

**In-person**  
March 13-16, 2024

**Virtual**  
May – July 31, 2024

## 45th National Conference on Pediatric Health Care

### Harder to Breathe: A Case Based Approach to Status Asthmaticus

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NAPNAP's Asthma & Allergy SIG is pleased to support this session

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Experts in pediatrics, Advocates for children. <sup>1</sup>

1

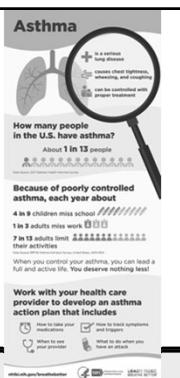
## Speaker Disclosure

- No disclosures

2

### Learning Objectives

- Define status asthmaticus
- Recognize and interpret escalating exam and diagnostic findings in severe asthma exacerbations
- Discuss limitations in pediatric asthma research
- Identify two alternative approaches for severe, refractory, status asthmaticus



**Source:** National Heart, Lung, and Blood Institute, National Institutes of Health, U.S. Department of Health and Human Services.

3

### Asthma and Healthcare Utilization

Each year, children with poorly managed asthma have more than:

- 10 million missed school days
- 74,000 hospital stays
- 787,000 trips to the emergency room

**National Data**

Characteristic <sup>a</sup>	Prevalence	Asthma Attacks	Healthcare Use	Mortality
Total	3,517	10.6 (5.18)		
Children (age 1-19 years) <sup>b</sup>	145	2.0 (0.16)		
Adults (age 18+ years) <sup>c</sup>	3,372	13.1 (8.22)		
<b>Age Group (years)</b>				
0-4	26	1.4 (0.27)		
5-11	68	2.4 (0.27)		
12-17	51	2.8 (0.27)		
18-24	113	3.8 (0.35)		

**Asthma Mortality by Select Sociodemographic Characteristics (2021)**

Characteristic <sup>c</sup>	Number of Deaths <sup>d</sup>	Death Rate <sup>e</sup> Per Million (SE)
Total	145	2.0 (0.16)
Children (age 1-19 years) <sup>b</sup>	145	2.0 (0.16)
Adults (age 18+ years) <sup>c</sup>	3,372	13.1 (8.22)

(Barrett et al., 2000; Centers for Disease Control, 2023; Lee et al., 2020; Nath & Hsia, 2015; L. and B. I. U. S. D. of H. and H. S. National Heart, 2022; R. Perry et al., 2019; Rogerson et al., 2023; Walensky et al., 2021; Weiss et al., 2019)

4

## Acute Severe Asthma: Status asthmaticus

- Asthma exacerbation = Airway obstruction triad
  - Edema/Inflammation
  - Bronchoconstriction
  - Hyperresponsiveness
- Severe asthma exacerbation that is unresponsive to conventional treatments
- NHLBI: Oxygen, SABA, steroids, "adjunct"
- No current consensus in United States, progressive data limitations



(Expert Panel Working Group, 2020; Hairston & McNamara, 2024; Miksa et al., 2021; NIHBI, 2007; Scottish Intercollegiate Guidelines Network, et al., 2019; Trotter et al., 2021)

5

## Our Journey Begins

6

## Presentation

- History: School-aged, moderate persistent asthma
  - Prior PICU admissions, no prior intubations
- Presents to ED: Significantly increased work of breathing, tachypnea
- HPI: Day 2 of illness
  - Wheeze yesterday evening, given albuterol
  - This AM, severe WOB → given q1h albuterol at home

Day 1

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7

## ED VS & Exam

- Exam:
  - PULM: Severe work of breathing. Retractions, nasal flaring. Auscultation= poor aeration
  - CNS: Anxious, intact
  - CV: Warm, well perfused. Tachycardia. 2+ pulses
- Vital signs: Temp 36.1 c, HR 122 bpm, BP 119/65 RR 50, SpO2 92% on RA.

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8

## Asthma scoring

- Positives: Objective evaluation, comparable multiple assessors, use in guiding pathways
- Negatives: MANY different systems: PAS, PASS, MPIS, etc
  - 2014 systematic review 36 different scoring instruments!!
- PAS: pediatric asthma severity score, developed 2000

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(Bekhof et al., 2014; Gorelick et al., 2004; Kelly et al., 2000) 9

9

## Initial PAS scoring

Score	1	2	3
RR:			
2-3 years	≤ 34	35-39	≥ 40
4-5 years	≤ 30	31-35	≥ 36
6-12 years	≤ 26	27-30	≥ 31
>12 years	≤ 23	24-27	≥ 28
Oxygen	>95% on RA	90-95% RA	<90% RA or O <sub>2</sub> requirement or contin. albuterol
Auscultation	No wheezing or minimal expiratory	Diffuse expiratory	Biphasic to diminished
Accessory muscle	None - 1 site	Two sites	≥ 3 sites
Dyspnea	Speaks in full sentences/coos and babbles	Partial sentence, short cry	Single words/short phrases, grunting

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(Kelly et al., 2000) 10

10

## Severe asthma: 1<sup>st</sup> line

Mild	Moderate	Severe
5-7	8-11	12-15

- Priority: Reverse obstruction, reduce inflammation, and correcting hypoxia
  - Short acting beta agonists- +/- additional ipratropium inhalation x 3 back to back
  - Systemic corticosteroids. IV vs PO
  - Oxygen to correct hypoxemia
- What about respiratory support?
- Do we add a 1<sup>st</sup> line IV option/2<sup>nd</sup> line medication?

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(Craig et al., 2020; Erumbala et al., 2021; Global Initiative for Asthma, 2021; Kelly et al., 2000; Miksa et al., 2021; Nhibi, 2007; Scottish Intercollegiate Guidelines Network, et al., 2019; Trottier et al., 2021) 11

11

## Bronchodilation: SABA +/- inhaled anti-cholinergic

- 1<sup>st</sup> step: REVERSED BRONCHOCONSTRICTION!
- SABA: First line, main stay of treatment
- Inhaled anti-cholinergic/Ipratropium: Benefit PRE-admission
  - Mild bronchodilation, ↓ edema, ↓ mucus production, no impaired mucociliary clearance
  - May reduce hospital admissions, improve oxygenation and functional expiratory volume (FEV)
  - DOSE: Combination with albuterol OR 0.5-1.5 mg separate dosing
  - SE: nausea, tremors, eye exposure → pupil dilation

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(Ewulonu & Dyer, 2021; Griffiths & Ducharme, 2013; Nhibi, 2007; Scottish Intercollegiate Guidelines Network, et al., 2019; Trottier et al., 2021; Vezina et al., 2014) 12

12

## Systemic Corticosteroids

- Early steroids for moderate & severe reduce hospital admission
  - Onset within 3-4 hours
- Moderate = PO steroids; Severe/Life-threatening = IV
- What do we choose?
  - Dexamethasone: PO, IM, IV
  - Prednisolone/prednisone: PO
  - Methylprednisolone: IM, IV

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(Craig et al., 2020; Doymaz et al., 2022; Ewulonu & Dyer, 2021; Keeney et al., 2014; Roddy et al., 2023; Trottier et al., 2021) 13

13

## Steroid dosing

Drug	Route	Dose	Max	Course of therapy
Dexamethasone	IV, IM, PO	0.6 mg/kg	16 mg/dose	1-2 days * Do NOT use > 2 days
Prednisone/ Prednisolone	PO	< 12 years: 1-2 mg/kg/day in 1-2 divided doses. > 12 years = 40-60 mg in 1-2 doses.	60 mg/day *G max 40mg <12 years old	Usual 5 days, may be 3-10 days
Methylpred- nisolone	IV/IM	IM: ≤4 years: 7.5mg/kg x1 ≥ 5 years: 240mg x 1  IV: (status asthmaticus) Load = 2mg/kg Maintenance: 0.5-1 mg/kg q6h	IM: Max 240mg  Load: Max Maintenance; Max 60 mg	IM: SINGLE dose. Replace "burst"  Therapeutic control: > 10 days may need taper

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(P and N. L-D. Lexicomp Online, 2024; P and N. L-D. O. Lexicomp Online, 2024, 2024) 14

14

## What is our 2nd line?

- When: First line partially effective or ineffective, or life-threatening presentation and lack of aeration
- What: IV/SQ bronchodilator
  - IV magnesium sulfate
  - IV/SQ terbutaline
  - IM/SQ epinephrine
- Drug of choice? Usually Magnesium Sulfate!

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(Craig et al., 2020; Erumbala et al., 2021; Ewulonu & Dyer, 2021; Griffiths & Kew, 2016; Nhibi, 2007; Scottish Intercollegiate Guidelines Network, et al., 2019; Singh et al., 2014) 15

15

## Magnesium sulfate

- Why does it work?
  - Supraphysiologic levels → Relaxation of smooth muscles → bronchodilation
  - Mast cell histamine inhibition → ↓ mucus production
- Magnesium level goal 4-6mg/dL
- Dosing: Max 2gm bolus, 2gm/hr continuous
  - **Bolus:** 25-75mg/kg over 20 - 30 minutes
  - **Continuous:** Loading dose/bolus + ~ 15-25 mg/kg/hr
- Side effects: Flushing, hypotension, vasodilation
- Toxicity: Nausea, vomiting, lethargy, bradycardia, arrhythmias

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(Craig et al., 2020; Erumbala et al., 2021; Griffiths & Kew, 2016; Gross Júnior et al., 2021; Johnson et al., 2022; P and N. L-D. Q6 Lexicomp Online, 2023; Liu et al., 2016; Mittal et al., 2020; Rogerson et al., 2023; Singh et al., 2014) 16

16

## Mag sulfate data

*J Respiratory and Critical Care Medicine* | Acute Exacerbation of Chronic Bronchitis. 2014 Dec;183(2):1897-8.

doi: 10.1177/0882693714540240. Epub 2014 Oct 2.

**Randomised comparison of intravenous magnesium sulphate, terbutaline and aminophylline for children with acute severe asthma**

Sunit Singh<sup>1</sup>, Sudhirchandra Dixit<sup>1</sup>, Arun Bansal<sup>1</sup>, Kishor Chandra<sup>1</sup>

Affiliations + expand

PMID: 25164315 DOI: 10.1177/0882693714540240



Cochrane Database of Systematic Reviews

intravenous magnesium sulfate for treating children with asthma in the emergency department (Review)

Griffiths R, Kew KM



Cochrane Database of Systematic Reviews

Interventions for escalation of therapy for acute exacerbations of asthma in children: an overview of Cochrane Reviews (Review)

Craig SL, Dabir SA, Powell CCE, Grullon A, Bell RL, Lumry C

[Craig et al., 2020; Griffiths & Kew, 2016; Gross Junior et al., 2021; Johnson et al., 2022; Mittal et al., 2020; Singh et al., 2014] 17

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17

## Epinephrine

• Non-selective  $\beta$ -agonist  $\rightarrow$  bronchodilator effects

• SQ epi vs SQ terbutaline  $\rightarrow$  similar bronchodilation, shorter effect

• Dosing IM or SQ:

- 0.01 mg/kg of 1:1000 (1mg/ml) solution, max 0.3-0.5mg, q20min x 3 doses

• IM more rapid, higher peak concentration

• ?Benefit  $\rightarrow$  ease of access!

- Epipen 0.15mg junior, 0.3mg adult

• Pyxis, code cart

[Bagnett et al., 2022; Craig et al., 2020; P and N. L.-D. O. Lexicomp Online, 2024b; Newth et al., 2012; Nhlbi, 2007]

18

## Terbutaline

- IV or SQ  $\beta_2$  agonist
- Dosing:
  - SQ: 0.01 mg/kg (max 0.25mg), q20min x 3 then q2-6hrprn. MAX 0.5mg/4 hours.
  - IV: 4-10 mcg/kg max of 400mcg load over 5 min + infusion at 0.2-0.4 mcg/kg/min.
    - Titrate to effect by 0.1-0.2 mcg/kg/min q30 min. Usual rate 1-5 mcg/kg/min, MAX 10mcg/kg/min
- SE: >10%: restlessness/tremors, hypokalemia; 1-10% = vomiting tachycardia, hypertension headache; <1% hypotension, arrhythmias, ST segment elevation, lactic acidosis
- Monitoring: ECG, telemetry, electrolytes, BP

(Bagnett et al., 2022; Doymaz & Schneider, 2016; Lexicomp, n.d.; P and N. L.-D. O. Lexicomp Online, 2024a; Nhlbi, 2007) 19

19

## Repeat assessment + PAS scoring

Score	1	2	3
RR:			
2-3 years	$\leq 34$	35-39	$\geq 40$
4-5 years	$\leq 30$	31-35	$\geq 36$
6-12 years	$\leq 26$	27-30	$\geq 31$
>12 years	$\leq 23$	24-27	$\geq 28$
Oxygen	>95% on RA	90-95% RA	<90% RA or O2 requirement or contin. albuterol
Auscultation	No wheezing or minimal expiratory	Diffuse expiratory	Biphasic to diminished
Accessory muscle	None - 1 site	Two sites	$\geq 3$ sites
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(Kelly et al., 2000) 20

20

## Respiratory support: High Flow Nasal Cannula (HFNC)

- Overall benefits:
  - Some end expiratory pressure, ↑ residual functional capacity
  - Increased inspired O<sub>2</sub>
  - Continuous flow through nasopharyngeal deadspace – more efficient
- HFNC & asthma
  - Benefits: less PICU admits when used on regular floor, well tolerated/comfort
  - Limitations: MAX 1ml/kg due to loss of inhalational agent. Balance respiratory support and SABA administration

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(Baudin et al., 2017; Chao et al., 2021a, 2021b; Craig et al., 2020; S. A. Perry et al., 2013; Viscusi & Pacheco, 2018; Wang et al., 2023) 21

21

## Respiratory support: Non-Invasive Ventilation (NIV)

- Provides additional pressurized air, overcomes higher intrinsic PEEP
  - CPAP: continuous pressure throughout respiratory cycle
  - BiPAP: Bilevel flow, higher inspiratory/IPAP and lower expiratory/EPAP
- Benefits:
  - End expiratory positive pressure, increased residual functional capacity
  - Reliable continuous inhalational agent
- Challenges & Risks:
  - Tolerance, may need sedation
  - Skin breakdown, small risk barotrauma and air leak syndromes

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(Dai et al., 2023; Korang et al., 2016; Nihbi, 2007; Scottish Intercollegiate Guidelines Network. et al., 2019; Smith et al., 2023; Viscusi & Pacheco, 2018) 22

22

## Patient update: PICU day 1

- Transfer to PICU → acutely agitated, pulled out IV
- With attempt at IV and NIV placement acute decompensation
  - SpO<sub>2</sub> 80s → 70s → 60s; HR drop to 80s → 40s
  - Acutely altered LOC
  - Loss of central pulses → CPR x 2 min, ROSC obtained.
- IO placed, epinephrine given
- Rapid Sequence Intubation with rocuronium, ketamine, and propofol

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23

## Diagnostics & Plan



pH, Venous (POC)	7.02 ▲
pCO <sub>2</sub> , Venous (POC)	38.8 ▲
pO <sub>2</sub> , Venous (POC)	515 ▲
HCO <sub>3</sub> Calculated, Venous (POC)	25.0 □
CO <sub>2</sub> Calculated, Venous (POC)	28.0 □
Base Excess, Venous (POC)	-6 □
O <sub>2</sub> Sat Calculated, Venous (POC)	100 □

- Received:
  - Methylprednisolone 2mg/kg load
  - Mag bolus 50mg/kg x 1
  - 20ml/kg NS bolus x 2
  - Ketamine 2mg/kg IVP x 1 for RSI
- Start:
  - 40mg/hr albuterol
  - Continue methylpred 1mg/kg q6h IV
  - Repeat Mag bolus and start drip
  - Terbutaline 10mcg/kg load + drip started
  - Ketamine Drip

23

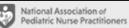
24

24

## Intubation and asthmatics

**Danger! Proceed with caution!**

- Severe, life-threatening asthma, possible cardiopulmonary arrest
- HIGH risk of hypotension, possible pneumothorax
  - Hyperinflation → increasingly negative intrathoracic pressures changes cardiac output, venous return. Intubation CHANGES pressures → relative hypovolemia
  - Air trapping, bagging with high pressures → Air leak syndromes
- Plan it out!
  - Sedation, rescue meds and vasoactives, plan for procedure

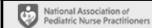


(Bolick et al., 2021; Rogerson et al., 2023) 25

25

## Ketamine

- Dissociative hypnotic, noncompetitive NMDA antagonist. Reduces bronchoconstriction
- Limited research! May improve pulmonary function and asthma scores
  - Pros: hemodynamically neutral, good for RSI
  - Cons: Increased tracheobronchial secretions, hallucinations
- Dosing:
  - RSI and prn dosing: 1-2 mg/kg/dose
  - Infusion: 0.5-3mg/kg/hr, titrate by 0.5 mg/kg to effect
- SE: HALLUCINATIONS, increased secretions



(Binaeedu et al., 2023; Craig et al., 2020; Goyal & Agrawal, 2013; Jat & Chawla, 2012; Rogerson et al., 2023; Sperotto et al., 2021; Tessari et al., 2023)

26

## Methylxanthines: Aminophylline

- NARROW THERAPEUTIC WINDOW! 10-20 mg/L
- Dosing: **Call your pharmacist!**
  - Load: 5-6mg/kg over 30 minutes.
  - Infusion: Varies per age from 0.5-1 mg/kg/hr
    - First drug level 60 minutes after load and then q12h. Titrate per level
- SE: GI effects, caffeine like/headache, bradycardia, hypotension
- TOXICITY: seizures, arrhythmias, cardiac arrest



(Aralihond et al., 2020; Cooney et al., 2016; Craig et al., 2020; Elsevier Drug Information, 2024; P. and N. L. O. Lexicomp Online, 2024; Rogerson et al., 2023)

27

## Patient update



Day 2

	H1	H2	H3	H4	H5	H6	H7
POC: GENERAL							
pH, Arterial (POC)	7.29 ♀	7.23 ♂	7.19 ♀	7.21 ♂	7.08 ♂	7.08 ♂	7.14 ♂
PCO <sub>2</sub> , Arterial (POC)	48.8	48	53.3	46	69.0	69.0	69.0
PCO <sub>2</sub> Set, Arterial (POC)	18.8 ▲	19.2 ▲	19.4 ▲	17.7 ▲	12.7 ▲	10.2 ▲	12.0 ▲
Beta Esterase, Arterial (POC)	8.8	8	8	11.1	11.1	11.1	11.1
PCO <sub>2</sub> Calculated, Arterial (POC)	22.8	20.0 ▼	20.3 ▼	18.4 ▼	19.0 ▼	18.7 ▼	19.6 ▼
CO <sub>2</sub> Calculated, Arterial (POC)	25.0	21.0 ▼	22.0	20.0 ▼	22.0	21.0 ▼	20.0 ▼
Qs Set Calculated, Arterial (POC)	99 ▲	99 ▲	97	99 ▲	97	94	90
Qs Set Calculated, Arterial (POC)	102	102	102	102	102	102	102
POC Potassium	3.9	4.1	4.3	4.5	4.70	4.70	4.70
POC Ionized Calcium	4.50	4.60 ▼	5.0	4.70	4.70	4.70	4.70
POC Glucose	68 ▼	59 ▼	59 ▼	66 ▼	70	70	70
POC Hematocrit	26.0 ▼	26.0 ▼	25.0 ▼	25.0 ▼	25.0 ▼	25.0 ▼	25.0 ▼

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28

## Inhaled Volatile Anesthetics: Sevoflurane

- What is it?
  - Inhaled anesthetic gas, reverses bronchospasm, unclear MOA
- SMALL amount of data, few patients are receiving!
  - Reports from 0.5-90 hours, improved pH and peak pressures
- Side effects:
  - Hypotension, seizures, nephrotoxicity
- Our patient?
  - ~ 72 hour duration. Weaned off due to rising CK, worsening hypotension. Phenylephrine for hypotension

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(Custer et al., 2022; Lew et al., 2021; Schutte et al., 2013) 29

29

## Trends while on Sevoflourane

POC GENERAL	H1	H2	H3	H4
pH, Arterial (POC)	7.40 ♀	7.48 ♀	7.30 ♂	7.32 ♀
pcO <sub>2</sub> , Arterial (POC)	49.7 ♂	49.7 ♂	48	43
paO <sub>2</sub> , Arterial (POC)	114 ▲	76 ▼	94	116 ▲
Base Excess, Arterial (POC)	-3 ▼	-3 ▼	-3 ▼	-4 ▼
HCO <sub>3</sub> Calculated, Arterial (POC)	26.9	25.3	23.5	22.0
CO <sub>2</sub> Calculated, Arterial (POC)	30.0	27.0	25.0	23.0
O <sub>2</sub> Sat Calculated, Arterial (POC)	96	90 ▼	96	98

Day 2-5

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30

## Patient update

- Off sevo x 24 hours → Worsening gas exchange
- Bronchospastic episodes → loss of tidal volume despite aggressive ventilatory attempts (50s/15s)
- <7.0pH, pcO<sub>2</sub> >130. Bradycardic and hemodynamically unstable
- What is left??

Day 6

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31

## What is left?? ECMO

- Cannulated to VV ECMO

POC GENERAL	H1	H2	H3	H5
pH, Arterial (POC)	7.00 ♀	7.29 ♀	7.40	7.47 ▲
pcO <sub>2</sub> , Arterial (POC)	>130 ♂	107 ♂	76 ♂	56 ♂
paO <sub>2</sub> , Arterial (POC)	95	172 ▲	69 ▼	42 ♀
Base Excess, Arterial (POC)	Comment... □ 26 ▲	23 ▲	17 ▲	
HCO <sub>3</sub> Calculated, Arterial (POC)	Comment... □ 51.8 ▲	47.7 ▲	40.8 ▲	
CO <sub>2</sub> Calculated, Arterial (POC)	Comment... □ >50.0 ♂	50.0 ♂	43.0 ♂	
O <sub>2</sub> Sat Calculated, Arterial (POC)	Comment... □ 99 ▲	92 ▼	80 ▼	

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32



## Extracorporeal Membrane Oxygenation (ECMO)

- Temporary cardiopulmonary support – allows lung rest, reversal of obstruction
  - Allows bronchoscopy, aggressive pulmonary hygiene
  - Rest settings ventilator
- More common than volatile anesthetics... but still low!
- High survival to discharge → 86%



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(Custer et al., 2022; Lew et al., 2021; Pineda et al., 2023) 33

33

## ECMO run

- **Day 6 hospital/Day 1 ECMO:** Cannulated, stopped terbutaline, aminophylline, mag, and albuterol. Continued steroids.
- **Day 8 hospital/Day 3 ECMO:** Bronchoscopy → diffuse inflammation, no mucus plugging. 2+ staph aureus BAL
- **Day 9 hospital/Day 4 ECMO:** Lung recruitment started, Continuous albuterol 40/hr, magnesium sulfate restarted
- **Day 11 hospital/ Day 6 ECMO:** Decannulated

Day 6-11

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34

34

## Post ECMO

- De-escalation of care!
- **Day 17 hospital** (6 days post ECMO): Extubated to HFNC, BiPAP overnight
- **Day 20 hospital** (9 days post ECMO): Room air, ongoing rehab. Transferred to regular pediatric floor
- **Day 28 hospital** (17 days post ECMO): Transferred to pediatric rehab facility!!

Day  
17-28

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35

35

## Conclusions

- Severe, refractory, asthma exacerbations often result in ICU care
- Lack of consensus and limited data for adjunctive therapies
- More research is needed!



References

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36

36

Questions?