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The Use of NAVA in severe BPD: Friend, Foe or Both?

Megan Lagoski, MD
Director of Lurie BPD Program
Assistant Professor of Pediatrics
Lurie Children's Hospital of Chicago
Feinberg School of Medicine/Northwestern University

BEST CHILDREN'S HOSPITALS U.S.News & WORLD REPORT HONOR ROLL

MAGNET RECOGNIZED AMERICAN NURSES CREDENTIALING CENTER

Disclosures

- I have nothing to disclose

VS

Our Program

- 65-80 referrals annually for chronic respiratory failure
  - Average length of stay = ~110-130 days after transfer (many transferred after 40 weeks gestation)
- Surgical breakdown:
  - 15-18 patients <32 weeks with severe BPD are discharged home on mechanical ventilation and with tracheostomies per year
  - Average PMA at trach insertion: ~49 weeks
  - Almost patients with tracheostomy get a g-tube (eventually)
  - Very few fundoplications (<5/year in NICU)
- Our team: 6 neonatologists on primary BPD service
  -- Weekly patient reviews
  - Weekly developmental rounds

Outline

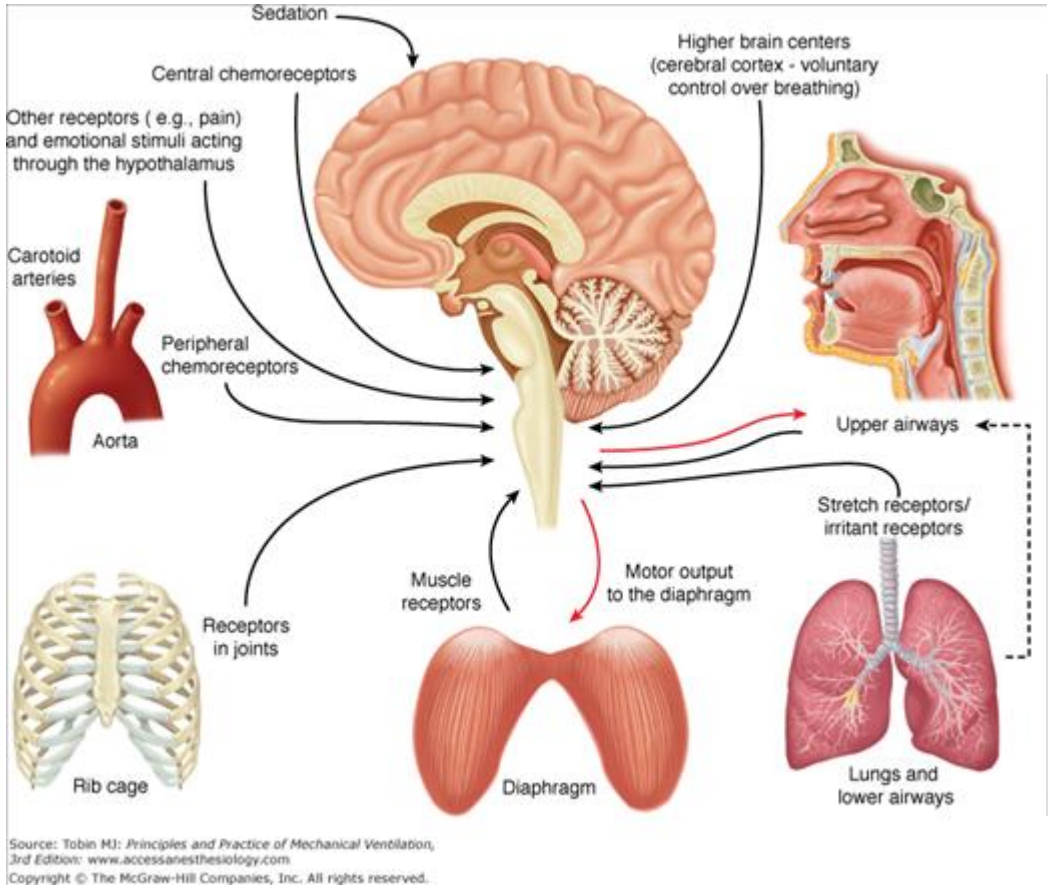
- Review
  - mechanics of spontaneous breathing and breathing on a ventilator
  - How NAVA works (invasive and non-invasive)
  - Pathophysiology of BPD: why NAVA should or shouldn't work
  - Available literature of NAVA use in severe BPD
- Non-Invasive NAVA in established BPD: Defining success and failure
- Invasive NAVA: Success and failure as a rescue therapy in established severe BPD
- Lessons learned: Setting the Intention

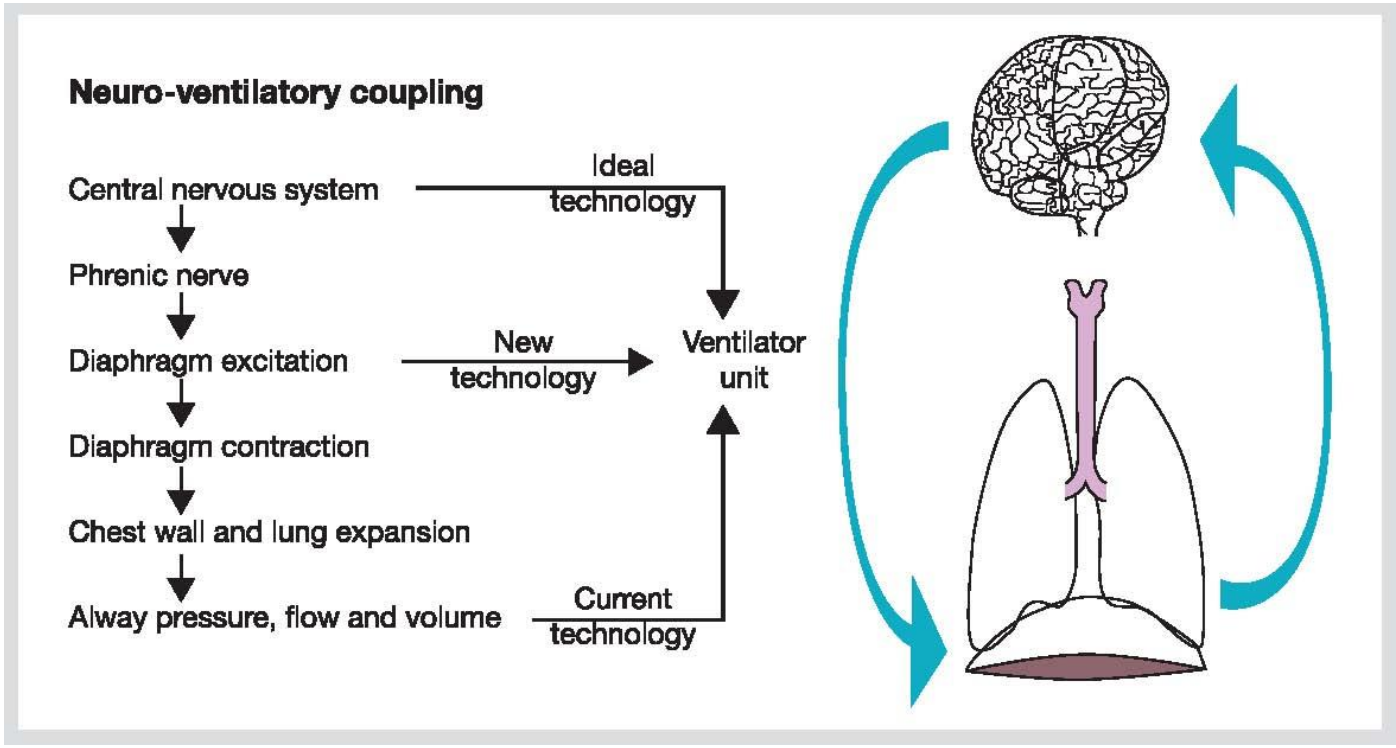
General info

- I am not here to convince anyone to use invasive or non-invasive NAVA
- We often use NAVA as a "rescue" therapy in patients with established BPD
- We have no idea how to get patients off of NAVA in a timely manner
- I used to believe that patients failed NAVA only because a provider skilled at transitioning someone to NAVA was not present
- Like so many therapies, defining success is difficult, and short-term success may not translate to long-term success

- This lecture is discussing NAVA for patients with *established* severe BPD/grade 2/3.

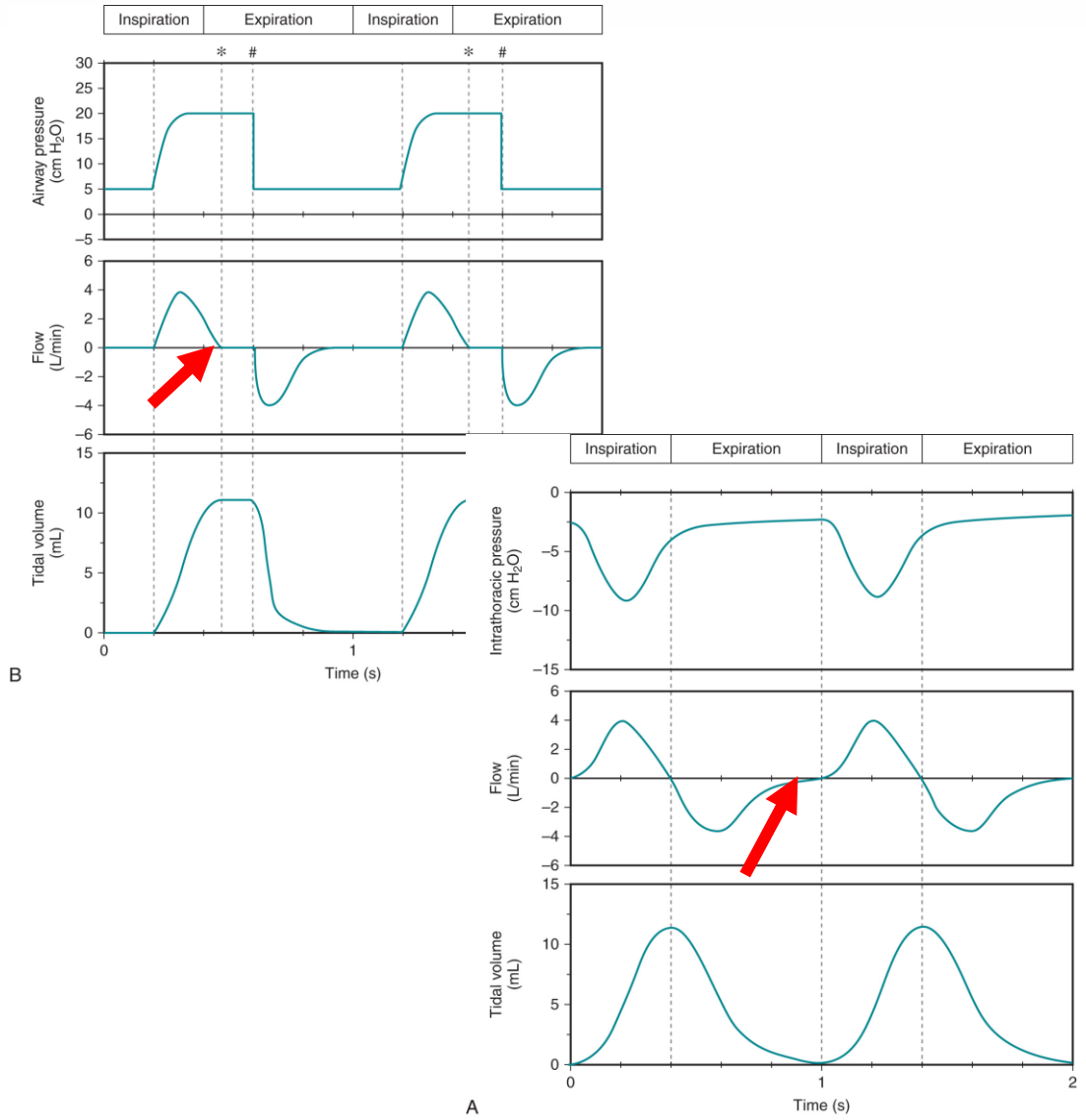
Control of breathing is complex and breaths vary based on needs and feedback from the body and environment





Breathing in and out is complicated

- Main driving force is diaphragm → contraction →expansion of thoracic cavity → decreasing intrathoracic pressure
- Inspiration ends when flow returns to zero and lung is hopefully filled to desired Vt. Depends on:
  - PIP
  - Inspiratory gas flow
  - Pressure-flow waveforms (indicates compliance of respiratory system and resistance of airways)
- Expiration ends when lung empties the inspired gas and depends on:
  - Chest wall elastic recoil
  - Expiratory resistance
  - PEEP



How does a patient trigger a ventilator breath?

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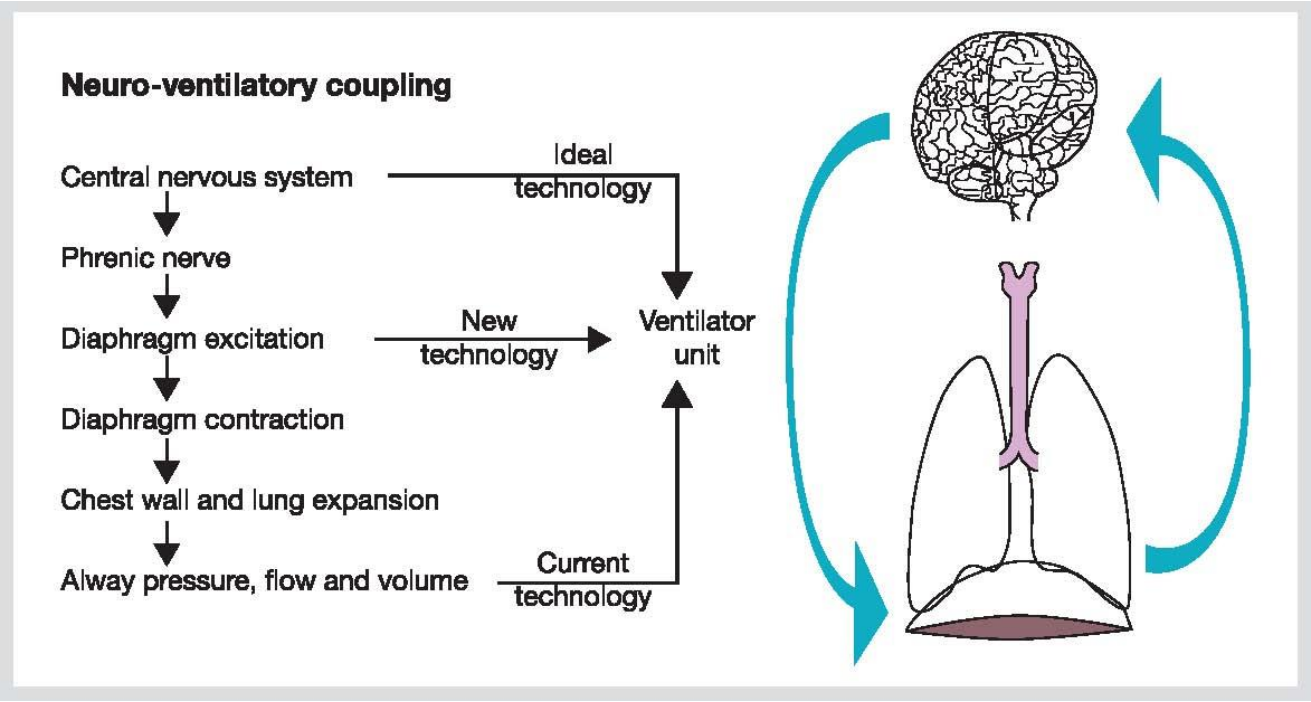
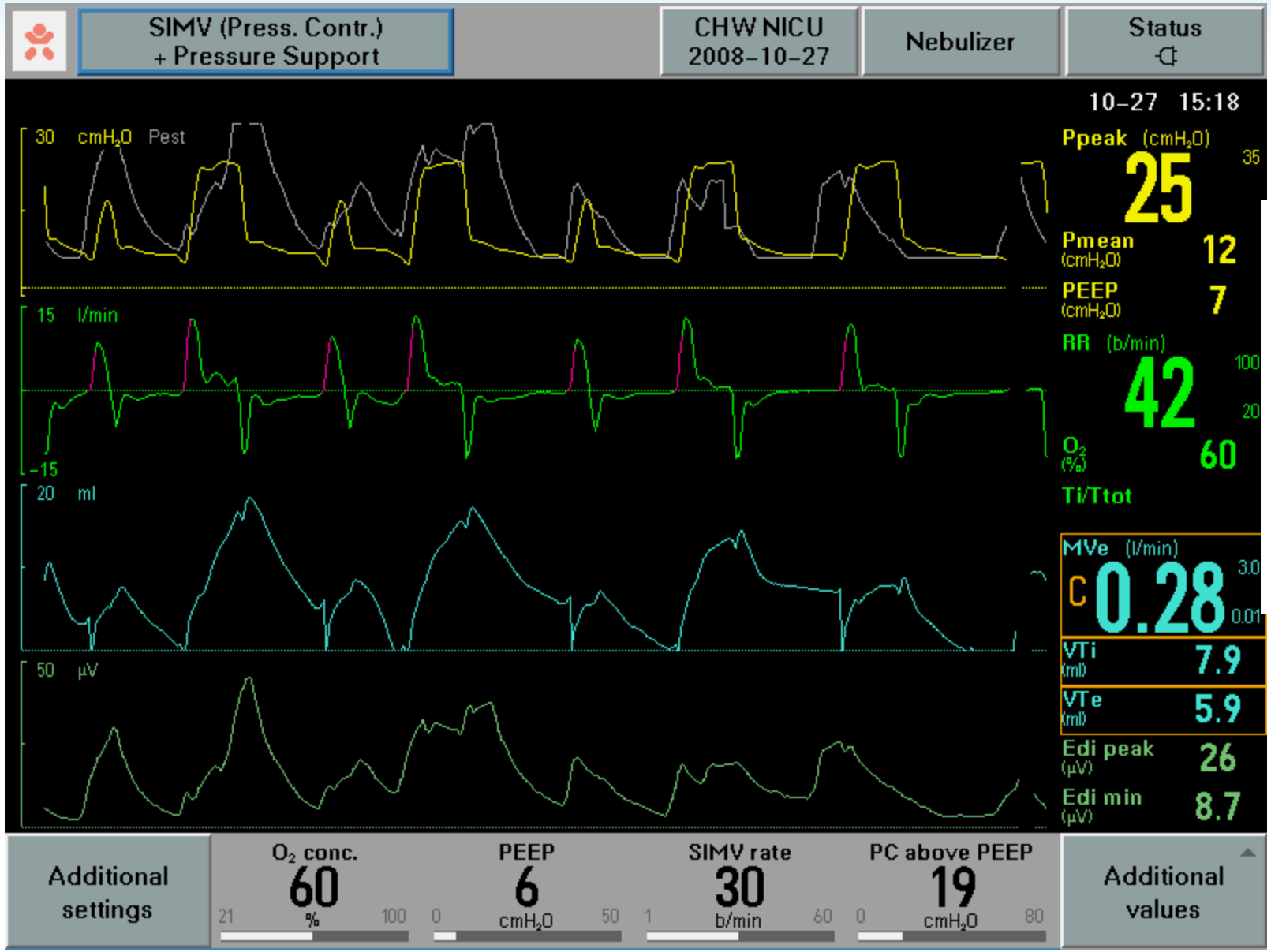
- Three trigger variables exist for conventional ventilation:
  - Time: Ventilator will initiate a new breath at set intervals regardless of patient efforts (used in IMV or PRVC)
  - Pressure:
    - Oldest technology, took IMV to **S**IMV
    - Baseline pressure drops to allow ventilator to sense the attempt at inspiration
  - Flow:
    - More sensitive and used in most modern ventilators
    - Senses a decrease in flow that happens before initiating a breath even with a leak in the system

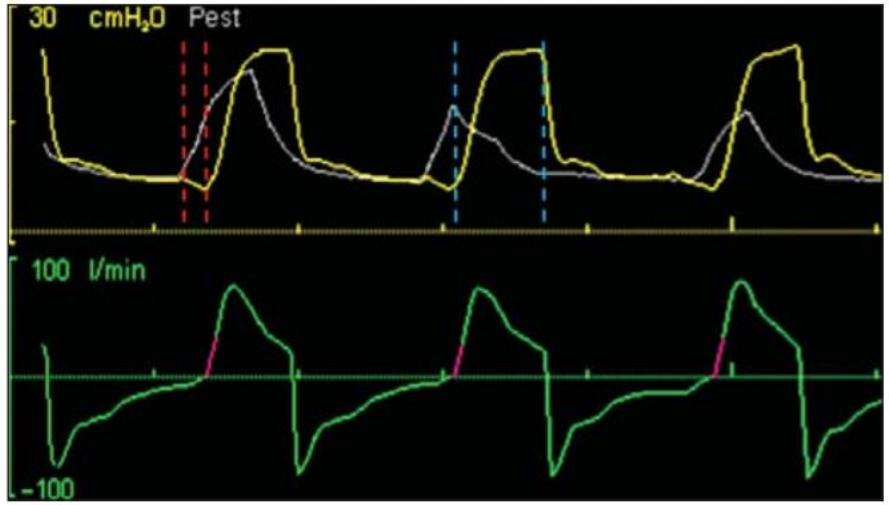


- NAVA senses diaphragm excitation and delivers a breath.
  - Delay is microseconds
  - Allows variability between breaths and sighs

Sinderby C, Navalesi P, Beck J, Skrobik Y, Comtois N, Friberg S, Gottfried SG, Lindstrom L. 1999. Neural Control of Mechanical Ventilation in respiratory failure. Nat. Med. 5:1433-1436.

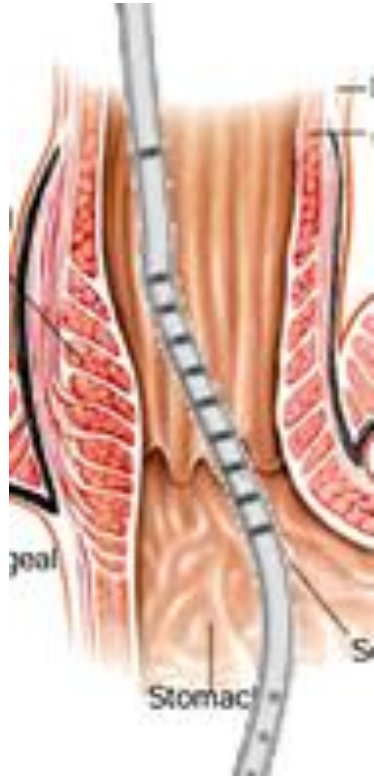
SIMV PC & PS with NAVA Preview





Neurally Adjusted Ventilator Assist

- The patient (specifically the brain) decides when and how to breathe
- Mode of ventilation that triggers based on **electrical activity** of the diaphragm (Edi signal)
  - Edi signal measured with specialized NG tube connected to the ventilator
- Provides support to a patient's spontaneous breaths based on the electrical activity of the diaphragm
  - Volume and duration of breath determined by electrical activity
- Servo-I and Servo-U (and N but we don't have those)
- Invasive and Non-invasive modes



Patient Selection

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- Who can go on NAVA?
  - Spontaneously breathing patients
  - Working diaphragm
  - >500 g
  - Ability to place NG/OG
- Who can't go on NAVA?
  - Paralyzed patients
  - Esophageal bleeding
  - Inability to place NG/OG
  - Absent electrical signal from brain
  - Abnormal diaphragm signal (phrenic nerve injury, absence of a diaphragm)

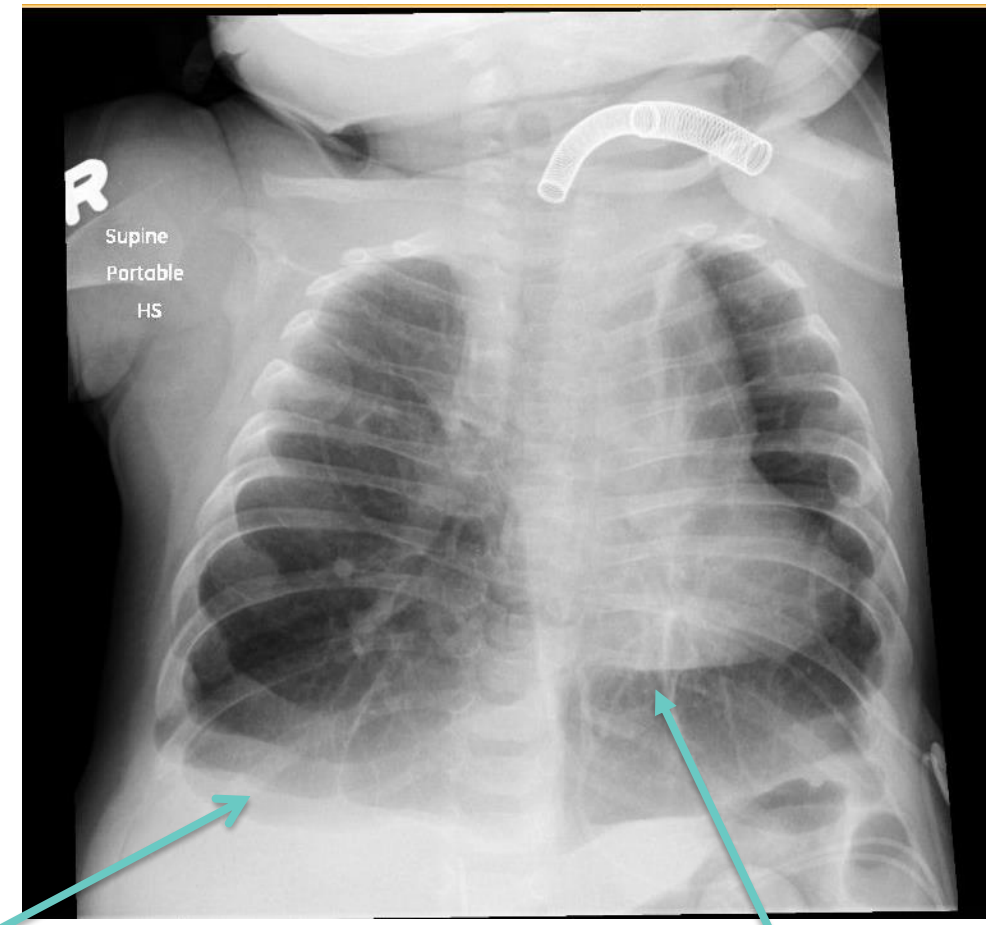
Selecting settings on NAVA

- NAVA level
  - should be set to achieve an Edi peak range of 5 to 20 μV
  - majority of time spent in the 10-15 range
  - Levels usually set between 0.5 to 3 (except for special circumstances)
  - The higher the level, the less work the diaphragm does
  - Pay attention to the "break point" – NAVA level increase results in Edi peak decrease rather than increase in support
- PEEP
  - Typically set to level equivalent to conventional vent
  - Monitor Edi min with goal of maintaining 0.5-2 μV
- Trigger
  - Measured in μV and usually set at 0.5 μV
  - If Edi mins are high, and sensitivity of trigger are low, diaphragm movement may auto-trigger a breath
- Apnea time
  - 2-10 seconds
  - Set higher for older patients who should breathe slower

Why should NAVA work in our BPD patients?

- Needs are often dynamic and an aging infant can have many states
- Synchrony can be challenging
  - If enough obstruction to flow exists, patients are unable to trigger the vent which can make stability challenging

- NAVA delivers *synchronous* breaths *in proportion* to the patient's spontaneous breathing efforts
  - Tidal volume/PIP and flow are variable and controlled by the patient and the NAVA level.



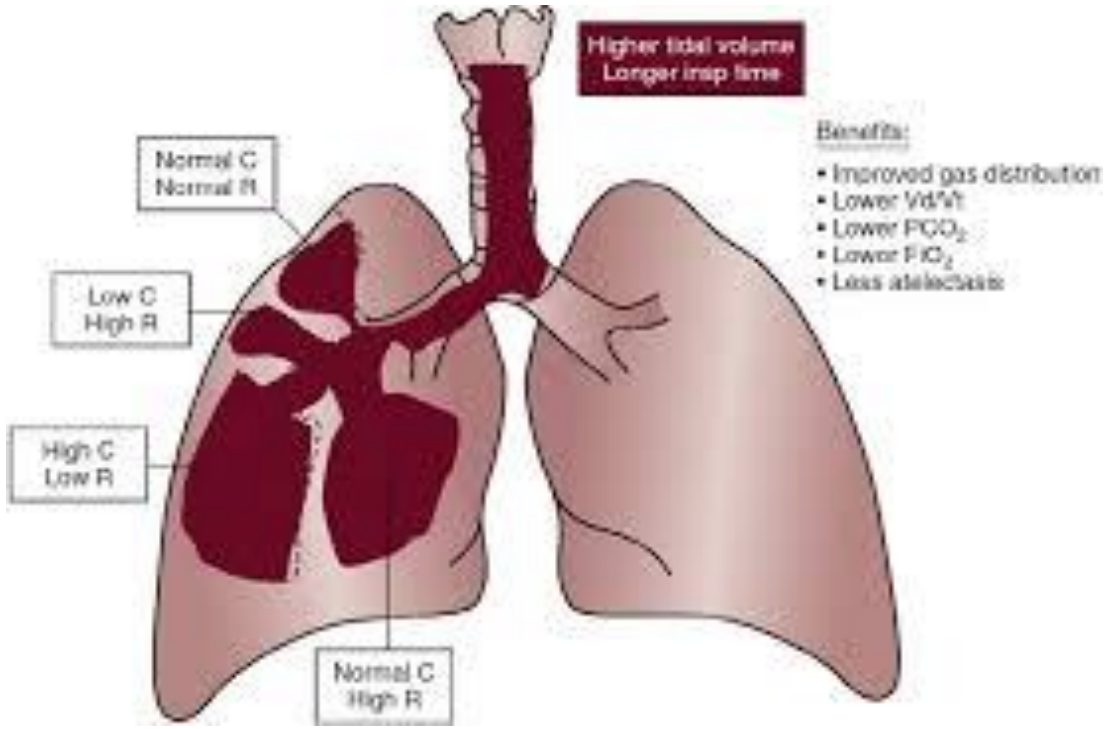
Flattened/inverted diaphragm

"Floating heart"

Why *wouldn't* NAVA work on BPD patients?

- Will patients regulate their i-time and volume to ventilate both healthy and unhealthy portions of the lung?
- In the areas of the lung that are slower to empty, will they regulate their rate to allow sufficient time to empty?

- Babies may get what they want, but do they get what they NEED?



Literature regarding NAVA in BPD

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Respiratory physiological changes post initiation of neurally adjusted ventilatory assist in preterm infants with evolving or established bronchopulmonary dysplasia

Basma Mohamed[1] · Anay Kulkarni[1] · Donovan Duffy[1] · Anne Greenough[3] · Sandeep Shetty[1,2]

Received: 17 November 2024 / Revised: 15 January 2025 / Accepted: 18 January 2025 / Published online: 29 January 2025

- 30 infants with established BPD
- CO_2 clearance and Oxygenation improved 48 hours after initiation
- Results similar when divided into NAVA vs NIV NAVA

Neurally adjusted ventilatory assist for infants under prolonged ventilation

Juyoung Lee,[1] Han-Suk Kim,[2] Young Hwa Jung,[2] Chang Won Choi[2] and Yong Hoon Jun[1]
[1]*Department of Pediatrics, Inha University College of Medicine, Incheon and* [2]*Department of Pediatrics, Seoul National University College of Medicine, Seoul, Korea*

- 14 patients
- Less steroid use
- Less sedation used

Crossover study of assist control ventilation and neurally adjusted ventilatory assist

Sandeep Shetty[1] · Katie Hunt[1] · Janet Peacock[2,3] · Kamal Ali[4] · Anne Greenough[1,3,5]

- 9 patients
- 1 hour on NAVA
- ALL had reduction in OI and MAP

Multicenter Experience with Neurally Adjusted Ventilatory Assist in Infants with Severe Bronchopulmonary Dysplasia

Robin L. McKinney, MD[1] Martin Keszler, MD[2] William E. Truog, MD[3] Michael Norberg, BS, MDiv[4]
Richard Sindelar, MD, PhD[5] Linda Wallström, MD[5] Bruce Schulman, MD[6] Jason Gien, MD[7]
Steven H. Abman, MD[8] and on behalf of the Bronchopulmonary Dysplasia Collaborative

- 4/13 centers used NAVA
- 67% of infants had stability on lower level of support
- Indications and strategies for using NAVA is highly variable among centers

Evidence of Non-invasive NAVA (NIV-NAVA) for BPD

Me looking for articles and not finding them

What question do we want answered?

- Can we avoid reintubation/tracheostomy?
- Time to liberation from respiratory support?
- Most studies are geared toward "evolving" BPD so ages at use were <28 days
- Is it better than CPAP (with same interface?)

Evidence for NIV-NAVA and COPD

- Decreases mortality and need for intubation
- Provides better synchrony (obvi)
- Interface is important!
- All are short term effects

So how do we select who should go onto NAVA?

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Does your patient have established BPD?

no

This lecture is not for you. However, if baby needs time before next extubation attempt, this is a reasonable option.

yes

Is your patient extubated or will extubate?

yes

Have you accepted the religion of Bubble CPAP?

yes

Me too, sister. However, bigger babies have interface woes, and if you've found the solution, find me later.

no

You probably should rethink this, but in this case NAVA is definitely for you.

no

Is your patient stable on current conventional support and comfortable?**

no

Consider the phenotype of BPD and then consider rescue NAVA especially if the goal is stability

yes

If getting tracheostomy and eventual portable ventilator, reasonable to continue conventional ventilation

**i.e. you tried all appropriate BPD settings including PEEP adjustments, low low rate, higher tidal volumes, long i-time and the baby still just cannot exist without heavy sedation and/or paralysis, or you tried all that and the baby is now delirious

Non-invasive NAVA: How to define success?

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NIV-NAVA in patients with BPD

- Case 1:
  - Former 28 week SGA infant now 2.5 months old, extubated for 1 month
  - "Could not tolerate bubble CPAP"
  - On ram cannula, tachypneic and dyspneic
  - Had worsening of respiratory distress over 2 weeks so was transitioned to bubble CPAP with improvement in respiratory status
  - PT/OT/SLP had limited interactions, and he was noted to have progressive sensitivity to touching his face, BSRIs 3-5 (when able to perform), could not wean sedation and kept breaking the seal on the mask
  - After 2 weeks, he was trialed on NAVA via cannula
  - NAVA level started at 3, quickly escalated to 4
  - Edi peaks solidly in the 30s, Edi mins all over the place

The good . . . and the bad

- All nurses reported the baby was more comfortable, and they were happier
- Rehab therapists were reporting better BSRIs (6-7)
- Therapies could last longer
- It was easier to move him
- Sleep/wake cycles were improved
- Echocardiograms were stable
- Linear growth was maintained
- Sedatives were discontinued soon after initiation

- Respiratory histograms were shifted with more tachypnea and mild retractions
- BSRI points taken off were due to work of breathing
- He needed breaks to recover from the tachypnea during his therapies
- It was hard to figure out when to wean the NAVA level and by how much
- It took 3 more months to get to a low flow cannula

Success?

Ultimate success

- Patient went home at 8 months of age on 0.5L nasal cannula without needing a tracheostomy
- His developmental skills were appropriate for age
- He was able to experience Costco on the way home

The interface woes of NIV-NAVA

- NAVA is designed to allow for leakage in the system so can be given through a cannula, BUT . . .
  - Most cannulas have a high resistance circuit resulting in lower flow at the patient despite increasing levels of "PEEP"
  - Synchrony may enhance minute ventilation, but maintaining/recruiting FRC effectively depends on interface
  - Numbers on the ventilator (Edi min/peaks, PIPs, tidal volume) are difficult to interpret
  - You can't determine success by numbers only
- NAVA can be given through a nasal mask and prongs, and may provide more support, BUT
  - Orogastric catheters may need to be placed to maintain a seal but may move more especially the bigger the baby
  - Nasogastric catheters may disrupt the seal
  - The bigger the baby, the harder a seal on the mask can be to maintain

Invasive NAVA: Can we given the patient what they want AND need?

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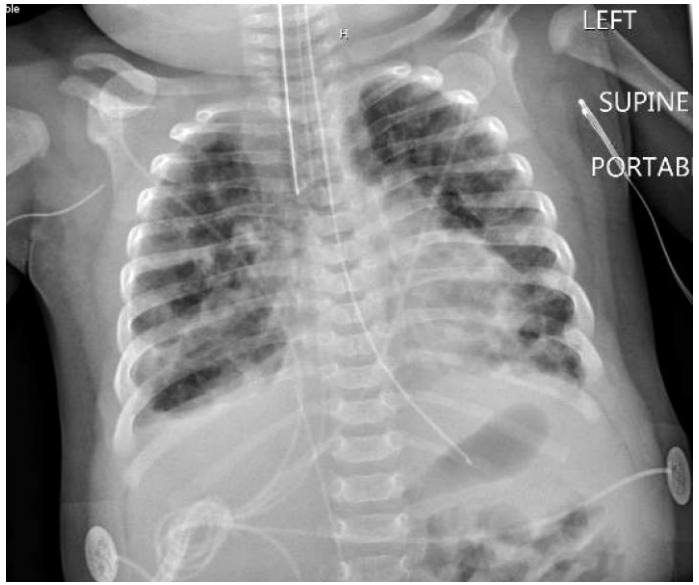
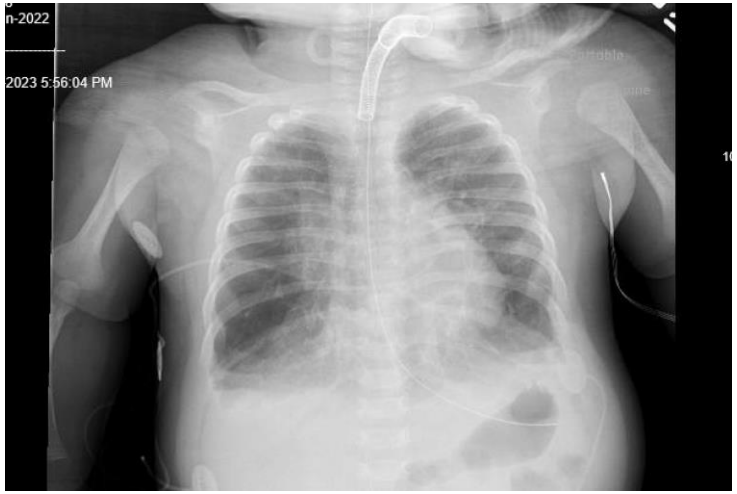
Case #2: EB

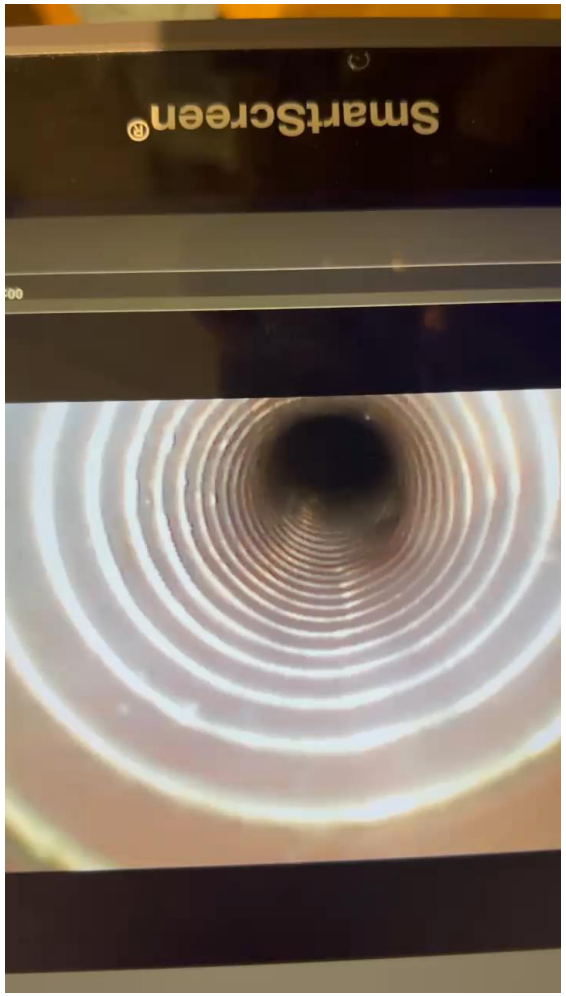
- Former 26 week AGA infant, twin
- Multiple intubations and extubations attempts over hospital course prior to transfer
- She was on heavy sedation with persistent need for FiO2>60% and frequent desaturation events and "agitation"
- After transfer, pt was quickly weaned off of iNO and milrinone with echo demonstrating mod. RVH, preserved function
- Vent settings changed to PEEP 12, low rate, higher i-time, etc, still with high FiO2
- Palliative care consulted with plans for deep sedation (paralysis unsuccessful and delirious on multiple sedatives) to get through tracheostomy and patient initiated on pentobarbital drip.





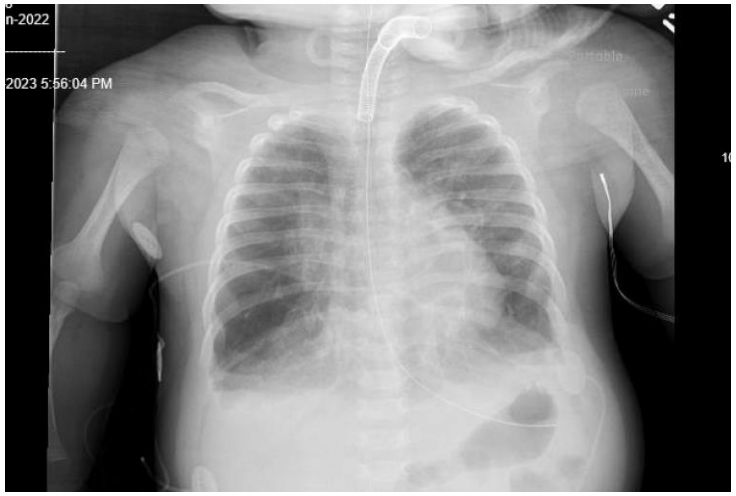
Peri-tracheostomy

- Pentobarbital drip titrated upward to reach desired sedation and stop Versed
- FiO2 decreased to 55% on day of tracheostomy
- After tracheostomy, pt was started on analgesic infusion (hydromorphone) and maintained on pentobarbital
- FiO2 requirement steadily rose to 100% with frequent desaturation events
- Attempts to muscle relax were unsuccessful again
- Bedside tracheoscopy demonstrated posterior wall collapse so PEEP increased to 14 and then 16.

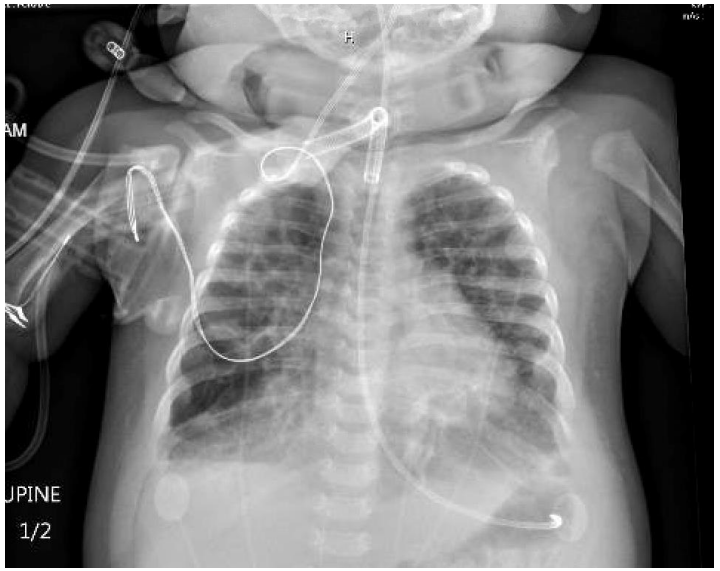


Events leading up to initiation of NAVA

- Despite higher PEEP, low rate, high tidal volume (>15 ml/kg) pt had significant dyssynchrony with vent and episodes of air hunger not improved by increasing sedation.
- EEG performed due to rhythmic movements (gasping against vent)
- Beta-agonists were trialed along with pulse steroids
- WHEN ALL FAILED, we switched to NAVA, level 5, PEEP 14.

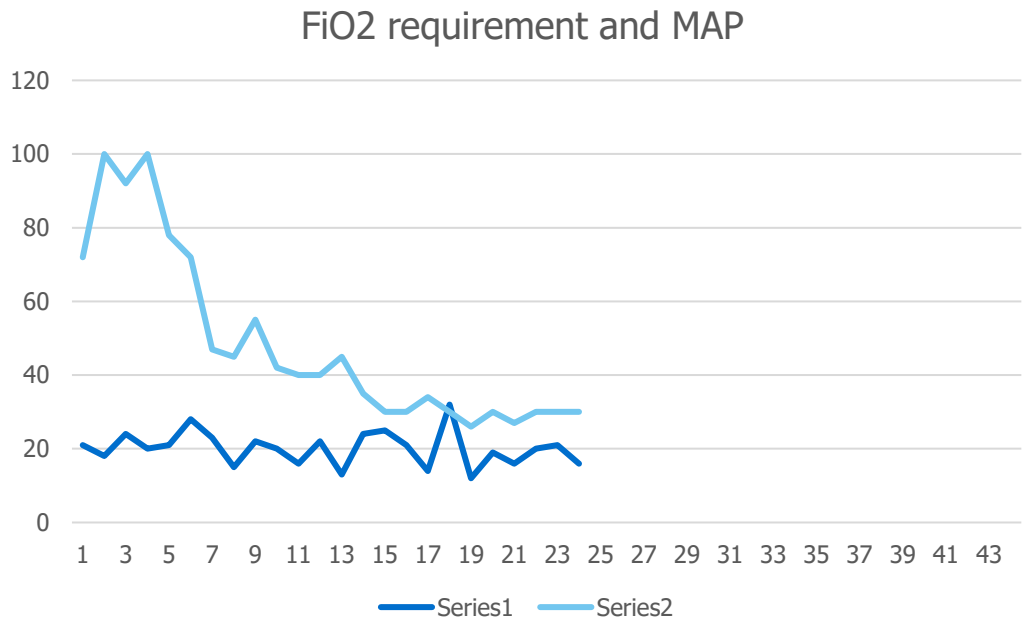


Prior to NAVA

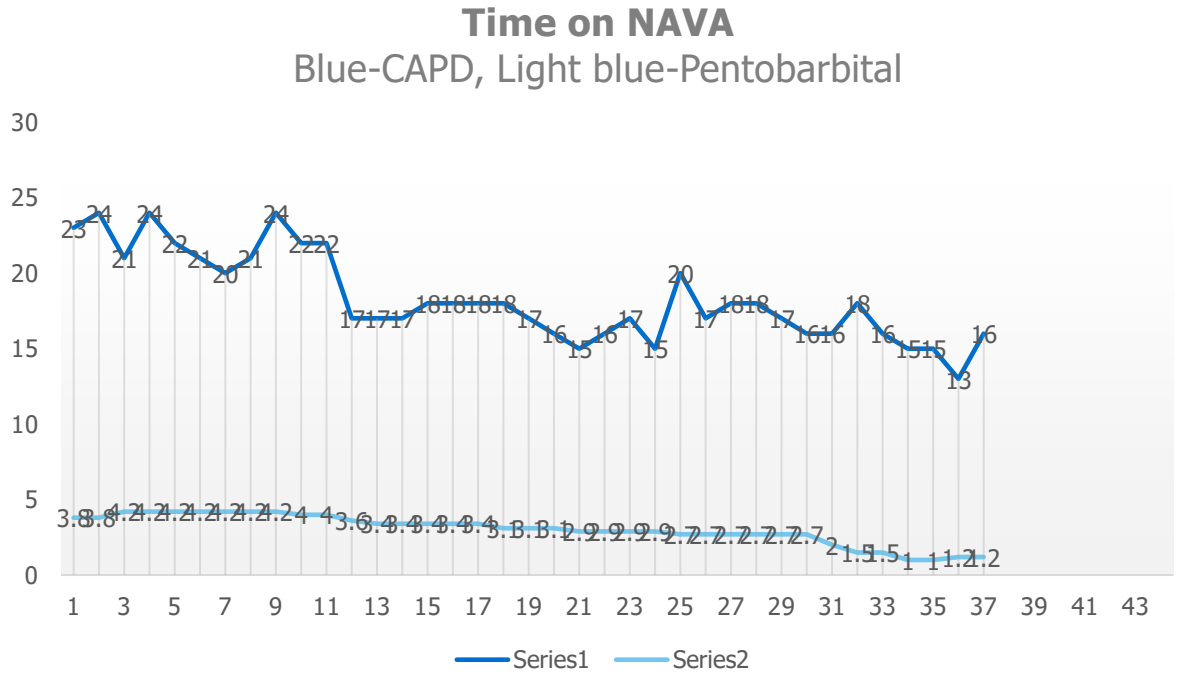


3 days after NAVA

Case progression



- Heart rate came down
- Saturations came up
- Gasping stopped
- CO2 went from undetectable to detectable



Case 2 (cont)

- On NAVA for a month
- She was eventually switched back to PRVC SIMV when she was found to be going into backup mode and remained on low FiO2, stable vent support with improved vent synchrony
- Able to transition off of Pentobarbital infusion to intermittent phenobarbital dosing
- Transitioned to portable ventilator 3 months later.*

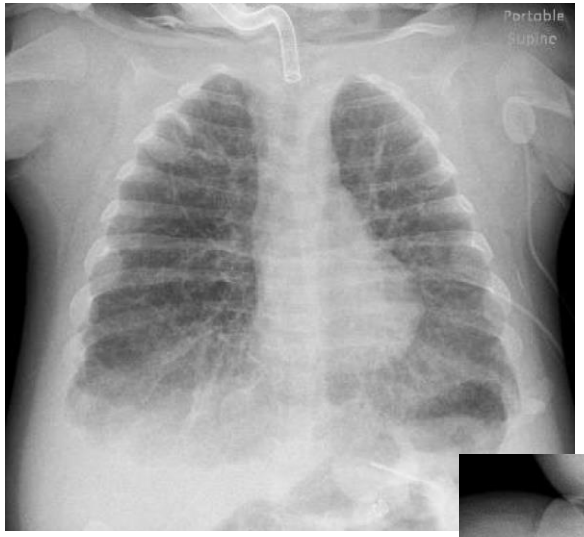
* She would have been discharged 3 months after conversion to home vent but caught rhinovirus, tried to die, and spent the next year in the ICU requiring a tracheopexy to be able to transition to portable ventilator. THEN she went home.*

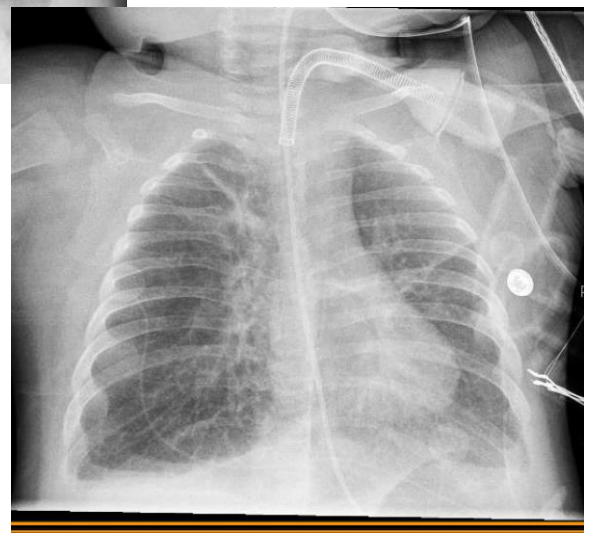
Case takeaways/points of discussion

- This was a rescue mode for this patient
- Allowed for decrease in sedation and better stability
  - Decreased FiO2 requirement
  - Stable amount of hyperinflation
  - Facilitated wean of deep sedation
  - Delirium scoring improved
- Pitfalls
  - Still had hyperinflation
  - Still had some ventilator dyssynchrony

Case #2: The one we couldn't get off NAVA

- Pt was IUGR 27 week twin infant on high vent support since birth, transferred to us at 3.5 months
- She had persistent hyperinflation and high FiO2 requirement (and sedation dependence)
- Able to get to 50% FiO2 with 15ml/kg volumes and low rate but had static hyperinflation and vent dyssynchrony
- Parents refused sedation +/- paralysis trial (mother wanted to focus on developmental therapies), so she was converted to NAVA, level 4, PEEP 15 (~5 months of age)





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Time on NAVA

- After 4.5 months on NAVA, and 3 failed attempts at conventional ventilation, she was started on scheduled PRVC SIMV-VG trials during the day that progressively lengthened.
- After 5 months, she was able to successfully transition to conventional ventilation.

Success?

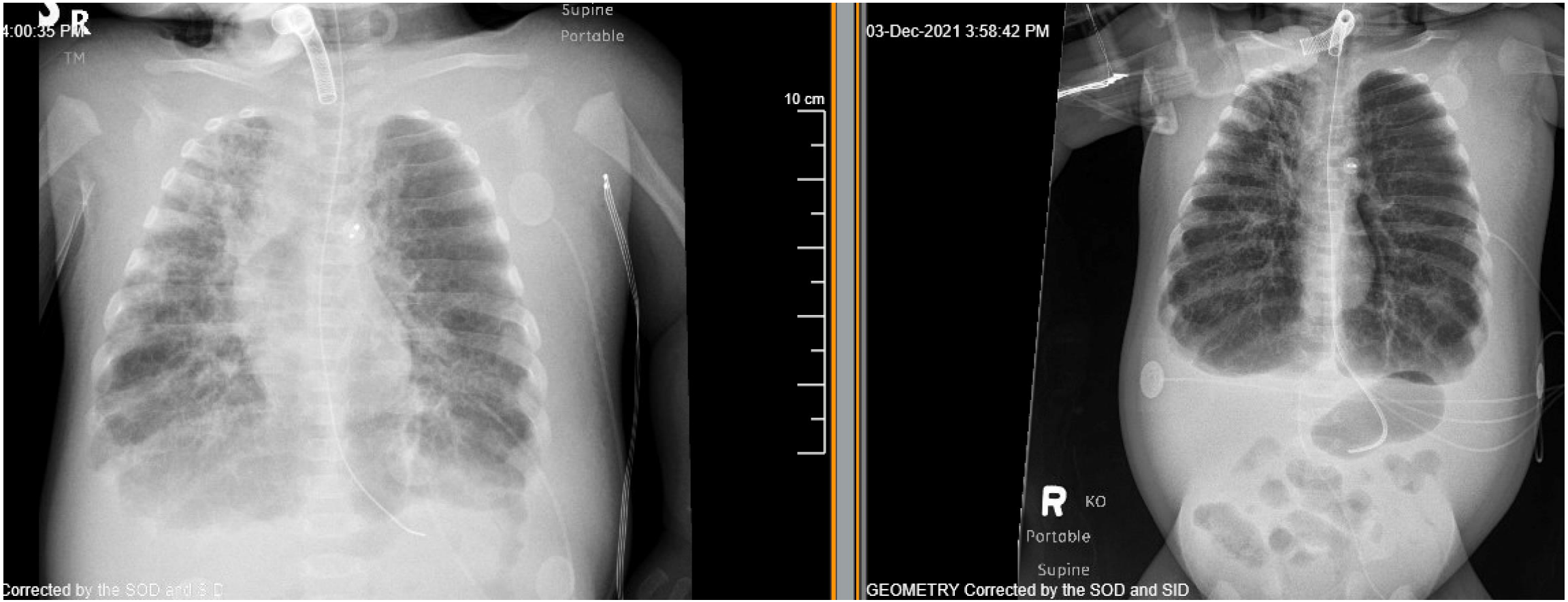
- Pros
  - She was able to work with rehab services ~4-5x/week (BSRI scores improved drastically after switching to NAVA)
  - She was able to wean off of sedation and avoid paralysis
  - After 5 months, despite persistent hyperinflation, she was able to trigger the ventilator
- Cons
  - She spent 5 months on a mode of ventilation that did not help her convert to the home ventilator (celebrating her 1st birthday in the NICU)
  - She had to have an (expensive) NG tube replaced *at least* 30 times despite having a g-tube that could be used for feedings

Case #3-LS, The NAVA Failure

- LS was the surviving 25 week twin referred at 3 months for a PDA occlusion with sBPD.
- Noted to have hyperinflation early in hospital course and difficulty triggering the ventilator
- Severely obstructive phenotype (no significant response to beta agonists) and early development of severe head and neck edema
- Had difficulty weaning off of sedation and eventually had prolonged course of sedation and paralysis
  - Decreased respiratory rate to 12
  - Aggressive diuresis
  - Allowed for tracheostomy to be performed
- After tracheostomy, paralysis was lifted but needed significant sedation due to continued asynchrony with the ventilator.
- PEEP titration via bronchoscopy did not lead to any improvement
- Pt was placed on NAVA, level 4, with rapid improvement in level of comfort.

Then this happened…

- After 6 hours on settings, he was noted to have more bradycardic events but otherwise stable blood pressures.
- After 18 hours, pt noted to have more bradycardic events and developed hypotension and low urine output



Case progression

- We tried one more time with higher NAVA level but had the same issue arise again (to a lesser degree)
- SO, we settled in for a long hospital course including
  - Prolonged deep sedation: >6-8 weeks without ability to wean sedation and maintain any awake state.
  - VERY VERY slow wean of sedation
  - Very gradual improvement
  - Hospitalized until 2+ years old, discharged with home ventilator

Common problems encountered in "rescue" NAVA and potential solutions

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- Patients breathe faster/have more breaths delivered
- Starting with a lower NAVA level and titrating upward can cause tachypnea and worsen the cycle of ineffective ventilation and air trapping
- NG placement may be different than standardized measurements-especially if hyperinflated lungs
- The vent kicks into backup mode especially while asleep and everyone is getting alarm fatigue
- Pmax alarms happen several times in an hour, day, etc

- Monitor for air trapping with x-rays, trends on vent, edema
- Start with a higher NAVA level and work downward (maybe 3-4). Watch for a break point and monitor numbers while awake before adjusting
- If Edi peaks/mins read low and infant is working hard to breath, the catheter is not in right position until proven otherwise
- Make sure apnea time is appropriate for age and disease process (could be 10 seconds)
- If infant is bigger, likely needs pediatric mode and pmax may be 60-80 for sigh breaths

So should we use NAVA as a rescue?

- Who is the ideal candidate? What phenotype of BPD?
  - Obstructive
    - Large airways
    - Small airways
    - Combination of the above
    - Poor supportive structure within the lungs/parenchymal disease
    - All of the above?
  - Restrictive
  - Combined
- What metrics can we collect to decide the benefit?
  - Number of successful therapies
  - Time to conventional vent synchrony
  - Delirium symptoms
  - Amount of sedation

Conclusions

- When deciding to use NAVA as an alternative therapy, one must decide *why* they are using it and set goals.
  - Overall stability
  - Ability to decrease sedation
  - Ability to tolerate and benefit from therapies
  - Optimal cardiorespiratory interactions/hemodynamic stability
  - Maintain adequate growth
- Do these benefits outweigh the risks?
  - Difficulty converting to home/portable vent
  - May not improve hyperinflation
  - May worsen hyperinflation and contribute to ongoing dyssynchrony
  - Repeated insertion of NG catheter a noxious stimuli for a developing patient who may already have a g-tube

So how do we select who should go onto NAVA?

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Does your patient have established BPD?

no

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yes

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yes

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yes

Me too, sister. However, bigger babies have interface woes, and if you've found the solution, find me later.

no

You probably should rethink this, but in this case NAVA is definitely for you.

no

Is your patient stable on current conventional support and comfortable?**

no

Consider the phenotype of BPD and then consider rescue NAVA especially if the goal is stability

yes

If getting tracheostomy and eventual portable ventilator, reasonable to continue conventional ventilation

**i.e. you tried all appropriate BPD settings including PEEP adjustments, low low rate, higher tidal volumes, long i-time and the baby still just cannot exist without heavy sedation and/or paralysis, or you tried all that and the baby is now delirious

Future directions (in my mind)

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- Don't forget the utility of a NAVA catheter!!
  - PEEP optimization
  - Understanding what size of breaths a baby wants
  - Detection of dyssynchrony
- Studies needed for longer-term outcomes
  - We need to understand the phenotype of disease better first to be able to design a study to case match patients.
- Can we create a hybrid vent that allows:
  - fast triggering (to decrease the dynamic airway collapse)
  - natural variations in breathing with gentle superimposition of longer i-times and e-times

Thank you!

Ann & Robert H. Lurie
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