CHAPTER 2

Respiratory Physiology and Protection Against Hypoxia

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> There is something fascinating about science. One gets such a wholesale return of conjecture from such a trifling investment of fact.
>
> —*Mark Twain, Life on the Mississippi*

RESPIRATORY PHYSIOLOGY

Respiration is the process by which an organism exchanges gases with the environment and, for most aerobic organisms, the critical portion of respiration consists of ensuring an adequate supply of oxygen. There is considerable geologic evidence that the Earth's original atmosphere was anoxic, and it seems probable that life began under anaerobic conditions. Because habitable environments available to anaerobic organisms became relatively scarce due to the shift toward an oxidizing atmosphere, the development of enzyme systems capable of both utilizing and detoxifying oxygen was a practical necessity. This evolutionary step had an added ramification because the utilization of a reactive element such as oxygen unleashed a source of energy that allowed the development of ever more complex multicellular organisms. In turn, this required a more or less elaborate system capable of effective oxygen delivery.

The process of respiration is a simple one for unicellular organisms with gases exchanged through passive diffusion. Even in the most complex multicellular organisms, individual cells continue to passively exchange gases with their local environment in a similar manner. In complex organisms, however, each cell is surrounded by other cells competing for the same oxygen and eliminating carbon dioxide, which leads to several requirements. One requirement is an adequate source of oxygen, the definition of ''adequate'' depending in part on the metabolic rate, and another is an efficient delivery system. The poor solubility of oxygen in water impacts both requirements. For mammals, the source must be gaseous, with a sufficient pressure of oxygen. Gills are adequate to support poikilothermic organisms but, even in a tumbling mountain stream, the oxygen content of water is trivial compared to air. Also, for all but the simplest of multicellular organisms, the solubility of oxygen requires that the delivery system includes a carrier molecule.

In humans, the limbs of the oxygen delivery system consist of the following:

- Ventilation—the process whereby pulmonary alveoli exchange gas with the atmosphere. Problems that may impact this part of the system include inadequate atmosphere, such as a hypoxic or hypercarbic environment, and airway obstruction.
- Pulmonary diffusion—the process whereby gases are exchanged between the alveolus and the pulmonary capillary. The process of diffusion itself is simple and efficient, and clinical problems are rare. Most pulmonary problems that result in systemic hypoxia represent a failure to topographically match ventilation with perfusion.
- Transportation—the shuttling of gases between lung and tissue, and back, through the vascular system. Clinical diseases related to oxygen transportation are common, and include anemia, hemorrhage, deficient cardiac output, and obstruction to blood flow.
- Tissue diffusion—the exchange of gases between systemic capillaries and tissue cells. Again this is a simple process, although it can be impeded by increasing the distance between capillary and target cell, such as by tissueb edema.
- Cellular utilization—the chemical reactions occurring within cells that employ oxygen. Compounds that interfere with these processes, such as cyanide, are toxic to most aerobic organisms.

Ventilation

Functional Anatomy of the Airways

In the normal human at rest, air is essentially completely humidified and warmed by the time it reaches the end of the trachea. From mainstem bronchi to the terminal bronchioles, the function of the airways is to conduct air to the respiratory zone. Because the airways from the nares to the terminal bronchioles do not participate in gas exchange, they constitute the anatomic dead space. In a normal adult male, this averages 150 mL at rest, although functional dead space may be increased by the addition of a rebreathing chamber, such as a mask. The resting bronchial tone found in normal airways serves to reduce anatomic dead space and thereby wasted ventilation, the trade-off being increased resistance to flow. Inflammation of the airways from a variety of causes commonly results in increased bronchial tone resulting in asthma, one of the most common diseases to afflict mankind.

Upon leaving the terminal bronchioles, gas flow enters the respiratory zone, comprising the respiratory bronchioles, alveolar ducts, and alveolar sacs. Although the total cross-sectional area of the airways increases as air flows peripherally, this increase is particularly dramatic as gas reaches the respiratory zone, and results in marked slowing of airflow velocity. Indeed, at this point the primary means of gas transport begins to be diffusion rather than convection, and gas movement is completely governed by diffusion at the level of the alveoli.

With levels of ventilation exceeding 8,000 L of air over a 24-hour period, the respiratory system is second only to the integument in exposure to the environment, and is necessarily far more delicate. Despite this constant assault, the parenchyma and distal airways are kept in a state of functional sterility by the mucociliary clearance system. The ciliated and secretory epithelial cells comprising this system constitute most of the cellls lining the conducting airways. Thin mucoid secretions float atop a watery sol layer, capturing particulate matter, and are wafted up the tracheobronchial tree to be passed through the glottis and swallowed. Although these secretions average approximately 100 mL/d, the normal individual is usually unaware of their production, a situation that changes when noxious stimuli such as infection, inflammation, or oxygen toxicity result in both impaired ciliary function and thickened secretions.

Lung Volumes

With each breath, the average adult at rest moves approximately 400 to 500 mL of air, an amount known as the *tidal volume* (TV). Inhalation is active, predominantly with the diaphragm, whereas exhalation is usually passive. The volume of air remaining in the lungs at the end of a passive exhalation is known as the *functional residual capacity* (FRC), and is determined purely by the balance between the elastic properties of the lung and the chest wall. If one exhales completely, the amount of air exhaled is designated as the expiratory reserve volume (ERV), and the remaining air that cannot be expelled (in the absence of a blow to the epigastrium) is known as the *residual volume* (RV). If instead one makes a maximal inspiratory effort from FRC, the volume inhaled is designated as the inspiratory capacity (IC), and the total volume of gas contained in the lungs is known as *total lung capacity* (TLC). The difference between TV and IC is designated the inspiratory reserve volume (IRV). The maximal amount of air that can be expelled from full chest expansion is the vital capacity (VC). These volumes and capacities are illustrated in Figure 2-1.

Average normal values for young adults are given in Table 2-1.

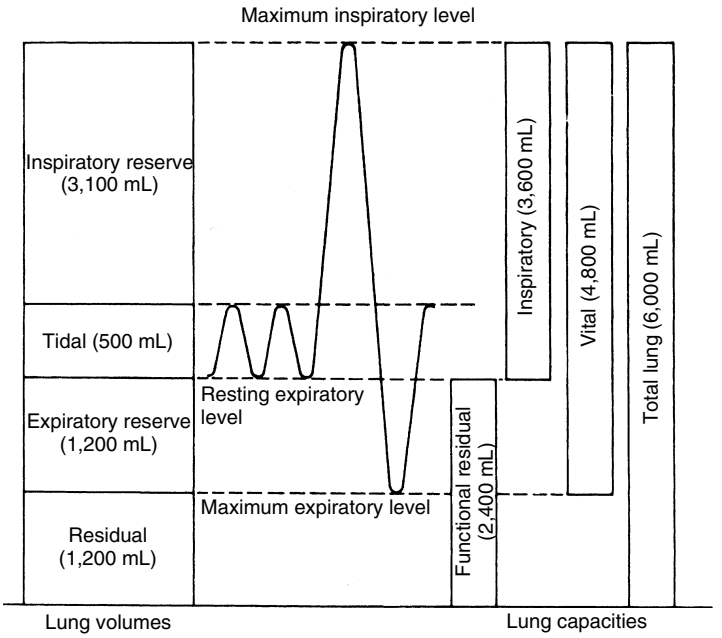


FIGURE 2-1 Lung measurements.

TABLE 2-1

Lung Volumes in Healthy Subjects 20 to 30 Years of Age

	Approximate Values (mL)	
Functional Measurements	*Males*	*Females*
Tidal volume (TV)	500	450
Inspiratory reserve volume (IRV)	3,100	1,950
Expiratory reserve volume (ERV)	1,200	800
Residual volume (RV)	1,200	1,000
Inspiratory capacity (IC)	3,600	2,400
Functional residual capacity (FRC)	2,400	1,800
Vital capacity (VC)	4,800	3,200
Total lung capacity (TLC)	6,000	4,200

(Modified from Comroe JH Jr. *Physiology of respiration*. Chicago: Yearbook Medical Publishers, 1965.)

Volumes vary directly with sitting height, explaining most differences between genders and races. Age tends to increase RV at the expense of VC. Note that because RV cannot be exhaled, neither RV nor any capacity that includes RV (TLC, FRC) can be measured by spirometry. Other techniques using gas equilibration or thoracic gas compression are required. The remaining volumes can be measured by a standard spirometer using a slow vital capacity maneuver. In modern clinical practice, spirometry has come to be synonymous with a forced vital capacity maneuver because this yields far more information about obstructive lung diseases, but an understanding of static lung volumes is fundamental to exploring the effects of pressure differentials and acceleration on the pulmonary parenchyma.

Inequality of Ventilation

With the partial exception of the larger airways, the lung is anything but rigid, and while the chest wall and the elastic recoil properties of the lung largely determine overall lung volumes, gravity plays a profound role in the relative expansion of different portions of the lung. In the upright individual, with gravity influencing the lung inside the chest cavity, intrapleural pressure is more negative at the apex than at the base, and the alveoli in the upper portion of the lung are significantly more distended than are those at the base. In essence, the lung is trying to "settle" toward gravity, and although the entire lung cannot move inferiorly due to a relatively rigid chest wall, the parenchyma will shift until restrained by its own internal elasticity. Compared with alveolar units in the lung bases, apical alveoli are functioning over a flatter portion of the lung pressure–volume curve; as a result, they experience a smaller change in volume with any given breath, and hence receive less ventilation. This is illustrated in Figure 2-2. That these changes are due to gravity rather than anatomy is demonstrated by the fact that, in the supine individual, the posterior portions of the lung are better ventilated, although the changes are less marked because of the smaller distances involved.

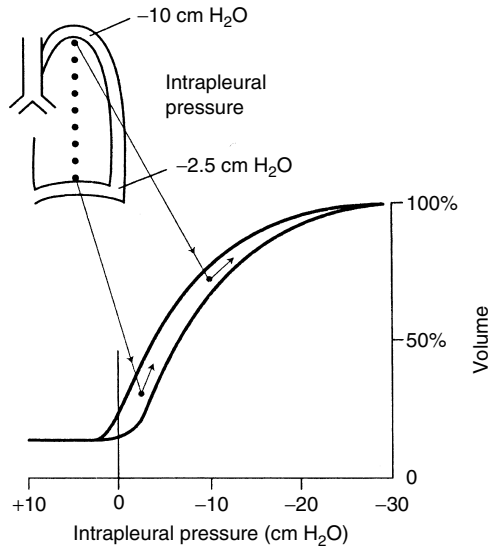


FIGURE 2-2 Explanation of the regional differences of ventilation down the lung. Because of the weight of the lung, the intrapleural pressure is less negative at the base than at the apex. As a consequence, the basal lung is relatively compressed in its resting state but expands more on inspiration at the apex. (From West JB. *Ventilation/blood flow and gas exchange,* 5th ed. Oxford: Blackwell, 1990, with permission.)

The relative compression of the basal portions of the lung has other effects. As subjects exhale below FRC, small airways in the bases begin to close, trapping air inside distal alveoli. The volume at which this occurs, known as *closing volume*, is close to RV in healthy young individuals, but because of loss of lung elasticity over time, closing volume rises with age and may even approach FRC. This probably accounts for most of the decrease in resting arterial oxygen tension with advancing age. As one would predict, single-breath nitrogen washout testing during weightlessness (parabolic flight) has documented an absence of dependent airway closure with zero gravity (1).

Because these effects are dependent on gravity, it would follow that sustained accelerative forces (defined as multiples of the Earth's gravity, or G) aggravate the topographic inequality in the lung. Dependent airway closure occurs routinely under G, and in combination with inequality of perfusion is responsible for a progressive decline in arterial oxygen levels with sustained acceleration. Ventilation with 100% oxygen partially offsets the hypoxia, but gives rise to a different problem, the syndrome of acceleration atelectasis (see Chapter 4). As noted earlier, airway closure in dependent lung parenchyma occurs before distal alveoli can collapse, which traps gas in those units. If 100% oxygen has been employed as the respirable gas mixture, the oxygen gradient from alveolus to pulmonary capillary will be such that the trapped gas is rapidly absorbed. (From the author's personal observations of intact animal preparations, the speed at which this occurs is remarkable.) The resulting atelectasis may cause dyspnea, retrosternal discomfort, and coughing. The use of less than 70% oxygen has been shown to prevent this syndrome (2).

Perfusion

Although the intent is to follow the course of oxygen through the process of respiration, a slight diversion is necessary. It is not possible to discuss gas flow to the lungs without discussing pulmonary blood flow, particularly because most causes of deficient oxygenation result from a failure to match perfusion to ventilation.

Pulmonary Vasculature

Pulmonary arteries, unlike pulmonary veins, are intimately associated with their respective airways, branching with each generation of the airways. This presumably facilitates the process of hypoxic pulmonary vasoconstriction. In a manner analogous to the airways, the total cross-sectional area in the pulmonary arterial bed increases progressively in the smaller vessels; for instance, the total surface area of the pulmonary capillaries is 50 times that of the pulmonary arterioles. This results in considerable slowing of blood flow velocity, allowing ample time for gas exchange.

The pulmonary circulation is a low-pressure system, the vessels displaying compliance characteristics more nearly akin to systemic veins than to systemic arteries. Indeed, under the microscope, small pulmonary arteries are difficult to distinguish from small pulmonary veins. The result is that the entire vascular bed in the lungs participates in blood volume redistribution in response to hypo- or hypervolemic states, and in response to hydrostatic pressure changes. For example, performance of a Valsalva maneuver may force half of the volume from the pulmonary vascular bed.

Inequality of Perfusion

If the lung has a relatively low degree of structural integrity, blood has essentially none, and is profoundly influenced by gravity. In the systemic circulation, the effect of gravity is largely counterbalanced by a high-pressure system, with vessels capable of withstanding such pressures. In the pulmonary circulation, the thinner structure and distensibility of the pulmonary arteries result in regional distribution of blood flow which is markedly influenced by gravity. Additionally, with an average distance of less than 0.5 μm between capillary blood and the alveolar space, pulmonary capillaries are minimally supported by surrounding tissue. The result is that capillary blood flow is also affected by intra-alveolar pressures, as well as by the pressure drop from arterial to venous sides. The lack of tissue support also puts the pulmonary capillaries at risk. Animal studies have shown that at a capillary transmural pressure of 40 mm Hg, disruption of vascular integrity occurs (3). Similar damage has been documented in cases of high-altitude pulmonary edema, and is felt to be etiologic to the disorder, the damage perhaps brought on by nonuniform hypoxic pulmonary vasoconstriction (4).

Average pulmonary arterial pressures (systolic 25 mm Hg, diastolic 8 mm Hg, mean 15 mm Hg) are just sufficient to perfuse the lung apices in the upright human, but the amount of flow to the apical segments is low. Blood flow increases in a roughly linear manner as one proceeds from the apex to the base. With exercise, blood flow increases throughout the lung, and differences are less marked. Under conditions of weightlessness, there appears to be a marked reduction in regional inequality of blood flow; measurements of pulmonary diffusing capacity (DL_{CO}) during a shuttle mission demonstrated dramatic improvement in DL_{CO}, which did not appear to be explained by increased pulmonary capillary blood volume (5). (Despite the name, changes in diffusing capacity more often reflect variations in the amount of wasted ventilation than changes in the alveolocapillary membrane.) In contrast, during sustained acceleration the regional differences in perfusion become more profound. At $+3$ G_z (an inertial force of three times the Earth's gravity, directed footward), the entire upper half of the lung is unperfused.

Another major determinant of regional inequality of pulmonary blood flow is hypoxic vasoconstriction. In contrast to systemic arteries, small pulmonary arteries constrict in response to hypoxia, but it is the intra-alveolar rather than the intraluminal oxygen tension that induces this response. Clearly a useful mechanism to blunt the hypoxemia that would otherwise occur with localized lung disease, hypoxic vasoconstriction occurs throughout the pulmonary vascular bed in response to environmental oxygen deficiency. In animal models, significant vasoconstriction has been shown to begin at an alveolar oxygen partial pressure (P_{AO_2}) of 70 mm Hg. In a healthy young adult, this would correspond to the expected P_{AO_2} at an altitude of 2,438 m (8,000 ft). Species differences do exist, and it is not known whether significant hypoxic vasoconstriction begins in the human at the same altitude, but it is worth noting that this represents the altitude above which high-altitude pulmonary edema begins to appear.

Ventilation—Perfusion Matching

With the topographic distribution of airflow and blood flow noted earlier, it should be evident that most of the gas exchange in the resting upright individual occurs in the bases of the lungs. Because gravity has a greater effect on blood flow, the ratio of ventilation to perfusion ($\dot{V}/\dot{Q}$ ratio) is maximal in the lung apices, and decreases as one proceeds to the bases. This is illustrated in Figure 2-3. The relative distributions of ventilation and perfusion result in a higher oxygen tension in the apical alveoli, which is thought to explain the proclivity of tuberculosis for the apices of the lungs.

Under normal conditions, the normal ventilation–perfusion inequalities merely result in a somewhat lower arterial oxygen partial pressure (P_{aO_2}) than might otherwise be expected. During sustained acceleration, the mismatch of ventilation and perfusion becomes highly significant. As gravity increases, the lung shifts caudally, stretching the apical alveoli and compressing those in the bases. At higher levels of $+G_z$, many of the basal alveoli never open at all. At the same time, pulmonary blood flow is almost entirely redirected to the bases. At high levels of G, physiologic shunting may account for half the pulmonary blood flow. The drop in P_{aO_2} is affected both by the intensity of $+G_z$ exposure, and by its duration. Even at $+3$ G_z, arterial blood gases do not reach a steady state after several minutes of exposure (see Chapter 4).

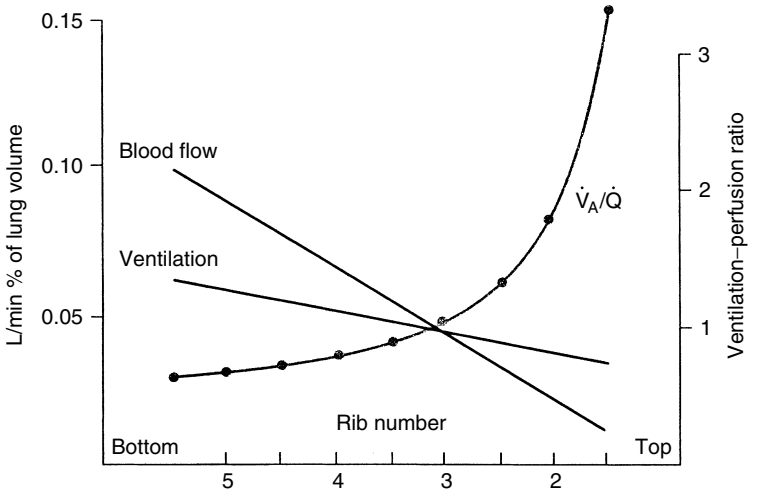


FIGURE 2-3 Distribution of ventilation and blood flow down the upright lung. Note that the ventilation–perfusion ratio decreases down the lung. (From West JB. *Ventilation/blood flow and gas exchange,* 5th ed. Oxford: Blackwell, 1990, with permission.)

Pulmonary Diffusion

The area of the gas exchange surface in the lung is huge, from 50 to 100 m^2, while the thickness of the membrane is usually under 0.5 μm. Diffusion is a passive process, determined in the case of a given gas by the difference in partial pressure across the membrane, by the diffusibility of the gas, and by the distance traversed. Diffusibility is a property of the gas itself, and is directly related to solubility, and inversely related to the square root of its molecular weight (see section Tissue Diffusion). Although carbon dioxide has a greater molecular weight than oxygen, it diffuses approximately 20 times as rapidly due to its much greater solubility. Pulmonary diffusion of carbon dioxide is not a limiting factor for gas exchange under any known circumstances. There are situations where oxygen diffusion limits pulmonary gas exchange, but in contrast to once-prevalent opinion, membrane thickness appears to rarely hamper oxygen diffusion even with diseased lungs. Under resting conditions oxygen equilibration between alveolar air and capillary blood is nearly complete before a third of the available time has elapsed. Therefore, there is enough of a reserve that equilibration can occur even when the membrane is thickened by interstitial disease, or when blood velocity increases with exercise. Diffusion limitation of oxygen may occur when both problems occur in combination, that is, exertion in the presence of interstitial lung disease. In the normal lung, diffusion limitation of oxygen only occurs in very hypoxic environments, particularly with exercise. At the summit of Mount Everest, for instance, diffusion limitation has been documented even at rest (6).

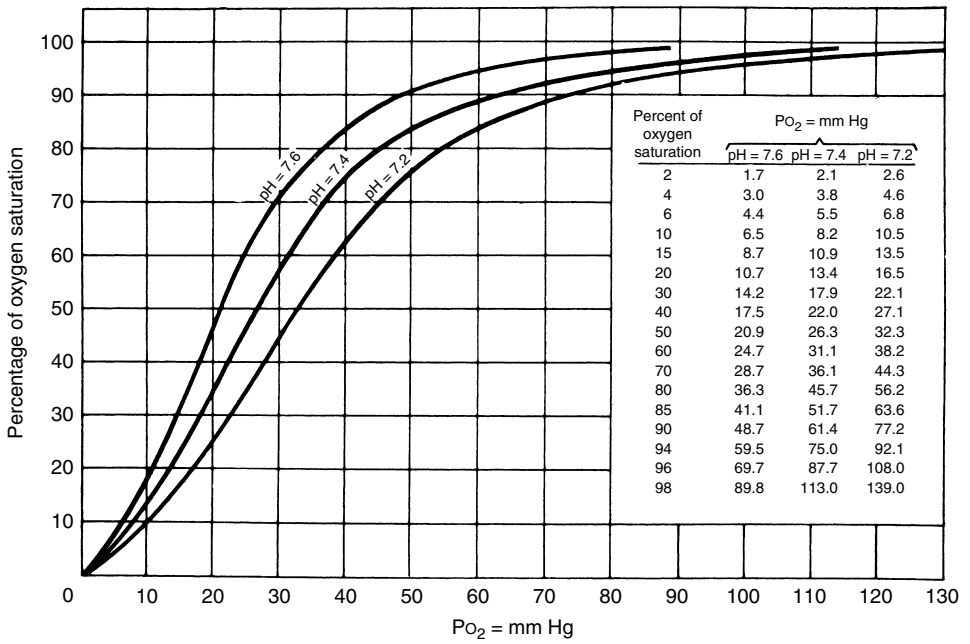
Gas Transport

Oxygen

Using Henry's Law, one should be able to estimate the amount of gas contained in the given volume of blood based on the partial pressure of the gas in the equilibrium atmosphere, the solubility of the specific gas in the liquid, and the temperature. In fact, in the case of oxygen and carbon dioxide, blood contains far more gas than predicted, because of chemical reactions that occur with the blood components. The amount of oxygen that is actually dissolved in plasma under normal conditions is almost negligible with respect to metabolic needs. The solubility of oxygen in blood is 0.003 mL 02/100 mL blood/mm Hg, so that even at sea level with a Pa_{O_2} of 100 mm Hg, 100 mL of arterial blood contains only 0.3 mL of oxygen. Ventilation with 100% oxygen, which typically results in a Pa_{O_2} of approximately 650 mm Hg, will raise the level of dissolved oxygen to approximately 2 mL 02/100 mL blood, which represents only approximately 40% of the amount of oxygen consumed at rest. In fact, 100 mL of blood at a Pa_{O_2} of 100 mm Hg actually carries approximately 21 mL of oxygen, nearly all of it complexed to a carrier molecule, hemoglobin. (Because hemoglobin is nearly oxygen saturated at that oxygen tension, a higher concentration of oxygen results in a relatively minor increase in oxygen transport, representing that dissolved in plasma.)

Hemoglobin is a complex substance, composed of a tetramer of polypeptide chains, each chain surrounding a single heme moiety, which is a protoporphyrin ring complexed with ferrous iron. The polypeptide chains consist of two α-chains and two slightly longer non-α chains; in normal adult hemoglobin A, the latter are designated as β chains. Single amino acid substitutions on the globin chains can result in marked differences in stability and oxygen affinity; for instance, a substitution of valine for glutamic acid on the β chains results in sickle cell disease. Each heme moiety can bind a single oxygen molecule, so that each hemoglobin molecule can carry up to four oxygen molecules. Each gram of hemoglobin can combine with 1.39 mL of oxygen so that ignoring the plasma content of dissolved oxygen, the oxygen-carrying capacity of 100 mL of blood is 20.8 mL 02, given a normal complement of 15 g of hemoglobin.

The tetrameric arrangement of hemoglobin is crucial, allowing rapid uptake and efficient delivery of oxygen over a narrow range of tensions. Monomeric forms such as myoglobin have a high affinity for oxygen but are incapable of releasing it except at very low oxygen tensions. In a tetrameric arrangement, the monomers interact such that the binding



Percent of oxygen saturation	Po_2 = mm Hg		
	pH = 7.6	pH = 7.4	pH = 7.2
2	1.7	2.1	2.6
4	3.0	3.8	4.6
6	4.4	5.5	6.8
10	6.5	8.2	10.5
15	8.7	10.9	13.5
20	10.7	13.4	16.5
30	14.2	17.9	22.1
40	17.5	22.0	27.1
50	20.9	26.3	32.3
60	24.7	31.1	38.2
70	28.7	36.1	44.3
80	36.3	45.7	56.2
85	41.1	51.7	63.6
90	48.7	61.4	77.2
94	59.5	75.0	92.1
96	69.7	87.7	108.0
98	89.8	113.0	139.0

FIGURE 2-4 Oxyhemoglobin dissociation curves for human blood.

of the first oxygen molecule increases the affinity for oxygen of the remaining monomers. The physiologic result of this interaction is the sigmoidal oxygen dissociation curve seen in Figure 2-4.

The shape of the curve is physiologically advantageous. In the relatively flat upper portion of the curve, a fall of 30 to 40 mm Hg in Pa_{O_2} from the "normal" level of 100 mm Hg, such as would occur at altitudes from 6,000 to 8,000 ft (1,829–2,438 m), results in only a 7% drop in arterial oxygen saturation. The curve accounts for some of the efficiency with which oxygen is loaded at the alveoli, because a large difference in partial pressure still exists when oxygen loading is nearly complete. The steepness of the lower portion of the curve means that a considerable amount of oxygen has been unloaded by the time the capillary oxygen tension has reached typical venous levels of 40 to 45 mm Hg. With a required oxygen tension at the mitochondrial level of 0.5 to 3 mm Hg, the large partial pressure difference between capillary and tissue facilitates diffusion into the tissues.

The actual position of the dissociation curve for normal hemoglobin A is influenced by temperature, by carbon dioxide tension, and by concentrations of hydrogen ion and intracellular 2,3-diphosphoglycerate; the last is a product of red cell metabolism, and increases in response to chronic hypoxia. A rise in any of these variables results in a shift of the curve to the right favoring oxygen unloading. The position of the dissociation curve is often expressed as the P50, the Po_2 at which 50% of oxygen is saturated; the normal value is approximately 27 mm Hg. Most of the effect of carbon dioxide on the oxygen dissociation curve, known as the *Bohr effect*, is actually mediated through pH change, but while the other factors shift the curve in response to particular situations such as exercise or chronic hypoxia, the Bohr effect is dynamic. As CO_2 is loaded at systemic capillaries the curve shifts rightward, resulting in further unloading of oxygen. Conversely, as CO_2 is off-loaded at the pulmonary capillary, the curve shifts leftward, favoring oxygen uptake.

Anemia reduces the oxygen-carrying capacity of blood in proportion to the reduction of hemoglobin. However, loss of hemoglobin through oxidation of the ferrous iron to the ferric form (methemoglobin), or through complexing with carbon monoxide (carboxyhemoglobin), causes an impairment of oxygen transport disproportionate to the loss of available hemoglobin. In both cases, the dissociation curve for the remaining hemoglobin shifts leftward, impairing off-loading of oxygen from that hemoglobin which is still available for transportation.

In the resting adult, the systemic circulation off-loads approximately 5 mL O_2 per 100 mL, resulting in a mixed venous Po_2 of approximately 50 mm Hg and an oxygen saturation of 75%. With a system relying on passive diffusion there are limits to how much oxygen can be extracted, but a mixed venous saturation of 75% means a considerable amount of oxygen remains as a reserve. On the basis of an average resting cardiac output of 5 L/min, the total oxygen consumption calculates to be 250 mL O_2/min in the 70-kg adult. Moderately active young men are able to increase their oxygen consumption to approximately 3 L/min (with up to 5 L/min in world class athletes), but cardiac output is incapable of matching this demand. With increased oxygen demand during maximal exercise, increased cardiac output accounts for approximately one third of the excess demand with the remainder being met by increased oxygen extraction from hemoglobin and a corresponding fall in mixed venous saturation.

The heart is in a unique situation regarding oxygen extraction. Even at rest, the myocardium removes approximately 12 mL oxygen per 100 mL blood. Therefore, blood

in the coronary sinus has a residual oxygen content of 8 mL per 100 mL blood, corresponding to a P_{O_2} of 18 mm Hg. (Of course, the heart is never really at rest, which accounts for some of the difference compared with systemic venous blood.) Increased demand must be met by increased coronary blood flow, which is largely mediated through coronary vasodilation. In the left ventricle, increases in coronary perfusion are limited by the fact that flow can only occur during diastole, and exercise-induced tachycardia limits the available time. Undoubtedly, these limitations play a role in the cardiac reserve available for periods of exertion.

Carbon Dioxide

Because carbon dioxide is much more soluble than oxygen in blood, with a solubility of 0.0697 mL CO_2/100 mL plasma/mm Hg, or approximately 24 times that of oxygen, dissolved carbon dioxide constitutes an appreciable percentage (approximately 10%) of the total elimination. Carbon dioxide, like oxygen, also undergoes chemical reaction with blood components, forming bicarbonate, which is responsible for approximately 60% of CO_2 excretion, and combining with proteins to form carbamino compounds, which account for the remaining 30%.

Carbonic anhydrase catalyzes the hydration of CO_2 to carbonic acid, which then readily forms hydrogen ion and bicarbonate. Most of the evolution of bicarbonate occurs within erythrocytes because carbonic anhydrase is absent from plasma. Bicarbonate moves into plasma by exchange with chloride. Within the erythrocyte, some of the hydrogen ions are bound to hemoglobin with the desaturated form proving to be the more efficient proton acceptor. Therefore, the off-loading of oxygen at the systemic capillary encourages the formation of bicarbonate, which reduces carbon dioxide tension, and increases its uptake. This mechanism is known as the *Haldane effect*. Desaturated hemoglobin also aids CO_2 transport through another process. Globins are the most important substrate for the formation of carbamino compounds, and oxygen desaturation enhances this reaction, which again facilitates the further uptake of CO_2 at the systemic capillary.

Nitrogen

Nitrogen is biologically inert, undergoing no chemical reaction with blood. Its concentration is determined by Henry's Law, being directly proportional to the partial pressure of nitrogen in the adjacent gas. The actual content is also determined by the solubility of the gas, which in plasma at body temperature is 0.0088 mL N_2/100 mL/mm Hg pN_2, approximately three times that of oxygen. Nitrogen is five times more soluble in fat than in plasma, an observation that partially accounts for nitrogen acting as an anesthetic at high partial pressures, as demonstrated by the development of nitrogen narcosis during diving. The differential solubility also plays a role in decompression sickness (DCS) because different tissues with equivalent partial pressures of nitrogen contain different amounts of the gas (see Chapter 3).

Tissue Diffusion

There exist approximately 50 billion capillaries in the human body, with a combined cross-sectional area more than a thousand times the cross-sectional area of the aorta. This ensures a slow enough flow to allow adequate time for exchange of gases and nutrients. It is rare for a cell to be more than 30 to 50 μm from the nearest capillary. This distance is considerably greater than the 0.5 μm between the alveolus and the capillary, but the latter's role is to provide gas exchange for the entire organism, and the pulmonary process must be more efficient.

The exchange of oxygen from capillaries to cellular mitochondria occurs along a gradient. Fick's Law of diffusion describes the rate of transfer of a gas through a tissue as inversely proportional to thickness (T), and directly proportional to tissue area (A), partial pressure difference, and a constant, D.

$$\text{Vgas} = \text{A/T} \times \text{D}(\text{P}_1 - \text{P}_2)$$

The value of the constant D is dependent upon the particular gas and tissue because it is directly proportional to the solubility of the gas in the tissue, and inversely proportional to the square root of the molecular weight of the gas.

To increase diffusion of oxygen into tissues, the systemic circulation can respond by increasing the flow through capillaries, which increases the partial pressure gradient ($P_1 - P_2$) for oxygen diffusion at the distal portion of the capillary. More importantly, it can also increase the number of open capillaries, which increases the area (A) for diffusion, and decreases the distance, or thickness (T), which the gas traverses. The recruitment or rarefaction mechanism seems to be constantly operative, with terminal arterioles fluctuating in their level of resistance as local tissue demands change. Decreasing oxygen tension, rising carbon dioxide tension, and falling pH all stimulate perfusion of local systemic capillary beds. There appear to be considerable differences between organs, both with respect to the potential recruitment of capillaries, and with respect to the major stimulus. The brain appears to be particularly sensitive to the tension of carbon dioxide, and there is relatively little difference in capillary flow between rest and exercise. Coronary blood flow to cardiac muscle appears to be most sensitive to oxygen tension, but capillary recruitment is limited by the diastolic interval, as noted earlier. In the renal and splanchnic circulations, flow decreases in response to exercise, as it does in muscle groups that are not involved with exertion. In actively exerting muscle groups, local endothelial control in response to oxygen and carbon dioxide tensions and to pH overrides sympathetic stimulation, resulting in striking recruitment of capillaries and increased local circulation.

Cellular Utilization

Approximately 95% of oxygen consumption by individual mammalian cells involves direct oxidation of substrates by the mitochondrial cytochrome system, in the process known as *oxidative phosphorylation*. The oxidative process is vital for the production of energy. Production of adenosine

triphosphate (ATP), the common coin of intracellular energy transactions, is possible in the absence of oxygen, but the initial step in carbohydrate metabolism, the cytosolic conversion of glucose to pyruvic acid through the glycolytic pathway, is inefficient, releasing only two molecules of ATP for each molecule of glucose. In the absence of oxygen, pyruvic acid is converted into lactic acid, which as a waste product is far more difficult to excrete than carbon dioxide. Furthermore, the process is incapable of catabolizing fatty or amino acids. The uptake of pyruvic acid into the mitochondrion, with its ensuing catabolism through the Kreb's cycle and oxidative phosphorylation, yields an additional 36 molecules of ATP, with the production of carbon dioxide and water. The former is excreted rapidly, and the latter is commonly beneficial; in certain desert animals the metabolic production of water functions as a significant source of hydration. The aerobic catabolic pathway is illustrated in Figure 2-5.

The electron transport system involved in the reduction of oxygen is tightly linked so that free radicals are not usually released into the cytosol. The intracellular oxygen tension required by the mitochondrion is only approximately 3 mm Hg, and values above this do not affect the rate of oxygen uptake. Additional energy requirements are met not by increased mitochondrial activity, but rather by additional numbers of mitochondria. A small lymphocyte will have only a few mitochondria, whereas a hepatocyte typically possesses approximately a thousand. Curiously, the cell responsible for the transportation of oxygen is the cell with the least use for it, because erythrocytes lose their mitochondria as well as their nuclei as they mature; erythrocytes are obligate anaerobes, utilizing glycolysis to meet their minor metabolic needs.

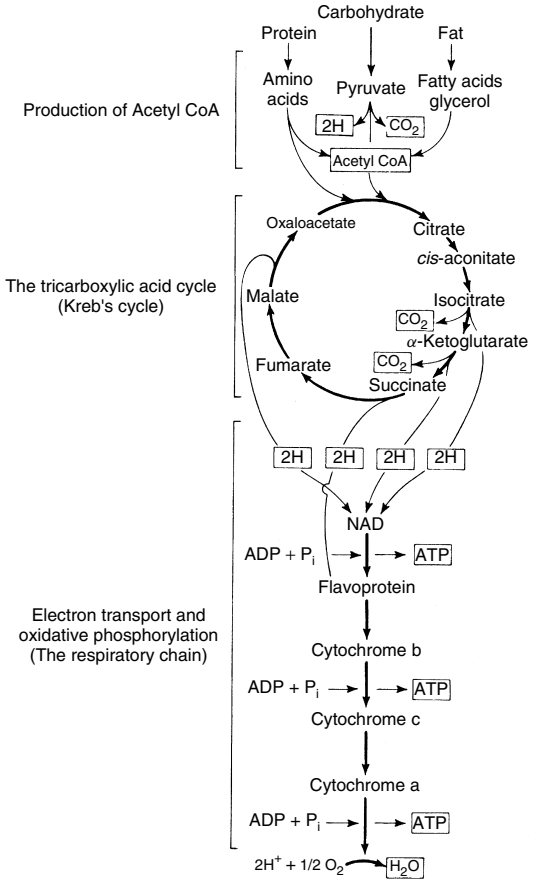


FIGURE 2-5 Cellular respiration. ADP, adenosine diphosphate; ATP, adenosine triphosphate.

During oxidative catabolism, the ratio of carbon dioxide released to oxygen consumed is known as the *respiratory exchange ratio*, or respiratory quotient (RQ, or simply R). Catabolism of carbohydrates results in an RQ of 1.0; fatty acids and amino acids release less carbon dioxide relative to oxygen consumption, and have an RQ of approximately 0.7. Because diets are generally a mixture of all three components, the RQ usually averages between 0.80 and 0.85.

Control of Ventilation

Ventilatory control is maintained through a feedback control mechanism comprising a controller, the central nervous system (CNS); effectors, the muscles of respiration; and a number of sensors. The mechanism is linked between sensors and controller by afferent neurons and between controller and effectors by efferent neurons. Although the primary controller is located in the brainstem, it can be at least partially overridden by instructions from the cerebral cortex. The sensors are designed to detect changes in blood chemistry (chemoreceptors), or physical distortion of the lungs or chest wall (mechanoreceptors).

Cardiac rhythm is determined by a group of pacemaker cells whose unstable transmembrane potential results in spontaneous electrical activity, but if such a focus exists in the ventilatory controller it has never been identified. The rhythmic pattern of ventilation appears to depend on interconnected neurons in the medulla and pons; the actual generation and maintenance of rhythmic inspiration is likely determined by reciprocal impulses between these centers. Medullary centers consist of the dorsal respiratory group, which is active during inspiration, and the ventral respiratory group, different portions of which are active during inspiration and expiration. In addition, the ventral group contains neurons innervating upper airway muscles and bronchial smooth muscles. The pontine apneustic and pneumotaxic centers appear to influence respiratory timing. Experimental damage to the pneumotaxic center, in combination with vagotomy, induces an apneustic breathing pattern (prolonged inspiration), which disappears with wakefulness, and returns with sleep.

Ventilatory control is complex, and is affected by a number of inputs. Coordination of the respiratory muscles is required for the primary task of maintaining respiratory homeostasis and activities such as phonation, defecation, and parturition to name a few. While these activities are controlled by the cortex and brainstem, the intrinsic ventilatory rate is influenced most significantly by input from chemoreceptors. Under normal conditions, carbon dioxide tension is the primary driver for changes in ventilation. Changes in arterial carbon dioxide tension ($Paco_2$) are

sensed predominantly by central chemoreceptors, with a small input from peripheral chemoreceptors. The location of the central chemoreceptors is unclear although they appear to be distinct from the respiratory centers described earlier. Stimulation of the central chemoreceptors appears to be largely mediated by a decrease in the pH of brain interstitial fluid. The process is a smooth one; increases in Pa_{CO_2} induce a linear increase in minute ventilation, first by increasing the depth and then the rate of ventilation. Decreases in Pa_{CO_2} depress ventilation; one can induce apnea in the sleeping or anesthetized individual through artificial hyperventilation.

It may seem counterintuitive that normal chemoreceptor input is based on carbon dioxide tension rather than oxygen tension but it is actually reasonable. Ventilation plays a minute-to-minute role in maintaining acid–base balance, whereas in healthy individuals the oxyhemoglobin dissociation curve ensures adequate arterial oxygen saturation despite such respiratory variation. This situation pertains unless oxygen tension reaches 60 mm Hg. From that point there is a rapid increase in minute ventilation in response to further reductions in Pa_{O_2}. Therefore, unlike the linear increase in ventilation with rising Pa_{CO_2}, there is a hyperbolic increase in ventilation with a falling Pa_{O_2}. The response is affected by Pa_{CO_2}, with a greater response to hypoxemia under hypercapnic conditions (7). The effect of different carbon dioxide tension on the hypoxic ventilatory response is displayed Figure 2-6.

The input from peripheral chemoreceptors is well illustrated by previously normal patients presenting with pneumonia. Those with milder cases and room air oxygen tensions reduced to 65–85 mm Hg will typically have near-normal pH and Pa_{CO_2} values. However, if the ventilation-perfusion mismatching is severe enough that the eupenic Pa_{O_2} would be reduced below about 60 mm Hg, then the usual pattern seen on arterial blood gases is a Pa_{O_2} maintained (if possible) near 60 mm Hg, with hyperventilation and respiratory alkalosis. Administration of supplemental oxygen typically raises the Pa_{O_2} and allows the return of Pa_{CO_2} and pH to more normal values.

The sensors responsible for this ''hypoxic override'' reside in the carotid and aortic bodies, innervated by the glossopharyngeal and vagal nerves respectively. These constitute the peripheral chemoreceptors. The carotid bodies, which appear to be more important in the human, also respond to changes in Pa_{CO_2} and pH. Physiologic responses to hypoxia seem to be entirely confined to these peripheral chemoreceptors, because in their absence hypoxia actually depresses respiration. The high arterial blood supply through the carotid allows carotid body oxygen needs to be met by dissolved plasma oxygen. As a result, Pa_{O_2} rather than oxygen content is the signal sensed by the chemoreceptor. This explains why anemia and carbon monoxide poisoning, which are accompanied by low arterial oxygen content but normal oxygen tension, generally fail to elicit tachypnea.

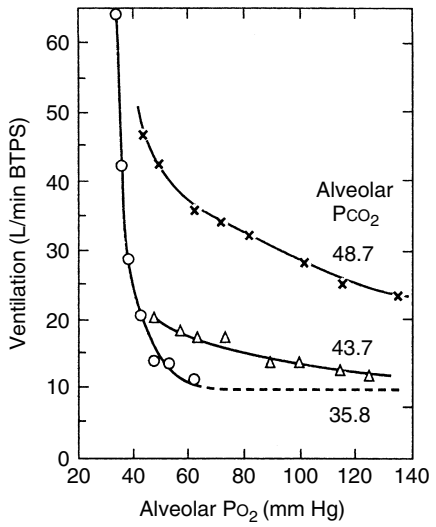


FIGURE 2-6 Hypoxic response curves. Note that when the P_{CO_2} is 35.8 mm Hg, almost no increase in ventilation occurs until the P_{O_2} is reduced to approximately 50 mm Hg. BTPS, body temperature and pressure, saturated with water vapor. (Modified by West JB Respiratory Phisiology, 2nd ed. Lippincott Williams & Wilkins, 1979, with permission; From Loeschke HH, Gertz KH. Einfluss des O2-Druckes in der Einatmungsluft auf die Atemtätigkeit der Menschen, geprüft unter Konstanthaltung des alveolaren CO2-Druckes. *Pflugers Arch* Ges *Physiol* 1958;267:460–477.)

Abnormal Ventilation

Ventilation is so closely tied to arterial carbon dioxide tension that hypoventilation and hyperventilation are usually considered to be synonymous with hypercarbia and hypocarbia, respectively. This construction is occasionally misleading. For instance, the patient with obstructive lung disease and carbon dioxide retention actually has increased minute ventilation, although the volume of effective ventilation is depressed. Nonetheless, carbon dioxide is closely linked to ventilation, and relatively immune from other influences, for several reasons. Unlike oxygen, the amount of environmental CO_2 is negligible with rare exceptions so that Pa_{CO_2} is determined by the rate of production and loss of carbon dioxide. While production of CO_2 definitely increases with conditions such as exercise, respiratory drive is modulated by Pa_{CO_2}, and under normal conditions an increase in production of CO_2 is matched by an increase in ventilation. Lastly, lung abnormalities that might raise Pa_{CO_2} can be effectively countered by increased ventilation. Because CO_2 is either carried in solution, or readily released through dissociation of bicarbonate or carbamino compounds, inadequate regional gas exchange in the lung can, in the case of carbon dioxide, be compensated by overventilating other areas of the lung. The result of such compensated ventilation–perfusion mismatching is that systemic Pa_{CO_2} levels are normal or even low. In contrast, arterial oxygen tensions in such situations cannot be made normal through increasing ventilation; blood traversing ventilated regions of the lung cannot carry more than approximately 21 mL/O_2/100 mL (i.e., saturated hemoglobin), regardless of how much ventilation is increased, and therefore cannot fully compensate for the low oxygen content of blood traversing poorly ventilated sections of lung.

Hypercapnia

With the exception of severe lung disease with $\dot{V}/\dot{Q}$ mismatching so severe that it cannot be fully compensated, hypercapnia in clinical practice is usually seen only with hypoventilation due to primary respiratory failure. This occurs either due to a state of altered consciousness, such as drug-induced sedation, or to muscular disease. Such problems are rare in the practice of aerospace medicine.

Oddly, where hypercapnia is typically of concern to aerospace medicine represents an exception to an earlier observation. Environmental carbon dioxide levels are usually negligible, but there is a distinct risk in a closed environment such as a sealed cabin in space flight vehicles (see Chapter 10). Even minor elevations in CO_2 concentration result in a prompt increase in ventilation. The result is to keep arterial P_{ACO_2} stable, but this becomes progressively more difficult as inspired CO_2 tensions approach 40 mm Hg, equivalent to approximately 5.6% CO_2 at sea level. Above that point, P_{ACO_2} begins to rise, with ventilation continuing to increase until it plateaus at a P_{ACO_2} of 80 to 100 mm Hg. Further increases in carbon dioxide tension lead to altered consciousness, and eventually death. In closed-loop systems such as aboard spacecraft, CO_2 is removed by chemical reaction with lithium hydroxide or by reversible absorption systems. The allowable P_{ICO_2} limit for shuttle missions is 7.6 mm Hg. The National Aeronautics and Space Administration (NASA) long-term spacecraft maximum allowable concentration (SMAC) is 5.3 mm Hg for 7-, 30-, and 180-day exposures.

Hyperventilation

To all intents and purposes, hypocapnia is equivalent to hyperventilation, because CO_2 production does not appreciably drop below baseline and environmental CO_2, normally close to zero, can hardly fall lower. The symptoms and signs of hyperventilation are mediated through the combined effects of alkalemia, which notably results in a fall in serum calcium due to increased protein binding, and the hypocarbia itself, which results in cerebral vasoconstriction. A sense of generalized weakness is a common complaint, often accompanied by a sense of impending doom. Neuromuscular manifestations typically include dysesthesias and paresthesias about the mouth, hands, and feet, as well as muscular cramping. Severe hyperventilation can result in tetany, seizures, or syncope.

Carbon dioxide is in equilibrium with serum bicarbonate through the intermediate formation of carbonic acid, as follows:

$$CO_2 + H_2O \leftrightarrow H_2CO_3 \leftrightarrow HCO_3^- + H^+$$

A sudden drop in P_{ACO_2} causes the reaction to proceed to the left by the law of mass action, resulting in the loss of hydrogen ions through combination with bicarbonate. The resulting respiratory alkalosis is buffered to an extent by tissues and by lactic acid production, but renal compensation is too slow to have much effect in acute hyperventilation.

Hyperventilation is a significant issue in aerospace medicine. Primary hyperventilation can occur in response to psychological or physical stress, or in response to drugs such as salicylates, progestins, or theophylline. Hyperventilation may also occur in response to pressure breathing. The usual diagnostic dilemma lies in sorting out such pure hyperventilation from secondary hyperventilation occurring in response to hypoxia. As noted earlier, a P_{AO_2} below 60 mm Hg typically results in hyperventilation. As a rule, this response is only partially effective in raising arterial oxygen tension, but carbon dioxide is unloaded as efficiently as ever. The difficulty is that many of the more noticeable symptoms of hypoxia, for example, circumoral and acral paresthesias, are actually due to hypocarbia. Those signs or symptoms that may specifically be due to hypoxia, such as alterations in color vision or impaired mental status, are more difficult to detect and furthermore the decreased cerebral perfusion that accompanies significant hypocarbia may also affect vision or mental status. Cyanosis is not a feature of primary hyperventilation, but in the cold environment typical of high altitudes, stagnant hypoxia in the extremities may cause local cyanosis. The similarities between primary hyperventilation and hypoxia are displayed in Table 2-2.

In clinical practice, primary hyperventilation is treated by reassurance to reduce the rate and depth of breathing, and by rebreathing exhaled air. At altitude, however, the strong

TABLE 2-2

Comparison of Hyperventilation and Hypoxic Hypoxia Syndromes

Signs and Symptoms	*Hyperventilation*	*Hypoxia*
Onset of symptoms	Gradual	Rapid (altitude dependent)
Muscle activity	Spasm	Flaccid
Appearance	Pale, clammy	Cyanosis
Tetany	Present	Absent
Breathlessness	X	X
Dizziness	X	X
Dullness and drowsiness	X	X
Euphoria	X	X
Fatigue	X	X
Headache	X	X
Poor judgment	X	X
Lightheadedness	X	X
Faulty memory	X	X
Muscle incoordination	X	X
Numbness	X	X
Performance deterioration	X	X
Increased respiratory rate	X	X
Delayed reaction time	X	X
Tingling	X	X
Unconsciousness	X	X
Blurred vision	X	X

X means that the sign or symptom can occur in either condition.

possibility that any such symptoms may represent hypoxia mandates a different approach. The aviator should first treat possible hypoxia, by administering 100% oxygen under pressure, before attempting to decrease the rate and depth of breathing. Oxygen supplementation is harmless in the setting of primary hyperventilation, and potentially life-saving for altitude hypoxia. Appropriate treatment of a hypoxic episode is discussed in the following section. The ultimate diagnosis is usually determined by a thorough ground check of the aircraft's life support equipment.

Abnormal Oxygenation

With the complexity of the oxygen delivery system, hypoxia at the tissue level may be caused by any of a number of abnormalities in uptake, transport, or utilization. Hyperoxia on the other hand is an artificially induced condition with the physiologic effects dominated by oxygen toxicity.

Hypoxia

Anaerobic metabolism in the human is inefficient and cannot be sustained for any period of time. Except for mature erythrocytes, all tissues require a more or less steady supply of oxygen, with the CNS being particularly susceptible to states of deficiency. As an example, cerebral resuscitation is seen as the immediate goal of cardiopulmonary life support, because cardiac arrest lasting longer than 3 minutes commonly causes CNS damage. Compared with anoxia, hypoxia causes more subtle deficiencies, but reduced visual function, cognitive impairment, and eventually altered consciousness are the principal manifestations.

Four types of hypoxia are recognized, and are discussed in order of increasing importance in aerospace medicine.

Histotoxic Hypoxia

Characterized by inability of the cell to use delivered oxygen, histotoxic hypoxia is usually due to poisoning of the cytochrome oxidase system. Cyanide is the prototype toxin. Carbon monoxide primarily acts through hypemic hypoxia but because it successfully competes with oxygen for cytochrome c oxidase when tissue oxygen tension is low, it also induces a degree of histotoxic hypoxia. Arterial oxygen tension is normal with histotoxic hypoxia, and cyanosis is absent.

Hypemic Hypoxia

Hypemic hypoxia results from a reduction in oxygen-carrying capacity by the blood. Anemia will cause a decrease in carrying capacity directly proportional to the reduction in hematocrit. A more complex, and probably more pertinent, cause of hypemic hypoxia is carbon monoxide poisoning. Carbon monoxide (CO), the leading cause of accidental poisoning in the United States, is the product of incomplete combustion and is present in aircraft exhaust fumes as well as cigarette smoke. The principal effect of CO poisoning is hypemic hypoxia, through two mechanisms. Like oxygen, CO binds hemoglobin reversibly, but it does so with an affinity more than 200 times that of oxygen, rendering those molecules of bound hemoglobin temporarily unusable. Furthermore, through the interrelated nature of the hemoglobin tetramer, the oxygen affinity of the remaining unbound hemoglobin is altered; the result is that the O_2 disassociation curve is shifted to the left, and peripheral oxygen release is impaired. Because CO is bound reversibly to hemoglobin, treatment of more than minimal poisoning consists of oxygen therapy. One hundred percent oxygen reduces the half-time for CO elimination from about 4 hours to 1 hour, while hyperbaric oxygen at 2.5 ATA (atmospheres absolute) decreases it to approximately 30 minutes.

In hypemic hypoxia, Pa_{O_2} is normal, although content is considerably reduced. Except for the rare case of methemoglobinemia, cyanosis is unusual; deoxyhemoglobin is in short supply with anemia, while carboxyhemoglobin is actually a cherry red color.

Stagnant Hypoxia

Inadequate blood flow, whether systemic or regional, may result in stagnant hypoxia to the affected tissue. Arterial oxygen tension and cyanosis are both variable. The common clinical causes, such as shock or peripheral vascular disease, are unlikely to be of concern to the flight surgeon, but two examples of stagnant hypoxia are of particular interest. DCS (see Chapter 3) causes localized stagnant hypoxia due to bubble formation. Sustained acceleration (covered in Chapter 4) induces pooling of blood in dependent areas, with stagnant hypoxia at the opposite end of the G axis. Because $+G_z$ is the force most likely to be encountered, the brain, the organ least likely to tolerate transient ischemia, is the one most often subjected to it under sustained acceleration.

Hypoxic Hypoxia

Hypoxic hypoxia, a deficiency in alveolar oxygenation, is the most common cause of hypoxia clinically, and is far and away the most common cause in aviation. In clinical medicine, the etiology is occasionally inadequate ventilation, but more often improper matching of ventilation to perfusion. In aviation medicine, the cause is more likely to be reduction in the oxygen partial pressure in inspired air. In either case, Pa_{O_2} is reduced, and cyanosis is often present. The remaining discussion of hypoxia will focus on a subcategory of hypoxic hypoxia, that is, altitude hypoxia.

Altitude Hypoxia

Hypoxia is of physiologic importance anytime humans exceed approximately 3,048 m (10,000 ft) altitude. This is true even for those who chronically live at such altitudes, although the physiologic considerations with chronic altitude exposure differ from those with acute exposure. It is important not to extrapolate the effects of altitude hypoxia from the highland to the lowland dweller, because altitude acclimatization profoundly affects human tolerance. A sea level dweller ascending suddenly to the summit of Mt. Everest [8,882 m (29,141 ft)] would be unconscious within a few minutes, and dead soon afterward, yet mountaineers have managed to carry out intense exertion at that altitude without oxygen. Because aviation systems attempt to maintain oxygen tensions

equivalent to 10,000 ft or less, and hypoxic episodes are usually acute exposures due to equipment failure, the effects of chronic altitude exposure will not be discussed in detail.

Barometric pressure varies in a nonlinear manner with altitude, due to the compressibility of air. By Dalton's Law, and given thorough mixing of gases in the homosphere, atmospheric partial pressure of oxygen will vary in the same manner. Table 2-3 shows total air pressure and oxygen pressure at 1,000-ft increments of altitude while breathing ambient air, up to an altitude of 7,620 m (25,000 ft). It also displays representative values while breathing 100% oxygen at altitudes of 10,058 to 14,041 m (33,000–46,000 ft).

Partial pressure of oxygen in alveoli is lower than the corresponding ambient P_{O_2} because of the displacement of oxygen by water vapor and because of exchange for carbon dioxide. Alveolar oxygen tension (P_{AO_2}) is calculated using the alveolar gas equation:

$$P_{AO_2} = P_{IO_2} - P_{ACO_2}/R + [P_{ACO_2} \times F_{IO_2} \times 1 - R/R]$$

R is the respiratory quotient, which is usually taken to be 0.85. P_{ACO_2} is the mean alveolar carbon dioxide pressure, which equals arterial CO_2 tension (P_{aCO_2}). P_{IO_2} is the partial pressure of inspired oxygen, which is calculated as:

$$P_{IO_2} = (P_B - P_{H_2O})F_{IO_2}$$

where P_B is ambient barometric pressure, F_{IO_2} is the fraction of inspired oxygen, and P_{H_2O} is water vapor pressure [47 mm Hg at body temperature and pressure, saturated

TABLE 2-3

Respiratory Gas Pressures and Gas Exchange Ratios

Altitude		*Pressure*		*Ambient*				*Respiratory Exchange*
(m)	*(ft)*	*(psia)*	*(mm Hg)*	P_{O_2} *(mm Hg)*	P_{AO_2}*(mm Hg)*	P_{ACO_2} *(mm Hg)*	P_{H_2O} *(mm Hg)*	*Ratio (R)*
Breathing Air								
0	0	14.69	759.97	159.21	103.0	40.0	47.0	0.85
305	1,000	14.17	733.04	153.57	98.2	39.4	—	—
610	2,000	13.66	706.63	148.04	93.8	39.0	—	—
914	3,000	13.17	681.23	142.72	89.5	38.4	—	—
1,219	4,000	12.69	656.34	137.50	85.1	38.0	—	—
1,524	5,000	12.23	632.46	132.50	81.0	37.4	47.0	0.87
1,829	6,000	11.77	609.09	127.60	76.8	37.0	—	—
2,134	7,000	11.34	586.49	122.87	72.8	36.4	—	—
2,438	8,000	10.91	564.64	118.29	68.9	36.0	—	—
2,743	9,000	10.50	543.31	113.82	65.0	35.4	—	—
3,048	10,000	10.10	522.73	109.51	61.2	35.0	47.0	0.90
3,353	11,000	9.72	502.92	105.36	57.8	34.4	—	—
3,658	12,000	9.34	483.36	101.26	54.3	33.8	—	—
3,962	13,000	8.99	464.82	97.38	51.0	33.2	—	—
4,267	14,000	8.63	446.53	93.55	47.9	32.6	—	—
4,572	15,000	8.29	429.01	89.88	45.0	32.0	47.0	0.95
4,877	16,000	7.96	411.99	86.31	42.0	31.4	—	—
5,182	17,000	7.65	395.73	84.50	40.0	31.0	—	—
5,486	18,000	7.34	379.73	79.55	37.8	30.4	—	—
5,791	19,000	7.05	364.49	76.36	35.9	30.0	—	—
6,096	20,000	6.76	349.50	73.22	34.3	29.4	47.0	1.00
6,401	21,000	6.48	335.28	70.24	33.5	29.0	—	—
6,706	22,000	6.21	321.31	67.31	32.8	28.4	47.0	1.05
7,010	23,000	5.95	307.85	64.49	32.0	28.0	—	—
7,315	24,000	5.70	294.89	61.78	31.2	27.4	—	—
7,620	25,000	5.46	282.45	59.17	30.4	27.0	47.0	—
Breathing 100% Oxygen[a]								
10,058	33,000	3.81	197.10	197.10	109	40	47.0	—
10,973	36,000	3.30	170.94	170.94	85	38	47.0	—
11,887	39,000	2.86	148.08	148.08	64	36	47.0	—
12,192	40,000	2.73	141.22	141.22	—	—	—	—
12,802	42,000	2.48	128.27	128.27	48	33	47.0	—
13,716	45,000	2.15	111.25	111.25	34	30	47.0	—
14,021	46,000	2.05	105.92	105.92	30	29	47.0	—

([a]From Holmstrom FMG. Hypoxia. In: Randall HW, ed. *Aerospace medicine*. Baltimore: Williams & Wilkins, 1971, with permission.)

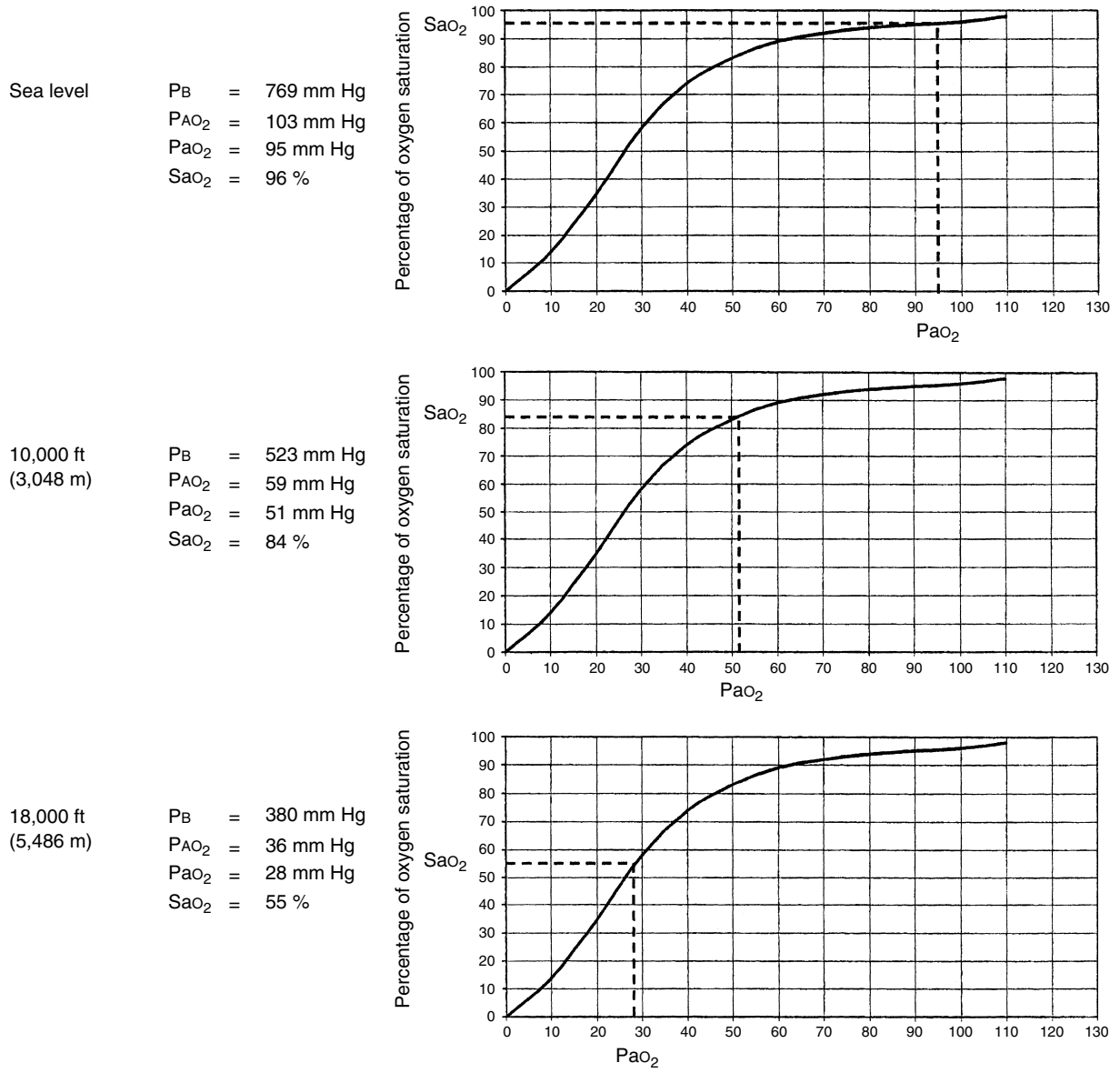


FIGURE 2-7 Expected oxyhemoglobin saturation at representative altitudes in normal individuals breathing ambient air.

with water vapor (BTPS)]. Because the term in brackets is small on ambient air (~2 mm Hg), it is usually ignored, and the equation may be written:

$$P_{AO_2} = (P_B - 47)F_{IO_2} - Pa_{CO_2}/R$$

Table 2-3 also displays the corresponding alveolar oxygen and carbon dioxide tensions at the given altitudes. The table ends at 25,000 ft for ambient air, and 46,000 ft for 100% oxygen; above these altitudes alveolar oxygen tensions cannot be calculated because altered consciousness supervenes before a steady state can be reached.

Although alveolar and arterial carbon dioxide tensions are essentially identical, arterial oxygen tension is slightly lower than alveolar oxygen tension because of imperfect matching of ventilation and perfusion. This alveolar–arterial (A–a) gradient for oxygen is approximately 8 mm Hg in a healthy young person, although it gradually rises with age, and may be markedly elevated with lung disease. Figure 2-7 shows the expected levels of hemoglobin saturation at three different altitudes, assuming normal hemoglobin, an RQ of 0.85, and a normal alveolar–arterial gradient of 8 mm Hg. At a height of 3,048 m (10,000 ft), Pa_{O_2} would measure approximately 51 mm Hg, yielding a saturation of approximately 84%. Note that this is just entering the steep portion of the dissociation curve. At 5,486 m (18,000 ft), Pa_{O_2} has fallen to 28 mm Hg, and oxyhemoglobin saturation has dropped to 55%, which is lower than normal mixed venous saturation. Actually, it is unlikely that the A–a gradient remains stable with altitude. With elevated pulmonary artery pressures,ventilation–perfusion matching appears to be more uniform, but because at higher altitudes diffusion begins to be a limiting factor, the end result is likely to be no net change.

Effects of Hypoxia

Acute altitude hypoxia affects critical organ systems in different manners. The respiratory and cardiovascular systems, which in the healthy individual are reasonably tolerant of moderate deficiencies of oxygen, respond by attempting to increase oxygen delivery, whereas the CNS becomes more or less dysfunctional as a result of oxygen deficiency.

The response of the respiratory system hinges on the peripheral chemoreceptors, the carotid and aortic bodies discussed earlier. The effect of acute exposure to altitude on ventilation is displayed in Table 2-4. Ventilatory response to hypoxia is not limited by effort, because maximum voluntary ventilation typically exceeds 100 L/min in healthy individuals. Instead, respiratory stimulation due to hypoxia is blunted by falling carbon dioxide levels. The effect of different carbon dioxide tensions on the hypoxic ventilatory response is displayed in Figure 2-6.

The cardiovascular response to altitude hypoxia is to increase cardiac output. The volume of oxygen extracted from the systemic circulation (oxygen consumption) is a product of the rate of delivery (cardiac output) and the proportion of oxygen off-loaded (the arteriovenous oxygen difference). As noted earlier, increased oxygen demand such as with exercise is usually met by increasing both cardiac output and oxygen extraction. However, mixed venous saturation can only fall so much. With progressively higher altitudes and falling oxygen tensions, the volume of oxygen that can be extracted from arterial blood becomes progressively limited and an increased cardiac output is required to meet even resting oxygen demand.

The CNS is disproportionately affected by hypoxia. It is the first tissue to malfunction with oxygen deficiency, and the first one to succumb to anoxic conditions. Oxygen consumption by the brain is characterized by its relative consistency; it is at a high level at rest, and does not change significantly in response to states such as exercise. The requirement by the CNS for an unfailing supply of oxygen is perhaps best illustrated by the physiologic lengths to which the organism will go after a traumatic episode, by supplying blood to the brain at the expense of nearly all other tissues.

Relative degrees of hypoxia result in subtle neurologic symptoms. These are amply illustrated in an extract of a report by Captain R. W. Schroeder in which he discussed his aviation altitude record of 29,000 ft (8,800 m) on September 18, 1918 (see Chapter 1):

> At 20,000 feet, while still climbing in large circles, my goggles became frosted, making it very difficult for me to watch my instruments. When I reached 25,000 feet I noticed the sun growing very dim. I could hardly hear my motor run, and I felt very hungry. The trend of my thoughts was that it must be getting late . . . I went on talking to myself, and this I felt was a good sign to begin taking oxygen, so I did. I was then over 25,000 feet, and as soon as I started to inhale the oxygen the sun grew bright again, my motor began to exhaust so loud that it seemed something must be wrong with it. I was no longer hungry and the day seemed to be a most beautiful one . . .
>
> I kept at it until my oxygen gave out, and at that point I noticed my aneroid indicated very nearly 29,000 feet. The thermometer 32° below zero C. and the R.P.M. had dropped from 1600 to 1560. This, considered very good. But the lack of oxygen was affecting me. I was beginning to get cross, and I could not understand why I was only 29,000 feet after climbing for so long a time. I remember that the horizon seemed to be very much out of place, but I felt that I was flying correctly and that I was right and the horizon was wrong.
>
> About this time the motor quit. I was out of gasoline, so I descended in a large spiral. When I had descended to about 20,000 feet I began to feel better . . . I did not see the ground from the time I went up through the clouds above Dayton, Ohio, until I came down through them again at 4000 feet above Canton, Ohio, over 200 miles from where I started (8).

Signs and Symptoms of Hypoxia

The warning symptoms of hypoxia tend to be subtle, and the symptom onset insidious. Recognition of developing hypoxia is also hampered by the fact that the cognitively impaired individual has difficulty recognizing his or her own cognitive impairment; an example is the intoxicated driver who is convinced he is in full control of his vehicle. Therefore, considerable attention should be devoted to acquainting the aviator with the early warning signs of hypoxia.

TABLE 2-4

Effect of Acute Exposure to Altitude on Pulmonary Ventilation

		Altitude in Meters (ft)				
	m	*Sea Level*	*3,700*	*5,500*	*6,700*	*7,600*
Pulmonary Function	*ft*	*Sea Level*	*12,000*	*18,000*	*22,000*	*25,000*
Minute volume (L/min)		8.5	9.7	11.1	15.3	—
Respiratory rate (per minute)		12.0	14.0	12.0	15.0	—
Tidal volume (L)		0.71	0.69	0.92	1.02	—
Alveolar P_{O_2}		103.0	54.3	37.8	32.8	30.4
Alveolar P_{CO_2}		40.0	33.8	30.4	28.4	27.0

Note: The ascent was accomplished at 1400 m/min (4,500 ft/min). The subjects remained at altitude for 30 to 60 minutes. Minute volume and respiratory rate are average values. The tidal volume was calculated.
(Adapted from Rahn H, Otis AB. Alveolar air during simulated flights to high altitudes. *Am J Physiol* 1947;150:202.)

Signs and symptoms associated with altitude hypoxia are due to either hypoxia itself, or to the associated hypocarbia, or to both. Objective signs include tachypnea, hyperpnea, and cyanosis. Signs of CNS dysfunction, some of which may also be noted as symptoms by the individual, include confusion; behavioral changes such as excitement or belligerence; loss of coordination; and eventually unconsciousness. Symptoms of hypoxia may include dyspnea, headache, lassitude, drowsiness, euphoria, and blurred or tunnel vision. Symptoms due to hypocarbia, such as circumoral or acral paresthesias, commonly accompany hypoxic symptoms and are often the first symptoms noted by the aviator. This is to be expected because the peripheral chemoreceptors will initially try to maintain an arterial oxygen tension near 60 mm Hg by hyperventilation.

Because there is always a risk of equipment failure at altitude, early recognition of hypoxic symptoms is mandatory. Unfortunately, the constellation of hypoxic symptoms and their sequence of appearance tend to be idiosyncratic to the individual. Subjecting the aviator to hypoxia under controlled conditions, such as in a hypobaric chamber, allows the flyer to experience his or her individual symptoms of hypoxia. As a rule, the individual's symptoms do not change dramatically over time, but refresher training in a chamber does reacquaint the individual with the symptoms, as well as identify any change in symptoms.

Effective Performance Time

Below 3,048 m (10,000 ft), few normal individuals notice hypoxic symptoms while at rest, although measurable deficiencies in color and night vision exist. Depending on the individual, scotopic visual function may be reduced by approximately 10% at 1,524 m (5,000 ft), with a 28% reduction at 10,000 ft. From altitudes of 10,000 ft to approximately 15,000 ft, cardiorespiratory compensation will allow the unacclimatized individual to function, typically for an indefinite period of time. Nonetheless, some degree of impairment is the rule with decreased alertness and impaired judgment and coordination. Above approximately 15,000 ft, the unacclimatized individual will usually become severely impaired usually within a matter of minutes or even seconds, depending on the altitude. However, it should be noted that individual tolerances vary markedly. The length of time an individual is able to perform useful flying duties is known as the *effective performance time* (EPT), or time of useful consciousness (TUC). This does not reflect the onset of unconsciousness *per se*—at 18,000 ft, for instance, the individual might not reach such a state—but rather the period of time beyond which the aviator would be unlikely to take corrective or protective action. Typical EPT values for resting individuals are given in Table 2-5.

Note that at higher altitudes, EPT values are considerably shorter than the period of time the average individual could breath-hold. Although at altitude mixed venous oxygen tension falls below its typical resting level of 40 mm Hg, at extreme altitude alveolar oxygen tension will fall lower still, resulting in a net diffusion of oxygen out of the pulmonary capillary. Therefore, EPT at that altitude is a function of circulation time. Exercise of even modest levels shortens the EPT because decreased circulation time and increased peripheral demand result in a faster loss of oxygen.

TABLE 2-5

Effective Performance Time at Altitude

Altitude		
m	*ft*	*Effective Performance Time*
5,500	18,000	20–30 min
6,700	22,000	10 min
7,600	25,000	3–5 min
8,500	28,000	2.5–3 min
9,100	30,000	1–2 min
10,700	35,000	0.5–1 min
12,200	40,000	15–20 s
13,100	43,000	9–12 s
15,200	50,000	9–12 s

Treatment of Hypoxia

With the onset of hypoxia, administration of 100% oxygen is critical. If the aviator was already using an oxygen system when symptoms began, either the concentration should be increased, or a different source of gas should be employed. At altitudes above 12,192 m (40,000 ft), oxygen must be administered under positive pressure. After oxygen administration, breathing rate should be slowed to 12 to 16 breaths/min, because otherwise persistent hypocarbic symptoms might incorrectly persuade the aviator that hypoxia was persisting. Oxygen equipment should be inspected because certain problems (e.g., disconnected hose) can be readily identified and corrected in the aircraft. If an immediately correctable cause cannot be identified, the aviator should if at all feasible descend to below 10,000 ft altitude. Recovery from hypoxia is usually immediate, but symptoms such as fatigue and headache may persist, particularly after prolonged episodes of hypoxia.

On occasion, administration of oxygen to correct hypoxia is followed by an increase in the severity of symptoms, a phenomenon known as *oxygen paradox*. Symptoms typically consist of confusion and worsened vision and even loss of consciousness may occur. This phenomenon is thought to occur because the reoxygenation may be accompanied by a fall in systemic blood pressure, and it seems most likely that the transient hypotension in the face of preexisting cerebral vasoconstriction due to hypocarbia causes cerebral ischemia. The cause of the hypotension itself is unclear. The direct cardiovascular effect of supplying oxygen in a hypoxic state is to reduce pulmonary vascular resistance, but the resulting increase in left ventricular preload and increased cardiac output would not explain systemic hypotension. It seems most likely that the phenomenon is due to transient release of a vasodilator substance such as oxygen radicals or nitric oxide, but the precise mechanism is unknown.

Oxygen Toxicity

Regardless of how vital any substance is to biologic processes, an excess is likely to be toxic, and oxygen is no exception. Aerobic organisms have managed to adapt to atmospheric oxygen tensions while avoiding toxicity, but the margin of safety is small. It should not be surprising that the existing antioxidant defenses are readily overwhelmed because exposure to oxygen at concentrations higher than 21% is largely a man-made phenomenon.

Prolonged exposure to oxygen tensions in excess of 400 mm Hg, or approximately 55% concentration at sea level, risks pulmonary damage. The time to onset of clinical toxicity is considerably shortened at higher partial pressures, with a latency of 1 to 3 days at a P_{IO_2} of 760 mm Hg, and 8 to 10 hours at 1,520 mm Hg. The time to onset of toxicity varies between individuals and species. Toxicity is hastened by certain drugs and by radiation, and may be delayed by prior sublethal oxygen exposure. Such provocative and palliative factors often appear to be paradoxical. For instance, disulfiram protects rats from hyperbaric oxygen toxicity, but potentiates normobaric toxicity. Pre-exposure of the same species to 80% oxygen renders the animal resistant to subsequent 95% oxygen, whereas pre-exposure to 60% oxygen actually increases the subsequent toxicity of 95% oxygen.

It is reasonably clear that toxicity is a function of oxygen partial pressure rather than concentration. Because of the engineering advantages of maintaining a sealed cabin at pressures lower than atmospheric, in the early years of the space program animal and later human research subjects were exposed to 100% oxygen at high altitudes (e.g., 10,200 m; 33,500 ft) for days to weeks. There were isolated reports of possible toxicity, such as instances of retrosternal discomfort that typically cleared with further exposure, and subjects who displayed an asymptomatic increase in pulmonary shunt fraction, but in general the absolute oxygen atmosphere was well tolerated at that altitude. Early astronauts were maintained in a similar atmosphere without evident toxicity, a practice that was abandoned after the disastrous Apollo fire of 1967.

Normal volunteers exposed to absolute oxygen at sea level typically experience substernal discomfort and mild dyspnea beginning 4 to 22 hours after onset of exposure. During this period, the only objective finding is decreased tracheal mucociliary clearance. Longer exposure to 100% oxygen typically results in decreases in vital capacity, pulmonary compliance, and diffusing capacity, with an increase in intrapulmonary shunting. Individual tolerance varies, but few volunteers have tolerated 100% oxygen for longer than 3 days. The longest voluntary exposure reported was 110 hours, but this resulted in severe dyspnea and acute respiratory failure (9).

In most part owing to idiosyncratic tolerances, it is difficult to specify safe limits for oxygen exposure. In general, normal humans appear to tolerate 24 to 48 hours of absolute oxygen at sea level, and oxygen concentrations of less than 50% can be tolerated for extended periods of time with little evidence of tissue injury. Given these findings, the risk of oxygen toxicity in civilian or military aviation appears to be negligible. An exception would have to be made in the case of an individual exposed to potentiating agents. Therapeutic doses of thoracic radiation, as well as certain drugs such as bleomycin, are synergistically toxic with oxygen. It is probable that the pneumonitis which occasionally complicates treatment with either bleomycin or radiation therapy represents potentiation of oxygen toxicity at ambient oxygen levels, due to increased free radical damage. Hyperoxia increases the risk of developing pneumonitis from either treatment. Of greater aeromedical concern is delayed toxicity, occurring when the previously treated individual is subsequently exposed to oxygen. Cases of delayed toxicity, most of them from the surgical literature, have been described months and occasionally even years following initial treatment; although most cases have been described within a year of exposure, this may well be artifactual, because it corresponds to the most likely period for delayed operative intervention in treatment of malignancy. The risk of such toxicity is controversial, because its occurrence is inconsistent, probably due to the multifactorial nature of oxygen toxicity itself. Pertinent aeromedical literature is essentially nonexistent. Although the risk is probably low, it seems wise to restrict those aviators who have received therapeutic doses of bleomycin or thoracic radiation from routine exposure to 100% oxygen.

Neural toxicity from oxygen is not a concern in aerospace operations because such toxicity requires exposure to 100% oxygen at pressures twice that of sea level (2 ATA). It is, however, of concern in hyperbaric treatment of altitude DCS, where absolute oxygen is administered at pressures of up to 2.8 ATA. The major risk is the development of generalized seizures, which may be preceded by muscle twitching and incoordination. Because the great majority of individuals can tolerate up to 30 minutes of 100% oxygen at 2 ATA, treatment regimens generally consist of 20 to 30-minute periods of pure oxygen, separated by 5- to10-minute periods of air breathing. This prolongs the latency of neural oxygen toxicity while allowing satisfactory resolution of DCS.

PROTECTION AGAINST HYPOXIA

The dominant theme of this chapter has concerned the central role of oxygen in the maintenance of aerobic life. Because adaptation to the hypoxic environment of altitude is limited to relatively low elevations, and furthermore is incompatible with the brief exposures typical of aviation, the answer is instead to engineer appropriate systems into the aircraft for hypoxia protection.

The value of the administration of supplemental oxygen as a means of alleviating hypoxia in rarefied atmospheric conditions was elegantly demonstrated by the great French physiologist Paul Bert in experiments he conducted in his hypobaric chamber in the 19th century (see Chapter 1). He used this evidence to advise balloonists about the value of breathing oxygen when flying at altitude. Indeed, it was the failure of

three balloonists during high altitude Zenith flights to properly use the stored oxygen they had taken that led to the deaths of two of them during an ascent above 26,200 ft (8,000 m).

Although heavier than air controlled flight began in 1903 with a short flight that attained only very limited altitude, flights of 600 mi were completed by 1913, the air speed record stood at 120 mph and an altitude of 20,000 ft had been reached. Georges Lagagneux, a French pilot, is credited with the first use of supplemental oxygen in an aircraft when he flew to an altitude of 20,014 ft in 1913. By the outbreak of war in Europe in 1914 most major powers had aircraft in military use and urgent efforts to improve performance were occurring. The tactical advantage of height in aerial combat soon became clear and drove the requirement for ascent to ever-higher altitudes. However, the physiological limits of unsupported ascent to altitude became a significant limiting factor in the advancement of air power. This limit was solved by the development of the first practical aircraft oxygen systems. German developments in this field allowed the aircraft and airship crews to achieve greater heights than their allied adversaries. The Dreager company even produced the first liquid oxygen (LOX) system for airborne use. Their designs were soon copied by the Allied Forces to redress this military advantage. Research conducted by the Royal Flying Corps demonstrated beyond a doubt the value of providing oxygen in flight, which resulted in efforts to make such systems easier for the aircrew to operate. This drove the change in delivery systems from a mouthpiece (commonly termed a *pipe-stem*) to a face mask molded to fit with a seal at its edge. The development of methods that economized the use of oxygen, through the use of a reservoir rather than simple continuous flow and eventually through systems that delivered oxygen on demand, improved capabilities still further.

Through the interwar years, developments continued at a slower pace but by the outbreak of the World War II aircrew oxygen systems were in routine use. Shortly after the end of World War I in the United Kingdom, J.S. Haldane was able to show that with the use of supplemental oxygen the alveolar partial pressure of oxygen could be maintained at acceptable levels, and that by breathing pure oxygen, hypoxia could be avoided up to 35,000 ft. Over 40,000 ft, however, he recommended that the individual be offered an alternative form of protection. This was the use of a pressurized suit, similar in some ways to a diving suit, filled with oxygen and maintained at a pressure of at least 130 mm Hg. This technique effectively removed the physiological limitation to ascent. By 1933 such a suit was developed and an American balloonist, Mark Ridge, was safely exposed to an altitude of 84,000 ft in a decompression chamber. In 1934 Wiley Post, the famous pioneering aviator, flew his aircraft, Winnie May, to an altitude of 40,000 ft wearing a similar suit (see Chapter 1).

It had been recognized for some time that an alternative solution to protect a pilot from the dangers of hypoxia would be to pressurize the cockpit. In 1931, a pressurized balloon gondola was used to allow Auguste Picard to attain an altitude of 51,795 ft. The first successful pressurized aircraft, the Lockheed XC-35, flew in 1935 but throughout World War II pressurized aircraft remained relatively rare, although a notable exception was the B-29 Superfortress. Since the end of World War II, however, cabin pressurization has become a standard feature of both combat and commercial aircraft, although the degree of pressurization commonly differs. Nonetheless, in the 50 years after the Wright Flyer 1 took to the air, the principal developments of personal oxygen systems, pressure suits, and cabin pressurization had all occurred. The remainder of this chapter will discuss the modern use of such systems.

Cabin Pressurization

Aircraft

Unpressurized aircraft are limited in altitude to avoid exposing crew and passengers to an unacceptable degree of hypoxia. National regulatory bodies apply limitations on the permissible service ceiling of each aircraft type. Commonly, aircraft with no pressurization capability are allowed to operate at altitudes no greater than 10 to 12,000 ft. This altitude limit may be lowered at night to take into account of the effect of low-grade hypoxia on night vision. The altitude to which pressurized aircraft may fly is regulated so that crew and, where appropriate, passengers will have an adequate oxygen supply available for use in the event of loss of cabin pressure. Commercial aircraft pressurization can provide a "shirt sleeve" environment within the cabin with an equivalent altitude no greater than 8,000 ft while the aircraft can operate up to approximately 40,000 ft. Commonly, military combat aircraft are pressurized to a lower degree than commercial or noncombat aircraft because they are more likely to sustain damage that may result in loss of pressurization. Such a system reduces the risk of DCS and reduces the utilization of oxygen, but makes it necessary for the crew to wear a personal oxygen system throughout flight.

Cabin pressurization systems are designed to pass compressed air into the cabin or cockpit and to control its outlet so as to raise the pressure within the cabin. A differential pressure is therefore established between the inside and the outside of the aircraft. The controlled entry and exit of air through the cabin ensures a supply of fresh air and is integrated into the cabin environmental control system to regulate the cabin temperature. Modern commercial aircraft commonly recirculate 50% of cabin air through high-efficiency particulate (HEPA) filters. This increases fuel efficiency without compromising cabin air quality although the latter has been a matter of some controversy.

Commercial aircraft are generally pressurized on ascent from ground level (Figure 2-8). The maximum pressure differential across the fuselage is on the order of 8.5 to 9 lb/in^2 and is termed a *high- differential pressurization system*. Once that differential has been reached, further ascent of the aircraft will lead to a further increase in cabin altitude and, given the requirement to maintain cabin altitude at or below 8,000 ft, a maximum acceptable aircraft altitude can be derived. A military combat aircraft may not pressurize at all until it has ascended to 8,000 ft but then holds the cockpit pressure at that altitude (termed *isobaric*) until its

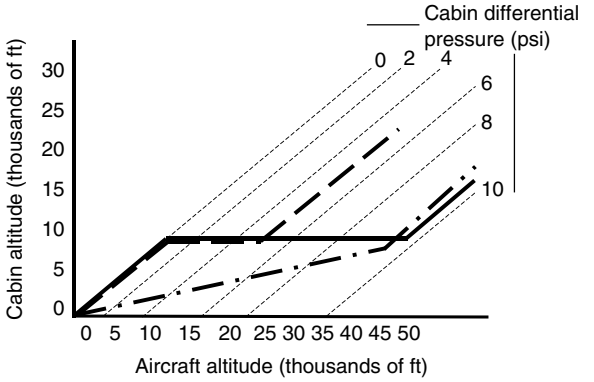


FIGURE 2-8 Graphs of the relationship between aircraft altitude and cabin altitude in a commercial transport aircraft (— ·), a high-differential military aircraft (—), and a low-differential military aircraft (— —). The pressurization of a commercial aircraft begins at ground level and cabin altitude rises more slowly than aircraft altitude until the maximum cabin differential pressure is reached. In military aircraft, the cabin is typically not pressurized until an altitude of 8,000 ft is reached. Thereafter an isobaric cabin altitude is held until the maximum cabin differential is reached. Further aircraft ascent will cause cabin altitude to rise again.

maximum pressure differential has been reached. In these aircraft this differential may be between 3.5 and 5.25 lb/in^2 in high-performance aircraft, whereas high-differential military aircraft may reach a maximum differential pressure of 9.2 lb/in^2. Other pressurization schedules have been used, including an enhanced high differential one in supersonic transport aircraft.

Spacecraft

At the altitudes of orbit for manned spacecraft the atmospheric pressure is so low that the compression of the relatively few molecules of air present is insufficient to provide a usable gaseous atmosphere inside the craft. Therefore, spacecraft must be pressurized by using systems that maintain the cabin environment without exchange of gases with the environment. Russian spacecraft have been designed from the early stages of their space program to provide a cabin environment pressurized to 1 atmosphere (sea-level equivalent) and composed of gas with a similar proportion of oxygen (21%) to air. This imposes challenges in terms of capsule strength and weight. Early U.S. spacecraft (Mercury and Gemini) had lower cabin pressures, thereby reducing weight, but had a high oxygen content to avoid hypoxia, giving rise to a greater risk of capsule fire. The accident and fire that killed three NASA Apollo astronauts led to a modification of this policy and design of the system in the Space Transportation System (STS). In the STS, the Orbiter is pressurized to a sea-level equivalent throughout much of the flight, but can be depressurized from 14.7 lb/in^2 to approximately 10 lb/in^2 in preparation for extravehicular activity.

Provision of Oxygen

Irrespective of the presence of a cabin pressurization system, the requirement for the provision of oxygen to the occupants of an aircraft is related to the ambient pressure to which they are exposed. The design of the system may also have to accommodate the need for physiological protection against hypoxia following a loss of cabin pressure, resulting in a sudden exposure to a much higher altitude. Such systems have to be designed to protect against hypoxia in an emergency in which the user is exposed to the ambient pressure at which the aircraft is flying (or even higher due to the effect of aerodynamic suction). The following pages will describe the requirements for oxygen systems pertinent to the challenges faced by the users, and therefore the altitudes and environmental pressures given refer to the conditions surrounding the occupants of the aircraft, rather than the aircraft itself.

Classes of Oxygen Systems

Closed Circuit Oxygen Systems

In closed circuit oxygen systems, advantage is taken of the relatively small proportion of the inspired air at sea level that is required to meet metabolic requirements. For example at sea level, 16% of the expired gas is oxygen. Therefore only approximately a quarter of the inspired oxygen is used and the rest exhaled. Therefore, recycling expired gas can economize on the amount of oxygen required to be delivered by an oxygen system.

However, this advantage diminishes with altitude because there are technical difficulties in ensuring that the correct amount of oxygen is delivered into the closed system to replenish the oxygen consumed. Furthermore, the gas in a closed system contains (a) expired water vapor that can condense and freeze at low temperatures, (b) an increasing concentration of carbon dioxide which must be removed from the circuit, and (c) a rising proportion of nitrogen, if there is any inward leakage of air. Therefore, such systems tend to be complicated by the need to address these aspects.

Closed circuit oxygen systems are used in space flight, and in some underwater breathing systems, but rarely in aviation, although some smoke hoods used by cabin crew during an on-board fire are based on oxygen systems of this type.

Open Circuit Oxygen Systems

In open circuit systems the expired gas is vented to the environment. Although this is relatively wasteful with regard to oxygen utilization, it has the considerable advantage of simplicity. The delivery of oxygen to the user may be continuous throughout the respiratory cycle or on demand, that is when an inspiratory effort initiates the flow of oxygen. The characteristics of such systems and the general and physiological design requirements are described in the subsequent text.

General Requirements of Oxygen Systems

Convenience

To the degree possible, a system should impose the minimum burden on the user and should be as automatic as possible.

The user should merely have to don the equipment (usually a mask) and connect to the system with ease.

Evaluation of Integrity

Having donned the system, the users should be able to assure themselves that it is functioning correctly and any failure should be immediately apparent. This requirement also include an indication of flow and, where appropriate, an indication of the oxygen contents held in storage. The latter is usually achieved with a pressure gauge visible to the user. Flow indication is commonly achieved with some form of "blinking" flow sensor. These sensors blink when flow occurs; a constant indication, with or without flow, indicates a fault in the system.

Safety Pressure

The primary aim of an oxygen system is to protect against hypoxia by the provision of an amount of oxygen sufficient to maintain adequate alveolar partial pressure. Inward leakage of ambient air may compromise this objective and is best prevented by a small overpressure of the system (safety pressure). This overpressure may be controlled so as to only be present when a significant altitude is reached, typically 12,000 to 15,000 ft in U.K. military oxygen systems and higher (>20,000 ft) in U.S. systems. In a similar manner, safety pressure can be used to protect the user from inhaling smoke or toxic fumes in the cockpit. In these cases no dilution of the inspired gas is acceptable so it must be possible to select the delivery of 100% oxygen and avoid the mixing of oxygen with cabin air. This capability can also be used to reduce the risk of DCS by "prebreathing" oxygen to reduce the nitrogen stored in the body.

Temperature

The inspired gas should be at a temperature that will be tolerable to the user. An inspired gas temperature within $\pm 5^{\circ}$C of the cockpit temperature is generally acceptable. The system itself should be resistant to the effects of temperature. In particular, exposure to low temperatures should not cause freezing of water vapor within the unit, which could prevent normal operation.

Duplication

Where a personal oxygen system is used as the primary means of protection against hypoxia, such as in a military combat aircraft, a degree of redundancy is essential in the delivery of oxygen. Simple continuous flow systems were utilized as a form of backup to the breathing regulator but have been mostly superseded by the provision of a secondary regulator with most of the features of the primary one. This allows for economical use of breathing gas and therefore has implications for mission effectiveness as well as crew safety. A form of redundancy is also required for the potential failure of the main oxygen supply system, be it stored oxygen or oxygen generation, and in ejection seat-equipped aircraft this function can be combined with the provision of post–ejection protection against hypoxia with a seat-mounted gas store.

Underwater Escape

A ditched aircraft will sink rapidly. Therefore, oxygen equipment can be designed to operate to a modest depth for a short time. In some air forces a short-term air supply is provided to assist escape from a helicopter underwater.

Physiological Requirements of Oxygen Systems

Oxygen Concentration

As ambient pressure reduces on ascent the partial pressure of respired gases, including oxygen, within the lungs will fall in parallel unless the proportion of a gas within the inspired air is raised. The amount by which the inspired oxygen concentration must be raised to maintain an alveolar partial pressure equivalent to breathing air at sea level can be calculated.

Figure 2-9 shows the concentration of oxygen required to be present in the inspired gas to maintain the P_{AO_2} at 103 mm Hg during ascent from ground level to an altitude of 34,000 ft. For example, raising the fractional inspired oxygen content from 21% to 63% at 25,000 ft will maintain a P_{AO_2} of 103 mm Hg. Although healthy individuals may tolerate some reduction in alveolar P_{O_2}, some reduction in memory and learning ability, as well as reduction in night vision, are known to occur when breathing air at an altitude of 8,000 ft. Furthermore, if a lower fractional increase in inspired oxygen were used, any inward leakage through a face mask that resulted in the in-drawing of ambient air would be even more hazardous because there would be a reduced margin of safety with respect to protection against hypoxia.

However, some compromise of the minimum acceptable oxygen partial pressure can be tolerated when a loss of cabin pressure occurs at high altitude. In this circumstance, and when positive pressure breathing is used to provide short duration protection against hypoxia, a P_{AO_2} of 30 mm Hg may be acceptable for a very limited duration, provided it rises rapidly to at least 75 mm Hg among aircrew while the aircraft descends.

A very basic oxygen system could provide 100% oxygen at all altitudes. This could have a number of advantages

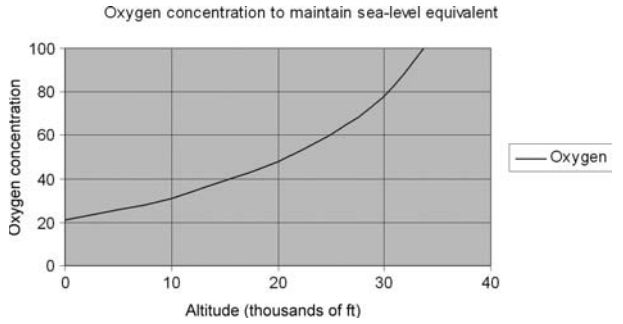


FIGURE 2-9 Graph of the concentration of oxygen required to be present in the inspired gas to maintain the P_{AO_2} at 103 mm Hg during ascent from ground level to an altitude of 34,000 ft.

including cost and mechanical simplicity. However, such a system has a number of significant disadvantages:

1. It is wasteful of oxygen at low altitudes because 100% oxygen is only required when altitudes in excess of 33,000 ft are reached.
2. Long periods of breathing 100% oxygen at altitudes below 18,000 ft can give rise to retrosternal discomfort.
3. Breathing high inspired oxygen concentrations will enter the middle ear cavity and its subsequent absorption can give rise to ear discomfort and deafness (delayed otic barotraumas), a process that is reduced by the presence of nitrogen in the inspired gas.
4. During increased acceleration, breathing 100% oxygen has been associated with the collapse of basal segments of the lung (acceleration atelectasis), giving rise to cough, dyspnea, and chest pain. The symptoms are aggravated by the use of anti-G trousers but are prevented by the presence of at least 40% nitrogen in the inspired gas.

In summary, an aircraft oxygen system should deliver a concentration of oxygen sufficient, but not greatly more than that required, to prevent hypoxia and ideally it should provide an inspired gas composition that will result in an alveolar P_{O_2} equivalent to breathing air at sea level. At very high altitudes (above 40,000 ft), the need for positive pressure breathing with 100% oxygen [pressure breathing for altitude (PBA)] to achieve an acceptable P_{AO_2} can give rise to compromise between the degree of pressure breathing required and the severity of hypoxia suffered for a short period before descent results in an improvement in the P_{AO_2}.

Pulmonary Ventilation

If an oxygen system is incapable of meeting the ventilatory demands of the user in terms of minute ventilation and instantaneous flow, the unmet ventilatory needs may be subjectively unpleasant and can give rise to significant disturbances of respiratory patterns. Respiratory measurements made during high-performance flights reveal that ventilatory demands can be very high, especially in air combat, and even when the pilot initially runs to his aircraft. Aircrew oxygen system should therefore provide a minute ventilation of 50 L/min [ambient temperature and pressure dry (ATPD)], and peak inspiratory flows of up to at least 200 L/min (ATPD). Standards to specify these performance criteria in aircrew oxygen systems in military aircraft have been defined by NATO and in AeroSpace Interoperability Command [formerly Air Standardization Coordinating Committee (ASCC)] Air Standards (3).

Resistance to Breathing

Most oxygen systems impose some additional flow resistance but this must be minimized or unacceptable physiological side effects may occur. The precise effects an individual experiences when confronted with subjectively persistent resistance to breathing are variable, with many individuals overbreathing (hyperventilating), whereas some try to moderate and reduce their demands so as to avoid the unpleasant sensation. Neither of these effects is desirable. Such respiratory resistance may be so uncomfortable as to make the user have sensations of impending asphyxia and compel them to discard their breathing system despite the risk of hypoxia. To reduce the risk to the aircrew from an inadequately designed oxygen system, there are Air Standards that define acceptable levels of mask cavity pressure at various flow rates.

Added Dead Space

In addition to the normal anatomic dead space, an oxygen system imposes a further functional dead space. To avoid significant rebreathing of expired carbon dioxide, the dead space in the mask should be kept to a minimum and ideally be less than 150 mL. In the event of a rapid decompression, gas trapped in the dead space of the oxygen system will contain an oxygen concentration inappropriate for the altitude to which the user of the system is now exposed. Therefore, it is critically important that this gas be replaced as quickly as possible by gas with an oxygen content high enough to prevent hypoxia. This is only possible if the gas trapped in the dead space is removed immediately and a breathing gas with the correct composition of oxygen to prevent hypoxia is supplied within one breathing cycle.

Airborne Oxygen Supplies

Gaseous Oxygen

The most common form of oxygen storage used in aircraft is a pressurized gaseous oxygen cylinder. Many cylinders have an operating maximum pressure of 1,800 lb/in^2, are made of steel, and are sometimes wire-bound in military aircraft to reduce the risk of release of shrapnel if shattered in combat. Cylinders with an even higher pressure, up to 3,600 lb/in^2, are sometimes used in commercial and some military aircraft. This has the benefit of reducing the space required to carry a large quantity of oxygen but can increase the logistic challenge of supporting such systems.

Gaseous oxygen is widely available although aviators' oxygen has to meet certain quality requirements, such as dryness, that are more stringent than therapeutic oxygen. For example, gaseous oxygen used in aviation must be 99.5% O_2 by volume and contain no more than 0.02 mg of water/L of gas at sea level. This is considerably more pure and dry than therapeutic oxygen used in hospitals. However, condensation and subsequent freezing of water vapor in the oxygen storage system could have disastrous consequences in flight as discussed earlier.

Aircraft cylinders can be charged until the pressure within it reaches its operating maximum. As it is used, the pressure in the cylinder will fall, although it is prudent to avoid complete discharge of the cylinder to prevent ingress of moisture.

The amount of oxygen held in aircraft cylinders will depend on the aircraft type and endurance. However, oxygen cylinders are relatively bulky and heavy. Whereas little or no stored oxygen may be acceptable in some types of aircraft, training aircraft and those in which the oxygen system

is not routinely used throughout flight, it is unacceptable in combat aircraft. Small cylinders of gaseous oxygen are commonly available on commercial aircraft for the in-flight treatment of passengers and as the emergency oxygen supply fitted to the ejections seats of combat aircraft.

Liquid Oxygen Storage

One liter of LOX can yield 840 L [normal temperature and pressure (NTP)] of gaseous oxygen. For this reason, it is the commonly used form of stored oxygen in combat aircraft because this economy of size and weight is critical in this type of aircraft. Moreover, LOX can be held in a relatively low-pressure vessel, but to be liquefied it has to be cooled to a temperature of $-183^{\circ}C$ at 1 atmosphere pressure.

Much LOX is wasted during production through vaporization and charging of vessels. Moreover, LOX is a hazardous substance to handle and there have been a number of serious fires in production plants, including shipboard ones.

Charging and using LOX vessel is a three-phase operation involving (a) the filling phase in which the vessel is exposed to LOX that initially evaporates and thereby cools the vessel sufficiently to retain oxygen in the liquid state, (b) the build-up phase in which liquid pressure rises in the vessel to approximately 70 to 115 lb/in^2, and finally (c) a delivery phase in which breathable oxygen can be derived from the vessel. The avoidance of thermal stratification within the LOX, which could lead to a loss of normal operating pressure when colder liquid is disturbed within the vessel, requires an additional process to be carried out that has the effect of warming the liquid contents to a consistent temperature. As it is used, the pressure within the vessel falls and more LOX vaporizes. Gaseous oxygen is channeled to the aircrew through a supply system that allows the gas to warm to an acceptable temperature before it is inspired.

In addition to the hazards of LOX production, there are hazards associated with the use of LOX because it can become contaminated by toxic materials, especially hydrocarbons, and these may accumulate so that a bolus of contamination may be released in a relatively high concentration to the user. The complexity and logistic requirements of LOX production and use are substantial. Therefore, LOX systems are now being superseded in combat aircraft by on-board oxygen production.

On-Board Oxygen Generation Systems

The generation of oxygen as a product of a chemical reaction can be used to produce breathable oxygen rapidly. Most chemical generators are designed to produce oxygen when sodium or potassium perchlorate reacts with iron. For example:

$$NaClO_3 + Fe = FeO + NaCl + O_2$$

Such reactions are exothermic and once initiated by raising the temperature of the reactants to more than $250^{\circ}C$, will usually proceed to exhaustion, with the coincidental release of significant amounts of additional heat. The active chemicals are usually formed with a binder into a cylindrical "candle." The initial heat source is generated within an iron-enriched zone which itself is activated by either percussion or an electrical heating wire.

Some solid candles have been used to provide oxygen in manned space activities, in particular on the Russian space laboratory Mir, and as a backup oxygen system on the International Space Station. In aviation, they are often used as a convenient means of providing emergency oxygen for passengers in commercial aircraft although incorrect storage of these units in transit has been associated with the loss of an aircraft. They have also been developed by some manufacturers as an alternative to seat mounted emergency oxygen in combat aircraft.

Chemical generation of oxygen by other means is also possible. For example, potassium superoxide reacting with water liberates oxygen during the formation of potassium hydroxide. This technique has been used in self-contained breathing escape devices and provides a further advantage in that the potassium hydroxide reacts with expired carbon dioxide, thereby reducing its accumulation within this closed system.

Concentrating oxygen from air has considerable logistic and operational advantages for airborne use. Pressure swing adsorption through a molecular sieve oxygen concentrator (MSOC) has now become practical, and such systems are being installed in most modern combat aircraft. The system is based on the supply of compressed air to a bed in which nitrogen is retarded within the matrix structure of the sieve material. This adsorption process does not result in the chemical combination of nitrogen with the sieve material, usually zeolite, but is dependent on the availability of adsorption sites within the bed and these will eventually be filled. However, when the bed is depressurized the nitrogen molecules are released and can be flushed from the bed.

Zeolites are aluminosilicates with a crystalline structure of SiO_4 and AlO_4 arranged tetrahedrally. The cavities within the tetrahedral structure are usually filled by water molecules but when heated these are driven off, leaving an open matrix within which molecules of an appropriate size can be held. Nitrogen is of such a size, but oxygen (and argon) molecules are too large.

The most basic form of the MSOC is therefore based on two beds pressurized in turn and then purged during their depressurized phase. A small proportion of the product gas from the active bed is used to flush the nitrogen from the resting bed. Once flushed the rested bed is again able to adsorb nitrogen when pressurized at the next cycle. By this means an effectively near continuous supply of product gas containing a high concentration of oxygen can be produced. The presence of a plenum in which product gas is held before use removes the potential problem of a respiratory demand being made at the point of change over between one bed and the other. MSOCs in which there are more than two beds can also alleviate this problem as well as assisting the control of product gas oxygen concentration (Figure 2-10).

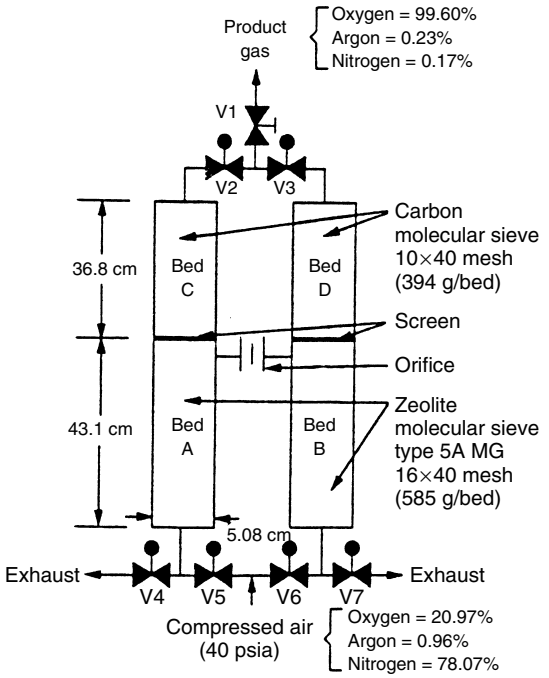


FIGURE 2-10 Two-stage molecular sieve oxygen-generating system. (From Advisory Group for Aerospace Research and Development (AGARD). *Advanced oxygen systems for aircraft.* AGARD-AG-286. Quebec, Canada: NATO Canada Communications Group, 1996:1–95.)

Because neither argon nor oxygen is adsorbed in the bed material, both are present in the product gas in elevated concentrations. This means that the maximum oxygen concentration delivered by an MSOC is approximately 94%, although this value can diminish over time as other factors, such as water contamination of the beds, may adversely affect the maximum achievable concentration. This problem is avoided in many aircraft by switching the breathing gas source to a backup system, which delivers 100% oxygen at high cabin altitudes or in the event of a loss of MSOC supply. In ejection seat–equipped aircraft, this backup oxygen system can be seat mounted to also provide postescape protection against hypoxia.

Aircraft MSOC systems have been designed so that compressed air is derived from the compressor stages of the jet engines. A separate compressor is not required to provide compressed air to the MSOC. However, engine failure does give rise to loss of the main oxygen system and, until an engine relight is achieved, the backup store of oxygen must be used. Despite this drawback, MSOC systems are now used successfully in military combat aircraft, including single-engine ones in which this disadvantage is most apparent.

In routine flight, the maximum oxygen concentration that could be provided from an MSOC is generally not required, and indeed too high an oxygen concentration has significant disadvantages in terms of acceleration atelectasis and delayed otic barotrauma (oxygen ear). Therefore, throughout flight the oxygen concentration should be controlled so as to be high enough to prevent hypoxia,

FIGURE 2-11 Photograph of molecular sieve oxygen concentrator (MSOC). (Courtesy of Honeywell Aerospace UK.)

also ensuring that the inspired oxygen concentration being breathed is sufficient for survival in the event of a rapid decompression, but not be so high as to induce the disadvantages described. The actual concentration of oxygen in the product gas can be influenced by a number of factors, including flow across the beds and the interval between their pressurization, known as *bed-cycle time*. Both of these factors can be employed in a feedback system in which the product gas oxygen concentration (or partial pressure) is measured and used to alter the operation of the MSOC, so as to maintain the appropriate oxygen concentration in the product gas within defined limits (Figure 2-11).

In addition to the use of MSOC systems as the main source of breathing gas in a military aircraft, this technique has also been used to provide therapeutic oxygen for respiratory patients traveling by air and is being investigated for use in large commercial aircraft as the means of providing emergency oxygen for passengers.

Oxygen Delivery Systems

Continuous Flow

The simplest form of delivery system is a continuous flow of oxygen from the storage vessel to the user. Usage is calculated easily and the whole apparatus is inexpensive to manufacture. However, a predefined flow has considerable disadvantages. In particular, the delivery of oxygen is not matched to requirements. Inspiration only occupies approximately one third of the normal respiratory cycle, and therefore during the rest of the cycle, the flow of oxygen is wasted. Also, there may be insufficient oxygen to protect against hypoxia, either at altitude or when ventilatory demand is high. If a high flow is provided to alleviate these problems, much of the oxygen will be wasted at low altitude or during quiet breathing.

Such problems can be partially addressed by the use of a range of metering orifices to regulate the flow of oxygen from a storage bottle. Progressive increases in the cross-sectional area of the orifice will allow greater flow to occur. Although this technique allows some form of variability, it

remains only a partial solution to compensate for increased altitude and does not compensate for variations in ventilatory requirements.

Incorporation of a reservoir bag between the flow regulator and mask allows oxygen to flow throughout the respiratory cycle and then a bolus of oxygen may be breathed during inspiration. This can reduce oxygen usage by more than 50% and the system may be enhanced further by using a bag which is in direct communication with the mask. If the gas available in the reservoir bag and that flowing from the regulator are insufficient to meet ventilatory demand, ambient air can be drawn in through a port in the mask. Exhaled gas in the respiratory dead space, which has not taken part in respiration and which has a high oxygen and low carbon dioxide content, is passed into the rebreathing reservoir and mixed with the continuous oxygen flow from the system. Such devices are very useful, for example in the provision of therapeutic oxygen to a sick passenger, but they are very vulnerable to the effects of freezing. Also, these systems are incapable of meeting the more sophisticated requirements of aircrew oxygen systems, for which demand flow delivery systems are necessary.

Demand Flow Delivery Systems

Within demand flow systems, it is possible to provide a volume of gas appropriate to meet the ventilatory demands of the user and a gas mixture in which the proportion of oxygen is appropriate for the altitude. This technique ensures protection against hypoxia without undue waste of oxygen, or oversupply leading to delayed otic barotrauma and in high-performance aircraft acceleration atelectasis.

As these systems respond to demand, a wide range of ventilatory requirements can be achieved, ideally up to 300 L/min instantaneous flow, and both safety pressure and pressure breathing can be provided. The altitudes at which safety pressure and positive PBA protection are delivered vary according to national standards. In the United States, safety pressure is generally provided from approximately 20,000 ft, and in the United Kingdom safety pressure is usually delivered when cabin altitude exceeds 12,000 to 15,000 ft. Positive pressure breathing is essential when exposed to altitude above 40,000 ft, where the alveolar partial pressure of oxygen falls below that seen at 10,000 ft breathing air, but some U.S. regulators initiate PBA at a lower altitude to maintain a sea-level equivalent alveolar partial pressure of oxygen. A demand regulator supplied with breathing gas from an MSOC has no requirement to conserve stored oxygen, so safety pressure may be provided from ground level.

Although these design requirements are common to most demand regulators the precise form of the regulator varies. Perhaps the most common is a panel-mounted unit, such as the crew regulator unit (CRU) series of regulators. These provide all the controls the pilot needs to access and display contents (as pressure) as well as an indication of flow (Figure 2-12). Similar panel-mounted units are in service in military aircraft around the world, although in the United Kingdom these were superseded by first man-mounted

FIGURE 2-12 T-38N pressure-demand regulator.

miniature regulators (similar to those used by the U.S. Navy) and more recently by ejection seat–mounted ones. Even smaller regulators have been used as mask-mounted units, although the disadvantages in terms of weight and movement have resulted in them being used mainly for emergency oxygen in transport aircraft. For aircraft in which aircrew use the breathing system throughout flight and during high-altitude escape, mounting the regulator on the ejection seat reduces the number of regulators required in an aircraft fleet and reduces the risk of damage associated with man-mounted units.

Air dilution demand regulators contain an aneroid that controls the degree to which ambient air is mixed with oxygen from the storage source. This is achieved by various means, either by suction dilution or injector dilution, but the end result is a system that is responsive to the physiological demands of the individual at the altitude it is operated. Loading of controls within the regulator can be used to induce the provision of safety pressure and PBA at appropriate altitudes.

The introduction of pressure breathing for G protection (PBG) has resulted in further modification of demand regulators so that a G-induced signal, pneumatic or electronic, will cause the regulator to deliver breathing gas at an elevated pressure, proportional to the acceleration to which the pilot is being exposed. The source of additional breathing gas pressure is the oxygen supply and therefore the F_{IO_2} is commonly raised during PBG. New electronic regulators have been developed which may result in increased reliability in service, but the need to ensure aircrew safety and mission completion suggests that a duplex (i.e., a main and stand-by) regulator will remain. In the most modern systems the breathing regulator and the anti-G valve may be combined in the same, seat-mounted unit (Figure 2-13).

Mask and Hose

The final link to the user is the hose and oxygen mask leading from the regulator to the face. The hose routing is related to the location of the regulator and, in ejection seat–equipped aircraft, must be designed to take account of escape requirements. There is considerable advantage in having a single point of connection between the aircrew and the ejection

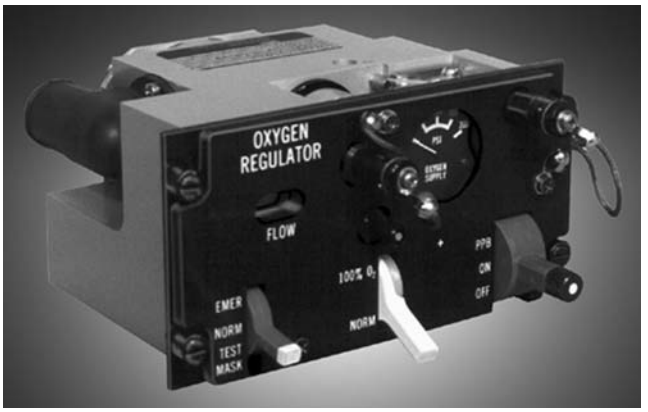


FIGURE 2-13 Combination anti-G valve and breathing regulator. (Courtesy of Carleton Life Support Systems.)

seat through which oxygen supply, anti-G trouser air, and communications pass. This reduces the number of separate connections to be made while strapping in, speeds emergency ground egress, and simplifies ejection seat sequencing.

Irrespective of the route to the mask, this final conduit of breathing gas is at low pressure but must meet wide respiratory demands. Therefore, the hose should be wide-bore and of low resistance. Movement of the hose should not induce significant fluctuations in gas pressure, and the passage of gas through it should not cause undue noise that would interfere with the use of the mask-mounted microphone (Figure 2-14).

Masks for aircrew that use oxygen throughout flight must fulfil a significant number of functions, fit adequately to prevent leakage, and be comfortable to wear throughout flight. In addition to being the final link in the oxygen system supply chain, these masks also support communication, protect the face in event of bird strike or ejection, and should not obscure vision or impede movement.

Masks worn by aircrew only in an emergency have somewhat easier criteria to meet, although the masks must still protect against hypoxia, including post decompression hypoxia, and not impede the aircrew. Emergency masks designed for passengers have somewhat different criteria. There is no way to ensure that the mask will fit the user, therefore it is designed to fit as wide a range of individuals as possible. The degree of acceptable hypoxia for passengers is greater so indrawing of ambient air is less significant; indeed it is necessary to meet ventilatory demand. The requirements for communication and facial protection are also absent, but the mask must be easy to fit by the untrained and unskilled (despite preflight briefs given in all commercial aircraft.) (Figure 2-15).

Pressure Suits

Full Pressure Suits

When encased in a full pressure suit, the user is exposed only to its internal pressure environment. Therefore, inflation of the suit to an acceptable pressure can provide protection against hypoxia, DCS, and ebullism (the evolution of water vapor from tissue water at altitudes above 63,000 ft). However, a suit inflated to a pressure adequate to allow the wearer to breathe air, that is, a pressure equivalent to 10,000 ft (523 mm Hg) is impractical because it would be impossible to move. Therefore, the inflation pressure is set so as to protect against extreme altitude, but the user must breathe 100% oxygen to ensure normoxia. The underlying principles of pressure suit design used in aviation and space flight are identical, although the practical implication of the differing usage influences design.

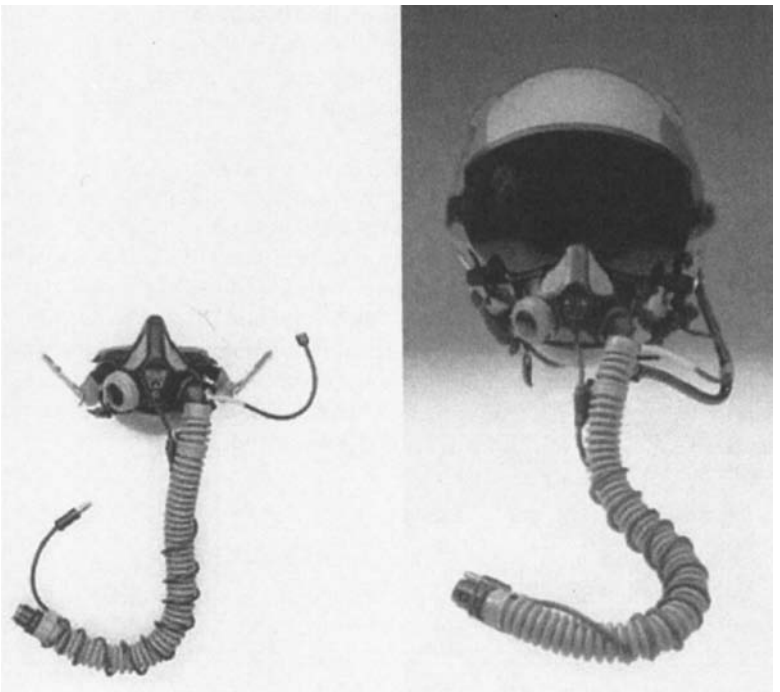


FIGURE 2-14 MBU-2X oxygen mask and connection to the aviator's helmet.

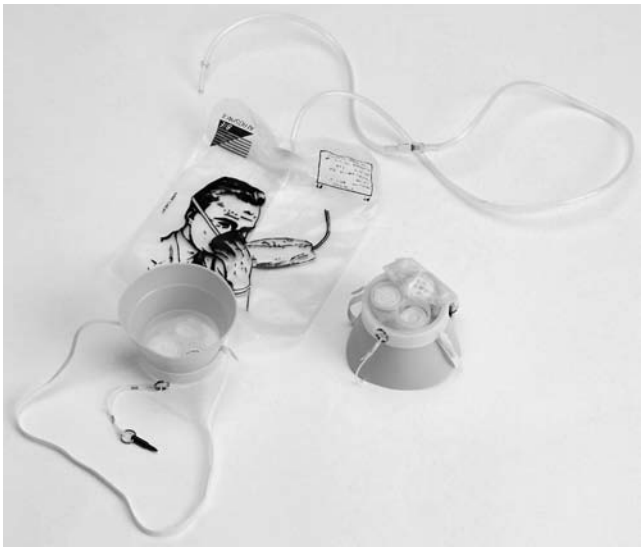


FIGURE 2-15 Passenger oxygen mask. (Courtesy of B/E Aerospace.)

Provided the absolute pressure within the suit is at least 141 mm Hg, and 100% oxygen is delivered to the respiratory tract, severe hypoxia will be prevented. However, to protect against DCS the absolute pressure within the suit should be at least 282 mm Hg, equivalent to an altitude of no higher than 25,000 ft. Some compromise can be reached so that a suit pressure of 226 mm Hg (0.3 bar, 4.3 lb/in^2), equivalent to an altitude of 30,000 ft, makes movement easier while wearing the inflated suit and, provided duration of use is relatively limited, such a pressure can be tolerated without undue difficulties.

The ability to perform extravehicular activity in the near vacuum of space requires a suit pressure of 226 mm Hg (0.3 bar, 4.3 lb/in^2) that is preceded by a period of 4 hours of breathing 100% oxygen, or a reduction in cabin pressure followed by a shorter period of 100% oxygen prebreathing (see Chapters 10 and 28). This prebreathing, or denitrogenation, removes nitrogen from the body stores thereby reducing the incidence and severity of DCS. If a higher suit pressure is available, a shorter period of denitrogenation is needed. Russian space suits have commonly been inflated to higher suit pressures, even up to 420 mm Hg (0.56 bar), although normal operating pressure is 0.4 bar or 5.88 lb/in^2.

Full pressure suits consist of a pressure garment that is impermeable to the gas which inflates the suit. This is contained within a retaining layer that prevents overexpansion on inflation. The outermost layer is a form of fabric that protects the functional elements within. Making a garment with the mechanical strength to withstand the pressure to which it is inflated is particularly difficult around joints, hands, and fingers. Nevertheless, the design of these garments has improved considerably throughout the manned space program, allowing astronauts to conduct complex physical actions while wearing a pressure suit.

Aviators need only wear pressure suits when the risk of decompression at very high altitudes exists. This is generally confined to a few high-flying reconnaissance and research aircraft. Even in the presence of an intact pressurized cabin, partial inflation of a pressure suit can provide a significant measure of protection against DCS during long, high-altitude flights.

In both aviation and space exploration, the thermal comfort of the wearer is important. A high ventilation airflow can conduct some heat away from the body. In aircraft, this can be taken from the engine compressors but a flow of oxygen to the pressure helmet is required to provide a breathing gas that allows adequate protection against hypoxia. Therefore the aircraft suit has two separate compartments. One protects against hypoxia and the other provides pressurization and thermal conditioning. It is necessary to keep the pressure difference between these two compartments as small as possible, but the pressure in the helmet must never be less than the suit body or air would be drawn into the face piece or helmet and hypoxia could ensue. Space suits are liquid cooled and have a one-compartment design.

Partial Pressure Suits

Although full pressure suits provide protection against hypoxia, DCS, and ebullism, they are expensive, complicated, and cumbersome. An alternative system that can be used to make positive pressure breathing tolerable for limited periods is based on providing a partial pressure garment assembly. Commonly this consists of a close-fitting oronasal mask that can deliver oxygen to the wearer at pressures considerably above ambient. The adverse physiological effects of positive pressure breathing include distension of the chest, reversal of the normal breathing cycle, fatigue, and circulatory disturbances leading to syncope. The application of counter-pressure over the chest can alleviate the overdistension of the chest and reduce the fatigue associated with pressure breathing. Inflation of counter-pressure garments over the limbs and abdomen reduce the circulatory disturbances too. Although this method provides no protection against DCS or ebullism it can make pressure breathing at mask pressure more than 30 mm Hg above ambient tolerable for limited periods. Therefore, this can provide short-duration protection following a loss of cabin pressurization at altitudes in excess of 50,000 ft. Immediate descent must be initiated because the degree of protection against hypoxia is limited and DCS may occur following a relatively brief exposure to such altitudes. Such systems provide very little protection against ebullism if the decompression occurs above 63,000 ft.

Lower body and lower limb counter-pressure can be provided by means of inflation of anti-G trousers. These are not being used to protect against acceleration but as an element of the high-altitude partial pressure assembly. Upper limb counter-pressure can also be used to give further circulatory support but this form of assembly is less convenient and rarely used in practice.

Advanced Life Support Systems

The advanced Life Support Systems (LSS) developed for the latest generation of combat aircraft are commonly based on

an MSOC oxygen generator, with an ejection seat–mounted emergency backup oxygen store. The pilot may wear a partial pressure assembly incorporating a chest counter-pressure garment and anti-G trousers, which may have extended body coverage, and use a demand breathing regulator that provides protection against hypoxia but also delivers positive PBG. The chest coverage element of the counter-pressure assembly can be inflated to make PBG more tolerable, and following a high-altitude decompression, the anti-G trousers can be inflated as part of the altitude protection system. Linkage between the breathing regulator and the anti-G valve automatically controls these functions, delivering the breathing gas at the pressure appropriate to requirements for altitude and G protection.

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