CHAPTER 3
Respiratory Physiology and Support

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Introduction

The primary function of the lung is to exchange gases between the bloodstream and the environment. The anatomy and physiologic control mechanisms of the lung and its associated pulmonary circulation allow for optimal efficiency of gas exchange. Due to a need for brevity, this chapter addresses only the features of lung development and pulmonary physiology that may impact the care of infants and children. The publications listed in the Suggested Reading at the end of this chapter present a more in-depth understanding of pulmonary physiology,

Pulmonary Physiology in the Neonate

Several unique aspects of neonatal pulmonary physiology related to lung maturation and growth as well as the transition from intrauterine to extrauterine life may significantly complicate management of the surgical neonate.

The structure of the bronchial tree is established by the 16th week of gestation, but alveolar maturation and growth continues throughout foetal life and into adulthood. Prenatal lung development is divided into four phases:

1. *embryonic phase* (3rd through 6th weeks of gestation), during which the primitive lung bud forms;

2. *pseudoglandular phase* (7th through 16th weeks of gestation), during which the bronchial airways are established;

3. *canalicular phase* (16th through 24th weeks of gestation), during which the structure of the distal airways and early vascularisation is established; and

4. *terminal saccular phase* (24th week of gestation to term), during which primitive alveoli are formed and surfactant production begins.

Throughout the period of prenatal lung development, interstitial tissue gradually decreases, resulting in thinning of the walls of the future alveoli. Even at birth, however, the lung does not contain mature alveoli; instead, it has approximately 20 million primitive terminal sacs. Postnatally, the relatively shallow, cup-like terminal saccules of the newborn lung gradually assume the more spherical, thin-walled structure of mature alveoli. In addition, new alveoli continue to develop up to 8 years of age. at which time approximately 300 million alveoli are present. After 8 years of age, lung growth is associated with increases in alveolar size but not number.

Lung hypoplasia is frequently associated with congenital surgical anomalies such as congenital diaphragmatic hernia or congenital cystic adenomatoid malformation that limit lung growth due to compression of the developing lung. Furthermore, because late foetal lung growth is stimulated by rhythmic lung expansion associated with foetal breathing, lung hypoplasia may also be associated with conditions that limit amniotic fluid volume (e.g., renal agenesis) and in patients with severe neurologic abnormalities (e.g., anencephaly). New bronchial development does not occur after the 18th week of gestation, so infants who experienced early inhibition of lung development will not develop completely normal lungs. Lung growth continues well after birth, however, so infants with adequate initial lung parenchyma to support extrauterine life may ultimately be left with little or no functional impairment.

Surfactant production in the foetal lung begins at about 20 weeks of gestation, but is not secreted by the lung until about 30 weeks gestation. Surfactant consists of about 90% glycerophospholipids, of which dipalmitoylphosphatidyl choline (DPPC) is the most important. During late gestation, the ratio of phosphatidyl choline (PC, or lecithin) to other lipid components (phosphatidylglycerol, sphingomyelin) changes, and thus the ratio of the different lipid components of surfactant in the amniotic fluid can be used as an index of lung maturity; that is, a lecithin/sphingomyelin (L/S) ratio >2.0, which normally occurs around 35 weeks gestation and is associated with a low risk of respiratory distress syndrome (RDS). Infants born prior to the age of lung maturity are prone to atelectasis and pulmonary oedema due to a relative lack of surfactant, which can result in the development of hyaline membrane disease.

Foetal lung maturation and surfactant production can also be affected by hormonal influences. Foetal stress associated with uteroplacental insufficiency accelerates lung maturation, probably as a result of the influence of elevated glucocorticoids and catecholamine levels, resulting in a relatively low incidence of RDS in these infants. Elevated insulin levels, however, inhibit surfactant production. Thus, even term infants of diabetic mothers may be prone to the development of RDS.

Due to the relatively greater tissue thickness in the normal newborn lung, lung compliance in the neonate is approximately equal to that of the adult. The chest wall of the newborn, however, is more compliant. Thus, the intrapleural pressure in the newborn is less negative (i.e., only slightly less than atmospheric pressure) than in adults. Given this relationship, one would expect the functional residual capacity (FRC) to be lower in the neonate than in the adult. However, the newborn infant augments FRC by maintaining inspiratory muscle activity throughout expiration thereby splinting the chest wall, and by increasing airway resistance via glottic narrowing during expiration. As a result, the percent FRC of the neonate is similar to that of adults.

Lung expansion and intrapleural pressures affect airway diameters and thus airway resistance. With forceful expiration, increased intrapleural pressure compresses the airways, thus restricting air flow and potentially causing air trapping. In the lung of the adult and older child, cartilaginous support of the airways prevents complete airway collapse. Less cartilaginous support of the central airways in premature infants, however, may result in air trapping during periods of increased respiratory effort.

Haemoglobin in the foetus has a higher oxygen affinity than the haemoglobin found in the normal older child and adult. The increased oxygen affinity of foetal haemoglobin appears to be primarily due to a decreased affinity for 2,3-DPG. This increased oxygen affinity allows for greater uptake of oxygen from the placenta at the lower oxygen tensions normally observed in the foetus. Greater oxygen uptake also reflects higher foetal haemoglobin concentrations. Postnatally,

however, the increased oxygen affinity of foetal haemoglobin may limit the delivery of oxygen during periods of hypoxaemia. In the newborn infant, the oxygen-haemoglobin dissociation curve gradually shifts to the right (toward decreased affinity), as adult haemoglobin levels increase and 2,3-DPG levels rise. Thus, by the time the child is 4 to 6 months of age, the oxygen affinity usually approximates that of an adult.

Haemoglobin concentrations also change during the first weeks after birth. The normal haemoglobin concentration of newborn infants varies between 16.7 and 17.9 g/dl. Postnatally, haemoglobin concentrations transiently increase initially, but then gradually fall to reach minimum levels at 8 to 12 weeks of age. The primary explanation for the postnatal decrease in haemoglobin concentration is believed to be the decreased stimulus for haemoglobin synthesis associated with markedly decreased erythropoietin levels in response to the higher oxygen environment of the neonate.

During intrauterine life, the placenta functions as the organ for gas exchange. In the foetus only about 12% of right ventricular output circulates through the pulmonary circulation. The remaining right ventricular output is shunted to the systemic circulation through the ductus arteriosus and foramen ovale. Blood is shunted away from the lung due to the high resistance to flow in the foetal pulmonary vasculature, likely due the combined effects of hypoxic pulmonary vasoconstriction, the local release of vasoconstrictor leukotrienes and anatomic compression of the pulmonary vasculature by the surrounding liquid-filled lung.

At birth, the lung must immediately assume the role of gas exchange. This remarkable transition depends upon the completion of several simultaneous events. First, the collapsed, fluid-filled alveoli of the prenatal lung must be expanded with air, which begins with the first breath. At birth, more than 25 mm Hg of negative pressure is required to overcome the surface tension and open the alveoli for the first time. To accomplish this, the initial inspiratory efforts of the newborn infant are extremely powerful, generating negative pressures of up to 60 mm Hg. In addition, as the newborn's lung fills with oxygen, blood flow must be redirected such that poorly oxygenated blood returning to the right atrium preferentially flows through the pulmonary circulation. The redistribution of blood flow in the newborn occurs as a result of the combined effects of an increase in systemic vascular resistance and an eightfold decrease in pulmonary vascular resistance. The former is due to loss of the low-resistance placental circulation. The latter is due to expansion of the pulmonary vasculature as the lung expands and the pulmonary vessels are no longer compressed by the fluid-filled lung, and due to vasorelaxation in response to increased alveolar oxygen tension. As a result of these adjustments, systemic pressure and left atrial pressure increase while right atrial and pulmonary artery pressure decrease, resulting first in functional closure and then anatomic closure of the foetal shunts (foramen ovale, ductus arteriosus).

Newborn infants with significant impairments in lung function (e.g., RDS, pulmonary hypoplasia) that result in hypoxaemia are prone to persistent pulmonary hypertension of the newborn (PPHN) due to hypoxic pulmonary vasoconstriction. In addition, abnormalities of lung structure are frequently associated with abnormalities of the pulmonary vasculature (i.e., pulmonary vascular hypoplasia), which may also contribute to pulmonary hypertension. As pulmonary blood pressure exceeds systemic blood pressure, blood flow will be shunted again through the anatomic foetal shunts (foramen ovale and ductus arteriosus), resulting in a condition referred to as persistent foetal circulation (PFC). The development of PFC further exacerbates hypoxaemia as unoxygenated blood is shunted away from the pulmonary circulation to the systemic circulation (right-to-left shunt). Occasionally, PFC will respond to measures that increase systemic blood pressure or decrease pulmonary vascular resistance, such as inhaled nitric oxide or oxygen. However, if a significant shunt already exists, these interventions are less unlikely to be successful. Therefore, the optimal strategy is to recognise and treat alveolar hypoxia before pulmonary hypertension develops.

Clinical Correlations

The following scenarios present typical situations and suggested treatments for paediatric respiratory problems.

Case Scenario #1

Presentation

You are seeing a newborn infant at 36 weeks gestational age. The child was born to a nulligravid 18-year-old mother who presented with preterm labor. The child was born after a prolonged labor and difficult assisted vaginal delivery. At the time of rupture of the amniotic membranes, meconium-stained amniotic fluid returned. Examination of the placenta revealed evidence of a partial abruption. The infant's Apgar scores were 7 at 1 minute and 8 at 5 minutes. Upon oropharyngeal suctioning in the delivery room, meconium-stained secretions were noted. The patient is tachypneic and has peripheral cyanosis. Auscultation reveals coarse bilateral breath sounds.

1. What is the likely cause of this patient's respiratory distress?
2. What are the options for supporting this patient?

Treatment

The newborn patient has respiratory distress syndrome. Given the difficult delivery and observed meconium staining of the amniotic fluid, it is likely this patient's respiratory distress is due to meconium aspiration syndrome. The management of patients with meconium aspiration syndrome is primarily supportive. Pulmonary physical therapy and frequent suctioning should be instituted to assist with clearance of the airways. Oxygen therapy with continuous positive airway pressures may improve the patient's cyanosis and decrease the atelectasis associated with disruption of surfactant function.

In many settings in Africa, the use of bubble continuous positive airway pressure, known as "bubble CPAP", may be an option in these types of cases. Bubble CPAP implies placing a short binasal pronged nasal cannulae into the nasal passages of newborns who need some extra airway pressure while their pathology improves and oxygenation increases. The nasal cannulae is attached to the oxygen wall outlet at 8–14 l/min in an effort to maintain pharyngeal pressure with a Y-connector so that an expiratory limb is produced. The expiratory limb can then be placed in 8 cm water pressure; bubbling that stops indicates an excessive loss of airway pressure and the need to confirm for leaks. The water pressure provides for continuous airway pressure, which could allow for these types of patients to improve without the need for intubation.

Steroid therapy may help to decrease airway inflammation, although corticosteroid therapy has not been shown to improve the course or outcome associated with this disease. In addition, antibiotic therapy should be instituted to prevent the frequent complication of secondary bacterial pneumonia, especially if steroids are used.

Case Scenario #2

Presentation

A 7-year-old boy is brought in after being rescued from a burning building. He was sleeping in his home when it caught fire. He was rescued by a neighbor who heard the child screaming for help and coughing. On examination, the child has soot around the nares and in the posterior pharynx, although there are no obvious facial burns. He is anxious and tachypneic, and his skin color is cherry-red.

1. What is the likely cause of this patient's anxiety and tachypnea?
2. What would be your initial treatment?

Treatment

This patient was exposed to a fire in an enclosed environment—a history that raises concern for an inhalation injury. Other findings including soot in the oropharynx and around the nares support the likelihood of inhalation injury, whereas the findings of the cherry-red skin and anxiety are consistent with carbon monoxide poisoning.

Carbon monoxide is a by-product of combustion. Inhaled carbon monoxide is rapidly transported across the alveolar membrane and preferentially binds to the haemoglobin molecule in place of oxygen. Binding of carbon monoxide to haemoglobin (carboxyhaemoglobin) impairs unloading of O_2. Carboxyhaemoglobin is bright red, which explains the cherry-red skin color, and the tachypnea and anxiety suggest tissue (central nervous system) hypoxia.

The most important first step in treating this patient is to provide supplemental oxygen in high concentrations. High oxygen concentration accomplishes two goals: (1) it optimises oxygen delivery to ameliorate tissue hypoxia, and (2) it accelerates unloading of carbon monoxide from the haemoglobin molecule (the half-life of carboxyhaemoglobin is about 90 minutes in 21% oxygen but decreases to 20–30 minutes in 100% oxygen).

An inhalation injury is not commonly due to direct thermal injury to the airways, but these injuries are associated with inhalation of toxic by-products of combustion, which can result in airway oedema due to inflammation. Therefore, fluid resuscitation should be judicious and the patient should have a bladder catheter placed to monitor urine output as an indicator of adequacy of hydration. Care should be taken, however, to avoid overhydration. At times, after fluid resuscitation, the airway can become oedematous, and one needs to monitor for airway obstruction, which may make a definitive airway more difficult. Steroids have been used frequently in the past to attempt to decrease airway swelling. Their use, however, has not been shown to decrease the morbidity or mortality in patients with inhalation injury, and they may increase the risk of infections. Similarly, prophylactic antibiotics have also not been shown to decrease pulmonary complications or mortality in patients with inhalation injuries.

Key Summary Points

1. The primary role of the lungs is to allow for exchange of respiratory gases (intake of oxygen and elimination of carbon dioxide).
2. Pulmonary function requires a balance of ventilation, gas transport, and blood flow.
3. Surgical diseases can negatively impact gas exchange by altering any or all of these factors.
4. Severe derangements may overcome compensatory mechanisms, resulting in hypoxia and acidosis.
5. Due to differences in lung maturation and respiratory mechanics, neonates may be at increased risk of altered gas exchange.
6. Recognition and treatment of causes of dysfunction are key to improving patient outcomes.

Suggested Reading

Cilley RE. Respiratory physiology and extracorporeal life support. In: Oldham KT, Colombani PM, Foglia RP, Skinner M, eds. Principles and Practice of Pediatric Surgery. Lippincott Williams & Wilkins, 2005, Pp 179–221.

Guyton AC, Hall JE. Respiration. In: Guyton AC, Hall JE, eds. Textbook of Medical Physiology, 10th ed. WB Saunders, 2000, Pp 432–492.

Piiper J, Respiratory gas transport and acid-base equlibrium in blood. In: Gregor R, Windhorst U, eds. Comprehensive Human Physiology, from Cellular Mechanisms to Integration. Springer-Verlag, 1996, Pp 2051–2062.

Piiper J. Pulmonary gas exchange In: Gregor R, Windhorst U, eds. Comprehensive Human Physiology, from Cellular Mechanisms to Integration. Springer-Verlag, 1996, Pp 2037–2049.

Staub NC, Dawson CA, Pulmonary and bronchial circulation. In: Gregor R, Windhorst U, eds. Comprehensive Human Physiology, from Cellular Mechanisms to Integration. Springer-Verlag, 1996, Pp 2071–2078.

West JB. Respiration. In: West JB, ed. Best and Taylor's Physiological Basis of Medical Practice, 11th ed. Williams and Wilkins, 1985, Pp 546–613.

Whipp BJ. Pulmonary Ventilation. In: Gregor R, Windhorst U, eds. Comprehensive Human Physiology, from Cellular Mechanisms to Integration. Springer-Verlag, 1996, Pp 2015–2036.

Wilson JW, DiFiore JW. Respiratory physiology and care. In: Grosfeld JL, O'Neill JA, Coran AG, Fonkalsrud EW, eds. Pediatric Surgery, 6th ed. Mosby Elsevier, 2006, Pp 114–133.