

Management of Acute Asthma Exacerbations in Children 2012 Update

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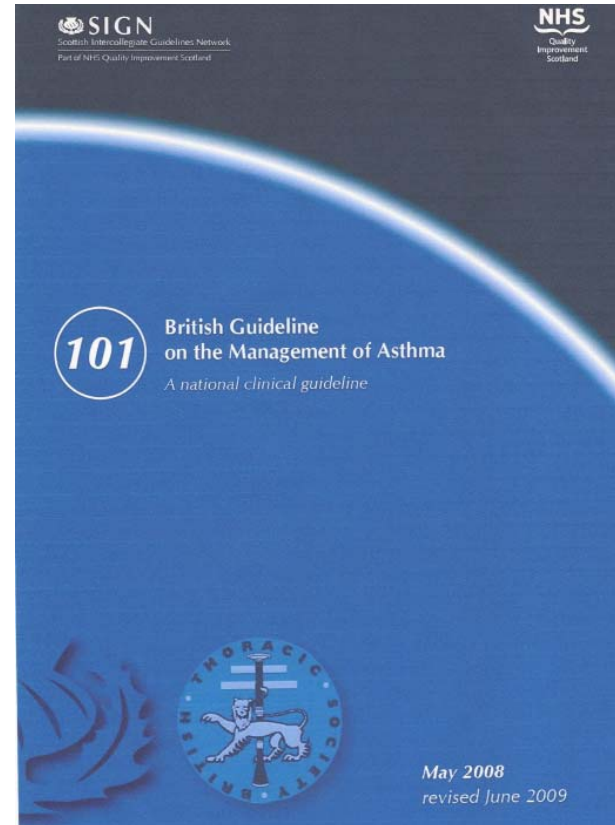
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- BTS/SIGN guidelines
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- NAEPP guidelines
- Presentation Prof Tex
Kissoon, CritSat Congress,
Cape Town 2008



Definition: ATS / ERS 2009

Severe asthma exacerbations:

- Events that require urgent attention on the part of the patient and physician to prevent a serious outcome, such as hospitalisation or death.
- The occurrence of either an asthma-related hospitalisation or visit to the ED or an urgent care facility, leading to treatment with systemic (oral, IM or IV) CS or use of CS for at least 3 days.

Moderate asthma exacerbations:

- The occurrence of at least one of the following events for at least 2 days (without the need for systemic CS): deterioration in symptoms, deterioration in lung function, and/or increased rescue bronchodilator use
- ED visits not requiring CS classified as moderate disease exacerbations

Mild asthma exacerbation:

- just outside normal range of variation for individual patient; difficult to distinguish from transient loss of asthma control

Severe asthma exacerbations

- Occur in patients with all degrees of asthma severity
- Even patients thought to have mild, easy-to-treat asthma can experience severe exacerbations, sometimes even fatal
 - 1 severe exacerbation per patient with mild asthma per year
 - Almost all develop over 5-7 days rather than acute catastrophic events; gradual increase in sx and deterioration in lung function
 - Most resolve over 7-10 days after Rx initiated

Environmental factors associated with asthma exacerbations

- Upper respiratory tract infections
 - Human rhinovirus infection
- Interaction with sensitisation & allergen exposure
- Passive smoke exposure
- Gene-environment interactions

Objective Evaluation

- Respiratory rate
- Retraction
- Ability to speak
- Ability to feed
- Peak flow
- O₂ saturation



Danger Signs in Acute Asthma

- Rising pulse rate
- Pulsus paradoxus
- Agitation, restlessness or ↓ consciousness
- Silent chest on auscultation
- Chest pain
- Cyanosis
- Peak flow < 50% predicted
- Rising PaCO₂

Assessment of severity



Life threatening asthma	Any one of the following in a child with severe asthma:	
	Clinical signs	Measurements
	Silent chest	SpO ₂ < 92%
	Cyanosis	PEF < 33% best or predicted
	Poor respiratory effort	
	Hypotension	
	Exhaustion	
	Confusion	
Acute severe asthma	<p>Can't complete sentences in one breath or too breathless to talk or feed</p> <p>SpO₂ < 92%</p> <p>PEF 33-50% best or predicted</p> <p>Pulse > 140 in children aged 2-5 years > 125 in children aged > 5 years</p> <p>Respiration > 40 breaths/min aged 2-5 years > 30 breaths/min aged > 5 years</p>	
Moderate asthma exacerbation	<p>Able to talk in sentences</p> <p>SpO₂ ≥ 92%</p> <p>PEF ≥ 50% best or predicted</p> <p>Heart rate ≤ 140/min in children aged 2-5 years ≤ 125/min in children > 5 years</p> <p>Respiratory rate ≤ 40/min in children aged 2-5 years ≤ 30/min in children > 5 years</p>	

Oxygen

- Administer in all cases if unable to monitor saturations
- Oxygen levels in patients with acute asthma should be maintained at SpO₂ 94-98%
- Oxygen saturation should be measured by pulse oximeters in adults and children. Pulse oximeters should therefore be available in both primary and secondary care settings
- **If SpO₂ <92% in air after initial bronchodilators, admit to hospital**

How would you treat?

- **β 2 agonist?**
 - Delivered how?
 - One or more?
- **Ipratropium?**
 - One or more?
 - How frequently?
- **Steroids?**
 - When? Route?
 - Which steroid? Dose?
- **If he doesn't improve, then what?**
 - Continue same therapy?
 - Other options?

The Golden Hour

- MDI with spacer (unless hypoxic)
- Repeated β 2 agonist aerosols
- Repeated ipratropium aerosols
- Early oral steroid



MDI & Spacer vs Nebuliser

- Mild asthma: MDI/spacer better Schuh J Pediatr 1999
- Cochrane Review Cates CJ 2006, updated 2008
 - 27 RCTs ED & community Settings
 - 2295 children > 2 years & 614 adults
 - 6 RCTs inpatients with acute asthma
 - 213 children & 28 adults
 - **MDI-spacer outcomes at least equivalent to nebulisers**
 - Spacers may have some advantages for children in acute asthma (shorter LOS, lower pulse rate)
- Home-made spacers no different from commercially produced spacers Zar Lancet 1999, Rodriguez-Martinez Cochrane Review 2008

β_2 agonist aerosols 1

Initial treatment

β_2 agonists should be given as first line treatment. Increase β_2 agonist dose by two puffs every two minutes according to response up to ten puffs.

Children with acute asthma at home and symptoms not controlled by up to 10 puffs of salbutamol via pMDI and spacer, or 2.5-5 mg of nebulised salbutamol, should seek urgent medical attention. Additional doses of bronchodilator should be given as needed whilst awaiting medical attention if symptoms are severe.

β 2 agonist aerosols 2

- Inhaled β 2 agonists are first line treatment for acute asthma
- 2-4 puffs of salbutamol 100 mcg repeated every 10-20 minutes depending on response
- Single puffs, one at a time, inhaled separately with 5 tidal breaths
- If hourly doses of bronchodilators required for > 4-6 hours, switch to nebulised bronchodilators

β 2 agonist aerosols 2

- Life-threatening asthma ($\text{SpO}_2 < 92\%$): give frequent doses of nebulised bronchodilators driven by oxygen (2.5-5 mg salbutamol)
- Repeat doses every 20-30 minutes

β 2 agonist x 3 over 60 minutes

- Continuous vs. Intermittent Nebulisation

Camargo CA Cochrane Review 2003, updated to 2011

- 8 RCTs, 461 patients total
 - **Hospital admission: those with severe airway obstruction benefitted most**
 - **Small but statistically significant improvement in pulmonary function tests**
 - No difference in side-effects
- BTS: no difference, but old references

Anticholinergic therapy for acute asthma in children

- Inhaled anticholinergic as single agent bronchodilators less efficacious than β 2 agonists
- Inhaled anticholinergic less efficacious than inhaled anticholinergic combined with β 2 agonists
- Six studies, unclear quality
 - Teoh Cochrane review April 2011, published 2012

Ipratropium x 3 over 60 minutes

- Combined inhaled anticholinergics and β 2 agonists for initial treatment of acute asthma in children (18 months to 17 years) Plotnick Cochrane Review 2000, published 2008
- Single dose - 5 RCTs, 453 patients
 - Small difference in PFTs, no difference in admissions
- Multiple doses – 7 RCTs, 1045 patients
 - Greater improvement in PFTs
 - NNT 12.5; if severe acute attack, NNT 7
- **Multiple doses preferred to single dose; use in school-age children with severe exacerbations**
- Safe, improves lung function

Early Steroids

- Early ED treatment of acute asthma with systemic corticosteroids (CS)(< 60 minutes)

Rowe BH Cochrane Review 2001

- RCTs, IV/IM or oral CS vs placebo
- 12 RCTs, 863 patients
 - **Significant reduction in hospital admission**
 - **Benefits greatest with more severe asthma**
- 3 RCTs using oral steroids in children
 - **Good response, reduced admission**

Summary: Golden Hour

- Strong Evidence
- MDI with spacer
- Repeated β 2 agonists
- Repeated ipratropium bromide
- Early oral steroids



What next?

- Observe response
- Good response: not tachypnoeic, minimal wheezing, no retraction, able to speak & feed, $PEF \geq 80\%$ predicted/best
- If good response, observe x 1 hour
- Discharge with written action plan and follow-up appointment

Poor response – what now?

- Incomplete / poor response:
 - Tachypnoeic
 - Persistent wheezing
 - Retraction present
 - Impaired speech or feeding
 - PEF \leq 79% predicted or personal best
- Admit to hospital
- Continue oxygen, nebulised SABA+IB, oral corticosteroids

Additional therapy?

- **What about?**
- Intravenous β 2 agonist?
- Intravenous magnesium sulphate?
- Intravenous theophylline?
- Adrenaline?

Intravenous β 2 Agonists

- IV salbutamol as once-off dose 15 mcg/kg over 10 minutes in children with acute asthma in ED
- IV + nebulised salbutamol vs nebulised salbutamol only
 - 29 children, severe symptoms
 - Discharged 10 hrs earlier

Browne Lancet 1997

- IV+nebulised salbutamol vs nebulised salbutamol + ipratropium
 - 55 children, severe symptoms
 - Discharged 28 hrs earlier

Browne Pediatr Crit Care Med 2002

Intravenous β 2 Agonists

- IV β 2 agonists for acute asthma in ED

Travers AA Cochrane Review 2000, published 2012

- 15 RCTs, 584 patients
- IV selective or non-selective β 2 agonists vs placebo, inhaled β 2 agonists or other standard of care
- Adults & children
- **IV β 2 agonists conferred no advantage over comparator regimens**

Intravenous Magnesium Sulphate

- Magnesium sulphate for treating exacerbations of acute asthma in ED

Bota G Cochrane Review 2000

- 7 trials (5 adult, 2 paediatric), 665 patients
- Non-significant improvements in PEF except in patients with severe acute asthma
- Hospital admissions reduced only in severe group
- **Probably provides additional benefit (less hospitalization) in severe acute asthma in children**

Cheuk DKL A meta-analysis on intravenous magnesium sulphate for treating acute asthma.

Arch Dis Child 2005

Aminophylline

- Narrow therapeutic index
- Potentially severe side effects
 - Cardiac arrhythmias
 - Hypotension
 - Convulsions
- Only used for severely ill children in ICU with cardiac monitoring & measurement of serum levels

Intravenous Aminophylline

- **IV aminophylline for acute severe asthma in children >2 years receiving inhaled bronchodilators**

Mitra Cochrane Review 2007, published 2009

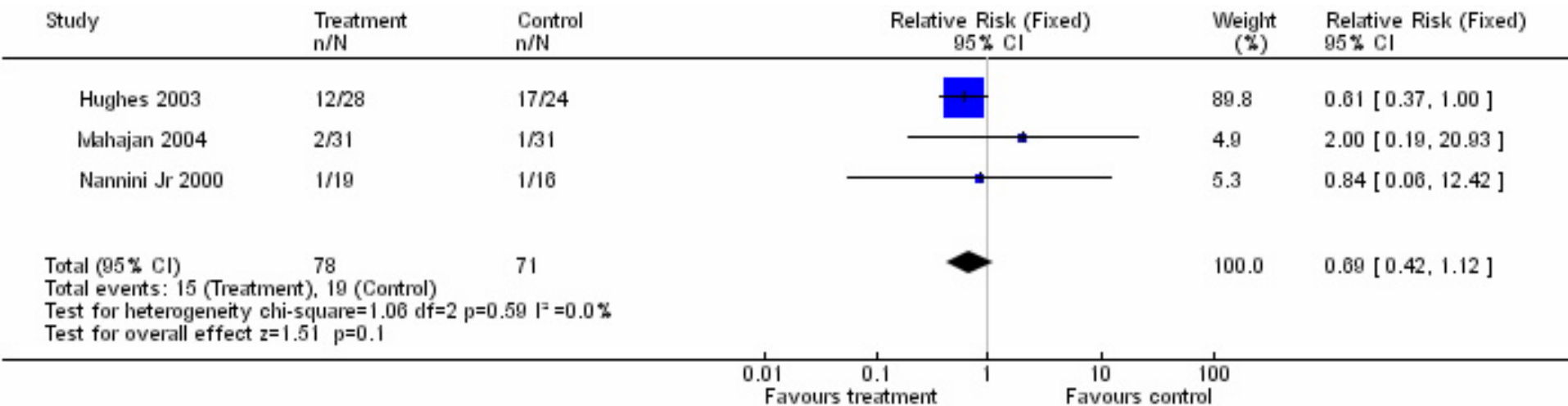
- Inpatients, severe asthma
- 7 RCTs, 380 children
- Improved lung function by 6 hrs
- No difference in LOS, no of nebs; unable to assess PICU admission or MV
- More vomiting

- **IV salbutamol bolus vs aminophylline infusion in children with severe asthma**

Roberts Thorax 2003

- Inpatients, severe, non-responsive to Rx
- RCT, 54 children
- IV salbutamol bolus vs aminophylline bolus + infusion
- No difference in clinical score in first 2 hours
- However shorter LOS in aminophylline group

Inhaled magnesium sulphate



MgSO₄ + β₂-agonists vs β₂-agonists alone; Outcome - admission to hospital

Six RCTs, 296 patients.

4 studies MgSO₄ + β₂-agonists vs β₂-agonists alone; 2 studies MgSO₄ vs β₂-agonists alone

Improved pulmonary function; *trend* towards benefit in hospital admission

Blitz M, et al. Inhaled magnesium sulfate in the treatment of acute asthma.

Cochrane Review 2005, edited & published 2009.

Adrenaline

- Given subcutaneously (0.01 ml/kg of 1:1000 solution)
- Only if no nebuliser or p-MDI available
OR
- If patient moribund and unable to benefit from inhaled therapy

Leukotriene receptor antagonists

- Oral montelukast as add-on therapy: decrease symptoms, hospitalisation, steroid use

Harmanci Ann Allergy Asthma Immunol 2006

Robertson AJRCCM 2007; Nelson Pediatr Emerg Care 2008

Capsomidis Arch Dis Child 2010

- IV montelukast added to standard care in adults improved FEV₁

Ramsay Thorax 2011

- Oral LTA + usual care in children (3 trials, 194 children): no difference

- IV LTA (1 trial, 276 children): decreased hospital admission, no difference FEV₁

Watts Cochrane review 2012

Respiratory failure

Features suggesting impending respiratory failure in children with acute asthma

- Disturbance in level of consciousness
- Inability to speak in sentences
- Inability to feed properly
- Severely decreased or absent breath sounds (“silent chest”)
- Central cyanosis very late sign
- Normal $p\text{CO}_2$ on arterial blood gas

Indications for admission to ICU

- Poor response to maximal pharmacologic therapy in ward / emergency room
- Cyanosis and hypoxaemia ($\text{PaO}_2 < 8\text{kPa}$) unrelieved by O_2
- $\text{PaCO}_2 > 4.5\text{kPa}$
- $\text{PEFR} < 30\%$ predicted or best
- Minimal chest movement, “silent” chest
- Severe retraction
- Deteriorating mental status, lethargy or agitation
- Cardio-respiratory arrest

ICU management of acute severe asthma

- Oxygen
- Continuous nebulised SABA; add ipratropium 4 hourly
- IV corticosteroids
- IV magnesium sulphate
- IV salbutamol and/or aminophylline infusions
- Intubation and ventilation
- Inhaled anaesthetic gas, ketamine

Acute asthma: unproven therapies

- Routine antibiotics Graham V Cochrane Review 2001
- Physiotherapy
- Mucolytics
- Antihistamines
- Heliox Rodrigo GJ Cochrane Review 2006

Other considerations

PEF

PEF measurements can be of benefit in assessing children who are familiar with the use of such devices. The best of three PEF measurements, ideally expressed as a percentage of personal best, can be useful in assessing the response to treatment.

A measurement of $< 50\%$ predicted PEF or FEV_1 with poor improvement after initial bronchodilator treatment is predictive of a more prolonged asthma attack.

Chest X-ray

Chest X-rays rarely provide additional useful information and are not routinely indicated.^{454,455}

- ☑ A chest X-ray should be performed if there is subcutaneous emphysema, persisting unilateral signs suggesting pneumothorax, lobar collapse or consolidation and/or life threatening asthma not responding to treatment.

Arterial blood gases

Blood gas measurements should be considered if there are life threatening features not responding to treatment. Arteriolised ear lobe blood gases can be used to obtain an accurate measure of pH and pCO₂.⁷⁸³ If ear lobe sampling is not practicable a finger prick sample can be an alternative. Normal or raised pCO₂ levels are indicative of worsening asthma. A more easily obtained free flowing venous blood pCO₂ measurement of < 6kPA (45mm Hg) excludes hypercapnia.⁷⁸³

Table 1 Arterial blood gas stages in acute severe asthma patients

Stage	pH (nl 7.35–7.43)	pCO ₂ (nl 35–40 mmHg)	pO ₂ (nl 90–100 mmHg)	Clinical Implications
I	Respiratory alkalosis	↓	Normal	Asthma exacerbation
II	Respiratory alkalosis	↓↓	↓	Common emergency room finding
III	Normal	Normal	↓↓	Impending respiratory failure
IV	Respiratory acidosis	↑↑	↓↓↓	Impending respiratory arrest

NB: initial response to acute asthma is to lower pCO₂, so if pCO₂ is within “normal” limits, the child is already in impending respiratory failure

Age > 5 years

ASSESS ASTHMA SEVERITY

Moderate asthma

- SpO₂ ≥ 92%
- PEF > 50% best or predicted
- No clinical features of severe asthma

NB: If a patient has signs and symptoms across categories, always treat according to their most severe features

Severe asthma

- SpO₂ < 92%
- PEF 33-50% best or predicted
- Heart rate > 125/min
- Respiratory rate > 30/min
- Use of accessory neck muscles

Life threatening asthma

SpO₂ < 92% plus any of:

- PEF < 33% best or predicted
- Silent chest
- Poor respiratory effort
- Altered consciousness
- Cyanosis

Oxygen via face mask/nasal prongs to achieve SpO₂ 94-98%

- β₂ agonist 2-10 puffs via spacer
- Increase β₂ agonist dose by 2 puffs every 2 minutes up to 10 puffs according to response
- Oral prednisolone 30-40 mg

Reassess within 1 hour

- β₂ agonist 10 puffs via spacer or nebulised salbutamol 2.5-5 mg or terbutaline 5-10 mg
- Oral prednisolone 30-40 mg or IV hydrocortisone 4 mg/kg if vomiting
- If poor response nebulised ipratropium bromide 0.25 mg
- Repeat β₂ agonist and ipratropium up to every 20-30 minutes according to response

- Nebulised β₂ agonist: salbutamol 5 mg or terbutaline 10 mg plus ipratropium bromide 0.25 mg nebulised
 - Oral prednisolone 30-40mg or IV hydrocortisone 4mg/kg if vomiting
- Discuss with senior clinician, PICU team or paediatrician
- Repeat bronchodilators every 20-30 minutes

ASSESS RESPONSE TO TREATMENT

Record respiratory rate, heart rate, oxygen saturation and PEF/FEV every 1-4 hours

RESPONDING

- Continue bronchodilators 1-4 hours prn
- Discharge when stable on 4 hourly treatment
- Continue oral prednisolone 30-40 mg for up to 3 days

At discharge

- Ensure stable on 4 hourly inhaled treatment
- Review the need for regular treatment and the use of inhaled steroids
- Review inhaler technique
- Provide a written asthma action plan for treating future attacks
- Arrange follow up according to local policy

NOT RESPONDING

- Continue 20-30 minute nebulisers and arrange HDU/PICU transfer
- Consider: Chest X-ray and blood gases
- Consider risks and benefits of:
- Bolus IV salbutamol 15 mcg/kg if not already given
- Continuous IV salbutamol infusion 1-5 mcg/kg/min (200 mcg/ml solution)
- IV aminophylline 5 mg/kg loading dose over 20 minutes (omit in those receiving oral theophyllines) followed by continuous infusion 1mg/kg/hour
- Bolus IV infusion of magnesium sulphate 40 mg/kg (max 2 g) over 20 minutes

Summary: Rx acute asthma

First line therapy

- Supplemental Oxygen (maintain SpO₂ 94-98%)
- Inhaled β ₂ agonist (pMDI-spacer)
- Steroids
- \pm Inhaled ipratropium bromide

Summary: Rx acute asthma 2

Second line therapy

- Add inhaled ipratropium bromide
- IV β_2 agonist
- IV magnesium sulphate
- IV aminophylline