CHAPTER 11

The Formerly Premature Infant

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With the advent of surfactant therapy, and the generalized improvement in care of extremely premature infants, mortality from medical problems of prematurity has decreased substantially. As a consequence, anesthesiologists are exposed to an increasing number of infants who were born prematurely. This chapter reviews the most important medical problems of former premature infants that are of importance to anesthesiologists – those related to the respiratory system. These include chronic neonatal respiratory disease (bronchopulmonary dysplasia), laryngeal and tracheal injury, and persistent respiratory center immaturity that manifests as postoperative apnea following general anesthesia.

BRONCHOPULMONARY DYSPLASIA

Bronchopulmonary dysplasia (BPD) describes the clinical, radiographic, and pathologic sequelae of respiratory distress syndrome (RDS), and is classified as mild, moderate, or severe (Table 11-1). It is the leading cause of chronic lung disease during infancy, occurring in up to 36% of infants born prematurely who require early mechanical ventilation. The risk of developing BPD increases with decreasing birthweight and younger gestational age. BPD has also been termed "chronic neonatal lung disease" and "chronic lung disease of prematurity," but it is more precisely characterized as one of many causes of "chronic lung disease of infancy" (CLDI). Additional causes of CLDI include pneumonia/sepsis, meconium aspiration pneumonitis, pulmonary hypoplasia, persistent pulmonary hypertension (see Chapter 1), apnea of prematurity (see Chapter 10), and any other systemic disease that affects lung function.

Various factors have been implicated in the pathogenesis of BPD. These include oxygen toxicity, barotrauma/volutrauma from prolonged mechanical ventilation, fluid overload, a persistent ductus arteriosus (PDA), congenital or nosocomial infection, and genetic predisposition, among others. No one factor appears to be primarily responsible and the etiology is likely to be multifactorial. Some authors have suggested that BPD is likely the end result of the reparative process of the lung after therapy for RDS as well as the arrest of lung growth during the neonatal period.

The clinical manifestations of the classic, more severe form of BPD include tachypnea, rales, bronchospasm, and a persistent requirement for supplemental oxygen. Carbon dioxide retention is a prominent finding and is presumably due to increased deadspace ventilation. Radiographic abnormalities include hyperinflation, bleb formation, and interstitial densities. The underlying pathologic findings include pulmonary fibrosis, necrotizing bronchiolitis, peribronchial smooth muscle hypertrophy, and widespread inflammatory changes in the distal bronchioles and alveoli.

Infants with severe BPD may demonstrate episodes of sudden, severe bronchospasm and cyanosis following agitation or physical stimulation ("BPD spell"), which is thought to be caused by nearly complete tracheal collapse as a result of underlying tracheomalacia, a common complication of prolonged mechanical ventilation. These episodes are treated with sedation or calming of the infant combined with application of continuous positive airway pressure (CPAP) or positive pressure ventilation in the event of unremitting hypoxemia.

Throughout the past several decades the clinical nature of BPD has evolved into a milder form ("new BPD") than seen in the past. This is primarily associated with an increased survival rate of extremely premature

Table 11-1 Classification and Diagnostic Criteria for Bronchopulmonary Dysplasia

	Gestational Age	
Classification	**<32 Weeks**	**≥32 Weeks**
Mild BPD	Breathing room air at 36 weeks postmenstrual age[a] or hospital discharge, whichever comes first	Breathing room air by 56 days postnatal age or discharge, whichever comes first
Moderate BPD	Need for <30% oxygen at 36 weeks postmenstrual age[a] or discharge, whichever comes first	Need for <30% oxygen at 56 days postnatal age or discharge, whichever comes first
Severe BPD	Need for ≥30% oxygen and/or positive pressure, at 36 weeks postmenstrual age[a] or discharge, whichever comes first	Need for ≥30% oxygen and/or positive pressure at 56 days postnatal age or discharge, whichever comes first

[a] Postmenstrual age is the postconceptional age (PCA) + 2 weeks.
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infants, and increased recognition of the role of oxygen toxicity and barotrauma/volutrauma in causing BPD. The newer, milder form of BPD is characterized by a minimal oxygen requirement in early life, although ventilatory therapy may be required for persistent central apnea. As the infant with mild BPD grows, there is a comparatively less bronchospastic component than with the more severe form.

With all forms of BPD, the ventilatory treatment is a two-pronged approach. First, the inspired fractional concentration of oxygen is minimized to prevent further oxygen toxicity. Second, "atelectrauma" is minimized by increasing PEEP (maximum 10 cmH_2O), which maintains functional residual capacity (FRC) and reduces the relative amount of chronically underventilated atelectatic areas of the lung.

Pharmacologic therapy includes diuretics, inhaled bronchodilators, theophylline, caffeine, and short courses of inhaled or oral steroids. Long-term treatment with diuretics results in hypokalemia, hypochloremia, and increased serum bicarbonate. Additional supportive therapy includes optimization of nutrition, fluid restriction, and aggressive treatment of infectious processes.

The vast majority of infants with BPD will regain normal lung function by 12 months of age. However, many will continue to demonstrate periodic episodes of bronchospasm, especially during upper respiratory tract infections. In severe cases, this predisposition can last into adolescence. Infants who develop the newer, milder form of BPD tend to be more premature and therefore more likely to suffer from an arrest in alveolar development. Long-term pulmonary function in these infants is unknown.

Anesthetic Management of Infants with BPD

Preoperative assessment of infants with BPD is focused on optimization of their respiratory status, with particular regard for treating underlying bronchoconstriction. Infants with severe BPD who are likely to develop bronchospasm and cyanosis during physical stimulation should receive an anxiolytic premedication. Principles of management of general anesthesia in these infants centers on the avoidance of endotracheal intubation. Whenever feasible, a laryngeal mask airway (LMA) is preferred. If endotracheal intubation is performed, a "deep extubation" may be warranted to avoid bronchospasm. In abdominal procedures, a regional analgesic technique is indicated for adequate postoperative pain control, as well as to avoid chest wall splinting and to preserve the ability to cough without pain. In infants with BPD, there are insufficient data with which to predict the incidence of intraoperative or postoperative pulmonary complications.

LARYNGEAL AND TRACHEAL INJURY

Premature infants who required prolonged endotracheal intubation and mechanical ventilation are prone to develop injury to the laryngeal and tracheal tissues, which results in scarring and upper-airway narrowing. Subglottic stenosis, a fibrotic narrowing usually located at the level of the cricoid cartilage, occurs in up to 15% of infants who survive prolonged mechanical ventilation in the neonatal period. When anesthetized, these infants will require an unexpectedly smaller diameter endotracheal tube. Following extubation, they may develop stridor as a result of further tracheal narrowing from acute subglottic edema. Therefore, the endotracheal tube should permit an air leak below 30 cmH_2O to help prevent excessive swelling of the subglottic mucosa.

Tracheal and bronchial injury that occurs during repeated deep suctioning techniques may result in lower-airway narrowing and granuloma formation. Tracheobronchomalacia may occur in up to 50% of

premature infants with CLDI. It is thought to be partially responsible for tracheal collapse that manifests as wheezing or cyanosis during "BPD spells."

POSTOPERATIVE APNEA

Formerly premature infants who are growing and otherwise doing well will often demonstrate central apnea following administration of general anesthesia for elective surgical procedures, such as an inguinal herniorrhaphy. These episodes of postoperative apnea may be accompanied by bradycardia and may require bag–mask assisted ventilation to relieve the hypoxemia. The cause of this phenomenon is unknown, but it is probably related to the effects of general anesthetic agents on the immature respiratory control center in the brainstem.

Both retrospective and prospective studies have been performed in an attempt to delineate the types of patients at risk for postoperative apnea. Characteristics of premature infants that are likely to develop postoperative apnea include low gestational age, low postconceptional age (PCA), preoperative apnea of prematurity, and anemia (usually defined as a hemoglobin level <10 g/dL). The PCA at which postoperative apnea will not occur is unknown; however, there are no reports of postoperative apnea in infants aged greater than 60 weeks PCA. The true risk for an individual patient is indeterminate and is likely a continuum based on the infant's gestational and chronological age, and coexisting medical conditions.

Strategies for Prevention of Postoperative Apnea

There are three main anesthetic strategies for preventing postoperative apnea in susceptible infants:

1. Performing a regional anesthetic instead of a general anesthetic
2. Perioperative administration of intravenous caffeine
3. Selection of general anesthetic agents or opioids that are characterized by their limited duration of action.

Spinal anesthesia for premature infants was popularized in 1984 by Chris Abajian from the University of Vermont (see Chapter 20). Since publication of that report, numerous additional publications have examined the benefits and risks of spinal or epidural anesthesia in this patient population for lower abdominal or groin procedures. Most reported series confirm that spinal or epidural anesthesia is associated with a lower incidence (but not complete absence) of postoperative apnea, provided additional systemic sedative agents are avoided. Comparative studies have not been performed with individual sedative agents; however, it appears that when systemic sedatives are administered intraoperatively to treat pain or agitation, the risk of postoperative apnea increases to a level similar to that after general anesthesia. This has been confirmed for ketamine as well. Therefore, infants at risk of postoperative apnea who receive regional anesthesia with sedative supplementation should receive the same postoperative apnea monitoring as that used after administration of general anesthesia.

Article To Know

Coté CJ, Zaslavsky A, Downes J et al: Postoperative apnea in former preterm infants after inguinal herniorrhaphy: a combined analysis. Anesthesiology 82:809–822, 1995.

Individually published studies that determine risk factors for postoperative apnea in former premature infants are unconvincing because of their retrospective nature or the relatively small number of patients studied. Therefore, in an attempt to determine true risk factors for postoperative apnea, Charlie Coté, at Children's Memorial Hospital in Chicago, obtained the original data from eight prospective studies that examined risk factors for postoperative apnea in former premature infants undergoing inguinal herniorrhaphy, and performed a reanalysis with the larger dataset. Dr Coté analyzed data from 255 patients from four institutions, and determined the influence of the following patient- or anesthetic-related factors on the incidence of development of postoperative apnea: a history of respiratory distress syndrome, BPD, apnea of prematurity, previous necrotizing enterocolitis, ongoing apnea at the time of surgery, use of narcotics or long-acting muscle relaxants, anemia (hematocrit level <30%), gestational age, and postconception age (PCA). Of these, only two, lower gestational age and lower PCA, were directly correlated with the risk of postoperative apnea (Fig. 11-1). Additional risk factors included ongoing apnea at home and presence of anemia, particularly in infants greater than 43 weeks PCA.

Coté's reanalysis showed that the risk for apnea does not decrease to below 1% with 95% statistical confidence until infants with a gestational age of 32–35 weeks reached a PCA of 56 weeks, and infants with a gestational age of 35 weeks or more reached a PCA of 54 weeks. He suggested that premature infants less than 55 weeks PCA are at sufficient risk to warrant overnight hospitalization and monitoring. The length of the required hospital stay is unknown; however, most pediatric institutions require monitoring for at least 12 apnea-free hours with a cardiopulmonary monitor (pulse oximetry and electrocardiography).

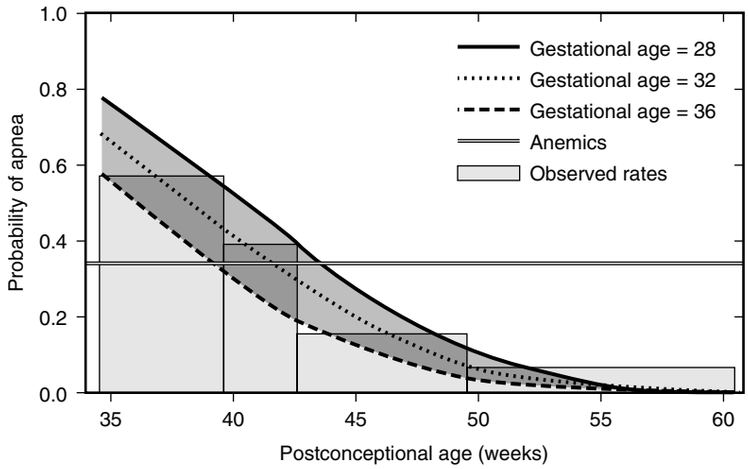

Figure 11-1 Influence of gestational age and PCA on risk of postoperative apnea in former premature infants. The risk of apnea is inversely related to the gestational age and PCA. The risk of anemia is represented by the horizontal hatched line, which is not altered by the gestational age or PCA. The shaded boxes represent the overall rates of apnea for infants within that gestational age range. (Redrawn with permission from Coté CJ et al: *Anesthesiology* 82:809–822, 1995.)

There is currently a debate in the pediatric anesthesia community concerning the appropriate level of postoperative monitoring in infants receiving regional anesthesia without sedative supplementation. Although some centers routinely discharge these infants on the day of surgery, the majority of pediatric centers require overnight monitoring.

The second strategy is perioperative administration of caffeine base, 10 mg/kg. Caffeine is a respiratory stimulant that, when administered during induction of general anesthesia, decreases the incidence of postoperative apnea, bradycardia, and hypoxemia in susceptible infants. Anesthesiologists caring for infants at risk of postoperative apnea should proactively consult with their center's neonatologists and develop a treatment plan for the administration of perioperative caffeine. At The Children's Hospital of Philadelphia, many of these susceptible infants will already be receiving caffeine as part of their prophylactic management of apnea of prematurity, so additional perioperative administration is not required. In formerly premature infants who present for elective surgery after discharge from the hospital, caffeine is administered on a case-by-case basis, after assessment of the risk factors and discussion with the infant's neonatologist.

Almost all studies on risk of postoperative apnea following general anesthesia were performed prior to the advent of short-acting anesthetic agents, such as sevoflurane, desflurane, and remifentanil. It is theoretically possible that use of these newer agents of limited duration will result in a decreased incidence of postoperative apnea, so they should be used in susceptible infants when available. However, definitive data on the association of postoperative apnea with use of these agents is lacking.

ADDITIONAL ARTICLES TO KNOW

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