Revista Mexicana de Anestesiología

CONFERENCIAS MAGISTRALES
Vol. 29. Supl. 1, Abril-Junio 2006
pp S76-S82

The Bronchospastic Patient

William E. Hurford, MD, FCCM*

* Professor and Chair Department of Anesthesiology
University of Cincinnati Medical Center Cincinnati, Ohio

I. INCIDENCE

A. Prevalence and mortality

Affects 14.9 million people in U.S.
Causes 500,000 hospitalizations and > 5,500 deaths annually
Costs $11.3 billion annually
Low socioeconomic status/blacks at higher risk

Eason J, Markowe HL. Controlled investigation of deaths from asthma in hospitals in the North East Thames region. Br Med J 1987;294:1255-8.
Evans R III. Recent observations reflecting increases in mortality from asthma. J Allergy Clin Immunol 1987;80:377-379.
McFadden ER Jr. Acute severe asthma. Am J Respir Crit Care Med 2003;168:740-759.
American Heart Association. Near-Fatal Asthma. Circulation 2005;112:IV-139IV-142. Available freely on-line at http://www.circulationaha.org.

B. Occurrence under Anesthesia

One case per 634 anesthetics in a retrospective Scandinavian study (Olsson, 1987). These events were serious enough to note in the medical record.
Most cases were unpredictable and had no known history of allergy or asthma prior to the anesthetic.
Triggering factor was most often mechanical (bronchoscopy, mediastinoscopy).

Olsson GL. Bronchospasm during anaesthesia. A computer-aided incidence study of 136,929 patients. Acta Anaesthesiol Scand 1987;31:244-52.

ASA Closed Claims Project Database – 88 claims (2.5%) in which bronchospasm was the damaging event or mechanism of patient injury (3,533 closed claims between 1975-1994)
28 (32%) had history of asthma; 10 (11%) had history of COPD.

Bishop MJ, Cheney FW. Anesthesia for patients with asthma. Low risk but not no risk. Anesthesiology 1996;85:455.

Overall, the incidence of perioperative pulmonary complications in asthmatic patients appears to approach that of the general population. In a retrospective study by Warner et al., 1.7% of asthmatic patients (n = 708) had bronchospasm during surgery or in the PACU. An additional 2.4% received supplemental bronchodilators.

Warner DO, Warner MA, Barnes RD, et al. Perioperative respiratory complications in patients with asthma. Anesthesiology 1996;85:460-467.

II. PATHOPHYSIOLOGY

A. Mechanisms in asthma and bronchoconstriction

Asthma- is an episodic, variable airflow obstruction with **increased responsiveness** of the airways to a variety of stimuli. Asthma is associated with marked submucosal **inflammation**.

1. Trigger (antigens and nonspecific stimuli)
2. Increased cellular activity
   Mast cell degranulation
   Eosinophils, macrophages
3. Mucosal edema; increased vascular permeability
4. Mucus secretion and cellular infiltrates
5. Airway smooth muscle contraction secondary to mast cell-derived mediators
6. Airway remodeling and fibrosis

Drazen JM, Boushey HA, Holgate ST, et al. The pathogenesis of severe asthma: A consensus report from the workshop on pathogenesis. J Allergy Clin Immunol 1987;80:428-437.
Hopewell PC, Miller RT. Pathophysiology and management of severe asthma. Clin Chest Med 1984;5:623-634.

B. Physiologic Effects

1. Airway narrowing.
2. Dynamic hyperinflation and auto-PEEP; increased RV.
3. Local hypoxemia and HPV.
4. V/Q mismatch; potential worsening of hypoxemia with vasodilators.
5. Dynamic hyperinflation and decreased venous return.

III. PREOPERATIVE ASSESSMENT

A. Signs and symptoms

Certain aspects of the patient's history suggests an increased risk of perioperative complications:

1. Frequent nocturnal awakenings from asthma (increased airway hyper-responsiveness).
2. Frequent or continuous use of systemic corticosteroids.
3. Recent hospitalizations or emergency room visits because of asthma.
4. Prior peri-operative complications.
5. Large amounts of sputum production.
6. Co-existent cardiovascular disease.
7. Alternative diagnoses (e.g., pulmonary edema, COPD, anaphylaxis, foreign body, airway obstruction).

B. Spirometry

Forced expiratory volume (FEV1), and/or peak expiratory flow rate (PEFR) compare with the patient's best value in the recent weeks:

80-100% of baseline:	Normal
50-80% of baseline:	Moderate exacerbation
< 50% of baseline:	Severe episode

National Asthma Education Program. Expert Panel Report. Guidelines for the diagnosis and management of asthma. *U.S. Department of Health and Human Services Publication 91-3042*, 1991.

IV. THERAPY FOR BRONCHOSPASM

A. Beta-2-adrenergic agonists

Treatment of choice for bronchospasm:
- Directly relaxes bronchial smooth muscle
- Decreases vascular permeability
- May modulate mediator release from mast cells and basophils

Choices:
- Inhaled agonists (Albuterol, salbutamol, etc.).
- No clear advantage to levalbuterol (isomer of albuterol).
- Subcutaneous epinephrine (0.3 mg subcutaneously at 20 min intervals).
- Intravenous epinephrine (caution).
- Terbutaline (0.25 mg subcutaneously).

Manthous CA, Hall JB, Schmidt G, Wood LDH. Metered-dose inhaler versus nebulized albuterol for treatment of bronchospasm in intubated patients. Am Rev Respir Dis 1993;148:1567-1570.
Manthous CA, Chatila W, Schmidt GA, Hall JB. Treatment of bronchospasm by metered-dose inhaler albuterol in mechanically ventilated patients. Chest 1995;107:210-213.
Newman KB, Milne S, Hamilton C, Hall K. A comparison of albuterol administered by metered-dose inhaler and spacer with albuterol by nebulizer in adults presenting to an urban emergency department with acute asthma. Chest 2002;121:1036-1041.

B. Concomitant use of beta-blocking agents

The use of beta-adrenergic antagonists may precipitate or worsen bronchospasm in patients with reactive airway diseases. The incidence of this complication is reduced but not eliminated when «cardioselective» beta blockers are used. Nevertheless, when β-1 adrenergic blockade is desirable in a patient with bronchospasm, the use of a more selective agent such as labetalol or esmolol is reasonable. These agents are unlikely to produce clinically significant worsening of pulmonary function.

Decalmer PBS, Chatterjee SS, Cruickshank JM, et al. Beta-blockers and asthma. Br Heart J 1978;40:184-189.
George RB, Monocha K, Burford JG, et al. Effects of labetalol in hypertensive patients with chronic obstructive pulmonary disease. Chest 1983;83:457-460.
Gold MR, Dec GW, Cocca-Spofford D, Thompson BT. Esmolol and ventilatory function in cardiac patients with COPD. Chest 1991;100:1215-1218.

Sheppard D, DeStefano S, Byrd RC, et al. Effects of esmolol on airway function in patients with asthma. J Clin Pharmacol 1986;26:169-174.

C. Anticholinergics

Bronchoconstriction, especially secondary to mechanical manipulation of the airway, can occur via cholinergically mediated pathways. Anticholinergic drugs cause bronchodilation directly and blunt bronchoconstriction resulting from cholinergically-mediated triggers.
Ipratropium (Atrovent) is an inhaled atropine derivative available as a metered-dose inhaler or as a solution for nebulization. Atrovent causes bronchodilation and enhances the action of β-2-adrenergic agents. Inhaled atropine and glycopyrrolate are also effective, used frequently, but are not FDA approved. Glycopyrrolate has the advantage of few, if any, systemic side-effects.

Anonymous. Ipratropium. Medical Letter 1987;29:71-72.
Fish JE, Rosenthal RR, Summer WR, Menkes H, Norman PS, Permutt S. The effect of atropine on acute antigen-mediated airway constriction in subjects with allergic asthma. Am Rev Respir Dis 1977;115:371-379.
Gal TJ, Suratt PM. Atropine and glycopyrrolate effects on lung mechanics in normal man. Anes Analg 1981;60:85-90.
Johnson BE, Suratt PM, Gal TJ, Wilhoit SC. Effect of inhaled glycopyrrolate and atropine in asthma. Precipitated by exercise and cold air inhalation. Chest 1984;85:325-328.
Rosenthal RR, Norman PS, Summer WR, Permutt S. Role of the parasympathetic system in antigen-induced bronchospasm. J Appl Physiol 1977;42:600-606.

D. Corticosteroids

Glucocorticoids are useful in patients with asthma and chronic obstructive lung disease who have not responded adequately to β-2-adrenergic agonists. While the reason for the efficacy of steroids is unclear, possible mechanisms of action include reduction of inflammation and histamine release and inhibition of arachidonic acid metabolism. Steroids may also increase the sensitivity of the airway to bronchodilation by β2-adrenergic agents and reduce airway hyperreactivity induced by propranolol.

For severe acute exacerbations, the equivalent of 60 to 80 mg of methylprednisolone can be administered intravenously every 6 to 8 hours and then tapered. For chronic administration, alternate-day dosage schedules or inhaled steroids, which reduce the incidence and severity of side effects, are often effective.

Patients who have received steroids within the last six months are assumed to have suppressed adrenal cortical function and probably should receive glucocorticoid coverage on the day of surgery. The equivalent of 100 mg hydrocortisone every 8 hours is traditional, but usually represents an overdosage. Postoperatively, steroids should be discontinued or quickly tapered.

Sauder RA, Lenox WC, Tobias JD, Hirshman CA. Methylprednisolone increases sensitivity to β-adrenergic agonists within 48 hours in Basenji greyhounds. Anesthesiology 1993;79:1278-1283.
Tobias JD, Sauder RA, Hirshman CA. Methylprednisolone prevents propranolol-induced airway hyperreactivity in the Basenji-greyhound dog. Anesthesiology 1991;74:1115-1120.
Van de Graff EA, Out TA, Roos CM, Jansen HM. Respiratory membrane permeability and bronchial hyperreactivity in patients with stable asthma. Effects of therapy with inhaled steroids. Am Rev Respir Dis 1991;143:362-368.
Silvanus MT, Groeben H, Peters J. Corticosteroids and Inhaled Salbutamol in Patients with Reversible Airway Obstruction. Anesthesiology 2004;100:1052-7.

E. Leukotriene receptor antagonists

Montelukast (Singulair 10 mg po qd) - leukotriene receptor (CysLT1) antagonist Inhibits activity of LTD4.
For long-term treatment of mild to moderate asthma.
Not for acute exacerbations asthma or bronchospasm.
Continue perioperatively.
Metabolized by cytochrome P450 enzymes.
Rarely, systemic eosinophilia and vasculitis (Churg-Strauss syndrome) may occur.

F. Magnesium

Relaxes bronchial smooth muscle.
Inhibits cholinergic neuromuscular transmission.
Adds to effects of β-adrenergic agents and corticosteroids.

Silverman RA, Osborn H, Runge J, et al. IV magnesium sulfate in the treatment of acute severe asthma: a multicenter randomized controlled trial. *Chest* 2002;122:489-497.
Hughes R, Goldkorn A, Masoli M, Weatherall M, Burgess C, Beasley R. Use of isotonic nebulised magnesium sulphate as an adjuvant to salbutamol in treatment of severe asthma in adults: randomized placebo-controlled trial. Lancet 2003;361:2114-7.

A Cochrane review concluded that IV magnesium sulfate improved pulmonary function and reduced hospital admissions, especially for patients with severe asthma.

Rowe BH, Bretzlaff JA, Bourdon C, et al. Magnesium sulfate for treating exacerbations of acute asthma in the emergency department. Cochrane Database Syst Rev CD001490, 2005.

Inhaled magnesium sulfate, nebulized and co-administered with albuterol, may also improve pulmonary function in acute asthma.

Blitz M, Blitz S, Beasely R, et al. Inhaled magnesium sulfate in the treatment of acute asthma. Cochrane Database Syst Rev CD003898, 2005.

A randomized placebo controlled trial of 40 mg/kg iv magnesium sulfate for moderate to severe asthmatic exacerbation in pediatric (6 to 18 yr old) ER patients demonstrated improved PFT's at 20 and 100 minutes; patients treated with magnesium were more likely to be discharged home (8/16 *vs* 0/14).

Ciarallo L, Brousseau D, Reinert S. Higher-dose intravenous magnesium therapy for children with moderate to severe acute asthma. Arch Pediatr Adolesc Med 2000;154:979-983.

G. Theophylline

Limited usefulness in the acute setting; less potent bronchodilator than adrenergic drugs; and toxic.
In chronic asthma and COPD, theophylline decreases the frequency and severity of asthmatic symptoms and decreases steroid requirements in some patients.
Its true mechanism of action is unknown. Theophylline inhibits cyclic AMP phosphodiesterase activity only at toxic concentrations. Alternative explanations are that theophylline acts as an adenosine receptor antagonist or decreases the availability of intracellular calcium.
At least in dogs, theophylline produces bronchodilation by increasing the release of endogenous catecholamines. Halothane blocks this effect.
No longer recommended for acute therapy.

Tobias JD, Kubos KL, Hirshman CA. Aminophylline does not attenuate histamine-induce airway constriction during halothane anesthesia. Anesthesiology 1989;71:723-729.

V. SPECIFIC ANESTHETIC TECHNIQUES AND CONSIDERATIONS

The goals of preoperative therapy are to reverse bronchospasm and inflammation, clear secretions, treat infection, and reduce the frequency and severity of acute exacerbations.

Barnes PJ. A new approach to the treatment of asthma. N Engl J Med 1989;321:1517-1527.
Hirshman CA. Perioperative management of the asthmatic patient. Can J Anaesth 1991;38:R26-R32.
Kingston HGC, Hirshman CA. Perioperative management of the patient with asthma. Anesth Analg 1984;63:844-855.

A. Conservative measures

1. Avoid triggers.

Environmental allergens and irritants (endotracheal intubation, cold air, latex products) may cause direct bronchoconstriction. Preoperative exposure to known irritants should be minimized. Ideally, elective surgery should be postponed during acute exacerbations. Be on the lookout for latex and aspirin sensitive patients.

2. Respiratory therapy.
Asthmatics and patients with chronic obstructive lung disease often have trouble clearing secretions postoperatively. Adequate perioperative hydration and humidification of inspired gases reduce drying of the airway and improve mobilization of secretions. Cold inspired gases may directly cause bronchoconstriction.

3. Treat infections.
Eradication of acute pulmonary infections prior to surgery may reduce the likelihood of postoperative pulmonary complications. Elective surgery should be postponed until acute infections are cleared. Broad spectrum prophylactic antibiotics are not indicated, as they may produce overgrowth of resistant organisms. Instead, antibiotic therapy should be directed at infections documented by sputum Gram stain and culture.

Laitinen LA, Elkin RB, Empey DW, Jacobs L, Mills J, Nadel JA. Bronchial hyperresponsiveness in normal subjects during attenuated influenza virus infection. Am Rev Respir Dis 1991;143:358-361.

B. Premedication

Preanesthetic medication should reduce anxiety and relieve the discomfort of transport, line placement, etc. Benzodiazepines are effective in allaying anxiety in most patients. Narcotics may be used to provide preoperative analgesia but should be titrated carefully in patients with CO2 retention. While

narcotics can cause systemic histamine release, there is no evidence to suggest that narcotics, in the doses used for premedication, cause clinically significant bronchoconstriction.
Avoid aspirin and non-steroidal anti-inflammatory drugs in patients with severe asthma, nasal polyps, or aspirin sensitivity.

C. Regional anesthesia

While it seems reasonable that regional anesthesia should avoid many of the pulmonary complications of general anesthesia and reduce the incidence of postoperative pulmonary complications, this hypothesis has been difficult to prove. Local or regional anesthesia for surgery on the extremities, eye operations, and other peripheral procedures appears, in general, to be the best choice for patients with asthma. Spinal or epidural anesthesia with levels of sensory anesthesia higher than T6 decreases functional residual capacity, expiratory reserve volume, and the patient's ability to cough. Airway reactivity, however, actually decreases, probably due to systemic absorption of the anesthetic.

McGough EK, Cohen, JA. Unexpected bronchospasm during spinal anesthesia. J Clin Anesth 1990;2:35-6.
Groeben H. Effects of high thoracic epidural anesthesia and local anesthetics on bronchial hyperreactivity. J Clin Monit Comput 2000;16:457-63.

D. General anesthesia

1. Induction
Induction may be performed with intravenous or inhalational agents, remembering that patients with bronchospasm have increased functional residual capacities and prolonged induction and emergence times.
Evidence suggests that induction of general anesthesia with propofol greatly reduces the incidence of wheezing after endotracheal intubation, compared with barbiturate induction, in both asthmatic (0% *vs* 45% incidence) and non-asthmatic patients (3% *vs* 16% incidence). Thiobarbiturates may release histamine and could worsen bronchospasm in the asthmatic. Induction with methohexital, an oxybarbiturate, has been associated with less histamine release. Ketamine or an inhalational agent also may be used.

Pizov R, Brown RH, Weiss YS, Baranov D, Hennes H, Baker S, Hirshman CA. Wheezing during induction of general anesthesia in patients with and without asthma. Anesthesiology 1995;82:1111-1116.

Intravenous lidocaine, 0.5-1.0 mg/kg, decreases airway reflexes and is a helpful adjunct to general anesthesia in bronchospastic patients.

Groeben H, Schwalen A, Irsfeld S, Stieglitz S, Lipfert P, Hopf H-B. Intravenous lidocaine and bupivicaine dose-dependently attenuate bronchial hyperreactivity in awake volunteers. Anesthesiology 1996;84:533-539.

Nebulized lidocaine can cause bronchoconstriction in some patients.

McAlpine LG, Thomson NC. Lidocaine-induced bronchoconstriction in asthmatic patients. Relation to histamine airway responsiveness and effect of preservative. Chest 1989;96:1012-5.

Avoid airway manipulations (tracheal intubation) when possible. Use of a laryngeal mask airway, when indicated, is an excellent alternative to endotracheal intubation in patients with increased airway responsiveness.

Kim ES, Bishop MJ. Endotracheal intubation, but not laryngeal mask airway insertion, produces reversible bronchoconstriction. Anesthesiology 1999;90:391-394.

2. Effects of anesthetics

a. Block parasympathetic irritant pathways.
b. Direct relaxation of bronchial smooth muscle.
c. Augment β-2-adrenergic responses (ketamine).

Aviado DM. Regulation of bronchomotor tone during anesthesia. Anesthesiology 1964;42:68-80.
Hirshman CA, Bergman NA. Halothane and enflurane protect against bronchospasm in an asthma dog model. Anesth Analg 1978;57:629-633.
Hirshman CA, Edelstein G, Peetz S, Wayne R, Downes H. Mechanism of action of inhalational anesthesia on airways. Anesthesiology 1982;56:107-111.
Hirshman CA. Airway reactivity in humans. Anesthetic implications. Anesthesiology 1983;58:170-177.
Shah MV, Hirshman CA. Mode of action of halothane on histamine-induced airway constriction in dogs with reactive airways. Anesthesiology 1986;65:170-174.

3. Inhalational anesthetics depress airway reflexes, cause bronchodilation, and are recommended for maintenance of general anesthesia in patients with bronchospasm. Enflurane, halothane, and isoflurane and sevoflurane all have bronchodilating properties. Of the commonly used volatile agents, on

average, sevoflurane appears to have the greatest effect on airway resistance.

Brown RH, Zerhouni EA, Hirshman CA. Comparison of low concentrations of halothane and isoflurane as bronchodilators. Anesthesiology 1993;78:1097-1101.
Rooke GA, Choi JH, Bishop MJ. The effect of isoflurane, halothane, sevoflurane, and thiopental/nitrous oxide on respiratory system resistance after tracheal intubation. Anesthesiology 1997;86:1294-1299.

4. Bronchospastic patients may be extubated while still under deep anesthesia, if they do not require airway protection or postoperative ventilatory support. This practice reduces reflex bronchoconstriction during emergence, since the continued presence of the endotracheal tube during light planes of anesthesia can increase airway reactivity.
5. Epidural local anesthetics and narcotics may be used to supplement a general anesthetic and provide postoperative analgesia as well.

E. Mechanical ventilation of the asthmatic

1. Controlled ventilation using slow rates and prolonged expiratory times reduces the bronchospastic lung's tendency towards air-trapping. Monitoring chest movements, inspiratory pressure, expiratory time, the end-tidal CO2, and the expiratory CO2 waveform is invaluable.
2. "Auto PEEP" - In patients with severe obstructive disease, expiratory flow rates may be very prolonged and/or respiratory rates increased. As a result, inhalation begins before the previous exhalation is complete. This traps gas in the lungs, often under surprisingly high pressure. This «auto-PEEP», like applied PEEP, can produce profound decreases of venous return and cardiac output. In extreme cases, electro-mechanical dissociation, leading to death, may occur!

Darioli R, Perret C. Mechanical controlled hypoventilation in status asthmaticus. Am Rev Respir Dis 1984;129:385-387.
Pepe PE, Marini JJ. Occult positive end-expiratory pressure in mechanically ventilated patients with airflow obstruction: the auto-PEEP effect. Am Rev Respir Dis 1982;126:166-170.
Wiener C. Ventilatory management of respiratory failure in asthma. JAMA 1993;269:2128-2131.

3. Overdistention and auto-PEEP may be reduced by limiting tidal volume and respiratory rate. Prolonged expiratory times may be required. In these cases, the $PaCO_2$ is allowed to rise passively—a strategy called permissive hypercapnia. The goal of permissive hypercapnia is simply to avoid regional or global overdistention of the lung.

Feihl F, Perret C. Permissive hypercapnia. How permissive should we be? Am J Respir Crit Care Med 1994;150:1722-1737.
Hickling KG. Ventilatory management of ARDS: can it affect the outcome? Intensive Care Med 1990;16:219-226.
Hickling KG, Henderson SJ, Jackson R. Low mortality associated with low volume, pressure-limited ventilation with permissive hypercapnia in severe adult respiratory distress syndrome. Intensive Care Med 1990;16:372-377.
Kacmarek RM and Hickling KG. Permissive hypercapnia. Respiratory Care 1993;38:373-387.
Quinlan JJ, Buffington CW. Deliberate hypoventilation in a patient with air trapping during lung transplantation. Anesthesiology 1993;78:1177-1181.

4. Some Guidelines for Mechanical Ventilation of the Asthmatic:

   a. Monitor expiratory airflow (physical exam, ET-CO2, spirogram)
   b. Ventilate Slowly! Decrease respiratory rate to limit auto-PEEP
   c. Provide adequate time for exhalation
   d. Allow $PaCO_2$ to rise, if necessary
   e. Limit peak alveolar pressure (end-insp. plateau pressure) < 30 cm H_2O
   f. Use low levels of PEEP (5 to 15 cm H_2O)

VI. ADDITIONAL TOPICS

A. Heliox

Heliox is a blend of helium and oxygen (usually an 80:20 or 70:30 mix) which is less dense than air and can decrease airway resistance in patients with airway obstruction and asthma. While breathing heliox, inspiratory and expiratory resistance may decrease, resulting in a decrease of $PaCO_2$. Evidence for the efficacy of heliox in the asthmatic remains largely anecdotal.

Kass JE, Castriotta RJ. Heliox therapy I acute severe asthma. Chest 1995;107:757-760.
Madison JM, Irwin RS. Heliox for asthma. Chest 1995;107:597-598.
Manthous CA, Hall JB, Caputo MA, et al. Heliox improves pulsus paradoxus and peak expiratory flow in nonintubated patients with severe asthma. Am J Respir Crit Care Med 1995;151:310-314.

Rodrigo GJ, Rodrigo C, Pollack CV, Rowe B. Use of helium-oxygen mixtures in the treatment of acute asthma: a systematic review. Chest 2003;123:891-6.

B. General Anesthesia for Treatment of Status Asthmaticus

Halothane was the classic drug of choice. The possibility of hepatotoxicity, arrhythmias and high bromide levels with prolonged administration decreases the utility of the drug. Both enflurane and isoflurane have been used to treat status asthmaticus. The main benefit of general anesthesia is sedation and the control of the patient's respiratory pattern Total intravenous anesthesia (propofol, ketamine, etc.) is a for more acceptable and practical alternative.

Bierman MI, Brown M, Muren O, Keenan RL, Glauser FL. Prolonged isoflurane anesthesia in status asthmaticus. Crit Care Med 1986;14:832-3.

Echeverria M, Gelb AW, Wexler HR, Ahmad D, Kenefick P. Enflurane and halothane in status asthmaticus. Chest 1986;89:152-4.

Parnass SM, Feld JM, Chamberlin WH, Segil LJ. Status asthmaticus treated with isoflurane and enflurane. Anesth Analg 1987;66:193-5.

Strube PJ, Hallan PL. Ketamine by continuous infusion in status asthmaticus. Anaesthesia 1986;41:1017-1019.

Howton JC, Rose J, Duffy S, Zoltanski T, Levitt MA. Randomized, double-blind, placebo-controlled trial of intravenous ketamine in acute asthma. Ann Emerg Med 1996;27:170-5.

Schultz TE. Sevoflurane administration in status asthmaticus: a case report. AANA J 2005;73:35-36.