LIFE THREATENING STATUS ASTHMATICUS:

Ventilatory Strategies: Treat the Patient and Not the Blood Gas

Lewis Rubinson MD, PhD
Professor of Medicine
University of Maryland School of Medicine
Assistant Chief Medical Officer
University of Maryland Medical Center
R Adams Cowley Shock Trauma Center
Site PI:
NIH sponsored multi-center influenza trial

Site PI and Protocol Working Group Co-chair:
US DHHS FDA/BARDA contract for the United States Critical Illness and Injury Trials Group Program in Emergency Preparedness (USCIIT-PREP)

Scientific/ Clinical Advisory Board Member in Past 12 Months
Ventec Life Systems Clinical Advisory Board Member
Philips/Respironics (novel mechanical ventilator platform for disasters)
Most ED visits (~75%) for asthma do not require hospitalization\(^1\)

A minority of hospitalized asthma patients (~10%) require ICU care\(^1\)
- Even fewer require mechanical ventilation (2-4%)

Inpatient mortality for asthma remains low (.5%) \(^2\)
- Mortality much higher (6.9%) if intub/mech vent
- Many asthma patients die before hospitalization

This talk will focus on the patients who require mechanical support:

Life Threatening Status Asthmaticus (SA)

\(^1\) Nanchal R et al. Respir Care 2014.
\(^2\) Krishnan V et al. AJRCCM 2006.
**LIFE THREATENING STATUS ASTHMATICUS (SA)**

<table>
<thead>
<tr>
<th>Category</th>
<th>Description</th>
<th>PEF Requirement</th>
<th>Treatment Recommendations</th>
</tr>
</thead>
</table>
| Mild          | Dyspnea only with activity (assess tachypnea in young children) | ≥ 70 percent predicted or personal best | Usually cared for at home  
                 |                                                  |                                        | Prompt relief with inhaled SABA  
                 |                                                  |                                        | Possible short course of oral systemic corticosteroids |
| Moderate      | Dyspnea interferes with or limits usual activity | 40–69 percent predicted or personal best | Usually requires office or ED visit  
                 |                                                  |                                        | Relief from frequent inhaled SABA  
                 |                                                  |                                        | Oral systemic corticosteroids; some symptoms last for 1–2 days after treatment is begun |
| Severe        | Dyspnea at rest; interferes with conversation     | <40 percent predicted or personal best  | Usually requires ED visit and likely hospitalization  
                 |                                                  |                                        | Partial relief from frequent inhaled SABA  
                 |                                                  |                                        | Oral systemic corticosteroids; some symptoms last for >3 days after treatment is begun |
| Subset: Life threatening | Too dyspneic to speak; perspiring | <25 percent predicted or personal best  | Requires ED/hospitalization; possible ICU  
                 |                                                  |                                        | Minimal or no relief from frequent inhaled SABA  
                 |                                                  |                                        | Intravenous corticosteroids  
                 |                                                  |                                        | Adjunctive therapies are helpful |

PREDICTORS OF LIFE THREATENING ASTHMA

HR > 110, RR >25, PEF <50%, Pulsus Paradoxicus >25 historically considered severe
- Not a good predictor of who will not respond to ED Tx

Perhaps better predictor is lack of peak flow improvement w/ albuterol

McFadden ER. AJRCCM 2003.
OTHER PREDICTORS OF LIFE THREATENING SA

Previous ICU admission (especially intubation)

2 or more hosp or > 3 ED visits in past year

Frequent use of SABA cannisters (> 2) per month

Poverty

Illicit drug use (tobacco use as well)

Psychiatric disease

AIRFLOW OBSTUCTION

3 S’s

Swelling
  – Airway edema

BronchoSpasm
  – Smooth muscle hypertrophy and bronchial constriction

Secretions
  – Mucus plugging
IMMEDIATE GOALS FOR LIFE-THREATENING ASTHMA

Improve airflow

Reduce and avoid hyperinflation

Reduce inflammation
MAINSTAY OF SA THERAPY

SABA
- Albuterol (inhaled)

Systemic corticosteroids
- IV when very ill

Inhaled short-acting anticholinergic
- Benefit less than SABA

May consider IV Mg
- Benefit uncertain but likely only in severe SA

May consider IV terbutaline

? Use of heliox

? When to use noninvasive ventilation (NIV)

Mechanical ventilation
- Sedation
- Paralysis
- Inhaled anesthetics
- ECMO
NON-INVASIVE VENTILATION

Benefit in COPD well established

Potential benefits in SA:
- Delivery of BDs
- Improved mechanics without ETT
- Most SA exacerbations are short duration
- Some cases of ETT worsening bronchospasm avoided
- Less HCAP

Potential pitfalls:
- Gastric inflation and worse mechanics
- Aspiration
- Urgent intubation converted to emergent intubation
- Harder to limit RR and min vent ($V_E$) if life threatening hyperinflation

Scala R Respir Care 2010.

Fig. 1. Potential goals of noninvasive ventilation (NIV) in severe acute asthma. ARF = acute respiratory failure.
Noninvasive Ventilation is an option, but it requires 2 things

1. Proper Patient Selection
2. Close monitoring
NIV BEING USED WITH INCREASING FREQUENCY

Noninvasive seems to be ok to use for a number of pts.

Again, though, pts must be watched very closely for signs of failure.
NIV AND Inv MECH VENT

Figure 1. Study cohort flow chart (criteria are not mutually exclusive). ICD-9 = International Classification of Disease, Ninth Revision, Clinical Modification; IMV = invasive mechanical ventilation; NIV = noninvasive ventilation.

Figure 3. Ventilation strategies by Laboratory Acute Physiology Score. IMV = invasive mechanical ventilation; NIV = noninvasive ventilation; vent = ventilation.

NIV IS REASONABLE FOR MANY PTS BUT MUST BE CAREFUL

pH, PaCO$_2$ range remains uncertain
  - pH > 7.2 probably reasonable

Close monitoring

Set iPAP to get Vt 6-8 cc/kg

Set ePAP (PEEP) for trigger sensitivity
  - Does pt look like trying to initiate breath and machine not delivering

Watch RR and monitor pt very closely (especially at first)
  - Re-check pH

I avoid in non-verbal pts

Avoid in hemodynamically unstable

If pt really does not tolerate mask ventilation than intubate
24 y/o woman with known asthma presents to outside ED with 3 days of worsening SOB
  - Unknown if intub in past
  - Only using SABA
  - Using tobacco

Recd albuterol, IV steroids, magnesium

Started on non-invasive ventilation (NIV)
  - Initial pH 7.15

NIV failure identified at 3 hrs
TRUE LIFE THREATENING
STATUS ASTHMATICUS

Large volume aspiration peri-intubation

Transient cardiac arrest, left needle decompression, left chest tube, then right chest tube

Paralyzed intermittently, being “hand bagged” when referred to my hospital for possible transfer
  – RR 25-30 per referring MD

pH 6.8, PaCO₂ >>100, PaO₂ 80
WHERE TO START?
pH 6.8, PaCO$_2$ > 100, PaO$_2$ 80

**Recommended to referring physician**

- Stop “bagging” pt especially stop fast rate
- NMBA paralysis
- Continuous SABA (ideally through mesh device)
- VC-AC

- Set PIP alarm very high
- RR 8-12, Vt 6-7 cc/kg
- Check Pplat and PEEP$_i$
- Ketamine for sedation
- Epinephrine if vasoactive needed
- ECMO (in this case because of sig CPR time and wanted to get to eucapnea quickly)
WHY DID I RECOMMEND WHAT I DID?
HOW DO PATIENTS WITH LIFE THREATENING SA DIE?

Hemodynamic collapse—mostly due to pulmonary hyperinflation

Barotrauma—unrecognized tension pneumothorax and collapse

Progression of anoxic CNS injury—from cardiac arrest (and possibly hypercapnea post arrest)

Most have NO irreversible sequelae from isolated hypercapnea
Induction with ketamine or propofol is reasonable
  - Caution with propofol if hypovolemic
  - Caution with ketamine if adrenergically maxed

May require intermittent NMBA to sort out initial mechanics and to maintain low RR if life threatening SA

If NIV was being used be very careful about peri-intubation aspiration

Do not manually ventilate at high rate peri-intubation

Anticipate Very High peak insp pressures (PIP) during ventilation
### CHALLENGES OF MECHANICAL VENTILATION

<table>
<thead>
<tr>
<th>Getting air in:</th>
<th>Allowing air out:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Avoiding high airway pressures</td>
<td>Higher RR to increase $V_E$ and hopefully $V_A$ will reduce $e_t$ if $i_t$ held the same</td>
</tr>
<tr>
<td><strong>Flow X Resistance</strong></td>
<td>Air trapping--- hyperinflation--- barotrauma, hypercarbia &amp; hemodynamic collapse</td>
</tr>
<tr>
<td>Vol X Elastance (lungs/chest wall/abd)</td>
<td></td>
</tr>
</tbody>
</table>

**Reducing hypercarbia:**

Want to increase $V_A$

Increasing $V_E$ (RR and Vt) may not increase $V_A$ (may even worsen)
Volume ventilation
- If PIP < $P_{\text{alarm}}$ will get set Vt
- Can have injurious pressures

Pressure ventilation
- Can limit injurious pressures and likely barotrauma (for same RR at VC)
- May more uniformly deliver inspired gas
- May get no effective Vt

Table 3. Optimal ventilator settings

<table>
<thead>
<tr>
<th></th>
<th>1–5 Yrs (n = 20)</th>
<th>6–10 Yrs (n = 13)</th>
<th>11–18 Yrs (n = 18)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Peak inspiratory pressure, cm H$_2$O</td>
<td>36 (20–45)</td>
<td>38 (26–49)</td>
<td>40 (30–60)</td>
</tr>
<tr>
<td>Rate, breaths/min</td>
<td>14 (10–20)</td>
<td>12 (10–14)</td>
<td>12 (8–12)</td>
</tr>
<tr>
<td>Inspiratory time, secs</td>
<td>1.0 (0.6–1.2)</td>
<td>1.0 (1.0–1.25)</td>
<td>1.2 (1.0–1.8)</td>
</tr>
<tr>
<td>PEEP, cm H$_2$O</td>
<td>4</td>
<td>4</td>
<td>4</td>
</tr>
</tbody>
</table>

I:E, inspiratory/expiratory; PEEP, positive end-expiratory pressure.
Data are median (range).

INITIAL VENT SETTINGS

Mode: VC-AC

Tidal Volume: 6-7 cc/kg IBW

Resp Rate: 8 - 14

FiO₂: Keep

SpO₂ > 88%

PEEP: < 80% PEEP₀
PIP vs $P_{\text{plat}}$

**Normal**
- PIP
- $P_{\text{plat}}$

**High R_{aw}**
- PIP
- $P_{\text{plat}}$

**High Flow**
- PIP
- $P_{\text{plat}}$

**Low Compliance**
- PIP
- $P_{\text{plat}}$

Interpretation of Ventilator Graphics v.1 ©2000 RespiMedu
High PIP w/ acceptable $P_{plat}$ is generally not injurious
- Like when bronchoscope inserted or prox secretion
- Can have some hyperinflated/ hypoinflated regions of lung

I usually turn the airway pressure alarm to tolerate very high PIP if necessary (again like w/ bronchoscopy)

Barotrauma tends to be correlated with elev $P_{plat}$, not elev PIP with low “ish” $P_{plat}$
CO$_2$ BASICS

PaCO$_2 \sim$ prod CO$_2$

\[
\frac{\text{VA}}{} \quad \text{VA} = V_T - V_D
\]

VA will usually increase with VE

VE is VT X RR

So we would normally want to increase either RR, V$_T$ or both for primary respiratory acidosis

CHALLENGES OF HYPERCAPNEA AND HYPERINFLATION

Leatherman J Chest 2015.
AIR TRAPPING

Inspiration

Expiration

Normal

Patient

Flow (L/min)

Time (sec)

Air Trapping

Auto-PEEP
ELEV PaCO$_2$ USUALLY DOES NOT KILL BUT HYPERINFLATION DOES

Need sufficient exp time to allow lungs to empty to near FRC for next breath

- Best way to prolong exp time is decrease RR
- Can also increase flow, reduce Vt and use square wave (constant) flow in VC-AC
- Limited addl benefit once exp time ~ 5 sec except in extreme situations

If pt does not have anoxia, another condition where worried about elev ICP, severe RV dysfunction, can usually tolerate significant hypercapnia and allow time to resolution

- “permissive hypercapnia”
In truly life threatening SA, I usually use Vol-AC, RR ~ 10, Vt 6-7 cc/kg
HOW DO YOU GAUGE WHEN/HOW TO MODIFY SETTINGS?

1) Air Trapping-due to mucus plugging and bronchospasm
   - **Exam**- Does pt finish expiration before vent initiated next inspiration?
   - **Graphics**- Does flow return to zero before next breath?
   - **End-expiratory hold maneuver**- Is there PEEP$_i$?

2) Dynamic Hyperinflation
   - **End-inspiratory hold maneuver**- What is Pplat?

In very serious SA, management as well as proper pressure measurement may require NMBA
GUIDANCE FOR VENT SETTINGS

Figure 4 – A, B. Schematic representation of airway pressure (A) and
AUTO PEEP

Occlude exhalation valve

Measure end occlusion-pre-occlusion

When Auto PEEP (PEEP$_i$-set PEEP) > 10, I get quite concerned

Laghi F et al. Minerva Anestesiol 2012
TRIGGERING WITH AUTO-PEEP

To Initiate Gas Flow, the Patient Must Generate An Effort That Exceeds the Amount of Auto-PEEP

Auto-PEEP = 8 cm H₂O
Trigger = -2 cm H₂O

Set PEEP = 0
To trigger > 10 cm H₂O
So can increase PEEP to reduce work of trigger
IS EXTRINSIC PEEP OK?

PEEP can reduce work of trigger
- ? Benefit in passive pt

PEEP could increase resistance to airflow during expiration

Theoretical benefit (work of breathing) and limited detriment up to certain levels

“The Waterfall effect”

5/8 pts with COPD or asthma had “paradoxical improvement”

Some do better, some no harm with PEEP up to a threshold (Waterfall) and some do worse.

EXTERNAL PEEP:

FOR SA I USUALLY START AT 5

IF PT W/ HIGH AUTOPEEP AND $P_{\text{PLAT}}$ I WILL INCREASE AND WATCH IMPACT ON $P_{\text{PLAT}}$
WHAT TO DO WITH RESP ACIDOSIS AND SEVERE AIRFLOW OBST?

If severe flow obstruction, elevated PEEP_{i} and Pplat >30

Severe hyperinflation can be life threatening due to development of pneumothorax and hemodynamic instability
  - Tolerate resp acidosis when life threatening hyperinflation

Need expiratory emptying
  - Best 1^{st} maneuver is to decrease RR (halving RR from 20 to 10 with t_{i} =1 sec changed t_{e} from 2 to 5 sec)

  - When RR is ~ 10, changes in flow (rate and contour) have less impact

Many will harass you to increase RR since pH low
  - When is it ok to increase RR?
PIP, PPLAT AND AUTO-PEEP BY RESP RATE

Leatherman J Chest 2015.
PERMISSIVE HYPERCAPNEA IS NOT DELIBERATE HYPERCAPNEA

I don’t maintain very low pH if patient is getting better---one has to assess

Use the pt-vent interaction data to inform the ventilator settings

If Pplat < 25 and Auto PEEP < 5, and flow getting back to zero

I consider increasing RR (eventually decision about NMBA and level of sedation) based on how pt tolerates of increasing $V_E$

Then recheck AUTO-PEEP and $P_{PLAT}$ after changes and periodically
Caution about using EtCO\textsubscript{2} changes as reflective of PaCO\textsubscript{2}

- When severe hyperinflation improves, EtCO\textsubscript{2} may increase and PaCO\textsubscript{2} decrease
- In other words pt may have safer physiology and higher EtCO\textsubscript{2} (since dead space improving)

\[
V_D/V_T = (P_{aCO_2} - P_{ECO_2})/P_{aCO_2}
\]

OTHER ADJUNCTS WHEN THE PATIENT IS VERY ILL
HELIOX

Mixture of helium: oxygen with low density

May improve turbulent flow especially in distal airways
- Theoretical reduction of $R_{aw}$

May improve BD effect as carrier for neb

13 pts with auto PEEP $\geq$ 8 cm H$_2$O

30 min after same settings but now w/ heliox (70:30 or 65:35)

<table>
<thead>
<tr>
<th>Table 1. Airway Pressures and Arterial Blood Gases During Ventilation With Air-O$_2$ and Heliox</th>
</tr>
</thead>
<tbody>
<tr>
<td>Variable</td>
</tr>
<tr>
<td>---------------------------</td>
</tr>
<tr>
<td>$P_{peak}$, cm H$_2$O</td>
</tr>
<tr>
<td>$P_{plat}$, cm H$_2$O</td>
</tr>
<tr>
<td>Total PEEP, cm H$_2$O</td>
</tr>
<tr>
<td>pH</td>
</tr>
<tr>
<td>$P_{acCO_2}$, mm Hg</td>
</tr>
<tr>
<td>$P_{ao2}$, mm Hg</td>
</tr>
</tbody>
</table>

Leatherman J et al. Respir Care 2017.
Fig. 1. Peak airway pressure (A), plateau airway pressure (B), and total PEEP (C) for individual subjects (N = 13) during ventilation with air-O₂ and heliox.
Fatal cases of asthma can have tenacious mucus

Bronchoscopy can be considered but not always essential to therapy


Marini JJ Crit Care Med 2006
ECMO “RESCUE”

Potential benefit:

- Minimize injurious ventilation settings since extracorporeal gas exchange (V-V)
  • Can more safely perform bronchoscopy if near-fatal airway obstruction with mucus
  • Can achieve timely eucapnea post-arrest or other reasons where elev PaCO₂ very undesirable

- If post arrest hemodynamic issues can also provide hemodynamic support (V-A)
~ 170 adult pts/ yr

V-V (~60 %)

1) ARDS
   - “Early” dz ≤ 7-10 days mech vent
   - P/F < 50 for > 3 hrs and no response to adjuncts
   - P/F < 80 for 6 hrs and no response to adjuncts
   - pH < 7.2 with RR 35 (or less with sig air trapping) and Pplat > 35

2) Bridge to transplant
3) Traumatic pneumonectomy
4) Inability to vent w/ large BPF or Refractory status asthaticus

BASIC PERIPHERAL ECMO CONFIGURATION

1) **Drains** blood from large central vein (V-)
2) CO$_2$ removed, O$_2$ added
3) Blood temp controlled
4) **Returns** to central vein/RA or artery (-V or –A)


ECCO$_2$R

CO$_2$ removal requires much less flow than trying to oxygenate refractory hypoxemia

Hence can have smaller cannulas and much lower flow and use sweep gas to remove CO$_2$

Anticipate such technology available in the US in the near future
Recommended to referring physician

- Stop “bagging” pt especially stop fast rate
- NMBA paralysis
- Continuous SABA (ideally through mesh device)
- VC-AC

Set PIP alarm very high
- RR 8-12, Vt 6-7 cc/kg
- Check Pplat and PEEP
- Ketamine for sedation
- Epinephrine if vasoactive needed
- ECMO (in this case because of sig CPR time and wanted to get to eucapnea quickly)
1. Severe SA failing initial therapies is a small but high consequence subset of asthma exacerbations

2. If one uses NIV, pt selection and close monitoring is crucial

3. PIP and PaCO₂ in isolation are not the targets

4. The pts level of obstruction will determine the initial vent settings
   Pplat and AUTO-PEEP

5. Patience is key since strategies to correct gas exchange may actually injure or kill the patient
   More rapid reduction in PaCO₂ is only needed in certain cases

6. The pts level of obstruction will determine the weaning course
Questions?

Lewis Rubinson
lrubinson@umm.edu