Anaesthetic management of the child with co-existing pulmonary disease

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Editor’s key points

- Asthma and bronchopulmonary dysplasia (BPD) are two of the most common pulmonary disorders encountered by paediatric anaesthetists.
- The prevalence of asthma is increasing; optimized preoperative treatment can reduce the risk for adverse respiratory outcomes.
- BPD, a common sequela of preterm birth, is associated with persistent airway disease and, in severe cases, pulmonary hypertension that increase perioperative morbidity.

Summary. Children with co-existing pulmonary disease have a wide range of clinical manifestations with significant implications for anaesthetists. Although there are a number of pulmonary diseases in children, this review focuses on two of the most common pulmonary disorders, asthma and bronchopulmonary dysplasia (BPD). These diseases share the physiology of bronchoconstriction and variably decreased flow in the airways, but also have unique physiological consequences. The anaesthetist can make a difference in outcomes with proper preoperative evaluation and appropriate preparation for surgery in the context of a team approach to perioperative care with implementation of a stepwise approach to disease management. An understanding of the importance of minimizing the risk for bronchoconstriction and having the tools at hand to treat it when necessary is paramount in the care of these patients. Unique challenges exist in the management of pulmonary hypertension in BPD patients. This review covers medical treatment, intraoperative management, and postoperative care for both patient populations.

Keywords: anaesthesia; asthma; bronchoconstriction; bronchopulmonary dysplasia; perioperative period

Maintaining oxygenation and carbon dioxide exchange is a fundamental component of anaesthesia practice. Anaesthetists frequently encounter children with co-existing pulmonary disease during preoperative assessments, intraoperatively, or in intensive care units. Their illnesses encompass a wide spectrum of disease ranging from mild upper respiratory tract infections to chronic lung disease and end-stage pulmonary failure. An in-depth review of all major paediatric pulmonary diseases is beyond the scope of a single article. Rather, this review focuses on the medical treatment, intraoperative anaesthetic management, and postoperative care for two of the most common paediatric pulmonary disorders encountered by anaesthesiologists: asthma and bronchopulmonary dysplasia (BPD). Although different in pathogenesis, these two disorders have overlap in physiology and anaesthetic management principles.

Asthma

Asthma is the most common chronic disease in children. All anaesthesiologists routinely encounter children with asthma and will likely encounter an increasing number of these children in the future. Worldwide, asthma prevalence varies widely, ranging from 0.7% to 18.4% with ‘Western’ countries topping the list. A recent governmental report found that the asthma prevalence in the USA is increasing; currently at 9.5% of children aged 0–17. Other reports have also found the prevalence of asthma and wheezing disorders to be on the rise, leading some to use the term ‘epidemic’. Children <3 yr old frequently have episodic respiratory symptoms (cough, wheezing), but most of these children do not go on to have a clinical diagnosis of asthma. Asthma is defined by chronic inflammation of the airways, associated with airway hyperresponsiveness, which leads to recurring episodes of wheezing, coughing, breathlessness, and chest tightness and reversible airflow obstruction within the lung. Contributing factors include genetic predisposition, atopy, and respiratory syncytial virus infection in infancy. Asthma patients carry a small but significantly increased risk for operative and postoperative complications.

Pharmacotherapy for asthma

β-Adrenergic agonists

β-Adrenergic agonists are commonly used to provide rapid relief of acute bronchospasm (short-acting β-agonists, SABAs) and are also used for chronic treatment (long-acting...
β-agonists, LABAs) but only in combination with inhaled corticosteroids. The inhaled β-2 adrenergic agents have a wide therapeutic window with a toxic dose that is far greater than their therapeutic dose. When these drugs activate the β-2 receptor, adenylyl cyclase increases cAMP levels, which cause smooth muscle relaxation and increased mucociliary clearance. Although they may be administered by oral or i.v. routes, inhalation administration provides faster peak bronchodilatation and fewer systemic side-effects.

Corticosteroids

Inhaled corticosteroids are the foundation of treatment for asthma because they target the inflammation that characterizes the disease. They should be seen as ‘controller’ medications because they do not cure the disease and their efficacy depends on consistent, appropriate administration. They have been shown to reduce airway reactivity, inhibit inflammatory cell migration and activation, and block reactions to allergens. High-dose inhaled corticosteroids may have some systemic side-effects, but the common side-effects of oral thrush and hoarseness seen in adults are rare in children. Systemic corticosteroids, either oral or parenteral, are reserved for severe, uncontrolled asthma.

Leukotriene pathway modifiers

Leukotriene modifiers are most commonly used as second-line controller medications. Leukotrienes are produced by mast cells, eosinophils and basophils inducing oedema, stimulation of airway secretions, and smooth muscle proliferation (by a non-histamine mechanism). These orally administered drugs are particularly useful in several specific areas, including: exercise-induced, intermittent (viral-induced), and aspirin-induced asthma.

Cromones

Cromolyn sodium and nedocromil sodium stabilize mast cells and interfere with chloride channel function. They are used as alternative treatment for asthma in adults but have recently been not recommended for use in children.

Anticholinergics

Ipratropium bromide inhibits mucous hypersecretion and decreases reflex bronchoconstriction by targeting airway muscarinic cholinergic receptors. It may be administered by metered dose inhaler (MDI) or nebulizer and is a quaternary amine with no significant systemic absorption or side-effects. Ipratropium is rarely used in chronic management of paediatric asthma patients. Several systematic reviews confirm its benefit in the setting of severe acute asthma when combined with other treatments.

Methylxanthines

Theophylline functions as a mild bronchodilator and anti-inflammatory. Because of the fact that its effect is less than that of low-dose inhaled corticosteroids, it is seldom used as first-line therapy. It has proven effective as a rescue medication in status asthmaticus. Because theophylline has a very low therapeutic index, serum monitoring is essential. Side-effects include nausea, vomiting, headache, and seizures.

Preanaesthetic evaluation

Paediatric asthmatic patients require careful preoperative evaluation and preparation. Asthmatic children well prepared for surgery (often with a multidisciplinary or ‘team’ approach) have significantly reduced risk for adverse outcomes (Fig. 1). Essential points to review in the preoperative evaluation are the level of asthma control and the current medication regimen. In addition, review of the level of activity, use of rescue medications, hospital visits (tracheal intubation or i.v. infusions required), allergies, and previous anaesthetic history are important. Also an inquiry regarding cough and sputum production should occur. Although otherwise healthy children can often be anaesthetized safely during an acute upper respiratory infection (URI), the risk of bronchospasm in asthmatics is very high. They should ideally be postponed 4–6 weeks after such an event. Physical examination should include vital signs, assessment for wheezing, cough, type of breath sounds, use of accessory muscles, and level of hydration. Room air oxygen saturation is useful as a baseline and for determining pre-existing hypoxaemia, but other laboratory data are not usually necessary.

Not all patients present with a diagnosis of asthma (true asthmatics are often undiagnosed), but an increased risk for bronchospasm can be determined by several key elements in the history. The diagnoses of atopy/eczema and allergic rhinitis often go hand in hand with a diagnosis of asthma as they are all thought to be conditions of chronic inflammation. A family history of asthma and atopy also contributes to intraoperative respiratory complications. As in adults, significant gastro-oesophageal reflux disease can often be a trigger for asthma symptoms. Obese patients present a variety of anaesthetic challenges. Relevant to this discussion is not only the association of obesity and asthma, but also the increase in intraoperative bronchospasm seen in obese children even without a diagnosis of asthma. Exposure to second-hand smoke should be considered a risk factor for poor asthma control, and also an independent risk factor for adverse respiratory events in children under general anaesthesia.

Risk factor optimization

Preoperative preparation for a controlled asthmatic can include a use of an inhaled β-2 adrenergic agonist 1–2 h before surgery. For moderately controlled asthma, additional optimization with an inhaled corticosteroid and regular use of inhaled β-2 agonists 1 week before surgery can be instituted. Poorly controlled asthmatics might need addition of one of the following: oral prednisone 1 mg kg⁻¹ day⁻¹ (60 mg max) 3–5 days before surgery, oral dexamethasone 0.6 mg kg⁻¹ (16 mg max), or oral methylprednisolone 1 mg
kg⁻¹ for 48 h before surgery. Preoperative use of systemic corticosteroids has been shown to suppress production of inflammatory cytokines and multiple studies confirm the safety of a perioperative pulse of systemic corticosteroids.

Mirroring the stepwise approach to treatment of asthma proposed by the Global Initiative for Asthma, Liccardi and colleagues have proposed a simple approach to preoperative treatment of asthmatic patients. Although not validated by randomized controlled trials, it represents a logical, easy-to-follow process for preoperative planning (Fig. 2).

**Perioperative management**

**Immediate preanaesthetic preparation**

Patients should continue all their controller medications as normal on the day of surgery. An extra dose of SABA may be efficacious if deemed necessary from the preoperative evaluation. Giving a routine ‘extra dose’ (in addition to the patient’s scheduled dose) to all asthmatics regardless of the level of control might not be warranted, although the beneficial effect of SABAs on reflex bronchoconstriction in response to tracheal intubation is clear. Premedication with oral midazolam, 0.5–1 mg kg⁻¹, is safe in asthmatics, and can be indicated since anxiety can precipitate acute bronchospasm. The use of systemic corticosteroids in the last 6 months or high-dose inhaled corticosteroids is an indication for stress dose coverage. If indicated by the preoperative evaluation, it is still not too late to give i.v. corticosteroids as their beneficial effect will extend into the postoperative period.

**Anaesthetic management**

If an i.v. catheter is in place before induction, several medications can be given to diminish the response to tracheal intubation. Lidocaine can prevent reflex bronchoconstriction and has little toxicity at a dose of 1–1.5 mg kg⁻¹ i.v., 1–3 min before tracheal intubation. Direct spraying of the airway can trigger airway reactivity, so the i.v. route is preferable. I.V. glycopyrrolate or atropine given long with an i.v. induction or after an inhalation induction may decrease secretions and provide additional bronchodilatation before tracheal intubation via their effect at muscarinic receptors.

The choice between i.v. and inhalation induction is often influenced by multiple clinical factors. There is little compelling evidence to suggest one technique over another in asthmatic children. If an i.v. induction is chosen, propofol is the i.v. induction agent of choice in haemodynamically stable asthmatic patients. It has been shown in multiple studies to attenuate the bronchospastic response to tracheal intubation, both in asthmatic and non-asthmatic patients. Its effect is likely mediated by suppression of vagally mediated stimulation of bronchial muscarinic receptors. Recent animal research suggests that propofol may mediate bronchodilation via other pathways including airway smooth muscle GABA receptors and diminishing the effect of tachykinins on airway smooth muscle. Neither thiopental nor
etomidate modulate the bronchospastic response to tracheal intubation as effectively as propofol. Ketamine is the induction agent of choice in haemodynamically unstable asthmatic patients. It likely produces smooth muscle relaxation and bronchodilatation directly, via release of catecholamines and vagally mediated mechanisms, although its bronchoprotective effect is not as pronounced as that of propofol. Its mucous-stimulating effects can be ameliorated by pretreatment with atropine or glycopyrrolate.

Volatile anaesthetics have long been known to depress airway reflexes to tracheal intubation and cause direct airway smooth muscle relaxation. Like propofol, this effect is likely mediated via a variety of pathways including inhibition of cholinergic neurotransmission, inhibition of tachykinin and leukotriene effect, and direct effects on intracellular calcium in bronchial smooth muscle. Sevoflurane seems to have the most pronounced effects of all the inhalation anaesthetics and is the agent of choice for mask induction. As a word of caution: in children with asthma, tracheal intubation with sevoflurane as the sole anaesthetic (even at 5% concentration) causes an increase in respiratory system resistance compared with non-asthmatic children.

It is important to recognize that having an asthmatic child use an SABA before induction with sevoflurane can decrease the risk of increased airway resistance and bronchospasm that occurs with tracheal intubation. During maintenance of anaesthesia, children with asthma have shown low airway resistance with a propofol infusion, but in most asthmatic children, switching to sevoflurane further improved this effect. In contrast, a switch to desflurane caused elevation in airway resistance in these susceptible children. Although some have questioned the mechanism by which desflurane increases airway resistance, it is clear that at typical, MAC-equivalent doses desflurane does increase airway resistance.

The decision regarding airway management is likewise influenced by multiple clinical factors. As tracheal intubation is one of the most potent triggers for bronchospasm, choosing a laryngeal mask airway (LMA) or simple mask may be useful. Little research defines the risks for asthmatic children with regard to tracheal intubation compared with LMA, but children with recent URI may benefit from the use of an LMA. Should tracheal intubation be required, the use of cuffed tracheal tubes allows for avoidance of multiple intubations due to air leak, more reliable \(\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{\text{E}}}CO_2}}}}}}}}\) waveform monitoring, and the use of lower fresh gas flows.

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**Fig 2** Suggested stepwise approach to the preoperative treatment of asthmatic patients based on their degree of asthma control. ICS, inhaled corticosteroids; LABA, long-acting \(\beta\)-2 agonist; OCS, oral corticosteroids; SABA, short-acting \(\beta\)-2 agonist. Modified from Liccardi et al. with permission.
Regional anaesthesia should be considered whenever possible to avoid airway manipulation, but might not be feasible for the uncooperative paediatric patient or for certain surgical situations.

Non-histamine-releasing neuromuscular blocking agents such as rocuronium, vecuronium, and cisatracurium are acceptable for use in children with asthma. Reversal of neuromuscular block with acetylcholinesterase inhibitors (e.g., neostigmine or edrophonium) can be undertaken with caution in asthmatics but carries the risk of residual neuromuscular block and muscarinic side-effects including bronchospsm. Sugammadex is a new and selective reversal agent that rapidly encapsulates steroidal neuromuscular blocking agents without activating muscarinic receptors. A recent phase IIIa study of sugammadex describes similar train-of-four recovery without activating muscarinic receptors. A recent phase IIIa study of sugammadex describes similar train-of-four recovery without activating muscarinic receptors. However, a study of sugammadex use in adults with underlying pulmonary disease found a 2.6% incidence of bronchospsm in this population. Therefore, sugammadex does not completely mitigate the risk of airway hyperreactivity in patients with pre-existing pulmonary disease. Currently, paediatric sugammadex use is limited by high cost and insufficient data on its efficacy and safety in children < 2 yr of age.

Airway irritation should be minimized by humidification of inspired gases. Stimulation of the trachea by suctioning should also be minimized and performed only with deep levels of anaesthesia. During mechanical ventilation, inspiratory pressures should be kept low and the expiratory time lengthened. Careful attention should be paid to the avoidance of intrinsically developed PEEP. On a theoretical basis, deep extubation should decrease the risk of bronchospsm evoked by coughing on the tracheal tube; however, little research has been done to answer this question for asthmatic children.

Treatment of intraoperative bronchospsm

Treatment of intraoperative bronchospsm in children presents a unique set of problems, particularly when the bronchospsm is severe. Inhaled β-2 agonists are the treatment of choice, yet the delivery of inhaled medications via small tracheal tubes is difficult. Previous research has shown that only 2.5–12.3% of the dose of albuterol by MDI into 3.0–6.0 mm ID tracheal tubes is delivered to the patient. Resourceful anaesthesiologists have sought ways to overcome this problem in various ways, including actuating the MDI canister into a long, 19 G i.v. catheter advanced out of the end of the tracheal tube. Although this method increases delivery of albuterol 10-fold, delivery of concentrated medication and other components of the MDI can cause damage to the airway. Most current research into the effective delivery of inhaled medications via small tracheal tubes comes from the critical care literature. Both MDI spacers and nebulizers have been modified in a variety of ways to fit into a ventilator circuit. Each technique has advantages and disadvantages, but in the operating theatre environment, simplicity and rapidity of deployment seem to favour MDIs with spacers (Fig. 3).

Occasionally, severe bronchospsm can make it difficult to deliver any inhaled medications necessitating an alternative route of administration. I.V. anticholinergic medications should be given and additional steroids (up to 2 mg kg⁻¹ of hydrocortisone or methylprednisolone) might not have immediate effect but can aid in avoiding postoperative bronchospsm. I.V. or subcutaneous β-agonists in the form of terbutaline (10 µg kg⁻¹ over 10 min), epinephrine, or isoproterenol can be used if previous therapy is unsuccessful in terminating the bronchospsm. I.V. or subcutaneous β-agonists in the form of terbutaline (10 µg kg⁻¹ over 20 min) can be added in refractory situations.

Magnesium (50 mg kg⁻¹ over 20 min) has been shown to benefit children with severe asthma already treated with β-agonists and corticosteroids. The final option for patients failing all the previously described treatments is extracorporeal membrane oxygenation. It has been used successfully, with good neurological outcomes, to treat refractory asthma in children.

Bronchopulmonary dysplasia

BPD is a chronic lung disease initially reported in 1967 by Northway and colleagues in 32 preterm infants with respiratory distress syndrome and characteristic radiographic changes after the initiation of positive pressure mechanical ventilation. Four stages of lung injury were originally described: exudative (age 1–3 days); necrosis and early repair (age 4–10 days); microcyst formation and pulmonary fibrosis (age 10–12 days); and severe cystic changes and cor pulmonale (after 30 days of age). Early ventilator therapies using high inspired oxygen concentrations and high ventilating pressures and volumes further contributed to lung injury. Until the 1980s, BPD remained a devastating disorder marked by prolonged hospital stays and a high incidence of mortality.

The clinical characteristics of BPD have evolved over the last three decades with advancements in neonatal care including antenatal steroid administration, surfactant therapy, and improved ventilator strategies designed to minimize lung injury. While the mean gestational age of Northway’s original patients was 34 weeks (during the time of alveolar development), most infants currently developing BPD are born at 24–28 weeks of gestation (during the time of canalicular and saccular development) and rarely later than 32 weeks of gestation. As a result, the obstructive bronchilolitis and alternating areas of overinflation and fibrosis seen in ‘classic’ BPD have been replaced in ‘new’ BPD by a uniform arrest of lung development featuring large, simplified alveolar structures and dysmorphic capillaries. Infants developing BPD today are more likely to present with a mild respiratory distress syndrome and a continued need for supplemental oxygen. The current definition of BPD has been validated in early infancy and determines three levels of severity (mild, moderate, or...
severe) using gestational age of the infant, oxygen dependency at 36 weeks post-conceptual age, total duration of oxygen supplementation, and positive pressure requirements (Table 1). The rate of BPD varies greatly among institutions depending on the definition utilized, gestational age distribution of the infants, and other population characteristics. Data from the National Institutes of Child Health Developmental Neonatal Research Network (NICHD Neonatal Network) and other centres suggest stable or increasing BPD rates due to improved survival of extremely preterm and low birthweight infants. The highest rates of BPD are found in infants with the lowest birth weights and lowest gestational ages. Among infants weighing 501–1500 g at NICHD Neonatal Network sites from 1997 to 2002, the incidence of BPD ranged from 57% at birth weights of 501–750 g to 6% at birth weights of 1251–1500 g with an average overall incidence of 23%. Thus, BPD remains one of the most prevalent long-term sequelae of premature birth.

### Risk factors

In addition to barotrauma, volutrauma, and oxygen toxicity, proposed risk factors for BPD-associated lung injury include surfactant deficiency, patent ductus arteriosus, pulmonary oedema, chorioamnionitis, and poor nutritional status. Laboratory evidence also points to an association between inflammatory mediators and BPD via direct injury of lung parenchyma, disruption of vasculogenesis, and immune priming leading to exaggerated pulmonary inflammatory responses.

### Sequelae of BPD

#### Airway disease and respiratory morbidity

Although BPD is primarily a disease of the small airways, large airway disease is frequently observed in this population during infancy. Prolonged tracheal intubation and mechanical ventilation are associated with the development of tracheomalacia and bronchomalacia. Older BPD infants may exhibit ‘BPD spells’, acute cyanotic events caused by

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**Table 1** Diagnostic criteria for bronchopulmonary dysplasia.
*Nasal CPAP or positive-pressure ventilation. PMA, post-menstrual age. Modified from Jobe and Bancalari* 

<table>
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<tr>
<th>Mild supplemental O₂ (for 28 days) and</th>
<th>Moderate supplemental O₂ (for 28 days) and</th>
<th>Severe supplemental O₂ (for 28 days) and</th>
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<tr>
<td>Breathing room air at 36 weeks PMA or discharge</td>
<td>( F_{IO2} &lt; 0.3 ) at 36 weeks PMA or discharge</td>
<td>( F_{IO2} \geq 0.3 ) and/or positive pressure* at 36 weeks PMA or discharge</td>
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<tr>
<td>Room air by 56 days postnatal age or discharge</td>
<td>( F_{IO2} &lt; 0.3 ) at 56 days postnatal age or discharge</td>
<td>( F_{IO2} \geq 0.3 ) and/or positive pressure* at 56 days postnatal age or discharge</td>
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**Fig 3** Options for the delivery of inhaled medications to intubated children. (a) MDI actuated inside a 60 ml syringe and connected to the gas-sampling port of the circuit elbow. (b) Delivery via a 19 G i.v. catheter advanced out of the end of the tracheal tube. (c) Valved MDI spacer positioned between the circuit ‘Y’ and the tracheal tube. (d) Jet nebulizer positioned in the inspiratory limb of a neonatal intensive care unit ventilator circuit.
increases in central airway compliance.\textsuperscript{105} Subglottic stenosis, airway granulomas, and pseudopolyps resulting from tracheal intubation and aggressive suctioning at times require surgical intervention.\textsuperscript{106}

Long-term BPD survivors experience persistent airway obstruction and hyperreactivity. A study of 28 subjects with a mean gestational age at birth of 26.5 weeks found children with ‘new’ BPD had decreased forced expiratory flows (FEV\textsubscript{0.5}, FEF\textsubscript{75%}, FEF\textsubscript{25 – 75%}) and increased FRC, RV, and RV/TLC ratios at an average chronological age of 17 months when compared with healthy infants. Infants with recurrent wheezing exhibited the greatest airway hyperreactivity and flow limitations.\textsuperscript{107} A study of 7-yr-old BPD survivors found increased prevalence of airway obstruction and bronchodilator responsiveness among preterm children with a history of BPD compared with preterm children with no BPD history.\textsuperscript{108} Few studies have assessed pulmonary function in adolescent and adult survivors of ‘new’ BPD. Most recently, a prospective cohort study by Vrijlandt and colleagues\textsuperscript{109} with up to 19 yr of follow-up demonstrated airway obstruction and decreased DL\textsubscript{CO} in children with BPD born at <32 weeks gestational age or with a birthweight <1500 g compared with healthy controls born at term. In addition, a study of lung function variables in BPD survivors with birthweights <1500 g now at a mean age of 18.8 yr found substantially diminished airflow in subjects with BPD without significant differences in lung volumes when compared with controls.\textsuperscript{110}

Rehospitalization for respiratory illness occurs at increased rates in BPD infants less than age 2 yr, even when compared with very low birthweight (VLBW) infants without lung disease.\textsuperscript{108, 111} Reactive airway disease, pneumonia, and respiratory syncytial virus infection cause the majority of readmissions.\textsuperscript{112} Over the age of 4–5 yr, rehospitalization becomes rare with reactive airway disease symptoms constituting the reason for most medical visits.\textsuperscript{106}

Pulmonary hypertension

Even in the post-surfactant era, pulmonary hypertension (PH) remains strongly linked to high morbidity and mortality in infants with BPD with reported mortality rates of almost 70% for infants with severe PH.\textsuperscript{113} In BPD, impaired angiogenesis reduces alveolar–capillary gas exchange, leading to hypoxaemia, increased pulmonary vascular resistance (PVR), and abnormal vasoreactivity of the pulmonary circulation. As a result, even mild hypoxaemia can cause significant increases in pulmonary artery pressure in infants with BPD.\textsuperscript{114} Retrospective studies estimate a 25–35% prevalence of PH in BPD infants.\textsuperscript{115, 116}

Echocardiography and cardiac catheterization

Echocardiography is a useful non-invasive tool in the diagnosis of PH and may improve late outcomes by allowing for earlier initiation of appropriate therapies. Clinical markers such as a continued need for positive pressure ventilation, oxygen requirements out of proportion to the degree of lung disease, recurrent cyanotic episodes, failure to thrive, recurrent hospitalizations, and elevated Pa\textsubscript{CO\textsubscript{2}} are frequently associated with more severe disease and warrant screening for PH.\textsuperscript{117}

Mourani and colleagues compared echocardiographic assessment of PH in infants with BPD and measurements of pulmonary artery pressure via cardiac catheterization, and found that while echocardiography often identified the presence of PH in infants with BPD, it did not reliably determine systolic pulmonary artery pressure and thus disease severity. In addition, echocardiographic findings suggestive of right heart strain such as right atrial enlargement, right ventricular hypertrophy, right ventricular dilatation, pulmonary artery dilatation, and septal flattening had relatively poor predictive value in the absence of a measurable tricuspid regurgitant jet.\textsuperscript{118} Despite these limitations, echocardiography remains an integral part of PH screening in children with BPD.

Cardiac catheterization is typically reserved for patients with PH by echocardiogram who have persistent cardiorespiratory disease despite optimal medical management or are candidates for chronic PH drug therapy. Data gathered during cardiac catheterization such as the presence and severity of anatomic lesions, left heart dysfunction, and pulmonary vascular reactivity may significantly inform clinical management.\textsuperscript{117}

Pulmonary vasodilator therapy

Inhaled nitric oxide (iNO) is a selective pulmonary vasodilator\textsuperscript{119} shown to diminish pulmonary oedema and inflammatory markers and promote lung growth in animal models of premature lung injury.\textsuperscript{100, 120} Despite the growing use of iNO as a treatment for PH in BPD, efficacy studies in humans have thus far focused on early iNO administration for the prevention of BPD\textsuperscript{121–125} rather than treatment of established disease. Routine use of iNO for patients with established BPD is not recommended.

Other vasodilator therapies include sildenafil, calcium channel blockers, and bosentan. Sildenafil, a type 5 phosphodiesterase inhibitor, augments cGMP content in vascular smooth muscle. It is approved for adults with PH and has been used for treatment of persistent PH of the newborn.\textsuperscript{126} Mourani and colleagues\textsuperscript{127} examined sildenafil use in 25 infants with chronic lung disease and PH (18 with BPD) and found that 88% of patients showed improvement in their PH by echocardiogram without significant adverse events.

Short-term benefit from calcium channel blockers has been reported in infants with BPD and PH,\textsuperscript{128} but the use is limited by systemic hypotension. Retrospective studies on bosentan, a non-selective endothelin receptor antagonist, suggest safe use for treatment of PH in children as young as 9 months.\textsuperscript{129} However, reports of use in younger children are limited to case reports. Bosentan requires monthly liver function testing due to potential hepatotoxicity.

Preanaesthetic evaluation

Several anaesthetic effects have the potential to produce life-threatening consequences in patients with BPD.
Intraoperative bronchospasm or airway collapse poses serious risks. As patients with BPD have limited respiratory reserve, airway obstruction can quickly lead to profound hypoxaemia, acute PH, right-sided heart strain, arrhythmias, and death. Similarly, anaesthetic effects on myocardial contractility can impair right ventricular function, leading to a reduction in cardiac output and cardiovascular compromise resembling cor pulmonale. Respiratory infections including pneumonia are frequent in this population and can significantly complicate the perioperative course. Because infants with BPD are at high risk of perioperative morbidity and mortality, these issues should be discussed with the parents before anaesthetic administration.

When caring for a patient with a diagnosis of BPD, the anaesthesiologist must thoroughly review the medical history and perform a detailed physical examination in order to minimize the risk of perioperative respiratory and cardiac complications. The preoperative history should specifically address prior anaesthetic history, current medications, allergies, cough or sputum production, prior hospitalizations (including the need for tracheal intubation or i.v. infusions), and exercise tolerance. Assessment of vital signs, type of breath sounds, presence of wheezing or cough, use of accessory muscles, cyanosis, altered mental state, and hydration status is essential during the physical examination. Room air oxygen saturation and $P_{aCO_2}$, available from capillary or venous blood gases, establish baseline oxygenation and acid/base status. Many children with BPD require long-term oxygen supplementation; parents should be questioned regarding home use and recent changes in supplemental oxygen requirements. Oxygen should be made available for operating theatre transport. The possibility of PH and right ventricular dysfunction should be considered and when indicated, evaluated via electrocardiogram and echocardiography.

BPD patients with reactive airway disease and bronchospasm can benefit from the use of nebulized β-2 adrenergic agonists 1–2 h before anaesthetic induction. Those with more severe airway disease might require several days of preoperative inhaled or oral steroid administration. Parents should be instructed to continue home pulmonary medications on the day of surgery. Owing to the high risk of bronchospasm, BPD patients should not be anaesthetized for elective surgery during an acute respiratory infection. Ideally, surgery should be postponed 4–6 weeks after respiratory illnesses.

Special attention must be paid to fluid and electrolyte balance in patients with BPD. Some children will present with electrolyte abnormalities due to chronic diuretic administration. In particular, furosemide can cause hypokalaemia and hypercalciuria, leading to nephrocalcinosis in some infants. Hydrochlorothiazide and spironolactone produce less severe metabolic abnormalities.130

**Perioperative management**

**Immediate preanaesthetic preparation**

Oral midazolam (0.5–1 mg kg$^{-1}$) can be useful for the reduction of anxiety-induced acute bronchospasm. Oversedation can be associated with hypercarbia, hypoxaemia, and airway obstruction. Caution is advised in children with PH and upper airway disease.131 Stress-dose steroid administration is indicated in children with a history of systemic corticosteroid use in the last 6 months.

**Anaesthetic management**

Etomidate is often used to induce anaesthesia in patients with limited haemodynamic reserve, yet its pulmonary vascular effects in children remain unclear. In a study of 12 children undergoing cardiac catheterization, etomidate administration led to only mild increases in PVR that were not statistically significant.132 Thiopental has been reported to decrease PVR but can also cause systemic hypotension due to histamine release.131 Airway instrumentation under thiopental may induce bronchospasm, as the drug provides only a light level of anaesthesia. Ketamine maintains arterial pressure and systemic vascular resistance (SVR) while enhancing smooth muscle relaxation and bronchodilatation directly and by the release of catecholamines. It can be of utility in the actively wheezing child for emergency surgery who is haemodynamically unstable. However, ketamine administration in children with PH remains controversial as some clinical studies suggest an association with elevations in PVR or pulmonary artery pressure (PAP).133–135 Recently, Williams and colleagues136 reported no increases in PVR or PAP in children with PH undergoing cardiac catheterization under 0.5 MAC sevoflurane and a ketamine infusion. The same group performed an investigation of 68 children with PH and found no increase in perioperative complications with ketamine administration.137 Propofol is a bronchodilator and, when compared with thiopental, results in significantly lower rates of wheezing after tracheal intubation. It is the agent of choice in the haemodynamically stable patient with reactive airway disease. Propofol has been used successfully in patients with PH, but large boluses can significantly decrease SVR, impairing biventricular function and perfusion in patients with severe disease.

Volatile anaesthetics mitigate hypoxic pulmonary vasoconstriction, thus decreasing ventilation–perfusion mismatch. Sevoflurane is excellent for an inhalation induction having a decreased incidence of laryngospasm and cardiac dysrhythmias but also bronchodilating effects. It is the agent of choice for mask induction. Volatile anaesthetics should be titrated with care in patients with PH, due to concerns for dose-dependent depression of cardiac contractility and reductions in SVR.

Histamine-releasing neuromuscular blocking agents should be avoided in patients with BPD. As in the asthmatic population, reversal of neuromuscular block with acetylcholinesterase inhibitors must be undertaken with caution due to the risk of muscarinic receptor activation and resultant bronchospasm. Sugammadex offers rapid reversal of neuromuscular block without muscarinic side-effects but has not been sufficiently studied in the infant and neonatal populations to recommend routine use.66
Anaesthetic management of infants and children with BPD parallels the anaesthetic management of asthmatics. Key goals are to provide adequate anaesthesia and analgesia while avoiding bronchospasm, increases in PVR, or decreases in cardiac contractility. Tracheal intubation is the most important risk factor for bronchospasm. Avoiding tracheal intubation by using a mask or LMA for appropriate cases may be useful. Ensuring a deep level of inhalation anaesthesia before tracheal intubation might decrease the risk of elevated airway resistance and bronchospasm that can occur with airway manipulation. I.V. glycopyrrolate or atropine after induction can decrease secretions and provide additional bronchodilatation before tracheal intubation. Properly sized cuffed tracheal tubes allow for lower fresh gas flows, avoiding airway manipulation. Deep extubation avoids the risk of bronchospasm from coughing on the tracheal tube but does not protect the airway from aspiration. Regional anaesthesia avoids airway manipulation but may not be feasible for paediatric patients or for certain sites of surgery.

The goal of mechanical ventilation should be to optimize gas exchange while avoiding ventilator-associated lung injury. There are few clinical studies investigating optimal ventilatory strategies in established BPD, thus most recommendations are based on physiological and structural changes associated with the disease. Most infants present with ventilation–perfusion mismatch and a compensated respiratory acidosis. The time constant is prolonged, thus high respiratory rates are not well tolerated and can lead to gas trapping. This is particularly true in infants with the cystic form of BPD. Oxygen saturation should be maintained higher than 90% to avoid PH and cor pulmonale. Permissive hypercapnia to the patient’s normal $P_{aCO2}$ is acceptable as long as the arterial pH remains above 7.25. Further recommendations are outlined in Table 2. High-frequency ventilation is of reduced utility in patients with established BPD as high airway resistance limits gas delivery and exchange.

Increases in PVR must be treated aggressively to avoid descent into a pulmonary hypertensive crisis. Moderate hyperventilation with 100% oxygen, correction of metabolic and respiratory acidosis, improved analgesia, and the administration of pulmonary vasodilators should be initiated. iNO is typically the pulmonary vasodilator of choice given its rapid onset and ease of administration. Inotropic support should be initiated for persistent systemic hypotension despite the initiation of pulmonary vasodilator therapy. Many clinicians prefer dopamine, epinephrine, and norepinephrine because they do not decrease SVR.

### Post-anaesthetic care

There are no real guidelines or requirements for admission or postoperative care. The postoperative care needed is dependent on age, severity of disease, PH, type of procedure, opioid requirements, parent education level, and distance from hospital. Paediatric intensive care unit admission needs to be available for younger, sicker patients and those requiring mechanical ventilation or continuous positive airway pressure (CPAP) and further diuretic administration.

### Conclusion

Asthma and BPD remain major causes of perioperative morbidity in the paediatric population, despite advancing medical therapies. While pulmonary pathology presents unique management challenges, the anaesthesiologist can make a difference in outcomes with proper preoperative evaluation and preparation for surgery. A multidisciplinary team approach can also significantly improve perioperative outcomes through risk factor modification and appropriate postoperative monitoring.

### Declaration of interest

None declared.

### Funding

None.

### References


### Table 2 Ventilator strategies and targets for children with early and established bronchopulmonary dysplasia. PIP, peak inspiratory pressure; PEEP, positive end-expiratory pressure. Modified with permission.

<table>
<thead>
<tr>
<th>Disease stage</th>
<th>Ventilator strategies</th>
<th>Targets</th>
</tr>
</thead>
<tbody>
<tr>
<td>Early (age 1–4 weeks)</td>
<td>Respiratory rate 25–40 bpm</td>
<td>$SpO_2$ 88–93%</td>
</tr>
<tr>
<td></td>
<td>Moderate PEEP (4–5 cm H$_2$O)</td>
<td>pH 7.25–7.35</td>
</tr>
<tr>
<td></td>
<td>Low PIP (10–20 cm H$_2$O)</td>
<td>$PaCO_2$ 6.7–9.3 kPa</td>
</tr>
<tr>
<td></td>
<td>Inspiratory time 0.35–0.45 s</td>
<td>$PaCO_2$ 6.7–9.3 kPa</td>
</tr>
<tr>
<td></td>
<td>Low tidal volume 3–6 ml kg$^{-1}$</td>
<td></td>
</tr>
<tr>
<td>Established (age &gt; 4 weeks)</td>
<td>Respiratory rate 20–40 bpm</td>
<td>$SpO_2$ 89–94%</td>
</tr>
<tr>
<td></td>
<td>Moderate PEEP 4–8 cm H$_2$O</td>
<td>pH 7.25–7.30</td>
</tr>
<tr>
<td></td>
<td>Lowest PIP required (20–30 cm H$_2$O)</td>
<td>$PaCO_2$ 6.7–9.3 kPa</td>
</tr>
<tr>
<td></td>
<td>Longer inspiratory time 0.4–0.7 s</td>
<td>$PaCO_2$ 7.3–9.3 kPa</td>
</tr>
<tr>
<td></td>
<td>Slightly larger tidal volume 5–8 ml kg$^{-1}$</td>
<td></td>
</tr>
</tbody>
</table>