Chapter 37

Pulmonary Disease

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Introduction

Patients with pulmonary dysfunction are often difficult to anesthetize safely. Most preanesthetic and anesthetic drugs depress respiratory function, further compromising patients with pulmonary disease and/or dysfunction. Knowledge of normal respiratory physiology and effective techniques for respiratory support is essential to provide favorable anesthetic outcomes.

Physiology of Ventilation

The primary function of the lungs is to exhale carbon dioxide generated by body metabolism and oxygenate venous blood. Alveolar ventilation can be assessed by measuring arterial carbon dioxide partial pressure ($PaCO_2$) or end-tidal carbon dioxide partial pressure ($ETCO_2$). Many factors can alter the ventilatory pattern (Table 37.1): (a) arterial carbon dioxide tension, (b) arterial pH, (c) arterial oxygen tension, (d) pulmonary stretch and upper airway receptors, (e) thermoregulation, (f) sensory input, and (g) emotional factors.[1] No conscious control is necessary to sustain ventilation.

The ventilatory control system is an integrated series of complex feedback loops made up of sensors, controllers, and effectors. The principal ventilatory receptors or sensors are (a) the peripheral carotid-body chemoreceptors (located at the bifurcations of the carotid arteries), (b) the central chemoreceptors (located near the surface on the ventrolateral aspect of the medulla oblongata), and (c) receptors sensing stretch, irritation, and proprioception in the lungs, airways, and muscles of respiration. The carotid-body chemoreceptors are responsive to oxygen and stimulate respiration when hypoxemia is present. The central chemoreceptors respond to carbon dioxide and stimulate ventilation when hypercarbia (respiratory acidosis) is present. Increased ventilation caused by metabolic acidosis may be mediated through either the central or peripheral chemoreceptors or the controllers of the ventilatory feedback loop located in the brain.[2] Automaticity of breathing is governed by specialized regions in the brain stem. The cortex controls voluntary and behavioral modifications of ventilation, and respiratory rhythm is controlled by the medulla. Control functions are integrated both centrally (brain stem) and peripherally (spinal cord). The effectors of ventilation are the muscles of respiration and include the intercostal muscles, the diaphragm, and the muscles of the upper airways.

Many preanesthetic and anesthetic agents can alter a patient's ventilatory pattern. Most preanesthetic and anesthetic agents alter ventilation by altering either the threshold or sensitivity of the respiratory centers to carbon dioxide and/or by relaxing the muscles of ventilation.[3]

Effects of Preanesthetic and Anesthetic Drugs on Ventilation

Most preanesthetic and anesthetic drugs depress respiratory function, thereby further jeopardizing a patient with respiratory dysfunction. Drugs depress or stimulate ventilation by acting directly or indirectly on one or more of the elements of the ventilatory control system.[4] Drugs used to treat respiratory disease may have significant interactions with anesthetics and anesthetic adjuncts.[5]

Atropine and glycopyrrolate decrease airway resistance by causing direct dilation of the airways. Atropine also increases respiratory dead space by dilating the larger bronchi. Both drugs will increase the viscosity of airway secretions.

Phenothiazine tranquilizers have minimal effects on ventilation at therapeutic doses, although large doses can depress ventilation. They decrease respiratory rate, but this is usually compensated for by an increase in tidal volume. Phenothiazines do not delay the central respiratory center response (threshold) to increases in arterial carbon dioxide, although the maximum ventilatory response (sensitivity) may be decreased.[3]

The α_2-adrenergic agonists (e.g., xylazine, detomidine, and medetomidine) vary in their pulmonary depressant effects and are somewhat unpredictable. Their depressant effects may range from mild to significant, depending on dose and individual patient response.[6] As with all general central nervous system (CNS) depressants, this effect is more pronounced in patients already suffering from respiratory distress caused by pneumonia, hydrothorax, or pneumothorax. When used in higher doses, α_2-adrenergic agonists may cause mucous membrane color to darken or appear cyanotic. Whereas cyanotic mucous membranes are normally interpreted as arterial hypoxemia and severe respiratory insufficiency, with α_2-adrenergic agonists the mechanism (and significance) is different. Arterial oxygen partial pressure is usually normal or near normal in these patients. The origin of the

Table 37.1. Factors affecting the ventilatory pattern

Arterial carbon dioxide tension
Arterial pH
Arterial oxygen tension
Pulmonary stretch and upper-airway receptors
Heat regulation
Sensory input
Emotional factors

increased concentration of desaturated hemoglobin in the mucous membranes is increased oxygen extraction during capillary transit rather than arterial hypoxemia. Oxygen extraction increases due to decreased tissue blood flow and increased capillary transit time. Vital organ blood flow (e.g., in the kidney, liver, and brain) may not decrease to the same extent as flow to superficial tissues (e.g., skin, mucous membranes, and skeletal muscle); therefore, the degree of darkening of the mucous membranes may not represent vital organ hypoxia. When α_2-adrenergic agonists are administered, the term *cyanosis* may not accurately reflect the true physiological status of the patient.

The benzodiazepine tranquilizers (diazepam and midazolam) usually produce minimal respiratory depression at therapeutic doses. However, both drugs have produced significant respiratory depression in isolated cases. This may be especially true when higher doses are administered intravenously.

Opioids are potentially respiratory depressant. The depression is drug and dose dependent, and may occur at doses that do not produce marked CNS depression or analgesia. The opioids directly depress the pontine and medullary centers, causing a decrease in respiratory rate and tidal volume. They also produce a delayed response (altered threshold) and a decreased response (altered sensitivity) to increases in arterial carbon dioxide.[3] The panting observed in some dogs after opioid administration (e.g., hydromorphone or oxymorphone) may be caused by an initial stimulation of the respiratory centers and/or alteration of the thermoregulation center.

The barbiturates are respiratory depressants. At anesthetizing doses, the respiratory centers of the brain are depressed. The barbiturates can depress both the respiratory rate and tidal volume, and thus minute ventilation. Barbiturates also produce a delayed response (altered threshold) and a decreased response (altered sensitivity) to increases in arterial carbon dioxide and depress the carotid-aortic chemoreceptors.

Dissociative anesthetics (ketamine and tiletamine) may have a dual effect on ventilation. They may affect ventilation at two or more anatomical sites, causing stimulation at one and depression at another. Both drugs can produce apneustic ventilation; that is, a ventilatory pattern characterized by a prolonged pause after inspiration. Although the respiratory rate may decrease, the tidal volume usually remains normal. In general, these respiratory alterations do not affect gas exchange or transport of gases to and from the lungs. However, in some patients, the dissociative agents can produce marked hypoxia and hypercarbia, especially when additional CNS-depressant drugs, such as tranquilizers, sedatives, or opioids, are used in combination with them. Dissociative agents do not depress the pharyngeal or laryngeal reflexes, and they may be activated with stimulation. Therefore, patients may be more prone to laryngospasm, bronchospasm, and coughing. Dissociative agents increase salivation and respiratory secretions, sometimes resulting in aspiration and respiratory obstruction. For this reason, the use of an antimuscarinic in combination with these drugs may be indicated.

Propofol is an injectable anesthetic that produces respiratory depression in much the same manner as the barbiturates. The incidence of apnea with propofol is comparable to that with barbiturates, but the duration of apneic episodes may be slightly longer. Etomidate is a carboxylated imidazole that can produce mild to moderate dose-dependent respiratory depression. Apnea following administration of propofol or etomidate can usually be avoided by limiting the rate of administration to achieve tracheal intubation.

The inhalant anesthetics halothane, isoflurane, sevoflurane, and desflurane depress ventilation by decreasing tidal volume. These anesthetics typically increase respiratory rate but not adequately to compensate for the decrease in tidal volume. Potent inhalation anesthetics increase the set point at which arterial carbon dioxide initiates spontaneous ventilation (i.e., the *apneic threshold*). The degree of elevation in apneic threshold is directly related to the depth of anesthesia. Inhaled anesthetics decrease the slope of the carbon dioxide response curve. There is both a delayed response (altered threshold) and a decreased response (altered sensitivity) to increases in arterial carbon dioxide. Inhaled anesthetics also depress the ventilatory response to hypoxemia, and the interaction between hypoxemia and hypercarbia in stimulating ventilation is greatly attenuated or eliminated by even moderate concentrations of these agents.

Nitrous oxide induces minimal respiratory depression. However, because of its low potency requiring high inspired concentrations and to prevent hypoxemia, this agent should be used cautiously, if at all, in patients with pulmonary dysfunction.

Anesthetic Considerations in Patients with Respiratory Dysfunction

Patients with pulmonary dysfunction may lack the ability to expand their lungs properly (extrapulmonary dysfunction) and/or may have impairment of oxygen and carbon dioxide transfer across the alveolar membranes (intrapulmonary dysfunction). Examples of extrapulmonary dysfunction include diaphragmatic hernia, pneumothorax, hydrothorax, space-occupying lesions of the thorax, flail chest, and any condition that restricts chest wall expansion. Examples of intrapulmonary dysfunction include pneumonia, pulmonary edema, intrapulmonary hemorrhage (contusions), atelectasis, interstitial disease, and upper-airway, tracheal, or bronchial obstruction.

Patients with respiratory dysfunction can be placed in one of four categories:

Category I: Dyspnea does not occur with exertion.
Category II: Dyspnea occurs with moderate exertion.

Category III: Dyspnea occurs with mild exertion.
Category IV: Dyspnea occurs at rest.

Patients in categories III and IV are at higher anesthetic risk. A thorough preanesthetic evaluation should be done on all patients with respiratory dysfunction. The thorax should be physically examined, and thoracic radiographs should be taken if the patient can tolerate handling and positioning without experiencing distress. Radiographs are valuable for arriving at a diagnosis, but the magnitude of the functional impairment is best measured with arterial blood-gas analysis. An ECG, arterial blood-gas analysis, baseline complete blood count, serum biochemistry panel, and serum electrolyte concentrations should be obtained.

Blood-gas analysis on an arterial sample obtained while the patient is breathing a low fraction of inspired oxygen (F_iO_2), such as room air ($F_iO_2 = 0.21$), and a high F_iO_2 is used by some to assess the ability of supplemental oxygen to improve arterial partial pressure of oxygen and calculate a pulmonary shunt fraction before administering anesthetic drugs. The oxygen partial pressure (PaO_2)-FiO_2 ratio is a simple way to quantify the ability to oxygenate at different levels of FiO_2. Dividing the value for PaO_2 by the decimal value of FiO_2 yields the ratio. A normal ratio is 500 (i.e., PaO_2 of 100 mm Hg divided by FiO_2 of 0.21). A PaO_2-FiO_2 ratio of 300 to 500 is consistent with mild disease, whereas a value of 200 represents significant pathology. This value is less accurate than the traditional alveolar-arterial gradients because it does not reflect the influence of PCO_2.[7] If a patient experiences cyanosis or respiratory distress when breathing a low F_iO_2, supplemental oxygen should not be withheld to obtain a measurement that can be estimated using an arterial sample collected during oxygen supplementation (e.g., alveolar-arterial gradient).

If possible, surgery and anesthesia should be delayed in patients with pneumonia, pulmonary edema, lung contusions, atelectasis, pneumothorax, and/or hydrothorax to allow time for these problems to be addressed and the condition of the patient to improve. A thoracentesis should be done in patients with moderate to severe pneumothorax or hydrothorax prior to anesthesia, and in some cases a chest tube may be needed.

Patients with respiratory dysfunction should be preoxygenated for 5 to 7 min prior to anesthetic induction.[8] A mask, nasal catheter, or oxygen chamber may be used. Supplemental oxygen should be immediately available both preoperatively and postoperatively.

Mild preanesthetic sedation may be necessary to enable the patient to be handled without causing stress and exacerbating dysfunction. Preanesthetic drugs that induce minimal respiratory depression should be considered. Several preanesthetic drugs or combinations may be used, such as the combination of acepromazine and butorphanol. Acepromazine is a phenothiazine derivative tranquilizer that produces minimal respiratory depression, especially in low doses. Butorphanol is a synthetic, opioid agonist-antagonist. Butorphanol can produce a dose-related respiratory depression similar to morphine; however, butorphanol seems to reach a ceiling beyond which higher doses do not cause significantly more depression.

After a patient has been sedated, rapid induction of anesthesia may be needed to gain quick control of the airway to enable positive pressure ventilation. Rapid anesthetic induction may be accomplished by intravenous administration of thiopental, propofol, etomidate, or ketamine. A rapid mask induction using desflurane, isoflurane, or sevoflurane may be used; however, because of the patient's inability to ventilate properly, this technique may result in delayed anesthetic induction and excessive struggling. Whichever induction technique is used, the trachea must be intubated rapidly and accurately.

Anesthesia is best maintained with an inhalant anesthetic and controlled or positive pressure ventilation. Nitrous oxide should be used with care in patients with respiratory dysfunction. It can increase the severity of a pneumothorax, and it should be discontinued if cyanosis is evident. Even if a patient with respiratory compromise seems to have adequate spontaneous ventilation, assisted or controlled ventilation is desirable unless a resolving pneumothorax is present and the patient's $PaCO_2$ and PaO_2 can be maintained at an acceptable level with spontaneous ventilation. High airway pressures from positive pressure ventilation in these patients may result in rapid development of a tension pneumothorax that requires immediate thoracentesis. Pulse oximetry, $ETCO_2$, and arterial blood-gas monitoring should be used to monitor respiratory status in these patients.

Controlled Ventilation

In spontaneously ventilating patients, the respiratory muscles increase the size of the thoracic cavity, the volume within it increases, and the pressure in the thorax falls. Thus, the intrapulmonary pressure falls, and the difference between the intrapleural pressure and alveolar pressure overcomes the elasticity of the lungs while the difference between the alveolar pressure and the pressure at the oral-pharyngeal area overcomes the airway resistance. There is a great difference between the intrapleural and alveolar pressures, and a small difference between the oral-pharyngeal pressure and airway resistance. The net effect is movement of air into the alveoli from the upper airway.

In contrast, controlled ventilation is usually *positive pressure* ventilation. Air is forced into the alveoli under pressure. Intrapleural pressure and intrapulmonary pressure increase during controlled ventilation. Controlled ventilation may be provided manually (by squeezing the rebreathing bag) or mechanically (using a ventilator).

One of three methods can be used to control a patient's ventilation and take over ventilatory effort: The patient can be hyperventilated to decrease the arterial carbon dioxide levels and decrease the stimulus for ventilation; the patient's anesthetic level can be increased (deepened); or the patient can be paralyzed by using peripherally acting muscle relaxants. Of the three methods, hyperventilating the patient (i.e., manually or mechanically increasing the patient's respiratory rate and depth) is the easiest and is usually quite effective.

Five components can be adjusted in the ventilatory cycle during controlled ventilation (Table 37.2): (a) peak airway pressure, (b) mean airway pressure, (c) length of inspiratory phase, (d) length of expiratory phase, and (e) the inspiratory-expiratory

Table 37.2. Adjustable components of the respiratory cycle during mechanical ventilation

Peak airway pressure
Mean airway pressure
Length of inspiratory phase
Length of expiratory phase
Inspiratory-expiratory ratio

ratio. Peak airway pressures are measured by a pressure manometer in the anesthesia circuit. Peak airway pressures of 15 to 20 cm water are necessary to overcome lung resistance to expansion in dogs and larger species. In cats, slightly higher pressures may be needed. Decreased lung compliance will increase the peak airway pressures needed to expand the lungs. An increase in airway resistance will increase the peak airway pressure needed to expand the lungs.

The mean airway pressure is the average pressure generated during the inspiratory and expiratory phases of positive pressure ventilation. Mean airway pressure should be kept low by minimizing the duration of positive airway pressure. Mean airway pressure most closely correlates with decreases in cardiac output.

To produce minimal cardiovascular alteration, the inspiratory phase should be shorter than the expiratory phase. Typically, the inspiratory phase should last 1 to 1.5 s. Prolonged holding of the tidal volume at peak airway pressure will not increase tidal exchange but will increase mean airway pressure and intrathoracic pressure, thereby decreasing venous return and cardiac output. The expiratory phase should begin as soon as the inspiratory phase is complete. The increased pressure within the lung must be allowed to return to 0 cm water pressure as soon as possible to prevent this preload impairment. The inspiratory-expiratory (I-E) ratio is very important during controlled or positive pressure ventilation. The inspiratory phase should be at least one-third and no more than one-half of the total ventilatory cycle. An I-E ratio of 1:2 or 1:3 will help provide an adequate period for proper cardiac filling. A 1:2 ratio will provide for a ventilatory rate of approximately 20 cycles per minute. A 1:3 or 1:4 ratio provides for a rate of 15 or 12 breaths per minute, respectively.

Although controlled or positive pressure ventilation is usually safe and effective, if it is done improperly, harmful side effects can occur.[9,10] As already described, interference with cardiac output can occur during controlled or positive pressure ventilation. During spontaneous ventilation, the intrapleural pressure at the height of inspiration is approximately a negative 8 to 10 cm water. This augments the movement of blood in the great veins into the chest (thoracic pump). However, during controlled or positive pressure ventilation, the intrapulmonary pressure increases and may reach plus 3 to 5 cm water pressure. Only during expiration is the intrapulmonary pressure the same in spontaneous ventilation and controlled ventilation. Increased alveolar pressure will also decrease pulmonary blood flow. This is why maintenance of proper peak and mean airway pressures and a proper I-E ratio is critical during ventilatory support of anesthetized patients.

Lung damage or *volutrauma* is a potential complication during positive pressure ventilation. Volutrauma (e.g., overextension or expansion of the lung tissue by excessive pressure) can range from mild trauma producing minimal alveolar hemorrhage to severe trauma producing airway rupture and a tension pneumothorax. Maintaining proper peak and mean airway pressures will help minimize pulmonary trauma.[11] A major airway blowout that occurs during positive pressure ventilation is often caused by excessive peak airway pressures and/or preexisting lung pathology. Vigilant monitoring of the anesthetic circuit's adjustable pressure limiting (e.g., pop-off) valve is crucial to preventing this type of misadventure.

Acid-base balance will be altered in accordance with changes in alveolar ventilation. Hyperventilation will cause a decreased arterial carbon dioxide level and an increased pH (alkalemia). Hyperventilation can also lead to cerebral vasoconstriction and may reduce cerebral perfusion pressure such that cerebral hypoxia occurs.[12] Hypoventilation will lead to increased arterial carbon dioxide and a decreased pH (acidemia), which may adversely increase intracranial pressure and lead to brain ischemia and/or herniation.

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