $PO_2$ is necessary, it is our general policy to try to keep the arterial $PO_2$ over 50 mm Hg. It must be recalled that there are a number of other factors which affect the adequacy of oxygen transport to tissues. In addition to the arterial $PO_2$, such factors as the hemoglobin concentration, the function of the hemoglobin and the cardiac output must be considered before it can be decided whether or not oxygen transport is indeed normal.

In attempting to oxygenate patients in respiratory failure, it is now accepted that continuous oxygen therapy should be used. However, there is some misconception about the use of low-flow continuous oxygen in the treatment of respiratory failure. This technique is extremely valuable in the treatment of patients with significant carbon dioxide retention; that is, in patients with arterial $PCO_2$'s of 50 mm of mercury or higher. These are usually the patients with emphysema or other types of obstructive pulmonary diseases. In these patients, because of the elevation of the $CO_2$ tension, there has been loss of $CO_2$ respiratory drive and the patient in many instances is receiving his stimulus to ventilation from hypoxic stimulation of the carotid bodies. Clearly, the sudden removal of the hypoxic drive by the rapid elevation of the arterial oxygen tension to high levels may lead to profound and sudden hypoventilation. With these patients, the use of carefully controlled, low-flow oxygen has been extremely successful, for it is possible in most instances to give just enough oxygen to raise the $PO_2$ to satisfactory levels, that is in the vicinity of 50 mm of mercury, without removing completely the hypoxic respiratory drive and thus not precipitating significant hypoventilation.\(^4\)

On the other hand, respiratory failure may occur with severe hypoxemia but without hypercarbia. This is likely to be the situation in such conditions as pulmonary fibrosis, pulmonary edema or the adult respiratory distress syndrome. In these patients, the arterial $PCO_2$ is usually normal or even low. It is usually impossible to oxygenate adequately these patients with low-flow oxygen. Since they do not have hypercarbia, there is no need to use it.\(^1\) Therefore, in these individuals, high-flow oxygen should be used at once by nasal cannula; i.e. 15 liters per minute and, in many instances, it will also be necessary to use an oxygen face mask. The guideline that we use in deciding whether or not low-flow oxygen will be used is the initial level of the arterial $PCO_2$.

**Improvement of Pulmonary Function**

Once adequate arterial oxygenation has been achieved, attention must rapidly be turned to attempts to improve pulmonary function. Efforts are directed at improving the total quantity, ease and distribution of
ventilation. If this can be accomplished, the patient with approximately the same expenditure of respiratory work will be able to lower arterial PCO$_2$ and improve arterial oxygenation. In attempting to improve total ventilation and decrease the work of breathing, major efforts are made to remove excessive bronchopulmonary secretions. The most effective way of doing this is by utilization of a good cough. Patients should be stimulated to cough frequently and effectively. An effective cough is characterized by the rapid exhalation of a large volume of air. Early in the management of the patient with respiratory failure, it must be determined whether or not he has the potential to cough effectively. Because of expiratory air-flow limitation present in patients with a severe obstructive airway disease such as bronchitis, emphysema and asthma, these patients frequently cannot cough effectively. If this is the case, other methods must be substituted to help them clear their pulmonary secretions. Other techniques which can be useful include good hydration, chest physiotherapy and the use of gravity to help in the drainage of secretions, i.e., positioning the patient in such a way that gravity will help secretions drain into large airways where they can either be coughed up or can be reached with a suction catheter.

In patients with ineffective cough, the use of endotracheal suction is strongly recommended. This is done most frequently by passing a catheter through the nose into the trachea. Once the catheter is in place, it is wise to leave it in the trachea for a matter of ten to fifteen minutes. While it is in the trachea, brief suctioning of the trachea or either of the main bronchi should be alternated with periods during which oxygen is given through the tracheal catheter. Suction should never be used for more than ten or fifteen seconds at one time. The patient then should be given adequate time to recover while receiving oxygen through the tracheal catheter. Before removing the nasotracheal catheter, one should listen to the chest to be sure that secretions have been removed from the main airways.

**Bronchoscopy**

Occasionally when there is segmental lobar collapse or a collapse of an entire lung secondary to retained secretions, bronchoscopy will be necessary. Routine bronchoscopy is a technically difficult procedure in a critically ill patient with pulmonary failure. However, with the development of the fiberoptic bronchoscope, it has become reasonably simple to bronchoscope these patients either by the transnasal route or by passing the small fiberscope through an endotracheal tube or through a tracheotomy tube. Using this technique, the patient can be ventilated simultaneously and a relatively leisurely bronchoscopy can be performed causing the patient very little discomfort. Even the small suction channel of the fiberscope, two mm in diameter, can be extremely effective in removing large quantities of obstructing bronchopulmonary secretions if adequate time is taken and if adequate amounts of irrigation are utilized. Occasionally, it may be necessary to insert an endotracheal tube either through the nose or mouth or to perform a tracheostomy to remove excessive bronchopulmonary secretions. However, it is rarely necessary to intubate for these purposes alone, intubation usually being reserved for the patient who also requires ventilatory assistance.

**Bronchopulmonary Infection**

The recognition and adequate treatment of bronchopulmonary infection is an extremely important part of the successful therapy of respiratory failure. A major pulmonary infection can significantly impair pulmonary gas exchange. The response of the host to such pulmonary infection depends largely upon the pre-existing level of lung function (figure 1). If it is postu-
lated that a patient has a pulmonary infec-
tion which is severe enough to drop the
arterial PO\textsubscript{2} by 20 mm of mercury, the
effect on the ability of the host to main-
tain adequate oxygenation will depend
chiefly on the arterial PO\textsubscript{2} before the infe-
tion began. If the arterial PO\textsubscript{2} was 80 be-
fore the infection and drops to 60, it is
shown in figure 1 that the arterial oxygen
saturation will have fallen from 95 to 89
percent, a relatively minor drop. If the
patient has enough underlying lung disease
that before infection his arterial PO\textsubscript{2} was
60, the same decrease in PO\textsubscript{2} will drop his
arterial oxygen saturation from 89 percent
to 75 percent. In an extreme example of a
patient with severe chronic lung disease
with a PO\textsubscript{2} of 40, the same drop in PO\textsubscript{2}
will decrease his arterial oxygen saturation
from 75 percent to 35 percent. Infection
appears to impair pulmonary function by
two general mechanisms: (1) actually de-
creasing the function of gas exchanging
surfaces of the lung and (2) by producing
bronchial obstruction from excessive secre-
tions. Infection as a contributing cause to
respiratory failure must be diligently
sought and treated when identified prop-
erly. In patients who are producing puru-
lent sputum, but from whom no obvious
bacterial pathogen can be isolated, empiric
therapy with penicillin is indicated for five
to seven days.

**Bronchial Narrowing**

The presence of significant, generalized
bronchial narrowing, indicated by the de-
tection of polyphonic wheezing, is an im-
portant finding in patients with pulmonary
failure. The bronchial narrowing may be
due to retained secretions, to mucosal
edema or, in some cases, to actual con-
traction of bronchial smooth muscle. When
generalized polyphonic wheezing is found,
efforts to clear secretions must be in-
creased. The use of agents known to pro-
duce bronchial muscle relaxation and to
decrease inflammation in the airways must

![Figure 1. Because of the shape of the oxyhemo-
globin dissociation curve, the change in hemo-
globin saturation resulting from a PO\textsubscript{2} drop of 20
mm Hg will vary greatly depending upon the
initial PO\textsubscript{2} value.](image)

be considered. The use of inhaled sympa-
athomimetic means such as isoproteranol
are useful particularly in the asthmatic.
Intravenous aminophylline given over a 15
to 20 minute interval in a dosage of about
7 mg per kilo is often effective. If wheez-
ing is not reversed by these procedures,
then the use of adreno-corticosteroids in
large doses should be considered.

The presence of increased amounts of
water in the lung may be an important
cause of impaired gas exchange in patients
with pulmonary failure.\textsuperscript{10} This may be due
to left ventricular failure, but it has fre-
quently been identified in patients without
heart failure, for example, in those who are
heroin addicts, have brain injuries or cer-
vical cord trauma. The presence of in-
creased pulmonary fluid can be identified
most readily by careful examination of
serial chest X-rays. Whether or not this is
due to left ventricular failure or to in-
creased pulmonary capillary permeability
may be a difficult question to answer. If
there is no history or physical finding sug-
gestig heart failure, it is probably due to
the latter. However, in some instances it
will not be possible to make this decision
without further measurements. With the
availability of flow guided pulmonary artery catheters, it is now possible to measure pulmonary artery and pulmonary capillary wedge pressure in patients in respiratory failure. The presence of a normal pulmonary capillary wedge pressure in a patient with the picture of increased lung water eliminates congestive heart failure, mitral stenosis or diseases of the pulmonary veins as causes of a pulmonary edema. The most effective treatment of pulmonary edema is the use of potent diuretics usually, in these situations, given intravenously. If need be, water intake is restricted. Daily weights of patients in respiratory failure and frequent measurements of the oxygen gradient between the inspired air or the pulmonary alveolus and the arterial blood are useful techniques which may give early warning that pulmonary edema is developing.

Occasionally, pulmonary failure will be precipitated or worsened by the presence of significant pleural disease. This should be sought carefully because pneumothorax or a large pleural effusion can be rapidly corrected; if missed, it can be a fatal complication in extremely ill patients. In particular, the patient who has suffered chest trauma should be watched carefully for the development of pneumothorax or hemothorax secondary to fractured ribs. Occasionally, pneumomediastinum will develop, particularly in asthmatic patients. This may be detected by the presence of subcutaneous emphysema, the visualization of mediastinal emphysema on the chest X-ray or by the presence of Hamman's sign (mediastinal crunch).

**MECHANICAL VENTILATORY ASSISTANCE**

If the above measures are not able to improve the patient to the point where he can maintain adequate oxygenation and CO₂ removal, then an additional measure, also designed to improve pulmonary function, must be considered. This is the use of mechanical ventilatory assistance. Most patients with respiratory failure, as defined in this article, do not require mechanical ventilatory assistance. The rationale underlying the use of mechanical ventilators is the belief that the patient is suffering from a condition which can be reversed if adequate time is provided. Therefore, the ventilator is just a device which allows the therapeutic measures, which have been discussed, an opportunity to become effective. The indications for mechanical ventilatory assistance are:

1. the worsening respiratory acidosis due to CO₂ retention,
2. the inability to maintain arterial oxygen tension over 50 mm of mercury using oxygen by nasal cannula and a mask,
3. the presence of uncontrollable pulmonary edema,
4. trauma to the chest producing large areas of paradoxical chest wall movement and
5. severe fatigue of the respiratory muscles, as may occur in such conditions as intractable asthma or severe pneumonia.

Some physiologic guidelines for applying ventilatory support have been suggested. These include: (1) respiratory rate greater than 35, (2) vital capacity of less than 15 ml per kilo, (3) a forced expiratory volume in one second (FEV₁) of less than 10 ml per kilo, (4) an inspiratory force less than 25 cm of water, (5) an arterial PO₂ less than 70 mm of mercury on a tight-fitting mask delivering oxygen and an alveolar arterial oxygen difference greater than 450 mm of mercury when the patient is breathing 100 percent oxygen, (6) an arterial PCO₂ greater than 55 or a (7) ratio between physiologic dead space to tidal volume (VD/VT) ratio greater than 0.6. Before placing a patient on a ventilator, the likelihood of significant reversibility of his disease should be considered. It is, we believe, inappropriate to use ventilator therapy on a patient with end-stage emphy-
sema or fibrosis unless there has been rapid and severe worsening and unless the patient's function a month before the episode was such that life was tolerable.

**Ventilators**

The choice of respirators is a somewhat complex subject which will not be considered in detail. There are two types of ventilators that are in common usage. These are so-called pressure-cycled and volume-cycled machines. The pressure-cycle machine delivers a quantity of air until a preset pressure has been reached and then it stops. The mode of operation of both types of ventilators is intermittent positive pressure. The pressure-cycle machines do have the advantage that they are much less expensive than the volume machines. They need no electrical connections. The volume machines which deliver a preset volume irregardless of the pressure required are, at the present time, becoming more popular. The reason being that they are more reliable. These machines will deliver the preset volume even if the mechanical properties of the airways or lung change so that more pressure is required. It is easier to regulate inspired oxygen concentrations with volume machines. It is also considerably easier to deliver various respiratory wave forms with these machines. This includes the use of an inspiratory plateau designed to provide better distribution of gas throughout the lung and positive end expiratory pressure, a technique which has been useful in patients who have generalized infiltrative disease, decreased functional residual capacity and severe arterial hypoxemia. When it becomes necessary to place a patient on a ventilator, it does become clear that continuous observation of the patient is necessary. His survival is now dependent upon the proper functioning of this machine. Precautions must be taken to avoid disconnection from the machine, twisting or kinking of tubing, obstruction of tubing by secretions and/or power failures. If any do occur, an adequately trained individual must be available immediately to provide continuing ventilation by the use of a self-inflating bag. A number of excellent monographs and reviews have been written in recent years which describe in detail the management of patients with respiratory failure requiring continuous ventilation.

### References


5. **Johnston, R. F.:** Definitions, causes and clinical presentations of pulmonary failure. Pulmonary Care, Johnston, R. F., ed. Grune and Stratton, in press.


