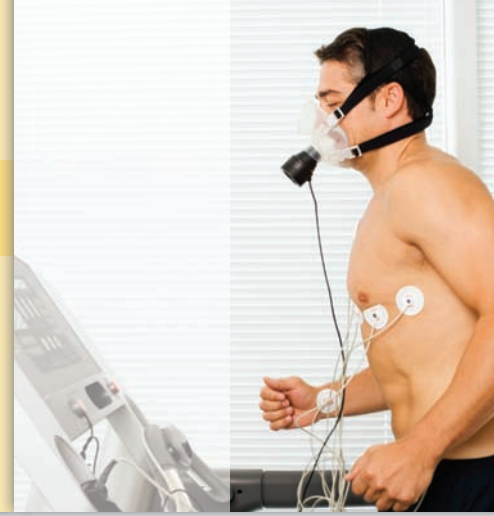


CHAPTER 1

Regulation of Ventilation



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Chapter Objectives

By studying this chapter, you should be able to do the following:

1. Describe the brain stem structures that regulate respiration.
2. Define central and peripheral chemoreceptors.
3. Explain what effect a decrease in blood pH or carbon dioxide has on respiratory rate.
4. Describe the Hering–Breuer reflex and its function.
5. Describe the chemoreceptor input to the brain stem and how it modifies the rate and depth of breathing.
6. Explain why it is that the arterial gases and pH do not significantly change during moderate exercise.
7. Discuss the respiratory muscles at rest and during exercise. How are they influenced by endurance training?
8. Describe respiratory adaptations that occur in response to athletic training.

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Brain stem The lower part of the brain connecting the brain to the spinal cord. It consists of the midbrain, pons, and medulla oblongata.

Passive expiration Lungs expel air when the alveolar pressure is higher than the atmospheric pressure.

Active expiration A forced exhalation using the internal intercostal and abdominal muscles.

Partial pressure The part of the total pressure exerted by a gas.

Passive and Active Expiration

Ventilation is controlled by a complex cyclic neural process within the respiratory centers located in the medulla oblongata of the **brain stem**. The neurons stimulate the diaphragm and external intercostals (**Figure 1-1**) to ensure that the rate, depth, and pattern of breathing at rest is sufficient to keep oxygen (O_2), carbon dioxide (CO_2), and pH at normal values.

Normal quiet breathing is accomplished primarily (~70%) by contraction of the diaphragm, which pulls the lower part of the lungs downward about 1.5 cm. Movement of the rib cage by the external intercostal muscles and several neck and chest muscles accomplishes the difference of ~30% in tidal volume change by lifting the ribs up and out. As the volume of the thoracic cavity increases, alveolar pressure falls about 1 mmHg below atmospheric pressure, and air flows into the alveoli. During exercise, the activity of the external intercostals is increased to make sure the ribs are moved up and away from the spine to assist inspiration.

During expiration, the diaphragm relaxes, and the elastic recoil of the lungs and chest compresses the lungs. The air pressure in the lungs increases above atmospheric pressure. Because alveolar pressure is now higher than atmospheric pressure, the lungs expel the air (**passive expiration**). During exercise, both the frequency of breaths (F_b ; also referred to as respiratory rate, or RR) and the depth of respiration (i.e., tidal volume; V_T) are increased.

Active expiration uses the muscles on the inside of the rib cage (internal intercostals). Contraction of these muscles pulls the ribs inward, which decreases the volume of the thoracic cavity. To help with active expiration, the abdominal muscles contract to move the diaphragm upward. During expiration, the lungs are released from the previous stretched position.

The RR and V_T are a function of an intricate mix of neural information from the brain, lungs, muscles, joints, and chemical sensors that regulates the respiratory system to maintain arterial **partial pressure** of oxygen (PaO_2) and carbon

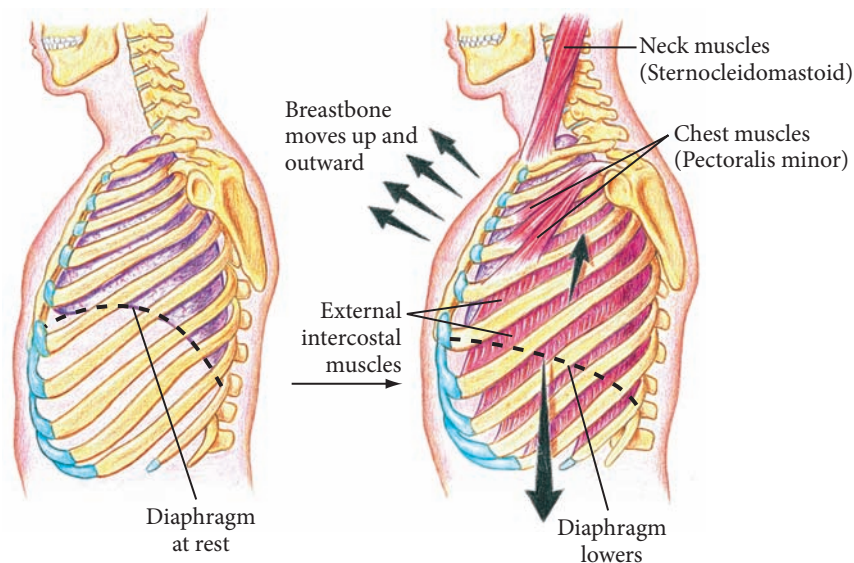


Figure 1-1 Normal inspiration.

dioxide (PaCO_2) levels in the body. The end result is normal arterial oxygen content, maintenance of the acid–base balance within the body, and alveolar ventilation that matches tissue metabolic requirements. At rest, the work of the respiratory muscles to ensure air flow is about 3–5% of the body's energy expenditure. The energy requirement of breathing during exercise is increased depending upon the resistance of the thoracic cage to stretch, compliance of the lungs, airway resistance, and the increase in metabolism of the skeletal muscles.

Respiratory Areas in the Brain Stem

The rhythmical pattern of breathing is carried out by four separate respiratory centers located in the medulla oblongata and pons (Figure 1-2). These centers control breathing whether a person is awake, asleep, or engaged in physical activity. The respiratory rhythm generated by these centers represents a neural network that is linked to pacemaker-like neurons known as the pre-Bötzinger complex located in the ventrolateral **medulla oblongata**. This complex is responsible for the activity of the **medullary respiratory (or rhythmicity) center**, which is divided into a **dorsal respiratory group** (DRG) and a **ventral respiratory group** (VRG). The dorsal group of neurons regulates the activity of the phrenic nerves to the diaphragm, which is responsible for inspiration. The ventral group controls the nerve impulses to the intercostal muscles. It is responsible for return of the thoracic cage to its original size, especially during exercise, when expiration is facilitated by contraction of the muscles that line the inside of the rib cage (internal intercostals).

Dorsal Respiratory Group

The DRG of neurons responsible for the basic rhythm of ventilation is located in the reticular formation of the medulla oblongata in the brain stem. Aside from their voluntary control over respiration during speaking, crying, laughing, singing, and other physical activities (including exercise and, particularly, strenuous exercise), the impulses originating from the DRG neurons are primarily responsible for inspiration.

Inspiratory activity is initiated by a rhythmical on–off pattern. During the “on” firing, neurons in the DRG cause the inspiratory muscles to contract. Motor neurons from the dorsal respiratory group (also termed the **inspiratory center**) innervate the diaphragm by way of bilateral phrenic nerves that originate from spinal nerves C3, C4, and C5. The inspiratory center is also responsible for stimulating the external intercostals to facilitate inspiration further. The motor neurons to the inspiratory muscles are inhibited when the motor neurons supplying the expiratory muscles are active and vice versa.

Ventral Respiratory Group

The VRG is located in the ventral part of the medulla. It consists of both inspiratory and expiratory neurons. Although it receives neural input from the DRG, it is chiefly for expiration. Both groups thus are responsible for the basic rhythm of the

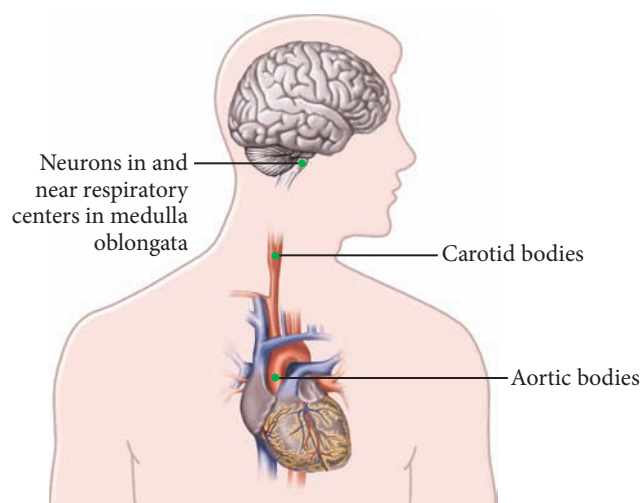


Figure 1-2 Regulation of breathing.

Medulla oblongata Part of the brain stem that controls respiratory and cardiovascular functions.

Medullary respiratory (or rhythmicity) center A collection of neurons in the reticular formation of the medulla involved in establishing or modifying the pattern of breathing.

Dorsal respiratory group Formerly the expiratory center; neurons in the medulla that generate the rhythm of breathing in response to the physiological needs of the body.

Ventral respiratory group Formerly the inspiratory area; it autorhythmically stimulates spontaneous ventilation.

Inspiratory center Region of the medulla that is active during inspiration.

Expiratory center Region of the medulla that is responsible for expiration.

Apneustic center The neurons in the brain stem that control normal respiration.

Pontine respiratory group Also known as the pneumotaxic center; located in the rostral dorsal lateral pons. It antagonizes the apneustic center.

Pneumotaxic center A neural center in the upper part of the pons that provides inhibitory impulses on inspiration and therefore prevents overdistention of the lungs.

Chemoreceptors Receptors that respond to changes in the chemical concentrations of a substance.

Central chemoreceptors Sensory nerve cells or chemical receptors located in the medulla.

Peripheral chemoreceptors A sensory neuron located outside the CNS, usually in the walls of blood vessels that respond to chemical stimuli.

Cerebrospinal fluid Fluid secreted by the choroid plexus into the ventricles of the brain.

respiratory cycle. It should be mentioned that although both groups have control over the respiratory muscles and that communication exists between the dorsal and ventral groups, the interrelationship between these groups of cells is not fully understood.

During the “off” part of the respiratory cycle, the neurons from the DRG stop firing. The inspiratory muscles relax, and passive expiration occurs. The ventral respiratory group, also known as the **expiratory center**, is a column of neurons located in the ventrolateral region of the medulla oblongata. It is primarily responsible for more forceful expiration. For example, when there is a need for more active expiration, the expiratory neurons stimulate the motor neurons to the internal intercostals and abdominal muscles.

Apneustic Center

The **apneustic center** is located in the posterior portion of the pons. It has a stimulating effect on the inspiratory center by preventing inspiratory neurons from being switched off, thus lengthening inspiration. This is accomplished by providing a constant stimulus to promote inspiration, which is inhibited by the activity of the pneumotaxic center.

Pneumotaxic Center

Located in the anterior part of the upper pons is a collection of neurons called the **pontine respiratory group**, which is more commonly termed the **pneumotaxic center**. Although the precise function of the group is unknown, it appears responsible for sending inhibitory neural impulses to the inspiratory center. Thus, its primary role is to shorten inspiration (or “switch off” the inspiratory neurons) and promote expiration. In addition to limiting the size of the tidal volume, it inhibits the impulses from the apneustic center, which helps to slow inspiration and control the rate of respiration.

Chemoreceptors

There are two groups of **chemoreceptors**. One is in the central nervous system, located on the ventrolateral surface of the medulla and bathed in brain interstitial fluid (a chemosensitive area termed the **central chemoreceptors**). These receptors are capable of responding to changes in PCO_2 and H^+ ion concentrations in the cerebrospinal fluid (CSF). The other group is located in the periphery and is exposed to the arterial blood (**peripheral chemoreceptors**). These receptors respond to increases in arterial H^+ ion concentrations and PCO_2 by sending signals to the medullary respiratory center, which, in turn, increases \dot{V}_E to correct the imbalance.

Central Chemoreceptors

At rest, most respiratory responses are mediated by specialized cells on the ventral surface of the medulla oblongata called the central chemoreceptors. These cells are sensitive to changes in CO_2 -induced H^+ ion concentrations in the brain interstitial fluid that bathes them. Because the **cerebrospinal fluid** has no protein buffers, the excess of H^+ ions (that decrease pH) in the CSF stimulates the central chemoreceptors in the medulla to increase RR and \dot{V}_T to decrease the acidity (i.e., increase pH). The excess CO_2 is exhaled into the atmosphere, and the arterial PCO_2 and H^+ ion

concentration of the CSF return to normal to maintain homeostasis of the gases. In contrast, if the levels of CO_2 and H^+ ions decrease, breathing decreases. This allows the blood concentrations of CO_2 and H^+ ions to increase.

Peripheral Chemoreceptors

The peripheral chemoreceptors are located in the arch of the **aorta** (the aortic bodies) and in the bifurcation of the internal and external carotid arteries in the neck (the carotid bodies). They sense changes in PCO_2 and H^+ ion concentrations in the arterial blood. If the PCO_2 and H^+ ion levels increase (with a decrease in pH), the peripheral chemoreceptors are strategically positioned to sense hypoxia in the arterial blood. This is accomplished by way of neural messages from the glossopharyngeal nerve (cranial nerve IX) from the carotid bodies and the vagus nerve (cranial nerve X) from the aortic bodies to the medullary respiratory center to increase \dot{V}_E (Figure 1-3). The network of neurons in the medulla then sends signals through motor neurons to the respiratory muscles to restore PCO_2 to a relatively constant level. This is done by increasing ventilation to increase CO_2 excretion and increase blood pH.

Aorta An artery that conducts blood from the left ventricle of the heart to the rest of the body.

Alveoli Grape-like sacs in the lungs designed to exchange oxygen and carbon dioxide between the air and the pulmonary blood.

Effects of Blood P_{O_2} on Ventilation

In the presence of a lack of oxygen that results in a low arterial level of oxygen content (P_{O_2} less than 60 mmHg whereby % Hb saturation drops precipitously), the carotid bodies are stimulated to send impulses to the inspiratory center to stimulate ventilation. However, it is important to point out that because a normal alveolar–capillary membrane and the high P_{O_2} of the **alveoli** allow for oxygen molecules quickly to diffuse from the alveoli to the pulmonary blood, very low P_{O_2} values should not occur. That is, given the low P_{O_2} of the mixed venous blood entering the pulmonary capillaries, the transfer of oxygen from the alveoli to the blood reaches equilibrium so rapidly that an alveolar P_{O_2} of 100 mmHg quickly translates into an arterial P_{O_2} of 100 mmHg. Thus, oxygen plays a minor role in the regulation of respiration.

Ventilation Control During Exercise

The increase in expired ventilation during exercise is proportional to the increase in the volume of oxygen consumed at the tissues. Alveolar ventilation (\dot{V}_A) may increase 20-fold during heavy exercise to keep pace with the increase in metabolic rate and the use of oxygen (\dot{V}_{O_2}) by the muscles. As the exercising muscles consume more oxygen, the increase in \dot{V}_A also keeps the arterial P_{O_2} and PCO_2 constant.

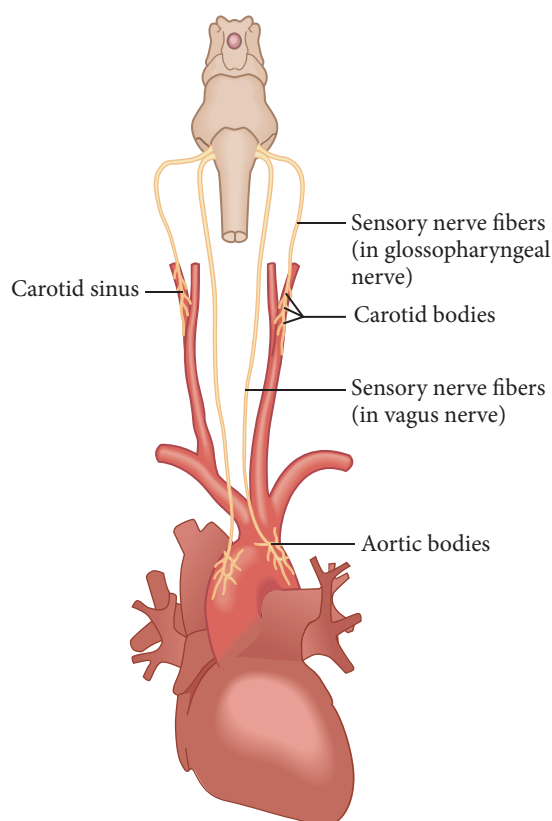


Figure 1-3 Peripheral chemoreceptors regulate the brain stem respiratory centers by means of sensory nerve stimulation.

Although both $\dot{V}O_2$ and CO_2 control ventilation, the need to remove CO_2 from the venous blood is probably more important in regulation of expired ventilation (\dot{V}_E) than is the need for O_2 at the cell level. This point is illustrated during light to moderate exercise (where $\dot{V}O_2$ is $< 2 \text{ L} \cdot \text{min}^{-1}$). Expired ventilation increases linearly with $\dot{V}O_2$, given that \dot{V}_T increases with the incremental workload. But, as $\dot{V}O_2$ approaches the $2.5 \text{ L} \cdot \text{min}^{-1}$ range, \dot{V}_E starts to deviate from linearity with $\dot{V}O_2$. The \dot{V}_E response is directly related to the need to remove CO_2 from the blood to counter a further decrease in pH. The disproportionate increase in \dot{V}_E with $\dot{V}O_2$ during graded exercise is termed ventilatory threshold (\dot{V}_T) or anaerobic threshold (AT), which typically corresponds with the steep rise in blood lactic acid (Figure 1-4).

Chemical Factors

The initial response of the respiratory system to exercise is to increase the V_T and the F_b . The ventilation (\dot{V}_E) response is driven primarily by changes in temperature and chemical status of the arterial blood. As exercise continues and becomes harder, the temperature of the muscles is increased along with the increased production of

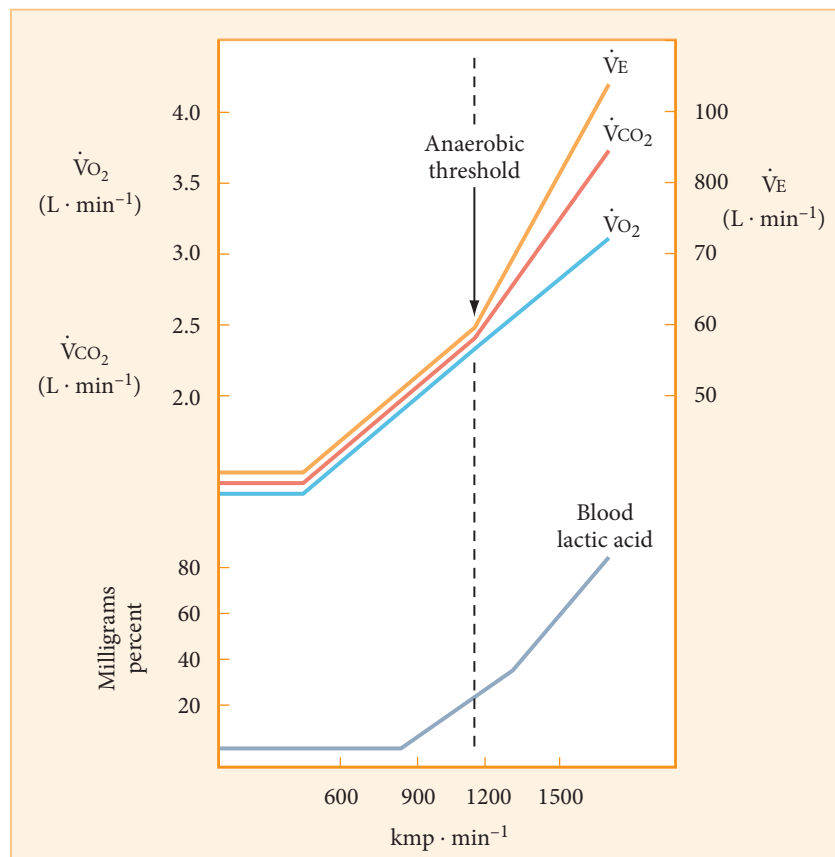


Figure 1-4 Relationship of \dot{V}_E to anaerobic threshold (AT). Expired ventilation (\dot{V}_E) and carbon dioxide production ($\dot{V}CO_2$) start to rise sharply at AT, coinciding with the steep rise in blood lactic acid.

carbon dioxide (\dot{V}_{CO_2}) from the muscles and the increased concentration of H^+ ions in the venous blood. While these factors increase the movement of oxygen from the arterial blood into the tissues, they also stimulate the inspiratory center in direct proportion to the body's metabolic needs. Once exercise is stopped, respiration takes several minutes to decrease to the resting level. The primary reason it remains elevated is to normalize the acid–base balance, PCO_2 , and blood temperature.

Effects of Blood PCO_2 and pH on Ventilation

The purpose behind the variety of methods to regulate ventilation is to ensure that the rate and depth of ventilation are normally adjusted to maintain an arterial PCO_2 of about 40 mmHg. Understandably, if ventilation is inadequate, PCO_2 is increased, and pH is decreased. This conclusion is a function of the decrease in pH due to the fact that CO_2 combines with water to form carbonic acid (HCO_3^-), which in turn releases H^+ ions into the solution. Conversely, during hyperventilation, blood PCO_2 falls, and **pH** is increased because of the excessive elimination of HCO_3^- . And yet, the oxygen content of the arterial blood remains constant. It is apparent that the blood PCO_2 and pH are affected by changes in ventilation more so than is the oxygen content. As a result, it should be clear that changes in the blood PCO_2 are primarily the most important stimulus in control of ventilation.

Proprioceptive Reflexes

At first, ventilation is increased as a function of anticipating the exercise itself. Then, as exercise gets under way, ventilation is further increased as the motor cortex sends impulses originating from body movements to the inspiratory center to increase ventilation reflexly. Thus, during exercise, the **proprioceptive reflexes** from muscle spindles, Golgi tendon organs, and joint pressure receptors are believed to help with the regulation of respiration. Although the neurogenic activity of the proprioceptive reflexes is detected by the medullary respiratory center, the increase in both depth and rate of breathing is small.

Other Factors

Other factors that play a role in the increase of ventilation during exercise include increase in body temperature, level of circulating **catecholamines** (**epinephrine** and norepinephrine), and motor impulses from the cerebral cortex. The catecholamines stimulate the nerve endings of the carotid sinus nerve, causing it to send impulses to the medullary respiratory center. In short, ventilation is regulated by an interaction of many factors that stimulate the medullary respiratory neurons. Furthermore, with exercise of a progressive intensity and effort, the work of the diaphragm may increase as much as 10-fold. The intercostals along with the expiratory abdominal muscles (internal and external obliques and transverse abdominis) significantly increase ventilation.

Hering–Breuer Reflex

This reflex is named for researchers Josef Breuer and Karl Ewald Konstantin Hering, who documented the reflex in the late 1800s. Their work demonstrated that once inspiration is under way, the lungs are prevented from overexpansion by the activation of pulmonary stretch receptors. The **Hering–Breuer reflex** arises outside the

Carbon dioxide (CO_2) The waste product of cellular metabolism.

pH A measure of the hydrogen ion concentration. A blood pH greater than 7.45 is called alkalosis. A blood pH of less than 7.35 is called acidosis.

Proprioceptive reflexes Receptor information from the musculoskeletal system.

Catecholamines A classification of hormones secreted by the adrenal medulla (epinephrine; also called adrenaline) and norepinephrine.

Epinephrine A hormone that stimulates the sympathetic nervous system.

Hering–Breuer reflex Mechanism that controls respiration via pulmonary fibers of the vagus nerves.

respiratory center in the brain. Stretch receptors in the smooth muscles of the walls of the bronchi and bronchioles respond to the air inflating the lungs. The reflex is mediated by the vagus nerve, which sends information to the medulla oblongata to terminate inspiration. This is a protective reflex. As the expiratory phase begins, the receptors are no longer stretched, impulses are no longer sent, and inspiration can begin again. The stretch receptors are probably not used during normal respiration but become more active during increased breathing associated with vigorous exercise.

Ventilation Response During Exercise

Within seconds of the beginning of exercise, expired ventilation increases very rapidly. The increase occurs too fast to be explained by changes in metabolism or blood gases. This means that the abrupt increase in ventilation must be triggered by other pathways. One in particular is the activation of motor pathways to bring about specific motor movements. These pathways have collateral fibers that stimulate the respiratory center. Moreover, the beginning stages of exercise (i.e., body movements) stimulate joint receptors that communicate with the respiratory center by way of ascending sensory nerve tracts.

As exercise continues at a steady-state level, ventilation tends to level off in about 5 min. As long as the exercise remains constant and there is sufficient oxygen to generate energy within the muscles (for muscle contraction), the average PO_2 , PCO_2 , and pH approximate resting values. However, if the exercise continues to increase in intensity, the changes in blood gases and pH play a more important role in regulation of ventilation. Stopping the exercise helps to normalize blood gases and pH, resulting in a sudden decrease in ventilation with a relative slow return toward resting values.

After endurance training, V_T at rest is usually unchanged. During submaximal and maximal exercise, V_T is increased along with an increase in alveolar ventilation. Frequency of breaths is slightly lower at rest and during submaximal exercise. At maximal exercise, f_b is slightly increased. Expired ventilation is generally unchanged or slightly decreased at rest and during submaximal exercise. In male athletes, maximal ventilation ($\dot{V}_{E\max}$) values are higher ($180\text{--}200 \text{ mL} \cdot \text{min}^{-1}$) compared with those of female athletes ($130\text{--}140 \text{ mL} \cdot \text{min}^{-1}$).

The capacity to increase ventilation is usually not considered as a limiting factor in the oxygen transport system ($\dot{V}_{O_2\max}$). Even with a 5- to 6-fold increase ($25\text{--}30 \text{ L} \cdot \text{min}^{-1}$) in cardiac output (\dot{Q}) relative to rest ($\sim 5 \text{ L} \cdot \text{min}^{-1}$), the transit time for red blood cells (erythrocytes) through the pulmonary capillaries is sufficient for oxygenation. Also, because the ventilation to cardiac output (ventilation/perfusion ratio; \dot{V}/\dot{Q}) can increase 5- to 6-fold during exercise, ventilation has a far greater capacity for increasing than does **cardiac output**.

Regular aerobic exercise improves $\dot{V}_{O_2\max}$ by structurally improving the heart and respiratory system, thereby making them more efficient in the delivery of oxygen to the working tissues. In addition to the enormous reserves of the lung at rest, the increases in the diffusing capacity of the membrane, and the increase in alveolar ventilation, the infrastructure of the muscles improves its capacity to use oxygen to produce more energy for muscle contraction. In particular, the number and size of mitochondria increase (along with the oxidative enzymes), as do the number of capillaries. As a result of these changes, the range for $\dot{V}_{O_2\max}$ is generally about

Cardiac output (\dot{Q}) The volume of blood pumped by the heart in 1 min.

65–85 mL of O_2 per kilogram of body weight per minute ($\text{mL} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$) in distance runners, 45–65 $\text{mL} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$ in non-distance athletes (football players), and 25–45 $\text{mL} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$ in sedentary college-aged subjects. The highest value that has been recorded is 94 $\text{mL} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$ in a male cross-country skier.

Ventilation Equivalent for Oxygen (\dot{V}_E/\dot{V}_{O_2})

The ventilation equivalent for oxygen is the ratio of \dot{V}_E ($\text{L} \cdot \text{min}^{-1}$) to \dot{V}_{O_2} ($\text{L} \cdot \text{min}^{-1}$). It is a good indication of the economy of respiration. At rest, given an average \dot{V}_E of $6 \text{ L} \cdot \text{min}^{-1}$ and an average \dot{V}_{O_2} of $0.25 \text{ L} \cdot \text{min}^{-1}$, \dot{V}_E/\dot{V}_{O_2} is 24 L of air breathed per liter of oxygen consumed. That is, the ratio indicates that 24 L of air must be respired to achieve a \dot{V}_{O_2} of 1 L. During light to moderate steady-state exercise, the range for \dot{V}_E/\dot{V}_{O_2} is 23–28 L of air per liter of \dot{V}_{O_2} . Ventilatory equivalent increases linearly with \dot{V}_{O_2} primarily as a function of V_T rather than F_b .

Figure 1-5 illustrates that with higher intensities of exercise, the increase in chemicals that drive the respiratory centers increases \dot{V}_E/\dot{V}_{O_2} above 28 L of air per liter of \dot{V}_{O_2} . Subject A's \dot{V}_E and \dot{V}_{O_2} of $95 \text{ L} \cdot \text{min}^{-1}$ and $2.7 \text{ L} \cdot \text{min}^{-1}$, respectively, during a non-steady-state exercise bout on the cycle ergometer at $1200 \text{ (kpm} \cdot \text{min}^{-1})$ produced a \dot{V}_E/\dot{V}_{O_2} ratio of 35 L of air per liter of \dot{V}_{O_2} consumed. The sharp upward increase in \dot{V}_E to \dot{V}_{O_2} is the point of ventilation threshold (\dot{V}_T) that correlates well with lactate threshold. The excess ventilation results from the increase in CO_2 in relation to buffering lactate that associates with an increase in anaerobic glycolysis. Theoretically, ventilation of a larger volume of air requires greater activity of the muscles of \dot{V}_E , which requires a greater percentage of the \dot{V}_{O_2} . This means there will be less oxygen available to the skeletal muscles involved in the exercise activity.

The more economical the respiratory effort is during exercise, the lower the \dot{V}_E/\dot{V}_{O_2} ratio. As expected, endurance training decreases the ratio and, therefore, indicates that the respiratory work is decreased during submaximal exercise. As an example, subject B's \dot{V}_E and \dot{V}_{O_2} of $75 \text{ L} \cdot \text{min}^{-1}$ and $2.7 \text{ L} \cdot \text{min}^{-1}$ at the same exercise intensity as that of subject A yields a ratio of 28 L of air breathed per liter of O_2 consumed. The lower \dot{V}_E/\dot{V}_{O_2} ratio of subject B indicates that the work of the respiratory system is properly matched to the need of the tissues for oxygen. Or, stated somewhat differently, the \dot{V}_E/\dot{V}_{O_2} ratio can be used as an index of ventilator efficiency. With endurance training, the athlete's lungs adapt by increasing the efficiency of gas exchange. So, for a given exercise intensity, the athlete will not need as high a \dot{V}_E for a given \dot{V}_{O_2} .

The training effect is achieved by specific oxidative adaptations within the muscles of the lower limbs that decrease lactate, which is responsible for the increase of breathing frequency. The decrease in breathing frequency is matched by an increase in V_T , thus allowing for an increase in oxygen extraction from the inspired air. With the respiratory muscles using a smaller percentage of the exercise \dot{V}_{O_2} , more oxygen is available to the active muscles.

Expired ventilation increases linearly with exercise \dot{V}_{O_2} until anaerobic threshold (AT) is reached.

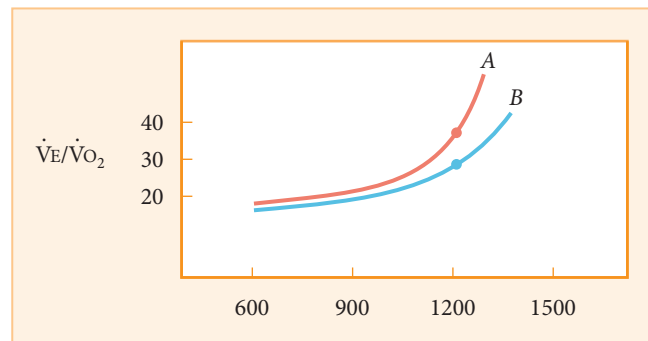


Figure 1-5 The lower \dot{V}_E/\dot{V}_{O_2} of subject B at $1200 \text{ kpm} \cdot \text{min}^{-1}$ compared with 35 for subject A indicates a more economical respiratory response.

At 55–70% of $\dot{V}O_2\text{max}$, ventilation increases dramatically in response to the increase in energy derived from glycolysis. This increases lactic acid and, ultimately, results in more CO_2 that stimulates the chemoreceptors which then signal the inspiratory center to increase \dot{V}_E . At low levels of exercise, the increase in ventilation is caused mainly by an increase in V_T . At higher work intensities, the increase in Fb accounts for most of the increase in exercise ventilation. Anaerobic threshold can be estimated when the ratio of $\dot{V}_E/\dot{V}O_2$ rises sharply while the ratio of minute ventilation to carbon dioxide $\dot{V}_E/\dot{V}CO_2$ remains constant.

Ventilation Equivalent for Carbon Dioxide ($\dot{V}_E/\dot{V}CO_2$)

The $\dot{V}_E/\dot{V}CO_2$ is the ratio of the volume of air expired (\dot{V}_E) to the volume of carbon dioxide produced ($\dot{V}CO_2$). It is an excellent indication of anaerobic threshold (also known as ventilation threshold), given that $\dot{V}_E/\dot{V}O_2$ increases in accordance with the exercise intensity without an increase in $\dot{V}_E/\dot{V}CO_2$. The ratio remains constant, thus indicating that \dot{V}_E is removing the excess nonmetabolic carbon dioxide. However, when the $\dot{V}_E/\dot{V}CO_2$ ratio begins to plateau for several workloads and then increases gradually with continued increase in exercise intensity, it indicates that the increase in carbon dioxide is disproportionate to the body's need to provide oxygen (Figure 1-6).

Ventilation Limitations to Exercise

Fortunately, aside from the highly trained athlete, there are few ventilation limitations during exercise. The lungs are very efficient at preventing an increase in carbon dioxide or a decrease in the partial pressure of oxygen in the alveoli. Respiratory muscles are well designed to sustain prolonged submaximal exercise (< 75% of $\dot{V}O_2\text{max}$). The diaphragm, in particular, has a cellular infrastructure that is significantly better adapted than skeletal muscles to the development of energy. This is primarily due to an increase in oxidative capacity (i.e., increased concentrations of oxidative enzymes and mitochondria) above that of other muscles.

Although the pulmonary ventilation can limit physical activity in people with severe asthma or obstructive respiratory disorders, airway resistance and gas diffusion do not limit exercise in healthy subjects. The tidal volume is roughly 500 mL for an average subject and may increase to about 2400–2600 mL in strenuous exercise of a short duration. The lungs are fully adaptable to an increase in \dot{V}_E from about $6 \text{ L} \cdot \text{min}^{-1}$ to 120 or 200 $\text{L} \cdot \text{min}^{-1}$ (or even higher) in heavy exercise for short periods of time. This is the equivalent of a 20- to 30-fold increase in ventilation over resting values.

By comparison, the heart can only increase cardiac output (\dot{Q}) by 5- to 7-fold with exercise (i.e., 25–35 $\text{L} \cdot \text{min}^{-1}$, respectively). Yet, the 7-fold or even higher increases in \dot{Q} among elite endurance athletes can occasionally have a limiting effect on the exchange of gas at the alveolar–capillary membrane. The problem is that the extremely fast blood flow through the pulmonary capillaries decreases transient time to the point of significantly reducing arterial oxygenation.

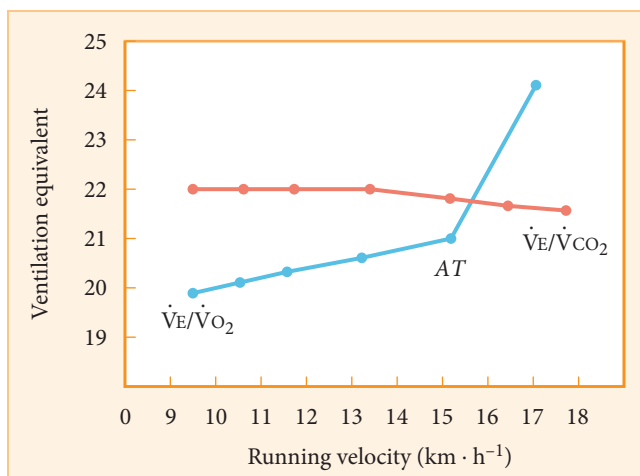


Figure 1-6 Changes in $\dot{V}_E/\dot{V}CO_2$ and $\dot{V}_E/\dot{V}O_2$ during increased intensity of running. Note the breakpoint of the anaerobic threshold.

Energy Cost of Breathing

Gas exchange requires expenditure of energy. The respiratory muscles at rest require on average 4% of the body's energy expenditure, which is the same as the body's "resting oxygen consumption" ($\dot{V}O_2$). The average $\dot{V}O_2$ for a 70-kg subject is $\sim 250 \text{ mL} \cdot \text{min}^{-1}$; energy cost of breathing at rest would be $10 \text{ mL} \cdot \text{min}^{-1}$ (e.g., 250×0.04). Divide this value by 1000 to convert $\dot{V}O_2$ in $\text{mL} \cdot \text{min}^{-1}$ to $\text{L} \cdot \text{min}^{-1}$, which is $0.01 \text{ L} \cdot \text{min}^{-1}$. Once $\dot{V}O_2$ is in liters, kilocalories of energy is calculated as the cost of respiration at rest. Because every liter of oxygen consumed is equal to approximately 5 kcal, the energy cost of respiration at rest is approximately $0.05 \text{ kcal} \cdot \text{min}^{-1}$. Clearly, the oxygen cost of breathing at rest is a small fraction of the total resting $\dot{V}O_2$.

As \dot{V}_T and RR increase with the transition from rest to exercise, the increased activation of the diaphragm and intercostal muscles along with the abdominal muscles increases the energy cost of respiration. The range is typically from 10% to 12% of the exercise $\dot{V}O_2$, which corresponds to a range of 10% to 15% of the exercise cardiac output (\dot{Q}). Given that 600 kilopond meters per minute ($\text{kpm} \cdot \text{min}^{-1}$) of work on the cycle ergometer requires a $\dot{V}O_2$ of $1.50 \text{ L} \cdot \text{min}^{-1}$, the total body energy cost of 1 min of exercise is $7.5 \text{ kcal} \cdot \text{min}^{-1}$. If the energy cost of respiration during exercise is 11%, respiration during exercise requires approximately $0.825 \text{ kcal} \cdot \text{min}^{-1}$.

As to cardiac output, 600 $\text{kpm} \cdot \text{min}^{-1}$ would require about $12.58 \text{ L} \cdot \text{min}^{-1}$ [given the regression equation $\dot{Q} = 6.12 \times \dot{V}O_2 (\text{L} \cdot \text{min}^{-1}) + 3.4$]. About 15% (or $1.9 \text{ L} \cdot \text{min}^{-1}$) of the exercise \dot{Q} goes to the diaphragm, the intercostal muscles, and the abdominal muscles to increase the rate and depth of ventilation during exercise. It is clear that training increases the strength and endurance of the respiratory muscles. Because training improves pulmonary function, trained individuals have lower ventilation values during exercise and, therefore, higher ventilation efficiency than those of untrained subjects. More oxygen goes to the skeletal muscles and less to the respiratory muscles (Figure 1-7).

Although the oxygen cost of respiration is not a limiting factor in athletic performance, it is reasonable to think that the pulmonary system (like other systems in the body) has a limit to its capacity to sustain or increase its gas exchange capabilities during extreme high-intensity exercise (85–95% of $\dot{V}O_{2\text{max}}$). Whether it is a matter of diaphragm fatigue leading to arterial hypoxemia or an interaction between the respiratory muscles and a reflex increase in sympathetically mediated vasoconstriction of the limb muscles remains to be determined.

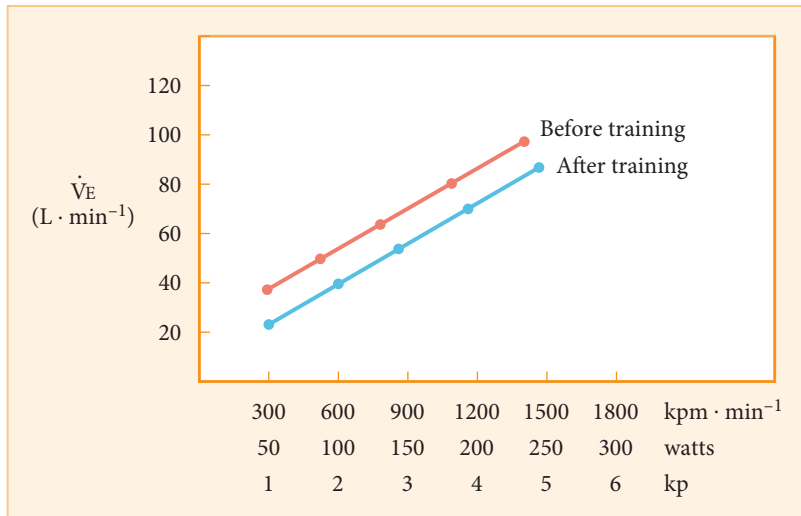


Figure 1-7 Effects of endurance training on \dot{V}_E during incremental exercise.

Study Questions

1. Where are the respiratory centers located, and what the central and peripheral regulators maintain respiration?
2. What are the chemical stimuli that help to regulate respiration?
3. What are factors throughout the body that stimulate ventilation?
4. Describe how ventilation changes during a graded exercise.
5. What is the ventilatory equivalent for oxygen? How is it calculated?
6. Explain why expired ventilation and perfusion need to be balanced to optimize gas exchange at the alveolar–pulmonary capillary membrane.
7. What is the ventilatory equivalent for carbon dioxide? How is it calculated?
8. Discuss the control of ventilation during steady-state exercise.
9. Explain why pulmonary ventilation does not limit endurance exercise performance among healthy people and athletes.
10. Why does the cost of ventilation increase with exercise?

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