Respiratory Failure

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Practice Gap

The primary cause of cardiopulmonary arrest in children is unrecognized respiratory failure. Clinicians must recognize respiratory failure in its early stage of presentation and know the appropriate clinical interventions.

Objectives

After completing this article, readers should be able to:

1. Recognize the clinical parameters of respiratory failure.
2. Describe the respiratory developmental differences between children and adults.
3. List the clinical causes of respiratory failure.
4. Review the pathophysiologic mechanisms of respiratory failure.
5. Evaluate and diagnose respiratory failure.
6. Discuss the various clinical interventions for respiratory failure.

WHAT IS RESPIRATORY FAILURE?

Respiratory failure is a condition in which the respiratory system fails in oxygenation or carbon dioxide elimination or both. There are 2 types of impaired gas exchange: (1) hypoxemic respiratory failure, which is a result of lung failure, and (2) hypercapnic respiratory failure, which is a result of respiratory pump failure (Figure 1). (1)(2)

In hypoxemic respiratory failure, ventilation-perfusion ($\dot{V}/\dot{Q}$) mismatch results in the decrease of Pao_2) to below 60 mm Hg with normal or low $Paco_2$. (1) In hypercapnic respiratory failure, $\dot{V}/\dot{Q}$ mismatch results in the increase of $Paco_2$ to above 50 mm Hg. Either hypoxemic or hypercapnic respiratory failure can be acute or chronic. Acute respiratory failure develops in minutes to hours, whereas chronic respiratory failure develops in several days or longer. In acute hypercapnic respiratory failure, the pH decreases below 7.35, and, for patients with underlying chronic respiratory failure, the $Paco_2$ increases by 20 mm Hg from baseline. (2) Acute and chronic hypoxemic respiratory failure cannot be readily distinguished from arterial blood gases. Clinical markers, such as polycythemia, pulmonary hypertension, or cor pulmonale, indicate chronic hypoxemia.

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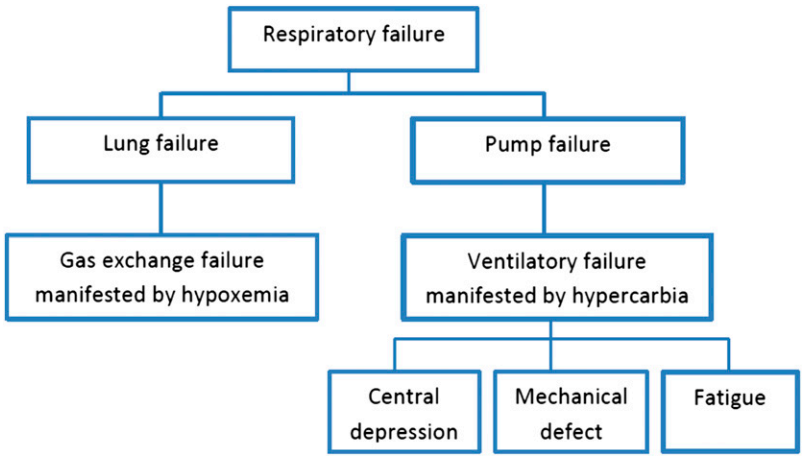
ABBREVIATIONS

ECMO	extracorporeal membrane oxygenation
VAP	ventilator-associated pneumonia
$\dot{V}/\dot{Q}$	ventilation perfusion

Figure 1. Types of respiratory failure.



EPIDEMIOLOGY

Infants and young children have a higher frequency of respiratory failure. (3)(4) Approximately half of respiratory failure cases are seen in the neonatal period, resulting from complications of prematurity and transitioning to extrauterine life. In addition, developmental differences between children and adults also explain the higher incidence. (1)(3)(4) First, infants and young children have a smaller upper airway, with the subglottic area being the narrowest. Any inflammatory process can result in airway narrowing and subsequently in increased work of breathing. Second, immature stages of lung growth and development present with fewer numbers of alveoli, smaller intrathoracic airway caliber with little cartilaginous support, and underdeveloped collateral ventilation, predisposing infants to atelectasis. Third, infant respiratory muscles have reduced type 1 muscle fibers, specifically the diaphragm, resulting in lower respiratory tract muscle bulk and reserve. Fourth, the chest wall is more compliant than in adults because of a less bony thorax, compromising thoracic expansion, and may result in accessory muscle use and paradoxical patterns of respiration. Fifth, bradypnea, apnea, or tachypnea commonly results from the immaturity of the respiratory center. All these factors result in a higher metabolic demand per kilogram of body weight, resulting in increased work of breathing and early fatigue.

PATHOPHYSIOLOGY

Respiration involves the nervous, cardiovascular, musculoskeletal, and respiratory systems. The causes of respiratory failure can come from any of these systems and are expansive. Common causes can be grouped based on underlying conditions, such as lung and airway disorders, respiratory pump failure, respiratory center failure, and failure to meet increased metabolic needs (Table 1).

The pathophysiologic mechanisms that lead to respiratory failure involve primarily either $\dot{V}/\dot{Q}$ mismatch or impairment of oxygen transfer at the alveolar-capillary membrane. (1)(2)(5) $\dot{V}/\dot{Q}$ mismatch most commonly contributes to respiratory failure. During gas exchange, perfusion and ventilation try to match each other ($\dot{V}/\dot{Q}=1$). (6) However, both do not perfectly match, even in healthy lungs. During alveolar ventilation, some capillary units are underperfused, whereas others are overperfused. Similarly, during perfusion, some alveolar units are underventilated, whereas others are overventilated. A high $\dot{V}/\dot{Q}$ ratio is when the alveoli are well ventilated but are not well perfused. High $\dot{V}/\dot{Q}$ ratios act like dead space. A low $\dot{V}/\dot{Q}$ ratio is when the alveoli units are well perfused but are not well ventilated. Low $\dot{V}/\dot{Q}$ ratios act like shunts.

Diffusion limitation is the impairment of transfer of oxygen at the alveolar-capillary membrane. (1)(2)(6) This can result from alveolar or interstitial inflammation and fibrosis. Diffusion limitation usually coexists with $\dot{V}/\dot{Q}$ mismatch.

These 2 common pathophysiologic mechanisms of respiratory failure are observed in a variety of diseases. Pulmonary conditions that involve the bronchi (eg, status asthmaticus and bronchiolitis) or inflammation or infection of the parenchyma (eg, pneumonia, aspiration, cystic fibrosis, and ciliary dysmotility) result in airway obstruction and/or parenchymal loss, leading to $\dot{V}/\dot{Q}$ mismatch and impaired gas exchange. Specifically, status asthmaticus occurs because of progression of airway inflammation, bronchospasm, and mucous plugging during days to weeks or sudden onset of asphyxia from bronchospasm. In either case, airway obstruction causes $\dot{V}/\dot{Q}$ mismatch, incomplete alveolar gas exchange, and lung

TABLE 1. **Causes of Respiratory Failure**

Lung and airway disorders
Lung parenchyma
• Bronchiolitis
• Severe asthma
• Aspiration
• Pneumonia
• Pulmonary edema
• Cystic fibrosis
Airway
• Laryngotracheobronchomalacia
• Croup
• Tracheitis
• Vascular malformations (ring, sling, right-sided aortic arch)
• Subglottic stenosis, complete tracheal ring
Respiratory pump failure
• Restrictive lung disorders (kyphoscoliosis)
• Chest wall abnormalities: congenital or traumatic (flail chest)
• Neuromuscular disorders (phrenic nerve paralysis, myopathies, muscular dystrophies)
• Diaphragmatic disorders (paralysis, congenital diaphragmatic hernia)
Respiratory center failure
• Brain injuries (traumatic)
• Central nervous system infection (controlled mechanical ventilation) or hypoxic encephalopathies
• Drug overdose or adverse effects
• Congenital (leukomalacia) or genetic disorders (congenital hypoventilation syndrome)
Failure to meet increased metabolic needs
• Septic shock

hyperinflation. End-expiratory alveolar pressure increases as a result, creating an autopositive end-expiratory pressure state. Work of breathing is increased to overcome the autopositive end-expiratory pressure for inspiratory flow to occur, eventually leading to inspiratory muscle fatigue and respiratory failure. (7) In cystic fibrosis, similarly, an acute pulmonary exacerbation can result in airway obstruction and mucous plugging, leading to $\dot{V}/\dot{Q}$ mismatch and reduced functional residual capacity. Increased work of breathing results in respiratory muscle fatigue, leading to hypoventilation, hypercarbia, and respiratory failure. In addition to $\dot{V}/\dot{Q}$ mismatch, impairment of gas exchange at the alveolar-capillary membrane is observed in progressive cystic fibrosis disease with pulmonary fibrosis and destruction. (8) Obstruction from infectious causes, foreign-body aspiration, burn injuries, anaphylaxis, or decreased muscle tone from depressed consciousness or neuromuscular disorders can result in complete or partial airway obstruction. Complete obstruction causes asphyxia, where the lungs are not ventilated but well perfused. Adequate airflow is usually initially observed in partial obstruction. As airflow obstruction increases from either a valvelike effect in foreign-body aspiration or airway inflammation and mucous secretions, respiratory failure can occur. (9) Central nervous system disorders include congenital malformations, such as absent corpus callosum; abnormal central control of respiration, such as periodic breathing; apnea of prematurity; central apnea; Ondine curse; acquired injuries, such as head trauma; intracranial bleeding; hypoxic ischemic encephalopathy; and cerebral palsy. In these conditions, respiratory efforts are inadequate and hypoventilation or apnea ensues, resulting in carbon dioxide retention and respiratory failure. (10)

CLINICAL PRESENTATIONS

The clinical presentations of respiratory failure depend on the underlying cause and the level of hypoxemia and hypercapnia. Infants and children most commonly present with increased work of breathing: tachypnea, grunting, nasal flaring, and retractions. (3)(11) These signs of increased work of breathing are blunted in those with neuromuscular disorders. These patients instead present with tachypnea and shallow breathing without retractions.

Additional signs and symptoms of respiratory failure may be observed, depending on the level of hypoxemia and hypercapnia (Table 2). (4) Impending respiratory failure can present as dyspnea, mood changes, disorientation, pallor, or fatigue. With acute hypercapnia, flushing, agitation, restlessness, headache, and tachycardia can occur. Children with chronic respiratory failure often present with worsening hypercapnia and hypoxemia. Reduced consciousness or coma and depressed tendon reflexes occur with severe chronic carbon dioxide retention. Cyanosis, polycythemia, cor pulmonale, and pulmonary hypertension are complications of chronic hypoxemia.

HISTORY AND PHYSICAL EXAMINATION

Determining whether there is any need for emergency intervention is the first step in assessing a patient with respiratory failure. Vital signs, work of breathing, and level

TABLE 2. **Signs and Symptoms of Hypoxia and Hypercapnia**

HYPOXIA	HYPERCAPNIA[a]
Mild	Mild
• None or depressed efficiency	• Flushed skin • Headaches
Moderate	Moderate
• Dyspnea	• Tachypnea
• Headaches, dizziness	• Tachycardia
• Fatigue	• Dyspnea
• Pallor	• Muscle twitches, depressed tendon reflexes
• Tachycardia, cardiac arrhythmias	• Drowsiness, confusion
• Hypertension • Mood changes: euphoria, disorientation, or depression • Ataxia, tingling	• Hypertension
Severe	Severe
• Cyanosis	• Papilledema
• Hypotension • Bradycardia • Visual impairment • Loss of consciousness, seizures, coma	• Coma

[a]In chronic hypercapnia, signs and symptoms of hypercapnia are observed when P_{CO_2} increases above baseline level.

of consciousness indicate which patients require immediate respiratory support. Respiratory support should be urgently provided for a patient with significant tachypnea, retractions, grunting, nasal flaring, and head bobbing. (11) Delay in respiratory support may lead to the patient becoming increasingly fatigued, resulting in shallow breathing, reduced consciousness, and cyanosis. Emergency intubation and mechanical ventilation should be initiated when such impending signs of respiratory failure are assessed. Airway control and ventilatory support should also be initiated in patients with impending cardiac arrest or central nervous system disorders with decreased responsiveness. (3)(11)

After determining whether emergency respiratory intervention is necessary, the next step is to obtain a comprehensive history to evaluate for likely causes of the respiratory failure. Risk factors, such as prematurity, immunodeficiency, anatomical abnormalities, and chronic pulmonary, cardiac, or neuromuscular disorders (eg, cystic fibrosis, asthma, unrepaired congenital heart disease, myasthenia gravis, or spinal muscular dystrophy) must be identified. (4) Additional factors, such as history of fevers, symptoms of respiratory infection (cough, rhinorrhea, or nasal congestion), history of seizures, head trauma, or possible exposures to sedatives, must be noted. (3)(4)

For the physical examination, vital signs are very helpful to indicate the severity of the respiratory failure. (3)(11) Tachypnea is a sensitive indicator of respiratory disease. Increased respiratory rate is one of the earliest compensatory mechanisms of respiratory failure. However, respiratory rates can be elevated during infancy, sleeping, eating, and increased activity in healthy children. Heart rate also increases to maintain adequate oxygen delivery. Blood pressure can be initially normal or high. When respiratory failure is in the decompensated phase, low blood pressure occurs. Pulse oximetry saturation estimates the oxygen saturation of hemoglobin. A 90% oxygen saturation on pulse oximetry correlates with a Pao_2 of 60 mm Hg based on the sigmoid shape of the oxyhemoglobin dissociation curve (Figure 2). (6) Pulse oximetry measures only saturation. It does not measure oxygen content or delivery. Thus, pulse oximetry has several limitations. The oxygen saturation can be falsely high with an elevated carboxyhemoglobin level in a patient with carbon monoxide or methylene chloride poisoning. (12) Carbon monoxide binds to hemoglobin with much greater affinity than oxygen, leading to tissue hypoxia. It also causes a left shift of the oxyhemoglobin dissociation curve, thereby decreasing the release of the oxygen and causing further tissue hypoxia. In a patient with an elevated methemoglobin level, the pulse oximetry saturation tends to be overestimated. In patients with poor tissue perfusion due to shock, hypovolemia, or hypothermia, the pulse oximetry is unable to detect the oxygen saturation accurately; these patients may have falsely low oxygen saturation.

The initial step of the physical examination of respiratory failure is assessing the work of breathing. (3)(11) One should assess the respiratory rate and quality, keeping in mind age-specific norms. When tachypnea is accompanied by retractions, nasal flaring, or grunting, respiratory support with either noninvasive or invasive positive pressure is needed. Bradypnea is often observed in respiratory center failure, indicating the need for emergency respiratory intervention. Bradypnea or hypoventilation is also observed in patients with neuromuscular disorders. These patients have shallow and ineffective breathing and usually do not present with retractions. In these patients, spirometric measurements with forced vital capacity less than 40% correlate with carbon dioxide retention and nocturnal hypoventilation. When assessing the respiratory rate, the chest wall should also be inspected. Asymmetric chest expansion indicates

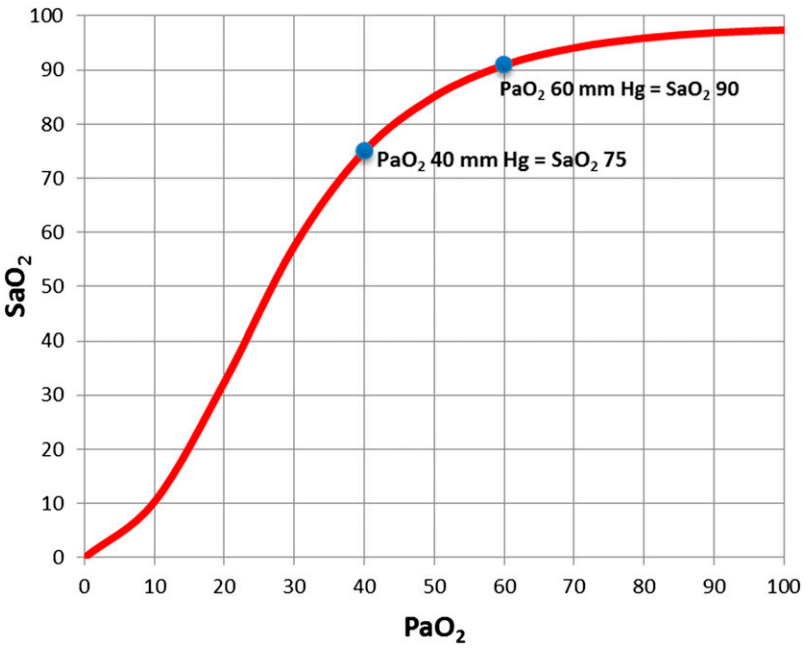


Figure 2. Oxygen dissociation curve.

possible pneumothorax, moderate to severe empyema or pleural effusion, or chest trauma. Paradoxical movement of the chest and abdomen during inspiration and expiration signals respiratory distress.

Auscultation of the chest provides information about the symmetry and quality of air movement and the presence of abnormal breath sounds. (3)(11) Wheezing can be heard on inspiration or expiration. Typically, expiratory wheeze reflects disease of the lower airways, such as asthma. In acute moderate to severe asthma, inspiratory wheeze may accompany expiratory wheeze. A local or asymmetric wheeze can indicate possible airway obstruction due to a foreign body or a mass. Stridor is a high-pitched inspiratory wheeze usually caused by upper airway narrowing or obstruction in such conditions as laryngomalacia, croup, tracheitis, subglottic stenosis, or vascular rings. Crackles or rales are heard when alveoli open and imply small airway diseases, such as pneumonia, congestive heart failure, pulmonary fibrosis, or other interstitial pulmonary processes.

In addition to the respiratory examination, examination of the heart for any abnormal heart sounds is important for assessing heart conditions that can lead to respiratory failure. (3)(11) Furthermore, a neurologic examination is also pertinent by assessing for mental status changes with the Glasgow Coma Scale. (4) Neurologic impairment is observed when the Glasgow Coma Scale score is low. A score of 8 or below indicates severe neurologic compromise. At this level of altered mental status, the patient is not able to control his or her airway and secretions. Intubation and mechanical ventilation are required. Aside from assessing for mental status changes, the neurologic examination should also include examination of muscle strength. Conditions in which muscle strength are decreased, such as mitochondrial diseases, Guillain-Barre syndrome, spinal muscular atrophy, or Duchenne muscular dystrophy, lead to respiratory failure. (3)(4)

DIAGNOSIS

Laboratory and radiographic studies are helpful in the assessment of respiratory failure and the monitoring of the response to therapeutic management. However, emergency respiratory support should be initiated when indicated and not be delayed while awaiting results of diagnostic studies.

Laboratory studies, such as an arterial blood gas, end-tidal carbon dioxide, oxygen saturation, a complete blood cell count with differential, and renal and liver functions, should be performed. The arterial blood gas accurately measures the extent of the gas exchange abnormality and confirms the type and chronicity of respiratory failure. (4) Normal arterial blood gas values are as follows: pH 7.4 (reference range, 7.38–7.42); P_{O_2}, 80 to 100 mm Hg; P_{CO_2}, 35 to 45 mm Hg; oxygen saturation, 95% on room air; bicarbonate, 22 to 26 mEq/L; and base excess, −2 to +2 mEq/L. In acute respiratory failure, P_{aO_2} is less than 60 mm Hg, pH is below 7.35, P_{aCO_2} is greater than 50 mm Hg, and serum bicarbonate concentration is low or normal. In chronic carbon dioxide retention, carbon dioxide is increased, pH

is normal, and serum bicarbonate concentration and base excess are increased. The arterial blood gas of the patient with an opiate overdose differs based on the severity of the overdose. In mild to moderate opiate overdose, respiratory acidosis is observed with a pH below 7.35, $Paco_2$ greater than 50 mm Hg, and a low or normal serum bicarbonate concentration. In severe opiate overdose, a mixed respiratory and metabolic acidosis is observed. End-tidal carbon dioxide is measured from expired air from the nose by a capnometer and is a common and reliable tool used in the emergency department and critical care setting.

The complete blood cell count helps to assess such causes as infection, anemia, or polycythemia. In addition, respiratory, blood, urine, and pleural cultures and polymerase chain reaction can be performed when indicated to identify the specific bacterial cause. Renal and liver function tests provide clues to the cause of or identify complications associated with respiratory failure. Electrolyte abnormalities, such as hypernatremia or hyponatremia, cause seizures, and hyperkalemia causes cardiac arrhythmia.

Chest radiography should be performed in patients who present with respiratory failure to help identify or confirm the cause of the respiratory failure. If a cardiac cause of acute respiratory failure is suspected, electrocardiography and echocardiography should be performed.

Pulmonary function testing evaluates the functional status of the respiratory system by measuring the volume and flow of air movement, gas exchange, and strength of the respiratory muscles. Pulmonary function testing includes a group of tests, such as spirometry, lung volumes, diffusion capacity, and maximal respiratory pressures, among others. It helps to determine the characteristics of the respiratory disease and to guide management. Pulmonary function testing is not typically performed when the patient is critically ill. Flexible bronchoscopy can also be performed to aid in diagnosis and therapeutic management.

Biopsies and bronchoalveolar lavage for microbiologic, cytologic, and histologic testing can be obtained with bronchoscopy. When a patient is critically ill, it may not be safe to perform the bronchoscopy because manipulation of the airway may induce bronchospasm or atelectasis.

MANAGEMENT

Early diagnosis, close monitoring, and timely intervention are of utmost importance in a patient presenting with respiratory distress. (3)(4) The primary cause of cardiopulmonary arrest in children is unrecognized respiratory failure. Interventions in a patient with respiratory failure range from close monitoring and supplemental oxygen to full respiratory support with mechanical ventilation. The initial step in the treatment of a patient with respiratory failure is rapid assessment of airway, breathing, and circulation to determine whether the patient needs urgent intervention. Indications for intubation and mechanical ventilation include the patient's inability to maintain an adequate airway and protect the airway from aspiration, failure of oxygenation and ventilation, and deteriorating status that will lead to inability to maintain airway patency and normal gas exchange.

The initial step and most basic airway management for a patient in respiratory failure is bag-mask ventilation, which allows for oxygenation and ventilation until a more definitive airway can be established. Although the patient is receiving bag-mask ventilation, necessary equipment (endotracheal tube, large-bore suction, fiberoptic scope, laryngoscope, carbon dioxide detector, and intubation drugs) can be prepared for intubation. (4) When possible, intubation should be performed by the most experienced medical professional (emergency care personnel, critical care physicians, and anesthesiologists) to ensure successful intubation and to avoid multiple unsuccessful attempts. Failure to

TABLE 3. **Interpretation of Blood Gas Results**[a]

CONDITION	pH	$Paco_2$	BASE EXCESS
Acute respiratory acidosis or acute hypoventilation	↓	↑	↔
Acute respiratory alkalosis or acute hyperventilation	↑	↓	↔
Acute or chronic respiratory acidosis	↓	–/↑	↑
Acute metabolic acidosis with respiratory compensation	↓	↓	↓
Chronic respiratory acidosis with metabolic compensation	Normal/slightly ↓	↑	↑

↓=*decrease;* ↑=*increase;* ↔=*no change.*

quickly secure an adequate airway can lead to morbidity or death.

Sedative agents alone or in conjunction with paralytic agents are used for intubation. When a difficult airway is anticipated (eg, Pierre Robin syndrome or anterior mediastinal mass), paralytic agents are avoided, and the patient is intubated in a more awake state or with a fiberscope. If successful intubation is unlikely, the airway can be secured with a laryngeal mask airway. (3) The laryngeal mask airway is a supraglottic airway device used as an important alternative airway device in the emergency setting when a very difficult airway is encountered. Placement of the laryngeal mask airway does not require laryngoscopy or paralytic agents. Although it is an easier device to secure an adequate airway, the laryngeal mask airway does not protect against aspiration.

Once patients are evaluated and emergency intervention with intubation and mechanical ventilation is not indicated, mild cases of respiratory failure may require only close monitoring and supplemental oxygen as needed by low- or high-flow nasal canula or a nonrebreather mask.

A nonrebreather mask can deliver a higher amount of oxygen (10–15 L/min) than a nasal cannula. (4) Respiratory drive in patients with chronic respiratory failure is stimulated primarily by hypoxia. Improving oxygenation in these patients can lead to blunting of the hypoxic drive of the respiratory center, resulting in decreased alveolar ventilation and increased carbon dioxide retention and leading to acute respiratory failure on top of chronic respiratory failure.

Noninvasive ventilation is used to manage both acute and chronic respiratory failure. (10)(13) It is now commonly used not only in the emergency department and critical care setting but also in the patients' homes. It is indicated in patients who are cooperative and have increased work of breathing or respiratory muscle fatigue. It is contraindicated in patients with altered mental status, cardiac instability, and inability to protect the airway because of a weak cough or swallowing. Its use in the pediatric intensive care unit is associated with decreased intubation rates. (14) Modes of noninvasive ventilation include continuous positive airway pressure or bilevel positive airway pressure. The positive pressure can be delivered through a variety of interfaces (mouthpiece, oronasal face mask, nasal pillow, or helmet mask). Continuous positive airway pressure provides a continuous level of positive airway pressure during the entire respiratory cycle to keep the airways open. Bilevel positive airway pressure provides an inspiratory positive airway pressure and an expiratory positive airway pressure. The inspiratory positive airway pressure is generated as the patient breathes in, providing effective inspiratory volume expansion, whereas the expiratory positive airway pressure is generated as the patient breathes out, maintaining positive end-expiratory pressure to prevent airway collapse and to keep the lungs expanded. Common complications of noninvasive ventilation include facial pressure skin injury from prolonged use, dry mucous membranes, and thickened secretions.

Positive pressure ventilation or mechanical ventilation is most commonly used to manage acute respiratory failure. (5) The goal of mechanical ventilation is to relieve respiratory distress by decreasing the inspiratory work of breathing, improving pulmonary gas exchange, allowing the lungs to heal, reversing respiratory muscle fatigue, and preventing further complications due to abnormal gas exchange. There are several types of mechanical ventilators that offer different modes and features. Mechanical ventilators provide positive pressure ventilation by pressure-limited ventilation or volume-limited ventilation. In pressure-limited ventilation, the gas is allowed to flow into the lungs until a preset airway pressure limit is reached, at which time a valve opens, allowing exhalation to ensue. In volume-limited ventilation, gas flows to the patient until a preset volume is delivered to the ventilator circuit, even if this entails a very high airway pressure. One of the factors to consider when deciding which ventilator to use is the mode of mechanical ventilation or the method of inspiratory support. There is limited evidence-based research to demonstrate that the mode affects clinical outcomes; therefore, the decision on which mode to use is based on the capability of available ventilators to manage small infant volumes and clinicians' experience with the mechanical ventilators. Common modes of mechanical ventilation include controlled mechanical ventilation, assist control, synchronized intermittent mandatory ventilation, and pressure support ventilation. In the controlled mechanical ventilation mode, the ventilator delivers a preset minute ventilation (preset tidal volume and respiratory rate), and the patient cannot trigger additional breaths above what is set. This mode is usually used for patients who are paralyzed, heavily sedated, or comatose. In the assist control mode, minimum minute ventilation is set, and the patient can trigger additional breaths. If the patient fails to trigger a breath within a selected time, the ventilator delivers the breaths. The assist control mode is not appropriate when the patient is ready to wean off the ventilator because it gives a full breath each time. The synchronized intermittent mandatory ventilation mode allows the patient to increase minute ventilation by preset breath rate synchronized with spontaneous breathing, rather than patient-initiated ventilator breathing as in the assist control mode. In the pressure

support ventilation mode, the ventilator delivers a preset pressure support level while the patient triggers each breath because there is no preset minute ventilation. In addition to these conventional modes of ventilation, high-frequency ventilation is commonly used, especially in premature neonates. The high-frequency oscillatory ventilator delivers small tidal volumes by oscillating air movements at an extremely rapid rate (300–1500 breaths per minute). A Cochrane review concludes no difference in benefit between high-frequency oscillatory ventilation compared with conventional ventilation in preterm infants. (15) A previous study found that length of mechanical ventilation, intensive care unit length of stay, and mortality were significantly higher in high-frequency oscillatory ventilation patients compared with the controlled mechanical ventilation patients ages 1 to 18 years who were hospitalized in the pediatric intensive care unit of a diverse group of hospitals that care for children in the United States. (16)

Newer modalities include neurally adjusted ventilatory assist and proportional assist ventilation. These modalities of assisted ventilation require that the patient spontaneously breathes and the delivered airway pressure changes, depending on the patient's breathing effort; thus, varying degrees of unloading of work by the respiratory muscles on inspiration on a breath by breath basis are delivered. In the neurally adjusted ventilatory assist, an esophageal sensor represents neural output from the respiratory center, controlling the timing and magnitude of the delivered pressure. (17)

Ventilator complications include infection and lung injury. Ventilator-associated pneumonia (VAP) has been described more in adult than children. The estimated incidence of VAP in pediatrics is 3 per 1000 ventilator-days. (18) Objective diagnosis of VAP is not well defined, even in adults. In a prospective study of a sample of children in the pediatric intensive care unit, Srinivasan et al (18) found that VAP was more likely in patients who were female, had undergone surgery, were taking narcotics, and were fed enterally. In 2011, the Centers for Disease Control and Prevention formed a VAP Surveillance Definition Working Group. Guidelines outline the identification of patients with respiratory status deterioration (eg, increased need of inspired oxygen or positive end-expiratory pressure) after having been stable while receiving ventilatory support; evidence of respiratory infection with abnormal white blood cell count, culture, or temperature; and initiation of antibiotic therapy. (19)

Ventilator-induced lung injury is another potential complication of mechanical ventilation. Ventilator-induced lung injury is a result of alveolar overdistension and cyclic atelectasis from high pulmonary pressure and oxygenation. The most common risk factor for ventilator-induced lung injury is acute respiratory distress syndrome. Strategies to prevent ventilator-induced lung injury include using small tidal volumes that range from 6 to 8 mL/kg, applying positive-end expiratory pressure, and maintaining a low plateau airway pressure of 30 cm H_2O or less. (20)(21)(22) These strategies are based on adult studies.

In premature infants particularly, prolonged mechanical ventilation not only leads to acute complications, such as infection and lung injury, but also results in long-term sequelae, such as chronic lung disease and neurodevelopmental delays. Strategies to minimize these complications include preservation of spontaneous breathing by applying patient-triggered and volume target ventilation, administering respiratory stimulants (eg, caffeine), and using nasal continuous positive airway pressure or nasal intermittent positive pressure ventilation after extubation. (23)

Extracorporeal membrane oxygenation (ECMO) can be considered when all other options have failed and the respiratory failure is a result of a reversible underlying illness. (24)(25) ECMO provides cardiopulmonary support extracorporeally to prevent further lung injury from high-pressure ventilation and allow the lungs to heal. ECMO was initially used almost exclusively in neonates. Its use to support older pediatric patients has increased throughout the years. In the past 5 years, there have been approximately 300 to 500 cases annually. (25) Relative contraindications for ECMO include patients who have irreversible respiratory or cardiac failure, who cannot undergo anticoagulation, and who undergo ventricular assist device implantation. Complications include bleeding, thromboembolism, and heparin-induced thrombocytopenia. (26) Prognosis depends primarily on the underlying illness. Mortality remains approximately 43%. Risk factors associated with death include older patient age, other nonpulmonary organ dysfunction, prolonged use of mechanical ventilation (>2 weeks) before ECMO, prolonged ECMO support, and complications during ECMO. (25)(26)

A small group of severely compromised children may require prolonged mechanical ventilation. Overall, their prognosis is good compared with adults. Outcomes data reveal that 65% of children who require a post–acute rehabilitation facility for prolonged weaning are eventually discharged to home and that 45% of children discharged to pulmonary rehabilitation were weaned on discharge. (27)(28) Weaning protocols have been established for the management of chronic respiratory failure in children. (29)

Summary

- On the basis of research evidence, (1)(2) numerous diseases and conditions can impair gas exchange, resulting in failure to meet the body's metabolic demands and leading to respiratory failure.
- On the basis of consensus, (1)(2)(7)(8)(9)(10) the clinical presentations of respiratory failure depend on the underlying cause and the level of hypoxemia and hypercapnia. Early diagnosis, close monitoring, and timely intervention are of utmost importance.
- On the basis of research evidence, (5)(14)(25) interventions range from noninvasive methods, such as close monitoring and supplemental oxygen, to full respiratory support with mechanical ventilation and in extreme cases even the use of extracorporeal membrane oxygenation.

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PIR Quiz

1. You are seeing 2 brothers ages 2 months and 6 years, respectively, for upper respiratory tract infection. Rapid antigen testing suggests infection with respiratory syncytial virus. Which of the following factors is most important in placing the younger sibling at greater risk of developing respiratory decompensation compared with his older brother?
    A. Decreased accessory muscle use.
    B. Decreased airway size.
    C. Decreased chest wall compliance.
    D. Decreased lung compliance.
    E. Greater reliance on mouth breathing.
2. Which of the following is a clinical marker of chronic hypoxemia?
    A. Depressed tendon reflexes.
    B. Flushed skin.
    C. Papilledema.
    D. Polycythemia.
    E. Tachypnea.
3. A 10-month-old girl presents with poor feeding, fever, cough, and respiratory difficulty for the last 2 days. Physical examination reveals axillary temperature of 38.9°C, respiratory rate of 65 breaths per minute, and heart rate of 170 beats per minute. Respirations are labored with nasal flaring and intercostal retractions. Auscultation of chest reveals diffuse crackles (rales) and wheezing throughout the chest. There are alternating periods of drowsiness and agitation. Use of 100% oxygen at 15 L/min via a nonrebreather face mask is initiated. Pulse oximetry recording reveals 93% oxygen saturation. Which of the following will prompt you to proceed with tracheal intubation and mechanical support of respiration?
    A. Arterial blood gas revealing Pa_{O_2} less than 60 mm Hg on currently administered oxygen.
    B. Arterial blood gas revealing pH less than 7.25 and P_{CO_2} less than 60 mm Hg.
    C. Chest radiograph revealing diffuse alveolar interstitial infiltrates.
    D. Lack of improvement after a trial of nebulized albuterol inhalation.
    E. No new information is necessary, so the patient should undergo tracheal intubation and mechanical support of respiration now.
4. A 12-year-old boy presents with tingling, numbness, and weakness of his lower extremities for 1 day. The weakness has gradually progressed, and now he is unable to walk. Physical examination reveals a comfortable-appearing child with normal sensorium. He is afebrile, with a respiratory rate of 18 breaths per minute and a heart rate of 74 beats per minute. Respiratory pattern appears normal. He has sensory loss to pinprick up to the midabdomen. He has decreased muscle strength: grade II/V in the lower extremities and IV/V in the muscles of the hand. He appears to have normal strength in his shoulders and arms. He has good gag and cough reflexes. Deep tendon reflexes are absent in the lower extremities and diminished in the upper extremities. The rest of his physical examination findings are normal. Which of the following is the best method of determining need for assisted ventilation?
    A. Assessment of respiratory distress by frequent physical examinations.
    B. Capnography to measure end-tidal P_{CO_2} in exhaled gas at the nose.
    C. Frequent assessment for mental status changes using the Glasgow Coma Scale.
    D. Pulse oximetry recording to measure oxygen-hemoglobin saturation.
    E. Serial arterial blood gas measurements.
5. A 16-year-old girl with cystic fibrosis is admitted for low-grade fever, productive cough, and shortness of breath. She is being followed up in the clinic for advancing lung disease. Her baseline vital capacity is 40% of normal. Vital signs on presentation are as follows: axillary temperature, 38.5°C; pulse, 100 beats per minute; and respirations, 24 breaths per minute. She has nasal flaring, intercostal retractions, and diffuse bilateral wheezes and crackles (rales) on chest auscultation. She is appropriately interactive. Her pulse oximetry oxygen hemoglobin saturation on 30% oxygen, which she receives at home, is 85%. Her

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arterial blood gas reveals the following: pH, 7.28; Pco_2, 62 mm Hg; and Po_2, 55 mm Hg. High-flow nasal cannula (15 L/min) with 100% oxygen is initiated. Fifteen minutes later, the patient becomes unresponsive with shallow respirations at rate of 10 breaths per minute; lung examination findings are unchanged. A subsequent arterial blood gas determination reveals the following: pH, 7.08; Pco_2, 110 mm Hg; and Po_2, 102 mm Hg. Which of the following is the most likely explanation of the change in this child's worsened clinical state?

A. Bilateral pneumothoraces.
B. Cerebral edema.
C. Exacerbation of cor pulmonale.
D. Respiratory muscle fatigue.
E. Suppression of peripheral chemoreceptors.

Respiratory Failure

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