

Intubation and mechanical ventilation of the asthmatic patient in respiratory failure

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Key words: Acute asthma, asthma exacerbation, emergency department, mechanical ventilation, respiratory failure, respiratory arrest, intubation, orotracheal intubation, nasotracheal intubation

There are approximately 2 million emergency department visits for acute asthma per year with 12 million people reporting having had asthma "attacks" in the past year.¹ Approximately 2% to 20% of admissions to intensive care units (ICUs) are attributed to severe asthma, with intubation and mechanical ventilation deemed necessary in up to one third in the ICU² and mortality rates in patients receiving intubation from 10% to 20% in this patient population.³

The onset of acute asthma symptoms ranges from hours to weeks. Type I acute asthma, also known as slow-onset asthma, often presents as a gradual deterioration of the clinical scenario, which is superimposed on a background of chronic and poorly controlled asthma. Type II acute asthma, or rapid-onset asthma, tends to be more dangerous and frequently presents with sudden narrowing of the airways.⁴

This article reviews the recent evidence-based data regarding the indications, techniques, and complications of intubation and mechanical ventilation in the treatment of acute asthma in the emergency department (ED). It also discusses possible strategies for preventing the need for intubation in patients with severe exacerbations who are not responding to conventional therapy. Finally, this article provides practical management recommendations in this clinical setting.

METHODS

Three sets of key words were used for the systematic literature review. The first set included the terms *acute asthma*, *acute severe asthma*, *acute bronchospasm*, *acute reactive airways disease*, *asthma exacerbation*,

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Disclosure of potential conflict of interest: B. Brenner has declared that he has no conflict of interest. T. Corbridge is on the speakers' bureau for GlaxoSmithKline. A. Kazzi has declared that he has no conflict of interest.

This article is part of the Joint Task Force Report: Supplemental Recommendations for the Management and Follow-up of Asthma Exacerbations, an official statement of the American Academy of Allergy, Asthma, and Immunology (AAAAI), the American Academy of Emergency Medicine (AAEM), and the American Thoracic Society (ATS). It was approved by the AAAAI Board of Directors, January 16, 2008, the AAEM Board of Directors, January 14, 2008, and the ATS Board of Directors, March 13, 2009.

The Joint Task Force Report is copublished in the *Journal of Allergy and Clinical Immunology*, the *Journal of Emergency Medicine*, and the *Proceedings of the American Thoracic Society*.

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J Allergy Clin Immunol 2009;124:S19-28.

0091-6749/\$36.00

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doi:10.1016/j.jaci.2009.05.008

Abbreviations used

ABG:	Arterial blood gas
ED:	Emergency department
ICU:	Intensive care unit
MDI:	Metered-dose inhaler
PEEP:	Positive end-expiratory pressure
Pplat:	Plateau pressure
RCT:	Randomized controlled trial
Rrs:	Respiratory system resistance
Vei:	Volume at end-inspiration

emergency asthma, and *status asthmaticus*. The second set of key words included the following terms: *mechanical ventilation*, *mechanical ventilator*, *invasive ventilation*, *mechanical ventilatory support*, *continuous mandatory ventilation (CMV)*, *assist-control ventilation*, *synchronized intermittent mandatory ventilation (SIMV)*, *intermittent positive-pressure ventilation*, and *complications of mechanical ventilation*. The third set of key words included the following terms: *hypercapnea*, *hypercapnia*, *hypopnea*, *hypercapnic*, *respiratory failure*, *respiratory insufficiency*, *respiratory arrest*, *arrest*, *hypoventilation*, *hypoxemia*, *intubation*, *endotracheal intubation*, *oral intubation*, *orotracheal intubation*, *nasal intubation*, *nasotracheal intubation*, *intratracheal intubation*, *respiratory acidosis*, *fatal*, and *life-threatening*. Additional details of the methodology for all literature reviews in this supplement are provided in the introduction to this supplement.⁵ The task force specified the level of evidence used to justify the recommendations being made, and the system used to describe the level of evidence is also defined in the introduction to this supplement.

RESULTS

The search for the topic of *intubation* produced 41 randomized controlled trials (RCTs) and 6 meta-analyses. Five RCTs were deemed appropriate for this review. The search for the topic of *mechanical ventilation* revealed 5 RCTs and 4 meta-analyses. None of these RCTs or meta-analyses was deemed appropriate for this review because they did not deal specifically with mechanical ventilation of asthmatic patients or effects of mechanical ventilation on airway function.

RCTs

Groeben et al⁶ conducted a study on 10 asthmatic patients (2 women and 8 men) to assess the effect on lung function of awake fiberoptic intubation after lidocaine or dyclonine inhalation with or without pretreatment with salbutamol. Baseline FEV₁ was recorded, and inhalational challenge with histamine was administered to confirm bronchial hyperreactivity. There were 3 hypotheses: (1) awake tracheal intubation during topical anesthesia leads to a decrease in FEV₁; (2) there is no difference in the response to awake tracheal intubation when either lidocaine or dyclonine are used for topical anesthesia; and (3) pretreatment with salbutamol attenuates the response to awake tracheal intubation and eliminates possible minor differences in the response after topical anesthesia with either lidocaine or dyclonine. On 4 different days in a randomized double-blind fashion, the volunteers inhaled either

dyclonine or lidocaine with or without salbutamol pretreatment. FEV₁ did not change significantly from baseline values with lidocaine inhalation versus placebo (4.43 ± 0.67 vs 4.29 ± 0.72 L) or dyclonine inhalation compared with placebo (4.53 ± 0.63 vs 4.42 ± 0.80 L); however, salbutamol slightly but significantly increased FEV₁ in the treatment group receiving lidocaine compared with the placebo group (4.45 ± 0.76 vs 4.71 ± 0.61 L, $P = .0034$) and with the treatment group receiving dyclonine versus the placebo group (4.48 ± 0.62 vs 4.71 ± 0.61 L, $P = .0121$). After awake intubation, FEV₁ decreased significantly with lidocaine topical anesthesia (4.29 ± 0.72 to 2.86 ± 0.87 L) and decreased to an even greater degree with dyclonine (4.24 ± 0.80 to 2.20 ± 0.67 L, $P < .0001$). The decrease in FEV₁ was significantly attenuated by salbutamol, both in the lidocaine group (4.72 ± 0.62 to 3.37 ± 1.03 L, $P = .0011$) and in the dyclonine group (4.73 ± 0.62 to 2.74 ± 0.98 L, $P = .0003$). The study concluded combined treatment with lidocaine and salbutamol can be recommended for awake intubation; however, bronchial hyperactivity might be a contraindication to the use of dyclonine.

A study by Conti et al⁷ was conducted to evaluate the effects of the last-generation opioid alfentanil on respiratory system mechanics in a group of American Society of Anesthesiology classification I nonasthmatic patients ventilated mechanically during general anesthesia. A total of 20 patients (10 men and 10 women) were randomized into 2 groups. Group A received alfentanil at 15 μ g/kg, and group B received alfentanil at a dose of 30 μ g/kg. Respiratory mechanics variables were obtained at baseline and after 3, 10, and 15 minutes. There were no statistically significant differences in respiratory mechanics variables after administration of alfentanil. The various components of respiratory system resistance (Rrs) were all within the standard limits for intubated patients and showed no variations after alfentanil administration. Furthermore, there were no other respiratory or hemodynamic side effects recorded during the study or surgical procedure, and no respiratory adverse effect was reported after intravenous alfentanil administration. Although opioids are believed to have a bronchoconstrictor effect, alfentanil did not appear to cause bronchoconstriction when administered intravenously to nonasthmatic patients; additional data are required to demonstrate safety in asthmatic patients.

Scalfaro et al⁸ tested the hypothesis that the preanesthetic administration of inhaled salbutamol would prevent the Rrs increase after tracheal intubation during sevoflurane-induced anesthesia in asthmatic children. Nineteen patients were randomly assigned to receive either salbutamol or placebo. When patients inhaled 3% sevoflurane in a mixture of 50% nitrous oxide in oxygen, there was no difference in ventilation variables and respiratory mechanics in patients pretreated with salbutamol or placebo. Mean Rrs was similar between groups; however, there was a significant difference in percentage change between the groups and the number of patients experiencing increased Rrs after tracheal intubation. With salbutamol, the Rrs decreased by a mean of 6.0% (95% CI, -25.2% to +13.2%) compared with a 17.7% mean decrease with placebo (95% CI, 4.4% to 30.9%; $P = .04$). A significantly larger proportion of patients in the placebo group manifested increased Rrs after tracheal intubation in comparison with pretreated patients (91% vs 46%, $P = .03$). The researchers concluded that salbutamol prevented increases in Rrs in asthmatic children having their tracheas intubated during sevoflurane induction. These data suggest that a preanesthetic treatment with salbutamol is useful in asthmatic children to protect against an increase in Rrs after tracheal intubation.

Maslow et al⁹ compared respiratory response during intubation after administration of intravenous lidocaine with that after inhaled albuterol in a group of patients with asthma scheduled for elective surgery requiring general anesthesia and tracheal intubation. These authors reported that inhaled albuterol blunted the airway response to tracheal intubation in asthmatic patients, whereas intravenous lidocaine did not. A total of 60 patients were randomized to receive 1.5 mg/kg intravenous lidocaine or placebo, which was administered 3 minutes before intubation. Fifty additional patients were randomized to receive 4 puffs of inhaled albuterol or placebo, which was administered 15 to 20 minutes before intubation. All patients were premedicated with midazolam and had anesthesia induced with propofol. The lidocaine and placebo groups were not different in terms of peak lower pulmonary resistance before isoflurane administration (8.2 vs 7.6 cm H₂O/L/s) or frequency of airway response to intubation (lidocaine: 6 of 30 vs placebo: 5 of 27). In contrast, the albuterol group had lower peak lower pulmonary resistance (5.3 vs 8.9 cm H₂O/L/s, $P < .05$) and a lower frequency of airway response (1 of 25 vs 8 of 23, $P < .05$) than the placebo group. Thus pretreatment with lidocaine administration did not blunt the intubation-induced bronchospasm compared with placebo, but pretreatment with albuterol did appear to blunt the hyperactive airway response.

Wu et al¹⁰ studied the efficacy of fenoterol and ipratropium in treating asthmatic patients with intraoperative bronchospasm. Sixteen asthmatic patients were enrolled in the study, all with a minimum 3-year history of clinically diagnosed asthma, regular treatment with β -adrenergic agents, and increased Rrs after intubation. They were randomized to receive either 10 puffs of fenoterol or 10 puffs of ipratropium through a metered-dose inhaler (MDI) with a spacer 5 minutes after intubation. All patients had an Rrs value at least 2 SDs greater than the previously established mean value, which confirmed the presence of hyperreactive airways. Rrs 30 minutes after treatment represented a 58% (SD, 6) decrease from 5 minutes after intubation (pretreatment) for fenoterol compared with 17% (SD, 5) for ipratropium. The percentage decrease in Rrs for patients in the fenoterol group was significantly greater than that for patients in the ipratropium group at all times ($P < .05$). The authors concluded that patients with a history of asthma were at high risk of having an exaggerated response to tracheal intubation and that fenoterol was effective in reducing Rrs after tracheal intubation in asthmatic subjects.

Other studies

A study was conducted by Tobin¹¹ to determine the incidence, risk factors, and outcome of barotrauma in a cohort of mechanically ventilated patients. A total of 5183 patients were studied, and barotrauma was present in 154 (2.9%) patients. Eighty percent of patients who had barotrauma did so within the first 3 days of mechanical ventilation. The incidence varied according to the reason for mechanical ventilation; 6% had asthma. The study found that patients with and without barotrauma did not differ in any ventilator parameter; however, patients with underlying lung diseases, such as adult respiratory distress syndrome and asthma, are more likely to have barotrauma with mechanical ventilation.

Behbehani et al¹² conducted a retrospective cohort study over a 10-year period of all asthmatic patients receiving mechanical ventilation at 2 centers in Vancouver to determine the incidence of acute myopathy and examine predictors of development. The authors reported there was a high incidence of acute myopathy when

TABLE I. Alternative therapies for possible prevention of intubation

Heliox
Ketamine
Glucagon
Leukotriene inhibitors
Nebulized clonidine
Nitroglycerin
Nebulized calcium channel blockers
Nebulized lidocaine
External chest compression

Modified with permission from Panacek and Pollack.¹⁵

neuromuscular blocking agents were used for near-fatal asthma. The development of myopathy was significantly associated with the duration of muscle relaxation, with an odds ratio of 2.1 (95% CI, 1.4–3.2) with each additional day of muscle relaxation. It was noted that the dose and type of corticosteroid were not significantly associated with myopathy in a multiple logistic regression analysis.

DISCUSSION

The ED task force identified 7 key areas for discussion from the review of the literature and their clinical experience:

1. prevention of intubation,
2. criteria for intubation,
3. recommendations for intubation technique,
4. recommendations for appropriate ventilator settings,
5. management in the immediate postintubation period,
6. medical management of asthma in the ventilated patient, and
7. prevention and treatment of complications.

Prevention of intubation

The decision to intubate a patient in the ED is multifactorial and must be weighed carefully. Studies have shown that most asthmatic patients are able to be treated without intubation. Braman and Kaemmerlen¹³ reported that of 2094 patients admitted for asthma over a 10-year period, 80 were admitted to the ICU, and only 24 required mechanical ventilation. Mountain and Sahn¹⁴ studied patients with hypercapnia and noted that only 5 of 61 patients required intubation.

Prevention of intubation is an important goal in the treatment of severe acute asthma because mortality rates range from 10% to 20% in patients requiring intubation.³ Patients with severe asthma exacerbations often respond to first- and second-line therapies, such as β_2 -adrenergic agonist use, corticosteroids, anticholinergic agents, magnesium, aminophylline, and systemic catecholamines. However, there are times when patients with severe acute asthma do not respond to first- or second-line therapies, and special therapies might be necessary for the possible prevention of intubation (Table I).¹⁵ Noninvasive ventilation is discussed in a separate article.

Criteria for intubation

Clinical. There are 4 indications for intubation, including (1) cardiac arrest, (2) respiratory arrest or profound bradypnea, (3) physical exhaustion, and (4) altered sensorium, such as lethargy or agitation, interfering with oxygen delivery or anti-asthma therapy. For example, a patient who repeatedly pulls off his or her oxygen mask and states “I cannot breathe” might require intubation (Table II).¹⁶

TABLE II. Consensus indicators for intubation¹⁶

Clinical
Cardiac arrest
Respiratory arrest
Altered sensorium
Progressive exhaustion
Silent chest
Laboratory
Severe hypoxemia with maximal oxygen delivery
Failure to reverse severe respiratory acidosis despite intensive therapy

Clinical judgment must determine whether intubation is appropriate in the setting of physical exhaustion and altered mental status. In the past, respiratory acidosis or an increasing $Paco_2$ was considered an indication for intubation; however, a systematic review of the literature by Leatherman¹⁷ determined that intubation might not be necessary for a successful outcome in most asthmatic patients with hypercarbia. Intubation is indicated with a progressively increasing $Paco_2$ that is unresponsive to therapy and possibly associated with a change in mental status; however, a high $Paco_2$ alone might not be an indication for intubation, provided the patient has no change in mental status and does not appear to be exhausted.

Arterial blood gases. In general, it is not necessary to obtain arterial blood gases (ABGs) for asthmatic patients presenting to the ED with bronchospasm. ABGs are usually obtained for patients who are refractory to therapy. The literature suggests the following ABG results are indications for intubation and mechanical ventilation: pH less than 7.2, carbon dioxide pressure increasing by more than 5 mm Hg/h or greater than 55 to 70 mm Hg, or oxygen pressure less than 60 mm Hg on 100% oxygen delivered through a mask.

In addition to the above clinical and laboratory indications for intubation, additional factors that might need to be taken into consideration include a respiratory rate of greater than 40 breaths/min, silent chest despite respiratory effort, complicating barotrauma, or unresolving lactic acidosis.¹⁸ Corbridge and Hall¹⁹ and Zimmerman et al²⁰ have emphasized that observation of a patient's clinical condition and course might be more valuable than laboratory testing.

Intubation technique

Once the decision to intubate the patient has been made, the appropriate method for achieving intubation is controversial. There are 4 methods of intubation, including awake nasotracheal intubation, awake orotracheal intubation, orotracheal intubation with sedation, or orotracheal intubation with sedation and neuromuscular blocks (Table III).

Although there are advantages to nasal intubation, such as more rapid preparation and less need for sedation, oral endotracheal intubation is generally preferred for patients in critical respiratory distress. Asthmatic patients are more likely to have nasal polyps and sinus pathology that complicate nasotracheal intubation.²¹ In addition, oral intubation allows the use of an endotracheal tube of a larger diameter, facilitating secretion removal and bronchoscopy, if needed.²¹

Because even minor manipulation of the airway during intubation can elicit laryngospasm and worsen bronchospasm, the

TABLE III. Benefits/risks of intubation methodology

Method of intubation	Benefits/risks	Contraindications
Nasotracheal	Benefits Minimal need for sedation Rapidly of preparation Greater postintubation comfort for awake patient Maintenance of semiupright posture Maintenance of spontaneous respiration Decreased likelihood of aspiration Risks Epistaxis Purulent sinusitis	Nasal polyps Coagulation disorder Thrombocytopenia Abnormal nasal anatomy
Orotracheal	Benefits Larger-sized endotracheal tube Direct visualization Relative ease of obtaining pharyngeal anesthesia Risks Oral or tracheal trauma Esophageal intubation Vocal cord injury Aspiration	
Awake oro tracheal	Benefits Avoid rendering patient apneic Risks Oral or tracheal trauma Esophageal intubation Vocal cord injury Aspiration Patient might be unable to tolerate the procedure Coughing reflex can be triggered	
Orotracheal with sedation	Benefits Rapid procedure, less traumatic than awake Intubation might be easier to accomplish Risks Oral or tracheal trauma Esophageal intubation Vocal cord injury Aspiration Hypotension caused by excessive sedation Opioids might cause bronchospasm	
Orotracheal with neuromuscular blockade	Benefits Increases the ease of intubation by reducing muscular resistance Eliminates the risk of coughing Might provide superior control during intubation compared with sedation alone (Baumgarten, <i>Can J Anaesth</i> 1988;35:5-11) Risks Few, rarely serious Side effects of neuromuscular blocking agents Sedation is necessary in addition to neuromuscular blockade Airway loss caused by inability to intubate, ventilate, or both	

airway should be established by experienced personnel. Atropine can be administered initially to attenuate the vagal reflexes that lead to these responses, and lidocaine can be used for topical anesthesia, as mentioned above.

Sedation can make intubation easier to achieve. Intubation with a rapid sequence of sedation and muscle paralysis is preferred, although some advocate awake intubation because of concern for the potential for apnea with sedation.²² Although there might be some concern about sedating a patient who is in respiratory distress, once intubation is planned, there is no contraindication to sedation.²³

Ketamine is one option to consider for preintubation sedation. It stimulates the release of catecholamines and might have a direct relaxation effect on bronchial smooth muscle, leading to bronchodilation.^{24,25} This, in turn, allows for easier ventilation in the peri-intubation period. Side effects associated with ketamine include hypersecretion, hypotension and hypertension, arrhythmias, and hallucinations, and its use is contraindicated in patients with ischemic heart disease, hypertension, preeclampsia, and increased intracranial pressure.

Propofol (2 mg/kg administered intravenously over 2 minutes) is an excellent alternative to ketamine to achieve sedation in the

peri-intubation period, particularly in the hypertensive patient. Propofol is a short-acting agent with bronchodilatory effects that allows for rapid awakening.²⁴ It does not cause hyperkalemia, except during rare cases of propofol infusion syndrome associated with high-dose use. Features of this syndrome include hyperlipidemia, hepatomegaly, hyperkalemia, rhabdomyolysis, severe metabolic acidosis, renal failure, and cardiovascular collapse.²⁶ A short-acting and rapid-onset benzodiazepine, such as midazolam, can also be used for patient sedation. Opioids, such as morphine sulfate, are not used in asthmatic patients for intubation because of the potential for histamine release, nausea and vomiting, and hypotension, and although the clinical significance of histamine release is doubtful in this setting, its other side effects preclude routine use.²¹

In addition to ketamine or propofol, succinylcholine or a competitive neuromuscular blocking agent can be used for muscle paralysis.²⁷ Succinylcholine offers the advantage of a rapid onset and short duration of action. Some authorities prefer a nondepolarizing agent, such as vecuronium, because succinylcholine causes a greater histamine release, which could theoretically worsen bronchospasm. On the other hand, the clinical significance of histamine release in this setting is once again doubtful.¹⁶ However, the increase in potassium levels caused by succinylcholine might cause severe cardiac arrhythmias if the patient has hyperkalemia from respiratory acidosis. Vecuronium does not carry the risk of hyperkalemia but produces a longer duration of paralysis.²⁸ Before inducing muscle paralysis, the physician should be sure that the patient can be ventilated and intubated, particularly with a longer-acting agent, such as vecuronium. This might be difficult to ascertain because of the severe bronchospasm preventing ventilation by means of bag valve mask. Facial features of patients and preintubation assessments (dentures, loose teeth, and Mallampati score) might provide important clues to the success of intubation.

In summary, rapid-sequence induction can be safely achieved in most patients by using 1.0 to 1.5 mg/kg ketamine administered intravenously and 1.0 to 1.5 mg/kg succinylcholine administered by means of intravenous push or 2 mg/kg propofol administered intravenously over 2 minutes with succinylcholine.²³ Propofol is preferred over ketamine for patients with hypertension, and succinylcholine should be avoided in patients with hyperkalemia.

Recommendations for appropriate ventilator settings

When an asthmatic patient is ventilated, severe hyperinflation can result from breath stacking, placing the patient at risk for hypotension and barotrauma.²⁹ It is essential to recognize, measure, and control hyperinflation and auto-positive end-expiratory pressure (PEEP) to ensure a good outcome in the intubated asthmatic patient.³⁰

Auto-PEEP occurs when diminished expiratory flow causes incomplete emptying of alveolar gas. As end-expiratory lung volume increases, so does end-inspiratory volume for a given tidal volume predisposing to lung hyperinflation.^{30,31} There are 3 ventilator strategies that can be used to reduce hyperinflation and auto-PEEP in the intubated asthmatic patient: (1) reduction of the respiratory rate, (2) reduction of tidal volume, and (3) shortening of inspiration by increasing inspiratory flow to allow greater time for exhalation with each respiratory cycle. Changes in

respiratory rate have the greatest effect on hyperinflation and auto-PEEP. In most intubated asthmatic patients, an inspiratory flow with decelerating waveform configuration is reasonable during the initial setup if inspiratory time is not excessively long. However, if one is unable to reduce the respiratory rate enough for reduction of hyperinflation and auto-PEEP to acceptable levels (10-15 cm H₂O, see below), inspiratory time can be shortened to allow for a proportionately longer time for exhalation per respiratory duty cycle by increasing the inspiratory flow rate. Reduction of tidal volume is appropriate; however, it is limited by its progressive effect on the dead-space fraction. Increasing pressure limitation to 100 cm H₂O might be necessary so that patient receives the full tidal volume. The use of a square wave-flow pattern and increasing flow rate shortens inspiratory time and might be appropriate because it does not represent a significant danger for barotrauma and should reduce auto-PEEP and hyperinflation.^{30,31} One concern regarding the use of high flow rates is that the patient's respiratory rate might increase in response to high flows, particularly during assist-control ventilation, thereby decreasing expiratory time and worsening auto-PEEP.³²

Decreasing respiratory rate can cause hypercapnia. Fortunately, hypercapnia is often well tolerated, even with arterial Paco₂ values as high as 90 mm Hg, and in selected, critically ill patients it might be safer to accept hypercapnia than to overventilate to a normal Paco₂ at the cost of critical hyperinflation. Anoxic brain injury and severe myocardial dysfunction are contraindications to permissive hypercapnia because of the potential for hypercapnia to dilate cerebral vessels, constrict pulmonary vessels, and decrease myocardial contractility.³³ In patients with mild-to-moderate myocardial dysfunction, the clinician must balance the benefits of decreasing lung hyperinflation with the potential adverse effects of hypercapnia.

Determining the severity of lung hyperinflation is central to assessing patients and adjusting ventilator settings. Several methods have been proposed to assess lung inflation, including the measurement of exhaled gases and the volume at end-inspiration (V_{ei}).³⁴ This volume is determined by collecting expired gas from total lung capacity to functional residual capacity during 40 to 60 seconds of apnea. A V_{ei} of greater than 20 mL/kg correlates with barotrauma; however, V_{ei} might underestimate air trapping if there are slowly emptying lung units. This measure requires staff training and patient paralysis and is not performed in routine ICU practice.

In common practice 2 relatively easy-to-measure pressures are used as surrogate markers of lung inflation: auto-PEEP and plateau pressure (P_{plat}). Auto-PEEP is an estimate of the lowest average alveolar pressure achieved during the respiratory cycle. It is obtained by measuring airway-opening pressure during an end-expiratory hold maneuver. The presence of expiratory gas flow at the beginning of inspiration (which can be detected by means of auscultation or flow tracings) also suggests auto-PEEP. Auto-PEEP can underestimate the severity of hyperinflation when there is poor communication between the alveoli and the airway opening.³⁵

P_{plat} (or lung distension pressure) estimates average end-inspiratory alveolar pressure. P_{plat} is affected by the entire respiratory system, including lung parenchyma, the chest wall, and the abdomen. It is determined by temporarily stopping flow at end-inspiration during a single delivered breath.

Accurate measurements of P_{plat} and auto-PEEP require patient-ventilator synchrony and absence of patient effort.

TABLE IV. Initial ventilator settings for the intubated asthmatic patient³¹

Controlled mechanical ventilation at 10 breaths/min
Tidal volume at 7-8 mL/kg (ideal body weight)
Peak inspiratory flow at 60 L/min (constant flow) or 80-90 L/min (decelerating flow)
Fraction of inspired oxygen at 1.0

Paralysis is generally not required. Unfortunately, neither auto-PEEP nor Pplat have been validated as a predictor of complications of mechanical ventilation. Still, many experts agree that complications are rare when Pplat is less than 30 cm H₂O and auto-PEEP is less than 15 cm H₂O.³⁶

Ventilator-applied PEEP is not recommended in sedated and paralyzed patients because it increases lung volume if used excessively. However, use of low levels of ventilator-set PEEP (eg, 5 cm H₂O) in spontaneously breathing patients decreases the inspiratory work of breathing by decreasing the pressure gradient required to overcome auto-PEEP without worsening lung inflation.¹¹

Table IV³¹ lists appropriate initial ventilator settings for the intubated asthmatic patient.

Management in the immediate postintubation period

Sedation. Effective sedation improves patient comfort, decreases oxygen consumption and carbon dioxide production, and allows synchronism between the patient and the ventilator.³⁷ Sedation also prevents the risk of an awakening patient becoming combative, self-extubating, or triggering auto-PEEP because of a rapid respiratory rate.³¹ Benzodiazepines are commonly used for this purpose, but other agents are used as well. Propofol is a useful sedating agent because it can be titrated to provide deep sedation and has bronchodilating properties.³⁷ However, propofol can lead to seizures, hypertriglyceridemia, and increased carbon dioxide production when used long-term.³⁷ High doses of propofol should be avoided to minimize the risk of propofol infusion syndrome.²⁶ To provide the best combination of amnesia, sedation, analgesia, and suppression of respiratory drive, a narcotic, such as fentanyl or alfentanil, should be added to either propofol or a benzodiazepine, such as lorazepam.³⁷

After intubation, inhaled anesthetic agents might be useful because of their potent direct bronchodilatory effect and their ability to decrease airway responsiveness.^{37,38} The benefits of the use of these agents must be balanced against the risk of inducing myocardial depression and arrhythmias³⁷ and the logistical problems associated with their use.³¹

Neuromuscular blockade. Continuing neuromuscular blockade during mechanical ventilation might reduce the risk for barotrauma, avoids coughing and dyssynchronous breathing, and allows the respiratory muscles to rest.³⁷ In this regard cisatracurium is a good choice because it is essentially free of cardiovascular effects, does not release histamine, and does not rely on hepatic and renal function for clearance.

Because paralytic agents can cause a myopathy, particularly when used concomitantly with corticosteroids, neuromuscular blockade after intubation is recommended only for patients who do not have adequate relaxation with deep sedation alone to allow for a passive response to the ventilator.³¹ Neuromuscular

blockade should be limited, when possible, to less than 24 hours to avoid an associated myopathy, particularly because deep sedation is generally all that is required by that time.³⁰ Full resolution of the myopathy generally occurs, although the recovery time might be prolonged.³¹

Heliox. Heliox is a mixture of oxygen and helium that decreases airway resistance by reducing airflow turbulence in the bronchial passages. The results of studies on the benefits of the use of heliox are conflicting, but there might be some benefit to its use in patients with severe asthma before intubation as a means of avoiding intubation. There is currently insufficient evidence to support the use of heliox in intubated patients.

Medical management of asthma in the intubated patient

Systemic corticosteroids. Because bronchospasm continues after intubation, inhaled bronchodilators and systemic corticosteroids should be continued.³⁰ Systemic corticosteroids are the gold standard of treatment in intubated asthmatic patients. Manser et al³⁹ conducted a systematic review of the literature and determined that 40 mg every 6 hours of methylprednisolone (or equivalent) is appropriate, and higher doses do not appear more efficacious.

Inhaled β -agonists. Inhaled β -agonists are also indicated; however, the most effective dosing is debated. The literature shows that delivery of sufficient puffs of β -agonists through an MDI using a well-designed reservoir system is cost-effective and has proved to be as effective as using a nebulizer in intubated asthmatic patients.⁴⁰ Table V³¹ summarizes guidelines for the use of MDIs and nebulizers in mechanically ventilated patients.

Other bronchodilators. The clinical benefits of intravenous theophylline in intubated patients are unknown, but outcomes in hospitalized asthmatic patients in general do not appear to improve with intravenous theophylline (Expert Panel Report 3).

Prevention and treatment of complications

Intubation-induced bronchospasm. It is well known that tracheal intubation increases airway resistance in patients with bronchial hyperreactivity.⁴¹ It is, however, unknown to what extent reflex bronchoconstriction in asthmatic patients occurs after awake tracheal intubation. Four studies addressed these issues.

Groeben et al⁶ (see the Results section) determined that dyclonine inhalation might be contraindicated in patients with bronchial hyperreactivity, given the greater than 50% decrease in FEV₁ in the asthmatic patients they studied. Furthermore, they found the decrease in FEV₁ was significantly mitigated (35%) by administration of lidocaine for topical anesthesia, and salbutamol pretreatment might have provided additional attenuation. Therefore they recommended combined pretreatment with lidocaine and salbutamol for awake intubation in patients with acute asthma.

In an attempt to better understand the ability of intravenous lidocaine to prevent intubation-induced bronchospasm, Maslow et al⁹ (see the Results section) found inhaled albuterol blunted the airway response to tracheal intubation in asthmatic patients, whereas intravenous lidocaine did not. Hence intravenous lidocaine cannot be recommended as a means of preventing intubation-induced bronchospasm.

Scalfaro et al⁸ (see the Results section) investigated the protective effect of an inhaled β_2 -adrenergic agonist in the setting of

TABLE V. Guidelines for the use of MDIs and nebulizers in mechanically ventilated patients³¹

MDI technique	Nebulizer technique
Ensure tidal volume >500 mL in adults during assisted ventilation	Place the drug solution in the nebulizer using a fill volume (2-6 mL) that ensures the greatest aerosol-generating efficacy <u>ll</u>
Aim for an inspiratory time (excluding the inspiratory pause) of >0.3 of total breath duration	Place the nebulizer in the inspiratory line at least 30 cm from the ventilator wye ^{ll}
Ensure that the ventilator breath is synchronized with the patient's inspiration	Ensure an airflow of 6-8 L/min through the nebulizer [#]
Shake the MDI vigorously	Ensure adequate tidal volume (>500 mL in adults); attempt to use duty cycle >0.3, if possible
Place the canister in the actuator of a cylindrical spacer situated in the inspiratory limb of the ventilator circuit*	Adjust minute volume to compensate for additional airflow through the nebulizer, if required
Actuate the MDI to synchronize with the precise onset of inspiration by the ventilator [†]	Turn off flow-by or continuous-flow mode on ventilator
Allow a breath hold at the end of inspiration for 3 to 5 seconds [‡]	Observe nebulizer for adequate aerosol generation throughout use
Allow passive exhalation	Disconnect nebulizer when all medication is nebulized or when no more aerosol is being produced
Repeat actuation after 20-30 seconds until total dose is delivered [§]	Reconnect ventilator circuit and return to original ventilator settings

*With MDIs, it is preferable to use a spacer that remains in the ventilator circuit to avoid disconnecting the ventilator circuit for each treatment. Although bypassing the humidifier can increase aerosol delivery, it prolongs each treatment and requires disconnecting the ventilator circuit.

[†]In ambulatory patients with an MDI placed near the mouth, actuation is recommended briefly after initiation of inspiratory airflow. In mechanically ventilated patients using an MDI and spacer combination, actuation should be synchronized with the onset of inspiration.

[‡]The effect of a postinspiratory breath hold has not been evaluated in mechanically ventilated patients.

[§]The manufacturer recommends repeating the dose after 1 minute. However, MDI actuation within 20 to 30 seconds after the prior dose does not compromise drug delivery.

ll The volume of solution placed in the nebulizer (ie, the fill volume) that achieves maximal efficiency varies among nebulizers.

^{ll}Bypassing the humidifier has been suggested as a means of improving aerosol delivery in mechanically ventilated patients. However, administration of dry gas might lead to drying of the airway mucosa; therefore administration with humidified gas is preferred for routine bronchodilatory therapy. This is the description of airway lines leading from the patient.

[#]The nebulizer can be operated continuously or only during inspiration; the latter method is more efficient. Some ventilators provide inspiratory gas flow to the nebulizer; alternatively, the nebulizer can be powered by continuous gas flow from an external source.

increased Rrs in children having their tracheas intubated and showed that in children with mild-to-moderate asthma, a preanesthetic treatment with inhaled salbutamol can prevent the increase of Rrs, as evidenced by a 6.0% decrease in Rrs with salbutamol treatment.

One additional study assessed medication effects on total Rrs. Wu et al¹⁰ (see the Results section) investigated the effects of a β -agonist and cholinergic antagonist on postintubation total Rrs in asthmatic patients who experienced an increase in resistance after tracheal intubation and concluded that fenoterol can reduce Rrs after tracheal intubation in asthmatic patients.

Overall, one can therefore conclude from these studies that (1) airway resistance does increase in response to intubation and (2) pretreatment with bronchodilators appears to be useful in decreasing or preventing this complication of intubation in patients with hyperreactive airways.

Persistent or worsening hypoxemia. Persistent or worsening hypoxemia during mechanical ventilation suggests the development of a complication of mechanical ventilation. Complications such as right main stem intubation (proper endotracheal tube placement is generally 21 cm at the incisors in a woman and 23 cm in a man), pneumothorax, endotracheal tube displacement, endotracheal tube blockage, leakage of air around the endotracheal tube, gastric distention decreasing respiratory system compliance, mechanical malfunction of the ventilatory apparatus, aspiration, and progressive bronchospasm can all contribute to hypoxemia and must be addressed individually as appropriate. In addition, appropriate settings for mechanical ventilation (see below), treatment of recurrent or persistent bronchospasm, nasogastric tube placement to decompress the stomach, and frequent

reassessment of the patient to determine the cause of hypoxemia and the response to interventions are critical.

Hypotension. Hypotension is another common complication that can develop after intubation. During periods of asthma exacerbations, patients typically have decreased oral intake and faster respiratory rates, both of which contribute to a negative fluid balance. This relative or actual dehydration can contribute directly to hypotension. Hypotension can also result from complications related directly to mechanical ventilation. The increase in intrathoracic pressure caused by mechanical ventilation leads to decreased systemic venous return, potentially leading to a decrease in cardiac output. These effects of ventilation can be avoided by preventing complications that increase intrathoracic pressure, such as hyperinflation, gastric distention, and tension pneumothorax. Lastly, medications used for sedation or medical management can cause hypotension. For example, the general anesthetic isoflurane improved Paco_2 in pediatric patients but caused hypotension severe enough to require vasopressor support in 8 of the 10 children studied.⁴²

A fluid bolus is an immediate measure that is useful for managing hypotension (unless there are contraindications to a fluid bolus, such as concurrent pulmonary edema). Decreasing the respiratory rate and adjusting the ventilatory cycle to allow for a shorter inspiratory cycle and longer expiratory cycle are typical strategies for avoiding complications caused by lung hyperinflation (see the discussion on ventilatory settings). In critical hypotension (defined as a decrease in systolic blood pressure to <90 mm Hg or a reduction of >40 mm Hg from baseline value), a trial of hypopnea (2-3 breaths/min) or apnea in a preoxygenated patient for 30 to 60 seconds can be both diagnostic and therapeutic

for lung hyperinflation. Critical hypotension for which a reversible cause cannot be immediately found is an indication for epinephrine.

Cardiac arrest. Cardiac arrest can occur as a result of critical lung hyperinflation by (1) decreasing preload to the right ventricle, (2) increasing pericardial pressure and tamponade physiology, (3) increasing total pulmonary vascular resistance and right ventricular strain, and (4) predisposing to tension pneumothorax. A trial of apnea or hypopnea for no more than 30 to 60 seconds, external chest compressions, volume challenge, and epinephrine are indicated for cardiac arrest presenting as pulseless electrical activity.

Tension pneumothorax is a clinical diagnosis. If lung examination suggests this complication (eg, tracheal shift with unilateral breath sounds or subcutaneous emphysema), proceed with needle thoracostomy followed by careful chest tube thoracostomy. Note that if the hyperinflated lung is punctured inadvertently, this could produce a rush of air similar to releasing a tension pneumothorax but result in ineffective ventilation. Note further that patients with tension pneumothorax might respond initially to a trial of apnea or hypopnea.

Other causes of cardiac arrest include hypoxemia, acidemia, electrolyte abnormalities (including lethal hyperkalemia if succinylcholine was used for intubation of a patient with respiratory acidosis), myocardial ischemia (particularly if high-dose β -agonists were used systemically), and endotracheal tube displacement, kinking, or plugging. Use of illicit drugs, such as heroin or crack cocaine, should also be considered.

Barotrauma. Increased morbidity and mortality are associated with barotrauma.⁴³⁻⁴⁶ The issue of development of barotrauma in relation to airway pressure, PEEP, and tidal volume is controversial. Amato et al⁴⁷ reported that the use of small tidal volumes and PEEP titrated to lung mechanics reduced the frequency of barotrauma in patients with acute respiratory distress syndrome. Conversely, Weg et al⁴⁸ found no relationship between the development of barotrauma and high airways pressures or high tidal volumes in patients with acute respiratory distress syndrome.

As noted above,¹¹ patients with underlying lung diseases, such as acute respiratory distress syndrome and asthma, are more likely to experience barotrauma with mechanical ventilation.

A case-control analysis showed increased mortality rates in patients with barotrauma (51.4% vs 39.2%, $P = .04$) and prolonged ICU stay (14 ± 13.6 days in patients with barotrauma vs 10.9 ± 11.4 days in patients without barotrauma, $P = .04$). In asthmatic patients Tuxen and Lane³⁴ have demonstrated that a Vei of greater than 20 mL/kg correlates with barotrauma (see above).

Myopathy. Acute muscle weakness after mechanical ventilation has been shown to be secondary to acute myopathy.⁴⁹ The pathogenesis of muscle injury has been linked to corticosteroids and neuromuscular blocking agents, such as pancuronium, vecuronium, and atracurium.⁵⁰ As noted above, Behbehani et al¹² reported that there was a high incidence of acute myopathy when neuromuscular blocking agents were used for near-fatal asthma, but corticosteroids were not independently associated with myopathy in their study.

Extubation. Because patients often have prolonged hold times in the ED while waiting for critical care beds, weaning and extubation have become germane to emergency medicine. Weaning and extubation criteria have not been validated for patients with acute asthma. One approach is to perform a spontaneous breathing trial in an awake patient once Paco_2 normalizes, airway resistance is

less than 20 cm H₂O, auto-PEEP is less than 10 cm H₂O, and neuromuscular weakness has not been identified. Extubation should proceed in a timely manner to avoid complications of mechanical ventilation, including endotracheal tube-induced bronchospasm. After extubation, observation in an ICU is recommended for an additional 12 to 24 hours. During this time, the focus can switch to safe transfer to the ward and outpatient management.

SUMMARY OF RECOMMENDATIONS (ALL STRONG)

1. Criteria for intubation (Evidence Category D)

- Clinical indications
 - Cardiac arrest
 - Respiratory arrest
 - Altered mental status
 - Progressive exhaustion
 - Silent chest
- Laboratory indications
 - Severe hypoxia with maximal oxygen delivery
 - Failure to reverse severe respiratory acidosis despite intensive therapy
 - pH <7.2, carbon dioxide pressure increasing by more than 5 mm Hg/h or greater than 55 to 70 mm Hg, or oxygen pressure of less than 60 mm Hg

2. Intubation technique (Evidence Category D)

- There are 4 choices of technique, each with its own benefits and risks:
 - nasotracheal intubation,
 - awake orotracheal intubation,
 - orotracheal intubation with sedation, and
 - orotracheal intubation with sedation and neuromuscular blockade.
- In general, orotracheal intubation with sedation and neuromuscular blockade are preferred for asthmatic patients in critical respiratory distress.
- The use of ketamine and propofol might be preferred over other sedative agents. Pretreatment with bronchodilators might reduce airway bronchospasm associated with tracheal intubation in patients with nonacute asthma requiring intubation. Patients with acute asthma almost invariably would have received bronchodilation before intubation unless presenting in arrest or near arrest.

3. Recommendations for appropriate ventilator settings (Evidence Category D)

- Control of hyperinflation and auto-PEEP
 - Reduction of respiratory rate might help control hyperinflation.
 - Reduction of tidal volume might help control hyperinflation.
 - An initial set-up of 80 L/min with a decelerating waveform configuration might be appropriate in adults.
 - Shortening of inspiration with a square wave pattern and an inspiratory flow rate of 60 L/min allows greater time for exhalation in each respiratory cycle and might help control hyperinflation.
 - Auto-PEEP and Pplat should be followed during mechanical ventilation.

- Hypercapnia is preferable to hyperinflation.
 - Hypercapnia should not be used in the presence of increased intracranial pressure.
 - An acceptable level of hypercapnia and acidosis is a pH as low as 7.15 and a PaCO_2 of up to 80 mm Hg.
- 4. Management in the postintubation period (Evidence Category D)
 - Verify endotracheal tube placement with a carbon dioxide detector, adequate oximeter readings, and chest radiography. Chest radiography will determine the depth of intubation but not esophageal intubation with the patient breathing “around the tube.”
 - Postintubation sedation should be provided with a benzodiazepine.
- 5. Medical management of the intubated asthmatic patient
 - Continued treatment with inhaled bronchodilators, such as nebulized albuterol or albuterol administered with an MDI (Evidence Category B)
 - Systemic corticosteroid treatment, such as 40 mg of methylprednisolone every 6 hours (Evidence Category B)
 - No routine use of heliox once the patient is intubated (Evidence Category D)
- 6. Prevention and treatment of complications (Evidence Category D)
 - Hypoxemia
 - Exclude right mainstem intubation (21 cm at incisors)
 - Exclude pneumothorax and place pleural drain
 - Tube obstruction (kinking, biting of tube, or plugging)
 - Exclude pneumonia and other lung disease
 - Hypotension
 - Consider pneumothorax early but first perform a trial of apnea or hypopnea to decrease intrathoracic pressure unless there is unequivocal evidence of pneumothorax, such as tracheal shift with unilateral breath sounds or subcutaneous emphysema
 - Tension pneumothorax is a clinical diagnosis. If a lung examination suggests this complication, proceed with a needle thoracostomy followed by a chest tube thoracostomy.
 - Fluids
 - Measure auto-PEEP and Pplat and apply reduction measures
 - Exclude other causes, such as myocardial infarction and sepsis
 - Cardiac arrest
 - A trial of apnea or hypopnea for no more than 30 to 60 seconds with external compressions and volume challenge is therapeutic for lung hyperinflation as a cause of cardiac arrest.
 - Consider tension pneumothorax early. If lung examination suggests this complication, proceed with a needle thoracostomy followed by a careful chest tube thoracostomy.

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