Management of Severe Acute Asthma in Pre-Schoolers

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OBJECTIVES

- Presumptive diagnosis of asthma in children 1-5 years of age.
- Pediatric Respiratory Assessment Measure [PRAM]-based Rx
- Timing of corticosteroid therapy & dose rationale
- Indications for IV Mg & evidence of benefit
- Discharge therapy-criteria for ICS and its duration

Case

A 16-month-old boy presents to your ED with a 2nd episode of wheezing. Previous ED visit 3 months ago with wheeze, good response to Rx.

Healthy, no atopy.

Grunting, neck and chest retractions, poor air entry, inspiratory and expiratory wheeze.

0_2 sat 88%, RR 60, HR 140, afebrile, weight 17kg.

Diagnosis of asthma possible?

Asthma Umbrella

- **CHILD Study Dr Subbarao**

- Majority (72%) of infants with a wheeze episode improve by school age

- Asthma diagnosis age 5 years:

- 55% preschool-onset wheeze
- 27% persistent wheeze
- 12% transient wheeze

- These groups have abnormal lung function at age 5 years
- This implies abnormal lung growth and high risk for COPD

CTS Statement 2015

High Risk for Asthma:

- ≥ 2nd wheeze in past 12 months and otherwise healthy AND

- ED visit for wheeze in past 12 months OR
- OCS or ICS therapy in past 12 months OR
- Cough with exercise/night in past 12 months

• Presumed Asthma:

- ≥ 2episodes wheeze ever OR
- ED presentation needing treatment
- Reversibility of respiratory distress after therapy
- 1st time wheeze: presumptive asthma if response to Rx

- Atopy not necessary for diagnosis

Bronchiolitis

<12 months

first episode

no response to Rx

PRAM Score

Signs	0	1	2	3
Suprasternal retractions	Absent		Present	
Scalene muscle contraction	Absent		Present	
Air entry	Normal	Decreased at bases	Widespread decrease	Absent/minimal
Wheezing	Absent	Expiratory only	Inspiratory and expiratory	Audible without stethoscope/ silent chest with minimal air entry
O2 saturation	≥95%	92%-94%	<92%	

Pediatric Respiratory Assessment Measure

- Asthma-like phenotype age 1 -17 years
- Validated in ED setting
- Strong association with hospitalization
- Standard across pediatric EDs in Canada

PRAM Based Asthma Pathway

- **PRAM ≤ 3:** Salbutamol x 1
  Corticosteroids PRAM 3
- **PRAM 4-7:** Salbutamol x 3
  Corticosteroids
- **PRAM 8-12:** Salbutamol x 3
  Ipratropium x 3
  Corticosteroids
  consider IV Mg after 3 salbutamol+IB

MDI and Chamber

- Short treatment time
- Allows close spacing of treatments
- Minimize side effects by minimizing drug deposition to upper airway and maximizing lower airway delivery
- Minimize risk of cross infection
- Educational opportunity
- Low cost

Use enough β2 agonist in young children

Tal J Peds 1996, Wildhaber J Peds 1999, Chua Eur Resp J 1994

- Lower inspiratory flows
- Small airway caliber
- Lower deposition when crying

- Dose of inhaled drugs should not be weight-based
- Big and small kids deposit same amount drug/kg body weight
- Can safely give same dose to all- 8-10 puffs per treatment

MDIs versus Nebulizers

Cochrane review by Cates 2006

- Shorter length of stay
- Fewer side-effects
- Preferable by parents and children
- Can be used in ED, ICU

Ipratropium

- Synergistic with β2 agonists
- Effective in severe disease only
- Give with PRAM ≥ 8
- Decreases hospitalizations in severe asthma (Qureshi F NEJM 1998)
- 3 treatments only

Corticosteroids

- Oral steroids decrease hospitalizations by 50% in 4 hours
- Indicated for virtually all ED patients

- Give in triage to avoid hospitalization

  lower admission rate, time to discharge

  [Zemek, Pediatrics 2012]

- Dexamethasone 0.3mg/kg x2 or single dose 0.6 mg/kg to last 5 days
- Prednisolone/prednisone 1-2 mg/kg for 5 days

Dexamethasone vs Prednisolone

Biologic half-life:

- Prednisolone: 12-36 hours
- Dexamethasone 36-54 hours

- Anti-inflammatory potency **dex vs pred: 6:1**

- Dexamethasone: one vs two doses?
  total dose required?

Translating Research Evidence in Kids Recommendation

- Total prednisone dose 2 mg/kg in ED and 1 mg/kg x 4 days is 6 mg/kg
- Corresponds to equivalent dexamethasone 1 mg/kg
- Currently recommend Dexamethasone 0.6 mg/kg x2
- Single dose often used but insufficient evidence

- epinephrine ?
- Inflammation: steroids ?
- Mucous Plugging: hypertonic saline ?
- Necrosis: nil

Challenges in Management

- Many children do not improve with standard therapy
- Benefit of steroids often not apparent until well beyond 4 hours
- Due to adreno-receptor and CS gene polymorphism, up to 30% resistant to initial therapy
- This population represents 84% of asthma hospitalizations
- Need for a second-line bridging agent

Case

A 6-year-old girl with acute asthma after a viral URI

2 ED visits for asthma in past year

Intermittent "wheeze" without colds

Flovent therapy but often forgets to take it

Difficulty talking in full sentences. Audible wheeze

Saturation 91%, RR 40, PRAM 11

Case

- Dexamethasone 20 mg po in triage
- Salbutamol 3 treatments (24 puffs) in 30 min
- Atrovent 3 treatments
- PRAM 8 at 30 minutes
- Next steps?

Escalation Therapies

- IV magnesium sulfate
- HFNC
- IV salbutamol
- Aminophylline
- Ketamine

Mechanistic Rationale for IV Mg

- Direct bronchodilator
- Calcium channel antagonist
- Inhibits acetylcholine release from nerve terminals
- Inhibits histamine release
- Up-regulates $ß_2$ receptors
- Reduces neutrophils in inflammatory response

- IV Mg doses **50-75 mg/kg** required to achieve Mg therapeutic concentration-time profiles *(Rower JE 2017, Vaiyani 2016).*

Consideration for IV Mg

- Extreme distress on arrival
- PRAM 8+ after initial hour of bronchodilator and CS
- Half-life 1.5 hr- observe at least 2 hours
- 50-75mg/kg IV over 30 minutes
- Hypotension with rapid administration (6%)
- Pre-treatment with saline bolus 20 ml/kg 30 minutes

Clinical Use of Magnesium

- **Johnson et al J Pediatr 2020**
- PECARN Registry PEDs 61,854 visits
- Only 26% of hospitalized children given IV Mg in the ED
- Discharge from ED in 11% post IV Mg
- Revisits within 72 hours: 1.8% after IV Mg
  3.6% without IV Mg
-

- **Mittal Hospital Pediatr 2020**
- *Pediatric Health System data collaborative database*
- Rate of IV Mg in pediatric asthma has doubled over past decade, no reduction in hospitalizations or ICU

Evidence of IV-Mg Benefit

- 3 pediatric RCTs: N=115
  Ciarallo 1996, 2000, Scarfone 2000

Disparate conclusions:

- Ciarallo: 50% decrease in admits Scarfone: No IV-Mg effect

- Systematic reviews: concluded IV Mg benefit OR 0.68

Griffiths SR 2016

- Critiques study limitations

- Random-effect re-analysis: Mg effect non-significant OR 0.18 (0.02-1.59)

- Calls for evidence of benefit

Recent Evidence

- **Arnold et al JACI 2022**
- **Schuh et al JAMA Open 2021**
- **Antoon Hosp Pediatr 2021**

- IV-Mg associated with 6-10 times higher odds of admission, independent of asthma severity or response to IV-Mg

- IV-Mg not associated with decreased LOS, need for airway support, time to q4h salbutamol

Mechanism of Action of HFNC

- Cold dry gas induces bronchoconstriction response
- Heated, humidified air/oxygen at flows higher than with traditional oxygen therapy
- Higher gas flow than what inspiratory demand is
- Flow rates ≥ 2 L/kg provide positive pressure throughout respiratory cycle
- Delivers modest incidental PEEP
- In ED, ward and ICU

Asthma and HFNC

- Increases functional residual capacity
- Decreases airway resistance
- Increases CO2 clearance by flushing nasopharynx dead space
- Maintains oxygen concentration

IV Salbutamol

- Recommended by BTS, CPS and AU/NZ guidelines
- Not recommended by NHLBI, GINA

Systematic Review Travers 2001

- No evidence that IV salbutamol better than inhaled

- Used in ICU setting in refractory asthma with increasing oxygen demands despite HFNC and maximized Rx

- Higher toxicity risk with IV than inhaled

- Anxiety, lactic acidosis, tachycardia, increase respiratory workload

Discharge Therapy

- Salbutamol via MDI 4-8 puffs q4h prn for 5-7 days

- Prednisone/Prednisolone 1mg/kg daily for 5 days
- Single ED dose of Dex 0.6 mg/kg

- ICS for 12 weeks (CTS 2015)

- Prescription for ICS in ED decreases ED visits & hospitalizations by 50%

Key Messages

- In ED, consider asthma diagnosis in all recurrent wheezers with response to bronchodilators/CS
- CS in triage in all kids needing ED Rx, 1-2 po dexamethasone doses
- PRAM-based treatment pathway
- MDI= educational opportunity.
- Consider IV-Mg 1 hour with PRAM 8+ post initial Rx
- ICS after discharge important for preventing relapses

Managing Pediatric Asthma in the Emergency Department

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2022

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Asthma Initial Treatment Order Set

For children aged 1-17 years who present to the ED with asthma-like event

LAST NAME	(FIRST)
MRN	VISIT NUMBER
DATE OF BIRTH YYYY-MM-DD	SEX
ADDRESS	

IMPRINT OR ENTER DETAILS BY HAND

Weight (kg)
Allergies ☐ NKDA

Time	Interval	PRAM	Signature
	Pre-treatment		
	1 hr post-treatment		

PRAM Score (Pediatric Respiratory Assessment Measure)

Signs	0	1	2	3
Suprasternal retractions	Absent		Present	
Scalene muscle contractions	Absent		Present	
Air entry*	Normal	Decreased at bases	Widespread decrease	Absent / minimal
Wheezing*	Absent	Expiratory only	Inspiratory expiratory	Audible without stethoscope / silent chest with minimal air entry
O_2 saturation	≥95%	92-94%	<92%	

* If asymmetric findings between right and left lungs, the most severe side is rated

Order time / MD signature	Initial orders	Date:	Time noted / RN signature
Monitoring			
	☑ heart rate, respiratory rate, O_2 sat ☑ PRAM q1h and prn ☐ consult RRT (consider for PRAM ≥ 5) ☐ apply continuous SpO_2 monitoring	☐ apply continuous cardiorespiratory monitoring (consider for PRAM ≥ 8) ☐ consider supplemental oxygen for SpO_2 < 90%	
	PRAM 1-3	☐ salbutamol MDI (100 mcg/puff) inhaled via spacer device 8 puffs x 1	
	PRAM 4-7	☐ salbutamol MDI (100 mcg/puff) inhaled via spacer device 8 puffs q15 min x 3	
	PRAM 8-12	☐ salbutamol MDI (100 mcg/puff) inhaled via spacer device 8 puffs q15 min x 3 ☐ IPRAtropium MDI (20 mcg/puff) inhaled via spacer device 4 puffs q15 min x 3	
Corticosteroids (consult eMAR for medications given by medical directive)			
	PRAM 1-12	☐ dexamethasone _____ mg PO x 1 (0.3 – 0.6 mg/kg/dose, max 20 mg/dose) ☐ predNISOLONE (liquid) _____ mg PO x 1 (2 mg/kg/dose, max 60 mg/dose) ☐ predniSONE (tablet) _____ mg PO x 1 (2 mg/kg/dose, max 60 mg/dose) ☐ hydrocortisone (IV) _____ mg IV now and q6h (5 mg/kg/dose)	
Magnesium sulfate			
	PRAM 8-12	☐ magnesium sulfate _____ mg IV (40 mg/kg/dose, max 2500 mg/dose)	
	☑ MD to reassess in _____ min (max 60 min)		
	☑ repeat PRAM score 1 hour post-initiation of treatment		
1 hour after initiation of treatment			

PRAM 0-3	PRAM 4-12
• if patient requires additional treatment, refer to *Asthma Continuing Treatment Order Set* • consider discharge if – mild distress at presentation – no co-morbidities – no history of ICU admission for asthma *and* – no other concerns	• for further treatment, refer to *Asthma Continuing Treatment Order Set* • consult CCRT if patient has impending respiratory failure

- Establish IV access
- NPO status (administer D5W NS plus 20mmol/l KCL if NPO)
- Check serum potassium (if Ventolin Q1h or less X 6hours)

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Asthma Continuing Treatment Order Set

For patients who have received treatment as per the *Asthma Initial Treatment Order Set* and require continuing treatment for their symptoms

LAST NAME	(FIRST)
MRN	VISIT NUMBER
DATE OF BIRTH YYYY-MM-DD	SEX
ADDRESS	

IMPRINT OR ENTER DETAILS BY HAND

Weight (kg)	Allergies ☐ NKDA

Time	Interval	PRAM	Signature
	1 hr post-treatment		
	2 hr post-treatment		

PRAM Score (Pediatric Respiratory Assessment Measure)

Signs	0	1	2	3
Suprasternal retractions	Absent		Present	
Scalene muscle contractions	Absent		Present	
Air entry*	Normal	Decreased at bases	Widespread decrease	Absent / minimal
Wheezing*	Absent	Expiratory only	Inspiratory expiratory	Audible without stethoscope / silent chest with minimal air entry
O_2 saturation	≥95%	92-94%	<92%	

* If asymmetric findings between right and left lungs, the most severe side is rated

Order time / MD signature	Continuing orders	Date:		Time noted / RN signature
1 hour	**salbutamol MDI (100 mcg/puff) inhaled via spacer device**			
	PRAM 1-3 ☐ 8 puffs x 1 ☐ continue to observe	**PRAM 4-7** ☐ 8 puffs q15 min x 3 ☐ 8 puffs q4h and q _____ min prn	**PRAM 8-12** ☐ 8 puffs q15 min x 3 ☐ 8 puffs q2h and q _____ min prn	
	magnesium sulfate			
		If minimal or no improvement, deteriorating, or PRAM ≥ 5 consider: ☐ magnesium sulfate _____ mg IV (40 mg/kg/dose, max 2500 mg/dose)		
	☑ MD to reassess in _____ minutes			
2 hours	**salbutamol MDI (100 mcg/puff) inhaled via spacer device**			
	PRAM 1-3 ☐ 8 puffs x 1 ☐ continue to observe	**PRAM 4-7** ☐ 8 puffs q15 min x 3 ☐ 8 puffs q4h and q _____ min prn	**PRAM 8-12** ☐ 8 puffs q15 min x 3 ☐ 8 puffs q2h and q _____ min prn	
	☑ MD to reassess in _____ minutes			
3 hours	**salbutamol MDI (100 mcg/puff) inhaled via spacer device**			
	PRAM 1-3 ☐ 8 puffs x 1 ☐ continue to observe	**PRAM 4-7** ☐ 8 puffs q15 min x 3 ☐ 8 puffs q4h and q _____ min prn	**PRAM 8-12** ☐ 8 puffs q15 min x 3 ☐ 8 puffs q2h and q _____ min prn	
	☑ MD to reassess in _____ minutes			
	Disposition			
	PRAM 1-3 • if previous ICU admission, observe for minimum 4 hr	**PRAM 4-7** • consider admission • consider transfer to peripheral paediatrics ward	**PRAM 8-12** • consider admission, consult Paediatrics or CCRT • consider alternative DDx	
	Discharge instructions			
	• additional systemic steroids ☐ dispense 2nd dose of dexamethasone _____ mg PO x 1 (0.3 mg/kg/dose, max 20 mg/dose) for home use the next day ***OR*** • prescribe predniSONE/predniSOLONE (1mg/kg/day, max 60 mg/day) PO as a single daily dose x 4 more days (consider for patients with previous PICU admissions) • recommend salbutamol inhaler (4-8 puffs q4h as needed) • recommend inhaled corticosteroids (eg. Flovent) twice daily for 12 weeks • review discharge instructions • review MDI and spacer technique (resources provided from AboutKidsHealth) • follow up with primary care physician for assessment and/or referral to an asthma specialist			

Critical Asthma & The PICU Admission

Despite increasing ED visits for patients with Asthma over the last decade, SickKids has seen a decrease in the proportion requiring PICU admissions.

This is largely due to changes in the intensive treatment delivered in the ED and the ability to manage less severe exacerbations on the Ward.

Pirie J, Cox P, Johnson D, Schuh S. Paediatric Emergency Care.

Children with acute severe asthma who fail to improve with proper aggressive treatment in the ED should be considered critical / non-responsive and CritiCall contacted ASAP for support.

Why are Asthmatics in the PICU?

1. Delayed Treatment
    - Delayed / Missed treatments
    - Delay in steroid use

2. Non-responsive or Atypical Asthma
    - Continuous Trigger (ie. virus)
    - Atypical Genotype
        - CDHR3 associate with severe asthma
        - Arg16Gly-Gln27Gln haplotype of the ADRbeta are four times more likely to be intubated and mechanically ventilated

Risk factors — Patients who are at risk for requiring ICU management for asthma include those who have a history of [6-13]

- Previous ICU admissions
- Seizure or syncope during asthma exacerbation
- Food triggered event
- Use of more than 2 B-agonist canister's/month
- Denial or failure to recognize illness severity
- Depression or other psychiatric disorder

However, as many as one-third of children who die from asthma would not have been classified as at risk for fatal asthma based upon these risk factors. (Madison 2016)

Critical/Non-Responsive Asthma Management

Activate CritiCall for guidance on the following:

- IV Magnesium Sulphate continued from the ED
- IV Corticosteroids continued from the ED
- IV/Continuous β agonists if unresponsive to Magnesium Sulphate
- HFNC +/ - Inhaled B-agonists Caution: Should not delay initiation of NIV if needed
- NIV +/ - Inhaled B-agonists
- Avoid Intubation whenever possible, however if required consider;
  - IV Ketamine / Propofol
  - General Anaesthesia –Sevoflurane, Isoflurane
- Invasive Ventilation +/- Inhaled B-agonists
  - Requires Obstructive Ventilation Strategy
  - Manual Compression on Exhalation

Added Resources

Community Hospitals Webinars

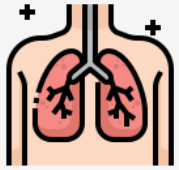
Connected Care delivers live and interactive competency-based education led by SickKids interprofessional providers (RNs, RTs, MDs, Pharmacists, and more). Interprofessional colleagues are encouraged to register and/or attend together.

Click on the icon to register for upcoming dates and view previously recorded webinar archives

Essentials in Paediatric Health Assessment

Nursing Care of the Child with Bronchiolitis

Essentials in Paediatric Oxygen Therapy & Heated High Flow



Essentials in Paediatric Airway Suctioning

Recognition and Management of Sepsis in Paediatrics

Nurse Extenders in Paediatric Acute Care

Basics of Invasive Mechanical Ventilation in Paediatrics

Equipment and Basics of NIV in Paediatrics

Webinars for MDs

PHYSICIANS

Managing Bronchiolitis & Asthma in Community Hospitals Pending Transfer to Tertiary Critical Care

Recommended for Physicians. This webinar will review approaches to the critical care of children with bronchiolitis, asthma or ARDS, and focus on medical management and use of NIV in stabilization of a child less than 14 years pending transfer to a paediatric intensive care unit.

Archived Webinars:

- Managing Bronchiolitis & Asthma in Community Hospitals Pending Transfer to Tertiary Critical Care

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The Department of Respiratory Therapy

High Flow Nasal Cannula

- The use of HFNC in children with asthma exacerbations is generally feasible and safe.

- Practitioners should be cautious of the risk of delaying escalation treatment to prevent negative outcomes.
  - HFNC provides a lower level of respiratory support than does NIPPV, which can potentially delay escalation treatment and cause safety and economic concerns.
    - does not ventilate
    - does not deliver CPAP

- The delivery of inhalation drugs via HFNC may not be optimal. Reducing the flow rate during HFNC or temporarily switching to routine therapy may be appropriate when performing inhalation therapy… to be discussed.

Ke-Yun Chao, Yu-Hsuan Chien, Shu-Chi Mu, High-flow nasal cannula in children with asthma exacerbation: A review of current evidence, Paediatric Respiratory Reviews, Volume 40, 2021, Pages 52-57, ISSN 1526-0542, https://doi.org/10.1016/j.prrv.2021.01.003.

Non-Invasive Ventilation (NIV)

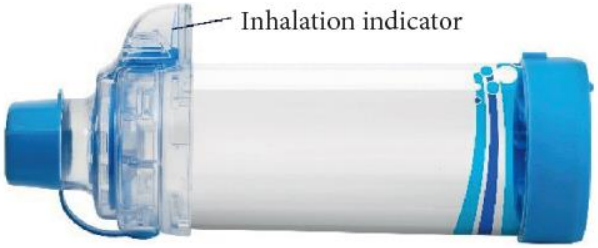
- NIV may help to avoid intubation in select patients while awaiting the maximum therapeutic benefit of pharmacotherapy. (Supportive Care) (Nagler, Cheifetz 2016)

- NIV is preferred to Invasive Ventilation as it maintains spontaneous breathing (active exhalation)

- Continue inhaled B-agonists whenever possible (potential for additive effect)
  - Bench Studies suggest that Jet Nebulization, pMDI, and Mesh Nebulization via NIV can deliver a therapeutic dose

(Hess 2015)

When to switch from MDI to Nebulizer



- When patients can no longer actuate the valved holding chamber or high O2 needs
- When a patient requests nebulization based on PmHx… take their word for it!
- Some with Tracheostomies not tolerate VHCs attached to their trach.

Practice:

ACTS

- The ACTS team will utilize Aerogen for nebulization during transport on a routine bases
- AGMP status is a serious consideration during transport via EMS
- This support may not continue once the patient arrives to SickKids…

SickKids Practice varies specific to the patient

TIPS & TRICKS

Nebulization Recommendations: HFNC

1) **For patients that tolerate removal of their HFNC:**
   - Delivery of inhaled medications will be either via pMDI with VHC (recommended) or jet nebulizer with mask (used for patients who cannot actuate the VHC valve, etc.)
   - *Masks should NEVER be administered on top of HFNC*

2) For patients who do NOT tolerate removal of HFNC:
   - HFNC + Aerogen can be used if dependent on HFNC
     - *Balance patient comfort, frequency*
     - *Refer to CritiCall for patient specific guidance*
     - Goal should be to decrease flow temporarily during administration as close to recommended rate as possible.

HFNC Titration Rates during Nebulization	
Infants <10kg or <1yr	2 LPM
Toddler/Child > 10kg	3-4 LPM
Adolescents	5-6 LPM

***Always follow manufacturer guidelines when available**

TIPS & TRICKS

Nebulization in Severe Asthma: HFNC or NIV

3) For patient's who do not tolerate decreased flow on HFNC or removal of their NIV:
- Salbutamol can be given to asthmatics while on NIV or HFNC on full therapeutic flows.
  - Perform under the guidance of CritiCall.
  - Titrate to patient response; know that patient dose may be suboptimal.
    - NIV may provide better deposition than HFNC.
  - Use a high efficiency nebulizer.
  - Serial or continuous dosing can be used.
  - Lower dosing only once IV bronchodilator takes effect.

- Rate (mL/hr) = $\frac{\text{Dose ordered(mg/hr)}}{\text{Concentration (mg/mL)}}$

Example: for a dose of 15mg/hr
Rate = $\frac{15\text{mg/hr}}{2\text{mg/ml}}$ = 7.5mL/hr

Do not delay treatments trying to figure out continuous dosing.

Questions?

Online evaluation form will be sent after the session or scan the QR Code to complete now.
We appreciate your feedback.
https://skconnect.typeform.com/to/jmP9E8IZ

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For Full List of References Contact diane.soares@sickkids.ca