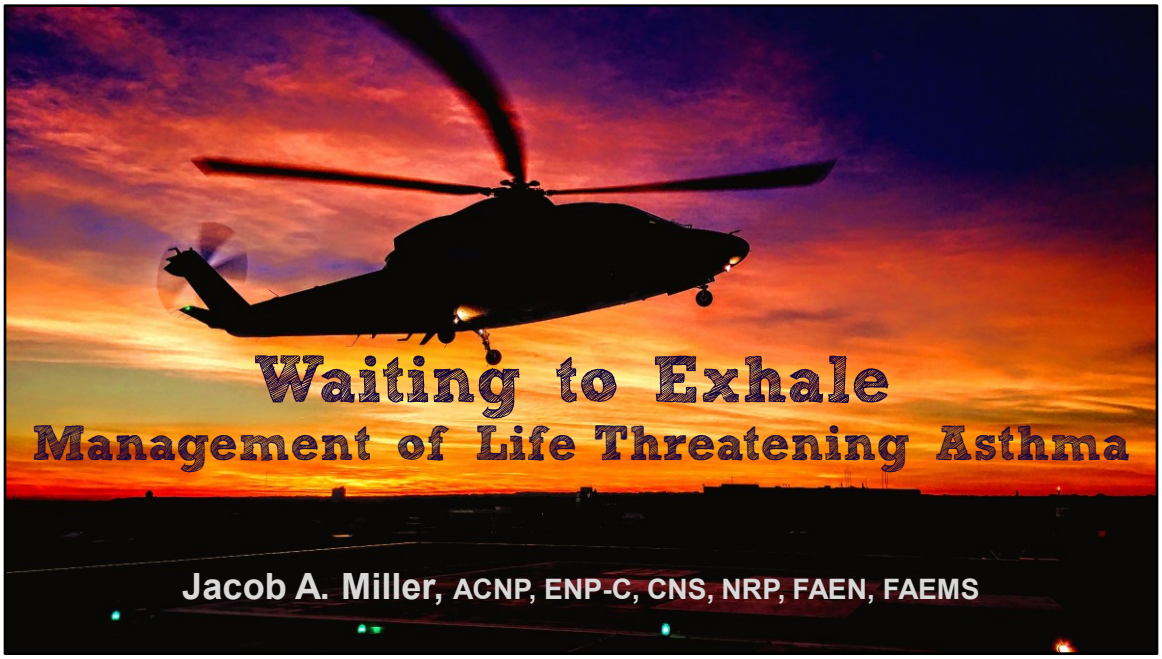
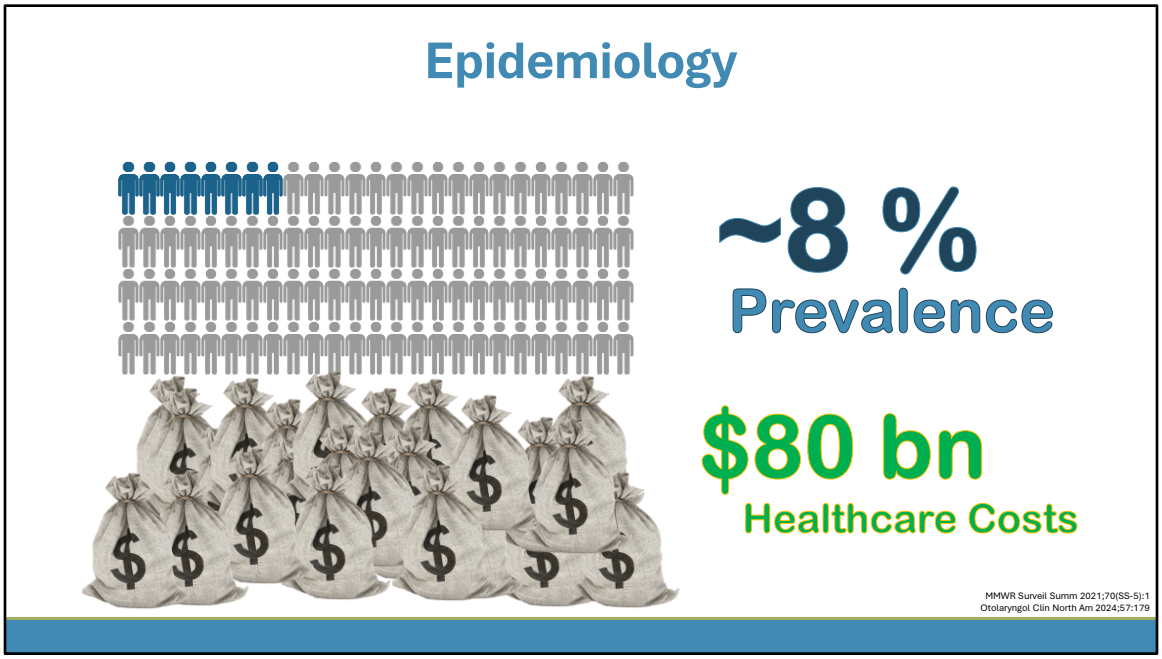
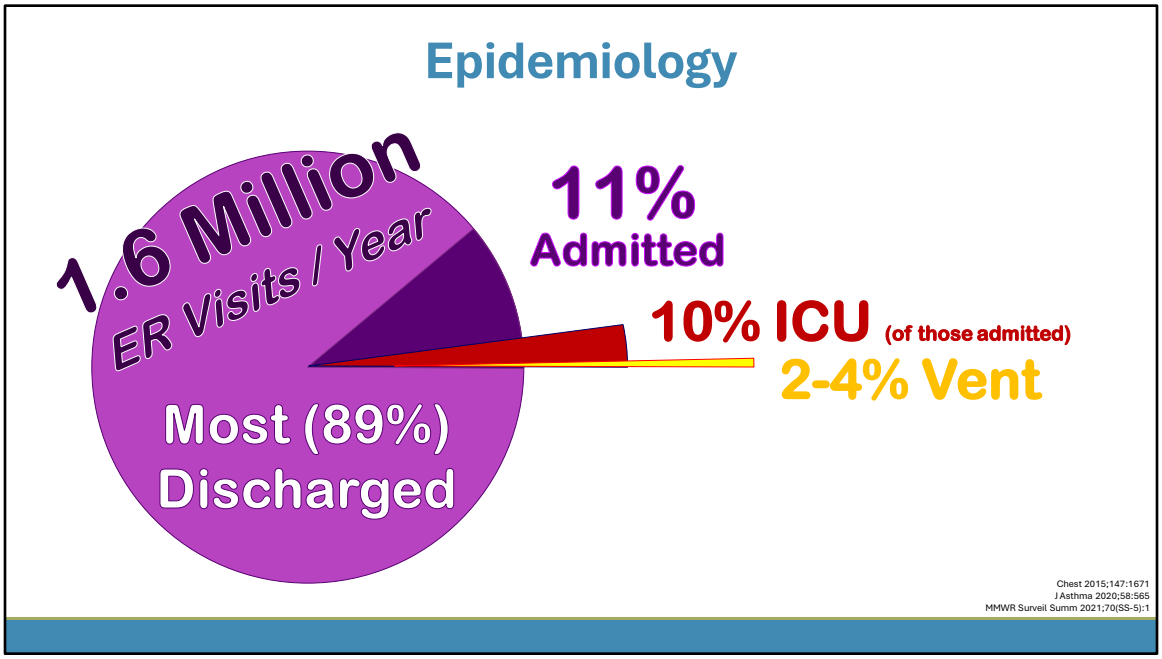

Waiting to Exhale
Management of Life Threatening Asthma
Jacob A. Miller, ACNP, ENP-C, CNS, NRP, FAEN, FAEMS

The term *asthma* comes from the Greek *ασθμαίνω* (pronounced “asthmaino”) meaning to gasp, wheeze, or pant.



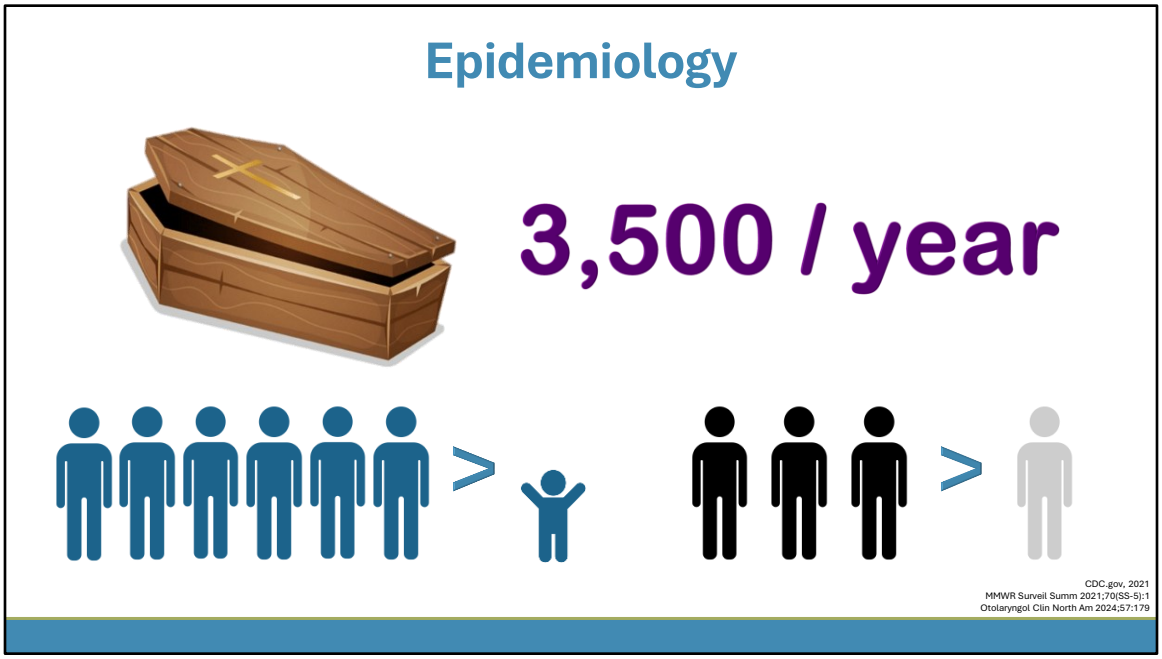
Asthma affects nearly 8% of the US population at any given time; this number may be closer to about 13.5% when referring to the number of patients *ever* diagnosed with asthma, including those who no longer have active disease.

The costs associated with treating asthma amount to nearly $80 billion dollars per year in the U.S. alone.



Depending on the source, asthma-related illness accounts for up to 1.6 million ER visits each year in the United States.

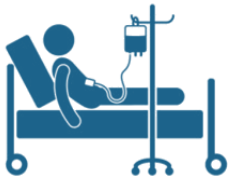
Fortunately, most of those patients can be safely discharged from home, and of those admitted to the hospital, only about 10% require critical care admission and only around 4% or fewer require intubation for their asthma.



Approximately 3,500 deaths per year are directly related to asthma.

Adult patients are around 4-6 times more likely to have a fatal asthma attack than pediatrics, and minorities are around 2-3 times more likely to die than their white counterparts.

Epidemiology

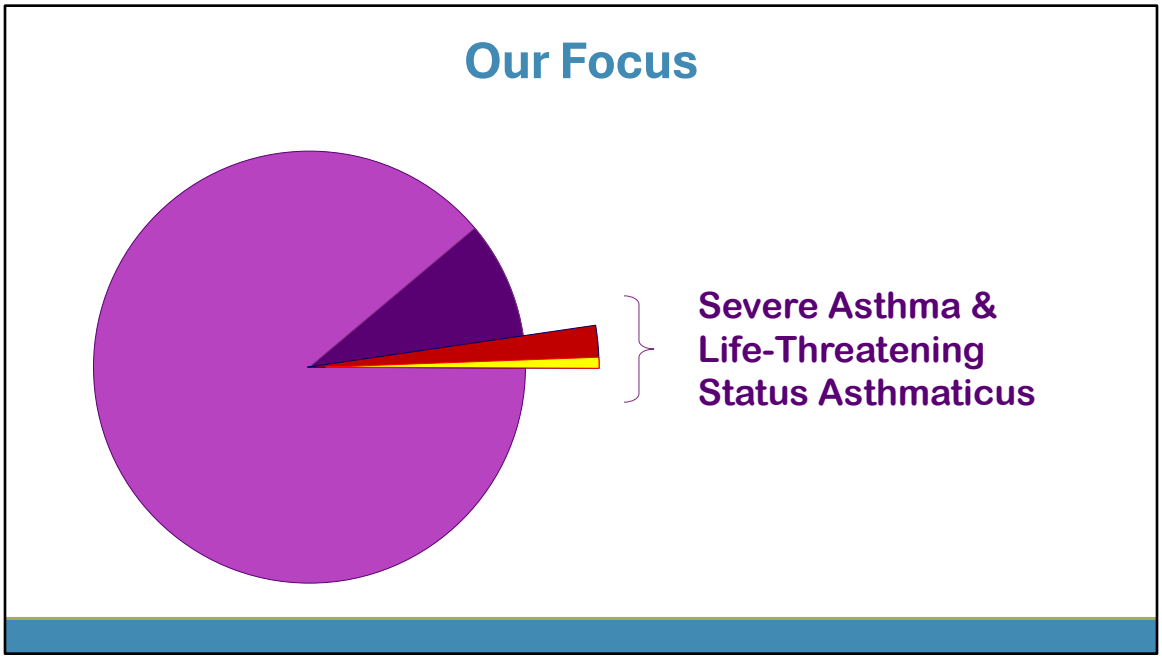


0.5% Inpatient Mortality Rate

6.9% On Mechanical Ventilation

Respir Care 2014;59:644

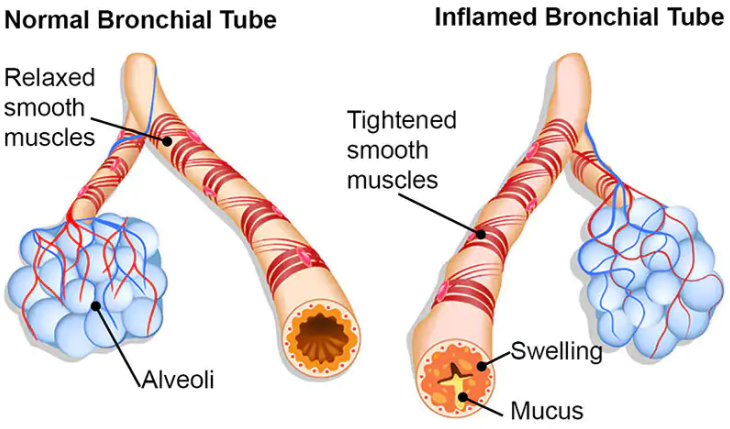
While the overall inpatient mortality rate from asthma is around 0.5%, this number rises considerably in patients critical enough to require mechanical ventilation to manage their asthma exacerbation.



Our focus for this presentation will be on the ***critical*** asthmatic with severe and life-threatening asthma exacerbation.

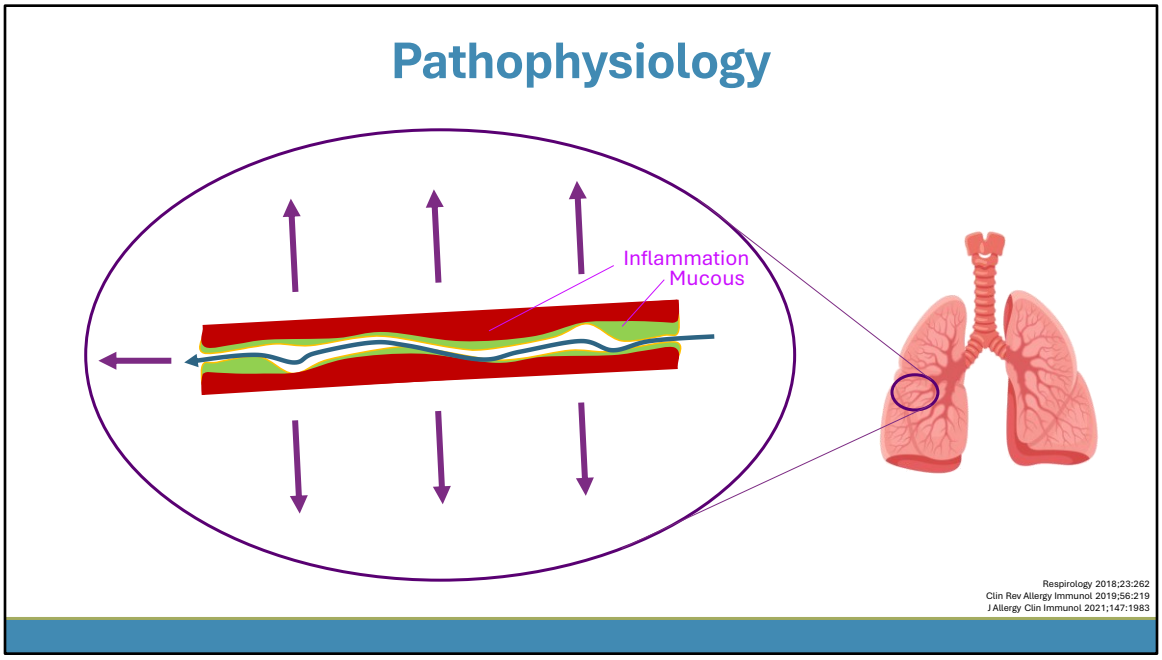
And remember that asthma is not just a simple reactive airway. As Murphy and O'Byrne state here, asthma truly is a complicated, heterogeneous inflammatory disorder that leads to permanent changes in the airway over time.

Pathophysiology

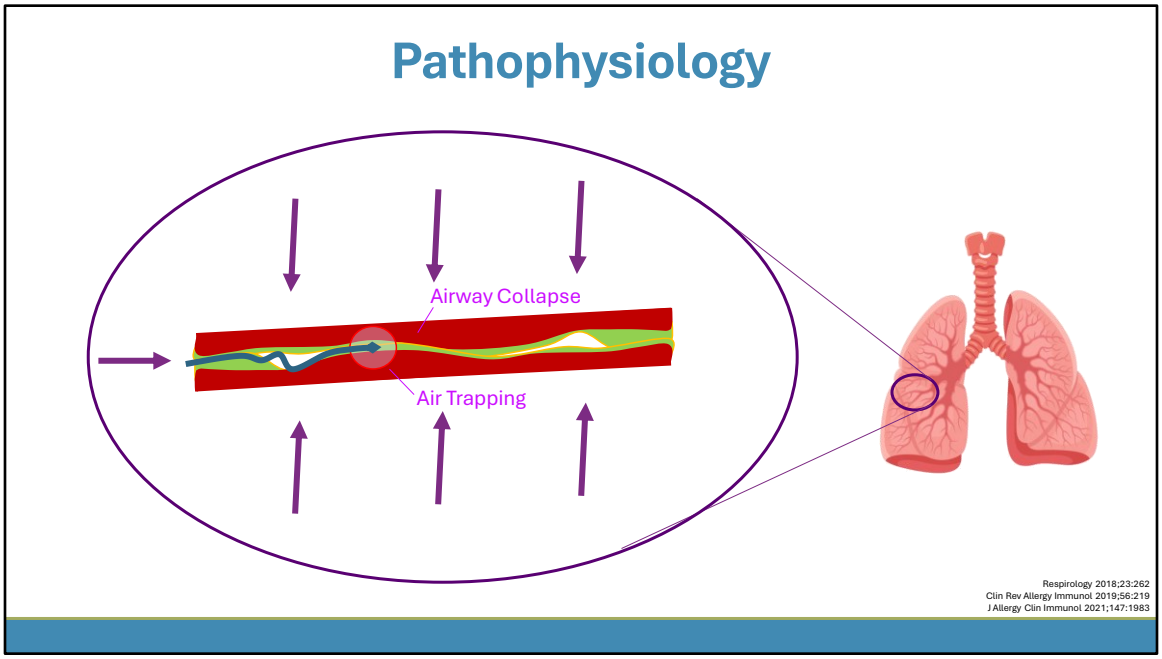


Respirology 2018;23:262
Clin Rev Allergy Immunol 2019;56:219
J Allergy Clin Immunol 2021;147:1983

When we compare the asthmatic airway to that of a normal, healthy individual, what we can see is that at baseline, there is hypertrophy of the airway smooth muscle, inflammation of the airway epithelium, and enlargement of the submucosal mucous glands. During an acute exacerbation, there is an increase in mucous secretion and worsening inflammation and constriction of the airway smooth muscle, further narrowing the airways.



During normal, negative pressure inspiration, contraction of the diaphragm and contraction of the intercostal muscles create a negative pressure which pulls air into the chest cavity.
Not only does this pull air into the chest cavity, but it also helps to pull open the inflamed and mucous-laden airways, allowing air to enter the alveoli relatively freely



During exhalation, however, as the chest wall and lung tissue relaxes, negative pressure subsides and the inflamed, mucous-filled airways begin to collapse. As long as there is still at least a narrow passageway for air to escape, air can leave the alveoli, although it may take a longer-than-normal time to escape through such a narrow passage. Movement of air through constricted airways is what causes wheezing.

However, depending on the degree of inflammation and mucus production, these airways may begin to completely collapse closed, leading to air trapping and dynamic hyperinflation of the lungs. Over time, this hyperinflation will prevent new air from entering the alveoli, because they're already full if they weren't able to exhale that volume at the end of the previous breath.

Asthma Mimics

1. All is not asthma that wheezes.

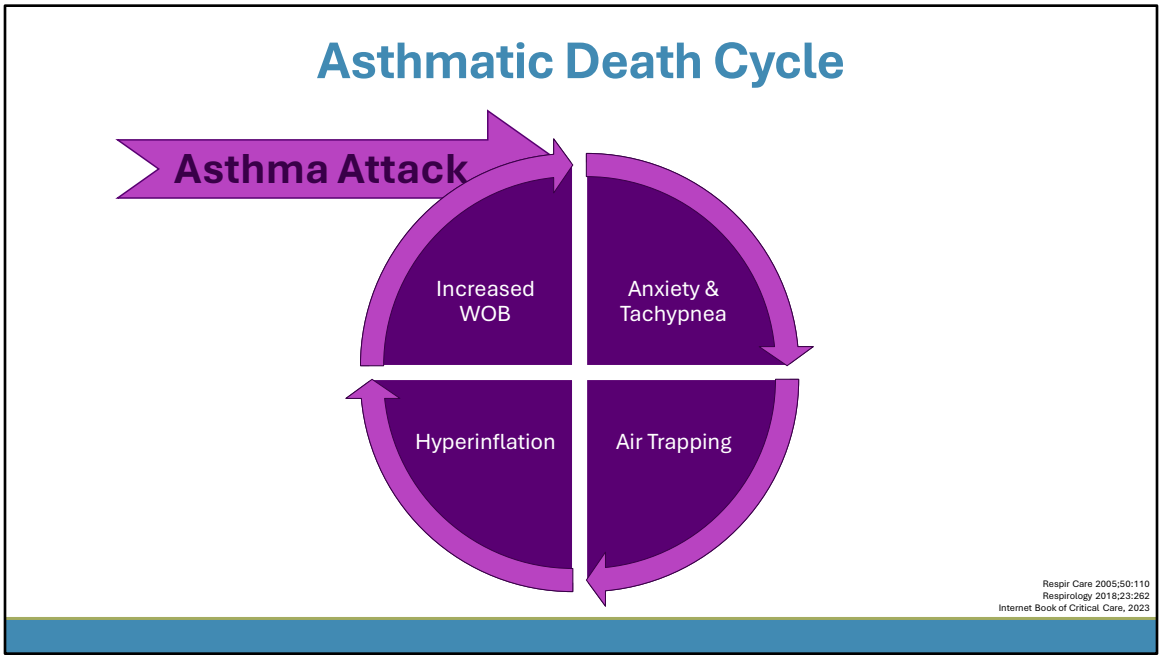
-C. Jackson, MD, 1931

Table 1. Common Asthma Mimics

Anaphylaxis
Angioedema
Central airway obstruction
Chronic obstructive pulmonary disease
Congestive heart failure
Drug reaction
Foreign body aspiration
Gastroesophageal reflux disease
Pulmonary embolism
Vocal cord dysfunction

Am J Dis Child 1931;41:153
J Emerg Med 2017;53:195
Med J Aust 2022;216:337

It's also helpful to consider that other processes can manifest with wheezing through similar pathophysiology. Carefully consider your differential diagnosis when presented with what appears to be an asthma exacerbation.



So, how does an asthma exacerbation worsen and lead to patient decompensation?

In general, when a patient has an asthma attack, they initially have a sense of anxiety which may lead to some degree of tachypnea. As the exacerbation continues, the tachypnea will lead to a decrease in the amount of expiratory time that's available, which in turn will lead to air trapping, hyperinflation of the lungs, and an increase in the patient's work of breathing. The increased work of breathing leads to even worsening anxiety, more tachypnea, additional air trapping, more hyperinflation, worse work of breathing, more anxiety, more tachypnea, and the spiral continues....

Predictors of Badness

RR > 30
HR > 120
Acc. muscle use
1-2 word dyspnea
Pulsus paradoxus

J Allergy Clin Immunol 2017;139:438

Carefully evaluate each patient for the presence of predictors of severe asthma exacerbation. Each of the above findings are suggestive of a patient who is progressing into severe asthma exacerbation or status asthmaticus.

Predictors of Uber Badness

BRADYCARDIA

INABILITY TO SPEAK

***ABSENT* PULSUS**

J Allergy Clin Immunol 2017;139:438

Patients who have critical asthma exacerbation or are peri-arrest may progress to these findings above. Keep in mind, the bradycardia here is a ***relative bradycardia***, meaning a patient who was previously to tachycardic to the 120s may present with a heart rate that "normalizes" into the 90s or 80s before progressing to a brady-PEA arrest. A normal-appearing heart rate *might* not be a good thing if the patient looks like they're actually getting worse and not better.

ABG Values

	RR	V_T	$PaCO_2$	PaO_2
Stage I	↑	NL	↓	NL
Stage II	↑	↓	**NL***	NL
Stage III		↓↓	↑	NL/↓
Stage IV (Peri-arrest)		↓↓	↑	↓

PulmCrit 2019
Allergy Asthma Proc 2019;40:406

If a blood gas (ABG or VBG) is obtained during an early asthma exacerbation, a normal (or slightly increased) tidal volume coupled with a mild tachypnea may result in a *respiratory* ***alkalosis*** early in the asthma exacerbation.

As the patient's exacerbation continues, and their tidal volume begins to fall (generally due to air trapping), they will begin to develop a *respiratory acidosis*. **Importantly**, however, that respiratory acidosis will begin *from a starting* ***alkalotic*** *state*. This means, is that as the patient gets worse, they will actually begin to have a *pseudo-normalization* of their blood gas results, looking relatively normal despite their worsening clinical appearance. Interpret a "normal" blood gas with extreme caution in these patients!

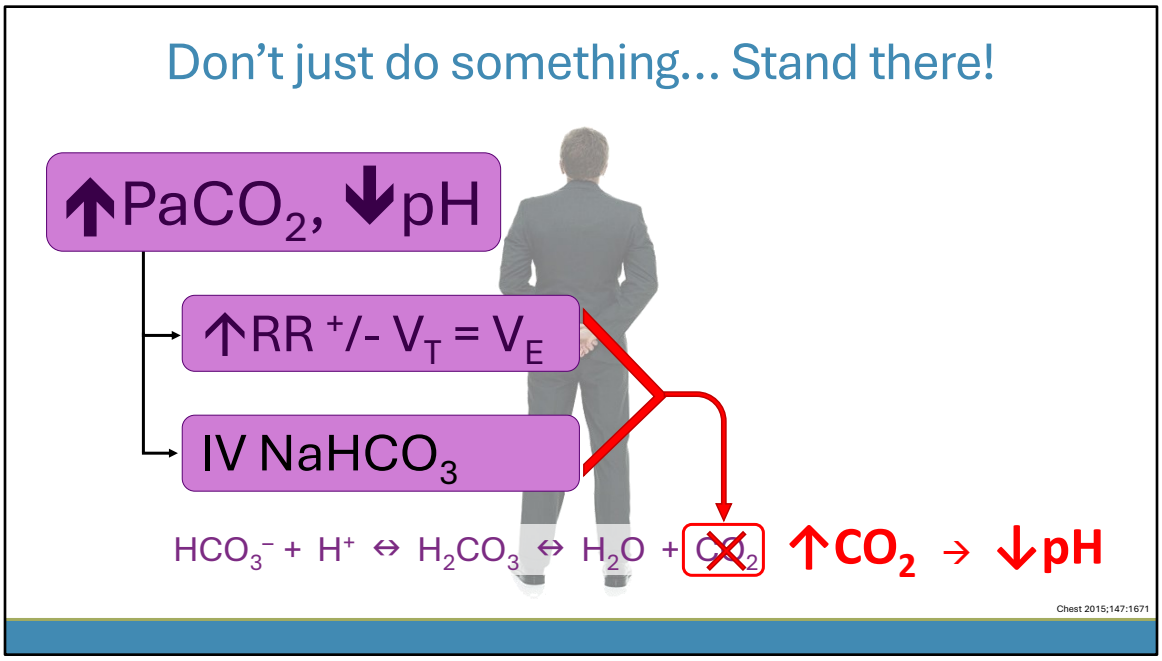
Later in the course of their exacerbation, they will move from a "normal" appearing blood gas toward the more commonly associated respiratory acidosis, with CO_2 retention and a low pH.

Generally speaking, acute asthma exacerbation shouldn't usually lead to significant hypoxia. A hypoxic asthmatic patient should be considered an ominous finding.

Management

"We used to think that they died from gas exchange abnormalities. But they die from us trying to normalize their gas exchange abnormalities."

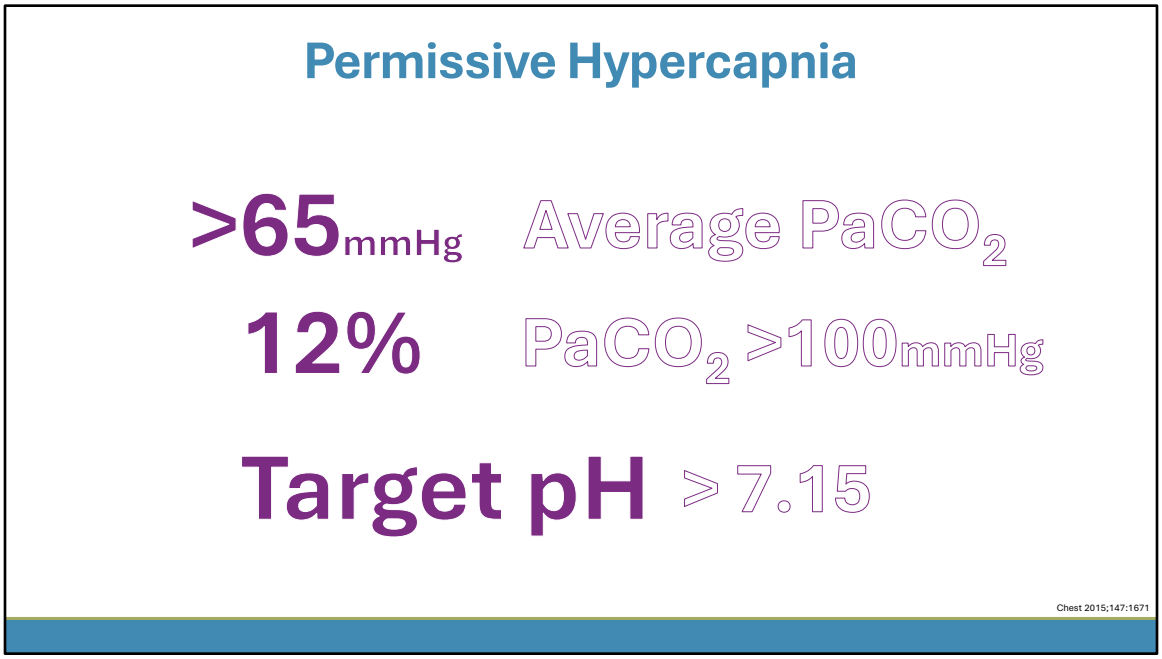
-L. Rubinson, MD, PhD



Be cautious about trying to fix a high PCO_2 or a low pH.

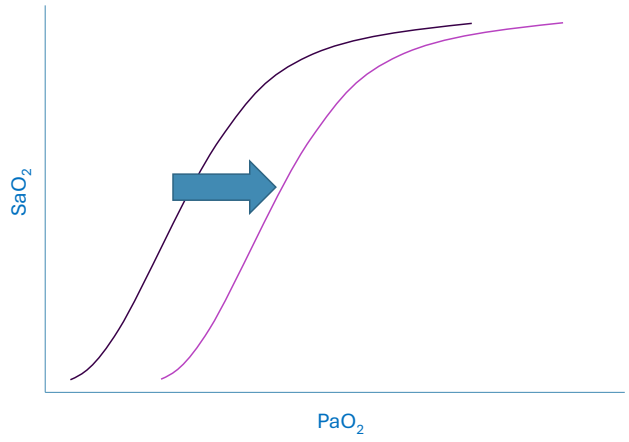
When encountering a high PCO_2, our normal inclination is to increase the patient's minute ventilation, by increasing their respiratory rate and or tidal volume, to try to blow that CO_2 off. In the asthmatic patient, however, increasing their respiratory rate and or tidal volume will lead to even worse air trapping, and paradoxically lead to even worse CO_2 retention.

Likewise, there are many individuals that would respond to a low pH by administering sodium bicarbonate. However, bicarb works by binding with an acid to form carbonic acid and then dissociating into carbon dioxide and water. Thus, the entire mechanism of action by which bicarbonate improves pH is *dependent upon the ability to remove the excess CO_2* that is generated. With our asthmatic patients, they are unable to clear CO_2 at baseline, so providing an additional "bolus" of CO_2 to that patient is unlikely to be helpful, and may actually be detrimental and lead to a paradoxically worsened pH with the administration of bicarb.



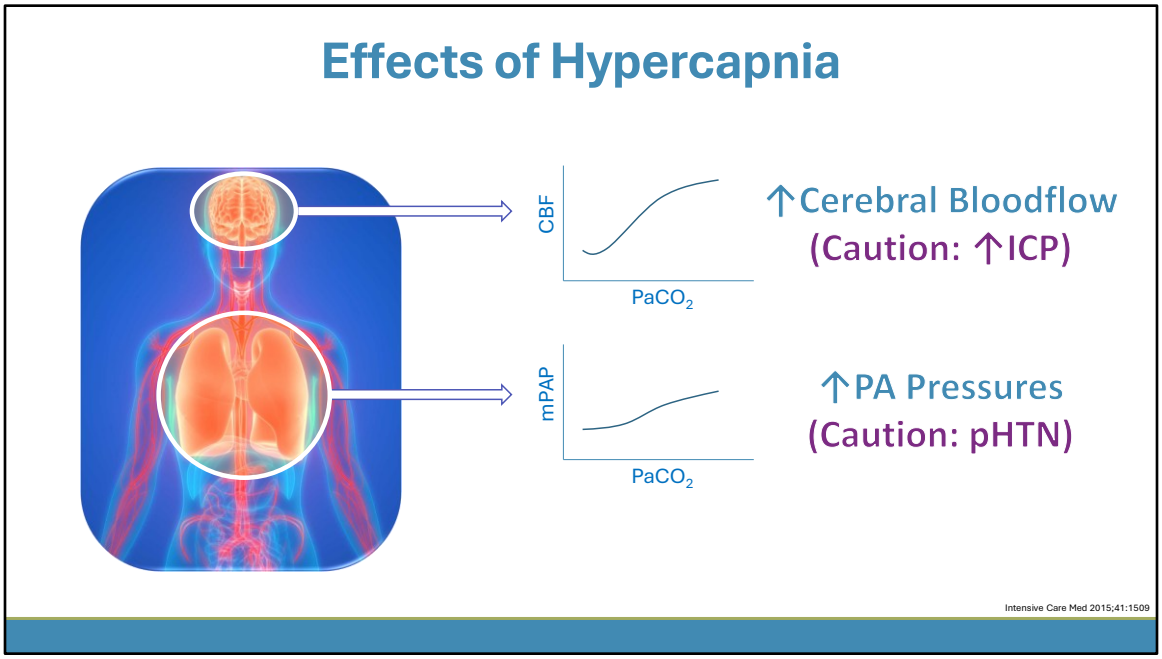
Thus, and the asthma patient, we can tolerate a higher CO_2 value, if necessary, during their resuscitation and care. That said, *permissive hypercapnia* is not the same as *deliberate hypercapnia*. We do want to keep their CO_2 as close to normal as possible, while trying to target a pH of at least 7.15 if able.

Effects of Hypercapnia



Breathe 2015;11:194

Elevated CO_2 levels can shift the oxyhemoglobin dissociation curve to the right, which will lead to increased oxygen delivery to the tissues. Thus, if you have a critical asthmatic that is having difficulty both oxygenating and ventilating, it's reasonable to maintain a lower-than-normal oxygen saturation, e.g., >88%, especially in the setting of hypercapnia. Even though the patient may look like they are mildly hypoxic on a pulse oximetry, they're probably going to be delivering adequate amounts of oxygen to the end organ tissues.



There are some negative consequences to hypercapnia, however. In the brain, carbon dioxide is a vasodilator, so increased CO_2 levels will lead to an increase in cerebral blood flow which may worsen intracranial pressure in a patient that is sensitive to those blood flow changes.

The opposite is true in the pulmonary circulation; the pulmonary capillaries respond to increased CO_2 levels with vasoconstriction. Thus, high levels of CO_2 will lead to an increase in pulmonary vascular resistance, which may worsen pulmonary hypertension or right ventricular dysfunction.

Basic Management

Short-acting β agonist

Inhaled anticholinergics

Systemic corticosteroids

Global Initiative for Asthma, 2024

With these patients, there is absolutely no change to the basic management of the asthma exacerbation itself. These patients are still managed with short acting beta agonists, like albuterol; inhaled anticholinergics, like ipratropium; and systemic corticosteroids, whether oral or intravenous, like prednisone, prednisolone, dexamethasone, or methylprednisolone.

Adjunct Therapy

Curr Emerg Hosp Med Rep 2015;3:154
Thorax 2022;77:563
Internet Book of Critical Care 2023

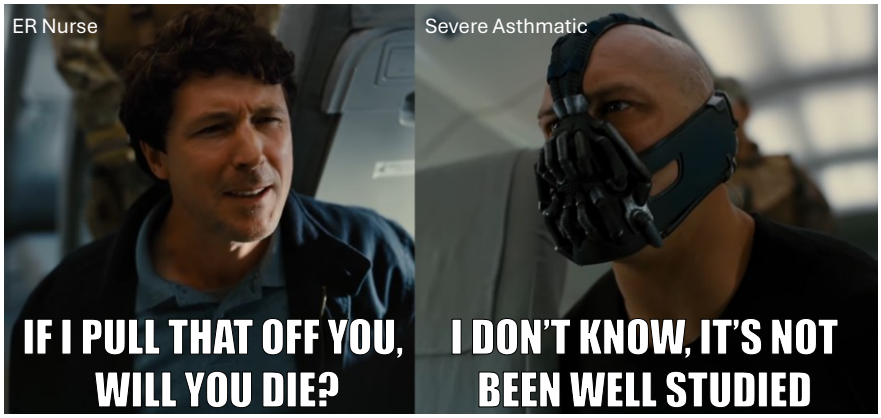
For patients not responding well to inhaled beta agonists, parenteral beta agonists can be considered. Epinephrine has shown some utility when administered parentally, whether IM or by IV bolus (or infusion). There's no good consensus on what the appropriate dose of IV epinephrine is in an asthma exacerbation, but it can be considered for a patient that is not responding effectively inhaled beta agonists like albuterol.

Adjunct Therapy

Cochrane Database Syst Rev 2014;CD010909
Cochrane Database Syst Rev 2016;CD011050
Internet Book of Critical Care 2023
Global Initiative for Asthma 2024

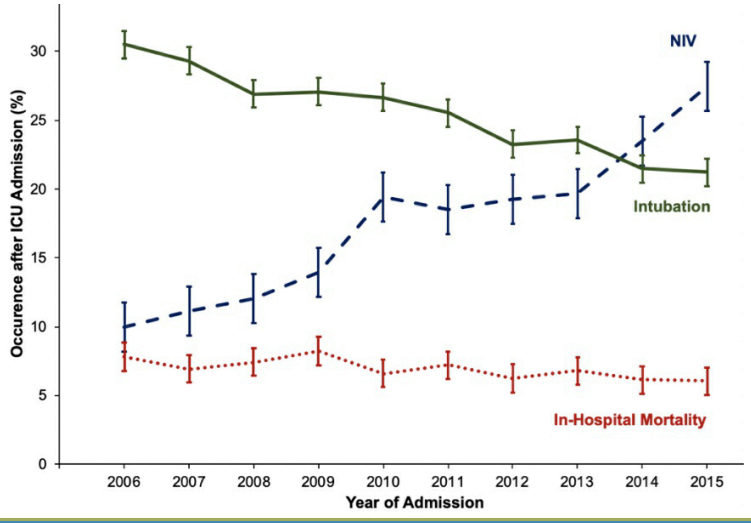
Magnesium sulfate has even less robust evidence supporting its use. In general, studies don't seem to find any significant harm, but the jury remains out on whether or not there is significant benefit to support using magnesium sulfate in acute asthma exacerbation. In my personal practice, I will typically go to epinephrine first for severe asthma, adding magnesium as an adjuvant therapy if the patient remains in acute exacerbation.

NIV?



J Intensive Care Med 2018;33:491
J Clin Med 2024;13:859
Cochrane Database Syst Rev 2024;CD012067
Expert Rev Respir Med 2025;19:165

Noninvasive Ventilation



Am J Respir Crit Care Med 2020;201:A1834
Am J Respir Crit Care Med 2020;202:1520

Over the last couple decades, the use of noninvasive ventilation has significantly increased. It appears this likely may reduce the rate of intubation in asthma exacerbations, but the in-hospital mortality curve has remained relatively flat during this time. Thus, the use of NIV and asthma exaggeration may prevent intubation, but doesn't appear to have much effect on overall mortality.

Noninvasive Ventilation

	LOS	☠
No ventilation *n* = 12676	2.9	0.2 %
Noninvasive *n* = 556*	4.1	2.3 %
Intubated *n* = 698	6.7	14.5 %
Intubated for NIV failure *n* = 26	10.9	15.4 %

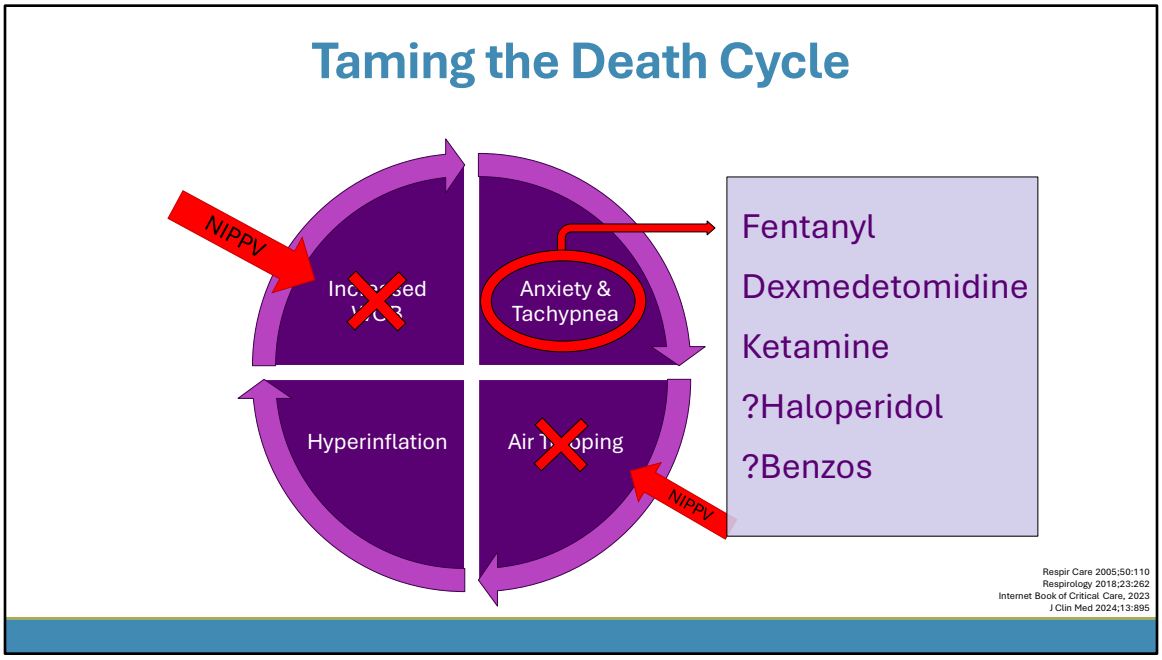
Ann Am Thorac Soc 2016;13:1096

One study evaluated nearly 14,000 patients with asthma exacerbation. The vast majority of them, over 90%, did not require any ventilatory support.

Of those receiving ventilator support, around 56% were intubated first, while 44% were placed on noninvasive ventilation. Overall, the patients on NIV did better than those that were intubated.

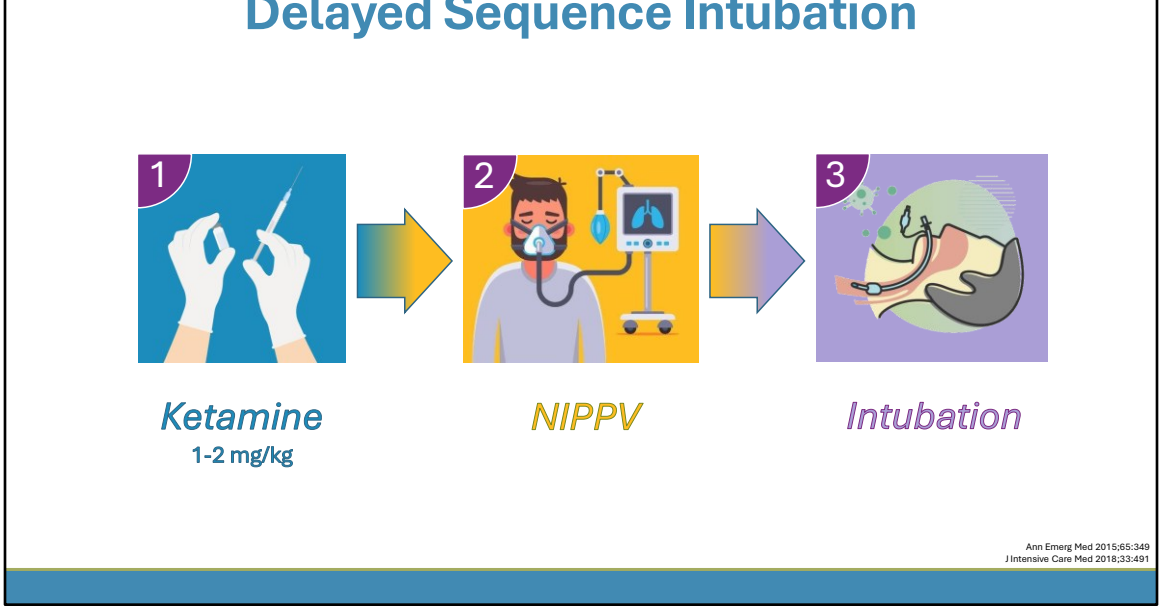
An important note, however, is that 4% of the patients initially started on noninvasive ventilation progressed to intubation due to failure of noninvasive support. That subgroup had the worst outcomes overall, with the highest length of stay and highest mortality.

What this tells me is that it may be reasonable to initiate noninvasive ventilation in the right patient population, but it's important to vigilantly monitor these patients for any sign of deterioration or simply any failure to improve, and consider early intubation if the patient does not appear to be improving with the noninvasive support.



Returning to the asthma death cycle, the use of noninvasive ventilation can help to improve the patient's work of breathing, and may also help to resolve some of the air trapping if you're able to stent open the patients Airways during exhalation.

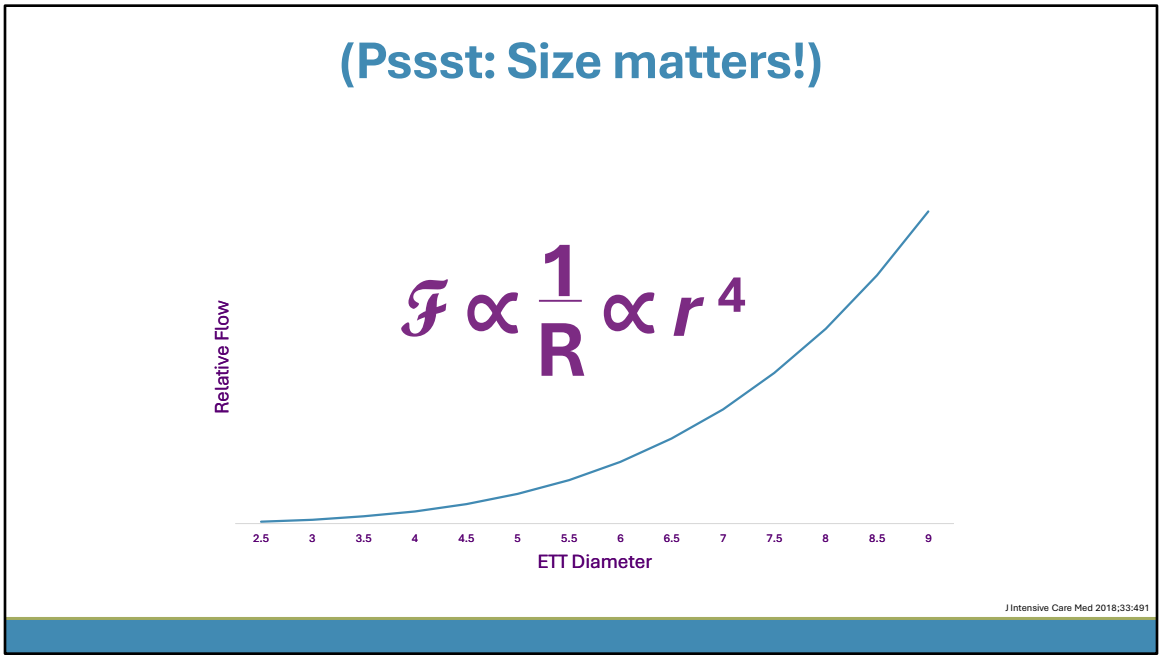
Anxiety and tachypnea can be managed with the administration of anxiolytics or similar medications. Fentanyl, dexmedetomidine, or subdissociative ketamine are all possible options. In extreme cases, full dissociative ketamine can help to remove the patient's anxiety while preserving a more physiologic respiratory drive. Ketamine also has the benefit of direct bronchodilator properties, which may directly help break the asthma exacerbation.



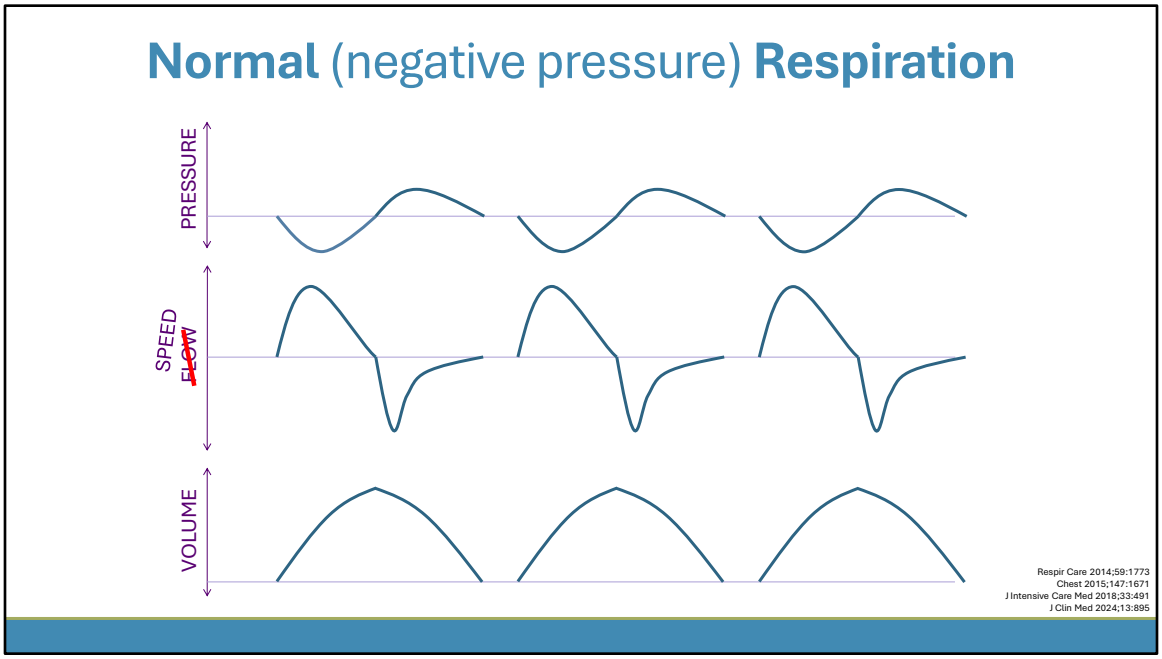
So what do we do if this patient fails noninvasive strategies and NEEDS to be intubated?

This may be a perfect candidate for *delayed sequence induction* for intubation.

Unlike typical RSI, in DSI, the patient is fully dissociated with ketamine, then allowed time to preoxygenate. In the severe asthmatic, this should be accomplished with noninvasive support. Hopefully, the combination of ketamine dissociation and noninvasive ventilation *may* be enough to break their asthma exacerbation and start improving their clinical course. However, if the patient does need to progress to intubation, a paralytic can then be administered and the patient may be intubated while still dissociated with the ketamine.



And remember that the size of the ET tube is important. The flow of any gas is going to be exponentially proportional to the diameter of the tube it is flowing through. These patients already have significant air flow limitations in their lungs, we don't need to add *additional* airflow limitation by using a small ET tube if we don't have to.

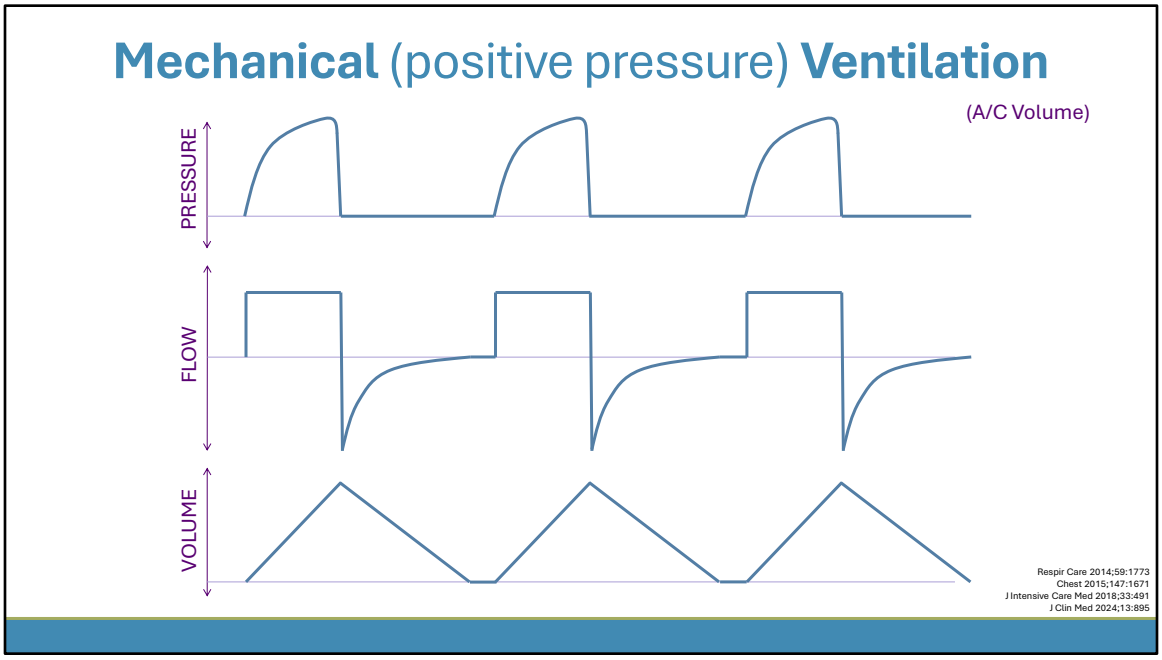


Here's a quick introduction to ventilator scalars. Depending on the ventilator available to you, you may have some or all of these waveforms visible to guide your ventilation.

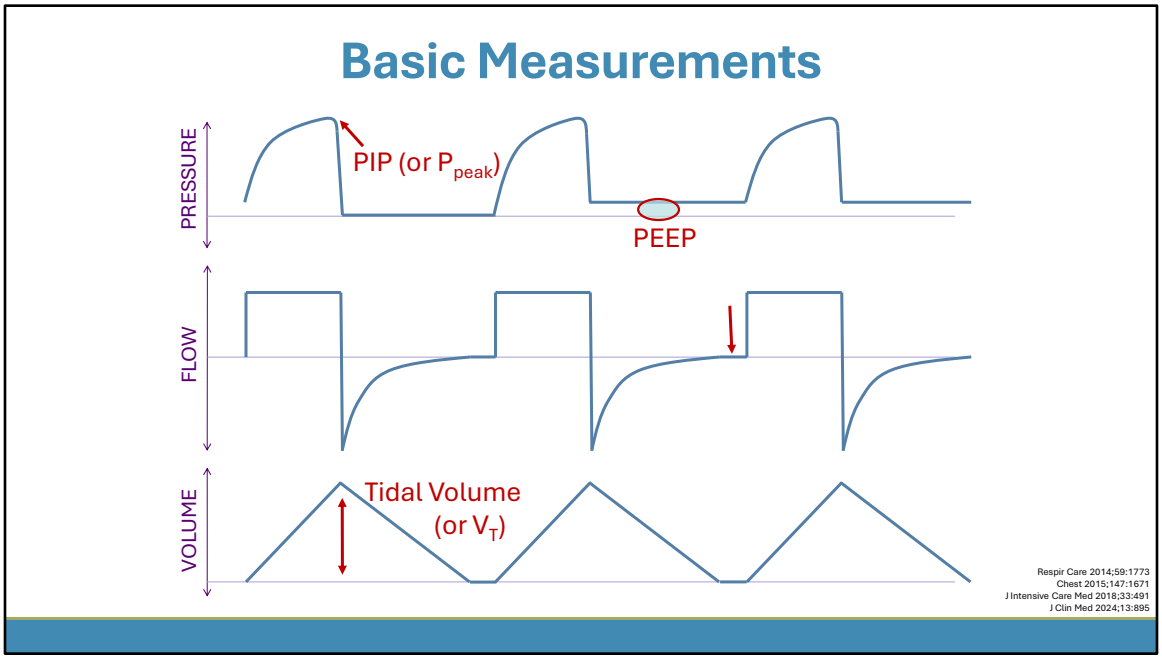
On the top scalar in this diagram, pressure, anything above the line is positive pressure, anything below the line is negative pressure. Thus, with normal (negative pressure) breathing, the inspiratory phase is negative (below the zero pressure line), and the expiratory phase incurs a slightly positive pressure as the chest wall relaxes and pressure slightly increases to cause air to leave the respiratory tract.

The middle scalar of this diagram, flow, can better be conceptualized as "speed" – in this case, speed (flow) increases in both directions as you go away from the center line. The difference here is that anything above the center line is speed of air movement *into* the lungs, while flow below the center line is the speed of air movement *out* of the lungs. Thus, with a normal breath, as you begin inhaling, the speed of air going into your lungs quickly rises, then slows down as your lungs fill. During exhalation, air rapidly starts to leave the lungs, then once again slows toward the end of exhalation.

The bottom scalar here, volume, is exactly how it sounds: absolute volume of air in the lungs (or, more technically, absolute value of the volume of air that has been delivered from, or retrieved by, the ventilator). Thus, during inspiration, the volume increases to the peak tidal volume, and during exhalation the volume returns back to zero.



This diagram shows a typical set of scalars for positive pressure ventilation, assuming a volume control mode of ventilation. Note that inspiration is a positive pressure (all above the zero pressure line) and at a constant “speed” of inspiratory air delivery (again, a constant line on the “inspiration” side of the flow scalar)

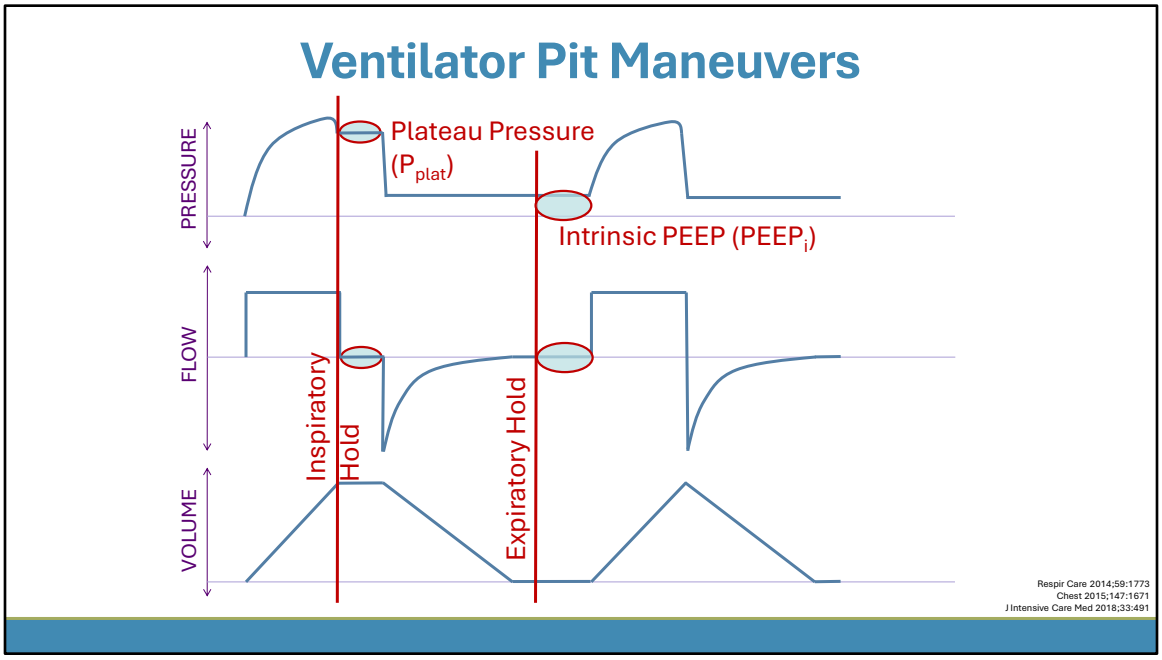


Here, you can note a few *basic* ventilator measurements.

On the pressure scalar, you can note the *peak inspiratory pressure* (PIP, or Ppeak), which represents the total highest pressure seen *in the circuit*, as measured from the ventilator. Note that this pressure accounts for both compliance (pulmonary tissue) ***and*** resistance (airway and tubing) factors.
Also on the pressure scalar, you can visually estimate the presence and amount of PEEP (positive end-expiratory pressure) by evaluating whether the pressure wave returns to zero (indicating no PEEP) or remains above the baseline (indicating some degree of PEEP). [Pro tip: you can also literally just look at the "PEEP" setting on the vent, but that's cheating…]

On the flow scalar, the most important thing to notice during normal breathing (negative pressure or positive pressure) is that *the flow should* ***return to zero*** at the end of one breath before the subsequent breath begins.

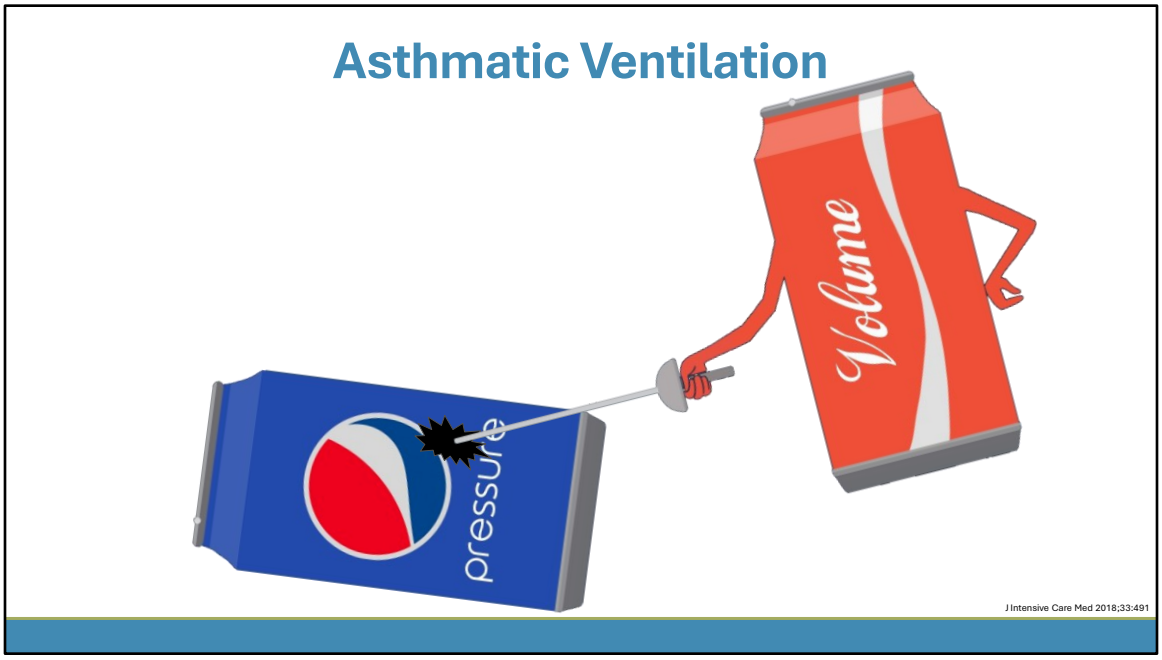
Lastly, on the volume scalar, the peak of the volume waveform represents the total inhaled tidal volume delivered to the patient.



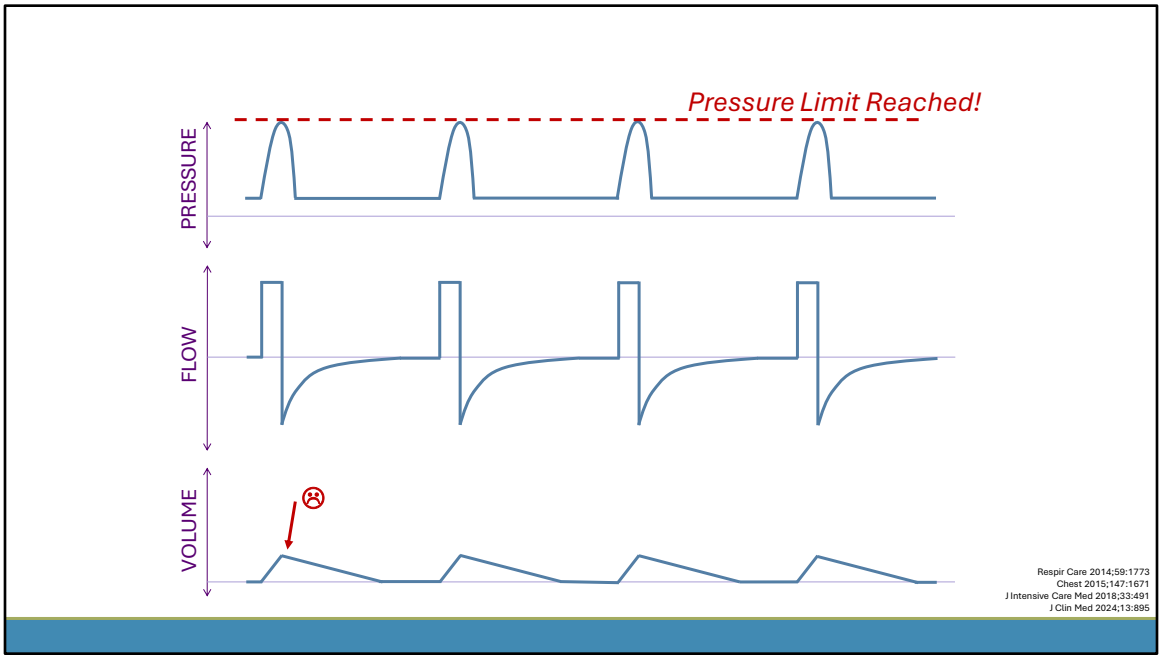
These are some “pit maneuvers” you (or your friendly neighborhood respiratory therapist) can do on most ventilators to provide additional data points.

An *inspiratory hold* will cause the ventilator to deliver the full tidal volume, then close both the inspiratory and expiratory valves, effectively “trapping” the air in the lungs. This is helpful because it allows a view of the *actual* static pressure felt by the alveoli and lung parenchyma by removing the resistance factors (i.e., by not pushing air through the tubing or airways). In most cases, the plateau pressure should generally be kept **below 30 cmH2O**.

An *expiratory hold* will cause the ventilator to close both valves after the patient has fully exhaled (or *should have* fully exhaled). If there is additional air trapped in the lungs that the ventilator was not accounting for, the additional air will generate additional pressure (often above the set PEEP). This total pressure is considered the *intrinsic PEEP*, or PEEPi.
You may have heard the term “Auto-PEEP” in the past; Auto-PEEP refers to the amount of *additional* pressure, above what is set, that exists in the lungs.
Thus, Intrinsic PEEP – Set PEEP = Auto PEEP



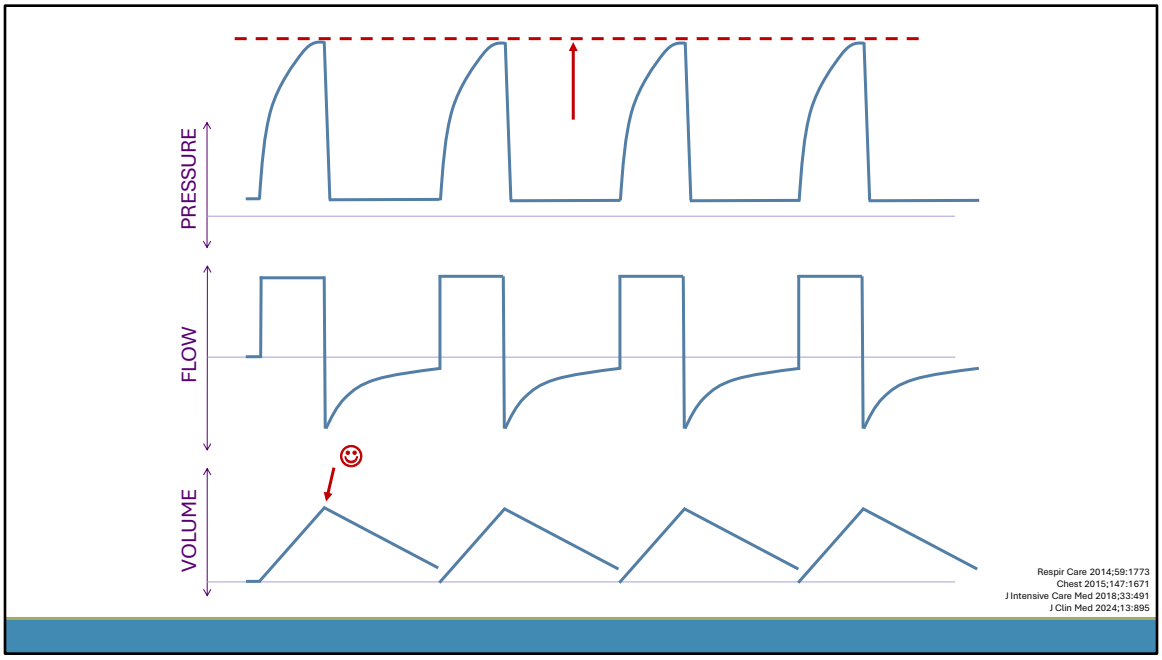
Although there is some debate about whether volume control or pressure control ventilation is more appropriate for general critical care patients (I would argue both are probably acceptable for most patients), in the case of a severe asthmatic, I tend to favor volume control ventilation because you have a better control of the *volumes* (and thus, to some degree, minute ventilation) being delivered.



The primary pathology behind ventilation in the severe asthmatic patient is **resistance** – the profound degree of airway inflammation creates resistance to airflow, causing a high pressure to overcome that resistance.

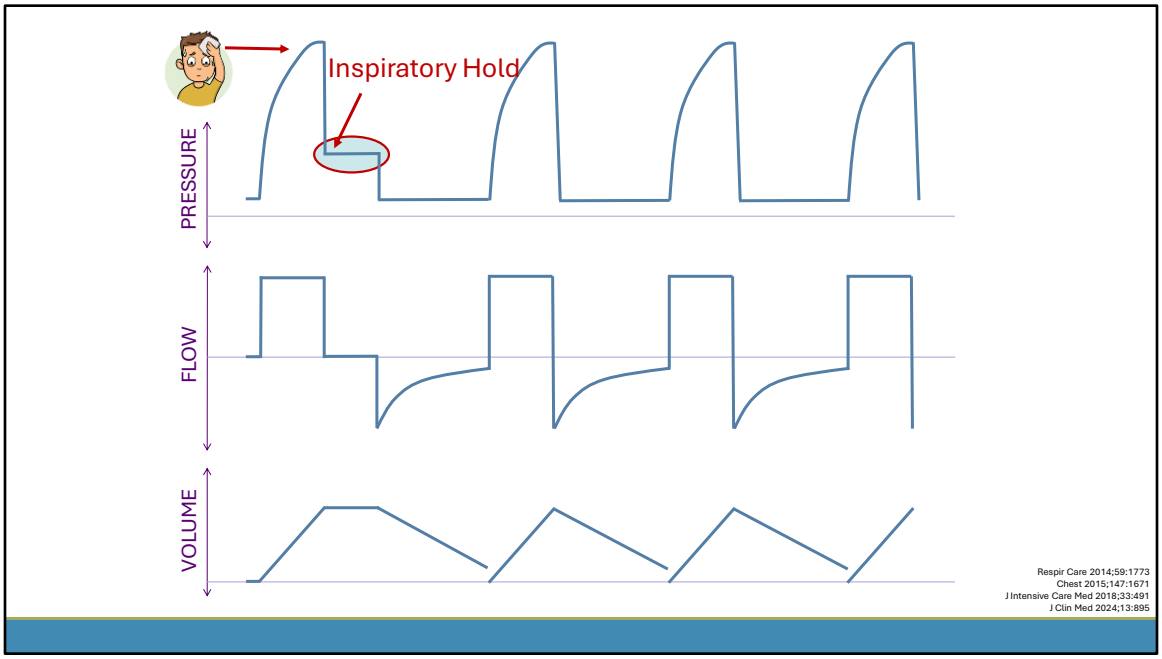
Consider, for example, taking a normal breath, then trying to exhale through your open mouth versus through a straw or even a coffee stirrer. There's considerably more pressure required to move the same volume of air as the diameter of your "airway" gets smaller.

As a result, the ventilator will quickly reach the set pressure limit and stop delivering volumes, resulting in significant hypoventilation.

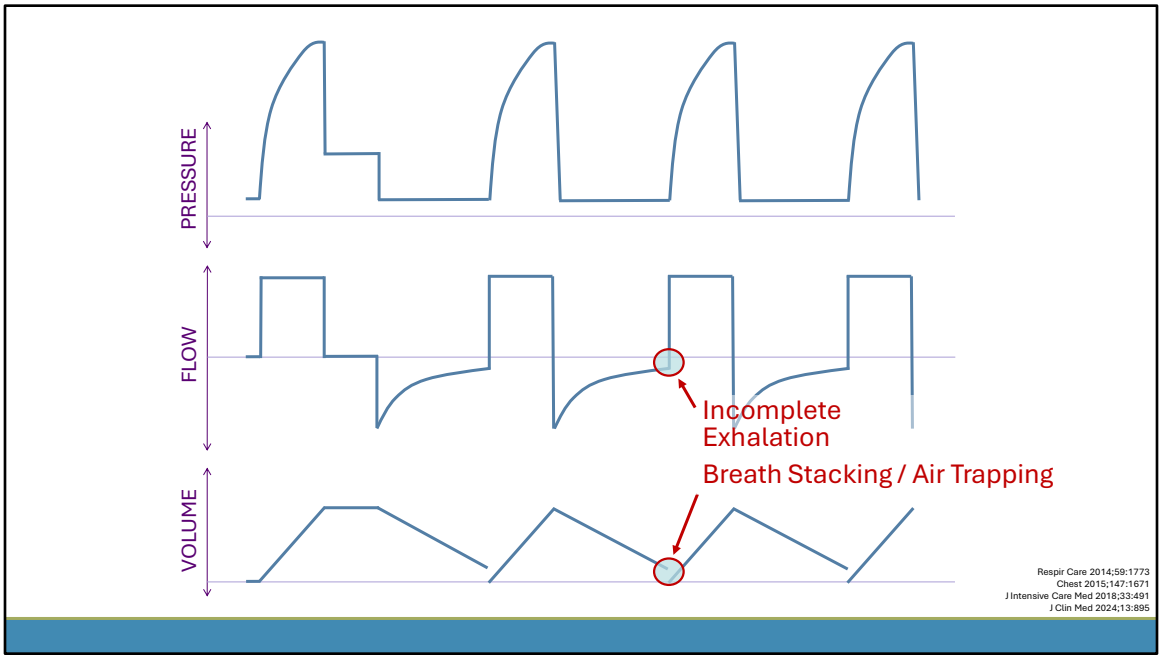


To combat this, it's necessary to *increase* the pressure limit on the ventilator to allow adequate tidal volumes to be delivered.

The pressure limit is usually set in one of two ways: Either directly (i.e., through a setting known as "pressure limit") and/or by raising the "high pressure" alarm. On most ventilators, the ventilator will automatically limit the pressure around 5 or 10 cmH2O below the pressure alarm setpoint. (Thus, if the "high pressure" alarm is set to 40 cmH2O, the ventilator will likely pressure-limit at 30 or 35 cmH2O).



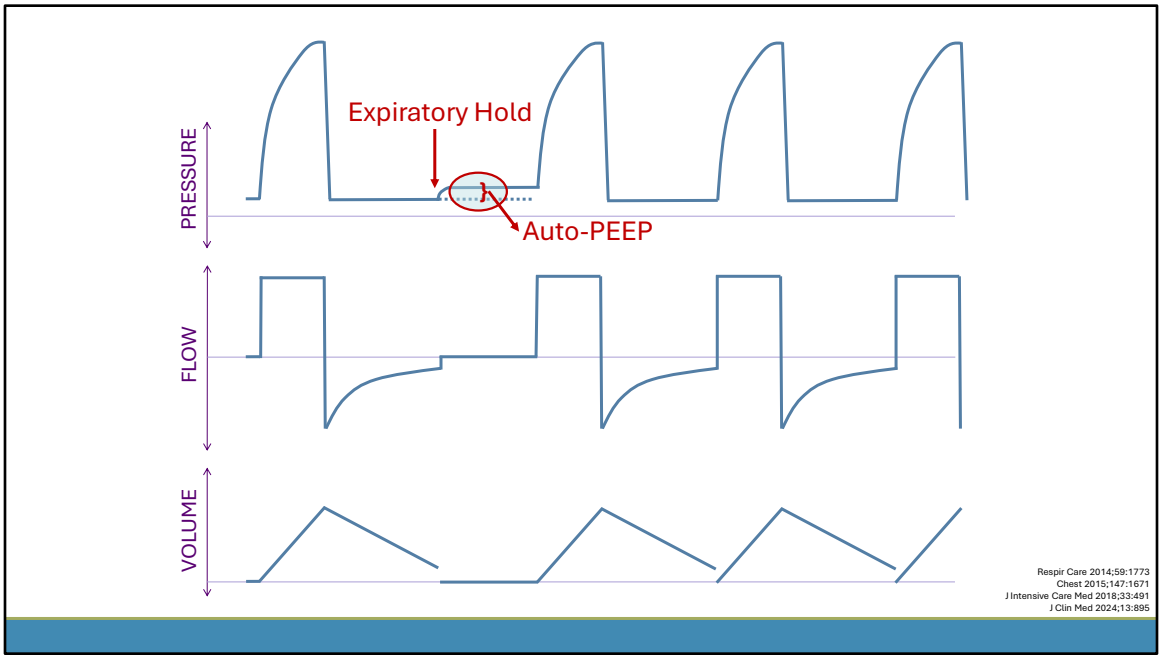
High peak pressures (possibly in excess of 60-80 cmH2O) can be unnerving, so remember to periodically check the plateau pressure to ensure you are still delivering safer pressures to the lung tissues. As long as the patient has a plateau pressure below 30 cmH2O, it's likely safe to continue tolerating high peak pressures.



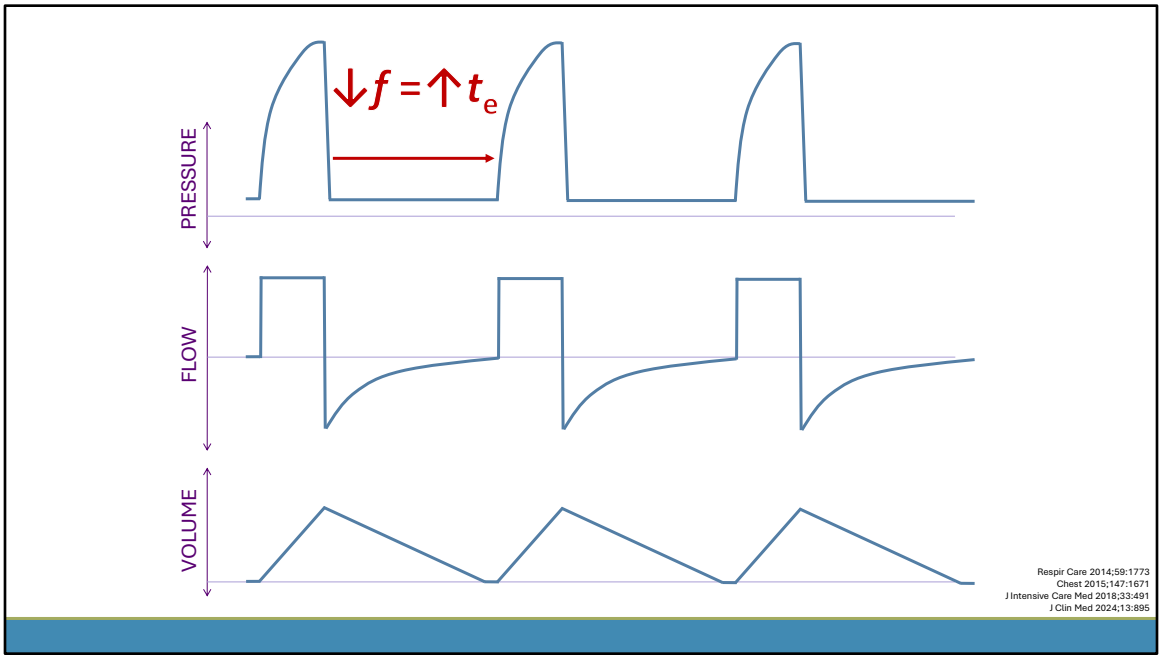
Once adequate *inspiratory* tidal volumes have been achieved through tolerating high Ppeak with safe Pplat, the next consideration is fixing the air trapping.

The two factors suggesting ongoing air trapping are outlined on this slide:

- An expiratory flow failing to return to zero before the next breath
- Expiratory volumes consistently less than inspiratory volumes (although this can also be seen with a cuff or circuit leak or other air volume loss)



When air trapping is suspected, an expiratory hold can help identify auto-PEEP. This can be ventilator specific, but for the in-hospital setting, your respiratory therapist should be able to help with this maneuver.

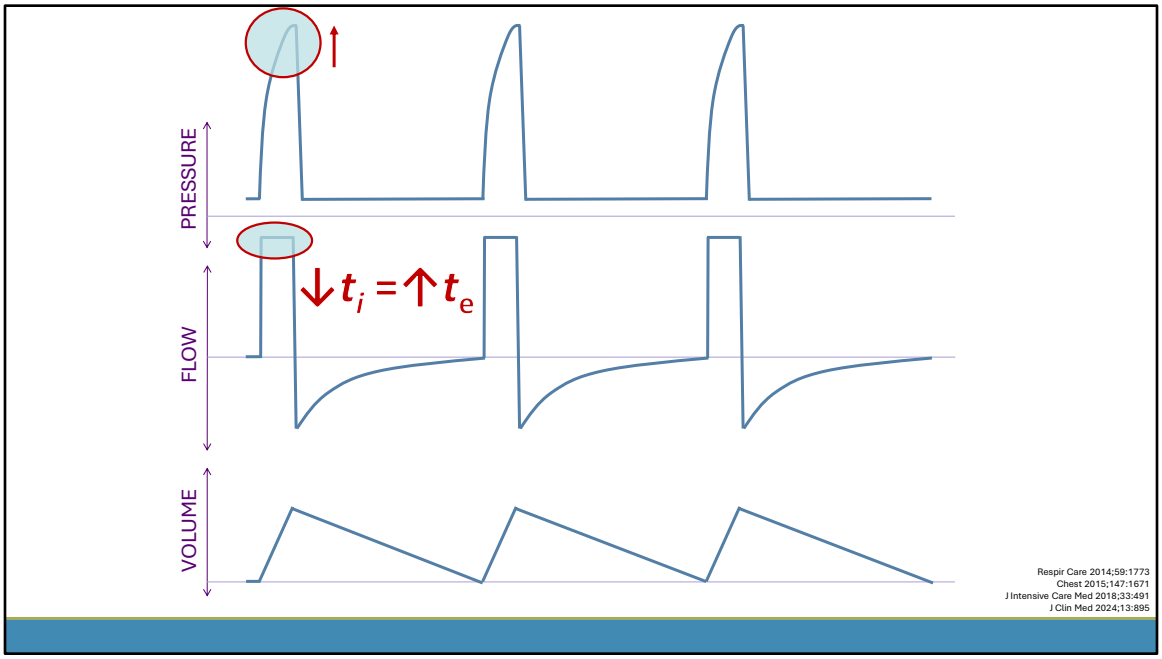


So, how do we *fix* air trapping?

With severe bronchoconstriction, the challenge for these patients lies with *exhalation* (again, consider the example of taking a normal breath and trying to exhale through your open mouth versus exhaling through a coffee stirrer or small straw – the latter options will take longer to move the same volume of air)

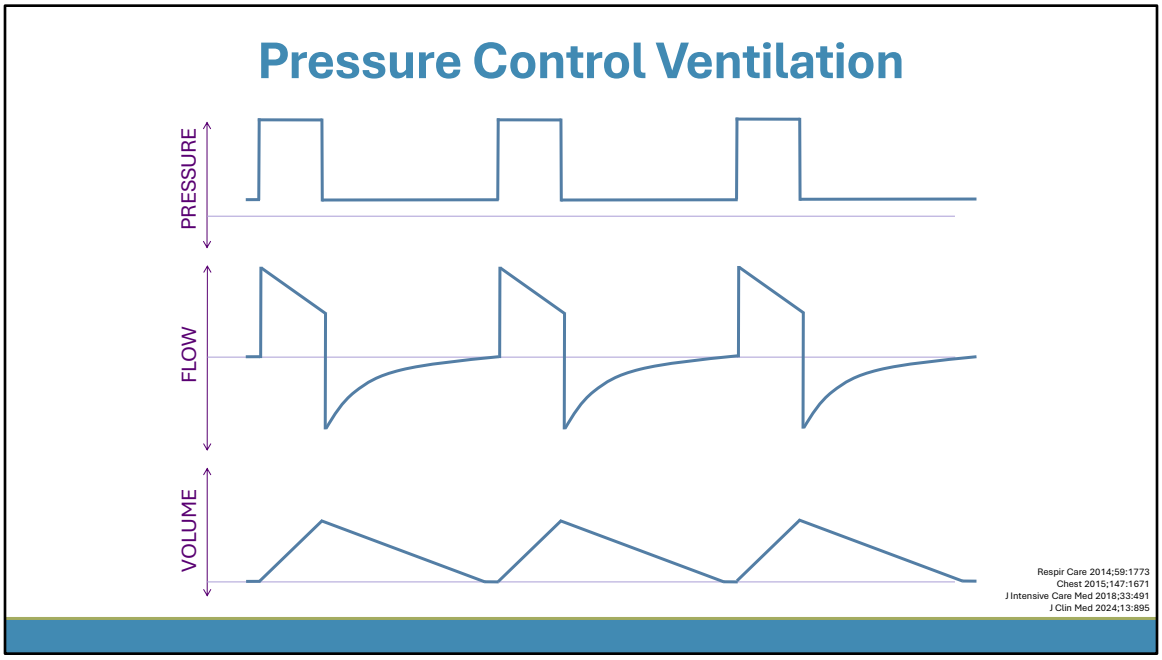
So, we need to give these patients more time to exhale; one way to do this is by decreasing the respiratory rate.

Consider the example of a set ventilator rate of 20: each breath (inhalation *and* exhalation, combined) is a total of 3 seconds. Reducing the rate to 12 will increase each breath to 5 seconds.



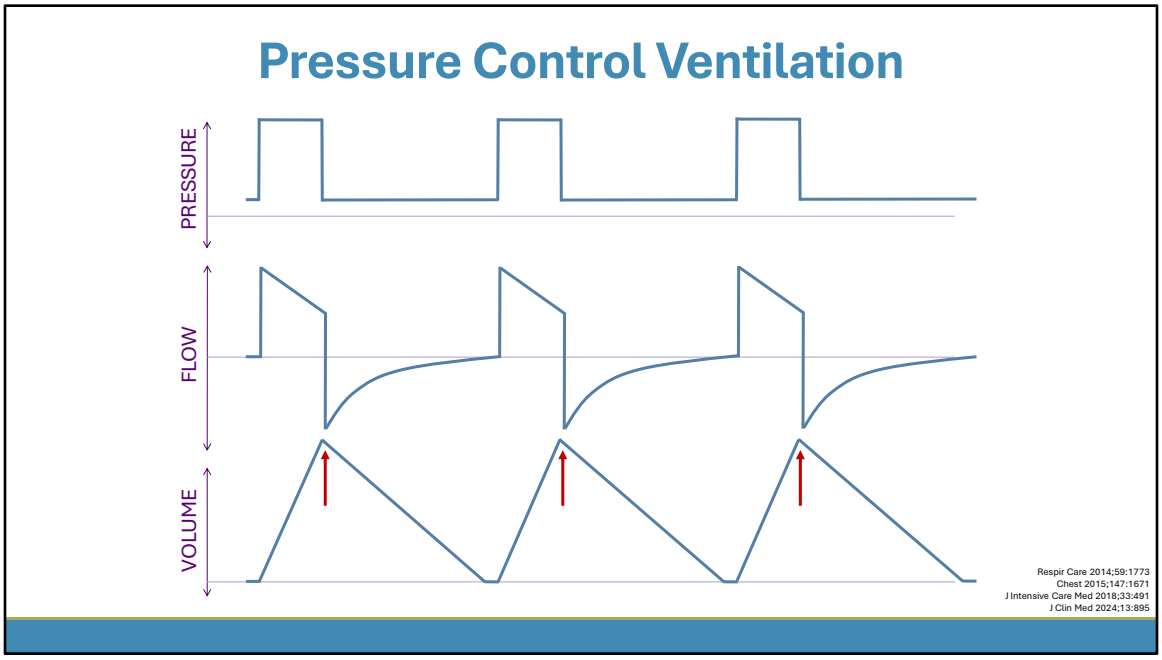
Once the rate has been decreased, shortening the *inspiratory time* can also provide more time for exhalation.

Taking the example from the previous slide, after reducing the rate to 12 (total breath time of 5 seconds), you can then drop the inspiratory time from 1 second (4 seconds exhalation) to 0.5 seconds (leaving 4.5 seconds for exhalation). While this seems miniscule, that will increase total exhalation time by about 6 seconds every minute.



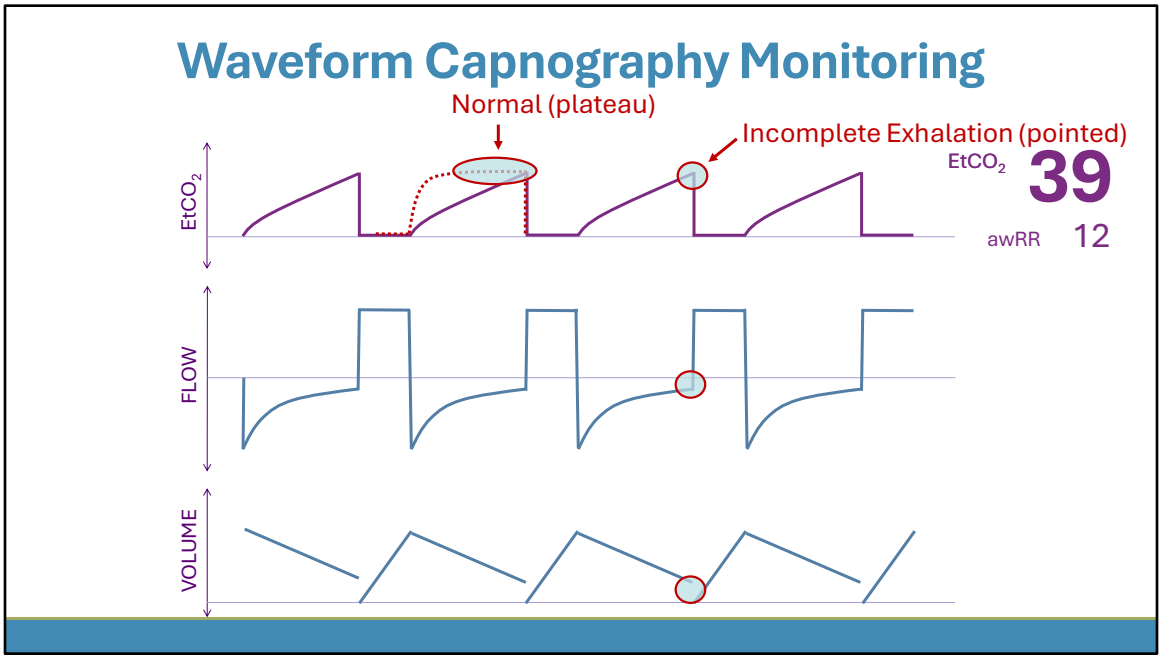
And this is why I prefer volume-control ventilation for severe asthma (or other *obstructive* lung disease).

With a constant pressure, the initial pressure is typically set based on a targeted tidal volume. As long as the patient's lung dynamics remain constant, the set pressure should achieve similar tidal volumes.



As the patient's condition and physiology improves, however, the same pressure will begin to achieve significantly higher tidal volumes (and, conceivably, more of that pressure may be delivered distally to the alveoli and lung parenchyma. Without close attention, this can quickly lead to volumtrauma and barotrauma with the same settings in pressure-controlled ventilation.

Now, of course, there are more advanced hybrid modes of ventilation that could be considered that may have less risk of downstream complications, but those are beyond the scope of this presentation.

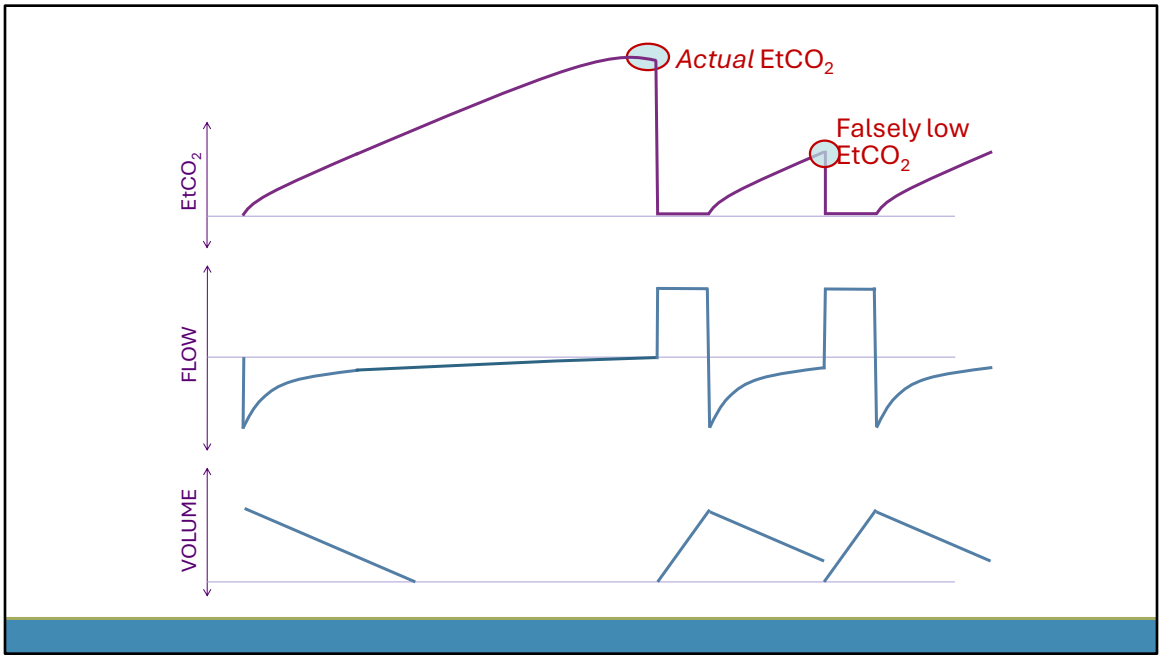


So now let's discuss monitoring these patients with waveform capnography.

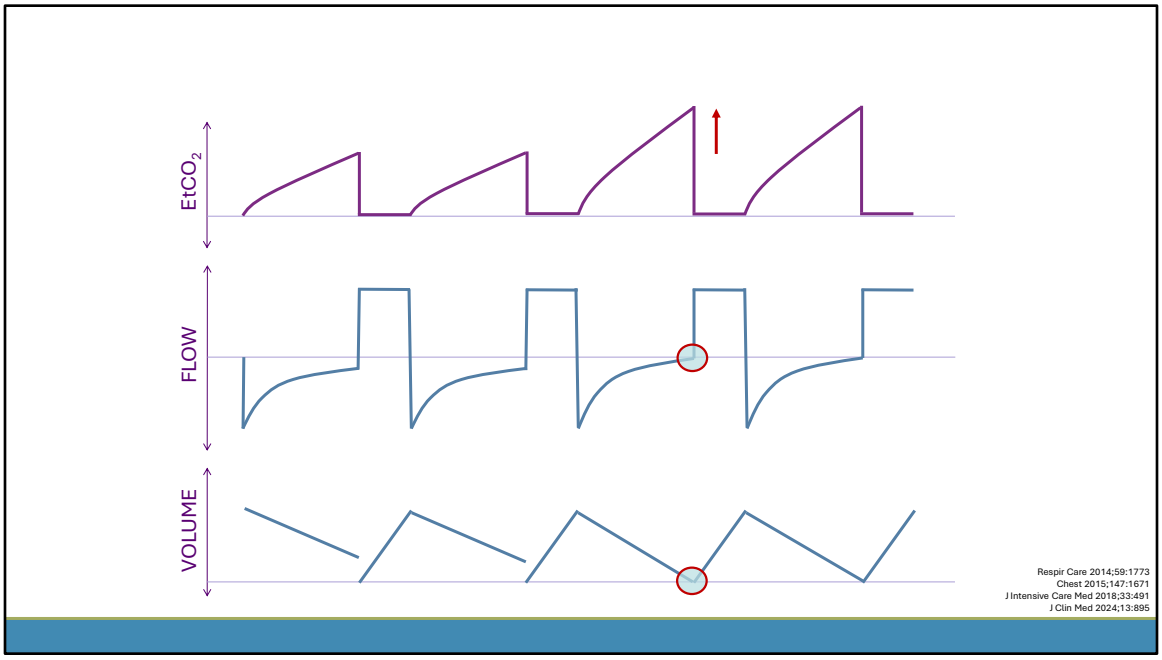
Remember that the value of the $EtCO_2$ represents the amount of measured carbon dioxide at the end of exhalation, just prior to the next inhalation. Exhaled CO_2 is dependent on diffusion of CO_2 from the blood into the alveoli, so, by definition, the true value of PCO_2 is *at least* as high as the $EtCO_2$, but possibly higher. Depending on a number of factors (including perfusion, ventilation, and obstruction), the true value of the PCO_2 in the blood may be *significantly higher* than the measured $EtCO_2$.
In other words, an $EtCO_2$ of 40, for example, means the PCO_2 in the blood is *at least* 40, but potentially 45, or 80, or 120…

The classic obstructive capnography pattern is the "sharkfin" waveform. There are two important components of this waveform:

1) The gradual upslope (or "increased alpha angle"), indicating a delayed emptying of alveolar gas (secondary to the severe bronchoconstriction), and
2) The sharp angle at the end-tidal position, suggestive of incomplete exhalation (i.e., the exhaled CO_2 concentration doesn't have a chance to "plateau" before ending the breath)

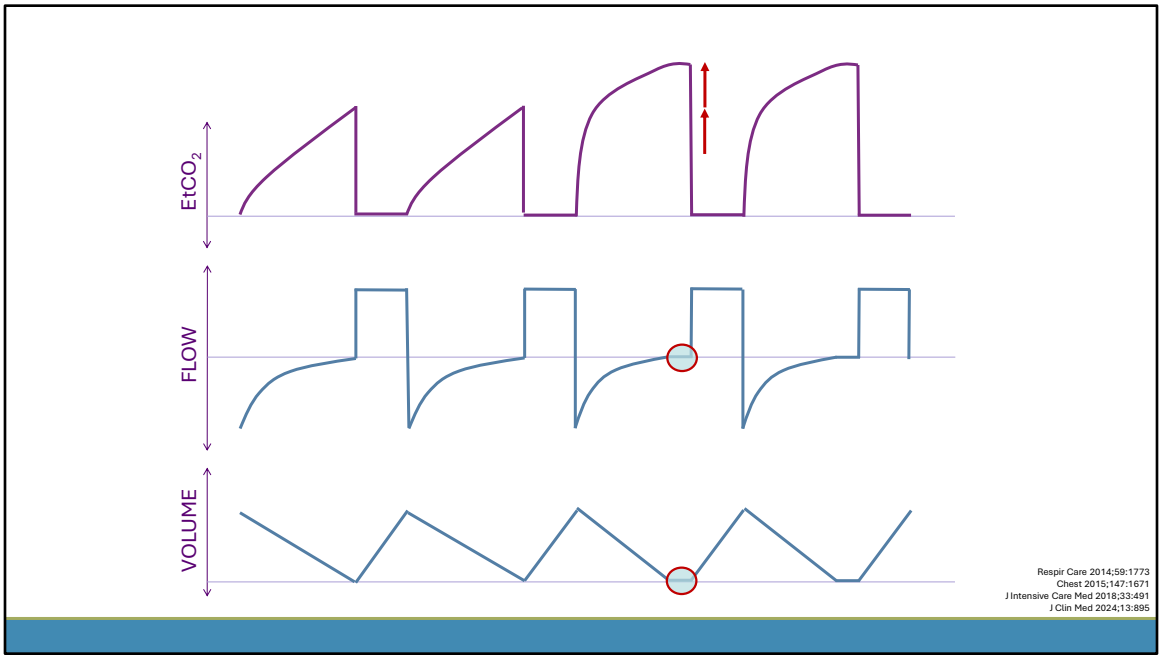


One way to identify this discrepancy is by disconnecting the patient from the ventilator (while keeping the EtCO2 sensor connected to the ET tube). As the patient continues to exhale the additional trapped air, the EtCO2 will continue to rise, until finally reaching the peak.

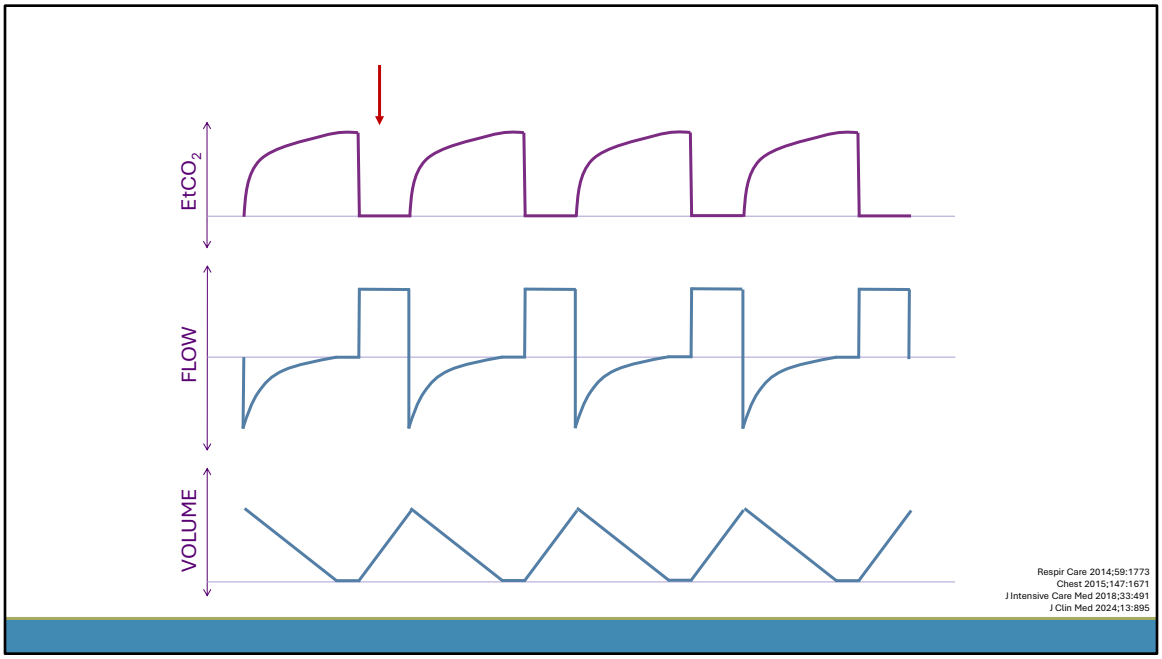


As the patient's obstructive pathology begins to improve, they will being to exhale more completely, thereby emptying more of their CO_2-rich alveoli. This will lead to an *increase* in their $EtCO_2$. Again, importantly, this doesn't necessarily reflect a rising PCO_2 – so this is quite likely be a ***GOOD*** thing to see supranormal $EtCO_2$ values in these patients.

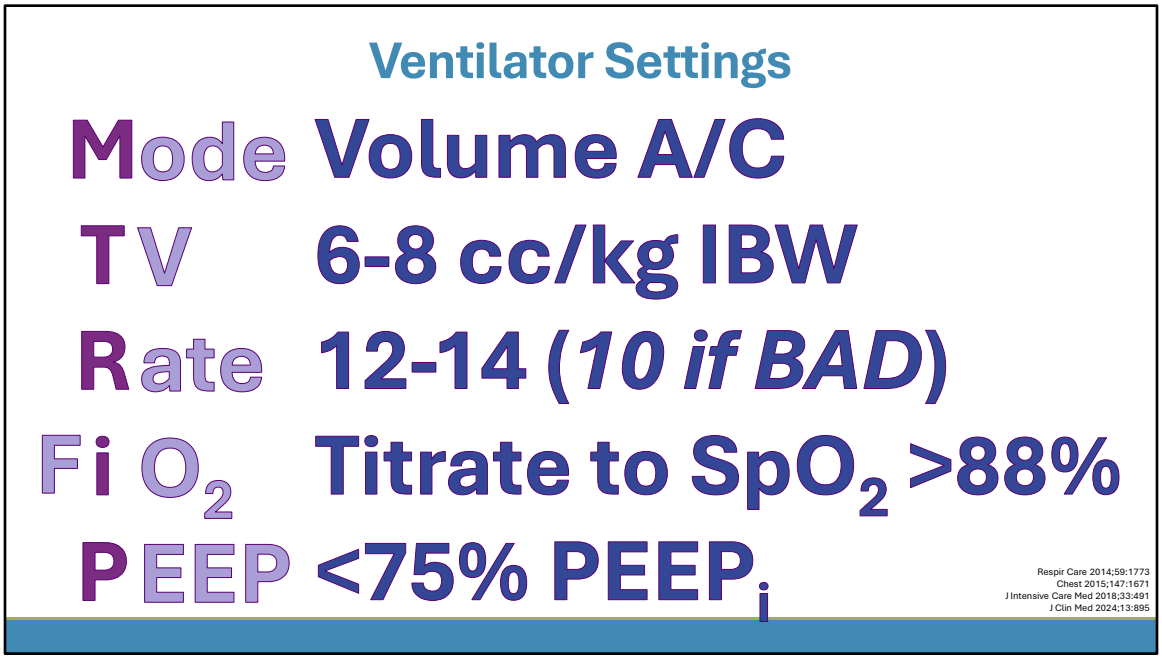
For example, if the PCO_2 is 80 and the initial $EtCO_2$ was 30, as the patient's condition begins to improve, the $EtCO_2$ will increase toward that value of 80 as the gap between the $PaCO_2$ and $EtCO_2$ begins to close.



Over time, with continue clinical improvement, the $EtCO_2$ will closely approximate the PCO_2, and the “sharkfin” waveform will start to plateau.



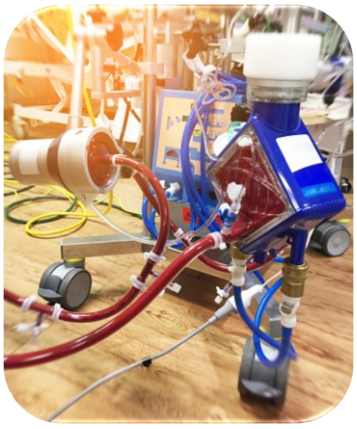
As the patient's condition continues to resolve, provided their minute ventilation is sufficient to blow off the excess CO_2 that has accumulated, the $EtCO_2$ (and PCO_2) will finally fall back to normal values. It's once you have resolved the air trapping and have a more normal capnogram that you can follow the absolute value of their $EtCO_2$ to guide your clinical therapies.



So, what is a good ventilator strategy for these patients?
My recommendation would be:

- **Mode**: Volume assist-control
- **Tidal Volume**: Target 6-8 cc/kg IBW, possibly as high as 10 cc/kg IBW if necessary for ventilation, recognizing that higher tidal volumes risk additional air trapping early in severe disease
- **Rate**: No more than 12-14, but possibly as low as 10 breaths per minute. Remember, the lower the rate, the longer the patient has for exhalation. Most experts agree, however, that below 10 breaths per minute, the loss of minute ventilation probably outweighs the marginal gains of expiratory time.
- **FiO2**: This can be titrated to target the goal SpO_2. In most patients, a goal SpO_2 of >88-90% is probably sufficient. Remember, especially in patients with hypercapnia and respiratory acidosis (elevated PCO_2), the patient's oxyhemoglobin dissociation curve shifts rightward, so cellular oxygenation is likely preserved despite a lower-than-normal pulse oximetry reading.
- **PEEP**: This should probably be set to about 75% of the patient's intrinsic PEEP. For example, if a patient has a measured PEEPi on expiratory hold of 10 cmH_2O, consider a set PEEP of about 8 cmH_2O.

When All Else Fails...



VV ECMO

85% survival

ECCO$_2$R

100%

Crit Care 2017;21:297
Crit Care Med 2020;48:e1226
Chest 2023;163:38
J Clin Med 2024;13:895
Lung 2024;202:91

So, what happens if the patient continues to deteriorate, or fails to improve, despite all of the therapies discussed previously?

Extracorporeal support has shown promising results in patients placed on circuit for severe asthma exacerbation. For example, studies looking at the use of venovenous extracorporeal membrane oxygenation (VV-ECMO) show survival rates approaching 83-85% (compared with ECMO survival rates of around 50% for other pulmonary indications).

Extracorporeal CO_2 removal ($ECCO_2R$) is a newer therapy (conceptually, it's like a lower-efficiency form of VV-ECMO) that can help with carbon dioxide removal without needing to significantly boost oxygenation. One $ECCO_2R$ study found a 100% survival to discharge; in this cohort, 77% of patients were able to be extubated while still on $ECCO_2R$ pump. In this cohort, the most common complication was bleeding, which required transfusion of at least one unit of PRBC in about 15% of the cohort. The first commercial $ECCO_2R$ system received FDA approval in 2021.

Summary

- Rare, but exists
- Beware "normal" ABG
- Don't fix "bad" ABGs
- Epi is your friend
- Monitor NPPV closely
- Ketamine for RSI
- LOWER rates better
  - Keep heavily sedated PRN
- V_T 6-8 cc/kg IBW
- Some PEEP okay
  - ZEEP if HD compromised
- Rising $EtCO_2$ *might* be okay
- Consider ECMO referral

In summary,

- Severe, life-threatening asthma exacerbation is rare, but certainly exists
- A *normal* ABG may not be reassuring, and my represent progressive disease (starting from a baseline of respiratory alkalosis)
- Don't necessarily try to fix *bad* ABGs. Significant hypercapnia can be well-tolerated. Ideally, just try to maintain a pH of >7.15 if possible.
- Epinephrine is a great second-line agent if the patient fails to respond to inhaled beta agonists
- If noninvasive support is used, monitor these patients closely and consider invasive support if they fail to respond appropriately
- Consider the use of ketamine for RSI (or consider DSI), since it has intrinsic bronchodilatory properties.
- Lower rates are better (and desired), which may necessitate *heavy* sedation (possibly down to a RASS of -5), possibly even temporary neuromuscular blockade, to prevent overbreathing
- Target tidal volumes at least 6-8 cc/kg IBW
- Some PEEP is probably okay, consider a PEEP of around 75% of the patient's measured intrinsic PEEP; in cases of severe hemodynamic compromise, consider minimal or even zero PEEP ("ZEEP").
- Rising $EtCO_2$ might be okay, and may simply be reflective of improving ventilation-perfusion matching and clearance of the patient's hypercarbia.
- In patients with severe disease, consider early consultation to the ECMO team (or early referral to an ECMO center) for consideration of extracorporeal therapy.

Jacob Miller, ACNP, ENP-C, CNS, NRP, FAEN, FAEMS

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