Asthma

January 28, 2017 by Josh Farkas

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Don't assume that every "asthmatic" with dyspnea is having an asthma exacerbation.

### evaluation to determine diagnosis

- **History** (to the extent that it is available).
- **Physical examination**
  - Asthma: Wheeze loudest over lung fields.
  - Upper airway obstruction: Wheeze loudest over throat.
- **Bedside ultrasonography**
  - Thoracic ultrasonography: Exclude pneumothorax or heart failure.
  - Cardiac ultrasonography: Evaluate volume status, function.
- **Chest X-ray**
  - Not immediately essential if bedside ultrasonography performed.
  - Useful to evaluate for pneumonia and obtain baseline for comparison.

### severity

- **Main indicators of severity**
  - Tachypnea (resp rate >30)
  - Work of breathing (patient looks bad)
  - Inability to speak
  - Wheezing may be absent if patient is moving very little air ("silent chest," an ominous finding).
  - Somnolence and bradycardia may be signs of impending respiratory arrest.

### diagnosis & initial assessment

<table>
<thead>
<tr>
<th>common diagnoses confused with asthma</th>
<th>Clues to reach this diagnosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anaphylaxis</td>
<td>Involvement of other organ systems (e.g. urticaria, vomiting, shock). Stridor due to angioedema.</td>
</tr>
<tr>
<td>Vocal cord dysfunction (or other upper airway obstruction)</td>
<td>Wheeze audible from across the room (this is not a feature of severe asthma!).</td>
</tr>
<tr>
<td>Pneumothorax</td>
<td>Thoracic ultrasound shows lack of lung slide on affected side. If lucky may see traditional signs (e.g., subcutaneous crepitus).</td>
</tr>
<tr>
<td>Pneumonia</td>
<td>Historical features (sputum production, fever) Infiltrate on chest X-ray; focal B-lines seen on thoracic ultrasound.</td>
</tr>
<tr>
<td>Heart failure (&quot;cardiac asthma&quot;)</td>
<td>Key finding = Diffuse B-line pattern visible on thoracic ultrasonography. Other supportive features may include peripheral edema, echo c/w heart failure.</td>
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</table>

Although patients will vary, the central pathophysiology often involves tachypnea leading to gas-trapping in the chest (autoPEEP) which exacerbates dyspnea in a vicious cycle:
Asthma involves a vicious cycle of airway obstruction and dyspnea that leads to tachypnea. Asthmatics will be unable to exhale properly if they are breathing fast, so they can’t tolerate tachypnea. Over time, this cycle will lead to diaphragmatic fatigue and exhaustion. Aggressive intervention before the point of exhaustion can generally avoid intubation.

The remainder of this section will unpack these various therapies:

### Initial management of severe asthma not requiring immediate intubation

- **Bronchodilation**
  - Stacked albuterol nebs (2.5-5 mg q20) or continuous neb (10-15 mg/hr)
  - Ipratropium (may use 1.5 mg over first hour, then 0.5 mg nebulized q4-6 hr)
- **Steroid**
  - Methylprednisolone 125 mg IV x1 (or equivalent dose of other steroid)
- **Magnesium sulfate**
  - 2 grams (8 mM) IV over 20 minutes.
- **BIPAP**
  - 1st line support device = BIPAP
  - If unable to tolerate BIPAP, HFNC may be used
- **Sedation if needed for BIPAP**
  - Start dexmedetomidine infusion at maximal rate (down-titrate as takes effect). This may be helpful as an anxiolytic agent, even if the patient is able to tolerate the BIPAP mask.
  - May use small doses of opioid while waiting for dexmedetomidine to take effect if severely dyspneic (e.g., fentanyl 25 mcg IV PRN).
- **Epinephrine infusion**
  - Indications
    - (i) failure of inhaled bronchodilators
    - (ii) unable to tolerate inhaled bronchodilators (re: coughing)
    - (iii) bradycardia related to dexmedetomidine
  - Start 5 mcg/min, titrate 1-10 mcg/min (peripheral IV is fine).
  - (Alternative with almost no evidentiary basis: 0.2 mg IV glycopyrrolate.)

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### Inhaled bronchodilators

#### high dose inhaled albuterol

- Patients should be started on high-dose albuterol. Two options are roughly equivalent:
  - (a) Stacked nebs: 2.5-5 mg via nebulizer Q20 minutes back-to-back.
  - (b) Continuous nebulized therapy (10-15 mg/hour initially).
As patients improve, this should gradually be weaned down and spaced out.

**inhaled ipratropium**

- Addition of ipratropium to *initial therapy* (e.g. 1.5 mg inhaled over the first hour of therapy) may be helpful. Subsequently 0.5 mg may be nebulized Q4-6 hours.

**systemic bronchodilators**

**epinephrine**

- Not supported by any high-quality evidence.
- Indications may include:
  - (a) Patient unable to tolerated inhaled bronchodilators (e.g. due to coughing).
  - (b) Failure to improve with inhaled bronchodilators.
- **Intramuscular epinephrine**
  - Dose is 0.3 – 0.5 mg IM, may repeat 1-2 times Q20 minutes.
  - Not preferred: lack of control over dose, unable to down-titrate if complications occur.
- **Intravenous epinephrine infusion**
  - Start at 5 micrograms/minute, rapidly titrate to effect over roughly 1-15 micrograms/minute range. Down-titrate as soon as possible.
  - Intravenous administration provides more flexibility than IM epinephrine (e.g. if hypertension or excessive tachycardia occurs, can down-titrate or stop it immediately).
  - Epinephrine is *safe for peripheral administration* ([link](https://emcrit.org/pulmcrit/phenylephrine-epinephrine-central-access/)). (It doesn't require a central line).
  - (More on IM vs IV epinephrine [here](https://emcrit.org/pulmcrit/iv-epinephrine-anaphylaxis/).)

**other IV beta-2 agonists**

- IV albuterol or salbuterol is available in some countries; this seems like a good alternative to IV epinephrine if available.
- IV terbutaline seems like a reasonable option, but there is very scanty evidence regarding its use in adult asthma. Given that terbutaline has a half-life of 3-4 hours, this may be less maneuverable than IV epinephrine. Finally, the logistics surrounding terbutaline aren't terrific (it's not widely available, there may be a longer delay time in obtaining the drug from pharmacy, and providers are unfamiliar with dosing and administration). Therefore, although tertubaline could have some theoretical superiority to epinephrine, in practice IV epinephrine is probably a better choice.

**IV anticholinergic agents ??**

- IV anticholinergic agents are a sensible consideration for the same reason that IV beta-agonists are: in severe patients with extreme obstruction or inability to tolerate nebulized medications the systemic route may be more effective.
- Glycopyrrolate 0.2 mg IV has been reported to be effective in one case report ([3619169](https://www.ncbi.nlm.nih.gov/pubmed/3619169)). Although the evidence level is obviously very low, mechanistically this makes sense. The utility of inhaled glycopyrrolate is better established than IV glycopyrrolate ([16236844](https://www.ncbi.nlm.nih.gov/pubmed/16236844), [3392363](https://www.ncbi.nlm.nih.gov/pubmed/3392363), [3792086](https://www.ncbi.nlm.nih.gov/pubmed/3792086), [2225951](https://www.ncbi.nlm.nih.gov/pubmed/2225951)). This should be used only in exceptional situations, with close monitoring of hemodynamics (there may be a risk of synergistic tachycardia if used in combination with systemic beta-agonists).

**BiPAP**

- **potential indications?**
  - Respiratory rate >25-30/min
  - Significant work of breathing
initial settings

- Start with standard settings (10 cm inspiratory pressure / 5 cm expiratory pressure).
- Titrate FiO2 to keep the saturation ~93-95%. Asthmatics shouldn't require much oxygen (if the FiO2 requirement is high, look for an alternative or additional diagnosis).
  - A prospective RCT suggests that excessive oxygen administration may impair ventilation-perfusion matching and thereby worsen hypercapnia [21597111](https://www.ncbi.nlm.nih.gov/pubmed/21597111).
- The role of various settings is shown below [7663804](https://www.ncbi.nlm.nih.gov/pubmed/7663804), [29131536](https://www.ncbi.nlm.nih.gov/pubmed/29131536), [30996631](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6422218/). Different patients may have different physiologies and thus individual titration to effect can be helpful.

**Optimal BiPAP settings ??**

<table>
<thead>
<tr>
<th>Expiratory pressure (EPAP)</th>
<th>Driving pressure (inspiratory pressure – expiratory pressure)</th>
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<tbody>
<tr>
<td><strong>Benefit</strong></td>
<td>- Main role = balances out intrinsic PEEP, thereby allowing patient to trigger breath easily.</td>
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<tr>
<td></td>
<td>- Possible theoretical role: stents open airways during exhalation.</td>
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<tr>
<td><strong>Situation where this is most beneficial</strong></td>
<td>- Extreme bronchospasm</td>
</tr>
<tr>
<td><strong>Risk</strong></td>
<td>- If set too high, will impair exhalation (decreases exhalatory pressure gradient)</td>
</tr>
<tr>
<td></td>
<td>- If patient doesn't reduce their own effort, then augmentation may increase the tidal volume and worsen gas trapping.</td>
</tr>
<tr>
<td><strong>Typical range</strong></td>
<td>5-8 cm</td>
</tr>
<tr>
<td><strong>How to titrate</strong></td>
<td>Patient comfort?</td>
</tr>
<tr>
<td></td>
<td>Tidal volume (target 4-8 ml/kg)</td>
</tr>
</tbody>
</table>

*Titration is only needed if patient is tachypneic or uncomfortable. The primary goal of titration is to achieve comfort and reduced respiratory rate. If this goal is achieved with higher tidal volumes (e.g. 8-10 cc/kg) that's probably fine.*


difficulty tolerating BiPAP

- (1) For patients with claustrophobia or anxiety, sedation (especially with dexmedetomidine) may be especially helpful. More on this below. It's generally worth making a real effort to get patients on BiPAP.
- (2) If patients genuinely cannot tolerate BiPAP, then high-flow nasal cannula (HFNC) may be used to reduce the anatomic dead space and thereby reduce the work of breathing.

evaluation of patient on BiPAP

- Respiratory rate is the key parameter.
  - As a rough rule, if the respiratory rate remains over ~25 breaths/minute, that's concerning. The ideal respiratory rate is probably around ~10-20 breaths/minute.
  - If the respiratory rate remains elevated, consider adjusting the BiPAP pressures or adding sedation (dexmedetomidine).
- Monitor tidal volume and minute ventilation.
  - These seem to be fairly accurate, as long as there isn't a large mask leak.
  - Tidal volumes should ideally be reasonably large (e.g. over ~5 cc/kg). If the tidal volumes are small (e.g. ~2-3 cc/kg) then the patient may get almost no effective ventilation (see dead space ventilation (#deadspaceventilation) below).
  - Minute ventilation should be reasonably large (e.g. at least ~4-5 liters/minute).

evidentiary basis

- The largest published series by Bond et al. describes 186 patients treated with noninvasive ventilation, of whom only 8 required intubation. Most patients were treated with CPAP alone with ~10 cm pressure. Many patients with poor mental status were successfully treated with noninvasive ventilation, proving that altered mental status alone is not an absolute contraindication to noninvasive support. This paper is strongly recommended reading (link [here](https://emcrit.org/wp-content/uploads/2017/01/bond2017.pdf))(29131536)
- BiPAP is supported by robust data in COPD. Since the physiology of asthma and COPD are somewhat similar (with some patients having asthma/COPD overlap), this evidence may be applicable to asthma as well.

The approach to sedation depends on how sick the patient is and how much time you have to titrate medications to effect. A general concept of how this might work is provided above, but there is no good data on any of this. Sedation plays a dual role of facilitating the use of BiPAP and also eliminating anxiety-driven tachypnea (which may exacerbate gas trapping in the chest).

**DEXMEDETOMIDINE MAY BE THE OPTIMAL AGENT FOR MOST PATIENTS**

- Dexmedetomidine has several excellent properties
  - (1) It's a titratable sedative, so it can be adjusted over time to match the patient's needs.
  - (2) It doesn't suppress the respiratory rate (in moderate cases, this allows respiratory rate to be used as an index of improvement).
  - (3) It may have bronchodilatory properties itself, which could directly improve asthma (26716866, 14739811).

- The main drawback of dexmedetomidine is that it can take a little while to work.
- Bolus doses are generally avoided, due to the associated risk of hemodynamic deterioration.
- Dexmedetomidine may be started at a high rate (e.g. 1.4 mcg/kg/hr) and then down-titrated over the next hour as levels accumulate.
- IV clonidine may be used in a similar fashion (if this is available, in lieu of dexmedetomidine).

**DELAYED SEQUENCE INTUBATION (DSI) WITH DISSOCIATIVE KETAMINE**

- This should only be done rarely, on extremely ill patients who look like they will likely require intubation.
- Some patients will improve immediately with ketamine, avoiding intubation. This is probably due primarily to ketamine's breaking a cycle of agitation-induced tachypnea (although ketamine-induced bronchodilation and facilitation of BiPAP probably help too).
● If patients don’t improve rapidly following ketamine administration, this will result in excellent pre-oxygenation prior to intubation (so it’s still a useful strategy).
● Ketamine may cause emesis, but this occurs as patients are waking up from dissociation. Close monitoring is required during this period. Nasal BiPAP may be considered during this period as a means of providing positive pressure ventilation with a lower risk of aspiration.
● More on delayed sequence intubation [here](https://emcrit.org/dsi/).

### opioids

- General properties:
  - It may be used to break a vicious cycle of hyperventilation-induced gas trapping.
  - Advantage compared to dexmedetomidine = immediate action, more powerful ability to reduce respiratory rate.
  - Advantage compared to ketamine = no risk of post-recovery emesis.
  - A rapid-acting, titratable opioid is usually most useful (e.g., IV fentanyl). Morphine should be avoided because histamine release could theoretically worsen bronchospasm.
- Potential situations where opioids could be useful:
  - (1) For a patient with moderate severity disease, as a stop-gap measure while waiting for dexmedetomidine to take effect (see figure above).
  - (2) If patients have pain for some other reason, then use of a low-dose opioid could be beneficial for pain (with mild blunting of the respiratory drive as a bonus effect).
- Evidentiary basis: There isn't any high-level evidence supporting opioid. However, studies have described the use of opioid to facilitate sedation on noninvasive ventilation ([25699177](https://www.ncbi.nlm.nih.gov/pubmed/25699177), [26164393](https://www.ncbi.nlm.nih.gov/pubmed/26164393)).
- Opioid changes the way patients must be monitored.
  - Without opioid on board, respiratory rate may be used as a general index of how sick patients are (as a reflection of ventilatory efficiency). Opioid directly suppresses respiratory rate, making this metric potentially unreliable.
  - Approaches to monitoring in a patient on opioids may include:
    - (1) Monitoring of mental status (worsening mental status over time suggests hypercapnia, but this is a late finding)
    - (2) Monitoring of tidal volume and minute ventilation in BiPAP (presuming an adequate mask seal).
    - (3) Periodic ABG/VBG monitoring may be needed in some situations. Please note that the goal of this monitoring isn't to see an immediate improvement in CO2, but rather to make sure that the patient isn't becoming much more hypercapnic. Often CO2 may take a while to improve, so the initial goal is to reduce the work of breathing and maintain a stable CO2.

### IV haloperidol or IV droperidol

- If dexmedetomidine isn't available, butyrophenones could be a reasonable sedative option.
- Advantages of these agents include
  - (a) Lack of respiratory suppression.
  - (b) No disinhibitory or paradoxical effects.
  - (c) Anti-nausea properties.
  - (d) Reasonably fast onset of action (within 10-20 minutes).

### benzodiazepines

- Benzodiazepines can sometimes be helpful, particularly for patients who chronically use benzodiazepines (and are known to respond favorably to them).
- However, in some patients benzodiazepines will induce delirium or agitation, which can be extremely counterproductive.
- Overall, the clinical effects of benzodiazepines are hard to predict, limiting their application.

### steroid

- (1) Loading dose: methylprednisolone 125 mg IV.
- (2) Maintenance dose

https://emcrit.org/ibcc/asthma/
No solid evidence on this.

- ~125 mg IV methylprednisolone daily seems reasonable (or roughly 2 mg/kg daily).
- One RCT found that 100 mg methylprednisolone was equally effective to 500 mg when administered in the emergency department (7781346). This suggests that optimal efficacy may be reached by a dose of ~100 methylprednisolone, and much higher doses may not be beneficial.

### other medications

#### IV magnesium

- This is a source of ongoing controversy. IV magnesium is safe and possibly effective, but hasn't been borne out in large adult RCTs such as the 3MG trial (25759905, 30633478, 24731521). A recent article summarizing available evidence is here. Some additional discussion of this may be found here.
- This therapy is reasonable. However, it's probably not enormously effective and definitely should not interfere with other treatments.
- Administration of two grams of magnesium over 20 minutes is reasonable (this dose of magnesium is extremely safe).

#### aminophylline

- May cause nausea and vomiting, which is very problematic on BiPAP (25164315).
- Evidence doesn't suggest that this improves outcomes.

#### leukotriene inhibitors (montelukast)

- Used in chronic asthma due to bronchodilatory and anti-inflammatory properties (20085924, 15539716).
- Some very weak evidence suggests a possible benefit from oral montelukast (10 mg daily) (20956393).
- The use of oral montelukast is limited in acute status asthmaticus because patients should be NPO.
- If intubation is required, enteral montelukast might be a reasonable consideration, especially if:
  - i) Patient is on chronic montelukast.
  - ii) Asthma is related to NSAIDs or aspirin (this type of asthma involves leukotriene overproduction).

### goals

**serial evaluation & goals**

- **(a)** Improvement in work of breathing.
  - Ideally respiratory rate will decrease to about 10-15 breaths/minute.
  - Persistent tachypnea (e.g. respiratory rate >>20 b/m consistently) is worrisome with regard to risk of respiratory fatigue.
- **(b)** Either normal mental status *or* absence of severe hypercapnia.
  - For patients with normal mental status, this is reassuring regarding absence of hypercapnia.
  - For patients with abnormal mental status due to sedation, periodic blood gas (VBG or ABG) may provide reassurance that patient is ventilating adequately.
- **(c)** BiPAP allows for monitoring of tidal volume and minute ventilation.
  - In absence of air leak, this may provide useful information.
  - Tidal volumes and minute ventilation may be trended.
- **(4)** Serial peak-flow monitoring not useful for critically ill asthmatic patients.
  - Very effort-dependent; patients often too sick to perform this properly.
  - May cause bronchospasm.
  - May turn into a random number generator.
ABG/VBG monitoring

- Ideally avoided (in situations where the patient’s mental status and ventilatory parameters can be monitored, this may be unnecessary).
- Goal of initial treatment is really to reduce the work of breathing, not immediate improvement in the ABG/VBG.
- May be useful in patients who are receiving sedation (if there is a concern for CO2 narcosis).
- If CO2 is increasing substantially (e.g. >20 mm increase), this is worrisome with regard to treatment failure. However, ultimately the overall clinical assessment is more valuable than any specific blood gas parameter.

beware of asthma treatment pseudo-failure

- Treatment pseudofailure is when the patient's lungs improve, but lactic acidosis occurs due to beta-agonist stimulation from albuterol and/or epinephrine. If severe, acidosis may trigger a compensatory respiratory alkalosis which will worsen dyspnea.
- Diagnosis of pseudofailure:
  - Lungs sound better.
  - Patient improves initially, then deteriorates.
  - Labs show metabolic (rather than respiratory) acidosis.
  - If measured, lactate is elevated.
- Management: these patients generally do well if you just cut back on the beta-agonists (e.g. stop epinephrine, wean albuterol as tolerated).

indications for intubation

- Intubation is a clinical decision, made primarily based on serial evaluation by experienced practitioners. This will often be a joint decision made by the physician, the respiratory therapist, and the nurse caring for the patient.
- Indications for intubation might include the following (with no high-quality evidence available):
  - (1) Progressive deterioration despite above therapies, with worsening work of breathing and impending respiratory exhaustion.
  - (2) Impending cardiopulmonary arrest (suggested by bradycardia, severe respiratory acidosis, very poor air movement, obtundation).
- When in doubt (e.g. about intubation) – continue to monitor the patient carefully, maximize therapy, and prepare for intubation. Evaluate the patient serially and elicit opinions from the entire team (including RN and respiratory therapists) regarding how the patient is doing. A team-based approach allows the decision to be based on numerous evaluations by several practitioners – which avoids fixation on any single data point.

risk of hemodynamic deterioration

- High airway pressures often cause hypotension after intubation, so prepare for this.
  - Consider administration of volume if there is any evidence or history of hypovolemia.
  - Start an epinephrine infusion prior to intubation if hemodynamics are tenuous (this may be beneficial for bronchospasm as well; see epinephrine infusion above).

use a large ETT

- Multiple reasons:
  - Will reduce airflow resistance, facilitating ventilation.
  - May facilitate procedures if necessary (e.g. bronchoscopy).
- Most sources recommend using at least a #8 ETT in adults (and an #8.5 or #9 on taller patients if this is available)(29105540 (https://www.ncbi.nlm.nih.gov/pubmed/29105540)).
**use a non-depolarizing paralytic (e.g. rocuronium)**

- Following intubation, it is extremely useful for the patient to be paralyzed briefly (e.g. 30-60 minutes). This allows for several tasks to be performed:
  - (a) Interrogation of respiratory mechanics (autoPEEP, plateau pressure).
  - (b) Gradual up-titration of other sedatives with close monitoring of hemodynamics (e.g. escalation of a propofol infusion).
  - (c) Determination of a reasonable ventilator setting (without the confounding effect of patient effort).
- The most seamless way to achieve this is to perform rapid sequence induction with rocuronium. An alternative, of course, is to intubate with succinylcholine and subsequently to administer a non-depolarizing agent.

**avoid aggressive bag-mask ventilation!**

- Aggressive bagging will rapidly precipitate severe gas-trapping in the lungs.
- Gas-trapping may cause pneumothorax or hypotension.

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**we're bagging the patient because the ventilator isn't working**

Sometimes an outside hospital may call regarding an asthmatic who has been intubated and is unable to ventilate. The problem is that airway pressures required to ventilate a patient in status asthmaticus will trigger alarms on standard ventilator settings. The following is an approach to set the ventilator over the phone, in such a way which is safe for the patient. Whenever possible, asthmatic patients should *not* be transferred with ongoing bag-mask ventilation (this will almost invariably lead to gas-trapping and pneumothorax).

**#1** Sedate the patient deeply (ideally with IV ketamine boluses +/- infusion).

**#2** Paralyze the patient with a long-acting agent (e.g. vecuronium or rocuronium).

**#3** Set the patient on a pressure-cycled ventilation (PC) with the following settings:

- Respiratory rate of 12 breaths/minute
- Inspiratory time (I-time) of 1 second
- Inspiratory pressure of 40 cm, with a PEEP of 5 cm
- FiO2 initially at ~60%, titrate against the patient’s oxygen saturation

These settings will ensure that the patient doesn't receive excessive pressures, but they won't ensure that the patient receives a sufficient *tidal volume*. This is prioritizing lung protection over CO2 normalization (more on this below). Attention is needed to ensure that adequate ventilation is obtained (e.g. tidal volumes of at least ~4 cc/kg and a minute ventilation of at least ~3-4 liters/minute). If this is achieved, then the patient can generally be stabilized sufficiently to transfer.

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**intubated asthmatic: overall strategy**

**foundational principles**

- (1) Intubated asthmatics almost never die or are harmed by hypercapnia (more on this below).
- Hypercapnia is a paper tiger. Once you can accept that, ventilation in asthma gets much easier.
- (2) Status asthmaticus *will* break eventually, but it may take a few days.
- (3) The major risks to the intubated asthmatic are *complications* – not the asthma itself.
  - Ventilator-associated pneumonia
  - Pneumothorax
  - Myopathy due to prolonged paralysis and steroid
  - Pulmonary embolism

**fundamental strategy**
• (1) Don't go crazy trying to reduce the pCO2 (permissive hypercapnia).
  • Less is often more – the key is often accepting hypercapnia and just waiting out the asthma.
• (2) Be vigilant for the development of complications (e.g. pneumothorax).
• (3) Avoid extended periods of paralysis.
  • Paralysis may be needed initially (e.g. first day on ventilator), but aggressive efforts should be made to wean this off as soon as possible.
  • Paralyzing the patient to achieve a small improvement in gas exchange is generally an unwise trade-off.

*This is an overview of management, which will be explored in the following sections:*

**management of the intubated asthmatic**

- **Bronchodilation**
  - Stacked albuterol nebs (2.5 mg q20) or continuous neb (10-15 mg/hr)
  - Ipratropium (may use 1.5 mg over first hour, then 0.5 mg q4-6 hr)
- **Steroid**
  - Methylprednisolone ~2 mg/kg/day probably reasonable.
- **Vent settings**
  - Key is low respiratory rate (~12 breaths/min)
  - Target tidal volume ~6-8 cc/kg
- **Deep sedation**
  - Initial goal is to render patient passive on vent.
  - High-dose Propofol infusion generally key (~60-80 ug/kg/min)
  - Fentanyl boluses & infusion is often necessary
  - Pain-dose ketamine (0.1-0.3 mg/kg/hr) primarily for analgesia and minimization of opioid side-effects.
  - (Avoid paralysis if at all possible, or limit duration.)
- **Alkalization**
  - May consider if pH remains <7.15-7.20 and/or if patient has bicarbonate <24 mM due to NAGMA or uremic acidosis.
  - Key is slow administration of bicarbonate. Formulation of bicarbonate and use of diuretics may vary depending on volume status (see table below).
- **Nutrition**
  - Start enteral nutrition early; this may reduce the risk of Propofol infusion syndrome and stress ulceration.
- **If refractory: Dissociative ketamine gtt**
  - Load with 1-2 mg/kg then infuse at 1-2 mg/kg/hr ketamine.
  - Glycopyrrolate to avoid bronchorrhea (e.g. 0.2 mg IV q6hr)
- **If all else fails: ECMO**

>Internet Book of Critical Care, by @PulmCrit

**principles of ventilating an asthmatic**

**intubated patients don’t die from hypercapnia**

• Hypercapnia is *extremely* well tolerated, especially in asthmatics (who tend to be young, and with good hemodynamic reserves).
  • This might not hold in patients with severe underlying pulmonary hypertension or elevated intracranial pressure – but those are generally not issues encountered here.
• The danger from hypercapnia is what we do about it. Our responses to hypercapnia can cause severe harm:
  • (a) Aggressive ventilation leading to a pneumothorax.
  • (b) Aggressive ventilation leading to autoPEEP and cardiovascular collapse.
• We need to revise our philosophy about asthma to fear these iatrogenic complications – *not* the hypercapnia.
• The goal of ventilation in asthma isn’t to reduce the CO2. It’s really just to keep the patient alive until their lungs improve.
  • The reason we intubate *isn’t* to reduce the CO2 – it’s to prevent patients from dying due to respiratory exhaustion and hypoxemia.
  • The pCO2 is often *higher* on the ventilator than it was before the patient was intubated!

**permissive hypercapnia and target pH**
When hypercapnia is imposed by rapidly deteriorating lung mechanics, as in acute severe asthma, there is little choice but to accept a brutal, at times extreme rise in pCO2 in order to prevent life-threatening barotrauma... In patients with sudden asphyxic asthma, our experience is that pCO2 much in excess of 80 mm (up to 200 mm) must often be accepted. -Feihl F and Perret C AJRCCM 1994

Permissive Hypercapnia is the core of safe ventilation in asthma. This simply refers to the concept that intentionally allowing the pH to fall is often safer than trying to strictly control it (which would involve more aggressive ventilation with risks of pneumothorax or barotrauma).

Contraindications to permissive hypercapnia would be the following:

- Active CNS disease with elevated intracranial pressure.
- Significant pulmonary hypertension with cardiac compromise, causing hypoperfusion or hypotension.
- Pregnancy (perhaps).

The precise target pH is unknown.

- There is no specific pH below which patients will deteriorate – this may vary between patients depending on their physiology.
- Young patients can often tolerate respiratory acidosis with pH <7 surprisingly well.
- Different providers have different pH targets, which are somewhat arbitrary and not evidence-based. It’s nice to see the pH >7.15 if possible, but ultimately this is a judgement regarding balancing the risks-vs-benefits of more aggressive ventilation vs higher pH.

autoPEEP is the main problem

- autoPEEP refers to trapping gas within the lungs during respiration. This occurs if one breath can't be fully exhaled prior to the next inhalation. The net result of this trapped gas is to create additional positive pressure (“auto PEEP”) within the chest, which is higher than the PEEP provided by the ventilator (the “set PEEP”).
- autoPEEP is inevitable with severe asthma. The goal is to minimize it as possible.
- autoPEEP can be measured in various ways:
  - If the expiratory flow curve never comes close to zero, then autoPEEP is present (this is basically inevitable in severe asthma).
  - In the paralyzed patient, an end-expiratory breath hold maneuver can measure the autoPEEP directly.
  - AutoPEEP will make it more difficult for the patient to trigger the ventilator (in order to trigger a breath, they need to overcome the autoPEEP). Thus, difficulty triggering the ventilator is an indirect sign of autoPEEP.
- autoPEEP management depends on increasing the expiratory time or decreasing the tidal volume. This may be done in a few different ways:
  - (a) Most effective: Decreasing the respiratory rate. Ventilating an asthmatic will often be impossible if the respiratory rate is >20 b/m.
  - (b) Decrease the inspiratory time (e.g. using a higher flow rate if you're using volume-cycled ventilation).
  - (c) Decreasing the tidal volume (this reduces the amount of gas which must be exhaled). Be careful though, because if the tidal volume approaches the patient's dead space volume (estimated as at least the patient's weight in pounds) then ventilation will become extremely inefficient.

how should the PEEP be set?

- This is a topic of considerable consternation, although it probably doesn't make a big difference (as long as it's not set too high).
- To get some basic terminology straight:
  - Set PEEP is the amount of PEEP dialed into the ventilator.
  - Intrinsic PEEP is the actual intrathoracic pressure at end-expiration (the “true” PEEP).
- Intrinsic PEEP may be measured by an end-expiratory breath hold maneuver:
  - At end-expiration the gas flow is stopped. This leads to equilibration between the intrathoracic pressure and the endotracheal tube, revealing the intrinsic PEEP.
  - An end-expiratory breath hold maneuver can be performed accurately only in a patient who is passive on the ventilator (either paralyzed or not triggering the ventilator).
- Benefits of set PEEP include the following:
  - (#1) May help stent open the airways during exhalation (otherwise the airways may tend to be compressed by adjacent lung tissue).
  - (#2) In order to trigger a breath from the ventilator, the patient needs to suck the pressure in their lungs down from intrinsic PEEP to below the set PEEP. Thus, the work of triggering the ventilator is proportional to the difference between the Intrinsic PEEP and the Set PEEP. Increasing the Set PEEP a bit will make it much easier for the patient to trigger the ventilator.
- How to set the PEEP?
If you want to keep things simple just set the PEEP at 5 cm and forget about it – this will be safe and fine. If you want to get fancy then...

(a) If the patient is not passive on ventilator (e.g. patient is triggering the ventilator), just use 5 cm PEEP (26033128).

(b) If the patient is passive on the ventilator, it may be reasonable to carefully titrate the PEEP. This begins with a measurement of the intrinsic PEEP. It may be reasonable to increase the PEEP to a level equal to ~75% of the intrinsic PEEP. Mechanics should be monitored during titration for signs of excess PEEP, which would be:

- Volume-cycled ventilation: Increasing PEEP causes an increase in plateau pressure.
- Pressure-cycled ventilation: Increasing PEEP causes a decrease in tidal volume.

**slow respiratory rate with normal-ish tidal volumes**

- (1) A slow respiratory rate is essential to avoid autoPEEP. This should be <20 breaths, and generally closer to ~10-14 b/m.
- (2) Ideally, tidal volumes should be maintained around 6-8 cc/kg (if possible). Dropping the tidal volume too low will cause problems with dead space ventilation.
  - Dead space is volume which enters the lungs but doesn't participate in gas exchange. The amount of dead space is the sum of the anatomic dead space (gas going into and out of the trachea and large bronchi) plus the physiologic dead space (gas going into and out of non-functional alveoli).
  - The anatomic dead space is roughly fixed, at 1 ml/pound ideal body weight (or ~2.2 ml/kg). So right off the bat, ~2 cc/kg of each breath is wasted in ventilating the anatomic dead space (this achieves nothing for the patient).
  - Asthmatic patients may have increased physiologic dead space, causing their total dead space to be relatively high (e.g. ~3 cc/kg). This means that if the tidal volumes are very low (e.g. 3-4 cc/kg), then the vast majority of ventilation will be wasted! This may cause the patient to be profoundly hypercarbic – even though the minute ventilation isn’t horribly low.
  - Maintaining reasonably sized tidal volumes (e.g. at least ~5-6 cc/kg) will ensure some effective ventilation.

**asthmatics should be difficult to ventilate**

- If the patient is easy to ventilate (e.g. with a normal peak inspiratory pressure), then they don’t have status asthmaticus. There must be some other form of upper airway obstruction, which has been alleviated by placement of the endotracheal tube.
  - The most common cause is vocal cord dysfunction.
  - Other possibilities include epiglottitis or neck abscess.
- If the diagnosis isn’t clear (e.g. if the patient doesn’t have vocal cord dysfunction), then consider a CT scan of the neck to exclude anatomic problems.

**pressure-cycled vs. volume-cycled ventilation**

- Either mode may be used; this is largely a matter of familiarity.
- Pressure-cycled ventilation has the advantage of achieving better control over alveolar pressure, but this comes at the expense of losing control over tidal volume. On the flip side, volume-cycled ventilation has the advantage of controlling tidal volume, but this comes at the expense of losing control over alveolar pressure.
  - Overall, my preference is pressure-cycled ventilation, because I’m more concerned with barotrauma than minute ventilation. Pressure-cycled ventilation also has the advantage of eliminating flow dyssynchrony once the patient starts waking up (flow rate inadequately matched to patient’s demands). However, either mode can work fine if it is monitored adequately.

**you shouldn’t need a lot of oxygen**

- Asthma causes impaired ventilation, but oxygenation should be intact.
- If the patient is requiring >55% FiO2, look for another process going on (e.g., pneumothorax, aspiration, pneumonia, mucus plugging, pulmonary embolism)(25759905).

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**initial vent settings: volume cycled ventilation**

(26033128)

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**initial settings**
Tidal volume: 8 cc/kg.
Respiratory rate: 12 breaths/minute.
Flow rate: 80 liters/minute (set this high in asthma to reduce inspiratory time).
FiO2: start ~60%, titrate for an oxygen saturation >88%.
PEEP: start at 5 cm.
Peak pressure alarm may need to be increased to prevent its constantly going off.

**monitoring for safety**

1. Plateau pressure should be monitored if possible (if the patient is passive on the ventilator). This may be achieved by an end-inspiratory breath hold maneuver. Plateau pressure should ideally be under ~35 cm.
2. Follow oxygenation; rapidly deteriorating oxygenation suggests an acute problem such as pneumothorax.

**initial vent settings: pressure cycled ventilation**

**initial settings**

- Inspiratory pressure: ~35 cm (titrate against tidal volume to achieve ~6-8 cc/kg)
- Respiratory rate: 12 breaths/minute
- Inspiratory time: 1 second
- FiO2: start ~60%, titrate for an oxygen saturation >88%
- PEEP: start at 5 cm

**monitoring for safety**

1. Tidal volume should be monitored. Ideally this should be ~6 cc/kg (but it may be lower, ~4-5 cc/kg, initially).
   - Falling tidal volume may be a sign of pulmonary deterioration (e.g. mucus plugging or pneumothorax).
   - Increasing tidal volume may be a sign of clinical improvement.
   - If the tidal volume is unnecessarily high, consider decreasing the inspiratory pressure.
2. Follow minute ventilation.
   - Initially this will be low (e.g. ~4-6 liters/minute).
   - With improvement, the minute ventilation may increase to a normal range (e.g. ~7-8 liters/minute).
3. Follow oxygenation; rapidly deteriorating oxygenation suggests an acute problem, such as pneumothorax.

**alkalinization**

**don’t forget metabolic acid-base status**

- pH is influenced by both metabolic considerations (bicarbonate level) and by respiratory acidosis (pCO2). There is a tendency to focus on the pCO2, but don’t forget about the metabolic component.
- Any metabolic acidosis should be aggressively treated. If the patient has a non-anion gap metabolic acidosis, IV bicarbonate should be given to target a normal bicarbonate level (e.g. 24 mEq/L).

**what will happen if you give a slow infusion of bicarbonate**

- If bicarbonate is given as a slow IV push (e.g. two 50-mEq ampules over 20 minutes), the following will happen:
  1. The CO2 level will increase by ~10 mm. This will increase the gradient driving CO2 excretion from the lungs. Over time (perhaps ~10 minutes), increased CO2 excretion will cause CO2 levels to decrease back to their previous equilibrium level. CO2 is constantly being produced by the body and excreted by the lungs. The CO2 level reflects a balance of this CO2 production vs. excretion. Giving a fixed amount of CO2 will cause only a transient increase in CO2.
  2. The bicarbonate level will increase by ~3 mM. Since the patient is acidemic, the kidneys are in a bicarbonate-avid state. Therefore, the kidneys will tend to retain this bicarb. This may lead to a sustained elevation in the bicarbonate level.
  3. The sodium concentration will increase by ~2 mM.
In summary, IV bicarbonate contains a lot of bicarbonate (50 mEq per ampule) with a little CO2 gas (~1 mEq per ampule). Following administration, the CO2 gas will be eliminated by the body, whereas the bicarbonate will be retained. So, giving bicarbonate is ultimately just... giving bicarbonate.

- The dissolved CO2 gas is problematic if bicarbonate is given as a bolus to patients in cardiac arrest without effective ventilation – which is why this shouldn't generally be done. Dissolved bicarbonate gas shouldn't be a significant problem in living humans if bicarbonate is given slowly.

**rationale for bicarbonate administration**

- Bicarbonate administration in respiratory failure (e.g. ARDS or asthma) hasn't been investigated rigorously, so the exact benefit is unknown. For severe acidemia, bicarbonate administration could make sense for the following reasons:
  1. Acceleration of normal compensatory mechanisms
     - Normally, the kidneys will retain bicarbonate in response to a respiratory acidosis. This renal compensation helps stabilize the pH, but it takes days.
     - Exogenous alkali administration merely speeds up this process.
     - The use of exogenous alkali might be particularly justifiable if the patient has renal dysfunction, which prevents their kidneys from compensating appropriately for the respiratory acidosis.
  2. Reduced respiratory drive
     - Bicarbonate administration may decrease the respiratory drive, which might theoretically reduce the amount of medication required to rest passively on the ventilator.
     - Pushing the bicarbonate level to ~30-35 mEq/L may facilitate extubation (again, by reducing the respiratory drive and allowing the patient to be comfortable in the face of mildly elevated pCO2).
  3. Avoid profound acidemia
     - At a certain point, profoundly low pH may be problematic.
     - The concept of using bicarbonate to avoid severely low pH isn't anything revolutionary (e.g. it was utilized in the classic ARDSnet ARMA trial).
  4. Avoidance of ventilatory & ECMO insanity
     - Low pH will induce some providers to do all sorts of bizarre interventions with the ventilator (e.g. prolonged paralysis) and ECMO.
     - Making the pH numbers look better may help the patient avoid iatrogenic harm.
Alkalization while maintaining volume and water balance

<table>
<thead>
<tr>
<th></th>
<th>Hyponatremia</th>
<th>Normonatremia</th>
<th>Hypernatremia</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Hypovolemia</strong></td>
<td>- Isotonic bicarbonate is mainstay of treatment. (May add some hypertonic bicarbonate if hypotension or acidosis are severe)</td>
<td>- Isotonic bicarbonate</td>
<td>- Isotonic bicarbonate &amp; Free water</td>
</tr>
<tr>
<td><strong>Euvolemia</strong></td>
<td>- Hypertonic bicarbonate (initially, until the sodium concentration increases)</td>
<td>- Isotonic bicarbonate &amp; Diuresis (loop diuretic +/- thiazide) (or, limited use of hypertonic bicarbonate)</td>
<td>- Isotonic bicarbonate &amp; Diuresis (loop diuretic plus thiazide) &amp; Free water</td>
</tr>
<tr>
<td><strong>Hypovolemia</strong></td>
<td>- Diuresis with only a loop diuretic (May add some hypertonic bicarbonate if hypotension or acidosis are severe)</td>
<td>- Diuresis (loop diuretic +/- thiazide) (or, limited use of hypertonic bicarbonate)</td>
<td>- Diuresis (loop diuretic plus thiazide) &amp; Free water</td>
</tr>
</tbody>
</table>

**Alkalization should be done thoughtfully, with attention to volume and water balance.** Further clarification of the interventions listed above:
- Isotonic bicarbonate: 150 mEq/L solution of sodium bicarbonate (typically 3 amps bicarb in a liter of D5W)
- Hypertonic bicarbonate: 1 mEq/ml solution of sodium bicarbonate (concentrated ampules of bicarbonate)
- Loop diuretic: Intravenous furosemide or bumetanide
- Thiazide diuretic: Usually oral metolazone or indapamide as an adjunctive diuretic to enhance sodium excretion.
In more severe cases, IV thioridazine may be useful.


- Unknown.
- May be reasonable if pH is consistently <7.15-7.20, despite adjustment of the ventilator ([26033128](https://www.ncbi.nlm.nih.gov/pubmed/26033128)).

**details of bicarbonate administration**

- An overall strategy for alkalization is shown above. Various forms of IV bicarbonate may be selected, depending on the patient's volume and sodium concentrations (more on IV bicarbonate [here](https://emcrit.org/ibcc/fluid/hypertonic_&_isotonic_bicarbonate)).
- The target bicarbonate level is unknown. The amount of compensatory alkalosis which would be expected normally is shown in the table above; this may be used as rough gauge of what could be reasonable.

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**Respirolytic Sedation**

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*Fairly deep sedation is needed initially. The best agents to use here are drugs which directly suppress the respiratory drive (opioids and propofol). A reasonable starting place is often a combination of propofol, opioid, and ketamine.*

**Propofol**

- Cornerstone of initial sedation for the intubated asthmatic.
  - (a) Sedative with powerful effects on respiratory drive.
  - (b) May cause some bronchodilation ([25759905](https://www.ncbi.nlm.nih.gov/pubmed/25759905); [8424280](https://www.ncbi.nlm.nih.gov/pubmed/8424280), [8669670](https://www.ncbi.nlm.nih.gov/pubmed/8669670)).
- Patients may require moderate to high doses (e.g. ~60 mcg/kg/min).
- Consider early initiation of enteral nutrition to reduce the risk of propofol infusion syndrome (carbohydrate administration appears to reduce the risk of propofol infusion syndrome).

**Opioid**

- Some opioid will generally be required, especially early on.
- Morphine should be avoided, because it may increase histamine release and cause bronchospasm (fentanyl or hydromorphone is preferable).
- Opioid dosing will depend to a large extent on how the patient responds to propofol.
  - Many patients can be rendered comfortable on a moderate dose of propofol with PRN doses of opioid.
  - Some patients may require considerable doses of both propofol and opioid to suppress their respiration enough to synchronize well with the ventilator.
- If a fentanyl infusion is used, this should ideally be limited as much as possible (e.g. to <100 mcg/hr). Note that 100 mcg/hr fentanyl is equivalent to 480 mg of oxycodone – a *lot* of opioid.
**pain-dose ketamine (0.1-0.3 mg/kg/hr)**

- This is generally useful here for several reasons:
  - (1) May reduce the incidence of *tolerance* and *opioid-induced hyperalgesia* among patients on opioid infusions (this may mitigate the harm caused by opioid infusions to a certain extent).
  - (2) Provides pain relief.
  - (3) May provide some bronchodilation (although probably not much).

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**dissociative-dose ketamine**

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**what is dissociative-dose ketamine sedation?**

- Continuous infusion of fully dissociative doses of ketamine (typically a loading dose of 1-2 mg/kg bolus followed by 1-2 mg/kg/hr).
- On dissociative-dose ketamine, other sedatives and analgesics (e.g. propofol, opioids) may often be stopped or down-titrated.
- Co-administration with an anti-cholinergic agent (e.g. glycopyrrolate 0.2 mg IV q6hr or atropine) may prevent problems with salivation and bronchorrhea ([25759905](https://www.ncbi.nlm.nih.gov/pubmed/25759905); [17301376](https://www.ncbi.nlm.nih.gov/pubmed/17301376); [8905436](https://www.ncbi.nlm.nih.gov/pubmed/8905436); [24082612](https://www.ncbi.nlm.nih.gov/pubmed/24082612)).
  - Note that using a systemic anti-cholinergic itself could theoretically promote bronchodilation.

**advantages of dissociative-dose ketamine sedation**

- (1) Ketamine has direct bronchodilatory effects on the lungs, which may be useful in refractory asthma.
- (2) Ketamine tends to increase the blood pressure. It also allows other sedatives and analgesics (e.g. propofol) to be discontinued – which is also beneficial for hemodynamics. Overall, a dissociative-dose ketamine strategy is arguably the best sedative strategy for hemodynamics.
- (3) Ketamine allows avoidance of toxicity due to other sedatives or analgesics:
  - High-dose fentanyl infusions rapidly lead to opioid tolerance and dependence. They also suppress gut motility, potentially leading to ileus.
  - Benzodiazepine infusions are sometimes used as a sedative-of-last-resort for hemodynamically unstable patients. These cause substantial problems with ICU delirium.

**disadvantages of dissociative-dose ketamine sedation**

- (1) Concerns exist with regard to causing ICU delirium.
- (2) Lack of large-volume or high-quality evidence (currently evidence is limited to patient series).
- (3) Potential to increase bronchial secretions (bronchorrhea) – although this should be avoided with use of an anti-cholinergic.

**potential indications for dissociative-dose ketamine**

- There is insufficient high-level evidence to know exactly where this should fit in the treatment rubric. Situations where this should be considered are the following:
  - (1) Refractory status asthmaticus with inability to ventilate safely.
    - However, even in this situation, the exact indication to pull the trigger on ketamine is unclear.
  - (2) Problematic *hypotension* due to conventional sedatives (e.g. propofol).
evidentiary basis

- Refractory intubated status asthmaticus is an unusual situation, so it's difficult to obtain RCT-level evidence on this.
- A before-after study demonstrated impressive improvements in blood gas parameters and chest mechanics, as shown above (17301376 [https://www.ncbi.nlm.nih.gov/pubmed/17301376]). A similar study in pediatric patients showed nearly identical results, supporting this concept (8905436 [https://www.ncbi.nlm.nih.gov/pubmed/8905436]).

paralysis

- Patients are usually intubated with rocuronium at moderate to high dose (e.g. 1.2 mg/kg). This will induce paralysis for about an hour.
- This initial period of paralysis should be used to settle the patient on the ventilator:
  - Evaluate pulmonary mechanics (e.g. peak & plateau pressures) and airflow patterns.
  - Note that low peak pressures or normal airflow excludes asthma (and suggests instead vocal cord dysfunction or upper airway obstruction).

avoid prolonged paralysis if at all possible

- Paralysis will make patients look beautiful and synchronize perfectly with the ventilator, but it carries significant risks (in terms of myopathy and delirium from the depth of sedation required).
- Prolonged paralysis should be avoided whenever possible. This may be achieved as follows:
  - (a) Respirolytic sedation (see above) may be used to suppress the patient's respiratory drive and thereby render the patient passive on the ventilator. If the patient is passive on the ventilator, there's really no added benefit to paralysis.
  - (2) Tailor the ventilator to minimize dyssynchrony, not with a goal of normalizing the ABGs. For example, use of pressure control mode may help reduce flow dyssynchrony (pressure control allows the patient to drive their own flow rate, which may be more comfortable).
- If ongoing paralysis is needed, the risk of myopathy may be minimized as follows:
  - (1) The duration of paralysis should be limited to the shortest period achievable. Every day there should be a strong effort to lift paralytics if at all possible. The odds of developing myopathy increase substantially with each additional day of paralysis (10378560 [https://www.ncbi.nlm.nih.gov/pubmed/10378560]).
  - (2) Cisatracurium may carry a lower risk of myopathy than aminosteroid paralytics (e.g. vecuronium) (23062076 [https://www.ncbi.nlm.nih.gov/pubmed/23062076]). Although the drug cost of cisatracurium is higher than vecuronium, using a cheaper paralytic won't be cost-saving overall if the patient develops a myopathy.
  - (3) Titrate the paralytic to the lowest dose that allows for ventilator synchrony.

inhalational anesthetics

Inhalational anesthetics have become popular in severe asthma, despite a lack of any high-quality evidence and despite the presence of several potential risks.
potential problems with inhalational anesthetics

- The main problem is that they generally require administration through an anesthesia ventilator. Such ventilators are generally not very sophisticated, and are unfamiliar to the ICU and respiratory therapy teams. Very simply, anesthesia circuits are not designed for prolonged use and they're not great at this purpose. Use of an anesthesia circuit may lead to a host of problems:
  - Anesthesia circuits aren't designed for continuous albuterol nebulization, so this may be impossible.
  - Anesthesia circuits often have limited ability to perform advanced modes of ventilation.
  - Alarm settings are typically unfamiliar, which may lead to delayed detection of complications (e.g. pneumothorax).
  - Anesthesia circuits require continuous maintenance with use of beads to absorb CO2. Failure to change out the CO2 absorber frequently enough will cause CO2 rebreathing (28612677).
  - The anesthesiology circuit will typically need to be managed by an anesthesiologist. This may increase the number of people involved in caring for the patient, with attendant communication issues.

- Hypotension
- Limits to the duration of inhalational anesthesia

my opinion on inhalation anesthetics via an anesthesia circuit

- There isn't enough evidence of benefit in order to justify using this treatment.
  - Case series in the pediatric literature suggest that isoflurane decreases pCO2 by ~17 mm and improves pH by ~0.11 units within two hours. These improvements aren’t that huge, and probably aren’t worth the risks incurred by using the anesthesia circuit (16614808).

- The vast majority of intubated asthmatics will respond to other measures described above (e.g., permissive hypercapnia, ketamine, and IV bicarbonate).
  - If a patient is truly refractory to all of these measures and genuinely needs more support, then they probably just need ECMO.

anaconda system

- Device which allows the use of inhalational anesthetic using a standard ICU ventilator.
- May be a good option if you have one.

ECMO

ECMO for severe asthma

- ECMO offers the ability to improve CO2 clearance. However, patients nearly never die from hypercapnia. Therefore, the vast majority of patients with asthma should be manageable without ECMO. In the pre-ECMO era, asthma patients didn't die from hypercapnia and overall had very good outcomes (18773325; 22188845).

- ECMO may be life-saving in complex patients with multiple coexisting problems (e.g. asthma complicated by a large broncho-pleural fistula).
  - Simultaneous presence of numerous problems may limit options with conventional ventilation.

potential indications for ECMO?

- (1) Inability to perform deep permissive hypercapnia
  - Active neurologic disease with elevated intracranial pressure
  - Severe pulmonary hypertension or right ventricular failure
  - Pregnancy
- (2) Inability to oxygenate
  - Profoundly severe asthma (possibly due to mucus plugging)
  - Asthma plus bronchopleural fistula with large air leak
  - Asthma plus pneumonia or ARDS

other strategies (extracorporeal CO2 removal)
• New devices are under development to remove CO2. These may be less invasive and easier to operate than ECMO (more akin to continuous renal replacement therapy).

• Further studies are underway. A safe and effective device for CO2 removal might facilitate early liberation from mechanical ventilation, which could improve outcomes (e.g. delirium and deconditioning). However, given the invasiveness and cost of such devices, benefit should ideally be demonstrated with RCTs prior to widespread adoption.

initial management of severe asthma not requiring immediate intubation

- Bronchodilation
  - Stacked albuterol nebs (2.5-5 mg q20) or continuous neb (10-15 mg/hr)
  - Ipratropium (may use 1.5 mg over first hour, then 0.5 mg nebulized q4-6 hr)

- Steroid
  - Methylprednisolone 125 mg IV x1 (or equivalent dose of other steroid)

- Magnesium sulfate
  - 2 grams (8 mM) IV over 20 minutes.

- BIPAP
  - 1st line support device = BIPAP
  - If unable to tolerate BIPAP, HFNC may be used

- Sedation if needed for BIPAP
  - Start dexmedetomidine infusion at maximal rate (down-titrates as takes effect). This may be helpful as an anxiolytic agent, even if the patient is able to tolerate the BIPAP mask.
  - May use small doses of opioid while waiting for dexmedetomidine to take effect if severely dyspneic (e.g. fentanyl 25 mcg IV PRN).

- Epinephrine infusion
  - Indications
    - i) failure of inhaled bronchodilators
    - ii) unable to tolerate inhaled bronchodilators (re: coughing)
    - iii) bradycardia related to dexmedetomidine
  - Start 5 mcg/min, titrate 1-10 mcg/min (peripheral IV is fine).
  - (Alternative with almost no evidentiary basis: 0.2 mg IV glycopyrrrolate.)

summary
management of the intubated asthmatic

- Bronchodilation
  - Stacked albuterol nebs (2.5 mg q20) or continuous neb (10-15 mg/hr)
  - Ipratropium (may use 1.5 mg over first hour, then 0.5 mg q4-6 hr)

- Steroid
  - Methylprednisolone ~2 mg/kg/day probably reasonable.

- Vent settings
  - Key is low respiratory rate (~12 breaths/min)
  - Target tidal volume ~6-8 cc/kg

- Deep sedation
  - Initial goal is to render patient passive on vent.
  - High-dose Propofol infusion generally key (~60-80 ug/kg/min)
  - Fentanyl boluses & infusion is often necessary
  - Pain-dose ketamine (0.1-0.3 mg/kg/hr) primarily for analgesia and minimization of opioid side-effects.
  - (Avoid paralysis if at all possible, or limit duration.)

- Alkalization
  - May consider if pH remains <7.15-7.20 and/or if patient has bicarbonate <24 mM due to NAGMA or uremic acidosis.
  - Key is slow administration of bicarbonate. Formulation of bicarbonate and use of diuretics may vary depending on volume status (see table below).

- Nutrition
  - Start enteral nutrition early; this may reduce the risk of Propofol infusion syndrome and stress ulceration.

- If refractory: Dissociative ketamine gtt
  - Load with 1-2 mg/kg then infuse at 1-2 mg/kg/hr ketamine.
  - Glycopyrrolate to avoid bronchorrhea (e.g. 0.2 mg IV q6hr)

- If all else fails: ECMO

- Internet Book of Critical Care, by @PulmCrit

podcast

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questions & discussion

To keep this page small and fast, questions & discussion about this post can be found on another page here.
Serial measurement of blood gases isn't very helpful and may be misleading (e.g. patient is feeling better but ABG remains unchanged). Treatment decisions are generally best based upon clinical appearance and serial evaluation.

Assumption that an asthma patient has asthma (rather than, for example, pneumothorax or pneumonia). Bedside BLUE-protocol ultrasound exam will go a long way to avoid this mistake.

Inadequate use of permissive hypercapnia for the ventilated asthmatic. Don't sweat the hypercapnia; trying to bring down the PaCO2 is often more harmful than helpful.

Over-bagging of the asthmatic after intubation. This carries a high risk of gas trapping and pneumothorax. It's probably ideal to connect these patients to a ventilator as soon as possible to provide controlled ventilation.

Note that “wheeze” or stridor you can hear across the room isn't due to asthma (suggests upper airway obstruction instead).

**Going further:**

- Some recent discussions of bleeding-edge concepts in asthma
  - Optimizing respiratory drive to avoid failure ([PulmCrit](https://emcrit.org/pulmcrit/respiratory-drive/))
  - Asthma guest post with Leo Stemp ([PulmCrit](https://emcrit.org/pulmcrit/crashing-asthmatic/))
  - Weingart & Farkas talk opioids & ketamine in asthma ([PulmCrit](https://emcrit.org/emcrit/discussion-guest-post-on-asthma/))
- [EMCrit 15 Asthma](https://emcrit.org/emcrit/severe-asthmatic/)
- [Crashing Asthmatic](https://rebelem.com/rebelcast-crashing-asthmatic/) (RebelEM, Salim Rezaie)
- [Life-threatening asthma](http://www.emdocs.net/core-em-life-threatening-asthma/) (EMDocs, Anand Swaminathan)
- Acute Severe Asthma ([LITFL](https://lit.com/acute-severe-asthma/)) (LITFL, Chris Nickson)
- Severe asthma ([First10EM](https://rst10em.com/asthma/)) (First10EM, Justin Morgenstern)