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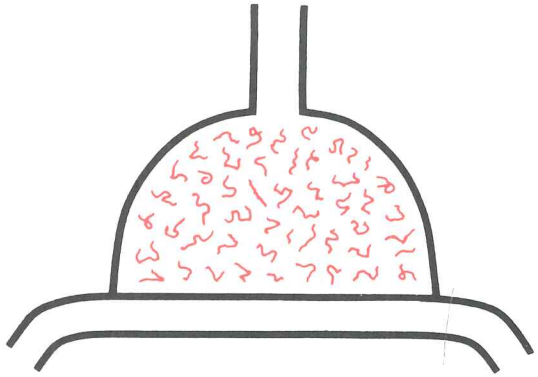


Respiratory Failure

Respiratory failure is said to occur when the lung fails to oxygenate the arterial blood adequately and/or fails to prevent CO_2 retention. There is no absolute definition of the levels of arterial P_{O_2} and P_{CO_2} that indicate respiratory failure. However, a P_{O_2} of less than 60 mm Hg or a P_{CO_2} of more than 50 mm Hg are numbers that are often quoted. In practice, the significance of such values depends considerably on the past history of the patient.

Gas Exchange in Respiratory Failure

Patterns of Arterial Blood Gases

Various types of respiratory failure are associated with different degrees of hypoxemia and CO_2 retention. Figure 8.1 shows an O_2–CO_2 diagram (See Respiratory physiology–the essentials, ed. 6: pp. 53 and 136) with the line for a respiratory exchange ratio of 0.8. Pure hypoventilation leading to respiratory failure moves the arterial P_{O_2} and P_{CO_2} in the direction indicated by the *arrow A*. This pattern occurs in respiratory failure caused by neuromuscular disease, such as poliomyelitis, or by an overdose of a narcotic drug (Figs. 2.2 and 2.3). Severe ventilation–perfusion ratio inequality with alveolar ventilation inadequate to maintain a normal arterial P_{CO_2} results in movement along a line, such as *B*. The hypoxemia is more severe in relation to the hypercapnia than in the case of pure hypoventilation. Such a pattern is frequently seen in the respiratory failure of chronic obstructive pulmonary disease (COPD).

Severe interstitial disease sometimes results in movement along *line C*. Here there is increasingly severe hypoxemia but no CO_2 retention because of the raised ventilation. This pattern may be seen in advanced diffuse interstitial lung disease or sarcoidosis. Sometimes there is a rise in arterial P_{CO_2}, but this is typically less marked than in obstructive diseases.

In respiratory failure caused by the adult respiratory distress syndrome (ARDS), the arterial P_{CO_2} may be low, as shown by *line D*, but the hypoxemia may be extreme. Such patients are usually treated with added inspired oxygen, which raises the arterial P_{O_2} but often does not affect the P_{CO_2} (*D* to *E*) although in some instances it may rise. Oxygen therapy to patients whose respiratory failure is caused by COPD improves the arterial P_{O_2} but frequently causes a rise in P_{CO_2} because of depression of ventilation (*B* to *F*).

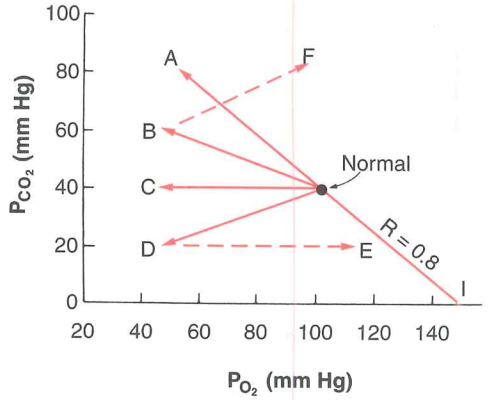


Figure 8.1. Patterns of arterial P_{O_2} and P_{CO_2} in different types of respiratory failure. Note that the P_{CO_2} can be high, as in pure hypoventilation *(A)*, or low, as in adult respiratory distress syndrome *(D)*. The *broken lines* show the effects of oxygen breathing. (See text for further details.)

Hypoxemia of Respiratory Failure

Causes

Any of the four mechanisms of hypoxemia, hypoventilation, diffusion impairment, shunt, and ventilation–perfusion inequality, can contribute to the severe hypoxemia of respiratory failure. However, the most important cause by far is ventilation–perfusion inequality (including blood flow through unventilated lung). This mechanism is largely responsible for the low arterial P_{O_2} in respiratory failure complicating obstructive diseases, restrictive diseases, and ARDS.

Detection

Severe hypoxemia causes cyanosis, cardiovascular signs such as tachycardia, and central nervous system effects such as mental confusion. However, a discussion of the detection of hypoxemia from these signs is largely academic because measurement of the P_{O_2} in the arterial blood is essential in determining the degree of hypoxemia in patients with suspected respiratory failure.

Tissue Hypoxia

Hypoxemia is dangerous because it causes tissue hypoxia. However, the arterial P_{O_2} is only one factor in the delivery of oxygen to the tissues. Other factors include the oxygen capacity of the blood, the oxygen affinity of the hemoglobin, cardiac output, and the distribution of blood flow.

Tissues vary considerably in their vulnerability to hypoxia. Those at greatest risk include the central nervous system and the myocardium. Cessation of blood flow to the cerebral cortex results in loss of function within 4–6 seconds, loss of consciousness in 10–20 seconds, and irreversible changes in 3–5 minutes.

If the P_{O_2} falls below a critical level in tissue, aerobic oxidation ceases and anaerobic glycolysis takes over with the formation and release of increasing amounts of lactic acid. The P_{O_2} at which this occurs is not accurately known and probably varies between tissues. However, there is evidence that the critical intracellular P_{O_2} is of the order of 1 mm Hg in the region of the mitochondria.

Anaerobic glycolysis is a relatively inefficient method of obtaining energy from glucose. Nevertheless, it plays a critical role in maintaining tissue viability in respiratory failure. The large amounts of lactic acid that are formed are released into the blood, causing a metabolic acidosis. If tissue oxygenation subsequently improves, the lactic acid can be reconverted to glucose or used directly for energy. Most of this reconversion takes place in the liver.

Effects of Severe Hypoxemia

Mild hypoxemia produces few physiologic changes. It should be recalled that the arterial oxygen saturation is still approximately 90% when the P_{O_2} is only 60 mm Hg at a normal pH (Fig. 2.1). The only abnormalities are a slight impairment of mental performance and visual acuity and perhaps mild hyperventilation.

When the arterial P_{O_2} drops quickly below 40–50 mm Hg, deleterious effects are seen in several organ systems. The central nervous system is particularly vulnerable, and the patient often has headache, somnolence, or clouding of consciousness. Profound acute hypoxemia may cause convulsions, retinal hemorrhages

and permanent brain damage. The cardiovascular system shows tachycardia and mild hypertension, partly caused by the release of catecholamines; in severe hypoxemia there may be bradycardia and hypotension. Signs of heart failure may occur if there is associated coronary artery disease. Renal function is impaired, and sodium retention and proteinuria may be seen. Pulmonary hypertension is common because of the associated alveolar hypoxia.

Hypercapnia in Respiratory Failure

Causes

Both of the two mechanisms of CO_2 retention–hypoventilation and ventilation–perfusion inequality–can be important in respiratory failure. Hypoventilation is the cause in respiratory failure resulting from neuromuscular diseases such as the Guillain-Barré syndrome, drug overdosage such as barbiturate poisoning, or a chest wall abnormality such as crushed chest (Fig. 2.3 and Table 2.1). Ventilation–perfusion inequality is the culprit in severe COPD and long-standing interstitial disease.

An important cause of CO_2 retention in respiratory failure is the injudicious use of oxygen therapy. Many patients with COPD gradually develop severe hypoxemia and some CO_2 retention over a period of months. It is not customary to refer to this situation as respiratory failure because these patients can continue in this state for long periods. However, such a patient usually has a high work of breathing (Figs. 3.3*B* and 4.12), and much of the ventilatory drive comes from hypoxic stimulation of the peripheral chemoreceptors. The arterial pH is virtually normal because of renal retention of bicarbonate (compensated respiratory acidosis), and the pH of the CSF is also nearly normal because of an increase in bicarbonate there. Thus, despite an increased arterial P_{CO_2}, the main ventilatory drive comes from the hypoxemia.

If this patient develops a relatively mild intercurrent respiratory infection and is treated with a high inspired oxygen concentration, a potentially dangerous situation can rapidly develop. The hypoxic ventilatory drive may be abolished while the work of breathing is increased because of retained secretions or bronchospasm. As a result, the ventilation may become grossly depressed and high levels of arterial P_{CO_2} may develop. In addition, profound hypoxemia may ensue if the oxygen is discontinued. This is because even if the ventilation does return to its previous level, the patient may take many minutes to unload the large accumulation of CO_2 in his or her tissues because of the large body stores of this gas.

A secondary cause of CO_2 retention in these patients may be the release of hypoxic vasoconstriction in poorly ventilated areas of lung as a result of the increased alveolar P_{O_2}. The consequences of this are increased blood flow to low $\dot{V}A/\dot{Q}$ areas and a worsening of $\dot{V}A/\dot{Q}$ inequality that exaggerates the CO_2 retention. This factor is probably less important than the depression of ventilation, but the rapid rise in arterial P_{CO_2} that is seen when some of these patients are given oxygen suggests that this mechanism may play a part.

Such patients present a therapeutic dilemma. On the one hand, oxygen administration is likely to cause severe CO_2 retention and respiratory acidosis. On the other hand, it is clearly essential to give some oxygen to relieve the life-threatening hypoxemia. The answer to this problem is to give a relatively low concentration (24–28% O_2) and to monitor the arterial blood gases frequently to

determine whether depression of ventilation is occurring. Intubation and mechanical ventilation may become necessary. The use of added oxygen is discussed further in Chapter 9.

Effects

Raised levels of P_{CO_2} in the blood greatly increase cerebral blood flow, causing headache, raised CSF pressure, and, sometimes, papilledema. In practice, the cerebral effects of hypercapnia overlap with the effects of hypoxemia. The resulting abnormalities include restlessness, tremor, slurred speech, asterixis (flapping tremor), and fluctuations of mood. High levels of P_{CO_2} are narcotic and cause clouding of consciousness.

Acidosis in Respiratory Failure

The CO_2 retention causes a respiratory acidosis that may be severe, especially after the injudicious administration of oxygen. However, patients who gradually develop respiratory failure may retain considerable amounts of bicarbonate, keeping the fall of pH in check (Fig. 2.10).

Metabolic acidosis frequently coexists with respiratory acidosis and complicates the acid–base abnormality. This is caused by the liberation of lactic acid from hypoxic tissues, and the dual factors of hypoxemia and an inadequate peripheral circulation are additive. In patients who are mechanically ventilated, the raised intrathoracic pressure may interfere with venous return and cardiac output and thus further reduce peripheral blood flow (Fig. 10.6).

Role of Diaphragm Fatigue

Fatigue of the diaphragm can contribute to the hypoventilation of respiratory failure. The diaphragm consists of striated skeletal muscle controlled by voluntary and automatic neural pathways via the phrenic nerves. Although the diaphragm is predominantly made up of slow twitch oxidative fibers and fast twitch oxidative glycolytic fibers, which are relatively resistant to fatigue, this can occur if the work of breathing is greatly increased over prolonged periods of time. Fatigue can be defined as a loss of contractile force after work, and can be measured from the transdiaphragmatic pressure resulting from a maximum contraction, or indirectly from the muscle relaxation time or the electromyogram. There is evidence that some patients with severe COPD continually breathe close to the work level at which fatigue occurs, and that an exacerbation of infection can tip them over into a fatigue state. This will then result in hypoventilation, CO_2 retention, and severe hypoxemia. Because hypercapnia impairs diaphragm contractility and severe hypoxemia accelerates the onset of fatigue, a vicious circle develops.

The dangers of diaphragm fatigue can be limited by reducing the work of breathing by treating bronchospasm and controlling infection, and by giving oxygen judiciously to relieve the hypoxemia. The force of contraction can be improved by a training program, for example, by breathing through inspiratory resistances. In addition, the administration of methylxanthines improves diaphragm contractility and also relieves reversible bronchoconstriction. However, the role of fatigue of the diaphragm in respiratory failure is still not fully understood.

Types of Respiratory Failure

A large number of conditions can lead to respiratory failure, and various classifications are possible. However, from the point of view of the physiological principles of management, five groups can be distinguished:

1. Acute overwhelming lung disease
2. Neuromuscular disorders
3. Acute on chronic lung disease
4. Adult respiratory distress syndrome
5. Infant respiratory distress syndrome

Acute Overwhelming Lung Disease

Many acute diseases, if severe enough, can lead to respiratory failure. These include infections such as fulminating viral or bacterial pneumonias, vascular diseases such as pulmonary embolism, and exposure to inhaled toxic substances such as chlorine gas or oxides of nitrogen. Respiratory failure supervenes as the primary disease progresses, and profound hypoxemia with or without hypercapnia develops. Oxygen administration is required for the hypoxemia, and mechanical ventilation may be necessary to tide the patient over the worst stage. A few patients have been treated by extracorporeal membrane oxygenators that largely take over the gas exchange function of the lung. Treatment of the underlying disease, for example, antibiotics for bacterial pneumonias, clearly is necessary. This group of conditions merges into ARDS (see later).

Neuromuscular Disorders

Respiratory failure may occur when the respiratory center is depressed by drugs such as heroin and barbiturates. Other conditions include central nervous system and neuromuscular diseases such as encephalitis, poliomyelitis, Guillain-Barré syndrome, myasthenia gravis, anticholinesterase poisoning, amyotrophic lateral sclerosis, and progressive muscular dystrophy (Fig. 2.3 and Table 2.1). Trauma to the chest wall also can be responsible.

In these conditions, the essential feature is hypoventilation leading to CO_2 retention with moderate hypoxemia (Figs. 2.2 and 8.1). Respiratory acidosis occurs, but the magnitude of the fall in pH depends on the rapidity of the increase in P_{CO_2} and the extent of the renal compensation.

Mechanical ventilation is often necessary in these conditions and occasionally, as in bulbar poliomyelitis, it may be required for months or even years. However, the lung itself is often normal and, if so, no additional oxygen is necessary to reverse the hypoxemia. Again, treatment of the underlying disease is always indicated, if available.

Acute on Chronic Lung Disease

This refers to an acute exacerbation of disease in a patient with longstanding underlying disease. It is an important and common group that includes patients with chronic bronchitis and emphysema, asthma, and cystic fibrosis. Many patients

with COPD follow a gradual downhill course with increasingly severe hypoxemia and CO_2 retention over months or years. Such patients are usually capable of limited physical activity even though both the arterial P_{O_2} and P_{CO_2} may be in the region of 50 mm Hg. As a result, this situation is not conventionally referred to as respiratory failure.

However, if such a patient develops even a mild exacerbation of his or her chest infection, the condition often deteriorates rapidly, with profound hypoxemia, CO_2 retention, and respiratory acidosis. The reserves of pulmonary function are minimal, and any increase in the work of breathing or worsening of ventilation–perfusion relationships as a result of retained secretions or bronchospasm pushes the patient over the brink into frank respiratory failure.

The management of these patients requires a delicate touch. Naturally, the underlying infection should be treated with antibiotics. In addition, bronchodilators may be indicated for bronchospasm, and diuretics and digitalis may be required if there is evidence of heart failure. Supplemental oxygen is necessary to relieve the severe hypoxemia. However, these patients frequently lose their ventilatory drive and develop severe CO_2 retention and acidosis if too much oxygen is administered. For this reason, it is usual to begin with 24–28% oxygen and monitor the arterial blood gases frequently (see Chapter 9).

Mechanical ventilation may be necessary, but the decision to employ this is often a difficult one. On the one hand, it may be impossible to prevent the rise of arterial P_{CO_2} without artificial ventilation. On the other hand, these patients often have such diseased lungs that, once they are on the ventilator, it may be difficult or impossible to wean them from it. Each case must be considered on its own merits, but mechanical ventilation should generally only be used if there is a substantial reversible component to the patient's condition.

Adult Respiratory Distress Syndrome

This condition is sometimes referred to as "acute respiratory failure." It is an end result of a variety of insults, including trauma to the lung or to the rest of the body, aspiration, sepsis (especially that caused by gram-negative organisms), and shock from any cause (40). There is evidence that many other organs are also affected, and the condition should probably be regarded as multi-organ failure.

Pathology

The early changes consist of interstitial and alveolar edema. Hemorrhage, cellular debris, and proteinaceous fluid are present in the alveoli, hyaline membranes may be seen, and there is patchy atelectasis (Fig. 8.2). Later, hyperplasia and organization occur. The damaged alveolar epithelium becomes lined with type 2 alveolar cells, and there is cellular infiltration of the alveolar walls. Eventually, interstitial fibrosis may develop, although complete healing can occur.

Pathogenesis

This is still unclear and many factors may play a role (41). The capillary endothelial and type 1 alveolar epithelial cells are damaged early,

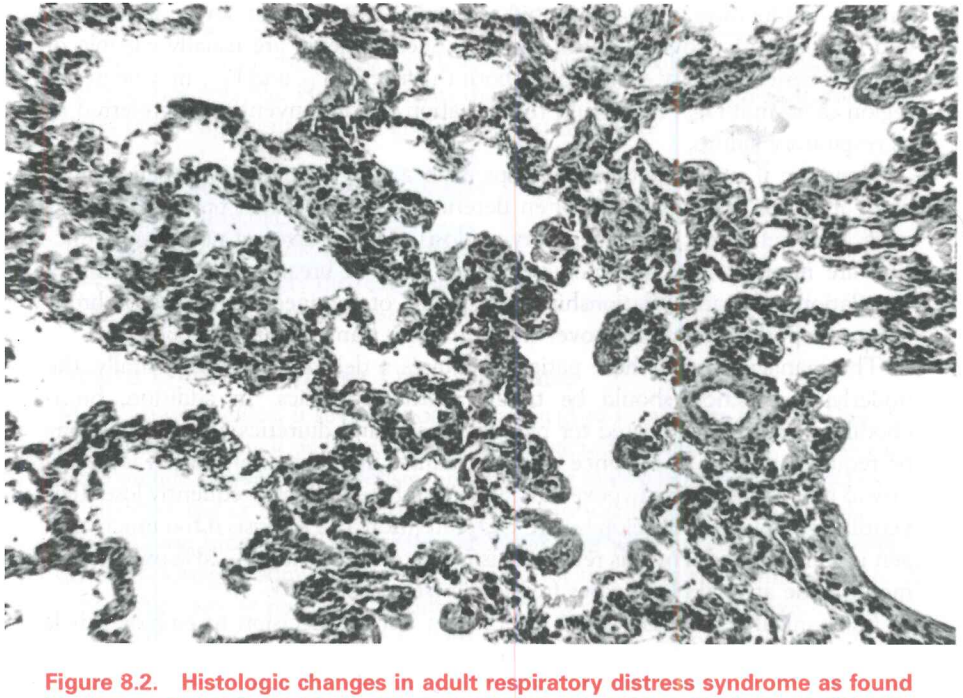


Figure 8.2. Histologic changes in adult respiratory distress syndrome as found by an open lung biopsy. There are patchy atelectasis, edema, hyaline membranes, and cellular debris in the alveoli. (From Lamy M, Fallat RJ, Koeniger E, et al. Pathologic features and mechanisms of hypoxemia in adult respiratory distress syndrome. Am Rev Resp Dis 1976;114:267–284.)

capillary permeability and flooding of the alveoli with proteinaceous fluid. Neutrophils accumulate partly as a result of complement or kinin activation. The activated neutrophils release mediators, including bradykinin, histamine, and platelet activating factor (PAF). In addition, toxic oxygen radicals are generated, together with cyclooxygenase products such as prostaglandins and thromboxane, and also lipoxygenase products such as leukotrienes. Platelets activated by PAF release proteases and kallikrein.

Clinical Features

ARDS is often associated with some severe underlying medical or surgical illness unconnected with the lung, and the onset of respiratory failure is often delayed. A typical history is that the patient is exposed to severe trauma, for example, an automobile accident with multiple fractures. There is some hemorrhagic shock with hypotension that is treated by fluid replacement. The patient appears to be doing well when, perhaps 2 days after the trauma, some increase in respiratory rate is noted, the arterial P_{O_2} and P_{CO_2} fall, and clouding is seen in the chest radiograph, which progresses to dense uneven opacification. Severe hypoxemia develops. The mortality rate is approximately 50%.

Adult Respiratory Distress Syndrome (ARDS)

End-result of a variety of insults including trauma, infection
Characterized by hemorrhagic edema with opacification on the radiograph
Severe hypoxemia
Low lung compliance
Typically requires mechanical ventilation
High mortality

Pulmonary Function

The lung becomes very stiff, and unusually high pressures are required to ve late it mechanically. Associated with this reduced compliance is a marked fal FRC. The cause of the increased recoil is presumably the alveolar edema exudate, which exaggerate the surface tension forces. As was pointed out ear (Fig. 6.3), edematous alveoli have a reduced volume. It is also possible that terstitial edema contributes to the abnormal stiffness of the lungs.

As would be expected from the histologic appearance of the lung (Fig. 8 there is marked ventilation–perfusion inequality, with a substantial fraction of total blood flow going to unventilated alveoli. This fraction may reach 50% more. Figure 8.3 shows some results obtained by the multiple inert gas metl in a 44-year-old patient who developed respiratory failure after an automobile cident and who was mechanically ventilated. Note the presence of blood flow

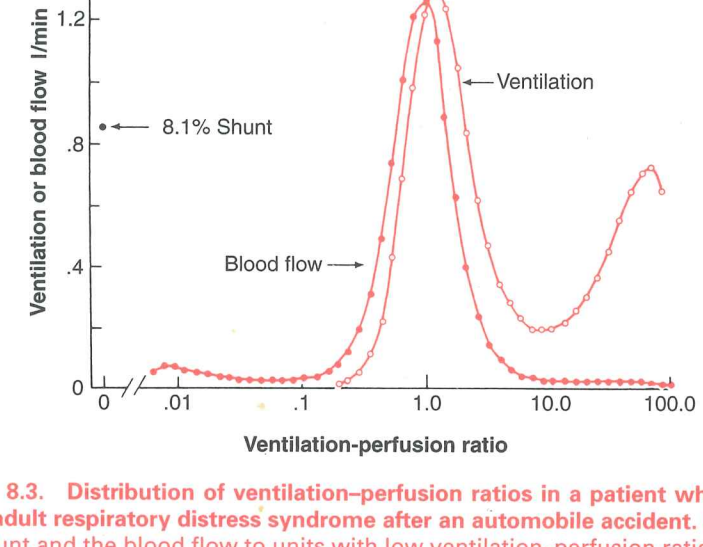


Figure 8.3. Distribution of ventilation–perfusion ratios in a patient who dev oped adult respiratory distress syndrome after an automobile accident. Note 8% shunt and the blood flow to units with low ventilation–perfusion ratios. In dition, there is some ventilation to high $\dot{V}_A/\dot{Q}$ units, probably as a result of high airway pressure developed by the ventilator (compare Fig. 10.4).

lung units with abnormally low ventilation–perfusion ratios and also the shunt of 8% (compare the normal distribution in Fig. 2.9). Figure 8.3 also shows a large amount of ventilation going to units with high ventilation–perfusion ratios. One reason for this is the abnormally high airway pressures developed by the ventilator, which reduces the blood flow in some alveoli (compare Fig. 10.4).

The ventilation–perfusion inequality and shunt cause profound hypoxemia. These patients usually must be given oxygen-enriched mixtures because air breathing, even with a ventilator, results in an arterial P_{O_2} that is dangerously low. Oxygen concentrations of 40–100% are sometimes necessary during mechanical ventilation to maintain an arterial P_{O_2} above 60 mm Hg. However, the possibility of oxygen toxicity should be kept in mind (Chapter 9). The addition of positive end-expiratory pressure (PEEP) often results in a substantial improvement in oxygenation in these patients (compare Fig. 10.4).

By contrast, the arterial P_{CO_2} is often low, even when severe hypoxemia develops; values in the 20s can occur. The reason for the increased ventilation is not known, although possibly the interstitial edema stimulates intrapulmonary J or stretch receptors. Another possible factor is stimulation of the peripheral chemoreceptors by the hypoxemia, although relieving this usually does not affect the level of ventilation.

Infant Respiratory Distress Syndrome

This condition, which is also called hyaline membrane disease of the newborn, has several features in common with ARDS (43). Pathologically, the lung shows hemorrhagic edema, patchy atelectasis, and hyaline membranes caused by proteinaceous fluid and cellular debris within the alveoli. Physiologically, there is profound hypoxemia, with both ventilation–perfusion inequality and blood flow through unventilated lung. In addition, a right-to-left shunt via the patent foramen ovale may exaggerate the hypoxemia. Mechanical ventilation with enriched oxygen mixtures is often necessary, and the addition of PEEP or continuous positive airway pressure (see Chapter 10) is frequently beneficial.

The chief cause of this condition is an absence of pulmonary surfactant, although other factors are probably also involved. The surfactant is normally produced by the type 2 alveolar cells (Fig. 5.2), and the ability of the lung to synthesize adequate amounts of the material develops relatively late in fetal life. Thus, a prematurely born infant is particularly at risk. The ability of the infant to secrete surfactant can be estimated by measuring the lecithin/sphingomyelin ratio of amniotic fluid, and maturation of the surfactant-synthesizing system can be hastened by the administration of corticosteroids. Treatment of the condition by administering exogenous surfactant via the trachea has been a major advance.

Management of Respiratory Failure

Although many factors enter into the management of an individual patient, it is useful to discuss the physiologic principles that underlie treatment. Naturally, attention must be directed to the primary cause of the disease. For example, antibiotic therapy may be required for an infection, or a specific treatment may be

available for a neuromuscular disorder. However, some aspects of management are common to many patients with respiratory failure.

Airway Obstruction

Respiratory failure is often precipitated by an increase in airway resistance. Many patients have COPD of many years' duration with hypoxemia and even some mild hypercapnia. Even so, they are able to maintain some physical activity. However, if they develop bronchospasm through exposure to smog or cold air or if they have a "chesty cold" with an increase in secretions, they may rapidly develop respiratory failure. The additional work of breathing becomes the straw that breaks the camel's back, and they develop profound hypoxemia, CO_2 retention, and respiratory acidosis.

Treatment should be directed at reducing the airway obstruction. Retained secretions are best removed by coughing when this is effective. Encouragement to cough and assistance by a respiratory therapist, nurse, or physician is often helpful, and changing the patient's position from side to side to assist drainage of secretions may be beneficial. Adequate hydration is important to prevent the secretions from becoming too viscid. It is especially important to humidify all gases given by a ventilator to prevent thickening and crusting of secretions. Drugs such as potassium iodide by mouth or acetylcysteine by aerosol to liquefy sputum are of doubtful value. Chest physiotherapy may help to clear airway secretions. However, aspiration of secretions by bronchoscopy may become necessary. Occasionally, respiratory stimulants are given to a drowsy patient but, more importantly, respiratory depressants must be avoided because they suppress coughing.

Any reversible airway obstruction should be treated by bronchodilators, such as albuterol or metaproterenol aerosol, intravenous aminophylline, or perhaps intravenous corticosteroids. Drugs such as isoproterenol that also stimulate β_1 adrenergic receptors in the heart should be avoided.

Respiratory Infection

An exacerbation of existing bronchitis in a patient with COPD, or a fresh respiratory infection in a patient with advanced interstitial lung disease, frequently provokes respiratory failure. There are at least two physiologic mechanisms for this. First, the increased secretions and, perhaps, bronchospasm increase the work of breathing as discussed earlier. Second, there is a worsening of ventilation-perfusion relationships, so that even if the ventilation to the alveoli remains unchanged, there will be increasing hypoxemia and hypercapnia. Treatment of the infection by antibiotics is indicated.

Even a mild exacerbation of bronchitis in a patient with COPD may precipitate respiratory failure. Moreover, the usual systemic responses to infection, such as pyrexia and leukocytosis, are often absent. However, treatment should not be delayed.

Cardiac Insufficiency

Many patients with incipient respiratory failure have a compromised cardiovascular system. The pulmonary artery pressure is frequently raised as a result of

several factors, including destruction of the pulmonary capillary bed by disease, hypoxic vasoconstriction, and increased blood viscosity caused by polycythemia. In addition, the myocardium is chronically hypoxic. Fluid retention often occurs as a result of retention of bicarbonate and sodium ions by the hypoxic kidney. Finally, some patients have coexisting coronary artery disease.

Patients with COPD frequently develop peripheral edema, hepatomegaly, and engorged neck veins. These and other patients may also show signs of left heart failure, with basal rales (crackles) on auscultation and engorged lung fields on the radiograph. The mild pulmonary edema further interferes with pulmonary gas exchange by causing uneven ventilation. Treatment with diuretics and digitalis is then indicated.

Hypoxemia

Hypoxemia can be relieved to some extent by treating the airway obstruction and the chest infection. However, the administration of long-term oxygen is frequently required, and this important topic is discussed in detail in Chapter 9.

Hypercapnia

Hypercapnia often responds to general measures directed at the airway obstruction and the infection. However, mechanical ventilation is frequently required. This is discussed in detail in Chapter 10.

QUESTIONS

1. Severe hypoxemia causes all of the following except:
- A. Bradycardia.
- B. Lactic acidemia.
- C. Retinal hemorrhages.
- D. Mental clouding.
- E. Proteinuria.

2. Carbon dioxide retention causes all of the following except:
- A. Acidosis.
- B. Reduced cerebral blood flow.
- C. Renal retention of bicarbonate.
- D. Mental clouding.
- E. Raised cerebrospinal fluid pressure.

3. A patient was admitted to the hospital with an acute pulmonary exacerbation of chronic pulmonary disease. When given 100% oxygen to breathe, his arterial P_{CO_2} increased from 50 to 80 mm Hg. A likely cause was:
- A. Increased airway resistance.
- B. Depression of ventilation.
- C. Depression of cardiac output.
- D. Reduced levels of 2,3 DPG in the blood.
- E. Bohr effect.

4. Acidosis in respiratory failure is likely to be increased by all of the followin except:
- A. Exacerbation of a chest infection.
- B. Depression of ventilation.
- C. Peripheral circulatory failure.
- D. Renal retention of bicarbonate.
- E. Administration of a narcotic drug.

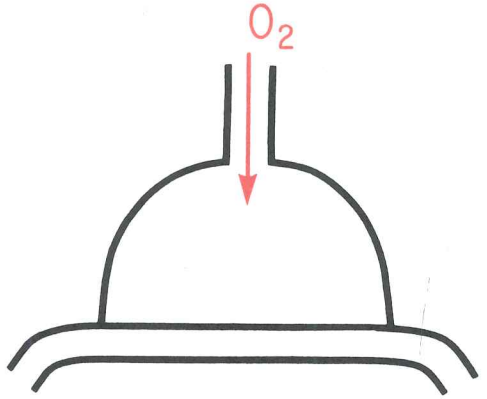
5. Features of the adult respiratory distress syndrome (ARDS) include all of the following except:
- A. Severe hypoxemia.
- B. Reduced lung compliance.
- C. Reduced FRC.
- D. Large shunt.
- E. Normal chest radiograph.

6. All of the following are thought to play a role in the development of ARDS except:
- A. Damage to capillary endothelial cells.
- B. Neutrophil accumulation in the lung.
- C. Release of platelet–activating factor (PAF).
- D. Generation of toxic oxygen radicals.
- E. Cigarette smoking.

7. Features of the infant respiratory distress syndrome include all of the following except:
- A. Patchy hemorrhagic edema and atelectasis.
- B. Normal amounts of pulmonary surfactant.
- C. Severe hypoxemia.
- D. Large shunt.
- E. Increased incidence in prematurity.

8. An acute exacerbation of bronchitis in a patient with advanced COPD typically results in all of the following except:
- A. Increased airway resistance.
- B. Worsening of ventilation–perfusion relationships.
- C. Severe hypoxemia.
- D. Carbon dioxide retention.
- E. Immediate requirement for mechanical ventilation.

9



Oxygen Therapy

Oxygen administration has a critical role in the treatment of hypoxemia and, especially, in the management of respiratory failure. However, patients vary considerably in their response to oxygen, and there are several potential hazards associated with its use. A clear understanding of the physiologic principles involved is necessary to prevent abuses of this powerful agent.

Improved Oxygenation After Oxygen Administration

Power of Added Oxygen

The great extent to which the arterial P_{O_2} can be increased by the inhalation of 100% oxygen is sometimes not appreciated. Suppose a young man has taken an overdose of a narcotic drug that results in severe hypoventilation with an arterial P_{O_2} of 50 and a P_{CO_2} of 80 mm Hg (Fig. 2.2). If this patient is mechanically ventilated and given 100% oxygen, the arterial P_{O_2} may increase to over 600 mm Hg; that is a 10-fold increase (Fig. 9.1). Few drugs can improve the gas composition of the blood so greatly and so effortlessly!

Response of Various Types of Hypoxemia

The mechanism of hypoxemia has an important bearing on its response to inhaled oxygen.

Hypoventilation

The rise in alveolar P_{O_2} can be predicted from the alveolar gas equation *if* the ventilation and metabolic rate, and therefore the alveolar P_{CO_2}, remain unaltered:

$$P_{A_{O_2}} = P_{I_{O_2}} - \frac{P_{A_{CO_2}}}{R} + F \qquad \text{(Eq. 9.1)}$$

where F is a small correction factor.

Assuming no change in the alveolar P_{CO_2} and the respiratory exchange ratio and neglecting the correction factor, this equation shows that the alveolar P_{O_2} rises parallel with the inspired value. Thus changing from air to only 30% oxygen can increase the alveolar P_{O_2} by approximately 60 mm Hg. In practice,

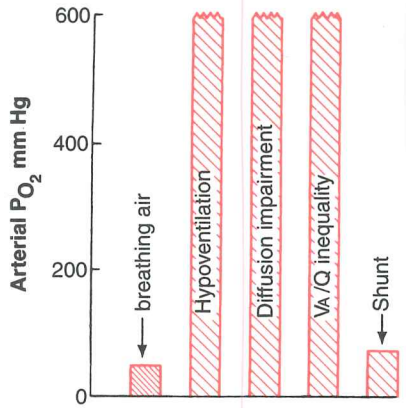


Figure 9.1. Response of the arterial P_{O_2} to 100% inspired oxygen for the different mechanisms of hypoxemia. The P_{O_2} breathing air is assumed to be 50 mm Hg. Note the dramatic increase in all instances except shunt where, nevertheless, there

the arterial P_{O_2} is always lower than the alveolar value because of a small amount of venous admixture. However, the hypoxemia of hypoventilation, which is rarely severe (Fig. 2.2), is easily reversed by a modest oxygen enrichment of the inspired gas.

Diffusion Impairment

Again, hypoxemia caused by this mechanism is readily overcome by oxygen administration. The reason for this becomes clear if we look at the dynamics of oxygen uptake along the pulmonary capillary (Fig. 2.4). The rate of movement of oxygen across the blood–gas barrier is proportional to the P_{O_2} difference between alveolar gas and capillary blood. (See Respiratory physiology–the essentials, ed. 6: p. 24.) This difference is normally approximately 60 mm Hg at the beginning of the capillary. If we increase the concentration of inspired oxygen to only 30%, we raise the alveolar P_{O_2} by 60 mm Hg, thus doubling the rate of transfer of oxygen at the start of the capillary. This in turn improves oxygenation of the end-capillary blood. Therefore, a modest rise in inspired oxygen concentration can usually correct the hypoxemia.

Ventilation–perfusion Inequality

Again, oxygen administration usually is very effective at improving the arterial P_{O_2}. However, the rise in P_{O_2} depends on the pattern of ventilation–perfusion inequality and the inspired oxygen concentration. Administration of 100% O_2 increases the arterial P_{O_2} to very high values because every lung unit that is ventilated eventually washes out its nitrogen. When this occurs, the alveolar P_{O_2} is given by $P_{O_2} = P_B - P_{H_2O} - P_{CO_2}$. Because the P_{CO_2} is normally less than 50 mm Hg, this equation predicts an alveolar P_{O_2} of over 600 mm Hg, even in lung units with very low ventilation–perfusion ratios.

However, two cautions should be added. First, some regions of the lung may be so poorly ventilated that it may take many minutes for the nitrogen to be washed out. Furthermore, these regions may continue to receive nitrogen as this gas is gradually washed out of peripheral tissues by the venous blood. As a consequence, the arterial P_{O_2} may take so long to reach its final level that in practice this is never achieved. Second, giving oxygen may result in the development of unventilated areas (Fig. 9.5). If this occurs, the rise in arterial P_{O_2} stops short (Fig. 9.3).

When intermediate concentrations of oxygen are given, the rise in arterial P_{O_2} is determined by the pattern of ventilation–perfusion inequality and in particular by those units that have low ventilation–perfusion ratios and appreciable blood flow. Figure 9.2 shows the response of the arterial P_{O_2} in lung models with various distributions of ventilation–perfusion ratios after inspiration of various oxygen concentrations (44). Note that at an inspired concentration of 60%, the arterial P_{O_2} of the distribution with a standard deviation of 2.0 rose from 40 to only 90 mm Hg. This modest rise can be attributed to the effects of lung units with ventilation–perfusion ratios less than 0.01. For example, an alveolus with a ventilation–perfusion ratio of 0.006 that is given 60% O_2 to inspire has an end-

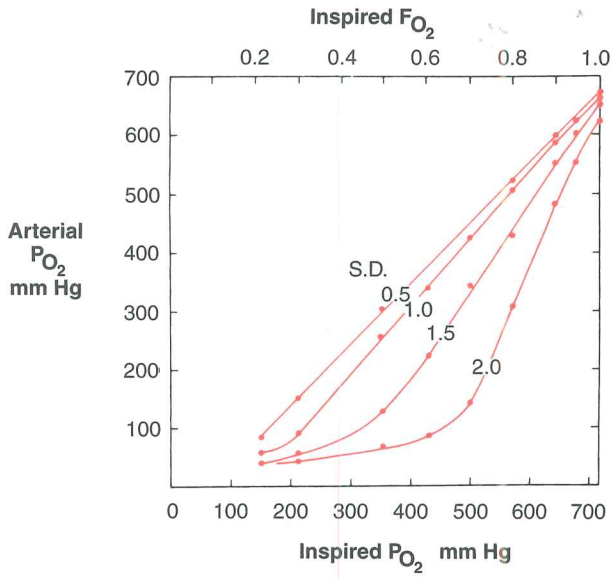


Figure 9.2. Response of the arterial P_{O_2} to various inspired oxygen values in theoretical distributions of ventilation–perfusion ratios. SD refers to the standard deviation of the log normal distribution. Note that when the distribution is broad (SD = 2), the arterial P_{O_2} remains low even when 60% oxygen is inhaled. (From West JB, Wagner PD. Pulmonary gas exchange. In: West JB. ed. Bioengineering aspects of the lung. New York: Marcel Dekker, 1977.)

the inspired oxygen concentration was increased to 90%, the arterial P_{O_2} of this distribution rose to nearly 500 mm Hg.

Figure 9.2 assumes that the pattern of ventilation–perfusion inequality remains constant as the inspired oxygen is raised. However, the relief of alveolar hypoxia in poorly ventilated regions of lung may increase the blood flow there because of the abolition of hypoxic vasoconstriction. In this case, the increase in arterial P_{O_2} will be less. Note also that if units with low ventilation–perfusion ratios collapse during high oxygen breathing (Figs. 9.5 and 9.6), the arterial P_{O_2} rises less.

Shunt

This is the only mechanism of hypoxemia in which the arterial P_{O_2} remains far below the level for the normal lung during 100% O_2 breathing. The reason is that the blood that bypasses the ventilated alveoli (shunt) does not "see" the added oxygen and, being low in oxygen concentration, depresses the arterial P_{O_2}. This depression is particularly marked because of the shallow slope of the oxygen dissociation curve at a high P_{O_2} (Fig. 2.6).

However, it should be emphasized that useful gains in arterial P_{O_2} often follow the administration of 100% O_2 to patients with shunts. This is because of the additional dissolved oxygen which can be appreciable at a high alveolar P_{O_2}. For example, increasing the alveolar P_{O_2} from 100 to 600 mm Hg raises the dissolved

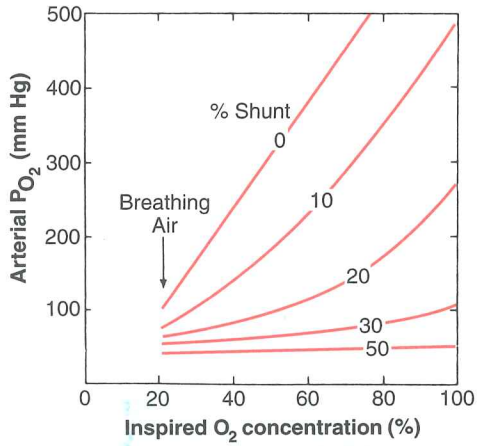


Figure 9.3. Response of the arterial P_{O_2} to increased inspired oxygen concentrations in a lung with various amounts of shunt. Note that the P_{O_2} remains a long way below the normal level for 100% oxygen. Nevertheless, useful gains in oxygenation occur even with severe degrees of shunting. (This diagram shows typical values only; changes in cardiac output, oxygen uptake, etc., affect the position of the lines.)

increase of 1.5 can be compared with the normal arterial–venous difference in oxygen concentration of approximately 5 ml/100 ml.

Figure 9.3 shows typical increases in arterial P_{O_2} for various percentage shunts at different inspired oxygen concentrations. The graph is drawn for an oxygen uptake of 300 ml/min and cardiac output of 6 liters/min; variations in these and other values alter the positions of the lines. However, in this example, a patient with a 30% shunt who has an arterial P_{O_2} of 55 mm Hg during air breathing increases this to 110 mm Hg if he or she breathes 100% oxygen. This increase corresponds to a rise in oxygen saturation and concentration of the arterial blood of 10% and 2.2 ml/100 ml, respectively. In a patient with a hypoxic myocardium, for example, these values mean an important gain in oxygen delivery.

Other Factors in Oxygen Delivery

Although the arterial P_{O_2} is a convenient measurement of the degree of oxygenation of the blood, other factors are important in oxygen delivery to the tissues. These factors include the hemoglobin concentration, the position of the oxygen dissociation curve, the cardiac output, and the distribution of the blood flow throughout the peripheral tissues.

Both a fall in hemoglobin concentration and cardiac output reduce the total amount of oxygen per unit time ("*oxygen flux*") going to the tissues. The flux may be expressed as the product of the cardiac output and the arterial oxygen concentration: $\dot{Q} \times Ca_{O_2}$.

Diffusion of oxygen from the peripheral capillaries to the mitochondria in the

Important Factors in Oxygen Delivery to Tissues

- Arterial P_{O_2}
- Hemoglobin concentration
- Cardiac output
- Diffusion from capillaries to mitochondria e.g., number of open capillaries
- Oxygen affinity of hemoglobin
- Local blood flow

blood, which reflects the average tissue P_{O_2}. A rearrangement of the Fick equation is as follows:

$$C\bar{v}_{O_2} = Ca_{O_2} - \frac{\dot{V}_{O_2}}{\dot{Q}} \qquad \text{(Eq. 9.2)}$$

This equation shows that the oxygen concentration (and therefore the P_{O_2}) of mixed venous blood will fall if either the arterial oxygen concentration or the cardiac output is reduced (oxygen consumption assumed constant).

The relationship between oxygen concentration and P_{O_2} in the mixed venous blood depends on the position of the oxygen dissociation curve (Fig. 2.1). If the curve is shifted to the right by an increase in temperature, as in fever, or an increase in 2,3-DPG concentration, as may occur in chronic hypoxemia, the P_{O_2} for a given concentration is high, thus favoring diffusion of oxygen to the mitochondria. By contrast if the P_{CO_2} is low and the pH is high, as in respiratory alkalosis, or if the 2,3-DPG concentration is low because of transfusion of large amounts of stored blood, the resulting left-shifted curve interferes with oxygen unloading to the tissues.

Finally, the distribution of cardiac output clearly plays an important role in tissue oxygenation. For example, a patient who has coronary artery disease is liable to have hypoxic regions in the myocardium, irrespective of the other factors involved in oxygen delivery.

Methods of Oxygen Administration

Nasal Cannulas

Nasal cannulas consist of two prongs that are inserted just inside the anterior nares and supported on a light frame. Oxygen is supplied at rates of 1–4 liters/min, resulting in inspired oxygen concentrations of approximately 25–30%. The higher the patient's inspiratory flow rate, the lower the resulting concentration. The gas should be humidified as close to body temperature as possible to prevent crusting of secretions on the nasal mucosa.

The chief advantage of cannulas is that the patient does not have the discomfort of a mask and he or she can talk and eat and has access to the face. The cannulas can be worn continuously for long periods, an important point because oxygen administration should usually be continuous rather than intermittent

(see later). The disadvantages of cannulas are the low maximum inspired con centrations of oxygen that are available and the unpredictability of the concen tration, especially if the patient breathes mostly through the mouth.

Masks

Masks come in several designs. Simple plastic masks that fit over the nose an mouth allow inspired oxygen concentrations of up to 60% when supplied wit flow rates of 6 liters/min. However because some accumulation of CO_2 occu within the mask (up to 2%), this device should be used with caution in patien who are liable to develop CO_2 retention. In addition, some patients report feelin smothered when this type of mask is used.

A useful mask for delivering controlled oxygen concentrations is based on th Venturi principle. As the oxygen enters the mask through a narrow jet, it entrai a constant flow of air, which enters via surrounding holes. With an oxygen flo of 4 liters/min, a total flow (oxygen + air) of approximately 40 liters/min delivered to the patient. At such high flow rates, there is negligible rebreathin of expired gas and, therefore, no CO_2 accumulation. Masks that give inspire oxygen concentrations of 24, 28, or 35% with a high degree of reliability are avai able and are particularly useful for treating patients who are liable to develop CO retention. Some patients complain of the noise and the breeze, while others enj the latter.

Transtracheal Oxygen

This can be delivered via a microcatheter inserted through the anterior trache wall with the tip lying just above the carina. It is an efficient way of deliveri oxygen, particularly for patients on long-term oxygen therapy, although care mu be taken to prevent infection.

Tents

These are now used only for children who do not tolerate masks well. Oxyge concentrations of up to 50% can be obtained but there is a fire hazard.

Ventilators

When a patient is mechanically ventilated through an endotracheal or tr cheostomy tube, complete control over the composition of the inspired gas available. There is a danger of producing oxygen toxicity if concentrations of ov 50% are given for more than 2 days (see later). In general, the lowest inspire oxygen that provides an acceptable arterial P_{O_2} should be used. This level difficult to define, but in patients with ARDS who are being mechanical ventilated with high oxygen concentrations, a figure of 60 mm Hg is often use

Hyperbaric Oxygen

If 100% O_2 is administered at a pressure of 3 atmospheres, the inspired P_{O_2} is ov 2000 mm Hg. Under these conditions, a substantial increase in the arterial ox gen concentration can occur, chiefly as a result of additional dissolved oxyge

For example, if the arterial P_{O_2} is 2000 mm Hg, the oxygen in solution is approximately 6 ml/100 ml of blood. Theoretically, this is enough to provide the entire arterial–venous difference of 5 ml/100 ml, so that the hemoglobin of the mixed venous blood could remain fully saturated.

Hyperbaric oxygen therapy has limited uses and is rarely indicated in the management of respiratory failure. However, it has been used in the treatment of severe carbon monoxide poisoning where most of the hemoglobin is unavailable to carry oxygen and therefore the dissolved oxygen is critically important. In addition, the high P_{O_2} accelerates the dissociation of carbon monoxide from hemoglobin. A severe anemic crisis is sometimes treated in the same way. Hyperbaric oxygen is also used in the treatment of gas gangrene infections and as an adjunct to radiotherapy where the higher tissue P_{O_2} increases the radiosensitivity of relatively avascular tumors. The high pressure chamber is also valuable for managing decompression sickness.

The use of hyperbaric oxygen requires a special facility with trained personnel. In practice, the chamber is filled with air and oxygen is given by a special mask to ensure that the patient receives pure oxygen. This procedure also reduces fire hazard.

Domiciliary and Portable Oxygen

Some patients are so disabled by severe chronic pulmonary disease that they are virtually confined to bed or a chair unless they breathe supplementary oxygen. These patients often benefit considerably from having a supply of oxygen in their home. This can take various forms. A central large tank with a long plastic tube and mask may enable the patient to climb stairs or go to the bathroom. In addition, portable oxygen sets are available, and these can be used for shopping or other activities. Some sets use liquid oxygen as a store; these are best for patient mobility. In others, oxygen is extracted from the air with a molecular sieve.

The patients who benefit most from portable oxygen are those whose exercise tolerance is limited by dyspnea. Increasing the inspired oxygen concentration can greatly increase the level of exercise for a given ventilation and so enable these patients to become much more active.

It has been shown that a low flow of oxygen given continuously over several months can reduce the amount of pulmonary hypertension and improve the prognosis of some patients with advanced COPD. Although such therapy is expensive, improvements in the technology of providing oxygen have made it feasible.

Hazards of Oxygen Therapy

Carbon Dioxide Retention

The reasons for the development of dangerous CO_2 retention after oxygen administration to patients with severe COPD were briefly discussed in Chapter 8. A critical factor in the ventilatory drive of these patients who have a high work of breathing is often the hypoxic stimulation of their peripheral chemoreceptors. If this is removed by relieving their hypoxemia, the level of ventilation may fall precipitously and severe CO_2 retention may ensue.

Intermittent oxygen therapy is especially dangerous. The physiologist Haldane compared this with bringing a drowning man to the surface–occasionally! The explanation is that if oxygen administration is seen to cause CO_2 retention and is therefore stopped, the subsequent hypoxemia may be more severe than it was before oxygen therapy. The reason is the increased alveolar P_{CO_2} as can be seen from the alveolar gas equation:

$$P_{A_{O_2}} = P_{I_{O_2}} - \frac{P_{A_{CO_2}}}{R} + F \qquad \text{(Eq. 9.3)}$$

This shows that any increase in alveolar P_{CO_2} will reduce the alveolar P_{O_2} and therefore the arterial value. Moreover, the high P_{CO_2} is likely to remain for many minutes because the body stores of this gas are so great that the excess is washed out only gradually. Thus, the hypoxemia may be severe and prolonged.

These patients should be given continuous oxygen at a low concentration, and the blood gases must be monitored. Initially, an oxygen concentration of 24% is often given by means of a Venturi mask, and the arterial P_{O_2} and P_{CO_2} are measured after 15–20 minutes. If the P_{CO_2} does not rise more than a few mm Hg and the patient remains alert, the oxygen concentration can be increased to 28%. This is generally adequate to relieve severe hypoxemia, although concentrations as high as 35% are sometimes used. The shape of the oxygen dissociation curve (Fig. 2.1) should be at the back of the physician's mind to remind him or her that a rise in P_{O_2} from 30 to 50 mm Hg (at a normal pH) represents more than a 25% increase in hemoglobin saturation!

Oxygen Toxicity

High concentrations of oxygen over long periods damage the lung. Studies on monkeys exposed to 100% oxygen for 2 days show that some of the earliest changes are in the capillary endothelial cells, which become swollen (45). Alterations occur in the endothelial intercellular junctions, and there is an increased capillary permeability that leads to interstitial and alveolar edema. In addition, the alveolar epithelium may become completely denuded and replaced by rows of type 2 epithelial cells. Later, organization occurs with interstitial fibrosis.

In humans, the pulmonary effects of high oxygen concentration are more difficult to document, but normal subjects report substernal discomfort after breathing 100% oxygen for 24 hours. Patients who have been mechanically ventilated with 100% oxygen for 36 hours have shown a progressive fall in arterial P_{O_2} compared with a control group who were ventilated with air. A reasonable attitude is to assume that concentrations of 50% or higher for more than 2 days may produce toxic changes.

In practice, such high levels over such a long period can only be achieved in patients who are intubated and mechanically ventilated. It is important to avoid oxygen toxicity because the only way to relieve the resultant hypoxemia is by raising the inspired oxygen, thus creating a vicious circle.

Atelectasis

Following Airway Occlusion

If a patient is breathing air and an airway becomes totally obstructed, for example, by retained secretions, absorption atelectasis of the lung behind the airway may occur. The reason is that the sum of the partial pressures in venous blood is considerably less than atmospheric pressure, with the result that the trapped gas is gradually absorbed. (See Respiratory physiology–the essentials, ed. 6: p. 123.) However, the process is relatively slow, requiring many hours or even days.

However, if the patient is breathing a high concentration of oxygen, the rate of absorption atelectasis is greatly accelerated. This is because there is then relatively little nitrogen in the alveoli and this gas normally slows the absorption process because of its low solubility. Replacing the nitrogen with any other gas that is rapidly absorbed also predisposes to collapse. An example is nitrous oxide during anesthesia. In the normal lung, collateral ventilation may delay or prevent atelectasis by providing an alternate path for gas to enter the obstructed region (Fig. 1.11C).

Absorption atelectasis is common in patients with respiratory failure because they often have excessive secretions or cellular debris in their airways and they are frequently treated with high oxygen concentrations. In addition, the channels through which collateral ventilation normally occurs may be obstructed by

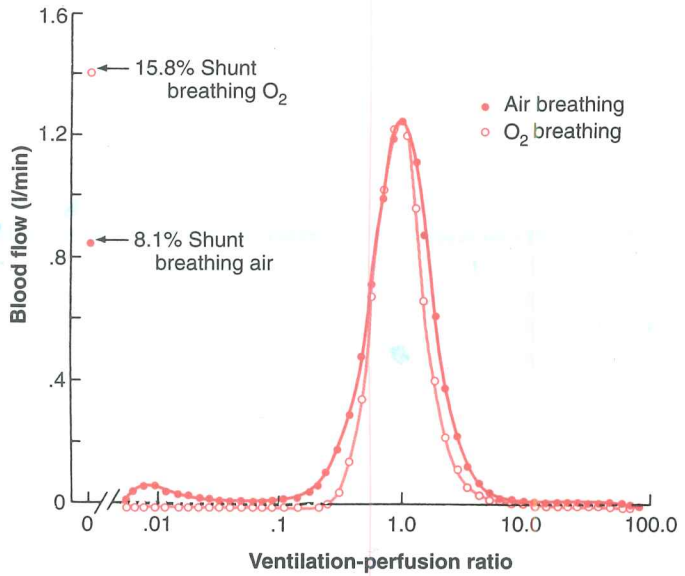


Figure 9.4. Conversion of low ventilation–perfusion ratio units to shunt during oxygen breathing. This patient had respiratory failure after an automobile accident (same patient as shown in Figure 8.3). During air breathing there was appreciable blood flow to units with low ventilation–perfusion ratios. After 30 minutes of 100% oxygen, blood flow to these units was not evident, but the shunt

disease. Collapse is common in the dependent regions of the lung because secretions tend to collect there, and those airways and alveoli are relatively poorly expanded anyway (Fig. 3.5). To the extent that atelectatic lung is perfused, hypoxemia develops, although hypoxic vasoconstriction may limit this to some extent.

Instability of Units with Low Ventilation–Perfusion Ratios

It has been shown that lung units with low ventilation–perfusion ratios may become unstable and collapse when high oxygen mixtures are inhaled. An example is given in Figure 9.4, which shows the distribution of ventilation–perfusion ratios in a patient during air breathing and after 30 minutes of 100% oxygen. This patient had respiratory failure after an automobile accident (Fig. 8.3). Note that during air breathing there were appreciable amounts of blood flow to lung units with low ventilation–perfusion ratios in addition to an 8% shunt. After oxygen administration, the blood flow to the low ventilation–perfusion ratio units was not evident but the shunt had increased to 16%. The most likely explanation of this change is that the poorly ventilated regions became unventilated.

Figure 9.5 shows the mechanism involved. The figure shows four hypothetical lung units, all with low inspired ventilation–perfusion ratios ($\dot{V}_{AI}/\dot{Q}$) during 80% oxygen breathing. In *A*, the inspired (alveolar) ventilation is 49.4 units but the expired ventilation is only 2.5 units (the actual values depend on the blood flow). The reason why so little gas is exhaled is that so much is taken up by the blood. In *B*, where the inspired ventilation is slightly reduced to 44.0 units (same blood flow as before), there is no expired ventilation because all the gas that is inspired is absorbed by the blood. Such a unit is said to have a "critical" ventilation–perfusion ratio.

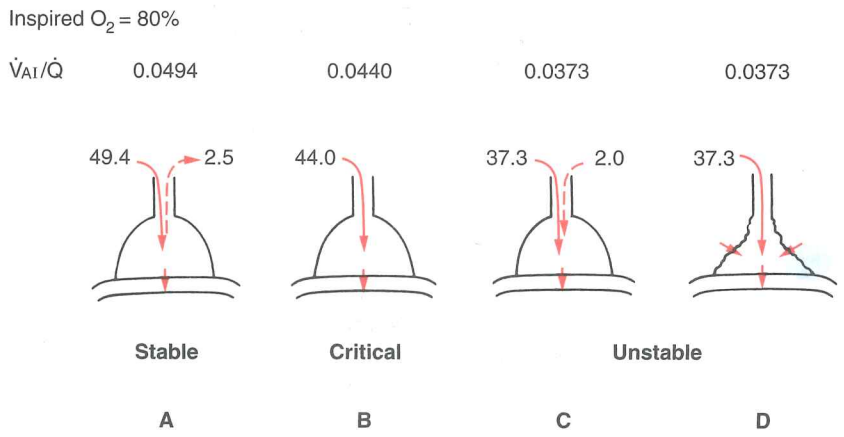


Figure 9.5. Mechanism of the collapse of lung units with low inspired ventilation–perfusion ratios ($\dot{V}_{AI}/\dot{Q}$) when high oxygen mixtures are inhaled. *(A)* The expired ventilation is very small because so much of the inspired gas is taken up by the blood. (*C* and *D*) More gas is removed from the lung unit than is inspired, leading

In Figure 9.5C and *D*, the inspired ventilation has been further reduced with the result that it is now less than the volume of gas entering the blood. This is an unstable situation. Under these circumstances, either gas is inspired from neighboring units during the expiratory phase of respiration as in C, or the unit gradually collapse as in *D*. The latter fate is particularly likely if the unit is poorly ventilated because of intermittent airway closure. This is probably common in the dependent regions of the lung in ARDS because of the greatly reduced FRC. The likelihood of atelectasis increases rapidly as the inspired oxygen concentration approaches 100%.

The development of shunts during oxygen breathing is an additional reason why high concentrations of this gas should be avoided if possible in the treatment of patients with respiratory failure. Also, the shunt that is measured during 100% oxygen breathing (Fig. 2.6) in these patients may substantially overestimate the shunt that is present during air breathing.

Retrolental Fibroplasia

If newborn infants with the infant respiratory distress syndrome are treated with high concentrations of oxygen, they may develop fibrosis behind the lens of the eye, leading to blindness. This has been successfully avoided by keeping the arterial P_{O_2} below 140 mm Hg. Recently, however, the disease has reappeared for reasons that are not clear.

QUESTIONS

1. A previously well young man was admitted to the emergency room with acute barbiturate poisoning that caused severe hypoventilation. When he was given 50% oxygen to breathe, there was no change in his arterial P_{CO_2}. Approximately how much would his arterial P_{O_2} (mm Hg) be expected to rise?
A. 25
B. 50
C. 75
D. 100
E. 200

2. When a patient with severe COPD and ventilation–perfusion inequality was given 80% oxygen to breathe, his arterial P_{O_2} rose to only 300 mm Hg after 5 minutes. Factors that might have contributed to this unexpectedly low level include all of the following except:
A. Severe inequality of ventilation.
B. Presence of units with low ventilation–perfusion ratios.
C. Atelectasis of low ventilation–perfusion ratio units as a result of the high inspired P_{O_2}.
D. Relief of hypoxic vasoconstriction in poorly ventilated areas.
E. Loss of alveolar surface area resulting in a low diffusing capacity

3. A patient with congenital heart disease has a right-to-left shunt and an arterial P_{O_2} of 60 mm Hg during air breathing. When he is given 100% oxygen to breathe, you would expect his arterial P_{O_2} to:
A. Fall.
B. Remain unchanged.
C. Increase by less than 10 mm Hg.
D. Increase by more than 10 mm Hg.
E. Rise to about 600 mm Hg.

4. A blood sample from a patient with carbon monoxide poisoning showed a reduction in P_{50} of the oxygen dissociation curve. The probable reason wa
A. Increased arterial P_{CO_2}.
B. The presence of carbon monoxide increased the oxygen affinity of th hemoglobin.
C. The concentrating of 2,3 DPG in the red cells was increased.
D. Reduced arterial pH.
E. Mild pyrexia.

5. Disadvantages of nasal cannulas for oxygen administration include all of the following except:
A. They are more uncomfortable than masks.
B. Inspired oxygen concentrations above 50% are difficult to obtain.
C. The inspired oxygen concentration is not accurately known.
D. Crusting of the nasal passages may occur.
E. The inspired P_{CO_2} tends to rise.

6. Advantages of oxygen masks based on the Venturi principle include all o the following except:
A. The inspired oxygen concentration can be accurately set.
B. The inspired P_{CO_2} is low.
C. They are useful for treating patients who are liable to develop carbon dioxide retention.
D. The high flow rate causes a breeze that some patients like.
E. The inspired oxygen concentration increases automatically if the ventilation falls.

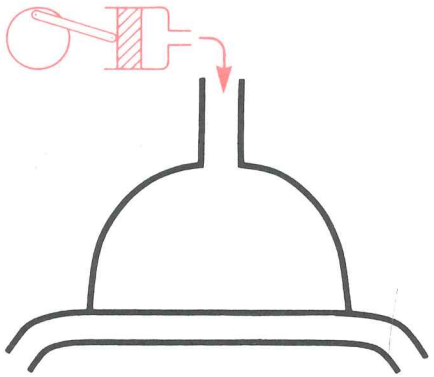
7. Hyperbaric oxygen therapy can be useful in the treatment of all of the following except:
A. Severe carbon monoxide poisoning.
B. Gas gangrene infections.
C. Spontaneous pneumothorax.
D. Some malignant tumors by radiotherapy.
E. Severe anemic crisis.

8. A patient with normal lungs but severe anemia in placed in a hyperbaric chamber, total pressure 3 atmospheres, and 100% oxygen is administere by mask. You can expect the dissolved oxygen in the arterial blood (in ml O_2/100 ml blood) to increase to:
A. 1

C. 3
D. 4
E. 6

9. If 100% oxygen is delivered to the lung over a long period of time, histological changes of oxygen toxicity occur. The first changes are probably in the:
A. Type 1 alveolar epithelial cells.
B. Type 2 alveolar epithelial cells.
C. Interstitial cells.
D. Capillary endothelial cells.
E. Alveolar macrophages.

10. Lung units with low ventilation–perfusion ratios may collapse when high concentrations of oxygen are inhaled for one hour because:
A. Pulmonary surfactant in inactivated.
B. Oxygen toxicity causes alveolar edema.
C. Gas is taken up by the blood faster than it can enter the units by ventilation.
D. Interstitial edema around the small airways causes airway closure.
E. Inflammatory changes occur in the small airways.



10 Mechanical Ventilation

Mechanical ventilation is of major importance in the management of patients with respiratory failure. Once used only as an emergency procedure in resuscitation or as a last resort in the treatment of the critically ill, it is now frequently employed to tide a patient over a respiratory crisis. Mechanical ventilation is a complex and technical subject, and this discussion is limited to the physiologic principles of its use, benefits, and hazards.

Intubation and Tracheostomy

Most ventilators require a port for connection to the lung airway. An exception is the tank type of ventilator (see later), which is now rarely used. The connection is made by means of an endotracheal or tracheostomy tube. These tubes are provided with an inflatable cuff at the end to give an airtight seal. Endotracheal tubes can be inserted via the nose or mouth.

These tubes have additional functions besides providing a connection for ventilators. They facilitate the removal of secretions by suction catheter, a serious problem in many patients with respiratory failure. Retained secretions are particularly troublesome in patients who are obtunded, who have a suppressed cough reflex, or in whom the secretions are particularly copious or viscid. In addition, a tracheostomy may be necessary to bypass upper airway obstruction caused, for example, by allergic edema or a laryngeal tumor. The tube may also prevent the aspiration of blood or vomitus from the pharynx into the lung.

The decision to intubate and ventilate a patient should not be lightly undertaken because it is a major intervention requiring a substantial investment of personnel and equipment, with many potential hazards. However, patients are frequently intubated too late in the course of respiratory failure. The precise timing depends on such factors as the nature of the underlying disease process, the rapidity of the progress of hypoxemia and hypercapnia, and the age and general condition of the patient.

Several complications are associated with the use of endotracheal and tracheostomy tubes. Ulceration of the larynx or the trachea is sometimes seen. This complication is particularly likely if the inflated cuff exerts undue pressure on the mucosa; furthermore, the subsequent scarring can result in tracheal stenosis. The use of large-volume, low-pressure cuffs has reduced the incidence of this problem. Also, care must be taken with the placement of an endotracheal tube. For example, if the distal end of the tube is inadvertently placed in the right main bronchus, atelectasis of the left lung may ensue.

Types of Ventilators

Constant-Volume Ventilators

These ventilators deliver a preset volume of gas to the patient, usually by means of a motor-driven piston in a cylinder (Fig. 10.1) or a motor-driven bellows. The stroke and frequency of the pump can be adjusted to give the required ventilation. The ratio of inspiratory to expiratory time can be controlled by a special switching mechanism. Oxygen can be added to the inspired air as required, and a humidifier is included in the circuit.

Constant-volume ventilators are robust, dependable machines that are suitable for long-term ventilation. They are used extensively in anesthesia. They have the advantage of having a known volume (or nearly so) delivered to the patient despite changes in the elastic properties of the lung or chest wall or increases in airway resistance. A disadvantage is that high pressures can be developed; how-

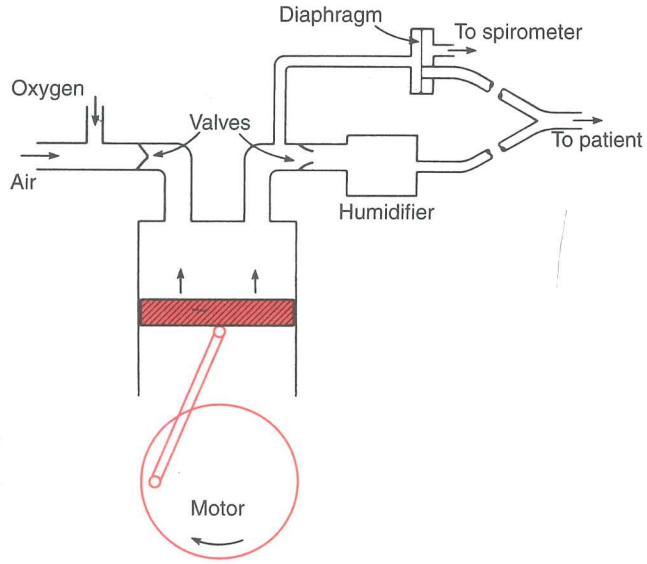


Figure 10.1. Example of a constant-volume ventilator (schematic). In pract
the stroke volume and frequency can be regulated. During the expiratory ph
as the piston descends, the diaphragm is deflected to the left by the redu
pressure in the cylinder, allowing the patient to exhale through the spirome

dangerous levels. Estimating the patient's ventilation from the stroke volume
frequency of the pump may lead to important errors because of the compr
ibility of the gas and leaks, and it is better to measure the expired ventilat
with a spirometer.

Constant-Pressure Ventilators

These ventilators deliver gas at a preset pressure and are small, relatively in
pensive machines. They do not require electrical power but instead work o
source of compressed gas having a pressure of at least 50 pounds/square in
Their chief disadvantage, if they are used as the sole method of ventilation
that the volume of gas they deliver is altered by changes in the compliance
the lung or chest wall. Also, an increase in airway resistance may decrease
ventilation because there may be insufficient time for equilibration of pressure
occur between the machine and the alveoli. Expired volume should, therefo
be monitored. This is difficult with some ventilators. Another disadvantage
some constant-pressure ventilators is that the inspired oxygen concentrat
varies with the inspiratory flow rate.

Constant-pressure ventilators are now mainly used for "pressure-assist ve
lation," that is to assist intubated patients to overcome the increased work
breathing occasioned by the relatively narrow endotracheal tube. This mode
use is valuable in weaning patients from a ventilator, that is in the transition fr

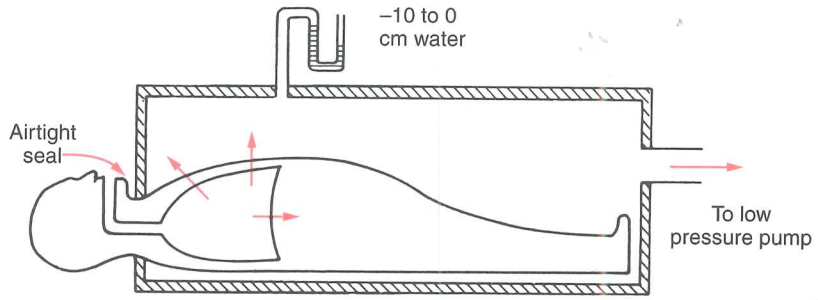


Figure 10.2. Tank respirator (schematic). The rigid box is connected to a large volume, low pressure pump which swings the pressure from about 0 to −10 cm H_2O.

Tank Ventilators

The ventilators we have discussed up to this point are called positive-pressure ventilators because they expand the lung by delivering positive pressure to the airway. By contrast, tank respirators deliver negative pressure (less than atmospheric) to the outside of the chest and rest of the body, excluding the head (Fig. 10.2). They consist of a rigid box ("iron lung") connected to a large volume, low pressure pump that controls the respiratory cycle. The box is often hinged along the middle so that it can be opened to allow nursing care.

Tank ventilators are no longer used in the treatment of acute respiratory failure because they limit access to the patient and because they are bulky and inconvenient. They were employed extensively to ventilate patients with bulbar poliomyelitis and they are still occasionally useful for patients with chronic neuromuscular disease who need to be ventilated for months or years. A modification of the tank ventilator is the cuirass which fits over the thorax and abdomen and also generates negative pressure. It usually is reserved for patients who have partially recovered from neuromuscular respiratory failure.

Patient-Cycled Ventilators

In these ventilators, the inspiratory phase can be triggered by the patient as he or she makes an inspiratory effort. The term "assisted ventilation" is sometimes given to this mode of operation. Many constant-pressure ventilators have this capability. These ventilators are sometimes useful in the treatment of patients who are recovering from respiratory failure and who are being weaned from a period of controlled ventilation.

Patterns of Ventilation

Intermittent Positive Pressure Ventilation (IPPV)

This is sometimes called intermittent positive pressure breathing (IPPB) and is the common pattern in which the lung is expanded by the application of positive pressure to the airway and allowed to deflate passively to FRC. With modern

ventilators, the main variables that can be controlled include the tidal volume respiratory frequency, duration of inspiration versus expiration, the inspirator flow rate, and the inspired oxygen concentration.

In patients with airway obstruction, there is an advantage in prolonging th expiratory time so that regions of the lung with long time constants have time t empty. (See Respiratory physiology–the essentials, ed. 6: p. 139.) This can be don by reducing the respiratory frequency and increasing the expiratory versus inspi ratory time. On the other hand, a prolonged positive airway pressure may imped venous return to the thorax (see later). Generally, a relatively low frequency an an expiratory time greater than inspiratory time are selected, but each patien requires individual attention.

Positive End-Expiratory Pressure (PEEP)

In patients who have ARDS, considerable improvement in the arterial P_{O_2} ca often be obtained by maintaining a small positive airway pressure at the en of expiration. Values as low as 5 cm H_2O are often beneficial, but pressures a high as 20 cm H_2O or more are sometimes used. Special valves are availabl to provide the pressure. A secondary gain from PEEP is that it may allow th inspired oxygen concentration to be decreased, thus lessening the risk o oxygen toxicity.

Several mechanisms are probably responsible for the increase in arterial P_{O_2} resulting from PEEP. The positive pressure increases the FRC, which is typicall small in these patients because of the increased elastic recoil of the lung. The lo lung volume causes airway closure and intermittent ventilation (or none at al of some areas, especially in the dependent regions (Fig. 3.5), and absorption a electasis ensues (Fig. 9.4). PEEP tends to reverse these changes. Patients wit edema in their airways also benefit, probably because the fluid is moved into sma peripheral airways or alveoli, allowing some regions of the lung to be reventilate

Figure 10.3 shows the effects of PEEP in a patient with ARDS (46). Note tha the level of PEEP was progressively increased from 0 to 16 cm H_2O and th caused the shunt to fall from 43.8 to 14.2% of the cardiac output. A small amoun of blood flow to poorly ventilated alveoli remained. The increase in PEEP als caused the dead space to increase from 36.3 to 49.8% of the tidal volume. Th can be explained by compression of the capillaries by the increased alveolar pres sure and also the increase in volume of the lung and consequent increased radia traction on the airways, which increases their volume. This situation is discusse further below.

Positive End-Expiratory Pressure (PEEP)

- Often valuable for raising the arterial P_{O_2} in patients with respiratory failure
- Values of 5–20 cm H_2O are commonly used
- May allow the inspired O_2 concentration to be reduced
- May reduce cardiac output by impeding venous return
- High levels of PEEP may damage pulmonary capillaries

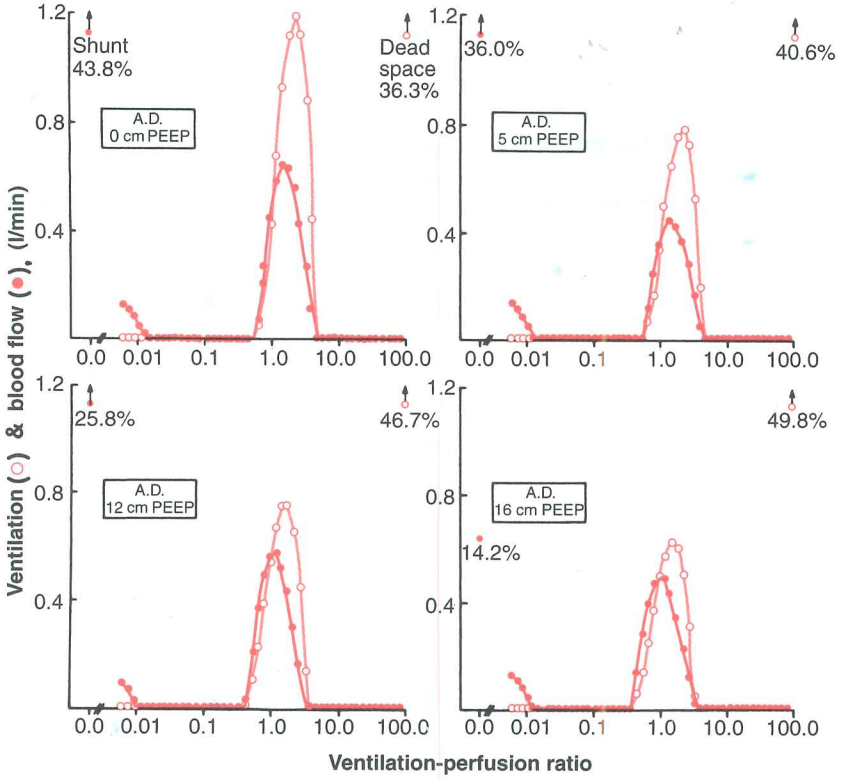


Figure 10.3. Reduction of shunt and increase of dead space caused by increasing levels of PEEP in a patient with adult respiratory distress syndrome (ARDS). Note that as the PEEP was progressively increased from 0 to 16 cm H_2O, the shunt decreased from 43.8 to 14.2% of the cardiac output, and the dead space increased from 36.3 to 49.8% of the tidal volume. (From Dantzker DR, Brook CJ, DeHart P, et al. Ventilation–perfusion distributions in the adult respiratory distress syndrome. Am Rev Respir Dis 1979;120:1039–1052.)

Occasionally, the addition of too much PEEP reduces rather than increases the arterial P_{O_2}. Possible mechanisms include: 1) a substantial fall in cardiac output, which reduces the P_{O_2} of mixed venous blood and therefore the arterial P_{O_2}; 2) reduced ventilation of well-perfused regions (because of increasing dead space and ventilation to poorly perfused regions); and 3) diversion of blood flow away from ventilated to unventilated regions by the raised airway pressure. These deleterious effects of PEEP on the arterial P_{O_2} are fortunately seldom seen.

PEEP tends to reduce cardiac output by impeding venous return to the thorax, especially if the circulating blood volume has been depleted by hemorrhage or shock. Accordingly, its value should not be gauged by its effect on the arterial P_{O_2} alone but in terms of the total amount of oxygen delivered to the tissues. The product of the arterial oxygen concentration and the cardiac output is a useful

index because changes in this alter the P_{O_2} of mixed venous blood and therefo the P_{O_2} of many tissues. Some physicians use the level of the P_{O_2} in mixed veno blood as a guide to the optimal level of PEEP.

However, in some extremely ill patients, the P_{O_2} of mixed venous blood ca be misleading. Under some conditions, the application of PEEP causes reduction in overall oxygen consumption of the patient (47). Although th raises the oxygen concentration and P_{O_2} of mixed venous blood (see equ tion 9.2), this is not beneficial to the patient. Apparently, the oxygen co sumption falls because the perfusion of some tissues is so marginal that if the blood flow is further decreased, they are unable to take up oxygen and pr sumably slowly die.

Another hazard of high levels of PEEP is damage to the pulmonary capilla ies as a result of the high tension in the alveolar walls. The alveolar wall can considered a string of capillaries. High levels of tension greatly increase the stress on the capillary walls causing disruption of the alveolar epithelium, capilla endothelium, or sometime all layers of the wall. This is another example "stress failure" that was discussed in Chapter 6 in relation to pulmonary eden caused by high capillary hydrostatic pressures.

Continuous Positive Airway Pressure (CPAP)

Some patients who are being weaned from a ventilator breathe spontaneously b are still intubated. Such patients may benefit from a small positive pressure appli continuously to the airway by a valve system on the ventilator. The improveme in oxygenation results from the same mechanisms as for PEEP. A form of CPA had been used successfully in the treatment of infant respiratory distress syndrom (IRDS). Another form of CPAP is useful in treating sleep disordered breathi caused by upper airway obstruction. Here the increased pressure is applied via face mask that is worn by the patient all night.

Intermittent Mandatory Ventilation (IMV)

This is a modification of IPPV (see previous text) in which a large tidal vo ume is given at relatively infrequent intervals to an intubated patient who breathing spontaneously. It is often combined with PEEP or CPAP. This pa tern may be useful in weaning a patient from a ventilator, and in preventi upper airway occlusion in obstructive sleep apnea by using nasal CPAP duri the night.

High Frequency Ventilation

It is possible to maintain normal blood gases by very high frequency (approx mately 20 cycles/sec) positive-pressure ventilation with low stroke volum (50–100 ml). The lung is vibrated rather than expanded in the convention way, and the transport of the gas occurs by a combination of diffusion ar convection. One use is in patients in whom gas leaks from the lung via bronchopleural fistula.

Physiologic Effects of Mechanical Ventilation

Reduction of Arterial P_{CO_2}

In general, mechanical ventilation is used to increase ventilation and improve pulmonary gas exchange in lungs where this is grossly impaired. The impairment may result either because the patient is not able to breathe spontaneously, as in neuromuscular disease, or because the lung itself is severely diseased, as in ARDS. Frequently, mechanical ventilation is begun because the arterial P_{CO_2} is rising or already elevated, and it is usually effective at keeping this in check or reducing it. In patients with airway obstruction in whom the oxygen cost of breathing is high, mechanical ventilation may appreciably reduce the oxygen uptake and CO_2 output, thus contributing to the fall in arterial P_{CO_2}.

The relationship between the arterial P_{CO_2} and the alveolar ventilation in normal lungs is given by the familiar equation:

$$P_{CO_2} = \frac{\dot{V}_{CO_2}}{\dot{V}_A} \cdot K$$

where K is a constant. In diseased lungs, the denominator $\dot{V}_A$ in this equation is less than the ventilation going to the alveoli because of alveolar dead space, that is, unperfused alveoli or those with high ventilation–perfusion ratios. For this reason, the denominator is sometimes referred to as the "effective alveolar ventilation."

Mechanical ventilation frequently increases both the alveolar and anatomic dead spaces. As a consequence, the effective alveolar ventilation is not increased as much as the total ventilation. This is particularly likely if high pressures are applied to the airway. This can be seen in the example shown in Figure 10.3. As the level of PEEP was increased from 0 to 16 cm H_2O in this patient with ARDS, the dead space increased from 36.3 to 49.8%. In some patients, high levels of PEEP also result in the appearance of lung units with high ventilation–perfusion ratios that cause a shoulder to form on the right of the ventilation distribution curve. This did not occur in the example shown. Occasionally, a large physiologic dead space is seen with IPPV even in the absence of PEEP. An example is shown in Figure 8.3.

There are several reasons why positive-pressure ventilation increases dead space. First, lung volume is usually raised, especially when PEEP is added, and the resulting radial traction on the airways increases the anatomic dead space. Next, the raised airway pressure tends to divert blood flow away from ventilated regions, thus causing areas of high ventilation–perfusion ratio or even unperfused areas (Fig. 10.3). This is particularly likely to happen in the uppermost regions of the lung where the pulmonary artery pressure is relatively low because of the hydrostatic effect. (See Respiratory physiology–the essentials, ed. 6: p. 37.) Indeed, if the pressure in the capillaries falls below airway pressure, the capillaries may collapse completely, resulting in unperfused lung (Fig. 10.4) (48). This collapse is encouraged by two factors: 1) the abnormally high airway pressure, and 2) the reduced venous return and consequent hypoperfusion of the lung. The latter is particularly likely to occur if there is a reduced circulating blood volume (see later).

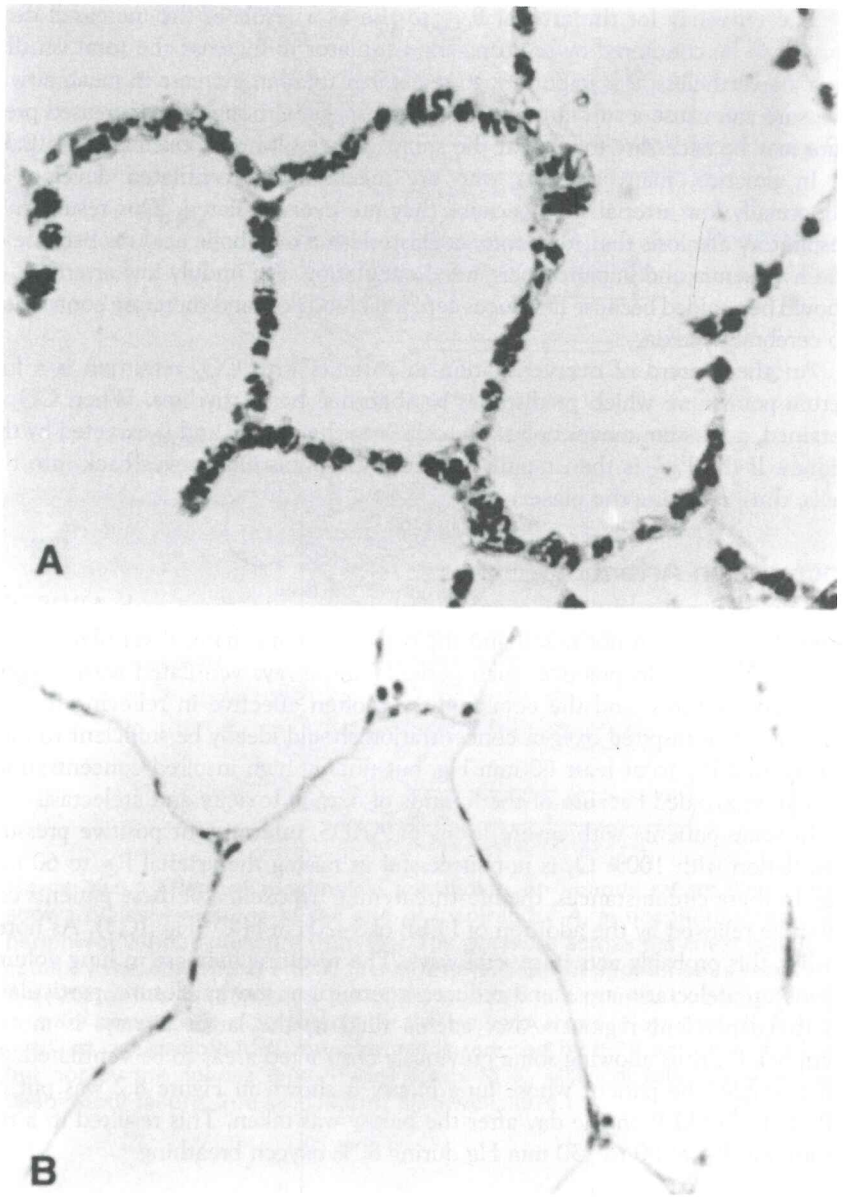


Figure 10.4. Effect of raised airway pressure on the histological appearance of pulmonary capillaries. *(A)* Normal appearance. *(B)* Collapse of capillaries when alveolar pressure is raised above capillary pressure. (From Glazier JB, Hughes JMB, Maloney JE, et al. Measurements of capillary dimensions and blood volume in rapidly frozen lungs. J Appl Physiol 1969;26:65–76.)

The tendency for the arterial P_{CO_2} to rise as a result of the increased dead space can be countered by resetting the ventilator to increase the total ventilation. Nevertheless, it is important to remember than an increase in mean airway pressure can cause a substantial rise in dead space, although the increased pressure may be necessary to combat the shunt and resulting hypoxemia (Fig. 10.3).

In practice, many patients who are mechanically ventilated develop an abnormally low arterial P_{CO_2} because they are overventilated. This results in a respiratory alkalosis that frequently coexists with a metabolic acidosis because of the hypoxemia and impaired peripheral circulation. An unduly low arterial P_{CO_2} should be avoided because it reduces cerebral blood flow and therefore contributes to cerebral hypoxia.

Another hazard of overventilation in patients with CO_2 retention is a low serum potassium, which predisposes to abnormal heart rhythms. When CO_2 is retained, potassium moves out of the cells into the plasma and is excreted by the kidney. If the P_{CO_2} is then rapidly reduced, the potassium moves back into the cells, thus depleting the plasma.

Increase in Arterial P_{O_2}

In some patients with respiratory failure, for example, those with ARDS, the arterial P_{CO_2} is often not raised and the objective of mechanical ventilation is to increase the P_{O_2}. In practice, such patients are always ventilated with oxygen-enriched mixtures, and the combination is often effective in relieving the hypoxemia. The inspired oxygen concentration should ideally be sufficient to raise the arterial P_{O_2} to at least 60 mm Hg, but unduly high inspired concentrations should be avoided because of the hazards of oxygen toxicity and atelectasis.

In some patients with severe forms of ARDS, intermittent positive pressure ventilation with 100% O_2 is not successful in raising the arterial P_{O_2} to 60 mm Hg. In these circumstances, the life-threatening hypoxemia of these patients can often be relieved by the addition of PEEP of 5–20 cm H_2O (Fig. 10.3). As noted earlier, this probably acts in several ways. The resulting increase in lung volume opens up atelectatic areas and reduces intermittent airway closure, particularly in the dependent regions. Also, edema fluid in the larger airways is moved peripherally, thus allowing some previously obstructed areas to be ventilated. As an example, the patient whose lung biopsy is shown in Figure 8.2 was put on 10 cm H_2O PEEP on the day after the biopsy was taken. This resulted in a rise in arterial P_{O_2} of 80 to 130 mm Hg during 80% oxygen breathing.

Effects on Venous Return

Mechanical ventilation tends to impede the return of blood into the thorax and thus reduce the cardiac output. This is true both for positive-pressure and negative-pressure ventilation. In a supine, relaxed patient, the return of blood to the thorax depends on the difference between the peripheral venous pressure and the mean intrathoracic pressure. If the airway pressure is increased by a ventilator, mean intrathoracic pressure rises and venous return is impeded (Fig. 10.5) (49). Even if airway pressure remains atmospheric, as in a tank respirator (Fig. 10.2)

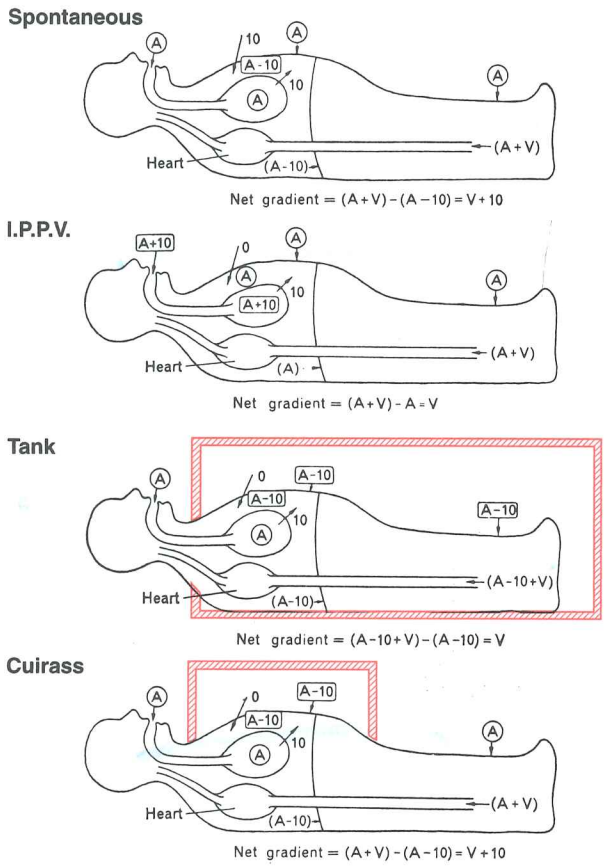


Figure 10.5. Effect of mechanical ventilation on venous return. The diagra shows typical pressures at the end of inspiration. *A*, atmospheric pressure; peripheral venous pressure (mm Hg). The pressure across the chest wall is in cated by the *downward arrow*; this is zero (except for spontaneous respiratio because at this lung volume the chest wall is in its relaxed position. Transp monary pressure is represented by the *upward arrow*. Note that the pressu gradient responsible for venous return is reduced by IPPV and tank respirato but not by the cuirass type. (From Sykes M K, McNicol MW, Campbell EJ Respiratory failure, 2nd ed. Oxford: Blackwell, 1976.)

venous return tends to fall because the peripheral venous pressure is reduced the negative pressure. Only in the cuirass respirator is venous return virtual unaffected.

The effects of positive-pressure ventilation on venous return depend on th magnitude and duration of the inspiratory pressure and, particularly, the additio of PEEP. The ideal pattern from this standpoint is a short inspiratory phase relatively low pressure followed by a long expiratory phase and zero (or slight negative) end-expiratory pressure. However, such a pattern encourages a low lu volume and consequent hypoxemia, and a compromise is generally necessary

An important determinant of venous return is the magnitude of the circulating blood volume. If this is reduced, for example, by hemorrhage or shock, positive-pressure ventilation often causes a marked fall in cardiac output. Systemic hypotension may ensue. It is therefore important to correct any volume depletion by appropriate fluid replacement. The central venous pressure is often monitored as a guide to this but should be interpreted in the light of the increased airway pressure. Positive airway pressure itself raises central venous pressure. An additional factor often contributing to the fall in cardiac output during mechanical ventilation is hypocapnia caused by overventilation.

Miscellaneous Hazards

Mechanical problems are a constant hazard. They include power failure, broken connections, and kinking of tubes. Apnea alarms are available to warn of these dangers, but skilled care by the intensive care team is essential.

Pneumothorax can occur, especially if PEEP and/or unusually large tidal volumes are used. *Interstitial emphysema* may develop if the lung is overdistended. The air escapes from ruptured alveoli, tracks along the perivascular and peribronchial interstitium (Fig. 6.1), and may enter the mediastinum and the subcutaneous tissue of the neck.

Pulmonary infection is a danger if the equipment is not scrupulously clean. Crusting of the large airways occurs unless the gas is efficiently humidified. *Cardiac arrhythmias* may be caused by rapid swings in pH and hypoxemia. There is also an increased incidence of *gastrointestinal bleeding* in these patients.

QUESTIONS

1. All of the following are true of a tracheostomy except:
- A. The tube facilitates the removal of retained secretions by suction.
- B. It provides port for mechanical ventilation.
- C. It can bypass a region of upper airway obstruction.
- D. The cuff can damage the airway wall.
- E. It increases the anatomic dead space.

2. All of the following are true of constant-volume ventilators except:
- A. They provide a nearly constant tidal volume even if lung compliance falls.
- B. Respiratory frequency can be changed.
- C. The ratio of inspiratory to expiratory time can be changed.
- D. They require electrical power.
- E. They are typically small and portable.

3. In the treatment of a patient with ARDS by mechanical ventilation, the addition of PEEP typically results in all of the following except:
- A. Increased arterial P_{O_2}.
- B. Increased FRC.
- C. Reduced shunt.
- D. Increased physiologic dead space.
- E. Tendency to reduce venous return to the thorax

4. A patient with paralyzed respiratory muscles but normal lungs is being treated by mechanical ventilation. In this patient the arterial P_{CO_2} can be reduced without changing total ventilation by:
- A. Reducing the FRC.
- B. Increasing the tidal volume.
- C. Increasing the respiratory frequency.
- D. Reducing the resistance of the airways.
- E. Adding oxygen to the inspired gas.

5. Hazards of mechanical ventilation include all of the following except:
- A. Pneumothorax.
- B. Interstitial emphysema.
- C. Pulmonary infection.
- D. Cardiac arrhythmias.
- E. Anemia.