# 12 The Physiological Effects of Flexible Bronchoscopy: Lessons for the Skilled Bronchoscopist

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## Introduction

> The health and well-being of my patient will be my first consideration. —World Medical Association Declaration of Geneva, *The Physician's Pledge*

Pediatric flexible bronchoscopy (FB) is an important diagnostic and therapeutic tool for the health of children. But what are the effects of FB itself on the patient? This chapter highlights the knowledge about the physiological effects of FB. Selected representative studies will be presented. There are many interesting and useful findings that have practical significance for judicious monitoring and prevention of adverse events during FB. Thus, this information will be valuable in helping to develop a more prudent and proficient practice of FB.

## The Effects of Flexible Bronchoscopy on Pulmonary Function

Placing a bronchoscope within the airway causes airway obstruction! To quantify physiological effects, pulmonary function studies have been obtained on patients and in model systems before, after, and, in some studies, during FB.

Study results in healthy controls after FB have been variable, including findings ranging from no significant effects [1, 2] to decreased pulmonary function [3]. In adult patients with asthma, Bellinger et al. reviewed prior inconsistent studies, which generally included single before and after FB lung function changes. Their recent, more comprehensive study performed serial pulmonary function measurements up to 24 hours following FB in control subjects and patients with non-severe and severe asthma. All subjects received albuterol during pulmonary function testing performed just prior to FB. Similar decreases in FEV1 and FVC were seen among the groups, with a trend of greater change associated with disease severity. The changes persisted longer in patients with severe asthma (Fig. 12.1). A subgroup of patients with asthma underwent a second FB. Those with a 14-day pretreatment with oral prednisolone experienced a faster recovery in lung function compared to controls The authors speculated that inflammation was the cause of the persistent changes in patients with severe asthma following FB [3].

In a NHLBI/NIAID workshop on investigative bronchoprovocation and bronchoscopy, a review evidenced the safety of research bronchoscopy, including bronchoalveolar lavage (BAL), bronchial biopsy with forceps, and brush biopsy in adult patients with asthma, including patients with FEV1 <50%. They also stated that "Premedication with atropine and bronchodila-

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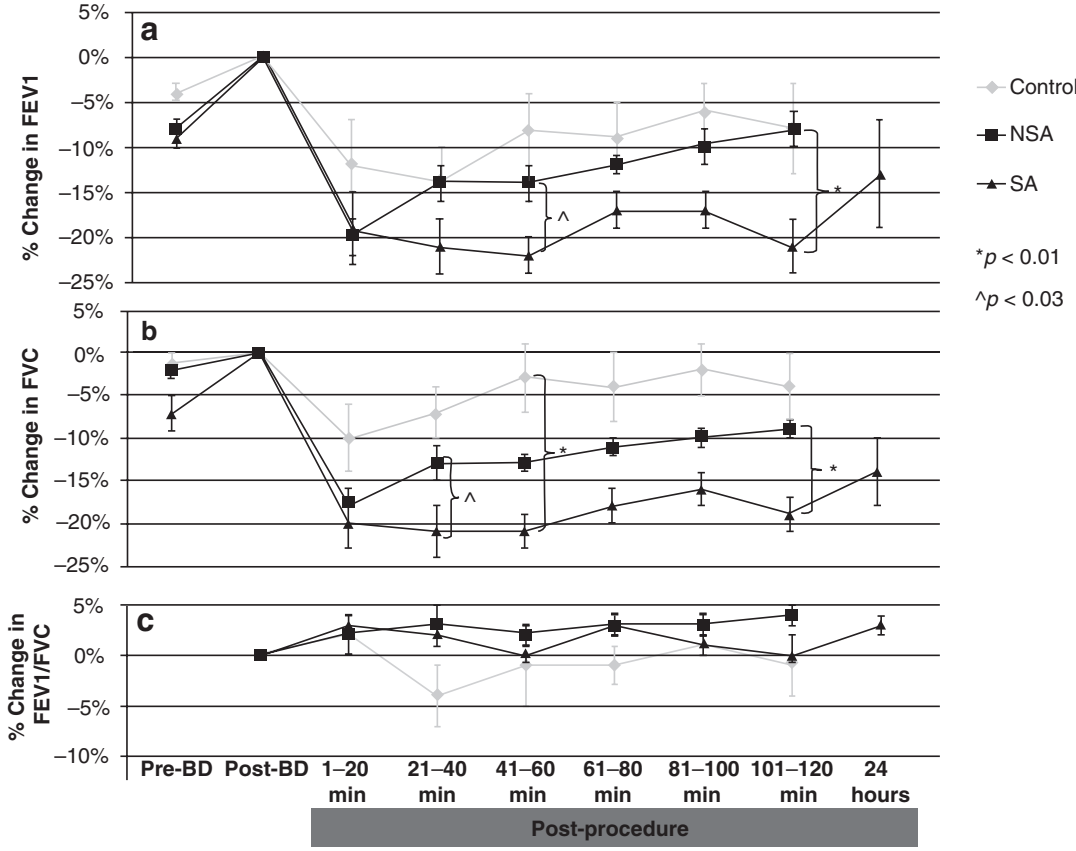


**Fig. 12.1** Changes in lung function following bronchoscopy. Spirometry post-bronchoscopy was compared to the post-bronchodilator, pre-procedure spirometry (baseline). Lung function was grouped in 20-minute intervals. (A) Percent drop in FEV1 among controls, nonsevere asthma (NSA), and severe asthma (SA) patients in 20-minute intervals. At 41–60 and 101–120 minutes post-procedure, the SA group patients were significantly slower to recover lung function compared to the NSA group. Only areas of significance are noted by brackets. (B) Percent drop in FVC among controls, NSA, and SA patients in 20-minute intervals. At 21–40 minute time post-procedure, the SA group was significantly slower to recover lung function compared to the NSA. At 101–120 minute time post-procedure, SA group was significantly slower to recover lung function compared to the control group and NSA group. At 41–60 minute interval, SA had significantly lower lung function than the control group. Only areas of significance are noted by brackets. (C) Change in FEV1/FVC ratio after bronchoscopy with no significant difference in any group at any time point. (Reprinted from Bellinger et al. [3], p. 869, Copyright 2017, with permission from Taylor and Francis. www.tandfonline.com)

tors can be given or omitted, depending on the procedures to be performed and the number of bronchoscopies a research subject may safely undergo over time" [4, 5].

Matsushima et al. studied lung function measurements, including functional residual capacity (FRC), *during* FB in adults, including a subgroup of ventilated patients. Evidence of airflow obstruction peaked during FB (Fig. 12.2) [6].

Measurements of intrabronchial pressures in a prospective, randomized study of intubated adults undergoing FB showed significant increases in peak airway pressures and end-expiratory pressures in volume control (VC) mode ventilation. No changes in tidal volume, $PaO_2$, or $PaCO_2$ were noted. In pressure control (PC) mode, peak airway pressures were unchanged, but tidal volumes decreased significantly while end-expiratory airway pressures (though less change than the volume control mode group) and $PaCO_2$ increased. No significant changes in oxygenation were noted. Thus, while VC mode maintained tidal

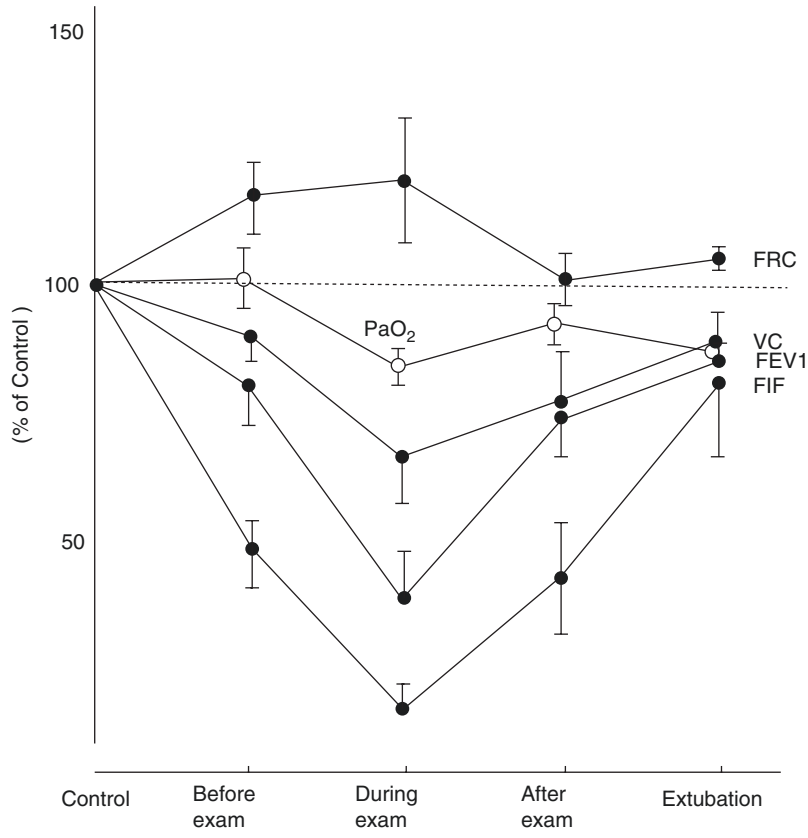


**Fig. 12.2** Changes in pulmonary function and blood gases during FFB examination through an 8-mm endotracheal tube in five patients. Values are mean ± 1 SEM. (Reprinted from Matsushima et al. [6], p. 186, with permission from Elsevier)

volumes and ventilation in these patients, significant airway pressures developed [7].

Lindholm et al. likewise noted significant development of incomplete expiration (auto-PEEP) during FB in ventilated patients in VC mode, leading to a recommendation to discontinue PEEP during VC ventilation while doing FB [8]. Using an adult lung model, Lawson et al. similarly observed auto-PEEP with insertion of the bronchoscope, also less in PC than VC mode. However, they found that adjusting respiratory rates and flow patterns could minimize auto-PEEP [9].

To further analyze lung function effects of FB during mechanical ventilation, Lindholm et al. also performed experimental studies in dogs. Elevated peak end expiratory and peak pressures along with decreased tidal volumes were greatest as the bronchoscope was placed in the airways. These effects became even more pronounced in narrower endotracheal tubes. Furthermore, they measured the effect of suctioning and consequent air removal in rapidly decreasing airway pressure to a negative measurement despite ongoing mechanical ventilation (Fig. 12.3). Analogous effects were noted in a small group of ventilated adult patients with increasing $PaCO_2$ and cardiac output with decreasing tidal volume and $PaO_2$ during FB with "intermittent suctioning"(Fig. 12.4). As a result, one of the study conclusions included the caution to "suction for short periods only" [8].

Moreover, studies in both a lung model and ventilated adult patients revealed that suction pressures of −20 to −80 KPa can lower lung volumes by exceeding minute ventilation and thus pose a risk for lung collapse [10]. Indeed, a case report concluded that unilateral pulmonary edema was caused by negative pressure from suctioning in an infant undergoing FB [11]. Thus, the wary bronchoscopist should take precautions during FB to avoid reduction of FRC and consequent effects on gas exchange by overly zealous suctioning.

Using a smaller bronchoscope can substantially decrease the respiratory and hemodynamic effects of FB as noted in a comparison study of

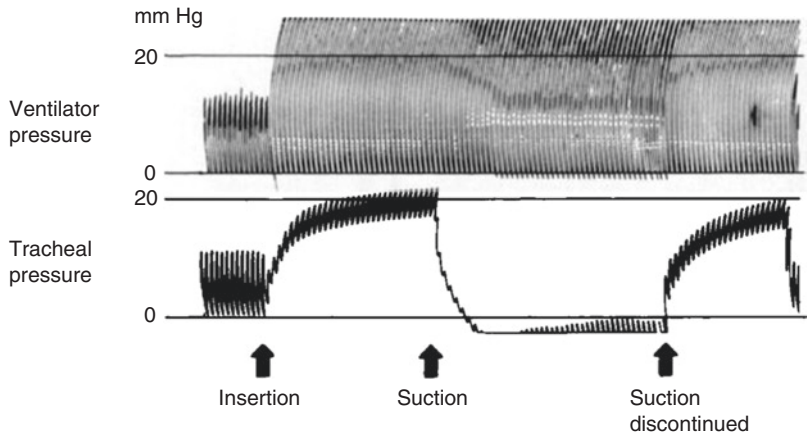


**Fig. 12.3** Simultaneous recording of ventilator and intratracheal pressure in a dog during controlled mechanical ventilation through a tracheal tube of 7.0 mm ID with a tidal volume of 30 ml/kg body weight and ventilator rate of 30 cycles/min. Insertion of the 5.7 mm ED bronchoscope resulted in immediate elevation of peak inspiratory ventilator pressure due to airway obstruction. Due to the narrow scale used, full deflection of the recording pen for ventilator pressure was precluded. The tracheal pressure tracing shows a more gradual elevation of peak inhalation pressure and a marked PEEP effect of 16 mm Hg, still rising when suction started after 1 minute. When a negative pressure of 62 mm Hg was applied to the suction port, in six ventilator cycles (12 seconds), the intratracheal pressure became continuously negative, indicating removal of air from the lungs in spite of unchanged ventilator function. Discontinuation of suction gradually restored presuction tracheal pressures, which finally returned to control values upon removal of bronchoscope (at the very end of the recording). (Reprinted from Lindholm et al. [8], p. 364, with permission from Elsevier)

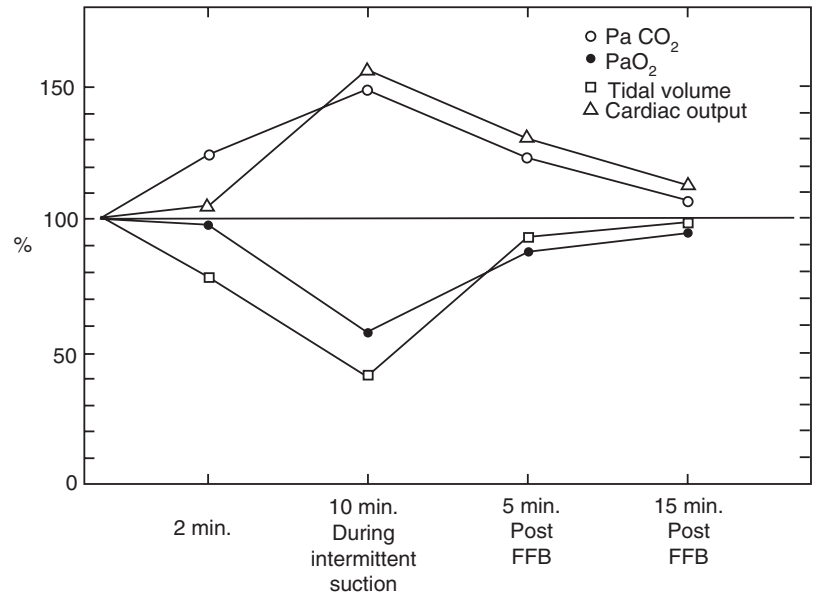


**Fig. 12.4** Variation of four variables during FFB in six critically ill patients during on-going controlled mechanical ventilation. Pre-bronchoscopy values set at 100%. Measurements were repeated at 2 minutes after insertion of the bronchoscope, at 10 minutes during on-going intermittent suctioning, and at 5 and 15 minutes following FFB. (Reprinted from Lindholm et al. [8], p. 366, with permission from Elsevier)

pediatric versus adult bronchoscopes in mechanically ventilated adults undergoing BAL [12].

The underlying anatomy and respiratory physiology of infants and young children would suggest that airflow and gas exchange would be even more dramatically compromised in contrast to adults. Utilizing an ultrasonic flow sensor, spirometry during FB with a 3.5-mm bronchoscope was studied in young children 3 days to 25 months of age. The results showed significant reductions in tidal volumes (from mean 5.0 ± 0.5 to 3.4 ± 0.5 ml/kg), minute ventilation (176 ± 17 to 121 ± 13 ml/kg/min), and peak expira-

tory (78 ± 12 to 52 ± 10 ml/s) and inspiratory flows (98 ± 15 to 66 ± 12 ml/s) from passing the instrument from the hypopharynx to mid-trachea. These changes decreased with application of CPAP [13].

Hsia et al. utilized a pediatric lung model to study the potential effects of FB during mechanical ventilation in the smaller airways of children. Dramatic changes were associated with increasing size of the bronchoscope relative to the endotracheal tube. With introduction of a pediatric flexible bronchoscope during pressure control ventilation, tidal volumes decreased significantly from 700 ml to 40–280 ml (Fig. 12.5). In volume control mode, tidal volumes were generally maintained, but peak inspiratory pressures rose dramatically. In addition, with increasing obstruction from higher ratios of bronchoscope to endotracheal tube size, expiratory flows decreased and increased inadvertent or high auto-PEEP developed during volume-control ventilation, but not during pressure control ventilation. Further obstruction from intrinsic airway abnormalities as well as underlying lung disease would be expected to further amplify these results.

The authors suggested that volume-controlled ventilation would be the preferred mode for FB in ventilated patients due to better maintenance of tidal volume, but at the greater risk of developing auto-PEEP. To avoid significant obstruction and allow adequate mechanical ventilation during FB, their model suggested a diameter guideline for bronchoscope-endotracheal tube difference of >1.3 mm for infants and toddlers, >2 mm for small children, and >2.5 mm for adolescents/young adults. However, the authors acknowledged limitations to these guidelines [14].

## Hemodynamic Effects

The most common and evident hemodynamic effects of FB are transient sinus tachycardia or bradycardia [15, 16]. These are felt to be due to reflex sympathetic or vagal stimulation. There have been several studies using Holter monitoring to evaluate for possible arrhythmias in adults during FB, though no similar studies in children. A prevalence of minor arrhythmias ranging from

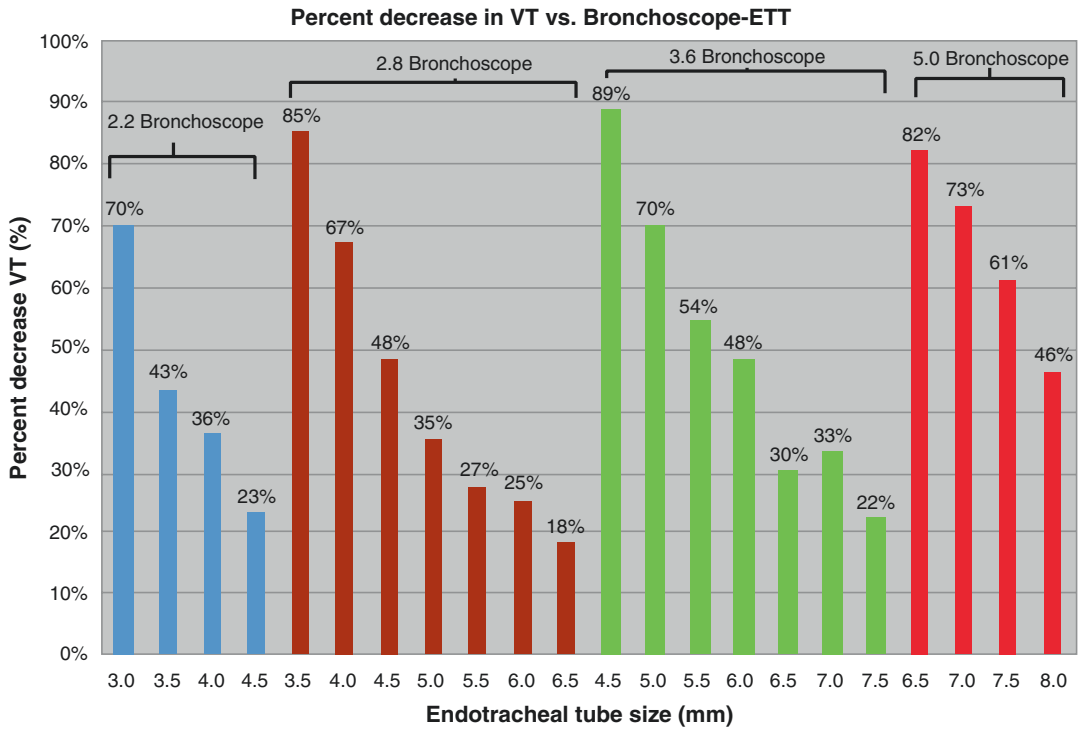


**Fig. 12.5** Percent decrease in tidal volume ($V_T$) after bronchoscope insertion during pressure control ventilation. (Adapted from Hsia et al. [14], p. 37, with permission from Elsevier)

60% to 77%, increasing in the presence of hypoxemia, has been found in adult studies [17].

Many of the details about the stimulatory hemodynamic effects from FB have been obtained from studies in adults on FB during mechanical ventilation. These effects include increases in heart rate, mean arterial pressure, cardiac index, and pulmonary wedge pressure [8, 18, 19].

In addition, mesenteric blood flow has been discovered to be decreased during FB in adult patients undergoing FB. As a result, Nayci et al. cautioned about the potential risk of FB for mesenteric ischemia and gastrointestinal bacterial translocation [20].

In a comparison study in infants undergoing intubation by either direct laryngoscopy or fiberoptic orotracheal intubation, no significant differences in hemodynamic changes were found. Both groups experienced mildly increased heart rates and mildly decreased blood pressures along with no significant changes in oxygen saturation and end-tidal $CO_2$ [21].

The potential lung function effects of suctioning were previously discussed. A prospective observational study evaluating the cardiovascular effects of suctioning during endotracheal intubation in sedated children revealed transient but clinically insignificant changes in heart rate, blood pressure, cerebral regional oxygen saturation, systemic oxygen saturation, and somatic regional (renal) oxygen saturation. In addition, saline instillation during endotracheal tube suctioning had no adverse effects on systemic or cerebral oxygenation [22].

## Gas Exchange Effects

The most significant physiological effect of bronchoscopy is hypoxemia due to hypoventilation and potentially due to other factors such as ventilation-perfusion inequality with bronchoalveolar lavage and depression of respiratory drive by sedation. An early study in adults using blood gas analysis revealed average declines in arterial oxygen pressure of 20 torr during the procedure with a return to baseline within 2 hours after FB [23]. As noted previously (Fig. 12.2), the peak abnormalities in gas exchange occur during the procedure. The effect of suctioning during bronchoscopy further alters gas exchange (Fig. 12.4) during mechanical ventilation, as shown in a study of adult patients on mechanical ventilation [8].

Studies in children have found that the frequency and degree of oxygen desaturation during FB is correlated with the degree of sedation, younger age (<2 years of age), and underlying laryngeal or tracheal abnormalities [16, 24].

Younger children are at greater risk for compromised ventilation from FB due to the relative size of the bronchoscope to their airways and consequent higher resistance. A study of pediatric FB utilizing pulse oximetry revealed that oxygen desaturations were frequent during FB and occurred more frequently in children who were less than 1 year of age, children with a history of prior oxygen therapy, and when the bronchoscope was located in the mid-trachea (Figs. 12.6 and 12.7). Pre-procedural assessment by pulse oximetry, supplemental oxygen, and shorter procedure time were suggested to reduce the risk of hypoxemia [24].

The evidence-based Practice Guidelines for Moderate Procedural Sedation and Analgesia 2018 recommends, "Use supplemental oxygen during moderate procedural sedation/analgesia unless specifically contraindicated for a particular patient or procedure." Their analysis indicated that the literature was insufficient to recommend a particular method of supplemental oxygen administration. Continuous monitoring by pulse oximetry with alarms is also recommended [25].

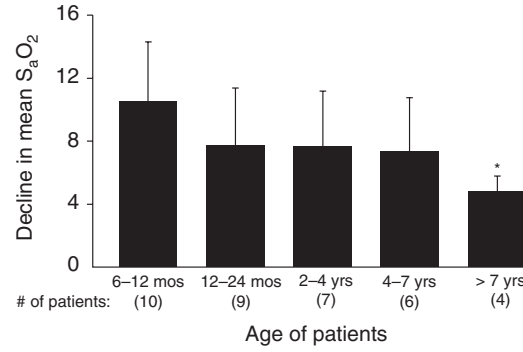


**Fig. 12.6** Age of patients vs decline in mean $SaO_2$. Data represent percent ± SD. Asterisk indicates $p < 0.05$. (Reprinted from Schnapf [24], p. 592, with permission from Elsevier)

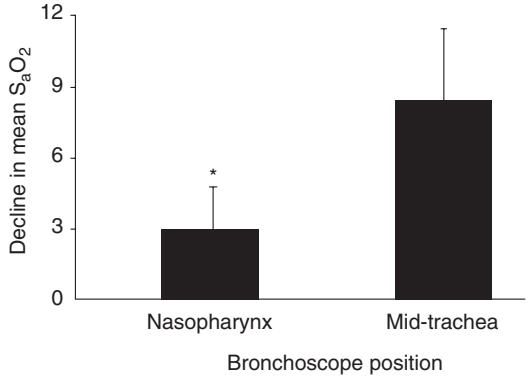


**Fig. 12.7** Position of bronchoscope vs decline in mean $SaO_2$. Data represent percent ± SD. Asterisk indicates $p < 0.05$. (Reprinted from Schnapf [24], p. 593, with permission from Elsevier)

However, pulse oximetry monitoring does not assess potential hypoventilation. Different studies on gas exchange in FB in adults have shown variable results from no change to increased $PaCO_2$ [6, 8, 23, 26, 27].

Studies have attempted to assess potential hypercapnia in children using techniques including nasal cannula, but the accuracy of such measurements are limited during FB because of suctioning, instillation, and supplemental oxygen administration. To address the issue of more accurate $PaCO_2$ measurement during FB in children, a prospective study was performed utilizing endoscopic intratracheal $CO_2$. Statistically significant changes in end-tidal $CO_2$ ($P_ECO_2$) were noted in all cohorts, including those without airway lesions. The changes were greater in the cohorts with either extra-thoracic or intra-thoracic lesions (increases in $P_ECO_2$ of 3, 4.5, and 8 mmHg for no, extra-thoracic, intra-thoracic lesions, respectively) (Fig. 12.8) [28].

Another technique to evaluate alveolar ventilation that is not compromised by issues of alveolar plateau measurements of end-tidal $CO_2$ or dilution of sampled gas by instillation of fluids, suctioning, or oxygen supplementation is transcutaneous $CO_2$ ($TcCO_2$). Sadot et al. utilized a newer $TcCO_2$ monitor with less calibration concerns. Their study in 95 children undergoing diagnostic FB (mean duration of FB was 33 minutes) showed a median $TcCO_2$ rise of 17 mm Hg with an interquartile range of 6.5, 23.7 (Fig. 12.9). Children receiving >3.5 mg/kg of propofol (sedation to be further discussed later in this chapter) had a higher rise in $TcCO_2$ of 22.5 mmHg compared to 13.6 mmHg receiving a lower dose. Of note, they found no correlation of the peak or amount of increase of $TcCO_2$ with age, weight, bronchoscope size, or diagnosis. Moreover, they detected no differences in peak or rise of $TcCO_2$ in patients who had bronchoalveolar lavage compared to those without BAL. The authors concluded that $TcCO_2$ monitoring is feasible and should be added to FB, especially when large amounts of sedation are expected and in patients at risk for complications of respiratory acidosis [29].

Based on a meta-analysis that revealed that continuous end-tidal carbon dioxide monitoring was associated with reducing frequency of hypoxemic events, the Practice Guidelines for Moderate Procedural Sedation and Analgesia 2018 recommended capnography "unless precluded or invalidated by the nature of the patient, procedure, or equipment" [25].

Ventilation support in order to safely perform FB may be required especially in patients with compromised lung function or airways or other significant underlying disorders. Strategies for improving oxygenation or ventilation during FB include use of supplemental oxygen with mask, nasal prongs, nasopharyngeal tube, or transnasal catheter, sedation reversal, bag-mask ventilation, CPAP via mask, laryngeal mask ventilation, including helium-oxygen, and/or intubation. However, some of these techniques will preclude a complete upper airway exam including vocal cord movement, increase the risk for laryngospasm, affect lower airway dynamics, limit the size of the bronchoscope that can be used, affect its manipulation, or require additional sedation [15, 30–34].

## Additional Effects of Bronchoalveolar Lavage

A common, additional procedure of FB is bronchoalveolar lavage (BAL). It has been shown to be tolerated even in critically ill children [35, 36]. What are the additional physiological consequences of BAL? The potential for hypoxemia is

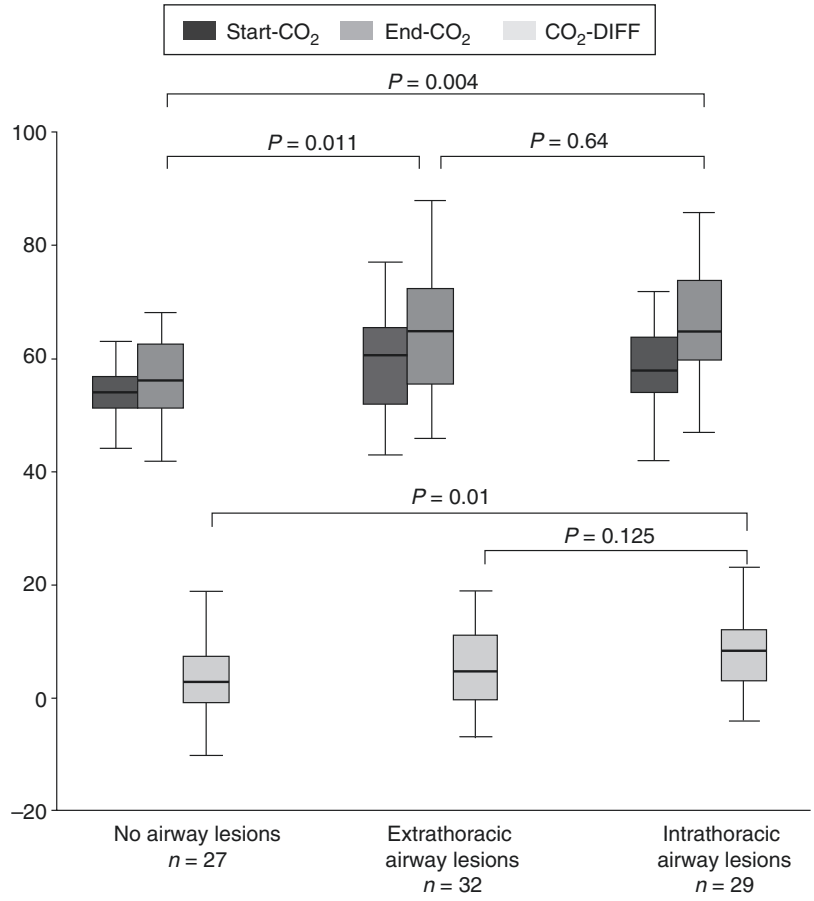


**Fig. 12.8** Box-plot of median and interquartile range of endoscopic intratracheal $CO_2$ measurements on the initial pass of the bronchoscope (Start-$CO_2$), at the completion of the procedure (End-$CO_2$), and the $CO_2$-change (End-$CO_2$ minus Start-$CO_2$), in the children grouped by airway lesion type (no airway lesions, extrathoracic, and intrathoracic airway lesions). The *P*-values refer to comparison between the groups using Wilcoxon test for unpaired data and Mann-Whitney for paired comparisons (*P*-values in the results section for comparison of more than two groups refers to Kruskal-Wallis test). (Reprinted from Chang et al. [28], p. 653, with permission from John Wiley & Sons, Inc.)

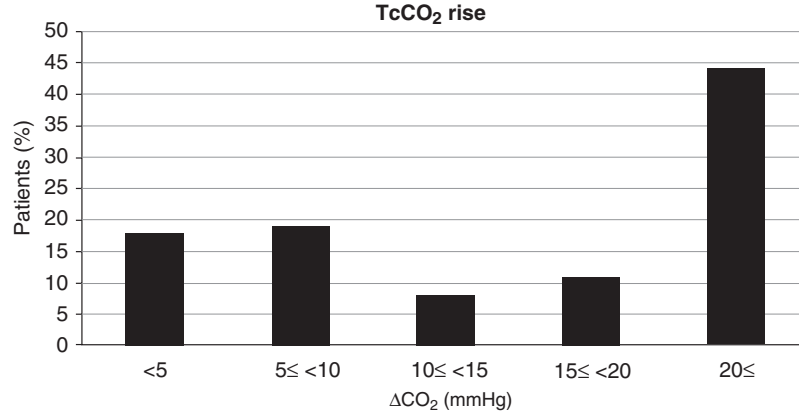


**Fig. 12.9** Distribution of elevation of transcutaneous pCO2 in children undergoing flexible bronchoscopy. (Adapted from Sadot et al. [29], p. 1180, with permission from John Wiley & Sons, Inc.)

further increased with BAL [18, 23, 36, 37]. Another physiological finding associated with BAL is transient fever, especially in young patients [36, 38–40].

The physiological effects of large volume BAL with 1000 ml saline lobar lavage was studied in a comprehensive fashion in healthy adult patients by Burns et al. They found a mean decrease of 30 torr in $PaO_2$ (Fig. 12.10), with the greatest decrease occurring during insertion of the bronchoscope and during lobar bronchus occlusion with an inflation cuff.

Ventilation and perfusion scans revealed abnormalities of decreased ventilation and perfusion persisting for hours with return to normal usually by 24 hours. Ventilation defects were not altered by use of supplemental oxygen. However, perfusion defects were decreased in those who were treated with supplemental oxygen.

$PaO_2$ was significantly lower after lavage in subjects who had received supplemental oxygen during FB and discontinued at the end of FB, and recovered more slowly than subjects receiving no supplemental oxygen! Hypoxemia was noted to persist up to 8 hours in the group who had received supplemental oxygen (Fig. 12.11). It was concluded that the use of supplemental oxygen resulted in less matching of the ventilation-perfusion abnormalities induced by lavage, with consequent effects on gas exchange following the procedure.

Furthermore, temperature differences of the lavage have been evaluated and found to lead to dissimilar results. Room temperature, compared to body temperature, saline lavage resulted in a greater changes in lung function, performed within 2–4 hours after lavage, including declines in vital capacity (VC), total lung capacity (TLC) (20% decrease), and $FEF_{25–75}$, and an increase in residual volume. In contrast, subjects lavaged with body temperature saline did not show significant declines in VC, TLC, $FEF_{25–75}$, but did have increased residual volume. No significant changes were noted in $PaO_2$, $FEV_1$, or Raw in either group. The authors stated that the reasons for the lavage temperature effect were obscure [26].

Ettensohn et al. studied the lung function effects of repeated BAL with 120 ml aliquots (3–5 procedures/person with an average interval

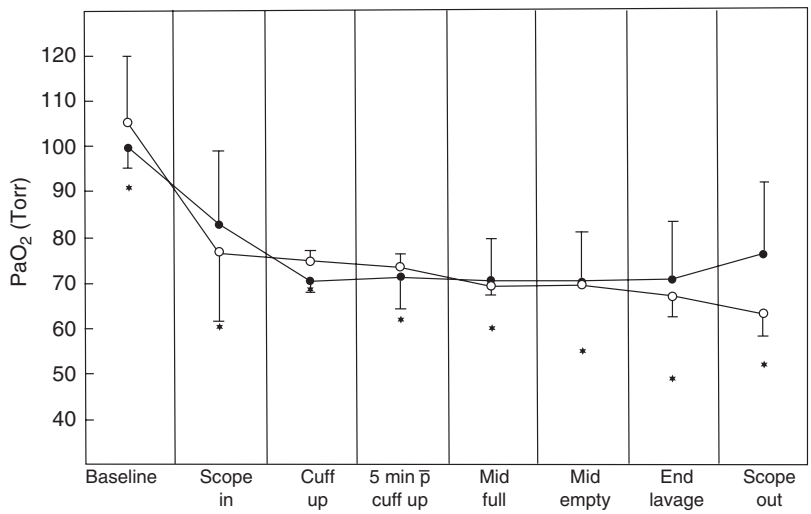


**Fig. 12.10** Arterial $PO_2$ during lavage with saline at room temperature with subjects breathing room air (• = mean values for lavaged subjects; O = mean values for control subjects; * = lowest Pao2 recorded in the entire group at each time point). Middle full and middle empty measurements were made after the fifth aliquot, with that aliquot in the lung (full) or after it had been aspirated (empty). Brackets indicate one standard deviation of the measurements. (Reprinted with permission of the American Thoracic Society. Copyright © 2019 American Thoracic Society. Burns et al. [26], p. 697)

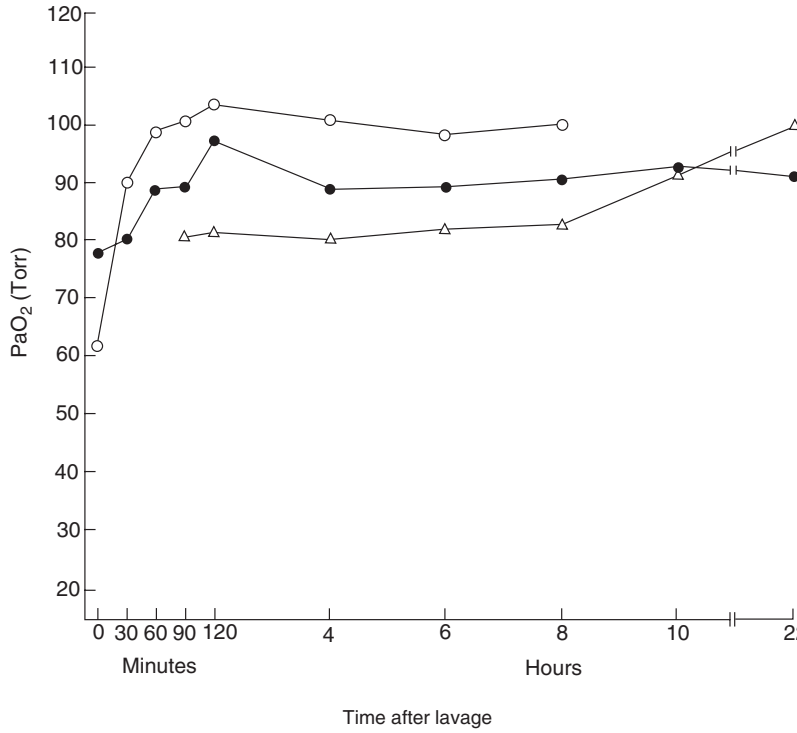


**Fig. 12.11** Arterial $PO_2$ after lavage (• = mean values for subjects lavaged while breathing room air; A = mean values for subjects lavaged while receiving supplemental oxygen; O = mean values for control subjects). The control values at 30 and 60 min are mean values for the three room air control subjects breathing room air; thereafter, the values are the mean values for the combined group of room air and supplemental oxygen control subjects. (Reprinted with permission of the American Thoracic Society. Copyright © 2019 American Thoracic Society. Burns et al. [26], p. 697)

of 4.7 months) in healthy adult volunteers. They found no persistent changes in pulmonary function tests, VC, TLC, $FEV_1$ or DLCO following repeated procedures [41].

In summary, BAL leads to additional physiological consequences, increasing with larger BAL volumes and room temperature more than body temperature lavage. While supplemental oxygen will moderate hypoxemia incurred during BAL, less matching of ventilation-perfusion abnormalities may lead to prolonged hypoxemia for hours after FB. Therefore, BAL should be performed with body temperature lavage and supplemental oxygen, with prolonged oxygen likely required after FB, especially with large volume BAL in sick patients.

## Body Temperature Effects

Another physiological response to FB is fever. One prospective study evaluating fever within 24 hours after FB in children showed an overall incidence of 48% (44/91 patients). This study reported a significant difference of 18.2% incidence of fever in patients having FB without BAL compared to 52.2% in the BAL group. The risk of fever was increased in children less than 2 years of age, presence of positive bacterial colonies in BAL, and abnormal bronchoscopic findings [38].

A fever incidence of 37.8% (56/148 children) was noted in another prospective study of fever following FB with BAL in children. In this study, a multivariate analysis revealed only one risk factor for fever, children less than 2 years of age

[39]. In a retrospective analysis, a 17% incidence of fever (defined ≥39 °C) was found after FB with BAL in non-critically ill, immunocompetent children with underlying pulmonary disease. In this study, an abnormal BAL fluid cell differential was associated with fever [40].

## Intracranial Pressure Effects

Due to prior reports of increased intracranial pressure (ICP) during FB in adults with severe brain injuries, Kerwin et al. carried out a prospective study on changes in ICP during FB. This study also evaluated possible pharmacological protection [42].

This study showed immediate changes with a substantial but transient increase in ICP along with concomitant increase in mean arterial pressure. Consequently, cerebral perfusion pressure (CPP) remained close to baseline. ICP increased from a mean baseline ICP of 12.6 mmHg to a mean peak ICP of 38.0 mm Hg (Fig. 12.12). The procedure time was 6 minutes, and the average time for return of ICP to baseline was 13.9 minutes. Subgroup analysis comparing patients with a baseline ICP ≤10 mmHg vs >10 mmHg showed comparable patterns of increases in mean ICP and MAP, close to baseline CPP, and time of return to baseline. No persistent changes in ICP and no evident neurological sequelae from FB were noted in the patients with brain injury following FB.

Based on prior studies, they used a sedation, analgesia, paralysis, and topical anesthesia protocol of vecuronium, morphine, midazolam and, in the subgroup of patients with ICP >10 mmHg, nebulized 4% lidocaine mmHg. However, they found that this protocol did not completely blunt the increase in ICP. The authors suggested that detecting rapid, high rises in ICP from routine suctioning might be useful in the "discretion" for doing a FB.

In another study of adult patients with severe head injury, similar findings of clinically insignificant increase of ICP, with a mean increase of

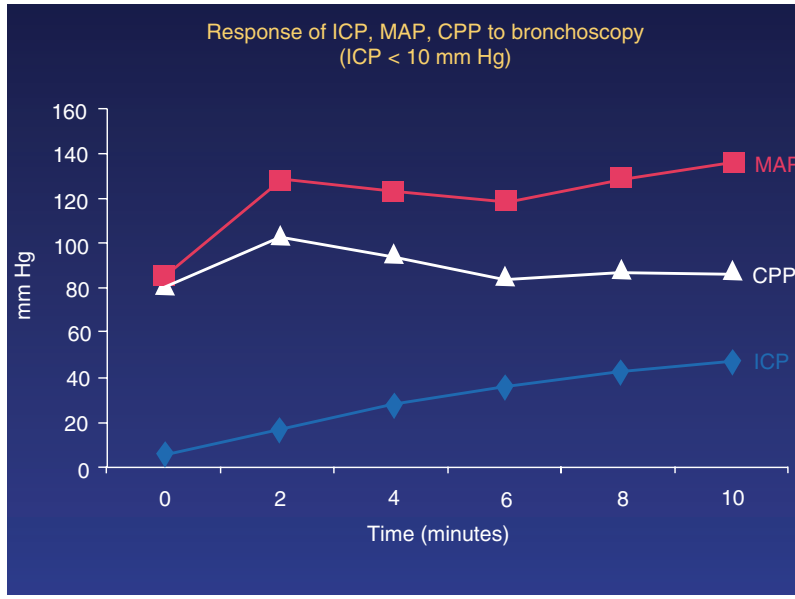


**Fig. 12.12** Response of intracranial pressure (ICP), mean arterial pressure (MAP, and cerebral perfusion pressure (CPP) to flexible bronchoscopy in patients with baseline ICP ≤ 10 mm Hg. (Adapted from Kerwin et al. [42], p. 879. https://journals.lww.com/jtrauma/pages/articleviewer.aspx?year=2000&issue=05000&article=00011&type=abstract)

13.5 mm Hg in ICP and a mean increase in MAP of 19.2 mm Hg with consequent increase of CPP of 14% were noted, returning to baseline immediately following the procedure. No patients had changes in Glasgow Coma Scale or neurologic exam following FB [43].

## Physiological Effects of Anesthetic Agents

While there is a specific consensus statement about sedation for FB in adults [44], no similar statement for pediatric FB sedation has been published. There are general pediatric guidelines about monitoring and management for sedation for diagnostic and therapeutic procedures by the American Academy of Pediatrics and American Academy of Pediatric Dentistry [45] and the Practice Guidelines for Moderate Procedural Sedation and Analgesia 2018 [25]. Adequate sedation with airway management for pediatric FB is considered a requirement in order to improve patient comfort and anxiety, maintain hemodynamics, provide for adequate gas exchange, and provide conditions for a successful FB [15, 31].

A confounding variable in evaluating the data about the physiological effects of FB is variation in sedation and topical anesthesia, which are often not specified or quantified in studies in FB. There are studies in adult patients evaluating FB with only topical anesthesia and comparing groups receiving sedation vs no sedation. For example, using a verbal analog scale, Gonzalez et al. found that patients receiving sedation during FB had less cough, pain, sensation of asphyxiation, higher global tolerance, and lower heart rate and blood pressure responses compared to the no sedation patients [46]. Yung-Lun et al. also found that sedation resulted in similar patient subjective scores along with less hypertensive but more hypoxemic episodes that were transient and non-life-threatening [47].

Some of the anesthetic agents commonly used for pediatric FFB and their direct, physiological consequences will be reviewed. The reader is referred to the chapter by Bruins, Laverriere, and Kilbaugh in this book for further information on anesthesia for FB.

The most important adverse concern about sedation is respiratory depression. Minor, usually clinically insignificant consequences from anesthesia during FB may occur including transient hypoxemia and hypercapnia, transient apnea, cardiac arrhythmia (transient bradycardia and tachycardia), transient hypotension, as well as nausea and vomiting. However, significant anesthesia complications during FB can occur, including significant episodes of apnea, hypoxemia, hypercapnia, hypotension, nausea and vomiting, and aspiration [15, 16].

Lidocaine is the most commonly used topical anesthetic agent for FB. The primary concern is lidocaine toxicity. Lidocaine maximum dose is stated as 7–8 mg/kg for adults [44]. For children, 4.5 mg/kg for children has been recommended by Drugs.com [48], whereas an ERS Task Force on pediatric FB has indicated a maximum dose of 5–7 mg/kg for topical lidocaine [31]. In a study of lidocaine for pediatric FB, serum levels were monitored and doses up to 7 mg/kg (175 mg/m$^2$) and up to 7–8.5 mg/kg for longer procedures were considered safe for children [49]. Toxic doses lead to dose-dependent effects including hypotension, myocardial depression, seizures, unconsciousness, apnea, coma, and cardiovascular depression (Table 12.1) [50].

At topical anesthesia doses, lidocaine has been shown to have physiological effects of note for FB. It attenuates cardiovascular responses to

**Table 12.1** Dose-dependent effects of lidocaine

| Plasma lidocaine concentration (μg/ml) | Effect |
|---|---|
| 1–5 | Analgesia |
| 5–10 | Circumoral numbness<br>Tinnitus<br>Skeletal muscle twitching<br>Systemic hypotension<br>Myocardial depression |
| 10–15 | Seizures<br>Unconsciousness |
| 15–25 | Apnea<br>Coma |
| >25 | Cardiovascular depression |

Adapted from Table 10-2, Maheshwai and Naguib [50], p. 293

awake intubation [50]. There was one published report that topical lidocaine for FB in children exaggerated laryngomalacia [51]. However, this finding was refuted in a subsequent study [52].

Among the more common agents used during FB are benzodiazepines, opiates, and propofol [16, 44]. Midazolam is the most commonly used benzodiazepine for intravenous sedation in pediatrics. The most significant side effect of midazolam is dose-dependent decrease in ventilation by decreasing hypoxic drive. This effect is further exaggerated by additional use of opiates and other CNS-depressant drugs.

Midazolam also decreases upper airway activity and depresses the swallowing reflex. Hemodynamic effects include decreased systolic blood pressure and elevated heart rate. It causes dose-dependent changes in regional cerebral blood flow in brain regions associated with the normal functioning of arousal, attention, and memory. Midazolam results in little to no change in ICP in patients with decreased CNS compliance. Midazolam does not prevent cardiovascular responses to intubation [53].

Opiates (short-acting agents such as fentanyl and remifentanil are primarily used for FB) may have the physiological consequences of dose-dependent and gender-dependent depression of ventilation, bradycardia, with consequent decrease in blood pressure and cardiac output especially in neonates, and modest increases in ICP. As noted previously, opiate–benzodiazepine combinations may result in synergistic depression of ventilation [53, 54].

Propofol is a commonly used non-barbiturate, non-opiate, non-benzodiazapine IV sedation agent for FB. Potential physiological effects include decreased cerebral blood flow, intracranial pressure, systemic blood pressure, and dose-dependent respiratory depression. It can produce bronchodilation. Profound bradycardia and asystole have been reported in healthy adults [53]. With regard to upper airway physiology, vocal cord and pharyngeal function, with consequent increased risk for aspiration, are compromised during procedural sedation. A prospective study of propofol anesthesia in children showed return of normal vocal cord movement upon emergence from anesthesia, thus permitting adequate assessment of vocal cord function at the conclusion of FB [55].

Ketamine can result in bronchodilator activity, no significant respiratory depression, emergence delirium, and increased cerebral blood flow and metabolic rate with subsequent increased ICP, though this latter finding has not been universally noted in studies. Unique among injected anesthetics, ketamine does result in cardiovascular stimulation including increases in systemic and pulmonary artery blood pressure, heart rate, and cardiac output [53].

An additional sedative agent that causes only mild respiratory depression is the alpha-2 adrenergic agonist, dexmedetomidine. It may lead to bradycardia and hypotension. In addition, it results in prolonged recovery times compared to other sedative agents [53].

Thus, anesthesia for FB may result in significant physiological changes in addition to the changes from the manipulation of the bronchoscope. In the largest prospective study of complications of FB in children (1153 children), transient oxygen desaturation was significantly higher in those undergoing deep sedation (6.3%) vs conscious sedation (0.7%) [16].

Consequently, the bronchoscopy team should be vigilant about both the anesthesia and operation of the flexible bronchoscope for possible adverse events while monitoring the patient. Patients with significant underlying conditions including chronic cardiovascular disease, significant congenital airway disorders, severe obstructive sleep apnea, and other disorders predisposing to potential of significant airway obstruction are at further risk for greater physiological effects from FB with sedation [16, 25, 45]. Furthermore, greater potential for physiological changes should be anticipated to occur during interventional FB due to the increased complexity and procedure time [56].

## Procedural Anxiety

In addition to the actual instrumentation and anesthesia for FB, other environmental factors may alter the physiological responses to procedures.

Preoperative anxiety is estimated to occur in up to 75% of children. As reviewed by Chow et al., preoperative anxiety can result in a number of negative postoperative outcomes including prolonged anesthesia induction, poorer postoperative recovery, and higher doses of postoperative analgesia [57]. Beyond increasing preoperative anesthesia, a number of non-pharmacologic measures have been utilized to reduce preoperative anxiety.

A Cochrane Collaboration analysis on non-pharmacological interventions to assist induction of anesthesia in children revealed that parental presence during induction of anesthesia does not diminish anxiety. Other measures such as parental acupuncture, clowns/clown doctors, playing videos of the child's choice during induction, low sensory stimulation, and hand-held video games were felt to be promising but not conclusively proven ways of reducing anxiety [58].

A recent systematic review suggested that audiovisual interventions are more effective than standard-of-care measures of non-intervention, parental presence, or low dose of sedative medication [57]. Preoperative music listening has also been shown to reduce preoperative anxiety in one study in children [59], with similar positive results on anxiety reduction in a study on music before FB in adults [60]. A meta-analysis in adults also found that music during FB lowered physiological responses of blood pressure and heart rate [61]. Reducing sensory stimuli and child life specialists are additional promising measures, which may reduce anxiety and possibly reduce sedation requirements for procedures [62]. Thus, non-pharmacological measures may be useful in reducing preoperative anxiety and, in the case of music, potentially reduce physiological responses during FB.

## Clinical Implications of the Physiological Effects of Flexible Bronchoscopy

Flexible bronchoscopy has been safely performed in the sickest neonates and children in intensive care units, and children undergoing more complex interventions [15, 31, 35, 63, 64]. A comprehensive review of FB studies among critically ill children revealed that the most commonly reported adverse events were transient and included hypotension, hypoxemia, and/or bradycardia requiring minimal intervention [35].

The physiological changes induced by fiberoptic bronchoscopy have been reviewed. There should be caution in interpreting the published data on physiological effects of FB. Much of the available data presented were from studies in adult patients. Circumspection must be exercised in extrapolating these effects in children. Presumably, these effects in children would be greater due to higher airway resistance and smaller airways along with the relative size of the bronchoscope to the airways, especially in infants. In addition, other precautions in evaluating the studies include the presence of different underlying health conditions that can affect the degree of physiological effects, the variable techniques of FB used such as trans-nasal vs use of face mask, LMA, or through an endotracheal tube, the variable strategies of anesthesia used, and the lack of information about other factors such as procedure time, the relative size of the bronchoscope(s) used in relation to patient size, amount of suctioning, and experience of the individuals performing the procedures.

Nonetheless, the available information does provide important lessons in understanding the pathophysiology of many of the potential complications and the basis for monitoring in FB. We have also learned that there are potentially multiple controllable factors that can reduce adverse consequences of FB. These include the relative size of the bronchoscope being used in relation to the size of the patient's airways, the length of the procedure, suctioning, and anesthesia.

Thus, the physiological consequences of fiberoptic bronchoscopy point to the following procedural caveats (Table 12.2):

**Twelve caveats for flexible bronchoscopy**

1. Use the smallest bronchoscope necessary to accomplish the procedure in order to reduce airway obstruction effects.
2. Adequate topical anesthesia should be administered to avoid potential barotrauma

**Table 12.2** Twelve caveats for flexible bronchoscopy (See text for details)

| |
|---|
| 1. Use the smallest bronchoscope necessary to accomplish the procedure |
| 2. Use and monitor topical anesthesia and sedation carefully |
| 3. Administer supplemental oxygen and monitor oxygenation |
| 4. Monitor for airway obstruction |
| 5. Monitor ventilation |
| 6. Keep suctioning to a minimum |
| 7. Keep the procedure time to a minimum |
| 8. Avoid "bronchoscopist's hypnosis" |
| 9. For patients undergoing bronchoalveolar lavage (BAL), a) oxygen may be needed for hours after the procedure; b) use body temperature rather than room temperature lavage fluid especially for large volume BAL |
| 10. In ventilated patients, monitor and adjust for hypoventilation and inadvertent auto-PEEP |
| 11. In patients with airway hyperreactivity, consider bronchodilator prior to procedure |
| 12. Carefully consider performing flexible bronchoscopy in children with high-risk conditions |

from coughing, as well as to avoid potential cough-receptor-induced bronchospasm or laryngospasm. In addition, proceeding with flexible bronchoscopy should be delayed to allow for sufficient topical anesthesia and attenuation of cardiovascular response from topical anesthesia. Appropriate level of sedation should be provided and closely monitored.

3. Provide supplemental oxygen to prevent hypoxic events and monitor oxygen saturation closely. Oxygen saturation will tend to be stable even in the face of significant hypoventilation when supplemental oxygen is provided to the patient.
4. Monitor for airway obstruction from flexible bronchoscopy by observation of chest excursions and auscultation of breath sounds, especially in neonates and premature infants in whom significant airway occlusion may occur with introduction of the bronchoscope.
5. Continual monitoring of ventilatory function, such as capnography, is advised to supplement standard monitoring by observation and pulse oximetry.
6. Keep suctioning to a minimum to minimize the potential of reduced FRC and compromised gas exchange.
7. Keep the procedure time to a minimum in order to minimize physiological effects from instrumentation and prolonged sedation.
8. Avoid "bronchoscopist's hypnosis," that is, avoid being spellbound on the airway finding(s) and losing awareness of procedure time, the patient's physiological status, and the communication and teamwork during FB.
9. For patients undergoing bronchoalveolar lavage, especially large volume BAL, supplemental oxygen may be necessary for hours after the procedure. In addition, in order to reduce adverse lung function changes, the BAL solution should be warmed to body temperature.
10. To avoid hypoventilation and barotrauma from excessive, inadvertent auto-PEEP while performing FB during mechanical ventilation, ventilator settings may need to be adjusted. This may include modifying or discontinuing PEEP during ventilation, especially in volume control mode. Another strategy to minimize inadvertent auto-PEEP would be to consider, if feasible, changing to a larger endotracheal tube for the procedure.
11. Bronchodilator administration prior to the procedure should be considered in patients at risk for further adverse effects due to increased airway hyperreactivity.
12. Carefully consider the indication(s) and safety of FB in children with significant underlying health problems who might be especially impacted by even small and transient or potentially more significant physiological effects of FB. Consequently, those with greatest concern would include infants and very small or young children, patients with significant health conditions such as severe pulmonary or cardiac disease, severe pulmonary hypertension, premature infants with necrotizing enterocolitis and other children with compromised mesenteric blood flow, unstable or severe intracranial hypertension, or patients with a complex febrile seizure disorder [65].

We look for medicine to be an orderly field of knowledge and procedure. But it is not. It is an imperfect science, an enterprise of constantly changing knowledge, uncertain information, fallible individuals, and at the same time lives on the line. There is science in what we do, yes, but also habit, intuition, and sometimes plain old guessing. The gap between what we know and what we aim for persists. And this gap complicates everything we do. —Atul Gawande, *Complications: A Surgeon's Notes on an Imperfect Science*

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