In this work, the authors provide an intensive analysis of the acute respiratory distress syndrome—giving initial background along with in-depth coverage of the etiology, pathophysiology, diagnosis, and treatment.

Before discussing the etiology, pathophysiology, diagnosis, and treatment of the acute respiratory failure in critically ill and injured patients, sometimes referred to as the Adult Respiratory Distress Syndrome (ARDS), it may be well to review some aspects of normal pulmonary function.

Ventilation
The four main processes involved in gas exchange in the lungs include ventilation (the movement of air in and out of the lungs), distribution (the partitioning of the ventilated gases into the various lobes, segments and lobules), diffusion (the movement of gases back and forth between the alveoli and the plasma and red blood cells), and perfusion (the circulation of blood through the pulmonary capillaries).

Lung volume
There are about 200-600 million alveoli in the normal lung, depending on stature, with an average total alveolar surface area of 40-100 sq. M. This area is directly related to the body length and decreases by about 5% per decade.

In most studies of ventilation, a number of terms have been used to describe the volume or capacity of the lung at various phases of the inspiratory-expiratory cycle. For example, the total lung capacity (TLC), representing the volume of the lungs, when maximally inflated is generally divided into the forced vital capacity (FVC) and the residual volume (RV). The FVC, by definition, is that volume of air which the patient can exhale after a maximum inspiration. The RV is that volume of air remaining in the lungs after a maximal exhalation.

The FVC in turn, can be divided into the inspiratory reserve volume (IRV), tidal volume (VT) and expiratory reserve volume (ERV). The VT is the amount of air moved in and out of the lungs during normal resting ventilation, the ERV is the amount of air that can be exhaled after a normal exhalation, and the IRV is the amount of air that can be inspired after a normal inspiration. The functional residual capacity (FRC) consists of the ERV plus the RV and represents the amount of air still present in the lungs after a normal exhalation. These relationships can be expressed as follows:

\[
\begin{align*}
\text{TLC} &= \text{FVC} + \text{RV} \\
\text{VC} &= \text{IRV} + \text{VT} + \text{ERV} \\
\text{TLC} &= \text{FRC} + \text{IC} \\
\text{FRC} &= \text{ERV} + \text{RV} \\
\text{IC} &= \text{IRV} + \text{VT}
\end{align*}
\]

An example of the lung volumes that might be expected in a seated young
adult who has a total lung capacity (TLC) of approximately 5.6 liters would be a residual volume (RV) of 1.2 liters, expiratory reserve volume (ERV) of 1.8 liters, a tidal volume (VT) of 0.5 liters, and inspiratory reserve volume (IRV) of 2.1 liters.

Table 1
Lung volume changes with age

<table>
<thead>
<tr>
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<th>20 Years</th>
<th>70 Years</th>
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<tbody>
<tr>
<td>TLC</td>
<td>5.6 L</td>
<td>4.2 L</td>
</tr>
<tr>
<td>IRV</td>
<td>2.1</td>
<td>1.2</td>
</tr>
<tr>
<td>VT</td>
<td>0.5 L</td>
<td>0.4 L</td>
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<tr>
<td>ERV</td>
<td>1.8 L</td>
<td>0.8 L</td>
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<tr>
<td>RV</td>
<td>1.2 L</td>
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The lung "capacities" in the same patient might consist of a forced vital capacity (FVC) of 4.2 liters, an inspiratory capacity (IC) of 1.6 liters, and a functional residual capacity (FRC) of 2.6 liters.

Table 2
Lung capacity changes with age

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<td>2.2 L</td>
</tr>
<tr>
<td>IC</td>
<td>2.6 L</td>
<td>1.6 L</td>
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<tr>
<td>FRC</td>
<td>3.0 L</td>
<td>2.6 L</td>
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</table>

With advancing age, total lung capacity (TLC) falls slightly, forced vital capacity (FVC) falls moderately, and expiratory reserve volume (ERV) and inspiratory capacity (IC) fall markedly. In 70-year-old patients who are in an apparently good state of health, the TLC might be 4.8 liters, FVC 3.0 liters, PV 1.8 liters, ERV 0.6 liters, FRC 2.4 liters, and the IC 2.4 liters. In the adult respiratory distress syndrome (ARDS), all the lung volumes and capacities, particularly the ERV, are markedly reduced.

Dead space and alveolar ventilation

Normal values

The tidal volume (VT) in a normal male at rest averages about 400–500 ml. Of this, approximately 150–200 ml never reach perfused alveoli, and this portion of the tidal volume is called dead space (VD). Under ordinary circumstances, the ratio of the dead space (VD) to tidal volume (VT) in healthy young adults is about 0.3–0.4.

To determine the alveolar ventilation with each breath (VA) one subtracts the dead space (VD) from the tidal volume (VT). The alveolar ventilation (VA) per minute can then be calculated and it is equal to the alveolar ventilation per breath multiplied by the respiratory frequency/minute (f).

\[
V_A = V_T - V_D
\]

\[
V_A = V_A \times f
\]

Changes with varying tidal volumes

Since dead space remains relatively constant, different tidal volumes can produce great changes in alveolar ventilation, even when the total minute ventilation remains constant. For example, if the minute ventilation is 8 liters/min., the respiratory rate is 16/min., the tidal volume is 500 ml, and the dead space is 150 ml, the alveolar ventilation will be about 5.6 liters/min.

On the other hand, if the tidal volume is 200 ml, the respiratory rate 40/min., and the dead space remains at about 150 ml/breath, the alveolar ventilation will only be about 2 liters/min.

At the other extreme, if the tidal volume is 1000 ml and the respiratory rate 8, alveolar ventilation will be approximately 6.8 liters/min. Although the total dead space does rise or fall somewhat as the tidal volume increases or decreases, at higher tidal volumes the VD/VT ratio does decrease and ventilation of the alveoli is much more efficient.

The shape of the inspired air front

If the movement of inspired air through the conducting airways had a square front and if the tidal volume were exactly equal to the anatomic dead space, there would theoretically be no
effective alveolar ventilation. However, the front of the inspired air movement apparently is shaped like a cone, so that even if the tidal volume is less than the anatomic dead space, there is still some alveolar ventilation.

Types of dead space

When considering dead space, it is important to think of the total dead space as being made up of anatomic dead space and pathologic or alveolar dead space. The "anatomic dead space" consists of the conducting airway which is roughly equivalent in ml to the body weight in pounds. Thus, a man with an ideal weight of 180 pounds has an anatomic dead space of approximately 180 ml.

Pathologic or "alveolar dead space" refers to the volume of alveoli that are ventilated and have no capillary blood flow. Increased alveolar dead space may be seen in patients with pulmonary emboli where the ventilated alveoli have impaired pulmonary capillary blood flow. It is also found in patients with emphysema, who have excessively distended alveoli and decreased alveolar septae so that the number of pulmonary capillaries exposed to the alveoli is reduced.

Calculating dead space

The ratio between dead space and tidal volume can be determined easily if one has equipment for measuring the arterial PCO₂ and the average PCO₂ in the patient's expired gas. Gas for such measurements can be obtained by having the patient breathe through a tube with a one-way valve and then collecting all of the expired gas in a Douglas or similar bag. Under ordinary circumstances, the arterial PCO₂ is about 40 mmHg and the average expired PCO₂ is about 28 mmHg, making the ratio of total or physiologic dead space to tidal volume approximately 0.3.

\[
\frac{V_D}{V_T} = \frac{(P_{aCO_2} - P_{eCO_2})}{P_{aCO_2}} = \frac{(40 - 28)}{40} = 12/40 = 0.3
\]

If there is a significant increase in alveolar dead space, the alveolar PCO₂ (P_{aCO_2}) will be significantly lower than the arterial PCO₂ (P_{aCO_2}) and the average expired PCO₂ (P_{eCO_2}) will also be lower than normal. For example, if a patient has a tidal volume (V_T) of 500 ml, PaCO₂ of 40 mmHg, P_{aCO_2} of 30 mmHg, and P_{eCO_2} of 20 mmHg, then:

\[
V_D (anatomic) = \frac{P_{aCO_2} - P_{eCO_2}}{P_{aCO_2}}(500) = \frac{30 - 24}{30}(500) = 167 \text{ ml}
\]

\[
V_D (total) = \frac{P_{aCO_2} - P_{eCO_2}}{P_{aCO_2}}(500) = \frac{40 - 24}{40}(500) = 250 \text{ ml}
\]

The alveolar dead space = 250 - 167 = 83 ml

Effect of alveolar ventilation on PCO₂

With a normal alveolar ventilation of about 4–5 liters/min., the PaCO₂ averages about 40 mmHg. If the alveolar ventilation falls to 2 liters/min., the PaCO₂ often rises to about 80 mmHg. On the other hand, if alveolar ventilation is increased to 8–9 liters/min., the PaCO₂ often falls to about 20–25 mmHg. Thus, the PaCO₂ provides a relatively accurate indication of the alveolar ventilation. The PaO₂, on the other hand, is affected by multiple factors in addition to the alveolar ventilation.

Distribution

The distribution of ventilated gas in the lungs is determined largely by local changes in the transpulmonary or distending pressures. Some other factors that also may alter gas distribution to various lobules include: position changes, airway closure, loss of surfactant, decreased elasticity of portions of the lung, and partial or complete obstruction of bronchi.
Transpulmonary pressure

The transpulmonary or distending pressure is equal to the alveolar pressure, which is generally considered to be the same throughout the lung, minus the pleural pressure. The pleural pressure is determined primarily by gravity, with each centimeter change in position up or down resulting in a corresponding decrease or increase in the pleural pressure of 0.2–0.3 cm H₂O. The vertical gradient that exists between the apex and base of the lung when the patient is standing is almost double the gradient present between the anterior and posterior surfaces of the lung when the patient is supine.

Because the pleural pressure is greater in the lower portions of the lung, there is less distending or transpulmonary pressure in that area, and as a consequence, the dependent alveoli are smaller than the apical alveoli. However, if the airways to the dependent alveoli are open during inspiration, they expand relatively more because they are in a more favorable position on the pressure volume curve (which describes the relationship between alveolar size and their distending pressure). Unfortunately, the small airways to these alveoli also tend to close earlier and open later than those associated with the larger, less dependent alveoli.

Airway closure

Ordinarily, all airways are open at the end of a full inspiration. During expiration, however, some of the small airways (0.5–0.9 mm in diameter) close relatively early. This phenomenon has given rise to the concept of “closing volume”, which is the lung volume present when a significant number of the small airways begin to close.

The important corollary of this is that those airways which close earliest during expiration also open latest during inspiration. Since those processes which increase closing volumes tend to have their greatest effect on the more dependent portions of the lung, ventilation tends to be distributed away from these areas in most critically-ill or injured patients.

Closing volumes increase with age and in the supine position. In an individual who is 65 years of age and standing erect, the closing volume is equal to the functional residual capacity (FRC). However, in the supine patient, the closing volume is greater and is equal to the functional residual capacity at only about 44 years of age.

Closing volume also tends to increase with obesity and abdominal distention; however, it is decreased by spontaneous sighing. If the functional residual capacity plus the tidal volume are less than the closing volume, as may happen in ARDS, the affected alveoli are not ventilated; such alveoli then become progressively more atelectatic as the gases they contain are absorbed. Thus, the more severe the ARDS, the higher the tidal volumes that are needed.

Surfactant

The surfaces of alveoli are normally lined by a surface-active agent called surfactant, which is primarily a phospholipid, dipalmitayl lecithin (DPL). Surfactant is essential in the lung because it reduces alveolar surface tension, thereby helping to prevent alveolar collapse (particularly at the lower transpulmonary distending pressures which are present in the lower portions of the lung).

Although surfactant production by the Type II granular pneumocytes appears to be decreased in experimental shock, it appears that surfactant metabolism can be maintained without perfusion of the pulmonary capillaries as long as there is adequate alveolar ventilation. Interestingly, mild over-distention of alveoli may increase surfactant production; however, excessive distention of alveoli may have the opposite effect.

Some of the clinical situations which may be associated with decreased surfactant production include inhalation of high concentrations of oxygen, cardiopulmonary bypass, and, possibly, pro-
longed ventilator assistance. Although there have been some suggestions that decreased surfactant might be an etiologic factor of ARDS, there seems to be an increasing feeling that decreased surfactant in such circumstances is a result and not a cause of the altered pathophysiology.7

**Diffusion**

The movement of gases back and forth between the alveoli and the plasma and red blood cells is accomplished largely by the process of diffusion. Since carbon dioxide diffuses so readily, hypercarbia due to impaired diffusion alone is extremely unlikely. Oxygen, on the other hand, is much less diffusible and impaired diffusion may be a significant cause of hypoxemia, particularly at low oxygen concentrations.

The most frequent cause of impaired or decreased diffusion in the lung is an increased distance between the alveolar and the red cell membranes caused by increased interstitial fluid, as may occur in ARDS or congestive heart failure. Under ordinary circumstances, the thickness of the alveolar-capillary membrane is about 0.1 micron and the distance between the alveolus and the interior of the red cell is less than 0.5-1.0 microns. However, apparently even mild changes in capillary permeability may cause an abrupt increase in the amount of interstitial fluid and a severe drop in the arterial PO2 (PaO2).

**Perfusion**

**Volume and pressure**

The total volume of blood in the pulmonary arteries, veins and capillaries is about 500 ml in an average adult male or about 10% of the total blood volume. Of this blood in the pulmonary circuit, approximately 60-65% is present in the pulmonary veins and about 15-20% each in the pulmonary arteries and capillaries. The pulmonary arteries are very compliant and the blood flow in them may increase two-to-four fold with no increase in pressure.

Pressures in the right side of the heart, pulmonary vessels, and left atrium are usually much lower than those in the systemic circuit. The pressure in the right atrium is normally about 0–5 mmHg, in the right ventricle it is 15–25/0–5, in the pulmonary artery it is 15–25/5–10, and the pressures in the pulmonary capillaries, pulmonary veins, and left atrium average about 5–10 mmHg. The pressures in the left ventricle are much higher and normally average 120/0–5; and in the aorta, the average pressure is about 120/80 mmHg.

**Flow**

The total perfusion or blood flow through the lung is essentially equal to the cardiac output. One method for determining the cardiac output is the Fick Principle. If one divides the oxygen uptake or oxygen consumption in ml/min. by the arteriovenous oxygen difference in ml of oxygen/liter. the result equals the cardiac output in liters/min.

For example, in an average adult male, oxygen consumption averages about 250 ml/min and the A-V oxygen difference is approximately 5 vol% or 50 ml/liter. Therefore, such an individual would be expected to have a cardiac output of about 5 liters/min.

\[
\text{Cardiac Output (C.O.)} = \frac{\text{O}_2 \text{ Consumption}}{\text{A-V O}_2 \text{ difference}}
\]

\[
\begin{align*}
\text{C.O.} &= \frac{250 \text{ ml/min}}{5 \text{ vol}% \times 10} \\
&= \frac{250}{50} \\
&= 5 \text{ L/min}
\end{align*}
\]

The average oxygen hemoglobin saturation in the pulmonary artery is approximately 70-75% and in the systemic arteries it is 95-98%. The blood from the superior vena cava ordinarily has an oxygen content similar to that of the mixed venous blood in the pulmonary artery. Inferior vena cava blood generally has a higher oxygen content than the superior vena cava, but this is usually balanced fairly well by the very low oxygen saturation of the coronary sinus blood.
Vascular resistance

Vascular resistance in the pulmonary circuit normally is only about 1/5 or 1/6 of that calculated for the systemic arteries. Since the mean pressure is normally about 15 mmHg in the pulmonary artery and about 5 mmHg in the pulmonary veins, the pressure drop across the pulmonary arterioles is approximately 10 mmHg.

If the pressure difference in mmHg across a vascular bed is divided by the flow in liters/min, the result, (if multiplied by 80 to change the units into the metric system), is equal to the vascular resistance in that circuit in dyne - sec/cm^5. Thus, the normal pulmonary arteriolar resistance is about 160 dyne - sec/cm^5.

\[
\text{TPR (dyne-sec/cm}^5\text{)} = \left(\frac{\text{pressure change (mm Hg)}}{\text{flow (L/min)}}\right) \times 80
\]

\[
= \frac{15 - 5}{5} \times 80
= 2 \times 80
= 160
\]

Thus, the total net hydrostatic pressure (P_C - P_T) tending to push fluid into the interstitial spaces averages about 24 mmHg.

\[
\pi_p = \text{plasma oncotic pressure, which is about 28 mmHg}
\]

\[
\pi_t = \text{tissue or interstitial oncotic pressure, which is estimated to average about 4-5 mmHg}
\]

As a result, the total net osmotic pressure (\(\pi_p - \pi_t\)) tending to keep fluid in the capillary space is about 23.5 mmHg. The resultant total net pressure of about 0.5 mmHg pushing the fluid into the interstitial space could gradually result in a fluid accumulation there if it were not removed by pulmonary lymphatics.

Movement of fluid out of the capillaries into the pulmonary tissue would be favored by any factors which increased capillary permeability (shock, sepsis), increased the capillary hydrostatic pressure (congestive heart failure), or decreased the plasma osmotic pressure (cirrhosis or administration of excessive crystalloids).

The formation of pulmonary edema fluid, particularly in patients with ARDS, is largely dependent on the permeability of the pulmonary capillaries, and to a much lesser extent on the balance of the intravascular and interstitial pressures. If the patient develops increased (less negative) interstitial fluid pressure, a higher left atrial or pulmonary venous pressure, or a lower colloid osmotic pressure, there is a progressively increased tendency toward pulmonary edema.

Regulation of ventilation

Of the various chemical factors stimulating ventilation, the three most im-
important are increased carbon dioxide, decreased oxygen, and decreased pH.

**Increased carbon dioxide**

Inhaling increased concentrations of carbon dioxide can increase tidal volume very quickly, primarily by direct stimulation of the medullary respiratory center. The medullary respiratory center is very sensitive to even slight rises in the arterial PCO₂ (PaCO₂), with a resultant increase initially in tidal volume and later in respiratory rate.

Interestingly it may not be until the inhaled CO₂ rises from a normal of 0.04% to over 2% in normal subjects that any significant change is produced. When the inspired concentration of carbon dioxide is increased to 5%, alveolar ventilation may be increased five-fold or more. If the PCO₂ is chronically elevated above 70–80 mmHg, however, the respiratory center may become depressed and unresponsive to PCO₂ changes, and the respiratory drive may then depend primarily on hypoxic stimuli from the chemoreceptors.

If a patient does not have an appropriate increase in ventilation when breathing an increased concentration of carbon dioxide or after stimuli such as shock, sepsis or trauma, one should look for the following:

1. Central nervous system damage or depression.
2. Airway damage or obstruction.
3. Chest wall damage or abnormalities.

In patients with chronic lung disease, additional problems may include:

1. CO₂ narcosis.
2. Removal of anoxic stimuli.
4. Cerebral spinal fluid pressure changes.

Interestingly, sudden severe hypocarbia may cause such severe cerebral vasoconstriction and ischemia that the resultant metabolic acidosis in various portions of the brain may act as a powerful stimulus to ventilation. This inappropriate hyperventilation will tend to become progressively worse until or unless the patient passes out, or he is allowed to rebreathe his expired air until his arterial PCO₂ has risen to a more normal range and the cerebral vasoconstriction can relent.

**Hypoxia**

Hypoxia normally is a much weaker stimulus to ventilation than hypercarbia. The concentration of inspired oxygen may have to decrease from a normal of 21% to approximately 16% before tidal volume is increased significantly. This response is mediated through reflexes initiated in the chemoreceptors of the carotid and aortic bodies by a decrease in the PaO₂. In anemia or carbon monoxide poisoning, the oxygen content of the blood may be greatly reduced with no appreciable change in PaO₂. Thus, there may be little or no increase in ventilation until tissue damage and/or lactic acidosis develop.

**Changes in pH**

Acidosis by itself (and without any changes in the PCO₂) increases both respiratory rate and tidal volume. It does this probably because of stimulation both centrally and peripherally. Much of the respiratory changes caused by the PaCO₂, however, are more than likely related to their effect on the pH of the cerebrospinal fluid.

Some of the other factors which influence ventilation include various reflexes such as the pulmonary stretch (Hering-Breuer), cough, upper respiratory, swallowing and submersion reflexes. The pulmonary stretch (Hering-Breuer) reflex is often thought of only as an “inhibito-inspiratory reflex” which stops further inspiration after the lungs have become moderately distended or inflated. However, the stretch reflexes also include “excitato-inspiratory reflexes” in which there is a stimulus to inspiration when the lungs become partially deflated and a “deep inspiration reflex” to inflate the lungs even further if the lung becomes more than moderately inflated.
Other factors

Other factors which may stimulate ventilation include infection, trauma, pain, hypotension, joint movements, and temperature changes. If shock, sepsis or trauma fail to increase the minute ventilation to at least 1½ to 2 times normal, something is usually wrong with the central nervous system, airway or chest wall. Such a condition should be corrected promptly.

Ventilation-perfusion ratios

Abnormal alveolar ventilation-perfusion (V/Q) ratios, or V/Q imbalance as it is often called, are generally considered to be the main cause of the abnormal blood gases in ARDS. Under normal circumstances, the entire lung has an average alveolar ventilation of about 4 liters/min and a perfusion of approximately 5 liters/min so that the total normal average V/Q ratio is about 0.8.

Perfusion in the lungs is largely determined by gravity, with the great portion of the pulmonary circulation going to those areas of the lung which are most dependent. Thus, in the erect subject, there is a decreased V/Q ratio at the bases and an increased V/Q ratio at the apices. In areas of the lung where there is increased dead space, that is, areas ventilated but perfused poorly or not at all, the V/Q ratio is high. If there is increased shunting, that is, areas perfused but poorly ventilated, the V/Q ratio is low.

Compliance

Compliance refers to the volume of air or gas that can move into the lung for each unit of pressure change and is generally expressed in liters or ml per cm H₂O pressure. Resistance is the reciprocal of compliance and is generally expressed in terms of cm H₂O pressure per liter or ml of inflation or deflation.

In general, resistance to ventilation can be divided into three parts: airway, lung, and chest wall. For example, it normally takes about 10-15 cm H₂O pressure to passively ventilate an adult with a tidal volume of about 500 ml. Of this total pressure, approximately 3-5 cm H₂O pressure are needed to overcome airway resistance (depending on the rate of air flow), 3-5 cm H₂O pressure are needed to overcome the resistance of the lung itself, and 3-5 cm H₂O pressure are needed to overcome the resistance of the chest wall. If the tidal volume is increased to 1000 ml, the pressures required to overcome the resistance of each component are 5-10 cm H₂O for the airway, 5-10 cm H₂O for the lungs, and 5-10 cm H₂O for the chest wall.

Airway resistance

Airway resistance \( (R_{AW}) \) can be calculated by dividing the pressure to overcome airway resistance \( (P_{AW}) \) by rate of airflow \( (F) \). If the rate of airflow is 1000 ml/sec or 1.0 liters/sec (which is often the flow rate used in ventilation but double the flow rate normally seen with spontaneous respiration), the airway resistance \( (R_{AW}) \) can be calculated as follows:

\[
R_{AW} = \frac{P_{AW}}{F} = \frac{5 - 10 \text{ cm H}_2\text{O}}{1.0 \text{ L/sec}}
\]

If the flow rate were slowed to 0.5 liters/sec, the \( P_{AW} \) would probably also decrease by about half. It must be emphasized that the airway resistance is much lower in patients who are breathing actively and spontaneously.

Some other important factors in airway resistance include the viscosity of the gas mixture, the length of the airways, the radius of the airways, and the type of flow. The resistance to flow through a tube is proportional to the viscosity of the gas and length of the tube and is inversely proportional to the radius to the fourth power. Whereas, the pressure required to maintain laminar flow is proportional to the velocity; when the flow becomes turbulent, the pressure required for flow is propor-
tional to the velocity squared. In other words, if doubling the air flow causes the flow to change from laminar to turbulent, the pressure required would increase four-fold. A mixture of 80% helium and 20% oxygen has about \( \frac{1}{3} \) the density of air and, therefore, is less likely to cause turbulence.

**Lung resistance**

Lung resistance \((R_L)\) can be calculated by dividing the pressure required to overcome the resistance of the lung \((P_L)\) by the volume \((V)\) to which the lung is inflated, thus:

\[
R_L = \frac{P_L}{V} = \frac{5 - 10 \text{ cm H}_2\text{O}}{1 \text{ liter}} = 5 - 10 \text{ cm H}_2\text{O/liter}
\]

Lung compliance \((C_L)\) which is the converse of the lung resistance will thus be:

\[
C_L = \frac{V}{P_L} = \frac{1 \text{ liter}}{5 - 10 \text{ cm H}_2\text{O}} = 0.1 - 0.2 \text{ liters/cm H}_2\text{O}
\]

\[
= 100 - 200 \text{ ml/cm H}_2\text{O}
\]

**Chest wall resistance**

Similarly, chest wall resistance \((R_{CW})\) can be calculated by dividing the pressure required to overcome the resistance of the chest wall \((P_{CW})\) by the volume \((V)\) of inflation:

\[
R_{CW} = \frac{P_{CW}}{V} = \frac{5 - 10 \text{ cm H}_2\text{O}}{1 \text{ liter}} = 5 - 10 \text{ cm H}_2\text{O/liter}
\]

Thus, chest wall compliance, the converse of chest wall resistance, will be:

\[
C_{CW} = \frac{V}{P_{CW}} = \frac{1 \text{ liter}}{5 - 10 \text{ cm H}_2\text{O}} = 0.1 - 0.2 \text{ L/cm H}_2\text{O}
\]

**Static resistance**

To differentiate between lung and chest wall resistance or compliance, it is necessary to know the intrapleural pressure changes on the ventilation. Since it is difficult to measure intrapleural pressure in most patients, we sometimes use the terms static resistance \((R_S)\) or static compliance \((C_S)\) to include the chest wall and lung resistance or compliance together. Thus, after the lungs are inflated and there is no airflow, the static resistance of the lungs plus chest wall would be:

\[
R_S = R_L + R_{CW} = 5 - 10 \text{ cm H}_2\text{O/L} + 5 - 10 \text{ cm H}_2\text{O/L} = 10 - 20 \text{ cm H}_2\text{O/L}
\]

\[
C_S = 1/R_S = 1/10 - 20 \text{ cm H}_2\text{O/L} = 0.05 - 0.1 \text{ L/cm H}_2\text{O}
\]

\[
= 50 - 100 \text{ ml/cm H}_2\text{O}
\]

**Effective resistance**

Although not strictly accurate, we sometimes use the terms total \((R_T)\) or effective resistance to include the sums of the resistance of the airway, lungs, and chest wall.

\[
R_T = R_{AW*} + R_L + R_{CW}
\]

In this instance, \(R_{AW*}\) is listed as pressure divided by volume (rather than flow), therefore:

\[
R_T = \frac{5 - 10 \text{ cm H}_2\text{O}}{1 \text{ liter}} + \frac{5 - 10 \text{ cm H}_2\text{O}}{1 \text{ liter}} + \frac{5 - 10 \text{ cm H}_2\text{O}}{1 \text{ liter}} = 15 - 30 \text{ cm H}_2\text{O/}
\]

\[
1 \text{ liter} = 33 - 66 \text{ ml/cm H}_2\text{O}
\]

Total compliance \((C_T)\) or "effective compliance" as it is sometimes called would be:

\[
C_T = 1/R_T = 1 \text{ liter}/5 - 30 \text{ cm H}_2\text{O} = 33 - 66 \text{ ml/cm H}_2\text{O}
\]

or an average of about 50 ml/cm H\(_{2}\)O.

**Causes of increased total resistance**

It is important to follow the total
resistance or compliance when the patient is on a ventilator. If the inflation pressure rises, it should indicate to the doctor, nurse, or therapist that there may be:

1. Partial obstruction somewhere in the system, such as a kinked tube, excess secretions, movement of the endotracheal tube into the right main stem bronchus, bronchospasm, and so on.
2. A pneumothorax.
3. Increasing lung stiffness.

Any pneumothorax or airway obstruction must be corrected as soon as possible. If these mechanical problems can be ruled out, the rising inflation pressure is relatively good evidence that the lung itself is becoming stiffer. For example, if a patient has a tidal volume of 800 ml with a system or inflation pressure of 30 cm H2O, and the system’s pressure rises to 35 cm H2O, with no apparent mechanical cause, one can estimate the change in lung resistance.

We assume that airway and chest wall resistance in the patients with ARDS are about 10 cm H2O/liter each. Thus, the lung resistance while the systems pressure was 30 cm H2O is 30 — (8+8) or 14 cm H2O/0.8 liters or 17.5 cm H2O/liter. When the systems pressure rises to 35 cm H2O, the lung resistance is 35 — (8+8) or 19 cm H2O/0.8 liter or 23.8 cm H2O/liter. Thus, the lung resistance is increased by[(23.8 — 17.5) ÷ 17.5] X 100% or 36%.

Since many ventilators now have the capability of providing an inspiratory hold of 0.5–1.0 sec or more, the static compliance or resistance of the lungs can be calculated directly very readily.

Although many assumptions are made in deriving these figures, they have provided us with some guidelines to evaluate changes in airway and lungs. It must also be emphasized that the changes or trends are far more important than the absolute numbers.

Gas concentrations

Inspired gases

The air we breathe at sea level has an average barometric pressure of 760 mmHg and contains approximately 20.93% oxygen and 0.04% carbon dioxide, with nitrogen making up almost the entire remainder. Thus, the partial pressure of O2 and CO2 in the air at sea level are 159 and 0.3 mmHg respectively.

When air enters the upper airway, it is warmed and saturated with water, thereby reducing the total partial pressure of the inhaled gases by 47 mmHg to about 713 mmHg. Thus, the inspired oxygen pressure (PiO2) in the trachea and bronchi falls to (713) (.2093) or 149 mmHg. If the patient is breathing 60% O2 (FiO2 = 0.6), the PiO2 in the trachea or bronchi will be (713) (0.6) or 428 mmHg.

Alveolar gases

As the water-saturated warmed air enters the alveoli, oxygen diffuses through the alveolar capillary membranes into the plasma and red blood cells, while carbon dioxide diffuses into the alveoli. On the average, for each ml of oxygen that leaves the alveolus, 0.8–1.0 ml of carbon dioxide enters it. This relationship is often referred to as the respiratory quotient (RQ) which refers to the ratio of the volume of CO2 excreted to the volume of oxygen taken up in the lungs.

The alveolar oxygen (PAO2) may then be calculated by the following formula:

\[ P_{A\text{O}_2} = P_{i\text{O}_2} - P_{A\text{CO}_2} \left( \frac{1 - F_{i\text{O}_2}}{RQ} \right) \]

The correcting factor \[ \left( \frac{1 - F_{i\text{O}_2}}{RQ} \right) \] is 1.2 if the RQ is 0.8 and is 1.0 if RQ is 1.0.

Since the alveolar PCO2 (PACO2) is generally equal to the arterial PCO2 (PaCO2), unless there is a significant increase in the alveolar dead space, the formula under normal circumstances (RQ=0.8), can be restated as:

\[ P_{A\text{CO}_2} = P_{i\text{CO}_2} - P_{A\text{CO}_2} (1.2) \]
If the $P_A CO_2$ is 40 mmHg,

\[
P_{\text{A O}_2} = 149 - 40 (1.2) = 149 - 48 = 101 \text{ mm Hg}
\]

If the RQ is 1.0, as frequently occurs in critically ill and injured patients, and the $P_A CO_2$ is 40 mmHg,

\[
P_{\text{A O}_2} = 149 - 40 (1.0) = 149 - 40 = 109 \text{ mm Hg}
\]

**Arterial gases**

Generally, we can assume that the average alveolar $P_{O_2}$ in patients breathing room air is about 105 mmHg. Because of the distance and interposing membranes between the alveoli and plasma, there is normally an alveolar arterial oxygen gradient or difference ($A-aDO_2$) of about 5–10 mmHg when breathing room air.

Thus, the arterial $P_{O_2}$ ($PaO_2$) in a healthy normal adult breathing will be about 95–100 mmHg with a hemoglobin oxygen saturation of about 97.0–97.4%. The arterial $PCO_2$ is generally the same as the alveolar $PCO_2$ (normally 35–45 mmHg). There is seldom a gradient for CO$_2$ between the alveolus and arterial blood unless there is a rather large increase in dead space.

The relationship between the oxygen saturation of the hemoglobin in the red blood cells, the plasma $P_{O_2}$, and the oxygen content of the blood is extremely important. This can be expressed by the following formula:

\[
O_2 \text{ Content (ml/100 ml blood)} = \frac{(Hb)(1.34)(Hb.02sat) + (pO_2)(0.003)}{100}
\]

In other words, each gram of hemoglobin when completely saturated with oxygen is capable of carrying 1.34 ml of oxygen. Thus, a patient with 15 grams% hemoglobin can carry 20.1 ml of oxygen on the hemoglobin in 100 ml of his blood. The amount or volume of oxygen dissolved in the plasma, represented by the $P_{O_2}$ is very small in comparison with the amount of oxygen carried by the hemoglobin.

In someone with an arterial $P_{O_2}$ of 100 mmHg, the volume of oxygen present in the plasma would be only (100) (0.003) or 0.3 ml/100 ml blood. Although the quantity of oxygen in the plasma (represented by the $P_{O_2}$) is very small, the $P_{O_2}$ determines the rate at which oxygen passes through the capillary walls and interstitial space into the tissue cells.

**Oxygen saturation and $P_{O_2}$**

Under circumstances of normal body temperature (37°C) and pH (7.40), there are certain standard relationships between the oxygen-hemoglobin saturation and plasma $P_{O_2}$.

<table>
<thead>
<tr>
<th>Hemoglobin Saturation (%)</th>
<th>Plasma $P_{O_2}$ (mmHg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>100.0</td>
<td>673</td>
</tr>
<tr>
<td>97.4</td>
<td>100</td>
</tr>
<tr>
<td>95</td>
<td>80</td>
</tr>
<tr>
<td>90</td>
<td>60</td>
</tr>
<tr>
<td>70</td>
<td>40</td>
</tr>
<tr>
<td>50</td>
<td>27</td>
</tr>
</tbody>
</table>

Thus, there is an almost linear relationship between oxygen saturation and the plasma $P_{O_2}$ when the saturation is 60% to 90%. However, as the oxygen saturation rises above 90%, the $P_{O_2}$ begins to rise somewhat faster; and once the saturation exceeds 97%, the $P_{O_2}$ rises very abruptly.

The effect of pH and temperature on the relationship between the oxygen saturation and the $P_{O_2}$ is often referred to as the Bohr effect.

For example, heat, acidosis or an increased 2.3-diphosphoglycerate (2.3-DPG) in the red blood cells will shift or move the oxygen-dissociation curve to the right, thereby increasing the $P_{O_2}$ present at a particular oxygen-hemoglobin saturation. In contrast, cold, alkalosis, and a decrease in the 2.3-DPG
(as may occur in stored blood and sepsis) shift the oxygen-dissociation curve to the left, thereby decreasing the PO₂ present at a particular oxygen-hemoglobin saturation.

As a general rule, a rise or fall of 0.01 in pH causes a 1% fall or rise in the PO₂. Thus, if the PO₂ is 100 mmHg at a pH of 7.40, a fall in pH to 7.30 will cause a rise in PO₂ to 110 mmHg, and a rise in pH to 7.50 will cause a fall in the PO₂ at 90 mmHg.

In relation to temperature, a rise or fall of 1°C causes a 5% rise or fall in the PO₂. Thus, given a PO₂ of 100 mmHg with a body temperature of 37°C, if the temperature rises to 38°C, the PO₂ will rise to 105 mmHg. Conversely, if body temperature falls to 36°C, the PO₂ will fall to 95 mmHg.

The compound present in greatest quantity, next to hemoglobin, in the red blood cell is 2,3 diphosphoglycerate (2,3 DPG). The more 2,3-DPG that is present, the more readily the hemoglobin gives up oxygen to the plasma and the higher the PO₂. The 2,3 DPG tends to rise in patients with anemia and those living at high altitudes. The effect of the 2,3-DPG is often correlated with the P₅₀ which represents the PO₂ present when the O₂ saturation is 50%. Thus, a decrease in 2,3-DPG causes a fall in the P₅₀.

**Oxygen consumption**

Under normal circumstances, only about a fourth (25%) of the oxygen present in the blood is picked up by the tissues as the blood passes through the capillaries in the systemic circulation. Thus, the arterial oxygen saturation is generally about 95-98% and the average oxygen saturation in the pulmonary artery is about 70-75%. If the cardiac output falls or the oxygen consumption rises, the arterio-venous (A-V) oxygen difference increases. This relationship, as mentioned previously, is often expressed by the Fick principle:

\[
\text{Cardiac Output} = \frac{O₂ \text{ Consumption}}{A-V O₂ \text{ difference}}
\]

**Acute respiratory failure**

Many names have been given to the adult respiratory distress syndrome (ARDS) that may develop in critically-ill or injured patients. Terms such as shock lung, traumatic wet lung, and septic lung refer to respiratory distress in association with certain well-defined clinical situations. Names such as congestive atelectasis and hemorrhagic at-
Electasis refer to pathologic changes noted by various investigators. It must be emphasized, however, that the lung is very limited in the ways it can respond to various insults and ultimately, the same pathophysiology appears to be present in all cases of ARDS.

Two of the more important historical studies of the acute respiratory distress syndromes include work by Burford and Burbank during World War II, when they described the pulmonary changes following thoracic trauma. They noted a vicious cycle of increasing pulmonary exudation, secretions, and atelectasis beginning in the area of the contused lung. It must be emphasized that once atelectasis develops in a particular portion of the lung, secretions and exudate tend to accumulate in that area, causing even more atelectasis. Therefore, if at all possible, atelectasis must be prevented right from the beginning; and secretions should be removed as rapidly as they develop.

Burke and co-workers from Boston later described a "high-output" respiratory failure syndrome in patients with peritonitis or ileus. These patients had a greatly increased minute ventilation; however, there was a decreased oxygen extraction from each liter of ventilated gas. It must be emphasized that patients with shock, sepsis, and trauma have a great need for increased ventilation. If ventilation is reduced or even normal in such patients, the decreased oxygen extraction per liter may result in dangerous hypoxia.

Some of the more frequently mentioned possible causes of acute respiratory insufficiency in adults include: ischemic pulmonary injury, fat embolism, vasoactive substances, fluid overload, massive transfusions, and aspiration.

Pulmonary ischemia
Pulmonary ischemia may cause respiratory insufficiency by interfering with local cellular metabolism, by reducing mucociliary clearance in the trachea and larger bronchi, and by decreasing surfactant production by the Type II granular pneumocytes. Since the half-life of surfactant is about 12-18 hours, it has been postulated that failure of continuing production of surfactant may account for the fact that respiratory distress often does not appear until 24-48 hours following shock or injury.

However, if the blood supply to one lung is completely occluded or clamped off during a period of shock or infection, the lung excluded from the circulation is relatively well preserved, whereas, the lung remaining in the circulation deteriorates rapidly. Thus, it appears that blood-borne chemicals and emboli are far more damaging than the pulmonary ischemia.

Fat embolism
The Classic Syndrome
The classic fat embolism syndrome is described as cerebral and respiratory dysfunction which develops approximately 24-72 hours after trauma, especially if long bone fractures are present. The syndrome was thought to be caused by fat from the marrow of the broken bones entering torn veins at the site of the fracture and then migrating to the lungs. It is now recognized that some of the fat emboli in the lung are chemically different from marrow fat, partially in their cholesterol content. Some of the fat emboli are now thought to come from the blood rather than marrow, and it is now recognized that significant fat emboli can develop without fractures. The catecholamine release that occurs following trauma apparently can greatly increase the quantity of fat, particularly triglycerides, in the blood.

Because the solubility of the fat is decreased following trauma, the fat tends to precipitate out as discrete particles or droplets. It takes 24-48 hours to convert the neutral fats (which are relatively innocuous) in the fat emboli to fatty acids (which may be very irritating), and the time required for this chemical change was thought to account
for the time-lag between the injury and the recognition of the pulmonary changes. The platelets trapped in the lungs with the fat emboli are a rich source of vasoactive materials which can cause further damage to the pulmonary capillaries.

There has been increasing attention to the role that intravascular coagulation may have in forming the fat emboli and various investigators have demonstrated an increased content of fibrin-split products together with reduction in platelets and other clotting factors. The thrombocytopenia in itself, may at least partially account for the petechiae which are occasionally found in the skin of the axilla or chest and in the conjunctivae in some patients with the fat embolism syndrome.

Subclinical fat embolism

In a prospective study that was performed on patients admitted to the orthopedic service with uncomplicated extremity fractures, it was found that the great majority of patients had pulmonary changes, as reflected by increased alveolar-arterial oxygen differences, and many had coagulation changes with particularly decreased platelet counts. Even more important, it was found that there was a relatively good correlation between the drop in the platelet count (presumably due to platelet trapping in the lung) and the increases in the alveolar arterial oxygen differences. This, together with the presence of fat in the urine of over 80% of the patients tested, suggests that even with uncomplicated extremity fractures, changes characteristic of fat embolism may occur.

Mammen found that, following experimental fractures in dogs, the fibrinogen and platelet concentrations in blood dropped precipitously during the first few minutes following fracture. However, within 24 hours, the fibrinogen concentration was back to normal. In addition, these animals, like the patients in our series, had progressively rising fibrinogen levels so that by the sixth to eighth day following injury, fibrinogen levels were often two to three times normal.

We have wondered if these increased fibrinogen concentrations may be part of the cause of the high incidence of venous thrombi and pulmonary emboli in patients with fractures.

Vasoactive substances

Damaged, necrotic or infected tissues and ischemic bowel may release a large number of chemicals which can adversely affect the function and structure of blood vessels, particularly capillaries, after they have been carried there by the blood stream. Some of the vasoactive substances which have been implicated in the development of the respiratory distress syndromes include catecholamines, serotonin, histamine, and vasoactive polypeptides such as bradykinin.

Fluid overload and congestive heart failure

Any tendency toward fluid overloading or congestive heart failure greatly increases the interstitial edema and congestion that can develop in patients with shock, sepsis, or trauma. Even without fluid overload, any increase in capillary permeability causes the lungs to greatly increase their water content thereby making them stiffer, more atelectatic, and less efficient in oxygenation of the blood.

Massive transfusions

Bank blood, as it is stored, contains increasing quantities of aggregated platelets, white blood cells, red blood cells, fibrin, and other particulate matter. If this material is not filtered out properly as it is administered to the patient, it can cause significant damage to the lung, both mechanically by obstructing small arterioles and capillaries, as well as chemically by releasing vasoactive amines.

Aspiration of gastric contents

Aspiration of gastric contents occurs far more frequently than is gen-
erally recognized clinically. Aspiration may occur during anesthetic induction or following trauma, particularly if the patient has been unconscious. This may also occur following the insertion of a naso-gastric tube, especially if it does not function well. Experiments by Dr. Carrasquilla and others have shown that when material is placed in the stomach of a dog restrained on its back or side with a poorly functioning naso-gastric tube, within 24-48 hours, that same material is almost invariably found in the lungs.

It is now clear that treatment of aspiration in order to be reasonably effective must be begun within 30 minutes. Unfortunately, the signs, symptoms and x-ray changes of aspiration may be delayed for up to 24-48 hours. Although there is much controversy in the literature about how aspiration should be treated, it is our own belief, based on our reading and experimental studies that, if one recognizes the aspiration as soon as it occurs, the immediate irrigation with an alkaline (NaHCO₃) solution and the administration of steroids, followed by positive pressure ventilation produces the best results.

Pathologic changes

Pulmonary capillary damage

The sequential changes in the lung that occur in the Adult Respiratory Distress Syndromes (ARDS) have been well described by James Wilson, from electron microscopic work he performed while at Duke University. The first abnormality noted is a swelling and disruption of the mitochondria in the pulmonary capillary endothelial cells. This appears to be at least partially related to release of lysosomal enzymes from polymorphonuclear leukocytes (PMN) which have accumulated in the pulmonary capillaries. The capillary endothelial cells then begin to swell and retract from adjoining cells leaving progressively enlarging intercellular spaces.

Interstitial edema

The second phase consists of increasing interstitial edema as fluid moves from the capillary space into the interstitial space through the defects between the pulmonary capillary endothelial cells. This increasing interstitial edema makes the lung stiffer and more difficult to ventilate, reduces oxygen diffusion from the alveoli into the capillaries, and causes bronchiolar mucosal swelling which further increases the tendency toward atelectasis.

Congestive atelectasis

The third phase is one of increasing congestive atelectasis, and it is at this state that the respiratory problem is usually first recognized. The pulmonary capillaries become progressively more engorged and congested, and there is an increasingly severe diffuse microatelectasis throughout the lungs. The disruption of the pulmonary capillary endothelium may become so great at this stage that even red blood cells can migrate into the interstitial space, producing an appearance of peribronchial hemorrhage.

Alveolar disruption and edema

In the fourth phase, increasing damage to alveolar cells and disruption of the alveolar lining are recognized and fluid begins to move from the interstitial space into the alveoli. The proteins in this fluid, particularly fibrinogen, may inactivate the surfactant present, further increasing the tendency toward atelectasis. If the patient survives long enough, the protein in the alveoli may precipitate along the alveoli as a hyaline-like membrane.

Pneumonitis

Superimposed upon all these processes is a varying amount of inflammation due to local infection. Even if infection or inflammation is not present initially, the increasing atelectasis and alveolar fluid seem to offer an ideal milieu for bacterial growth and invasion.

Phases of the acute respiratory insufficiency syndromes

The development of respiratory in-
sufficiency following injury has been divided into four phases. In an attempt to further clarify the progression of this entity before and after clinical recognition, we have elaborated on the characteristics of each phase somewhat.

Phase I (Injury and resuscitation).

This phase is characterized by altered tissue perfusion and metabolism. Unless there is a problem with CNS depression or damage to the airway, chest wall, or lungs, there is generally a persistent moderate respiratory alkalosis due to hyperventilation (PCO$_2$=30–35 mmHg). The A-aDO$_2$ on room air is generally only slightly elevated or in the range of 20–30 mmHg. The lungs are frequently clear on physical examination except for a few basilar rales or rhonchi, and x-rays generally are normal or show only minimal congestion or atelectasis.

Phase II (Stabilization and early respiratory distress).

In this phase, the hyperventilation continues and may be slightly increased with a PCO$_2$ often in the range of 25–35 mmHg. The alveolar arterial oxygen differences on room air may increase to approximately 35–40 mmHg, but there is little or no evidence of any respiratory problem. At this time, x-rays may again be normal, or there may be minimal diffuse infiltrates, compatible with multiple small areas of atelectasis and/or pulmonary congestion.

Phase III (Mild-moderate respiratory distress).

During this phase, it becomes increasingly apparent clinically that the patient has a respiratory problem. Although it often appears as if the problem has developed rather suddenly, serial blood gas determinations would reveal that the problem had indeed been developing progressively and was only recognized suddenly.

The patient may hyperventilate even more with a further drop in the PCO$_2$, and the PaO$_2$ may begin to fall to about 60 mmHg. The A-aDO$_2$ is often 55 mmHg or more, the shunt often exceeds 40%, and increasing pulmonary edema and progressive confluence of the previously scattered diffuse infiltrates are noted on the x-ray.

Phase IV (Terminal respiratory failure).

This phase is often characterized by a gradual rise in the PCO$_2$ towards normal and then finally, if the patient lives long enough, to levels above normal. Carbon dioxide is normally excreted very easily by the lungs at a rate which correlates quite closely to the alveolar ventilation. In spite of an increased alveolar ventilation, when the PCO$_2$ begins to rise in ARDS, the lungs are severely and often irreversibly damaged.

At this stage, increasing metabolic acidosis eventually may also be noted. These pre-mortem patients generally cannot tolerate room air, the physiologic shunt often exceeds 50 or 60%, and the lungs may become almost completely opaque on the chest x-ray.

Diagnosis

Clinical anticipation

The diagnosis of the various respiratory distress syndromes in their earliest phases is extremely important. Therefore, anticipation of the problem in certain clinical situations is probably the most effective method for diagnosing these problems early—when treatment is most apt to be effective.

For example, in a study of patients with flail chest at Detroit General Hospital, it was found that some of the more frequent clinical factors associated with death in these patients were: the presence of shock, injury to three or more organs or large bones, more than seven rib fractures, head injury, previous pulmonary disease, and an age factor of 65 or more years. If two or more of these were present in an individual, particularly shock or injuries of three or more large bones or organs, the mortality rate exceeded 70% when ventilatory assistance was delayed for more than 48 hours.

Physical examination

The physical examination of pa-
Patients with early or impending respiratory failure may be remarkably unrevealing. In the earliest phases, the only abnormality noted may be some tachypnea. This is a relatively non-specific sign; but it may be the only evidence of developing shock, sepsis, or respiratory failure, and its cause must always be sought after diligently. Rales may develop relatively early, but sometimes do not develop until rather late in the syndrome. By the time the classic signs of respiratory failure, such as use of the accessory muscles of respiration, flaring of the alae nasae and restlessness appear, respiratory failure is usually far advanced and extremely difficult to reverse.

X-ray examination

The radiographic features of the acute respiratory distress syndrome are relatively non-specific and generally are not present until the process is rather far advanced. The earliest changes usually consist of a patchy, bilateral alveolar infiltration which is frequently confused with pulmonary edema. Later, these diffuse patchy infiltrates become confluent and eventually take on the appearance of consolidation. If a large round infiltrate is present in one area of the lung, especially posteriorly or in a lower lobe, one must suspect that aspiration may have contributed to the problem.

Blood gas studies

It is extremely difficult to judge a patient's blood gases by looking at him, until it is too late. Relying on the patient's color, particularly if his hemoglobin is less than 10.0 Gm%, is an extremely poor practice because there must be at least 5 Gm% of reduced hemoglobin at the capillary level before a patient begins to look cyanotic, and venous oxygen saturation seldom falls below 35%.

Time and time again, we find patients who clinically appear to have developed respiratory failure rather suddenly. However, on retrospective analysis of blood gases, it can be clearly shown that the process has been developing and progressing for at least 24-48 hours. Under most circumstances when respiratory failure “suddenly” appears, it is probable that it was already there and increasing for some time. This “sudden” aspect of ARDS (late diagnosis) is one of its most unfortunate and frequent features.

In looking at the blood gases, the PCO₂ (at least in the initial phases of respiratory failure) is generally the best indicator of the adequacy of alveolar ventilation. In most of these patients, the arterial PCO₂ is in the range of 25–35 mmHg, reflecting the hyperventilation which is so characteristic of the acute respiratory insufficiency syndromes.

One can often gain some impression of the acuteness of the respiratory changes by noting the effects of the PCO₂ on the pH. For each 1 mmHg acute rise or fall in the PCO₂, the pH decreases or increases approximately by about 0.01. This assumes that the plasma bicarbonate levels remain relatively constant, as they often will for up to one or two hours because the plasma bicarbonate can change only about 1/100 to 1/200 as fast at the PCO₂.

Thus, if a patient with a pH of 7.40, PCO₂ of 40 mmHg, and plasma bicarbonate of 24 mEq/L suddenly began to hyperventilate and reduced his PCO₂ to 32 mmHg within a few minutes, the plasma bicarbonate would change only minimally and the pH would rise to about 7.48.

On the other hand, if the patient suddenly began to breathe slowly and shallowly and his PCO₂ change had been present for more than a few hours, the plasma bicarbonate would have a chance to compensate somewhat. In addition, the pH change from normal will be less than what might be expected on the basis of the PCO₂ alteration alone. For example, if the PCO₂ is 25 mmHg and the pH is 7.45, one can generally assume that low PCO₂ has been present for some time and that the plasma bicarbonate has fallen somewhat to par.
tially compensate for the respiratory alkalosis.

Table 5
Effects of PCO$_2$ on the pH

<table>
<thead>
<tr>
<th>PCO$_2$ (mm Hg)</th>
<th>pH</th>
<th>Plasma-HCO$_3$ (mEq/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td>60</td>
<td>7.22</td>
<td>24</td>
</tr>
<tr>
<td>50</td>
<td>7.30</td>
<td>24</td>
</tr>
<tr>
<td>40</td>
<td>7.40</td>
<td>24</td>
</tr>
<tr>
<td>30</td>
<td>7.53</td>
<td>24</td>
</tr>
</tbody>
</table>

The arterial PO$_2$ is generally followed very closely in patients with impending or established respiratory failure. Evaluated properly, it can provide important information on lung function and the adequacy of oxygen supply to the tissues. There are, however, several factors which must be kept in mind when interpreting the arterial PO$_2$.

1. The concentration of oxygen in the inhaled gases (FiO$_2$).
2. The effects of pH, temperature, and RBC 2,3-DPG concentrations.
3. Age.
4. The PCO$_2$.

Unfortunately, the fraction of oxygen in the inspired gases (FiO$_2$) is often not considered adequately in evaluating the PaO$_2$. The approximate PO$_2$ that might be expected in normal patients with various amounts of oxygen are listed.

Table 6
Effects of FiO$_2$ on the PaO$_2$ in normal patients

<table>
<thead>
<tr>
<th>FiO$_2$</th>
<th>Expected* PaO$_2$ (mmHg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.21 (Room Air)</td>
<td>100</td>
</tr>
<tr>
<td>0.4</td>
<td>236</td>
</tr>
<tr>
<td>0.6</td>
<td>378</td>
</tr>
<tr>
<td>0.8</td>
<td>520</td>
</tr>
<tr>
<td>1.0</td>
<td>663</td>
</tr>
</tbody>
</table>

*Assuming an A-aDO$_2$ of 5-10 mmHg and PCO$_2$ of 40 mmHg

In the patient with a pulmonary problem, the PaO$_2$ will be quite a bit lower than expected on room air but may be near expected values at a high FiO$_2$. Thus, a patient with a severe diffusion problem and no other abnormality might have a PaO$_2$ of only 50 mmHg on room air but a PaO$_2$ of 500 while breathing 100% O$_2$.

If the patient’s primary problem is increased physiologic shunting in the lung due to ventilation-perfusion imbalance, the PaO$_2$ will increase only moderately with a high FiO$_2$. Thus, a patient with a very large physiologic shunt might have a PaO$_2$ of 50 mmHg on room air and a PaO$_2$ of only 100 mmHg on 100% O$_2$.

The position of the oxygen dissociation curve must always be considered when evaluating the PaO$_2$. The most common error is failure to correct for the moderate to severe respiratory alkalosis that is found in many of these patients. For example, given that the patient has a PaO$_2$ of 68 mmHg at a pH of 7.55 and if his pH were reduced to 7.40, then his PaO$_2$ (even if there were no change in the PaCO$_2$ or oxygen saturation) should rise to 78 mmHg.

Even in healthy individuals with no apparent respiratory problems, there are pulmonary changes that occur with advancing age which cause a fall in the PaO$_2$. On the average, one can expect a fall in the PaO$_2$ of about 3-4 mmHg for each decade after the patient reaches 20-30 years of age. Thus, an otherwise normal 20-year-old patient with a PaO$_2$ of about 90-95 mmHg on room air would be expected to have a PaO$_2$ of about 70-75 mmHg at 80 years of age.

The level of the PCO$_2$ may change the PO$_2$ by (1) altering the pH (which has already been discussed), and (2) by altering the alveolar PO$_2$ (PaO$_2$). It is not unusual as acute respiratory insufficiency develops to see patients with blood gas values of PaCO$_2$ of 25-35 mmHg, PaO$_2$ of 65-75 mmHg, a pH of 7.45-7.55, and O$_2$ saturation of 92-95%. Most physicians looking at such blood gas values would not consider them to be a cause for alarm.
However, it is often forgotten that if the PaCO₂ falls because of hyper-
ventilation, the PaO₂ should rise by an almost equivalent amount. One method
of evaluating this relationship between the PO₂ and PCO₂ is to measure or
estimate the A-aDO₂, which often re-

dicts much more serious changes than
might be appreciated from either the
PO₂ or PCO₂ alone.

The A-aDO₂ in a patient who is
breathing room air can be estimated
rapidly and relatively accurately by add-
ing the arterial PO₂ and PCO₂ together
and subtracting the sum from 145. Thus, the
patients described earlier having an
average PCO₂ of 30 and PO₂ of 70
mmHg would have an A-aDO₂ of about
45 mmHg. This is significantly above
the 10-20 mmHg which we consider to be
within the normal range in a young
adult.

Interestingly, if the patient previ-
ously had normal lungs and has a rel-
atively normal cardiac output, the
amount of shunting in his lungs can be
estimated by subtracting 15 from the
A-aDO₂ on room air. Thus, this patient,
under such circumstances, would have
a pulmonary shunt equivalent to about
30% of his cardiac output.

Though the A-aDO₂ has received
much attention from a number of in-
vestigators, many prefer to work with
the value obtained while the patient is
breathing 100% O₂. The alveolar PO₂
(PA0₂) expected at sea level while the
patient is breathing 100% O₂ is equal
to 760 mmHg minus water vapor pres-
sure (47 mmHg) and the PCO₂. Thus,
if the PCO₂ were 40 mmHg, the PAO₂
would be about 723 mmHg. If one ob-
tains an arterial sample after the
patient has been breathing 100% O₂
(FI0₂ = 1.0) for 15-20 minutes, one
can simply apply the formula for cal-
culating the PAO₂ and subtract the
measured PAO₂ from it.

For example, if the PAO₂ is 300
mmHg on an FI0₂ of 1.0, the A-aDO₂
on 100% O₂ or P(A-aDO₂) 1.0 will be
373 mmHg. Some investigators feel that
P(A-aDO₂) 1.0 of more than 300 mmHg
is cause for concern and indicates sig-
nificant respiratory insufficiency. Most
of our patients with any significant res-
piratory problems have had a P(A-
aDO₂) 1.0 much greater than this.

Although alveolar arterial oxygen
differences on room air are relatively
easy to obtain and estimate, we have
found that the amount of physiologic
shunting in the lungs (perhaps better
referred to as pulmonary-venous admix-
ture) is the most accurate test for diag-
nosing frank or impending respiratory
failure.24 As mentioned previously, the
shunt refers to the amount of blood pass-
ing through the lungs without being
oxygenated to the value theoretically
possible at the particular FI0₂ being
delivered (usually FI0₂ = 1.0). Nor-
maUy, the amount of venous-arterial admix-
ture is about 3-8% of the cardiac
output; and this small amount of shunt-
ing is largely due to some bronchial veins draining into pulmonary veins and
the drainage of some of the small intra-
myocardial veins into the left side of the
heart.

Physiologic shunting is somewhat
harder to measure than the A-aDO₂ be-
cause it requires administering 100%
oxygen for 20 minutes and then drawing
arterial and mixed venous samples.
Mixed venous samples from the pul-
monary artery are preferable to those
obtained from central venous catheters;
however, the central venous blood does
give a reasonable estimate of the amount
of shunting present, unless the cardiac
output is quite high.

Although an FI0₂ of 1.0 is gen-
erally used when obtaining the Qs/Q,
some investigators have found that the
high FI0₂ in itself may cause increased
shunting, and they believe that the shunt
present when the FI0₂ is 0.6 is a better
indicator of the status of the lung.25
We have found that if the physiologic
shunting of the lung exceeds 40% and
the patient has acute tissue damage or
necrosis due to shock, sepsis or severe
trauma, he should be put on a respi-
rator and treated aggressively with high
tidal volumes, and possibly, PEEP. If
such patients are not given ventilatory support, many of them will die.

The amount of physiologic shunting in the lung \( QS/QT \) can be easily calculated from a modification of Berggren's formula, \( QS/QT = MOC - AOC + MOC - VOC \). Thus, if the maximum oxygen content \( MOC \) that can be present in the blood with 100.0% saturation and a \( \text{PaO}_2 \) of 667 mmHg is 20 volumes%, the venous oxygen content \( VOC \) is 15 volumes%, the arterial oxygen content \( AOC \) is 19 volumes%, and the shunt is approximately 0.20 (20%). One can also estimate the amount of shunting in the lung from the arterial blood alone, using an assumption that the AV oxygen difference is approximately 5 volumes%.

A number of tables have been constructed to relate the A-aDO\(_2\) on 100% O\(_2\) with the amount of physiologic shunting present in the lung. However, these tables are calculated on the assumption that 15 gms of hemoglobin are present, and that the oxygen consumption is approximately 250 ml/min and the cardiac output is 5 L/min. If all of these factors are not present, however, estimations from standard tables using the A-aDO\(_2\) on 100% O\(_2\) may be seriously in error. For example, if the \( \text{PaO}_2 \) were 100 mmHg on 100% O\(_2\), the A-aDO\(_2\) would be about 560 mmHg, the shunt in a patient with a cardiac output of 5 liters/min. would be 31% (which we usually do not consider to be life-threatening). However, in a patient with a cardiac output of 10 liters/min., this A-aDO\(_2\) would be associated with a shunt of 47%, which could indeed be life-threatening if not treated aggressively.

It is important to note when looking at the \( \text{PO}_2 \), A-aDO\(_2\) or shunt that a low cardiac output with a high AV oxygen difference may produce a low \( \text{PO}_2 \) with a relatively mild-moderate amount of pulmonary dysfunction. Thus, the arterial \( \text{PO}_2 \) is also controlled to a certain extent by the cardiac output and the \( \text{PO}_2 \) in the venous blood as it gets to the lungs. Although a patient with a high cardiac output and normal hemoglobin can generally tolerate a moderately low \( \text{PO}_2 \) fairly well, similar blood gases in a patient with severe anemia or low cardiac output tend to be tolerated very poorly.

**Nursing care**

Nursing care for patients who may develop any type of respiratory complication should include: stimulation of the patient to cough and take deep breaths, frequent position changes, elevation of the head and chest as much as possible, and chest physiotherapy. In order to institute early preventative measures such as these, the nurse must have a strong index of suspicion for patients who are prime candidates to develop complications.

The cough is particularly important and should be taught to patients preoperatively and as early after trauma as possible. A cough can generally be divided into three phases: the inhalation phase, the bearing-down phase, and the blast phase. If the patient has severe pain, he is often unable to inhale and bear down properly, and therefore, cannot produce an effective cough.

The bearing-down phase is particularly important because, as some feel, it may help to “squeeze” material out of the alveoli and smaller bronchioles into the bronchi where the blast of air may carry the material out of the lungs. Therefore, judicious use of pain medication is required. Enough should be given to facilitate coughing and proper breathing, but if too much is given it may depress the cough reflex and ventilation. Inspiratory effort also may be improved by using an incentive spirometer, blow bottles, or a number of other devices.

An effective cough cannot be readily achieved with an endotracheal tube or with a tracheostomy present. This is because of the patient's inability to close the glottis which results in increased intrathoracic pressure. Consequently, it is not unusual for “tubed” patients to have many rales or rhonchi with little or no mucus being recovered.
on aspiration of the trachea and major bronchi.

In such patients, a more effective cough may be obtained by temporarily occluding the tube after a deep inspiration. As expiration begins against the blockage, an effect similar to the normal bearing down may be produced. This is then followed by the blast phase when the airway is opened. We believe that patients should be turned frequently, at least every half-hour to hour. Thus, at any one time, at least one-third of the patients in the intensive care unit should be on one or the other side or sitting relatively upright. Elevation of the head and chest decreases the pressure on the diaphragm produced by the viscera; and we believe this produces the best overall ventilation-perfusion ratios throughout the lung.

Chest physiotherapy, which is an important adjunct to our regimen, is beginning to become increasingly important in many hospitals in the United States. Maneuvers such as vibration and/or careful clapping on the chest, with the patient in various positions, can be helpful in removing mucous plugs and for treating or preventing atelectasis.

General measures

Some of the general measures which may be performed to help reduce the tendency toward pulmonary complications in any sick, injured, or postoperative patient include: early recognition and control of infection, reduction of abdominal distention, reduction of pain, reduction of oxygen demand, and in selected instances, thoracentesis.

Control of infection is particularly important in a patient who has any tendency towards ARDS. At this time, the patients that we lose from respiratory failure are primarily those in whom infection, particularly peritonitis, cannot be adequately controlled.

Abdominal distention must be prevented and vigorously treated if it develops, by naso-gastric suction. Once swallowed air reaches the small bowel, and ileus develops, it becomes difficult or impossible to remove this air. Therefore, early and persistent decompression of the stomach is important.

It must be emphasized that the patency of the naso-gastric tube must be frequently checked and is chiefly the responsibility of the nurse. If the nasogastric tube is not functioning properly, its presence is harmful for several reasons. With the patient lying flat, gastric contents can run along the tube to the pharynx and larynx where they subsequently can be aspirated into the lungs. Secondly, any tube in the pharynx or larynx irritates the upper airway, not only producing increased secretions, but also reducing the effectiveness of and tendency to cough. In patients who require prolonged gastrointestinal intubation and who have pre-existing respiratory disease, it may be wiser to insert a gastrostomy tube rather than rely on prolonged nasogastric intubation.

If ascites is present, the careful removal of excessive intraperitoneal fluid may be of great help. Proper attention must be paid to the blood volume to ensure that hypovolemia or hypotension do not develop following paracentesis.

Pain should be reduced to allow the patient to cough properly, but medication should not be given in doses high enough to depress ventilation and the cough reflex. If the patient has an unusually high temperature or is very restless, antipyretics and careful sedation may help to reduce excessive oxygen demands. However, any sedation is dangerous in these patients, unless the ventilation is either controlled or watched very carefully. The nurse, therefore, must be acutely aware of the effects of analgesic or sedatives administered to any sick, injured, or postoperative patient. Restlessness in such patients should be considered as due to hypoxia until proven otherwise.

Insertion of any needles, including subclavian vein catheters, in these patients must be done very cautiously. There are a certain number of patients (particularly those with peritonitis)
who may have increased pleural fluid. One might suspect this condition upon reading an upright chest x-ray or by observing increased resistance to ventilation. If increased pleural fluid is recognized in a patient requiring high ventilatory pressures, one should remove the fluid very cautiously, preferably with a plastic needle, so as not to damage the lung. Many of these patients will require ventilatory assistance, and any damage to the lung greatly increases the tendency to develop a tension pneumothorax later, particularly if high ventilatory pressures are required.

**Fluid therapy**

Because much of the pathophysiologic change occurring in ARDS is due to excess lung water, particularly in the pulmonary interstitial fluid space, fluid therapy in these patients is very critical. Our general approach, once the patient has been properly resuscitated, is to gradually dehydrate them as much as possible. But, careful attention must be paid to maintaining adequate tissue perfusion and urine output. Sudden, abrupt dehydration can very easily cause severe hypovolemia and oliguric renal failure. The object of dehydration is to pull fluid from the interstitial fluid space slowly enough so that there is only a minimal decrease in the intravascular volume.

Many patients can be dehydrated and given large amounts of fluid at the same time if there is assurance that the measured output is equal to or slightly greater than the intake every hour. The insensible water loss in most adults averages about 30-40 ml/hour. If one is careful to maintain an adequate urine output with diuretics but keeps the fluid intake equal to or slightly less than the measured fluid output (including urine output), the patient will be gradually dehydrated by approximately one liter a day.

Dehydration in septic patients is often very difficult or impossible to accomplish. These patients often require large amounts of fluid to maintain an adequate intravascular volume and any tendency to restrict intake relative to output can quickly cause hypotension or oliguria, which in turn, may be extremely difficult to reverse.

One method for determining the effectiveness of the dehydration efforts is to follow the serum osmolarity. In most instances, however, we can only raise the serum osmolarity from a normal of about 270-290 to about 320 mOsm/L.

There is much controversy about the use of colloids in these patients. If pulmonary capillary permeability were normal, an increased colloid osmotic pressure might help to draw fluid from the interstitial space into the vascular space. Because of the increased capillary permeability found in these patients, it appears that any infused protein, particularly albumin, may quickly enter the interstitial fluid space where it can then draw more fluid to it. As a consequence, we currently use colloids, particularly albumin, very cautiously in ARDS unless there is severe hypoproteinemia.

In the past, we were usually content to keep the hemoglobin level in the blood around 10 Gm% feeling that this level provided the best overall cardiac output and oxygen transport. However, on reviewing our data it appears that our patients have done much better with a higher hemoglobin, preferably 12.5-14.0 gm%. The mortality rate and the amount of physiologic shunting in the lung decreased significantly at these hemoglobin levels in relation to similar patients with a hemoglobin of less than 10 gm%.

**Drugs**

Bronchodilators should be given if there is any evidence or history of broncho-spasm or increased airway resistance, since the airway resistance often has to be raised to more than four times normal before it becomes clinically evident. Digitalis and diuretics should be used if there is any evidence of heart failure; diuretics may also be required to help dehydrate patients with ARDS.
and no evidence of CHF. If there is a moderate to severe metabolic acidosis, sodium bicarbonate should be given, but very cautiously so as not to overload the patient with sodium or water.

If there has been any evidence of significant smoke inhalation or aspiration of gastric contents, we believe that steroids should be given in doses of at least 50–100 mg of hydrocortisone every 4-6 hours. It must be emphasized that the clinical and x-ray signs of massive smoke inhalation or aspiration are often inapparent or absent for the first 24-48 hours, and one can easily be lulled into a false sense of security by the absence of evidence of pulmonary damage during that time.

Although there is much controversy about the value of massive steroids in these patients, we believe that if the patient with respiratory insufficiency is not responding appropriately and rapidly to vigorous therapy (including ventilatory assistance with PEEP and dehydration), massive steroids should be given. Experimentally, the greatest benefits noted with massive steroids appear to be their ability to stabilize lysosomal and capillary membranes.

Some of the benefits of massive steroids on the lung noted in experimental animals by James Wilson include platelet preservation, preservation of polymorphonuclear leukocyte (PMN) membranes, preservation of the ability of PMN’s to form pseudopods, decreased diapedesis of red blood cells, decreased endothelial cell swelling, decreased epithelial Type I cell swelling, and decreased destruction of the mitochondria in the alveolar Type II pneumocytes (which make surfactant). Other possible benefits of massive steroids reported by investigators include “normalizing” of cardiac function in clinical shock and improvement of cell metabolism by increasing gluconeogenesis in experimental animals.

To be effective, massive steroids should be given as early as possible. In the terminal phases of shock or ARDS, they have little or no value. We generally give either methylprednisolone succinate (Solu-medrol®) 30 mg/kg or dexamethasone phosphate (Decadron®) 6 mg/kg. Two doses are given IV over a 10-15 minute period, 4-6 hours apart with careful objective studies (particularly of the blood gases and inflation pressures), before and after each dose. If any improvement is noted, these doses are repeated as needed for up to 24-48 hours.

**Respiratory therapy**

Oxygen, aerosolization, nebulization, and intermittent positive pressure breathing (IPPB) all may be of value if used judiciously in these patients. When ventilation is adequate but the arterial PO₂ is below 70-80 mmHg, we will give up to 40% oxygen. However, if more than 40% oxygen is needed to keep the PO₂ above 60-70 mmHg in the patient with previously normal blood gases, we generally place him on a ventilator regardless of how well he is ventilating.

Proper aerosolization and nebulization may help reduce insensible water loss and decrease the viscosity of mucoid material in the bronchi, making it easier for the patient to cough up his tracheobronchial secretions. IPPB may be very helpful if it stimulates the patient to breathe and cough properly or brings appropriate moisture or medication into the tracheobronchial tree. However, if it accomplishes none of these, it may actually cause impaired pulmonary function. It is now well recognized that routine use of IPPB postoperatively does not reduce the incidence of pulmonary complications. However, any technique, ranging from “blow bottles” to “blowing up gloves,” which causes the patient to breathe and cough better, is of great value. The incentive spirometer, if used properly, may be particularly beneficial.

**Airway**

Maintenance of the airway may be accomplished in many ways. Positioning of the patient is sometimes all that is needed. Positioning may be particularly
important in the emergency room situations where we find patients with severe CNS depression. In such cases, the tongue tends to fall back and occlude the pharynx when the patient is lying on his back. If no other injuries are present, this airway obstruction can be corrected simply by turning the patient on his side with his face down.

If this technique is not successful, an oral or nasopharyngeal airway may be used to maintain the airway. Excessive secretions in the lower airways may necessitate naso-tracheal suction and bronchoscopy. If these maneuvers are inadequate or have to be repeated with excessive frequency, an endotracheal tube or tracheostomy may be required.

A tracheostomy is rarely indicated in the initial management of acute respiratory failure. However, if there is evidence of damage to the larynx or trachea or if there is excessive bleeding in the mouth or pharynx, it may be difficult or dangerous to insert an endotracheal tube. If the patient has excessive secretions that are difficult to remove or if the patient will require prolonged ventilatory support, a tracheostomy is generally indicated.

In a few centers, some patients have been kept on ventilators for prolonged periods of time, 4-8 weeks or longer, with endotracheal tubes. However, if a special protocol has not been established to accomplish this procedure and the management of these patients is not supervised by someone with particular interest and expertise in this area, such efforts are often unsuccessful. Even in the most experienced hands, prolonged endotracheal intubation may be impossible to manage if the patient has excessive secretions.

**Ventilator assistance**

If ventilatory assistance in critically-ill and injured patients is delayed until there is obvious clinical evidence of respiratory failure, many of these patients will die.

**Clinical indications**

There are several clinical situations in which early ventilator assistance may be of benefit for patients with severe trauma, sepsis or shock (even with relatively normal ventilation and blood gases). These include: flail chest, coma, generalized peritonitis (especially if it involves the subdiaphragmatic areas), and previous severe pulmonary disease. Massive smoke inhalation or aspiration of gastric contents also may be indicative of early ventilator assistance even if no other problems are present.

**Laboratory indications**

Some of the laboratory indications for ventilator assistance might include: (1) an arterial PO$_2$ less than 55 or 60 mmHg on room air, particularly if the blood gases do not improve adequately with 40% oxygen; (2) an arterial PCO$_2$ greater than 45-55 mmHg in patients with previously normal lung function and without metabolic alkalois; (3) an alveolar arterial oxygen difference on room air greater than 55 mmHg; and (4) a physiologic shunt in the lung of 40% or more.

Other indications which have been described include: greatly increased respiratory effort, greatly increased dead space, greatly reduced vital capacity, prolonged high respiratory rates, and certain x-ray changes. Isolated laboratory values in themselves are not nearly as valuable as the trend that the patient’s condition or these numbers are taking. If the patient’s general condition or any of these values are progressively deteriorating (particularly if underlying sepsis has not been adequately corrected), the patient should be put on a ventilator.

**Ordering ventilatory assistance**

When ordering ventilatory assistance, it is extremely important to understand that the patient is being put on the ventilator primarily for ventilation, that is, to expand the alveoli optimally; obtaining normal blood gases is only a very secondary consideration.

Not infrequently, we see patients with ARDS who have relatively normal
blood gases, despite low tidal volumes. This is because these patients are given oxygen. When the physician in charge is asked to use a higher tidal volume, not infrequently, he is reluctant to do so. As far as he is concerned, the patient is doing all right because his blood gases are normal.

There is, however, a lot of evidence that such patients need high tidal volumes (much higher than those needed to produce adequate blood gases) in order to provide optimal alveolar distention and reverse the tendency toward atelectasis. We prefer volume-cycled ventilators because they will more reliably ventilate the alveoli. Pressure-cycled ventilators can be used if they are all that is available. However, the patient must be kept under close observation to ensure that he is getting adequate tidal and minute volumes.

Serial blood gas analyses are necessary to determine which ventilator settings and FiO₂ are optimal.

We generally use the highest tidal volume possible, in the range of 12–15 ml/kg. However, we prefer not to use ventilation pressures greater than 35–40 cm of water because of the increased risk of causing a pneumothorax. While the patient is on the ventilator, it is very important to watch the inflation or system pressure. If this pressure progressively rises, it indicates obstruction to the free inflow of gases from the respirator. At this point, one must assume that a mechanical problem is present, which can be caused by: a kinking or malpositioning of the endotracheal tube or tracheostomy, excessive secretions or, on occasion, a pneumothorax. It has been suggested that “prophylactic” chest tubes should be inserted if the inflation pressure exceeds 40 cm H₂O for more than a few hours.

If the rise in inflation pressure is gradual and the above problems can be ruled out, the lung is probably becoming stiffer due to increasing congestive atelectasis and interstitial edema. One can use system pressures to calculate or estimate the so called “effective pulmonary compliance”, which is equal to the tidal volume divided by the peak inspiratory pressure. This provides an objective measurement of the progression of the ARDS.

After the initial resuscitation, we generally use the lowest FiO₂ possible, preferably 0.4 or less, to maintain a PO₂ of at least 70 mmHg. Although there is minimal good clinical data on the effect of an FiO₂ less than 1.0, we feel that prolonged administration of an FiO₂ greater than 0.4 may, in itself, cause damage to the lung.

We prefer to keep the respiratory rates relatively low, about 10–14 times/min because the combination of a fast respiratory rate coupled with high tidal volumes may cause a severe respiratory alkalosis. If the respiratory rate cannot be controlled and severe respiratory alkalosis does develop, rather than reduce the tidal volume, we will add up to 300 ml dead space (50–100 ml at a time) to keep the PCO₂ in the range of 30–35 mmHg.

We “sigh” the patients 6–12 times/hour using a sighing volume of approximately 1½ times the tidal volume, but not allowing the inflation pressure to exceed 50–60 cm H₂O. Nebulization and humidification are kept at a maximum.

Positive end-expiratory pressure (PEEP) is added if the pulmonary problem does not rapidly improve. Although there has been increased enthusiasm for using PEEP in patients with ARDS, it should be emphasized that PEEP is not always beneficial, particularly if it exceeds 8 cm H₂O. If the functional residual capacity is low and blood volume is adequate, PEEP may greatly improve the FRC and pulmonary function.

However, PEEP does retard venous return and may cause an abrupt fall in blood pressure and cardiac output if the patient is hypovolemic. Consequently, vital signs, skin perfusion, and urine output must be monitored closely in any patient on PEEP. If tissue perfusion is impaired after PEEP is applied and does not improve after appropriate administration of additional fluids, the
PEEP should be discontinued, at least until the patient’s hemodynamic status is improved.

In some instances, the PEEP, rather than expanding atelectatic alveoli, may overexpand relatively normal alveoli. This is particularly apt to occur in patients with pre-existing obstructive lung disease. Under such circumstances, one may note an increase in the dead space in the lungs, and occasionally, a decreased \( \text{PO}_2 \) and elevated \( \text{PCO}_2 \). Consequently, it is important to follow arterial and venous blood gases and the vital signs closely when patients are placed on PEEP. A falling central venous or pulmonary arterial oxygen saturation or content often suggests that the cardiac output is falling and that the PEEP should be reduced, at least temporarily, until venous return can be improved. One can also use these gases to calculate the physiologic shunt in the lungs.

"Respirator brain"

Some physicians believe that ventilators should be used less than they are because of the change that they may cause in the brain. The so-called, "respirator brain," which refers to the softened, almost necrotic, brain tissue found in patients who have died after having been on respirators for long periods of time, has been recognized for many years. It is our own feeling, however, that these brain changes can occur with or without the respirator if a terminal patient or one with poor tissue perfusion or impaired metabolism is kept alive long enough.

Oxygen toxicity and "respirator lung"

The pulmonary changes noted in patients who have been on a ventilator for long periods of time are probably caused by the underlying shock, sepsis or trauma, or by oxygen toxicity rather than the ventilator itself. Pulmonary oxygen toxicity has received a great deal of attention in the literature. Caldwell in 1966 reported that normal subjects breathing two atmospheres of oxygen had similar decreases in vital capacity and in compliance in only 6–11 hours. Demonstrations of pulmonary changes are more difficult to find when one atmosphere of \( \text{O}_2 \) is used for shorter periods of time or when concentrations of less than 100% \( \text{O}_2 \) are used. In 1970, Singer reported that in patients ventilated for 24 hours following cardiovascular surgery, there appeared to be no difference in pulmonary function whether the patients were kept at an \( \text{FiO}_2 \) of 0.5 or an \( \text{FiO}_2 \) of 1.0. However, in a study reported by Barber in 1970, it was noted that patients with central nervous system disease and normal lungs (when ventilated for 50 hours with 100% \( \text{O}_2 \)) tended to have a \( \text{PO}_2 \) of only 120 mmHg. Similar patients who were ventilated with air had a \( \text{PO}_2 \) of about 300 mmHg when tested for brief periods on 100% \( \text{O}_2 \).

Various pulmonary morphologic changes have been reported with prolonged administration of high concentrations of \( \text{O}_2 \). Nash in 1967 reported that 7–10 days of ventilation with 80–100% \( \text{O}_2 \) resulted in pulmonary changes characterized by an early exudative phase and a late proliferative phase. The early exudative phase consisted of congestion, edema, and intra-alveolar hemorrhage. The later proliferative phase consisted of alveolar and septal edema, fibroblastic proliferation, and hyperplasia of the alveolar lining cells. Mechanical ventilation with air produced none of these changes. Therefore, it was felt that the term "respirator lung" was a misnomer.

In our own experience, an \( \text{FiO}_2 \) of 0.4 or less does not appear to be harmful to the lungs. Nevertheless, concern for oxygen toxicity should not preclude the use of a higher \( \text{FiO}_2 \) if it is necessary to maintain a \( \text{PaO}_2 \) of at least 60–70 mmHg.

Special problems

Some special problems to consider.
in patients with respiratory distress syndrome include: obesity, hyperinflation of the lungs, sudden reversal of respiratory acidosis, and pulmonary emboli.

The severely obese patient should be nursed on his side or in a semi-Fowler's position whenever possible. Following surgery, the endotracheal tube should not be removed until it is clear that the patient's vital capacity has almost returned to normal.

Hyperinflation of the lungs is increasingly being recognized as a problem when high tidal volumes are used in patients with advanced shock or sepsis. Alveoli may rupture with these high inflation pressures producing a pneumothorax, interstitial emphysema, and on occasion, air emboli to the left side of the heart.

In patients with chronic, severe respiratory acidosis, sudden reversal of the respiratory acidosis may cause a severe combined alkalosis with a drop in ionized calcium producing cardiac arrest or severe arrhythmias. In such patients, it is generally suggested that the PCO₂ not be reduced by more than 5 mmHg/hour.

In critically ill and injured patients with respiratory insufficiency syndromes, the incidence of pulmonary emboli is extremely high, particularly if the patient has been bedridden or has underlying congestive failure. Any sudden impairment of cardiac or pulmonary function in such patients should be considered, until proven otherwise, as due to the pulmonary emboli.

A sudden rise in the CVP or particularly the pulmonary artery pressure, EKG changes suggesting increased right heart strain, or increases in arterial-alveolar CO₂ differences should strongly suggest this diagnosis. If it is possible for the patient to have a lung scan or pulmonary angiography, these will often confirm the diagnosis. However, even if the diagnosis is only suspected, we believe that administration of heparin by continuous IV infusion should be considered.

Summary

We believe that there is a great similarity between all the acute respiratory distress syndromes and that they can be characterized by progressively increasing interstitial edema and congestive atelectasis. Early diagnosis is mandatory and is often best accomplished by one's clinical suspicion based on the patient's injury or illness and the previous condition of his lungs. Shock, sepsis, CNS or thoracic disease and trauma are particularly important etiologic features.

Blood gas changes cannot usually be appreciated clinically until the respiratory problem is quite severe. Accordingly, serial blood gas analyses should be performed in any patient who has an increased chance of developing ARDS. We have found that changes in the estimated A-aDO₂ on room air are especially helpful.

Any deterioration in the patient's condition, blood gases or ventilatory effort should be considered as an indication for early ventilator assistance using high tidal volumes coupled with careful dehydration in the properly selected patient. PEEP should be used early if there is any evidence that the ARDS will be severe or if there is failure to respond promptly to dehydration and high tidal volumes. If the patient is deteriorating in spite of all these efforts, a trial of massive steroids should be considered. However, if the underlying problem, particularly sepsis, cannot be controlled, it is unlikely that any of these measures will be successful.

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