Wheezeing in the young: How to approach and treat?
Physiology / Mechanism of wheezing

- Continuous musical, high pitched whistling sounds usually associated with prolonged expiration caused by vibration of airway wall due to turbulent airflow through narrow airways.
Physiology / Mechanism of wheezing

Polyphonic (heterophonous) → Monophonic (homophonous)

Wheeze
- Indicates airflow limitation
  - Loudness – does not indicate severity of obstruction
  - Biphasic wheeze – indicates more severe obstruction
  - Quality of wheeze – indicates site of obstruction
Anatomic & physiologic predisposition to wheezing in infants and young children

- Anatomic:
  - Smaller airways
  - Spiral airway smooth muscles extend to peripheral airways
    → increased BHR

Paediatr Respir Rev 2004; 5: S77-S79
Taussig: Pediatric Respiratory Medicine 2008
Anatomic & physiologic predisposition to wheezing in infants and young children

• Physiologic:
  – Increased nasal airway resistance
  – Increased peripheral airway resistance
  – Decreased elastic recoil pressure
  → early airway closure

Paediatr Respir Rev 2004; 5: S77-S79
Taussig : Pediatric Respiratory Medicine 2008
Common causes of *acute wheezing* in infants & young children

- Infection
  - Acute bronchiolitis
  - Viral pneumonia
  - Acute bronchitis (*Mycoplasma pneumoniae, Chlamydia pneumoniae*)
  - Severe viral croup
- Foreign body aspiration
- Anaphylaxis
Causes of recurrent/persistent wheezing in infant & young children

- **Congenital malformations:**
  - Airway anomalies
  - Vascular ring
  - Congenital lobar emphysema
  - Bronchogenic cyst, etc.

- **Inflammation:**
  - Asthma / Reactive airway disease
  - Cow’s milk protein allergy
  - Bronchopulmonary dysplasia (BPD)

- **Infection:**
  - Pertussis, Chlamydia, Endobronchial TB

- **Gastroesophageal reflux (GERD) & other pulmonary aspiration syndrome**

- **Foreign body aspiration**

- **Others**
How to approach a child with acute wheezing?
Case example

ผู้ป่วยเด็กชายอายุ 8 เดือน
• ไข้ไอ น้ำมูกไหล 3 วัน หายใจหอบมากวันที่มาโรงพยาบาล
• ไม่เคยพบมาก่อน แข็งแรงดี ไม่เคยเจ็บป่วยร้ายแรง เป็นหวัดนาน ๆ ครั้ง

PE: BT 39°C, RR 80/min, PR 140/min, BW 9 kg.

- Nasal flaring, intercostal & subcostal retractions
- Generalized diminished bronchovesicular breath sounds,
  inspiratory & expiratory wheezing
- Normal heart sound, no murmur
- No chest deformity, no clubbing fingers
Case example:

A previously healthy 8-month-old male infant with URI for 3 days and dyspnea for 1 day. Generalized inspiratory & expiratory wheezing

Not respond to nebulized salbutamol x 2 doses

NP secretion: + ve RSV

Dx: RSV bronchiolitis
• How to manage this patient?
• What are the updates on management of acute bronchiolitis in children?
RSV bronchiolitis

Inflammation of small airway
- Edema
- Secretion
- Bronchospasm

Necrosis of bronchiolar epithelium

In bronchiolitis, the airway becomes obstructed from swelling of the bronchiole walls.
Treatment of acute bronchiolitis

The aim of all treatments is

- to reduce respiratory distress, mortality, economic and social burden (such as decrease length of stay),
- and long term sequelae: consequent wheezing, asthma
Treatment of acute bronchiolitis

Acute phase

1. **Supportive treatment**
   - Oxygenation & hydration
   - Pharmacological interventions

2. **Specific treatment**
   - Antiviral - ribavirin
   - RSV-specific humanized monoclonal antibody (Palivizumab)
Treatment of acute bronchiolitis

Acute phase
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Treatment of acute bronchiolitis

Pharmacological interventions

- Bronchodilators: $\beta_2$ agonist, epinephrine
- Nebulized hypertonic saline
- Corticosteroid
Clinical Practice Guidelines

• Released before 2007: recommend
  - Oxygenation and fluid replacement
  - All pharmacological agents are still controversy, should not be routinely used
• Recommendations of treatment were based on the existed evidences
• Those supported evidences had some limitations
Clinical Practice Guidelines

• The limitation of supported evidences
  - Inadequate power: small sample size
  - Variation of the eligible criteria especially enrolled recurrent wheezing or asthma
  - Variation of the studied medications especially systemic corticosteroids
  - Different outcome measurements
Bronchodilators
Bronchodilators

- $\alpha$ adrenergic agents: epinephrine
- $\beta_2$ agonist: albuterol/salbutamol
- Anticholinergic: ipratropium bromide
Bronchodilators

• Most previous studies with small samples showed conflicting results among
  β-agonist (albuterol or salbutamol) and
  α-adrenergic agents (epinephrine)

• 2 Cochrane Reviews

• A large RCT
Epinephrine for bronchiolitis

Selection criteria:
- RCTs comparing epinephrine with placebo or other bronchodilators
- children < 2 years with bronchiolitis
- presented at least one quantitative outcome

Main results:
14 RCTs - 6 adequate allocation concealment, 8 unclear

Epinephrine for bronchiolitis

Epinephrine vs placebo

IPD - only one RCT significant change in clinical score at 60 min

OPD - no different in admission rate and oxygen saturation at 60 min

Hartling L, et al. Cochrane Database 2004
Epinephrine for bronchiolitis

Epinephrine vs salbutamol

- IPD - only 1/7 RCTs showed significant change in respiratory rate at 30 min
- OPD - no different in admission rate

Hartling L, et al. Cochrane Database 2004
Author’s conclusion

There is insufficient evidence to support the use of epinephrine among IPD.

There is some evidence to suggest epinephrine may be favourable to placebo and salbutamol among out-patient.

Selection criteria:

RCTs comparing bronchodilators (other than epinephrine) with placebo

Main results:

22 trials with 1428 infants

Main results:

8 trials - bronchodilator showed no significant improvement in clinical score compared with placebo

Subgroup - a slightly greater effect on oximetry, clinical score in out-patients

Author’s conclusion

Bronchodilators produce small short term improvements in clinical score. This small effect must be weighed against the costs and adverse effects.

Comparison of nebulized epinephrine to albuterol in bronchiolitis

Objectives:
To compare the effect of nebulized racemic epinephrine to nebulized racemic albuterol on successful discharge from the emergency department (ED)

Methods: Children age less than 18 month, presenting to two EDs (n=703) randomly allocated - one dose of racemic epinephrine plus two saline nebulizations (n=351) or - 3 doses of racemic albuterol (n=352)

**Comparison of nebulized epinephrine to albuterol in bronchiolitis**

**Conclusions:**
Treatment at emergency department of bronchiolitis with nebulized racemic albuterol led to more successful discharges than nebulized epinephrine.

Hypertonic saline nebulization
Hypertonic saline nebulization

Mechanism

- reduces mucosal edema, secretion plug
- 2 RCTs in the past 2 years
  - Both were quite small sample studies
- 1 Cochrane Review
Hypertonic saline/epinephrine treatment in hospitalized infants with viral bronchiolitis reduced hospitalization stay: 2 years experience


Nebulized hypertonic saline in the treatment of viral bronchiolitis in infants

Results:

The combination of 3% hypertonic saline with epinephrine significantly reduced the hospital stay in hospitalized infants with viral bronchiolitis.


Results:

- The infants in the HS group had a clinically relevant reduction in LOS, compared with the NS group (p=0.05).
- The treatment was well tolerated, with no adverse effects attributable to the use of HS.

Nebulized hypertonic saline solution for acute bronchiolitis in infants

Selection criteria:
- RCTs and quasi-RCTs using hypertonic saline alone or in conjunction with bronchodilators
  - children < 2 years with bronchiolitis
  - 3%NaCl compared with 0.9%NaCl

Main results:
4 trials - 254 infants (189 IPD, 65 OPD)

Zhang L, et al. Cochrane Database 2008
Nebulized hypertonic saline solution for acute bronchiolitis in infants

Main results:
3%NaCl - significantly shorter mean LOS, lower clinical score in the first 3 days
   The effect was greater among OPD than IPD

Author’s conclusion
Nebulized 3%NaCl may significantly reduce LOS and improve clinical severity score

Zhang L, et al. Cochrane Database 2008
Systemic corticosteroid
Systemic corticosteroid

- 2 RTCs published in 2007
  - Dexamethasone single high dose
- 1 RCT in the last 5 years
Efficacy of dexamethasone injection for acute bronchiolitis in hospitalized children: a randomized, double-blind, placebo-controlled trial

Patient:
- 179 children with 1st wheeze, age 1–24 months, hospitalized

Intervention:
- Dexamethasone 0.6 mg/kg; n = 89
- Placebo IM at enrollment; n = 85

Primary outcome:
- Time from study entry to resolution of respiratory distress, determined by clinical score

Secondary outcome
- Duration of $O_2$ therapy
- Length of stay
- Additional drug use
- Later medical visit or admission,
- Adverse events

Fig. 1. Flow diagram of the progress through the phases of the clinical trial.
Efficacy of dexamethasone injection for acute bronchiolitis in hospitalized children: a randomized, double-blind, placebo-controlled trial

Teeratakulpisarn J. Pediatr Pulmonol 2007; 42:433
Efficacy of dexamethasone injection for acute bronchiolitis in hospitalized children: a randomized, double-blind, placebo-controlled trial

Results:
Dexamethasone significantly decreased in:
- the time needed for resolution of respiratory distress
- the mean duration of respiratory symptoms
- the mean duration of oxygen therapy and
- the mean length of hospital stay

Teeratakulpisarn J. Pediatr Pulmonol 2007; 42:433
Efficacy of dexamethasone injection for acute bronchiolitis in hospitalized children: a randomized, double-blind, placebo-controlled trial

**Conclusions:**

A single injection of dexamethasone provided a significant clinical benefit for the treatment of previously healthy young children hospitalized with acute bronchiolitis

Teeratakulpisarn J. Pediatr Pulmonol 2007; 42:433
A multicenter, randomized, controlled trail of dexamethasone for bronchiolitis

Patient:
- 600 children with 1st wheeze, age 2 - 12 months at ED

Intervention:
- Dexamethasone 1 mg/kg; n = 305
- Placebo oral; n = 295
  at emergency department

Primary outcome:
- Hospital admission after 4 hours

Secondary outcome
- Respiratory assessment change score (RACS),
- Length of stay,
- Later medical visit or admission,
- Adverse events
A multicenter, randomized, controlled trial of dexamethasone for bronchiolitis

Results:
No significant difference between the two groups in
- admission rate at 4 hours after enrollment and
- mean 4 hours Respiratory assessment change score (RACS)

A multicenter, randomized, controlled trial of dexamethasone for bronchiolitis

<table>
<thead>
<tr>
<th>Conclusions:</th>
</tr>
</thead>
<tbody>
<tr>
<td>A single dose of 1 mg/kg dexamethasone did not significantly altered the rate of hospital admission, the respiratory status after 4 hours of observation, or later outcomes</td>
</tr>
</tbody>
</table>

How to explain the difference of those results?

Has there any influence factors?

- Age
- Viral etiology
- Atopy
- Severity of disease
- ?
Conflicting results of usefulness of dexamethasone

Baseline characteristics

<table>
<thead>
<tr>
<th></th>
<th>5.1, 5.1</th>
<th>10.2, 11.2</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Mean age, mo</strong></td>
<td>5.1, 5.1</td>
<td>10.2, 11.2</td>
</tr>
<tr>
<td><strong>Male, %</strong></td>
<td>62, 60</td>
<td>62, 65</td>
</tr>
<tr>
<td><strong>Clinical score</strong></td>
<td>9/17, 9.2/17</td>
<td>7.1/12, 6.9/12</td>
</tr>
<tr>
<td><strong>RSV +, %</strong></td>
<td>66.9, 57</td>
<td>-</td>
</tr>
<tr>
<td><strong>Days of illness</strong></td>
<td>3.7, 3.6</td>
<td>3.6, 3.6</td>
</tr>
<tr>
<td><strong>Passive smoker, %</strong></td>
<td>39, 36</td>
<td>60, 62</td>
</tr>
<tr>
<td><strong>Atopic, family, %</strong></td>
<td>63.4, 69</td>
<td>29, 28</td>
</tr>
</tbody>
</table>
Oral prednisolone in the acute management of children age 6 to 35 months with viral respiratory infection-induced lower airway disease: a randomized, placebo-controlled trial

Patient:
- 230 children with 1st wheeze, age 6 - 35 months, at emergency department

Intervention:
Prednisolone 2 mg/kg first dose, oral, then 2 mg/kg/day bid for 3 days (six total doses) (n=113) vs placebo (n=117)

Oral prednisolone in the acute management of children age 6 to 35 months with viral respiratory infection-induced lower airway disease: a randomized, placebo-controlled trial

Results:
- The hospitalization rates were similar
- For admitted children, prednisolone significantly reduced the length of stay, the median duration of symptoms of respiratory distress
- Less need for additional asthma medications in the prednisolone group

Oral prednisolone in the acute management of children age 6 to 35 months with viral respiratory infection-induced lower airway disease: a randomized, placebo-controlled trial

The results of this study were similar to those two previous studies of dexamethasone that
• systemic corticosteroid did not demonstrate its usefulness in admission rate but
• in hospitalized children, it significantly reduced the length of stay and duration of respiratory distress

Are there any relation of viral etiology, age and atopy of affected children to the response of treatment?
Role of rhinovirus in wheezing children

- Rhinovirus was found to be the second most common etiologic agent in hospitalized children after RSV.
- It was also associated with recurrent wheezing and particular risk of later asthma.

Respiratory picornaviruses and respiratory syncytial virus as causative agents of acute expiratory wheezing in children

Objective:
To determine the viral etiology of acute expiratory wheezing (bronchiolitis, acute asthma) in 293 hospitalized children in a 2-year prospective study from Finland

Respiratory picornaviruses and respiratory syncytial virus as causative agents of acute expiratory wheezing in children
Rhinovirus-associated wheezing in infancy: comparison with RSV bronchiolitis

Objective: To compare clinical characteristics of rhinovirus and respiratory syncytial virus (RSV) bronchiolitis

Results: The children with RV infection, compared with RSV patients, were
- older (median, 13 vs 5 months),
- presented more often with atopic dermatitis
- blood eosinophilia

Treatment of acute bronchiolitis

Acute phase
1. Supportive treatment
   - Oxygenation & hydration
   - Pharmacological interventions
2. Specific treatment
   - Antiviral – ribavirin
   - RSV-specific humanized monoclonal antibody (Palivizumab)
Treatment of acute bronchiolitis

Acute phase
1. Supportive treatment
   - Oxygenation & hydration
   - Pharmacological interventions
2. Specific treatment
   - Antiviral - ribavirin
   - RSV-specific humanized monoclonal antibody (Palivizumab)
### Ribavirin

- A nucleoside analogue, broad spectrum antiviral activity (esp. RSV)
- Small studies of its efficacy
- Recommend only in high risk children: immunocompromised host, heart diseases, chronic lung diseases, etc
- Safety problem during administration and cost
<table>
<thead>
<tr>
<th>Palivizumab</th>
</tr>
</thead>
<tbody>
<tr>
<td>• A human recombinant monoclonal antibody direct against a surface glycoprotein of RSV</td>
</tr>
<tr>
<td>• Recommend for prevention of RSV infection in high risk infants who will suffer severe diseases especially in RSV season</td>
</tr>
<tr>
<td>• No sufficient evidence to support the role in acute phase infection (Fuller H. Cochrane Database 2006)</td>
</tr>
</tbody>
</table>
Summary
Pharmacological interventions

- There is insufficient evidence to support the use of any medication in acute phase RSV bronchiolitis
- The clinical presentations of bronchiolitis causes by RSV, rhinovirus or other respiratory viruses are similar
- Rhinovirus is found to be the second most common cause of bronchiolitis after RSV and trends to infect older child than RSV
- Identification of causative viruses is not routinely performed in many hospitals
Pharmacological interventions

- Practically, although systemic corticosteroid did not provide the usefulness in children less than one year at the emergency department.
- But it should be considered in older, hospitalized children with viral bronchiolitis.
- Moreover, most of all studies reported few or minor side effects of corticosteroid.
Pharmacological interventions

- Nebulized racemic albuterol also provided a clinical benefit over epinephrine in a large study.
- Aerosolized hypertonic saline alone or with epinephrine may be beneficial in acute phase bronchiolitis.
Case example:

A 13-month-old boy with history of RSV bronchiolitis at 8 month of age and recovered after hospitalization for 6 d.

What is the cause or diagnosis of recurrent wheezing in this patient?
How to approach a child with recurrent wheezing?
Evaluation of wheezy infant

- Clinical history
- Physical signs
- Lab / Diagnostic investigations
Wheezy infants & preschool children age 0-6 yrs

Typical wheezy infants
- Early transient wheeze
- Non-atopic (viral) wheeze
- Persistent (atopic) wheeze

Atypical wheezy infants
- GER / aspiration syndrome
- Foreign body aspiration
- Congenital anomalies of CVS & RS
- Bronchiolitis obliterans
- Congenital esophageal anomalies
- Bronchiectasis, BPD, TB, PCD, CF

Types of wheezy infants & preschool children
Clinical presentations suggestive of atypical wheezers

- Onset in newborn period
- Symptoms associated with feeding
- History of feeding difficulty
- History of endotracheal intubation
- Failure to thrive / failure to gain weight
- Choking or chronic aspiration
- Barrel shaped chest
- Digital clubbing
Evaluation of wheezing child: Investigations

- Chest X-ray
- Tuberculin test
- Pulmonary function test
- Esophagogram & upper GI study
- GER scan & esophageal pH monitoring
- Allergic evaluation
- CT scan chest
- Bronchoscopy & BAL
Wheezy infants & preschool children age 0-6 yrs

Types of wheezy infants & preschool children
Schematic representations of prevalence of wheezing phenotypes in childhood

Taussig : Pediatric Respiratory Medicine 2008 :128
Wheezing phenotypes

- **Transient infant wheeze**
  - Maternal smoker, young mother

- **Non-atopic (viral associated) wheeze**
  - Recurrent wheezing during childhood
  - No increased atopy
  - Transient BHR
  - Risk of COPD ?

- **Persistent (atopic) asthma**
## Predictors for wheezing phenotypes in the first 10 years of life (n= 2711)

<table>
<thead>
<tr>
<th>Baseline factors</th>
<th>Preschool wheezers OR (95% CI)</th>
<th>Primary-school wheezers OR (95% CI)</th>
<th>Intermittent wheezers OR (95% CI)</th>
<th>Persistent wheezers OR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Respiratory infection</td>
<td>5.15 (2.57–10.33)</td>
<td>4.76 (1.83–12.37)</td>
<td>8.44 (3.05–23.33)</td>
<td></td>
</tr>
<tr>
<td>Gender, male</td>
<td></td>
<td></td>
<td></td>
<td>1.89 (1.17–3.05)</td>
</tr>
<tr>
<td>Breastfeeding</td>
<td>1.54 (1.13–2.09)</td>
<td></td>
<td>1.94 (1.22–3.09)</td>
<td>1.89 (1.17–3.05)</td>
</tr>
<tr>
<td>Prematurity (&lt;37 weeks)</td>
<td></td>
<td></td>
<td>2.37 (1.18–4.76)</td>
<td>1.89 (1.17–3.05)</td>
</tr>
<tr>
<td>Personal history of allergy</td>
<td>2.25 (1.50–3.39)</td>
<td></td>
<td>2.42 (1.40–4.17)</td>
<td>4.84 (3.03–7.74)</td>
</tr>
<tr>
<td>Health status rated low at birth</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Daycare attendance</td>
<td>1.50 (1.11–2.03)</td>
<td>0.36 (0.14–0.94)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>History of parental asthma</td>
<td>2.35 (1.49–3.71)</td>
<td>2.38 (1.23–4.61)</td>
<td></td>
<td>7.21 (3.99–13.06)</td>
</tr>
<tr>
<td>History of parental smoking</td>
<td>1.53 (1.14–2.06)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Crowding (n ≥ 1.5/bedroom)</td>
<td>0.69 (0.50–0.94)</td>
<td>0.44 (0.26–0.74)</td>
<td></td>
<td>1.74 (1.05–2.87)</td>
</tr>
<tr>
<td>Dwelling needing repairs</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*Respirology 2008; 13: 53-45*
Study in 259 children 0-6 yrs. of age with parental respiratory allergies

Figure 2. Risk of asthma at age 6 years in children who wheezed during the first 3 years of life with rhinovirus (RV), respiratory syncytial virus (RSV), or both (*P < 0.05 vs. Neither; †P < 0.05 vs. RSV only). OR = odds ratio.
Relationship between virus-induced wheezing in infancy and childhood asthma

Predisposed infant
- Lung function decreased
- Antiviral response

Healthy infant
- Immune deviation

First excuse to wheeze

VRI

Asthma
- Decreased lung function
- Structural changes
- Allergies

Birth  Infancy  School age

Pediatr Infect Dis J 2008;27: S97- S103
Respiratory virus infection

Activation of innate or adaptive immune defense mechanism

Atopic sensitization

Aeroallergen re-exposure

Airway DC– induced Th2 activation

Airway inflammation

Altered postnatal lung & airway growth & differentiation

Disturbed respiratory function

Persistent asthma
Case example: A 13-month-old male infant with history of RSV bronchiolitis recovered after hospitalization for 6 days.

หลัง discharge จากโรงพยาบาล ผู้ป่วยเป็นหวัดและหายใจหอบ ตรวจพบเสียงหายใจมี wheezing อีก 3 ครั้ง ตอนอายุ 10 เดือน, 11 เดือน และ 1 ปี ต้องไปพยาบาลขยายหลอดลมที่คลินิก และที่ รพ.จังหวัดขึ้น ขณะนั้นอายุ 1ปี 1 เดือน

ประวัติเพิ่มเติม: - คลอดก่อนกำหนด 36 wk GA. ไม่ต้องใช้เครื่องช่วยหายใจตอนแรกเกิดกินนมแม่ประมาณ 3 เดือน
- ไม่มีประวัติสลายกั้น หรืออาเจียนหลังกินนม
- คุณแม่เป็นภูมิแพ้ที่จมูก เคยเป็นหายท้องเด็ก คุณพ่อสูบบุหรี่

PE: No barrel chest, no clubbing fingers, BW 10 kg.
Chest x-ray

A 13-month-old male infant with

- Recurrent wheezing (RAD) after RSV bronchiolitis
- Maternal history of asthma & allergic rhinitis
- Tobacco smoke exposure
Asthma predictive index

• Child with \( \geq 3 \) episodes of wheezing by 3 years of age has 1 major criteria or 2 minor criteria:

  
  **Major criteria :**
  - Parental asthma (physician diagnosed)
  - Eczema / Atopic dermatitis (physician diagnosed)

  **Minor criteria :**
  - Allergic rhinitis (physician diagnosed)
  - Wheezing apart from colds
  - Peripheral eosinophilia (\( \geq 4\% \))

  *Amer J Respir Crit Care Med 2000;162: 1403-6*
- How to treat this child with recurrent wheezing?
- How to prevent post-bronchiolitis wheezing or asthma?
How to treat recurrent wheezing?

- Treat as asthma
- According to GINA or Thai guideline for asthma in children

แนวทางการวินิจฉัยและรักษา
โรคติดในประเทศไทย
สำหรับผู้ป่วยเด็ก พ.ศ. 2551
Children ≤ 5 years

ICS or LTRA
(200 µg BDP equivalent) (dose depends on age)

Insufficient control**

Increase ICS dose (400 µg BDP equivalent) or Add ICS to LTRA

Insufficient control**

Increase ICS dose (800 µg BDP equivalent)
Or Add LTRA to ICS
Or Add LABA

Insufficient control**

Consider other options
* Theophylline
* Oral corticosteroids
How to prevent post-bronchiolitis wheezing or asthma?

- Inhaled/systemic corticosteroid
- Montelukast
- Ribavirin
How to prevent post-bronchiolitis wheezing or asthma?

• Inhaled/systemic corticosteroid
• Montelukast
• Ribavirin
How to prevent post-bronchiolitis wheezing or asthma?

Inhaled/systemic corticosteroid

- 2 RCTs
- 1 Cochrane Review
Objective: to assess the efficacy of inhaled budesonide vs placebo after 1st episode of wheezing in reducing subsequent respiratory symptoms during the first 3 years of life.

Patients:
- 1-month old infants with 3-consecutive days of wheezing episode
- Maternal history of asthma

Intermittent inhaled corticosteroids in infants with episodic wheezing

**Intervention:** 2 weeks of 400 ug budesonide/placebo

**Results:**
- 149 budesonide group vs 145 placebo group
- were cohort for 3 years

Intermittent inhaled corticosteroids in infants with episodic wheezing

Conclusions

- Intermittent inhaled budesonide had no effect on progression from episodic to persistent wheezing

- No short-term benefit during episodes of wheezing in the first 3 years of life

Inhaled corticosteroids during acute bronchiolitis in the prevention of post-bronchiolitis wheezing

Objective: to evaluate the effect of ICS, started during the acute phase, on the prevention of post-bronchiolitis wheezing

Selection criteria
- RCTs of ICS in children < 2 years with clinical diagnosis of acute bronchiolitis

Inhaled corticosteroids during acute bronchiolitis in the prevention of post-bronchiolitis wheezing

**Main results:** 5 studies, involving 347 infants
- No effect of ICS in the prevention of wheezing (dairy records or GP diagnosis), re-admission, use of corticosteroid, bronchodilator

**Author’s conclusion**
ICS does not demonstrate an effect in the prevention of post-bronchiolitis wheezing

Preemptive use of high-dose fluticasone for virus-induced wheezing in young children

**Objective:** to determine the efficacy and safety of preemptive treatment with high-dose fluticasone in reducing the severity of recurrent virus-induced wheezing

**Patients:**
- age 1-6 years with ≥ 3 wheezing episodes triggered by URI

Preemptive use of high-dose fluticasone for virus-induced wheezing in young children

Interventions:

750 ug fluticasone or placebo twice daily for a maximum of 10 days at the beginning of URI, over a period of 6-12 months

Primary outcome:
- rescue oral corticosteroid use

Preemptive use of high-dose fluticasone for virus-induced wheezing in young children

Conclusions

- Preemptive treatment with high-dose fluticasone significantly reduced the use of rescue oral corticosteroids
- But fluticasone was associated with a smaller gain in height and weight
- No different in basal cortisol level and bone density or adverse events

How to prevent post-bronchiolitis wheezing or asthma?

- Inhaled/systemic corticosteroid
- Montelukast
- Ribavirin
Montelukast

• A large multicenter study published this year of 979 children

To evaluate the efficacy and safety of montelukast on recurrent respiratory symptoms of post-RSV bronchiolitis
Study of montelukast for the treatment of respiratory symptoms of post-RSV bronchiolitis in children

**Patients:** RSV-positive 3-24 months admitted for at least 24 hours for a 1\textsuperscript{st} or 2\textsuperscript{nd} episode of bronchiolitis:
- Montelukast 4 mg (n=327),
- Montelukast 8 mg (n=324)
- Placebo, n=328: period I 4-wks, period II 20-weeks,

**Results:**
Montelukast at two separate doses did not alleviate post-RSV bronchiolitis respiratory symptoms in 3 to 24 months old infants over a period of 4 weeks and subsequent 20 weeks

Summary: Prevention of persistent wheeze/asthma

- The effect of corticosteroid on recurrent wheezing should be further investigated in a large and long term cohort.
- Montelukast did not alleviate post-bronchiolitis respiratory symptoms over a period of 20 weeks.
## Conclusion

**Acute wheezing in young children:**

- Acute bronchiolitis is the most common cause
- Currently, there are insufficient evidence to support the use of any medications
- Supportive treatment including oxygen therapy and hydration are still the mainstay of management
- Some medications i.e. corticosteroid, nebulized hypertonic saline, racemic albuterol may be helpful in certain patients (further research studies are required)
- Palivizumab is not effective in acute wheezing
Recurrent / persistent wheezing in young children:

- Careful history taking & physical exam are essential for identifying the cause (atypical wheezy infant)

- Among those without specific cause of wheezing, risk factors for persistent wheezing or persistent asthma should be identified in order to give appropriate management and follow ups

- There is currently no conclusive evidence on the effectiveness of corticosteroid and leukotriene antagonist