



American College of Chest Physicians Consensus Statement on the Use of Topical Anesthesia, Analgesia, and Sedation During Flexible Bronchoscopy in Adult Patients

Momen M. Wahidi, MD, MBA, FCCP; Praseon Jain, MD, FCCP;
Michael Jantz, MD, FCCP; Pyng Lee, MD, FCCP; G. Burkhard Mackensen, MD, PhD;
Sally Y. Barbour, PharmD; Carla Lamb, MD, FCCP; and Gerard A. Silvestri, MD, FCCP

Background: Optimal performance of bronchoscopy requires patient's comfort, physician's ease of execution, and minimal risk. There is currently a wide variation in the use of topical anesthesia, analgesia, and sedation during bronchoscopy.

Methods: A panel of experts was convened by the American College of Chest Physicians Interventional/Chest Diagnostic Network. A literature search was conducted on MEDLINE from 1969 to 2009, and consensus was reached by the panel members after a comprehensive review of the data. Randomized controlled trials and prospective studies were given highest priority in building the consensus.

Results: In the absence of contraindications, topical anesthesia, analgesia, and sedation are suggested in all patients undergoing bronchoscopy because of enhanced patient tolerance and satisfaction. Robust data suggest that anticholinergic agents, when administered prebronchoscopy, do not produce a clinically meaningful effect, and their use is discouraged. Lidocaine is the preferred topical anesthetic for bronchoscopy, given its short half life and wide margin of safety. The use of a combination of benzodiazepines and opiates is suggested because of their synergistic effects on patient tolerance during the procedure and the added antitussive properties of opioids. Propofol is an effective agent for sedation in bronchoscopy and can achieve similar sedation, amnesia, and patient tolerance when compared with the combined administration of benzodiazepines and opiates.

Conclusions: We suggest that all physicians performing bronchoscopy consider using topical anesthesia, analgesic and sedative agents, when feasible. The existing body of literature supports the safety and effectiveness of this approach when the proper agents are used in an appropriately selected patient population.

CHEST 2011; 140(5):1342-1350

Abbreviations: ACCP = American College of Chest Physicians

EXECUTIVE SUMMARY

Performing Bronchoscopy With No Sedation

1. There is an equal safety record of sedation vs no sedation in bronchoscopy, but patients' satisfaction and procedure tolerance are significantly improved with sedation.
2. Sedation is suggested in all patients undergoing bronchoscopy unless contraindications exist.
3. The extent of sedation (minimal, moderate, deep, or general anesthesia) used during bronchoscopy can vary based on

the procedural settings (office, ICU, or operating room) and complexity and duration of the procedure (advanced diagnostic or therapeutic bronchoscopy).

Use of Topical Anesthesia

4. Topical anesthesia before and during bronchoscopy decreases cough and reduces the dose of sedation needed during the procedure.
5. Cocaine (4%), benzocaine (20%), tetracaine (1%), and lidocaine (1%-10%) have been shown to be equally effective

in achieving topical anesthesia during bronchoscopy.

6. Cocaine use is discouraged because of its habit-forming predisposition and adverse effects on the cardiovascular system.
7. Benzocaine and tetracaine should be used with extreme caution because of the risk of induced methemoglobinemia.
8. Lidocaine is the suggested preferred topical anesthetic for bronchoscopy. The minimum effective dose should be used and caution should be exercised in patients with advanced age, impaired liver function, or congestive heart failure.
9. Transcrioid or transtracheal injection of lidocaine and nerve block achieve high levels of topical anesthesia with good patient acceptance and comfort but are discouraged as first-line techniques because of their invasive nature and required special training.

Use of Sedative and Analgesic Agents

Benzodiazepines

10. Benzodiazepines are the suggested preferred sedation agents for use during flexible bronchoscopy because of their favorable effects, including sedation, anterograde amnesia, decreased patient discomfort, improved tolerance of procedure, willingness of patients to undergo a repeat procedure, and improved working conditions for physicians.
11. Benzodiazepine use may lengthen recovery time, but is not associated with an increase in complication rate.
12. The suggested preferred benzodiazepine agent in bronchoscopy is midazo-

lam because of its quick onset of action, rapid peak effect, and relatively short duration of effect.

Opioids

13. The use of combination of benzodiazepines and opioids is suggested because of synergistic effects on patient tolerance during the procedure and the added antitussive properties of opioids.
14. The suggested preferred opioid agent in bronchoscopy is fentanyl because of its quick onset of action, rapid peak effect, and relatively short duration of effect.

Propofol

15. Propofol is an effective agent for sedation in bronchoscopy and can achieve similar sedation, amnesia, and patient tolerance compared with the combined administration of benzodiazepines and opioids.
16. There is no difference in adverse events, particularly hypoxia, between propofol and the combined administration of benzodiazepines and opiates, with the added advantage of shorter recovery time for patients sedated with propofol.

Anticholinergic Agents

17. Atropine and glycopyrrolate, when administered prebronchoscopy, do not produce a clinically meaningful improvement in lung function or decrease in bronchial secretions, and their use is discouraged.

Complementary Nonmedicinal Adjunct Tools During Bronchoscopy

18. Complementary nonmedicinal tools, such as visual and sound effects, during bronchoscopy have not been shown to reduce patients' anxiety.

Manuscript received January 4, 2011; revision accepted May 1, 2011.

Affiliations: From the Department of Medicine (Dr Wahidi), the Department of Anesthesia (Dr Mackensen), and the Department of Pharmacy (Dr Barbour), Duke University Medical Center, Durham, NC; the Louis A. Johnson VA Medical Center (Dr Jain), Clarksburg, WV; the University of Florida (Dr Jantz), Gainesville, FL; the National University Hospital (Dr Lee), Singapore; the Lahey Clinic (Dr Lamb), Burlington, MA; and the Medical University of South Carolina (Dr Silvestri), Charleston, SC.

Correspondence to: Momen M. Wahidi, MD, MBA, FCCP, Interventional Pulmonology and Bronchoscopy, Division of Pulmonary, Allergy, and Critical Care Medicine, Duke University Medical Center, Box 3683, Durham, NC 27710; e-mail: momen.wahidi@duke.edu

© 2011 American College of Chest Physicians. Reproduction of this article is prohibited without written permission from the American College of Chest Physicians (<http://www.chestpubs.org/site/misc/reprints.xhtml>).

DOI: 10.1378/chest.10-3361

Bronchoscopy is one of the most common procedures performed by chest physicians. The procedure is generally uncomfortable, and most patients express some fear of pain, difficulty breathing, nasopharyngeal irritation, or other complications.¹ The use of topical anesthesia, analgesia, and sedation during flexible bronchoscopy varies among physicians, institutions, and geographic locations in the world. Practice patterns range from no sedation to general anesthesia.

Sedation is defined as a continuum of altered consciousness levels, including minimal sedation (anxiolysis), moderate sedation (conscious sedation), deep sedation, and general anesthesia.² Moderate sedation is commonly used in bronchoscopy and is defined as a drug-induced depression in consciousness wherein patients can respond purposefully to verbal commands while maintaining a functional airway, spontaneous ventilation, and cardiovascular function. Deep sedation is less commonly used in bronchoscopy and causes a deeper state of depressed consciousness in which patients cannot be easily aroused but respond purposefully to repeated or painful stimulation and may have compromised airway function and spontaneous ventilation; cardiovascular function is usually maintained. Optimal procedural conditions are achieved when patients are comfortable, physicians are able to perform the procedure, and risk is minimized. The purpose of this consensus statement is to provide suggestions for the use of topical anesthesia, analgesia, and sedation during flexible bronchoscopy based on best available data. For the purpose of this document, adequate monitoring of the level of consciousness and physiologic variables (including BP, respiratory rate, oxygen saturation by pulse oximetry, and ECG monitoring) is assumed and will not be further discussed.

MATERIALS AND METHODS

The American College of Chest Physicians (ACCP) Interventional/Chest Diagnostic Network steering committee appointed a panel of experts to review the published literature and reach a consensus. The panel consisted of a pharmacist, a cardiothoracic anesthesiologist, and interventional and general pulmonologists with representation from academic and private practices and a wide geographic distribution.

Each panel member was assigned a subtopic, and a literature search (1969 to December 2009) was performed on MEDLINE; articles in languages other than English, on pediatric population, or on rigid bronchoscopy were excluded from the search. The search terms included bronchoscopy combined with terms of sedation or generic and brand names of specific medications. Data from studies were organized in tables displaying the type of study, patient population, main objectives, and outcomes. The panel met face to face twice during the annual ACCP meeting in 2008 and 2009 and discussed the literature and potential recommendations. Consensus was reached by the panel members in the second meeting after a comprehensive review of the data. Randomized controlled trials and prospective studies were given highest priority when building the consensus.

It is important to recognize that this is a consensus statement and not evidence-based practice guidelines. A consensus statement is defined as a written document that represents the collective opinions of a convened expert panel. The opinions expressed in the consensus statement are derived by a systematic approach and a traditional literature review as outlined by the ACCP Health and Science Policy Committee Recommendation.³ The panel's suggestions should not be used for performance measurement or for competency purposes but rather as a forum that provides opportunities for scientific debate and additional clinical research.

Performing Bronchoscopy With No Sedation

Bronchoscopy can be performed with and without moderate sedation. In the early days of flexible bronchoscopy, there was a concern about the adverse events of sedation, so it was rarely used. Earlier studies showed no difference in complications rate when comparing the two approaches and concluded that performing diagnostic bronchoscopy without sedation is safe and acceptable; however, these studies did not take into consideration patient's preferences.^{4,5}

Subsequent randomized studies have shown that sedation led to better tolerance of the procedure by patients⁶⁻⁹ and higher physician satisfaction.¹⁰ No difference in complications was seen, but patients did require a longer recovery time when sedation was used.

A survey of bronchoscopy practice in North America in 1991 showed that sedation was routinely used in 50.7% of patients. A more recent survey in the United Kingdom showed a higher percentage (73%),^{11,12} indicating a shift in attitude among bronchoscopists.

Topical Anesthetics

Commonly used topical anesthetic agents before and during bronchoscopy include cocaine (4%), benzocaine (20%), tetracaine (1%), and lidocaine (1%-10%) and can be administered as soaked cotton pledgets, dropper instillation, aerosol spray, nebulization, transcricoid or transtracheal injection, local nerve block, or "spray-as-you-go technique" (through the working channel of the bronchoscope).^{13,14}

Cocaine has a special property of causing vasoconstriction by inhibiting norepinephrine reuptake at the sympathetic nerve endings. This causes shrinkage of nasal mucosa and is particularly advantageous for transnasal intubation.¹⁵ However, myocardial infarction has been reported with topical cocaine where myocardial ischemia is caused by coronary artery vasoconstriction and intracoronary thrombosis.^{16,17} Because of its habit-forming predisposition, potential for abuse, high cost, decreased commercial availability, and adverse effect on the cardiovascular system, alternative topical anesthetic agents are strongly suggested.

Benzocaine and tetracaine sprays have been used as topical anesthetics for the nasal and oral passages prior to bronchoscopy. Their use has been discouraged due to their narrow therapeutic range and potential toxicity with drug-induced methemoglobinemia, a condition that is characterized by abnormal levels of oxidized hemoglobin that cannot bind and transport oxygen and can result in cyanosis and life-threatening complications.¹⁸⁻²¹

Lidocaine is the most commonly used topical anesthetic for flexible bronchoscopy because of its efficacy in

suppressing cough, short half-life, wide safety margin, and minimal tissue toxicity.²² Lidocaine blocks both initiation and conduction of nerve impulses by decreasing ionic flux through the neuronal membrane. It is available in different preparations, including gel, solution, and spray, and at concentrations ranging from 1% to 10%.²³ When lidocaine is applied to the mucous membranes of the airways, peak serum concentrations occur within 20 to 30 min from the beginning of local anesthesia. Cardiac and neurologic toxicity (circumoral paraesthesia, seizures, and cardiac arrhythmias) are dose-related and can occur if the total topical dose exceeds 7 mg/kg or serum lidocaine level exceeds 5 mg/L. Particularly at risk are patients with advanced age, impaired liver function, or congestive heart failure, although no dose adjustment is required for renal failure.²⁴ The total dose of lidocaine used before and during the procedure should be carefully tracked, including the dose applied to the upper airways and the tracheobronchial tree.

A randomized study demonstrated that the use of topical lidocaine through the bronchoscope significantly reduced the frequency of cough and the total dose of sedation needed during the procedure.²² A study comparing 1% vs 2% solutions of topical lidocaine found similar efficacy and therefore suggested the use of the lower concentration to enhance safety.²⁵

Scant data exist with respect to the preferred modes of administration for topical anesthetics. Two small studies found that patients preferred nasal lidocaine gel over lidocaine spray when the transnasal route is chosen for bronchoscopy.^{26,27}

Nebulized lidocaine became popular after two earlier prospective studies demonstrated patients' preference for nebulized lidocaine over spray^{28,29}; however, more recent placebo-controlled trials comparing prebronchoscopy administration of nebulized lidocaine to nebulized saline (given in addition to topical administration of lidocaine in the nose, oropharynx, vocal cords, and airways, as well as sedation) showed no difference in cough scores by patients or physicians or discomfort scores by patients.^{30,31}

Transcricoid or transtracheal injection involves the direct injection of topical anesthetics into the upper trachea through the cricothyroid membrane or between the tracheal rings. Three studies have shown that this method, when compared with nebulization or spray-as-you-go techniques, produced less cough and was tolerated by patients with no increased risk of complications.³²⁻³⁴ Transtracheal injections of equivalent concentrations of cocaine and lidocaine were compared in one study and were found to be equally effective for cough suppression, patient comfort, and operator acceptability.³⁵

Local nerve block anesthesia consists of injecting anesthetic solutions around a nerve root to produce

anesthesia in the distribution of that nerve. Applicable to bronchoscopy are two blocks: glossopharyngeal nerve block, which causes temporary abolition of the gag reflex and loss of tactile sensation over the posterior one-third of the tongue and the lateral and posterior wall of the oropharynx and hypopharynx, and the superior laryngeal nerve block, which results in loss of tactile sensation over the posterior surface of the epiglottis and the mucosa of the larynx and upper trachea. Knowledge of anatomy and special training are required to master this technique. Efficacy of local nerve block using lidocaine was evaluated in a large trial in which 313 awake patients underwent glossopharyngeal and laryngeal nerve blocks prior to bronchoscopy, achieving excellent anesthesia with minimal morbidity and good patient acceptance.³⁶

The Use of Analgesic and Sedative Agents

Table 1 summarizes the pharmacokinetics of analgesic and sedative agents commonly used in bronchoscopy. Table 2 summarizes pertinent information about available reversal agents.

Benzodiazepines: Benzodiazepines exert their actions through potentiation of γ -aminobutyric acid, the major inhibitory neurotransmitter in the brain, and have several pharmacologic properties, such as antianxiety effect, anterograde amnesia, and sedation, that can be very helpful during bronchoscopy.³⁷ The availability of an effective reversal agent for benzodiazepines further solidifies their suitability as a sedation agent in bronchoscopy. Commonly used benzodiazepines include midazolam, diazepam, and lorazepam. Midazolam has become the most common benzodiazepine agent used in bronchoscopy because of its quick onset of action, rapid peak effect, and relatively short duration of effect.¹² Adjustment in dosages is recommended in patients with advanced age and liver cirrhosis because these patients may metabolize benzodiazepines more slowly and are more prone to adverse effects, including drowsiness, ataxia, hangover effects, confusion, and falls.

Randomized studies comparing the use of benzodiazepines in bronchoscopy with placebo show that benzodiazepine administration causes sedation^{6-5,38} and anterograde amnesia for the procedure.^{38,39} Patients report less discomfort^{6,7} and tolerate the procedure better when the procedure is done under benzodiazepine sedation rather than placebo.⁷ In some studies, operators reported better working conditions and were less likely to abandon the procedure when benzodiazepine sedation was used.^{7,10} Patients who received benzodiazepine sedation were also more likely to agree to a repeat procedure at a future date.^{38,39} Sedation with benzodiazepines is not associated with higher

Table 1—Pharmacokinetic Properties of Commonly Used Analgesic and Sedative Agents

Agent	Fentanyl	Alfentanil	Meperidine	Morphine	Diazepam	Lorazepam	Midazolam	Propofol	Fospropofol
Onset of action	5-10 min	Immediate	5-10 min	5-10 min	1 min	8-15 min	30 s to 1 min	30 s	6.5 min
Peak effect	5 min	Immediate	15 min	15-30 min	2-3 min	15-30 min	5-10 min	2 min	12 min
Duration of action	1-2 h	1-2 h	3-4 h	1-6 h	1-3 h	8 h	2 h	3-5 min	17 min
Metabolism	Hepatic	Hepatic	Hepatic	Hepatic	Hepatic	Hepatic	Hepatic	Hepatic	Hepatic
Renal excretion	<5%	<1%	<5%	90%	<1% Unchanged, 75% of metabolites	<1% Unchanged, 60%-80% of metabolites	<1% Unchanged, 70%-75% of metabolites	70%	70%
Elimination half-life	3-4 h	1 h	3-4 h	2 h	20-50 h	11-22 h	1.6-3.2 h	3-12 h	45 min
Major adverse events	Respiratory depression	Respiratory depression	Respiratory depression, bronchospasm, hypotension, nausea, reduction of seizure threshold	Respiratory depression, histamine release (itching and hypotension), bronchospasm	Respiratory depression, chemical phlebitis	Respiratory depression	Respiratory depression, hypotension	Injection site pain, respiratory depression, bradycardia, hypotension	Paresthesia, pruritus, hypoxemia, and hypotension

incidence of complications,^{6-8,10,35,39} but may lead to a longer time in recovery.⁶

When comparing benzodiazepines alone to opioids alone, the former agents demonstrated better amnesia, less discomfort in nose and throat, and lower risk of respiratory depression, but more cough and more drowsiness.^{40,41} Randomized studies have reported better comfort and tolerance⁴² and improved cough control^{42,43} with the combination of benzodiazepines and opiates over benzodiazepines alone. Similar benefits are also reported in a randomized study in which a combination of dextromethorphan (a cough suppressant) and midazolam was compared with midazolam alone.⁴⁴ Although the combination of benzodiazepine and opiate produced greater decrease in oxygen saturation in one study than benzodiazepine alone,⁴³ the combination was safe without any major clinically relevant adverse effect in several other studies.⁴²⁻⁴⁵

The dose of midazolam in most recent studies is 0.06 to 0.07 mg/kg.^{43,46-48} In two uncontrolled studies, higher doses of 0.13 to 0.24 mg/kg of midazolam were used without clear advantage over smaller doses, and a significant number of patients required reversal agents to eliminate the effects of benzodiazepines.^{49,50} Older patients appear to be more sensitive to benzodiazepine effects, need smaller doses to achieve sedation, and require longer time to recover after the bronchoscopy.^{50,51} Conversely, higher doses of midazolam are needed in recipients of stem cell transplantation, patients with cystic fibrosis who received lung transplantation, and HIV-infected patients with history of drug dependence.^{47,52}

Opioids: Opioids have been the cornerstone of the treatment of pain for many years and have been referred to as “God’s medicine” by Sir William Osler.⁵³ Most of the clinically used opioid agents are relatively selective for the mu receptors with primary action in the brain and exert physiologic effects, such as analgesia and cough suppression. These effects, as well as the availability of an effective reversal agent, make opioids ideal agents for use in bronchoscopy. Fentanyl is the most commonly used drug in the setting of bronchoscopy because of its lipophilic properties resulting in a rapid onset of action and short half-life.

Data on the use of opioids as single agents for bronchoscopy are limited; three randomized studies found opioids to be inferior to benzodiazepines in terms of procedure recall and amnesia^{40,54} and patient comfort.⁴¹ The main additive advantage of the use of opioids over benzodiazepines during bronchoscopy is better suppression of cough.^{41-43,55} One randomized study has demonstrated that the combination of opioids and benzodiazepines over benzodiazepines alone led to better patient tolerance of the procedure.⁴²

Table 2—Reversal Agents for Benzodiazepines and Opioids

Reversal Agent	Antagonized Drug	Metabolism	Excretion	Dosage and Administration	Onset of Action	Duration of Action	Special Considerations
Flumazenil	Benzodiazepines via the GABA benzodiazepine receptor	Hepatic	Renal	0.2 mg IV over 15 s, may repeat same dosage at 60-s intervals (maximum dosage: 1 mg/dose; 3 mg/h)	1-2 min	30-60 min	May lower seizure threshold in predisposed patient population; may cause benzodiazepine withdrawal in patients with chronic benzodiazepine use
Naloxone	Opioids via the opioids receptors (μ , κ , σ)	Hepatic	Renal	0.1-0.2 mg IM/IV/SQ over 2-3 min (may need to repeat dosage relative to half life of opioids)	IV: 1-2 min IM/SQ: 2-5 min	1-4 h	May result in opioid withdrawal in patients with chronic narcotic use

GABA = γ -aminobutyric acid; SQ = subcutaneous.

Propofol: Propofol is an IV anesthetic that produces sedation, anxiolysis, and amnesia but has no direct analgesic properties.⁵⁶ Although used less commonly in clinical practice than other sedatives, a number of studies have evaluated the use of propofol for sedation during bronchoscopic procedures. One small randomized study evaluated propofol vs topical anesthesia only and found that patients in the propofol group had less pain, sensation of asphyxiation, and cough.⁹

A few randomized clinical trials have compared the efficacy of propofol vs analgesics and opioids, including a combination of fentanyl and diazepam,⁵⁷ hydrocodone and midazolam,⁵⁸ and midazolam alone⁵⁹⁻⁶¹; only one study found better patient tolerance in the propofol arm,⁶¹ whereas the rest of these studies found equal patient satisfaction with either approach. Additionally, there was no difference in the degree of hypoxia. One advantage of propofol is the faster recovery time and quicker return to baseline mental status.⁵⁸⁻⁶¹

In a study of patient-controlled sedation, 276 patients were randomized to receive sedation with either propofol and ketamine or propofol and alfentanil using a patient-controlled analgesia device.⁶² Amnesia for the procedure and patient satisfaction were higher in the propofol-ketamine group, and all patients reported they would be willing to undergo repeat bronchoscopy with patient-controlled sedation.

The administration of propofol in the endoscopy suite by nonanesthesiologists has been an area of debate and is currently subject to local regulation. As initially discussed, sedation represents a continuum, and it is impossible to predict how individual patients may respond to agents such as propofol. Therefore, even if moderate sedation is desired, patients receiving propofol should be monitored and receive care consistent with that required for deep sedation. Non-anesthesia personnel administering propofol should be qualified to adequately treat patients whose level of sedation becomes deeper than initially intended. The

use of nurse-administered propofol sedation for bronchoscopy without the support of an anesthesiologist was described in a recent retrospective study.⁶³ Propofol was administered by nurses who had completed a training protocol. An analysis of 498 bronchoscopy procedures with nurse-administered propofol demonstrated a favorable safety profile with an overall complication rate of 6.6%. Prospective trials are needed to validate these findings.

Other Agents

Anticholinergic: Atropine and glycopyrrolate are anticholinergic agents that antagonize the muscarine-like activity of acetylcholine with therapeutic actions stemming mainly from inhibition of smooth muscles and glands innervated by postganglionic cholinergic nerves. Because of effects on bronchial smooth muscle and salivary and bronchial glands, these agents cause bronchodilatation and inhibit secretions production in the nasopharynx/oropharynx and bronchi. The theoretical benefits of prebronchoscopy administration of these medications include drying of secretions to allow better examination of the tracheobronchial tree and protection against vasovagal reaction and bronchospasm.

Both atropine and glycopyrrolate have been shown to improve pulmonary function when given through the IV or IM route prior to bronchoscopy; however, this improvement was not sustained through the post-bronchoscopy period.⁶⁴⁻⁶⁹ One small study has suggested that administration of atropine via nebulization prior to bronchoscopy may lead to continued improvement in pulmonary function after the procedure.⁷⁰

A number of studies have evaluated the antisialagogic effects of atropine and, except for one study,⁷¹ found no clinically meaningful reduction in bronchial secretions.^{64,65,67,69,72,73} In the largest randomized, double-blind, placebo-controlled trial of the effects

of atropine and glycopyrrolate on bronchoscopy, 1,000 patients were randomized to IM premedication with atropine 0.01 mg/kg, glycopyrrolate 0.005 mg/kg, or saline.⁷⁴ Glycopyrrolate, but not atropine, was associated with reduced bronchoscopist-reported airway secretions, but neither drug was associated with any significant reduction in cough, patient discomfort, oxygen desaturation, or procedure time. Increase in heart rate and BP was significantly greater with anticholinergic agents than placebo.

Complementary Nonmedicinal Methods

Adjunctive nonpharmacologic tools in the form of imagery, music, relaxation training, and hypnosis have been used as safe means to reducing discomfort in patients undergoing invasive medical procedures.⁷⁵ Two studies have attempted such an approach in bronchoscopy. One study used nature scene murals and provided patients with nature sounds to listen to before, during, and after the procedure; this intervention reduced patients' pain but not anxiety.⁷⁶ A second study randomized patients to receive music during bronchoscopy but failed to show a reduction in procedure-related state anxiety.⁷⁷

Emerging Agents

Fospropofol: Fospropofol disodium is a water-soluble prodrug of propofol with a pharmacokinetic and pharmacodynamic profile that distinguishes it from propofol lipid emulsion. Following IV administration of fospropofol, propofol is liberated by tissue alkaline phosphatase in a manner characterized by a smooth and predictable rise and decline in the plasma concentration of fospropofol-derived propofol, rather than a rapid spike as observed following administration of the lipid emulsion formulation of propofol.⁷⁸

Because of its unique pharmacokinetic properties, fospropofol can be titrated to a predictable level of moderate sedation. In a phase III randomized dose-controlled trial, fospropofol was found to be safe and efficacious in producing moderate sedation in patients undergoing bronchoscopy.⁷⁹ In that study, the drug was administered by pulmonologists without anesthesia support. However, because fospropofol is converted to propofol after administration and carries identical risks to propofol, the drug received US Food and Drug Administration approval with guidelines similar to propofol, thus requiring the presence of an anesthesiologist and continuous monitoring during drug administration outside the ICU.

Future Directions

The use of topical anesthesia, analgesia, and sedation during bronchoscopy has evolved over time, and con-

siderable progress has been made. Although a single perfect sedation agent for bronchoscopy does not currently exist, most procedures can be performed adequately with combinations of benzodiazepines and opiates. As the field of bronchoscopy and interventional pulmonology advances, procedure complexity and length are increasing. Thus, the ideal sedation agent should provide safe and predictable sedation for lengthier procedures with minimal side effects. As new agents are introduced, randomized controlled trials should be the standard by which new drugs or combinations of drugs are evaluated for their suitability in clinical practice.

CONCLUSIONS

This consensus statement was created to provide suggestions for the use of topical anesthesia, analgesia, and sedation during bronchoscopy. The panel reached agreement on 18 suggestions as summarized in the executive summary. Although heterogeneity is common in the clinical practice of bronchoscopy, the reviewed body of literature supports topical anesthesia, analgesia, and sedation as a means of enhancing patient satisfaction and achieving optimal procedural conditions for physicians. Additional research is needed to augment our knowledge of optimal performance of bronchoscopy on all fronts.

ACKNOWLEDGMENTS

Financial/nonfinancial disclosures: The authors have reported to *CHEST* the following conflicts of interest: Dr Wahidi was an investigator on the multicenter trial of Fospropofol. Dr Lamb has been an Educational Board Consultant for the following: Boston Scientific 2007 to current, Cardinal Health 2007 and 2008, and Super Dimension 2007. Dr Silvestri was an investigator on the multicenter trial of Fospropofol; he was a recipient of grant funding from Olympus America and MGI Pharma for a project assessing fospropofol for bronchoscopy and from Allegro Diagnostics Corp for assessing malignancy in patients with abnormal chest radiographs. Drs Jain, Jantz, Lee, Mackensen, and Barbour have reported to *CHEST* that no potential conflicts of interest exist with any companies/organizations whose products or services may be discussed in this article.

Other contributions: This study originated as a project of the Interventional Chest/Diagnostic Procedures Network of the American College of Chest Physicians.

REFERENCES

1. Poi PJ, Chuah SY, Srinivas P, Liam CK. Common fears of patients undergoing bronchoscopy. *Eur Respir J*. 1998;11(5):1147-1149.
2. American Society of Anesthesiologists Task Force on Sedation and Analgesia by Non-Anesthesiologists. Practice guidelines for sedation and analgesia by non-anesthesiologists. *Anesthesiology*. 2002;96(4):1004-1017.
3. Baumann MH, Gutterman DD. American College of Chest Physicians evidence-based guidelines—the next generation:

- considering resource use and evolution to a single grading system. *Chest*. 2006;129(1):10-12.
4. Aslam M, Beg M. Desirability of using buprenorphine and diazepam as an adjunct to atropine in patients undergoing fibre-optic bronchoscopy. *J Pak Med Assoc*. 1993;43(6):120-122.
 5. Colt HC, Morris JF. Fiberoptic bronchoscopy without premedication. A retrospective study. *Chest*. 1990;98(6):1327-1330.
 6. Maguire GP, Rubinfeld AR, Trembath PW, Pain MC. Patients prefer sedation for fibreoptic bronchoscopy. *Respirology*. 1998;3(2):81-85.
 7. Putinati S, Ballerin L, Corbetta L, Trevisani L, Potena A. Patient satisfaction with conscious sedation for bronchoscopy. *Chest*. 1999;115(5):1437-1440.
 8. Rees PJ, Hay JG, Webb JR. Premedication for fibreoptic bronchoscopy. *Thorax*. 1983;38(8):624-627.
 9. Gonzalez R, De-La-Rosa-Ramirez I, Maldonado-Hernandez A, Dominguez-Cherit G. Should patients undergoing a bronchoscopy be sedated? *Acta Anaesthesiol Scand*. 2003;47(4):411-415.
 10. Hatton MQ, Allen MB, Vathenen AS, Mellor E, Cooke NJ. Does sedation help in fibreoptic bronchoscopy? *BMJ*. 1994;309(6963):1206-1207.
 11. Pickles J, Jeffrey M, Datta A, Jeffrey AA. Is preparation for bronchoscopy optimal? *Eur Respir J*. 2003;22(2):203-206.
 12. Prakash UB, Offord KP, Stubbs SE. Bronchoscopy in North America: the ACCP survey. *Chest*. 1991;100(6):1668-1675.
 13. Perry LB. Topical anesthesia for bronchoscopy. *Chest*. 1978;73(suppl 5):691-693.
 14. Fry WA. Techniques of topical anesthesia for bronchoscopy. *Chest*. 1978;73(suppl 5):694-696.
 15. Smith RB. Cocaine and catecholamine interaction. A review. *Arch Otolaryngol*. 1973;98(2):139-141.
 16. Benzaquen BS, Cohen V, Eisenberg MJ. Effects of cocaine on the coronary arteries. *Am Heart J*. 2001;142(3):402-410.
 17. Osula S, Stockton P, Abdelaziz MM, Walshaw MJ. Intratracheal cocaine induced myocardial infarction: an unusual complication of fibreoptic bronchoscopy. *Thorax*. 2003;58(8):733-734.
 18. Moore TJ, Walsh CS, Cohen MR. Reported adverse event cases of methemoglobinemia associated with benzocaine products. *Arch Intern Med*. 2004;164(11):1192-1196.
 19. Clary B, Skaryak L, Tedder M, Hilton A, Botz G, Harpole D. Methemoglobinemia complicating topical anesthesia during bronchoscopic procedures. *J Thorac Cardiovasc Surg*. 1997;114(2):293-295.
 20. Kotler RL, Hansen-Flaschen J, Casey MP. Severe methaemoglobinemia after flexible fibreoptic bronchoscopy. *Thorax*. 1989;44(3):234-235.
 21. Noorily AD, Noorily SH, Otto RA. Cocaine, lidocaine, tetracaine: which is best for topical nasal anesthesia? *Anesth Analg*. 1995;81(4):724-727.
 22. Antoniadis N, Worsnop C. Topical lidocaine through the bronchoscope reduces cough rate during bronchoscopy. *Respirology*. 2009;14(6):873-876.
 23. Loukides S, Katsoulis K, Tsarpalis K, Panagou P, Kalogeropoulos N. Serum concentrations of lignocaine before, during and after fibreoptic bronchoscopy. *Respiration*. 2000;67(1):13-17.
 24. Milman N, Laub M, Munch EP, Angelo HR. Serum concentrations of lignocaine and its metabolite monoethylglycinexylidide during fibre-optic bronchoscopy in local anaesthesia. *Respir Med*. 1998;92(1):40-43.
 25. Mainland PA, Kong AS, Chung DC, Chan CH, Lai CK. Absorption of lidocaine during aspiration anesthesia of the airway. *J Clin Anesth*. 2001;13(6):440-446.
 26. Zainudin BM, Rafia MH, Sufarlan AW. Topical nasal anaesthesia for fibreoptic bronchoscopy: lignocaine spray or gel? *Singapore Med J*. 1993;34(2):148-149.
 27. Webb AR, Woodhead MA, Dalton HR, Grigg JA, Millard FJ. Topical nasal anaesthesia for fibreoptic bronchoscopy: patients' preference for lignocaine gel. *Thorax*. 1989;44(8):674-675.
 28. Keane D, McNicholas WT. Comparison of nebulized and sprayed topical anaesthesia for fibreoptic bronchoscopy. *Eur Respir J*. 1992;5(9):1123-1125.
 29. Foster WM, Hurewitz AN. Aerosolized lidocaine reduces dose of topical anesthetic for bronchoscopy. *Am Rev Respir Dis*. 1992;146(2):520-522.
 30. Charalampidou S, Harris E, Chummun K, Hawksworth R, Cullen JP, Lane SJ. Evaluation of the efficacy of nebulized lignocaine as adjunctive local anaesthesia for fibreoptic bronchoscopy: a randomised, placebo-controlled study. *Ir Med J*. 2006;99(1):8-10.
 31. Stolz D, Chhajed PN, Leuppi J, Pflimlin E, Tamm M. Nebulized lidocaine for flexible bronchoscopy: a randomized, double-blind, placebo-controlled trial. *Chest*. 2005;128(3):1756-1760.
 32. Webb AR, Fernando SS, Dalton HR, Arrowsmith JE, Woodhead MA, Cummin AR. Local anaesthesia for fibreoptic bronchoscopy: transdermal injection or the "spray as you go" technique? *Thorax*. 1990;45(6):474-477.
 33. Isaac PA, Barry JE, Vaughan RS, Rosen M, Newcombe RG. A jet nebuliser for delivery of topical anesthesia to the respiratory tract. A comparison with cricothyroid puncture and direct spraying for fibreoptic bronchoscopy. *Anaesthesia*. 1990;45(1):46-48.
 34. Graham DR, Hay JG, Clague J, Nisar M, Earis JE. Comparison of three different methods used to achieve local anesthesia for fibreoptic bronchoscopy. *Chest*. 1992;102(3):704-707.
 35. Teale C, Gomes PJ, Muers MF, Pearson SB. Local anaesthesia for fibreoptic bronchoscopy: comparison between intratracheal cocaine and lignocaine. *Respir Med*. 1990;84(5):407-408.
 36. DeMeester TR, Skinner DB, Evans RH, Benson DW. Local nerve block anesthesia for peroral endoscopy. *Ann Thorac Surg*. 1977;24(3):278-283.
 37. Olkkola KT, Ahonen J. Midazolam and other benzodiazepines. *Handb Exp Pharmacol*. 2008;182:335-360.
 38. Kolek V, Jezdinsky J. Comparative study of midazolam and diazepam in premedication of bronchoscopy. *Acta Univ Palacki Olomuc Fac Med*. 1991;131:233-241.
 39. Maltais F, Laberge F, Laviolette M. A randomized, double-blind, placebo-controlled study of lorazepam as premedication for bronchoscopy. *Chest*. 1996;109(5):1195-1198.
 40. Dorward AJ, Berkin KE, Elliott JA, Stack BH. A double-blind controlled study comparing temazepam with papaveretum as premedication for fibreoptic bronchoscopy. *Br J Dis Chest*. 1983;77(1):60-65.
 41. Houghton CM, Raghuram A, Sullivan PJ, O'Driscoll R. Pre-medication for bronchoscopy: a randomised double blind trial comparing alfentanil with midazolam. *Respir Med*. 2004;98(11):1102-1107.
 42. Stolz D, Chhajed PN, Leuppi JD, Brutsche M, Pflimlin E, Tamm M. Cough suppression during flexible bronchoscopy using combined sedation with midazolam and hydrocodone: a randomised, double blind, placebo controlled trial. *Thorax*. 2004;59(9):773-776.
 43. Greig JH, Cooper SM, Kasimbazi HJ, Monie RD, Fennerty AG, Watson B. Sedation for fibre optic bronchoscopy. *Respir Med*. 1995;89(1):53-56.
 44. Schwarz Y, Greif J, Lurie O, Tarrasch R, Weinbroum AA. Dextromethorphan premedication reduces midazolam requirement: objective and subjective parameters in peribronchoscopy. *Respiration*. 2007;74(3):314-319.
 45. Fox BD, Krylov Y, Leon P, et al. Benzodiazepine and opioid sedation attenuate the sympathetic response to fibreoptic

- bronchoscopy. Prophylactic labetalol gave no additional benefit. Results of a randomized double-blind placebo-controlled study. *Respir Med*. 2008;102(7):978-983.
46. Banerjee A, Banerjee SN, Nachiappan M. Premedication for fiberoptic bronchoscopy (is sedation a must?). *Indian J Chest Dis Allied Sci*. 1986;28(2):76-80.
 47. Chhajed PN, Wallner J, Stolz D, et al. Sedative drug requirements during flexible bronchoscopy. *Respiration*. 2005;72(6):617-621.
 48. Sury MR, Cole PV. Nalbuphine combined with midazolam for outpatient sedation. An assessment in fiberoptic bronchoscopy patients. *Anaesthesia*. 1988;43(4):285-288.
 49. Williams TJ, Nicoulet I, Coleman E, McAlaney C. Safety and patient acceptability of intravenous midazolam for fibre optic bronchoscopy. *Respir Med*. 1994;88(4):305-307.
 50. Williams TJ, Bowie PE. Midazolam sedation to produce complete amnesia for bronchoscopy: 2 years' experience at a district general hospital. *Respir Med*. 1999;93(5):361-365.
 51. Korttila K, Saarnivaara L, Tarkkanen J, Himberg JJ, Hytönen M. Effect of age on amnesia and sedation induced by flunitrazepam during local anaesthesia for bronchoscopy. *Br J Anaesth*. 1978;50(12):1211-1218.
 52. Chhajed PN, Aboyou C, Chhajed TP, et al. Sedative drug requirements during bronchoscopy are higher in cystic fibrosis after lung transplantation. *Transplantation*. 2005;80(8):1081-1085.
 53. Golden RL. William Osler, urolithiasis and God's own medicine. *Urology*. 2009;74(3):517-521.
 54. Webb AR, Doherty JF, Chester MR, et al. Sedation for fiberoptic bronchoscopy: comparison of alfentanil with papaveretum and diazepam. *Respir Med*. 1989;83(3):213-217.
 55. Tsunozuka Y, Sato H, Tsukioka T, Nakamura Y, Watanabe Y. The role of codeine phosphate premedication in fibre-optic bronchoscopy under insufficient local anaesthesia and midazolam sedation. *Respir Med*. 1999;93(6):413-415.
 56. Vanlersberghe C, Camu F. Propofol. *Handb Exp Pharmacol*. 2008;182:227-252.
 57. Randell T. Sedation for bronchofiberscopy: comparison between propofol infusion and intravenous boluses of fentanyl and diazepam. *Acta Anaesthesiol Scand*. 1992;36(3):221-225.
 58. Stolz D, Kurer G, Meyer A, et al. Propofol versus combined sedation in flexible bronchoscopy: a randomised non-inferiority trial. *Eur Respir J*. 2009;34(5):1024-1030.
 59. Clarkson K, Power CK, O'Connell F, Pathmakanthan S, Burke CM. A comparative evaluation of propofol and midazolam as sedative agents in fiberoptic bronchoscopy. *Chest*. 1993;104(4):1029-1031.
 60. Crawford M, Pollock J, Anderson K, Glavin RJ, MacIntyre D, Vernon D. Comparison of midazolam with propofol for sedation in outpatient bronchoscopy. *Br J Anaesth*. 1993;70(4):419-422.
 61. Clark G, Licker M, Younossian AB, et al. Titrated sedation with propofol or midazolam for flexible bronchoscopy: a randomised trial. *Eur Respir J*. 2009;34(6):1277-1283.
 62. Hwang J, Jeon Y, Park HP, Lim YJ, Oh YS. Comparison of alfentanil and ketamine in combination with propofol for patient-controlled sedation during fiberoptic bronchoscopy. *Acta Anaesthesiol Scand*. 2005;49(9):1334-1338.
 63. Bosslet GT, Devito ML, Lahm T, Sheski FD, Mathur PN. Nurse-administered propofol sedation: feasibility and safety in bronchoscopy. *Respiration*. 2010;79(4):315-321.
 64. Belen J, Neuhaus A, Markowitz D, Rotman HH. Modification of the effect of fiberoptic bronchoscopy on pulmonary mechanics. *Chest*. 1981;79(5):516-519.
 65. Hewer RD, Jones PM, Thomas PS, McKenzie DK. A prospective study of atropine premedication in flexible bronchoscopy. *Aust N Z J Med*. 2000;30(4):466-469.
 66. Inoue H, Aizawa H, Takata S, et al. Ipratropium bromide protects against bronchoconstriction during bronchoscopy. *Lung*. 1994;172(5):293-298.
 67. Neuhaus A, Markowitz D, Rotman HH, Weg JG. The effects of fiberoptic bronchoscopy with and without atropine premedication on pulmonary function in humans. *Ann Thorac Surg*. 1978;25(5):393-398.
 68. Thorburn JR, James MF, Feldman C, Moyes DG, Du Toit PS. Comparison of the effects of atropine and glycopyrrolate on pulmonary mechanics in patients undergoing fiberoptic bronchoscopy. *Anesth Analg*. 1986;65(12):1285-1289.
 69. Williams T, Brooks T, Ward C. The role of atropine premedication in fiberoptic bronchoscopy using intravenous midazolam sedation. *Chest*. 1998;113(5):1394-1398.
 70. Zavala DC, Godsey K, Bedell GN. The response to atropine sulfate given by aerosol and intramuscular routes to patients undergoing fiberoptic bronchoscopy. *Chest*. 1981;79(5):512-515.
 71. Grønnebech H, Johansson G, Smedebøl M, Valentin N. Glycopyrrolate vs. atropine during anaesthesia for laryngoscopy and bronchoscopy. *Acta Anaesthesiol Scand*. 1993;37(5):454-457.
 72. Cowl CT, Prakash UB, Kruger BR. The role of anticholinergics in bronchoscopy. A randomized clinical trial. *Chest*. 2000;118(1):188-192.
 73. Roffe C, Smith MJ, Basran GS. Anticholinergic premedication for fiberoptic bronchoscopy. *Monaldi Arch Chest Dis*. 1994;49(2):101-106.
 74. Malik JA, Gupta D, Agarwal AN, Jindal SK. Anticholinergic premedication for flexible bronchoscopy: a randomized, double-blind, placebo-controlled study of atropine and glycopyrrolate. *Chest*. 2009;136(2):347-354.
 75. Lang EV, Benotsch EG, Fick LJ, et al. Adjunctive non-pharmacological analgesia for invasive medical procedures: a randomised trial. *Lancet*. 2000;355(9214):1486-1490.
 76. Diette GB, Lechtzin N, Haponik E, Devrotes A, Rubin HR. Distraction therapy with nature sights and sounds reduces pain during flexible bronchoscopy: a complementary approach to routine analgesia. *Chest*. 2003;123(3):941-948.
 77. Colt HG, Powers A, Shanks TG. Effect of music on state anxiety scores in patients undergoing fiberoptic bronchoscopy. *Chest*. 1999;116(3):819-824.
 78. Fechner J, Ihmsen H, Hatterscheid D, et al. Pharmacokinetics and clinical pharmacodynamics of the new propofol prodrug GPI 15715 in volunteers [retracted in: *Anesthesiology*. 2010;112(4):1056-1057]. *Anesthesiology*. 2003;99(2):303-313.
 79. Silvestri GA, Vincent BD, Wahidi MM, Robinette E, Hansbrough JR, Downie GH. A phase 3, randomized, double-blind study to assess the efficacy and safety of fospropofol disodium injection for moderate sedation in patients undergoing flexible bronchoscopy. *Chest*. 2009;135(1):41-47.