Wheezing in the young : How to approach and treat ?

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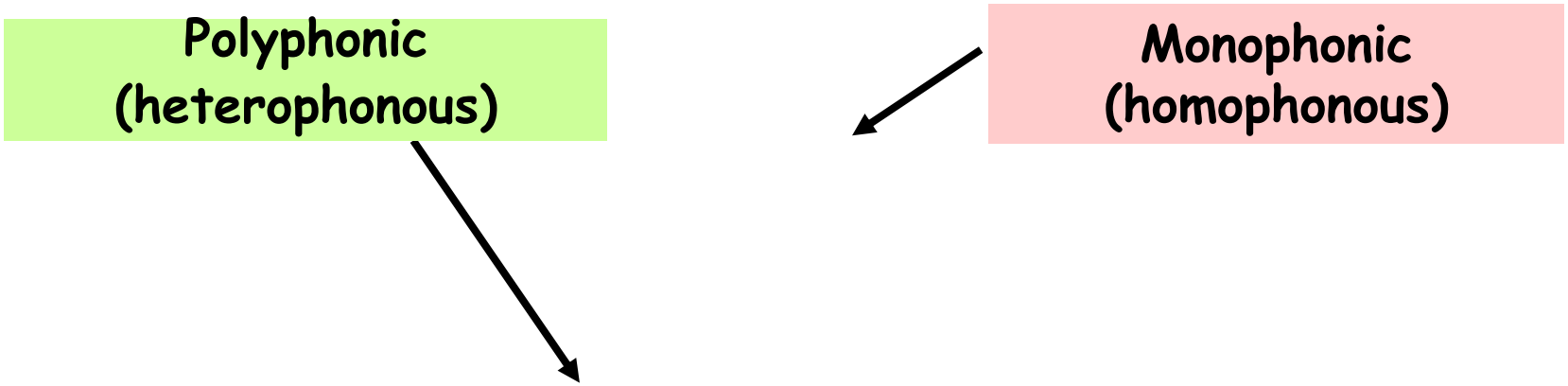
1 /04/2009

Physiology / Mechanism of wheezing

: **Continuous musical, high pitched whistling sounds usuallly associated with prolonged expiration caused by vibration of airway wall due to turbulent airflow through narrow airways**

Physiology / Mechanism of wheezing



Wheezing – 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**
- **ไม่เคยหอบมาก่อน แข็งแรงดี ไม่เคยเจ็บป่วยร้ายแรง เป็นหวัดนาน ๆครั้ง**

PE : BT 39^{O}C, RR 80/min, PR 140/min, BW 9 kg.

- Nasal flaring, intercostal & subcostal retractions

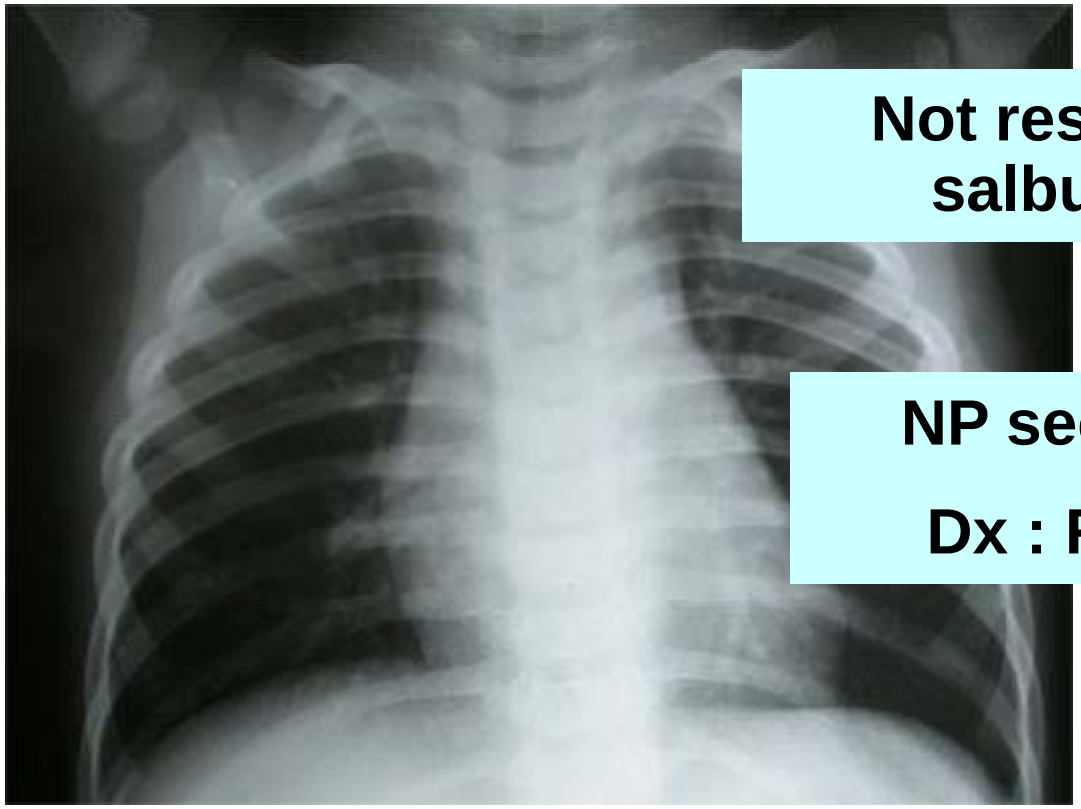
- Generalized diminished bronchovesicular breath sounds, inspiratory & expiratory wheezing

- 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

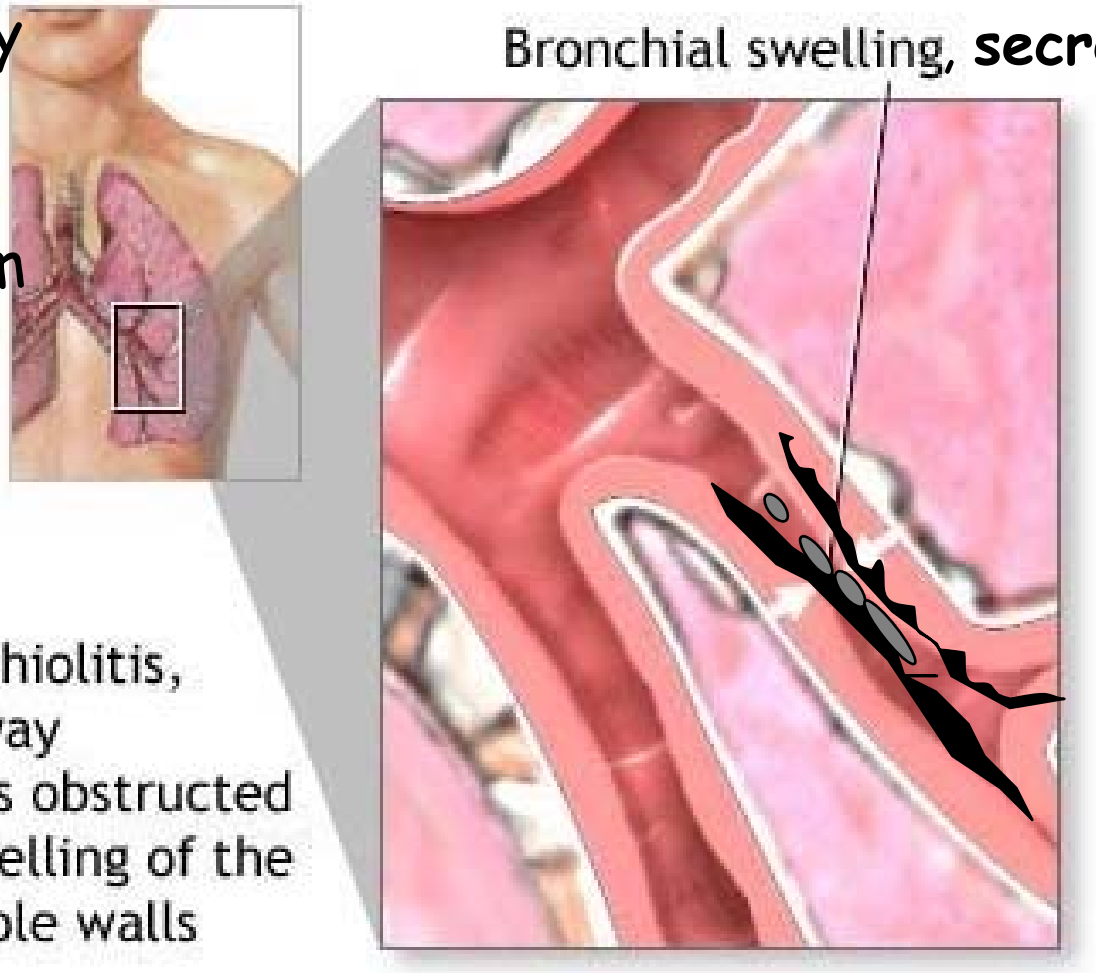
Dx : RSV bronchiolitis

- 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



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

1. Supportive treatment
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   - Antiviral – ribavirin
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Treatment of acute bronchiolitis

Pharmacological interventions

- Bronchodilators: β_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

- α adrenergic agents : epinephrine
- β_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

Hartling L, et al. Cochrane Database 2004

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

Epinephrine for bronchiolitis

Author's conclusion

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

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

Hartling L, et al. Cochrane Database 2004

Bronchodilator for bronchiolitis

Selection criteria:

RCTs comparing bronchodilators (other than epinephrine) with placebo

Main results:

22 trials with 1428 infants

Gadomski AM, et al. Cochrane Database 2006

Bronchodilator for bronchiolitis

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

Gadomski AM, et al. Cochrane Database 2006

Bronchodilator for bronchiolitis

Author's conclusion

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

Gadomski AM, et al. Cochrane Database 2006

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)

Walsh P. Acad Emerg Med 2008; 15: 305-13

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

Walsh P. Acad Emerg Med 2008; 15: 305-13

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

Tal G, et al. IMAJ 2006; 8: 169.

Nebulized hypertonic saline in the treatment of viral bronchiolitis in infants

Kuzik BA, et al. J Pediatr 2007; 151: 266.

Results:

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

Tal G, et al. IMAJ 2006; 8: 169.

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

Kuzik BA, et al. J Pediatr 2007; 151: 266.

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

Teeratakulpisarn J, et al. Pediatr Pulmonol 2007; 42:433

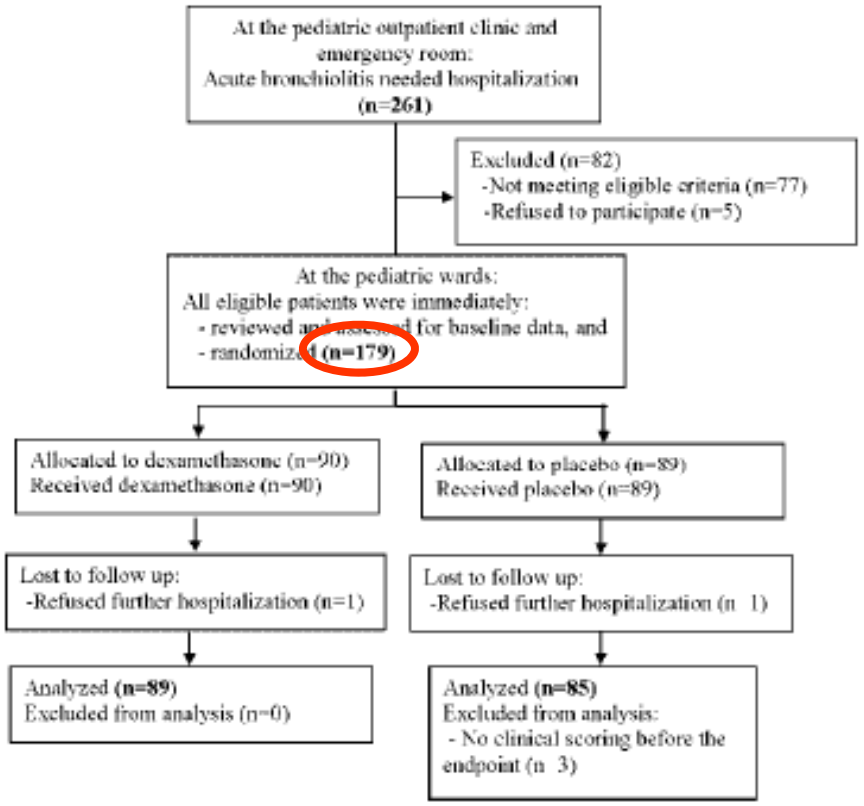

Fig. 1. Flow diagram of the progress through the phases of the clinical trial.

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

Efficacy of dexamethasone injection for acute bronchiolitis in hospitalized children: a randomized, double-blind, placebo-controlled trial

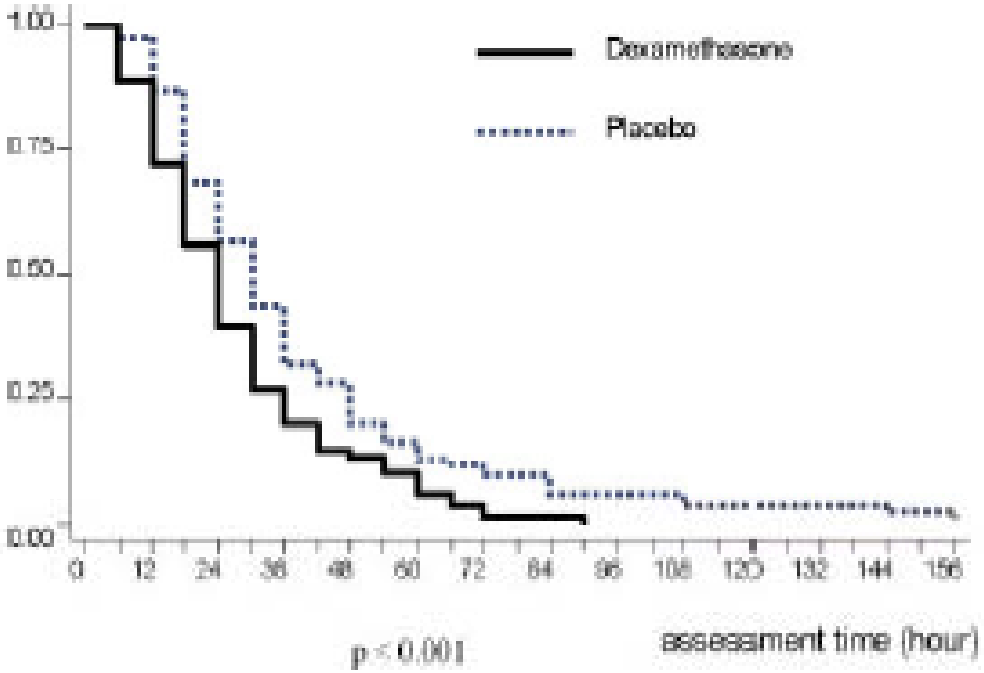

Fig. 2. Comparison of time to resolution of respiratory distress (total clinical score ≤3) between the dexamethasone and placebo groups.

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

Corneli HM, et al. N Engl J Med 2007; 357

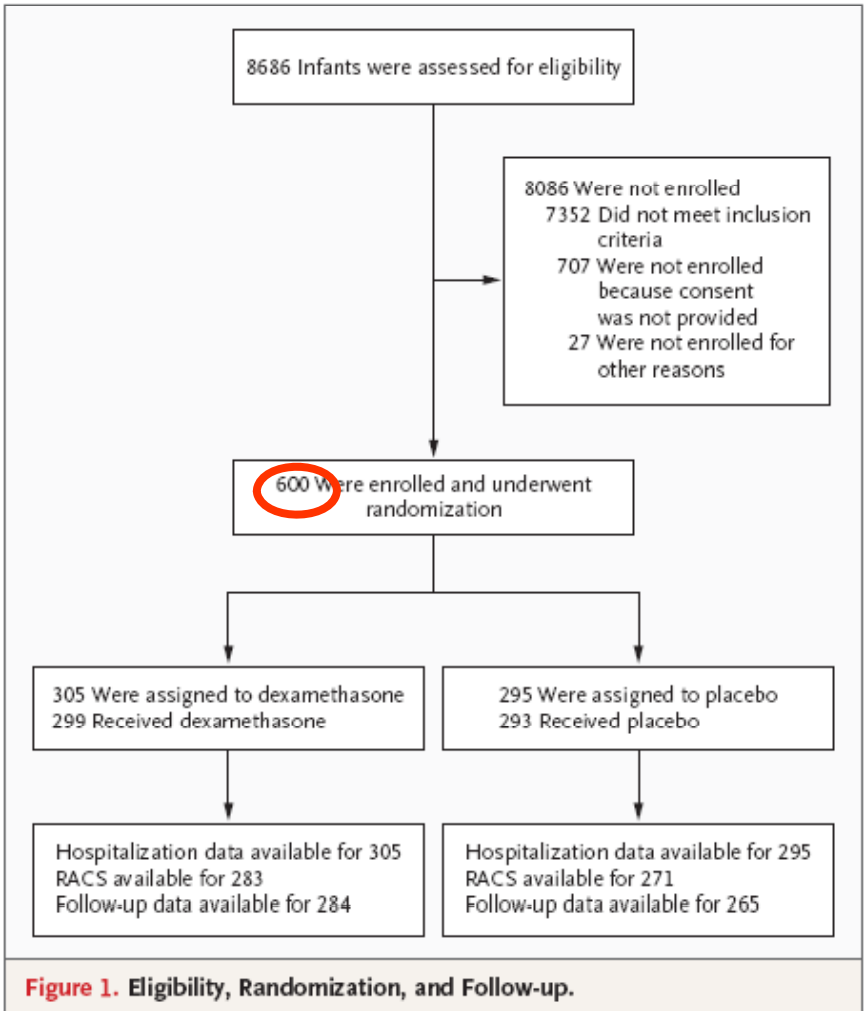

Figure 1. **Eligibility, Randomization, and Follow-up.**

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 brocnhiolitis

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)

Corneli HM, et al. N Engl J Med 2007; 357

A multicenter, randomized, controlled trial of dexamethasone for brocnhiolitis

Conclusions:

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

Corneli HM, et al. N Engl J Med 2007; 357

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

The NEW ENGLAND JOURNAL of MEDICINE

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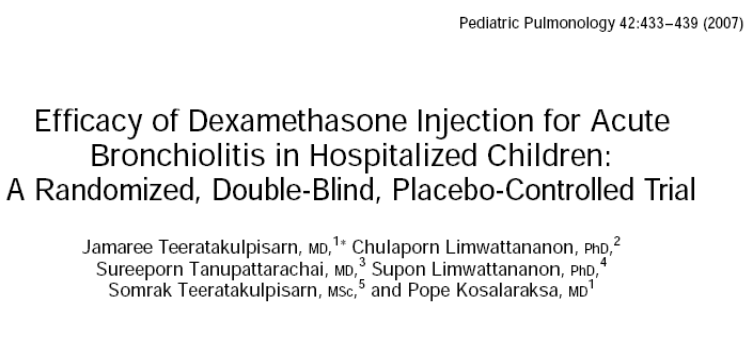
A Multicenter, Randomized, Controlled Trial of Dexamethasone for Bronchiolitis

Howard M. Corneli, M.D., Joseph J. Zorc, M.D., Prashant Mahajan, M.D., M.P.H., Kathy N. Shaw, M.D., M.S.C.E., Richard Holubkov, Ph.D., Scott D. Reeves, M.D., Richard M. Ruddy, M.D., Baqir Malik, M.D., Kyle A. Nelson, M.D., M.P.H., Joan S. Bregstein, M.D., Kathleen M. Brown, M.D., Matthew N. Denenberg, M.D., Kathleen A. Lillis, M.D., Lynn Babcock Cimpello, M.D., James W. Tsung, M.D., Dominic A. Borgialli, D.O., M.P.H., Marc N. Baskin, M.D., Getachew Teshome, M.D., M.P.H., Mitchell A. Goldstein, M.D., David Monroe, M.D., J. Michael Dean, M.D., and Nathan Kuppermann, M.D., M.P.H., for the Bronchiolitis Study Group of the Pediatric Emergency Care Applied Research Network (PECARN)*



Pediatric Pulmonology 42:433–439 (2007)

Efficacy of Dexamethasone Injection for Acute Bronchiolitis in Hospitalized Children: A Randomized, Double-Blind, Placebo-Controlled Trial

Jamaree Teeratakulpisarn, MD,[1]* Chulaporn Limwattananon, PhD,[2] Sureeporn Tanupattarachai, MD,[3] Supon Limwattananon, PhD,[4] Somrak Teeratakulpisarn, MSc,[5] and Pope Kosalaraksa, MD[1]

Baseline characteristics

Mean age, mo	5.1, 5.1	10.2, 11.2
Male, %	62, 60	62, 65
Clinical score	9/17, 9.2/17	7.1/12 , 6.9/12
RSV +,%	66.9, 57	-
Days of illness	3.7, 3.6	3.6, 3.6
Passive smoker,%	39, 36	60, 62
Atopic, family,%	63.4, 69	29, 28

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)

Csonka P, et al. J Pediatr 2003; 143:725

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

Csonka P, et al. J Pediatr 2003; 143:725

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

Csonka P, et al. J Pediatr 2003; 143:725

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

Mansbach JM. Acad Emerg Med 2008; 15: 111-8

Garcia-Garcia ML, et al. Pediatr Infect Dis J 2007; 26: 904.

Manoha C, et al. J Clin Virol 2007; 38: 221.

Jacques J. et al. J Clin Virol 2006; 35: 463.

Pitrez PMC, et al. J Pediatr (Rio J) 2005; 81:417.

Lemanske RF, et al. J Allergy Clin Immunol 2005; 116:571.

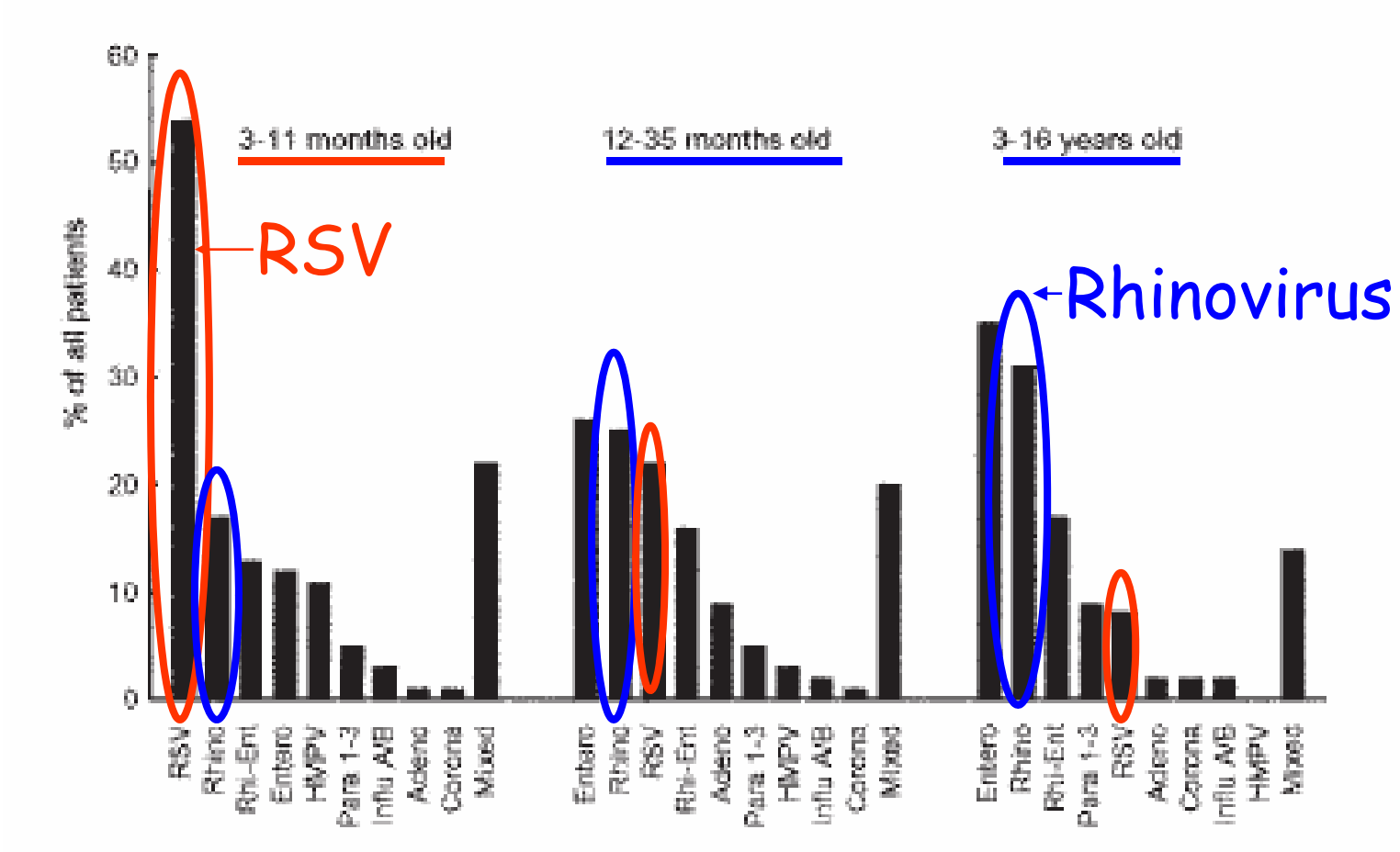
Respiratory picornaviruses and respiratory syncytial virus as causative agents of acute expiratory wheezing in children

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

Jartti T, et al. Emerg Infect Dis 2004; 10:1095

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**

Korppi M, et al. Pediatr Infect Dis J 2004; 23:11.

Treatment of acute bronchiolitis

Acute phase

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

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Ribavirin

- A nucleoside analoque, 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

Palivizumab

- A human recombinant monoclonal antibody direct against a surface glycoprotein of RSV
- Recommend for prevention of RSV infection in high risk infants who will suffer severe diseases especially in RSV season
- No sufficient evidence to support the role in acute phase infection (Fuller H. Cochrane Database 2006)

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 benefit 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.

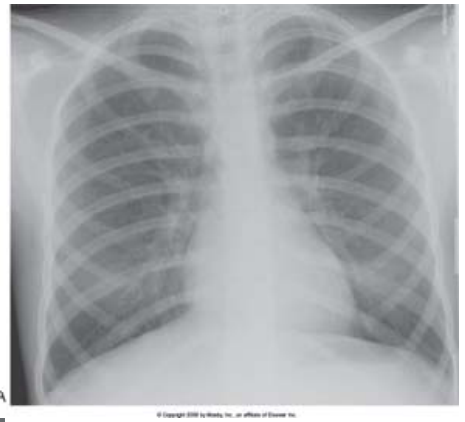
หลัง discharge จากโรงพยาบาล ผู้ป่วยเป็นหวัดและหายใจหอบ ตรวจพบเสียงหายใจมี wheezing อีก 3 ครั้ง ตอนอายุ 10 เดือน 11 เดือน และ 1 ปี ต้องไปพ่นยาขยายหลอดลมที่คลินิก และโรงพยาบาลจึงดีขึ้น ขณะนี้อายุ 1 ปี 1 เดือน

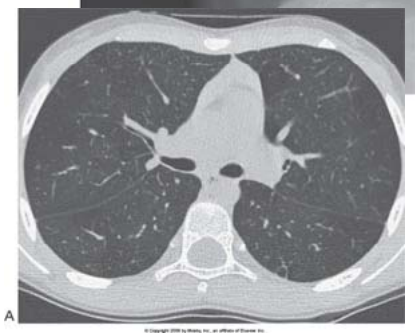
What is the cause or diagnosis of recurrent wheezing in this patient ?

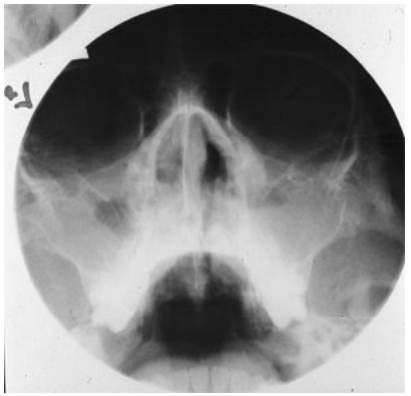
How to approach a child with recurrent wheezing ?

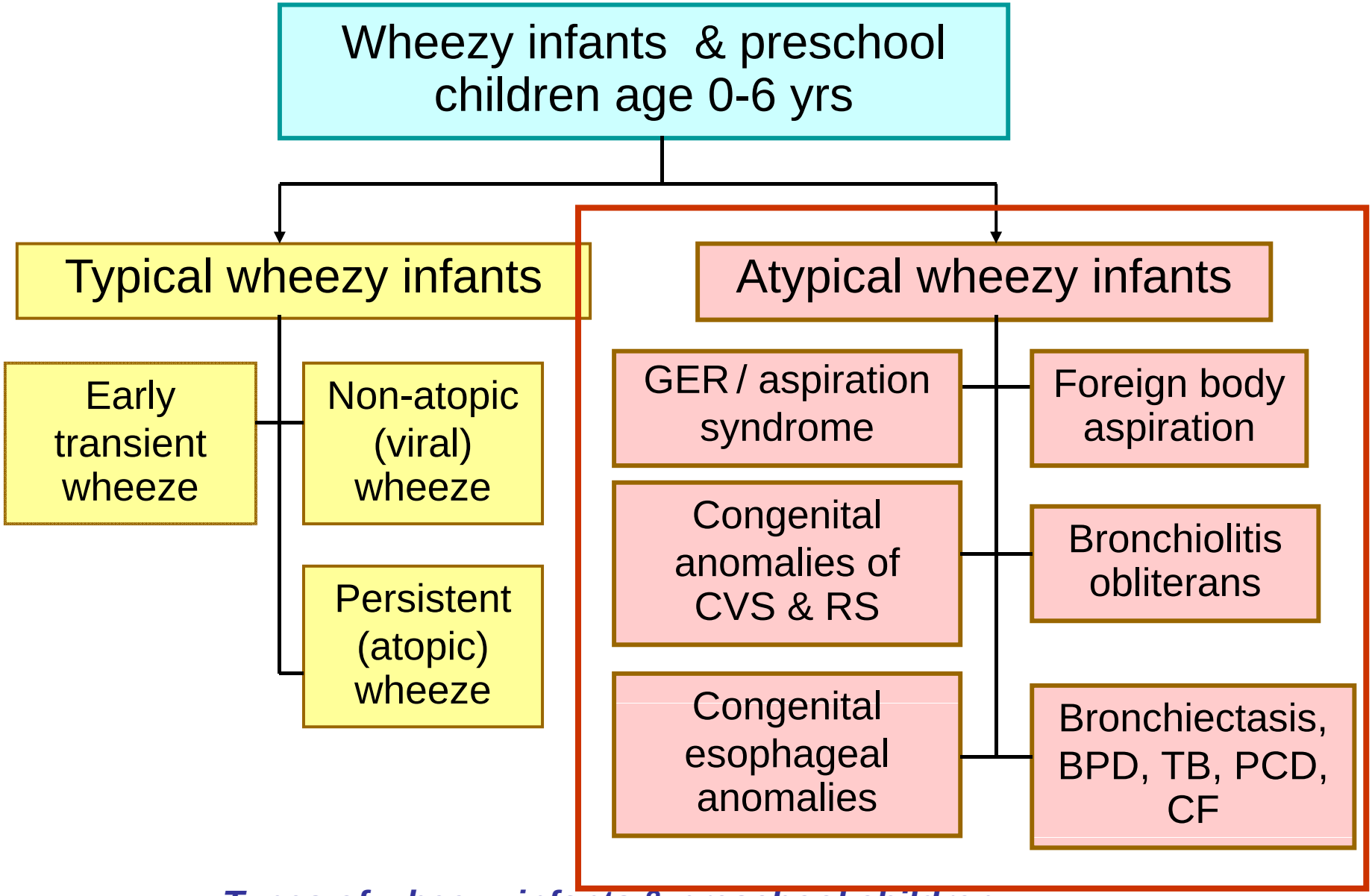
Evaluation of wheezy infant

- Clinical history
- Physical signs
- Lab / Diagnostic investigations









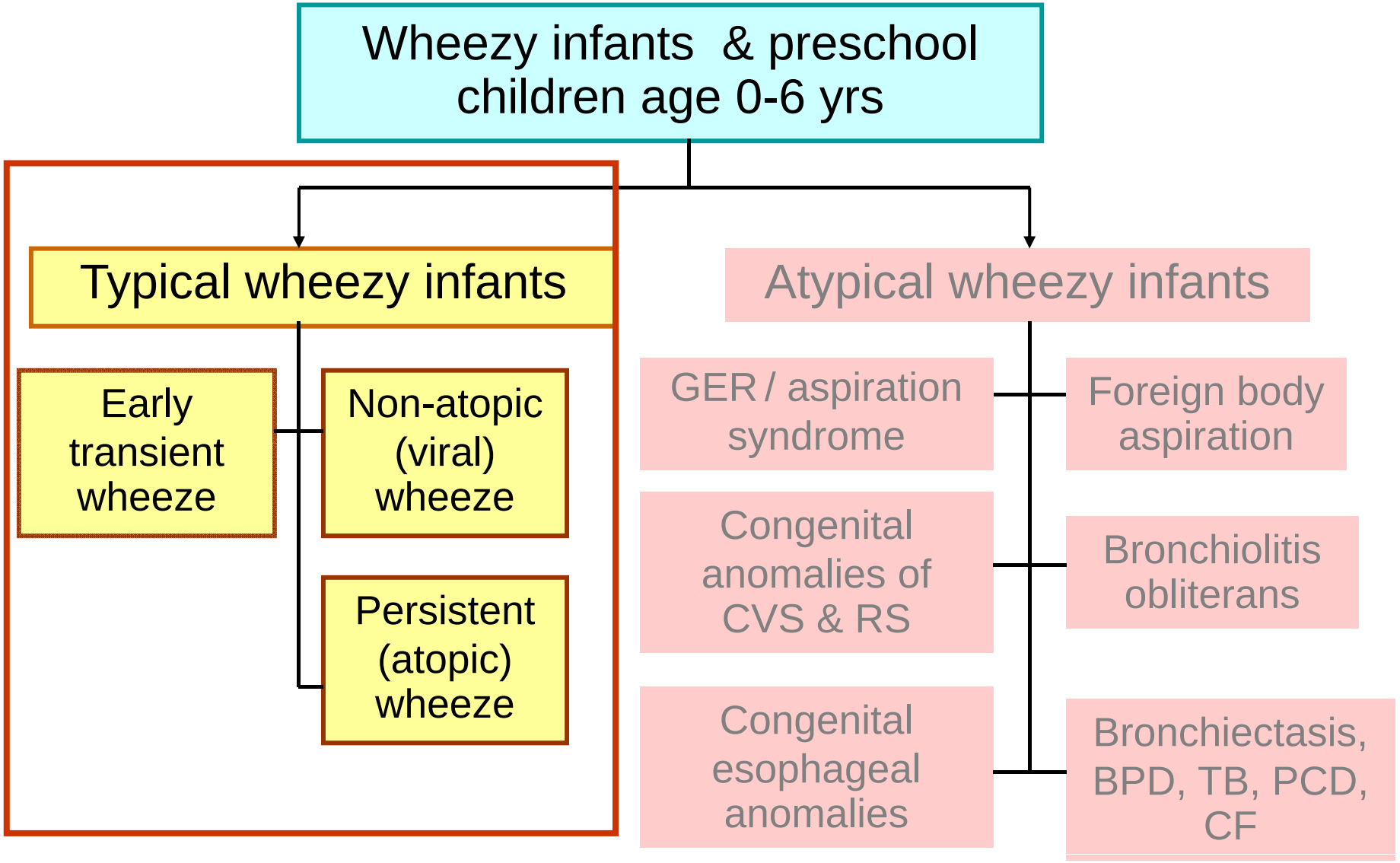
Types of wheezy infants & preschool children

Clinical presentations suggestive of atypical wheezers

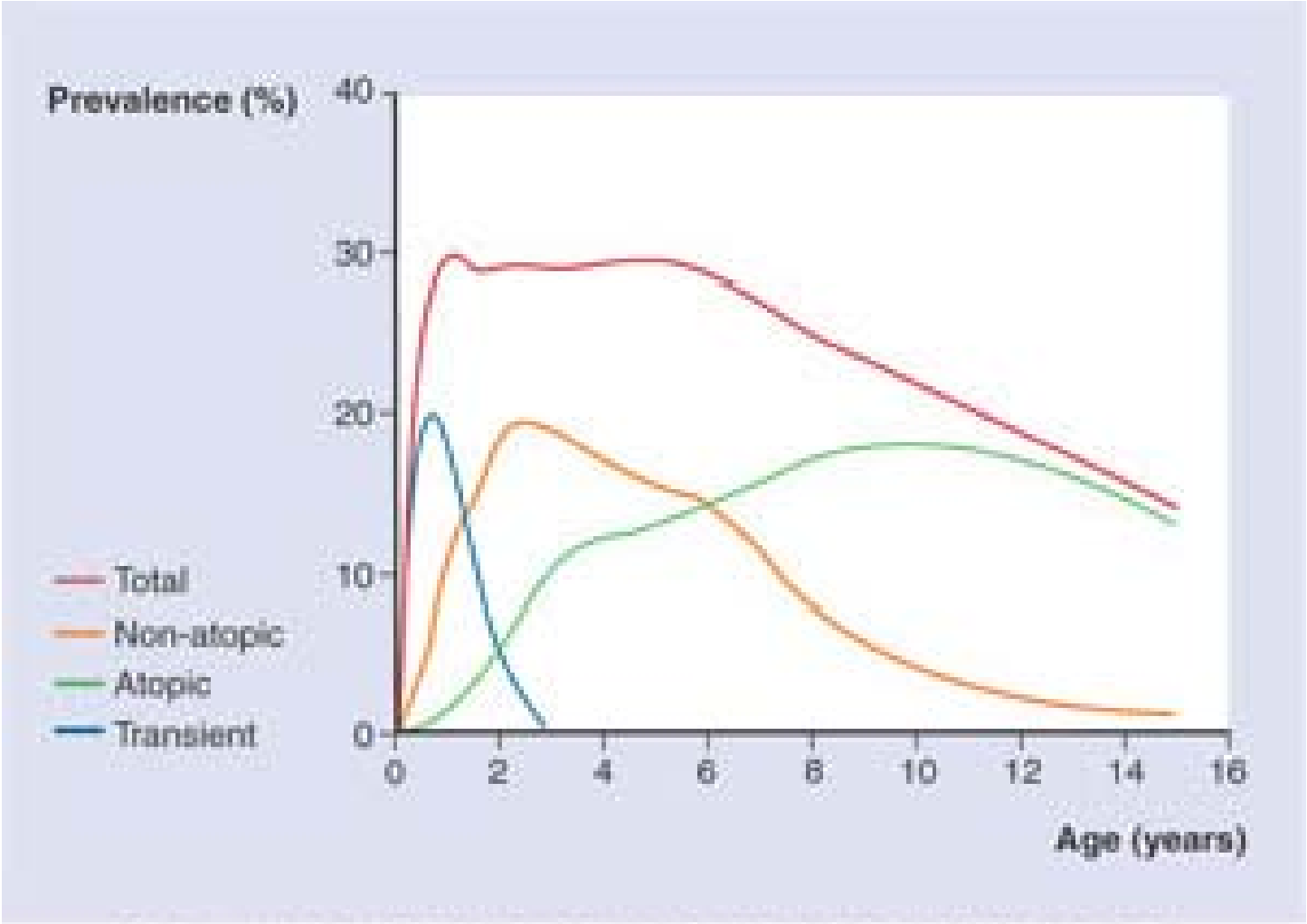
- Onset in newborn period
- Symptoms associated with feeding
- History of feeding difficulty
- History of endotracheal intubation
- Failure to thrive / failure to gain weight
- Choking or chronic aspiration
- Barrel shaped chest
- Digital clubbing

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



Types of wheezy infants & preschool children



(Redrawn with permission from Martinez FD, Godfrey S. Wheezing Disorders in the Preschool Child. New York: Martin Dunitz, Taylor & Francis Group; 2003. p 15.)

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***

Taussig : Pediatric Respiratory Medicine 2008 :128

Predictors for wheezing phenotypes in the first 10 years of life (n= 2711)

Table 4 Multivariate odds ratio (OR) and 95% confidence interval (95% CI) for factors associated with wheezing phenotypes[†]

	Wheezing phenotypes			
Baseline factors	Preschool wheezers OR (95% CI[‡])	Primary-school wheezers OR (95% CI[‡])	Intermittent wheezers OR (95% CI[‡])	Persistent wheezers OR (95% CI[‡])
Respiratory infection	5.15 (2.57–10.33)		4.76 (1.83–12.37)	8.44 (3.05–23.33)
Gender, male				1.89 (1.17–3.05)
Breastfeeding	1.54 (1.13–2.09)		1.94 (1.22–3.09)	
Prematurity (<37 weeks)			2.37 (1.18–4.76)	
Personal history of allergy	2.25 (1.50–3.39)		2.42 (1.40–4.17)	4.84 (3.03–7.74)
Health status rated low at birth				2.18 (1.10–4.33)
Daycare attendance	1.50 (1.11–2.03)	0.36 (0.14–0.94)		
History of parental asthma	2.35 (1.49–3.71)	2.38 (1.23–4.61)		7.21 (3.99–13.06)
History of parental smoking	1.53 (1.14–2.06)			
Crowding ($n \geq 1.5$/bedroom)	0.69 (0.50–0.94)	0.44 (0.26–0.74)		
Dwelling needing repairs				1.74 (1.05–2.87)

Respirology 2008; 13: 53-45

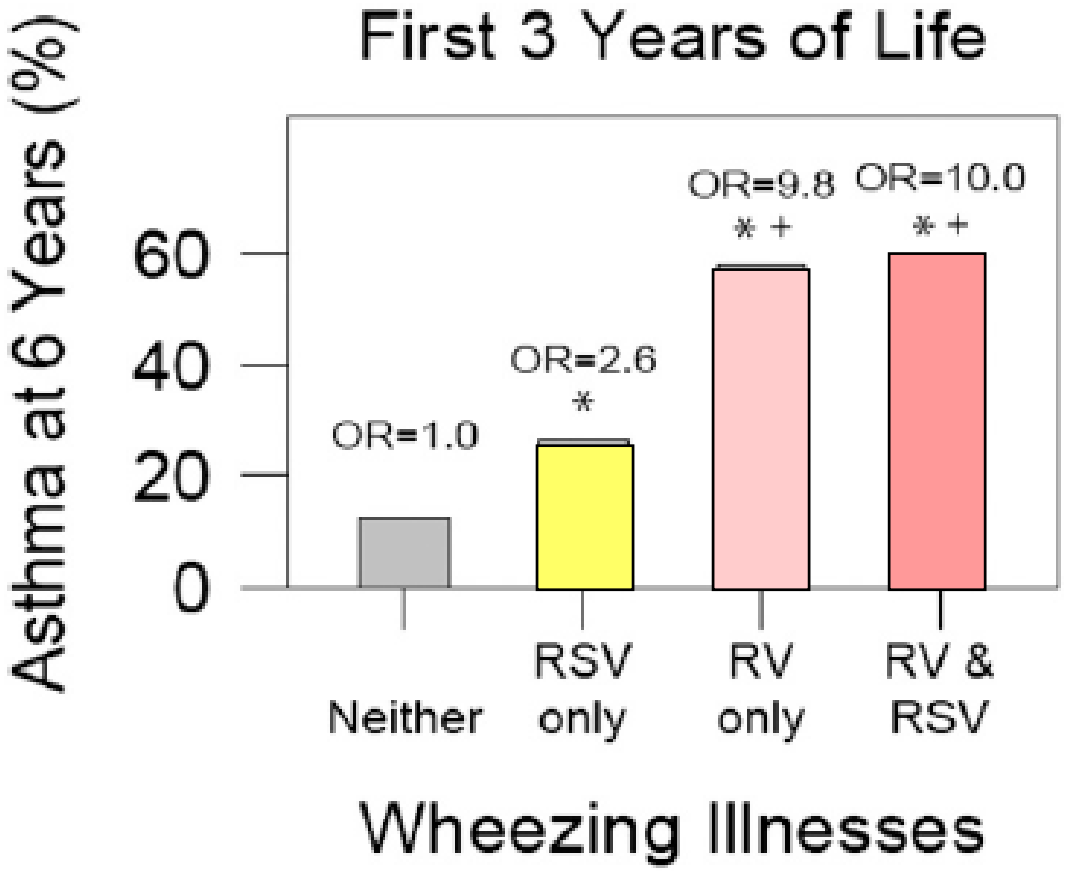
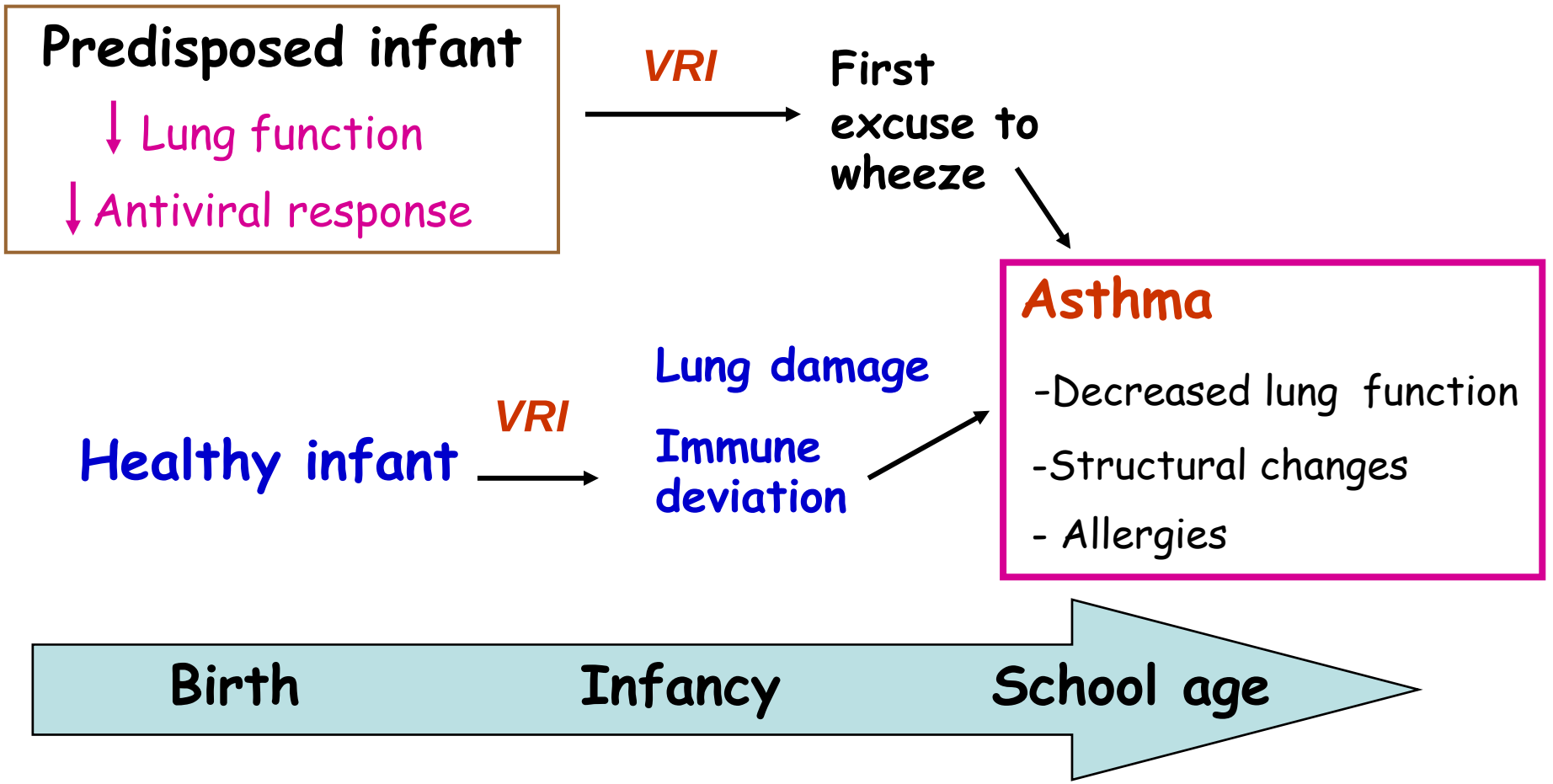


Figure 2. Risk of asthma at age 6 years in children who wheezed during the first 3 years of life with rhinovirus (RV), respiratory syncytial virus (RSV), or both (*$P < 0.05$ vs. Neither; $^{+}P < 0.05$ vs. RSV only). OR = odds ratio.

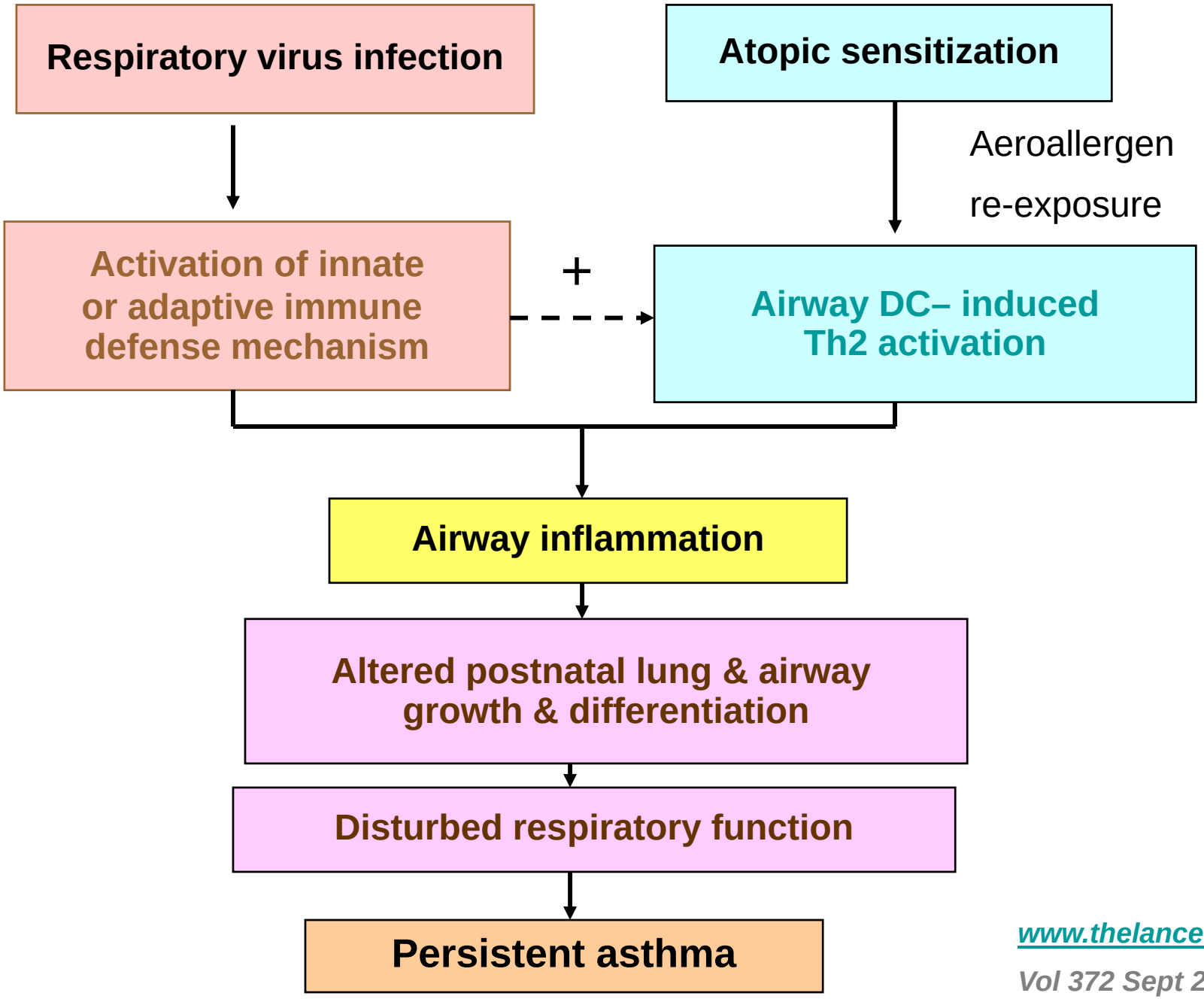
Study in 259 children 0-6 yrs. of age with parental respiratory allergies

Amer J Respir Crit Care 2008; 178 : 667

Relationship between virus-induced wheezing in infancy and childhood asthma



Pediatr Infect Dis J 2008;27: S97- S103



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Vol 372 Sept 20,2008

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 ต้องไปพ่นยาขยายหลอดลมที่คลินิก และที่ รพ.จึงดีขึ้น ขณะนี้อายุ 1ปี 1 เดือน

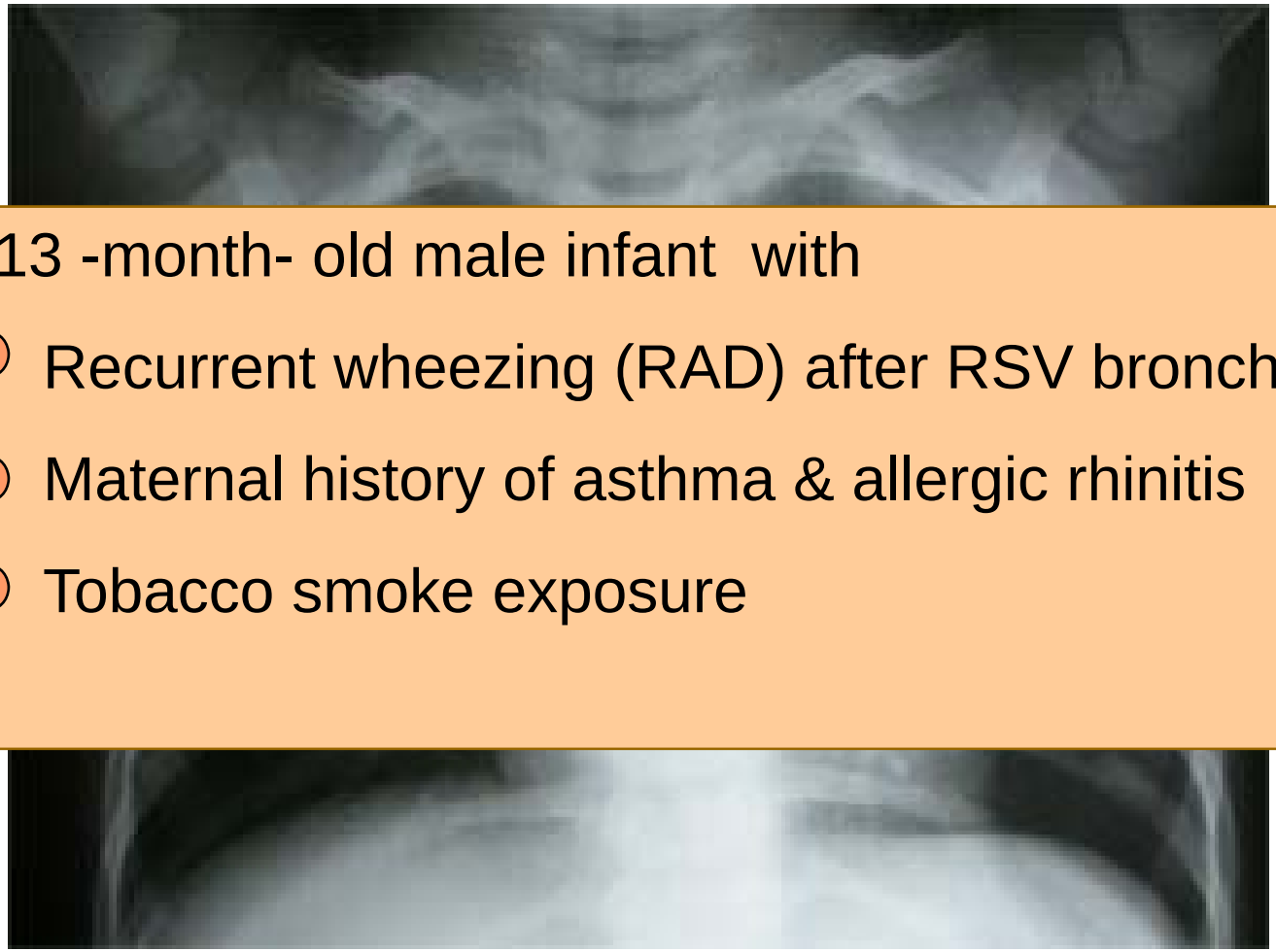
ประวัติเพิ่มเติม : - คลอดก่อนกำหนด 36 wk GA. ไม่ต้องใช้เครื่องช่วยหายใจตอนแรกเกิด กินนมแม่ประมาณ 3 เดือน

- ไม่มีประวัติสำลักนม หรืออาเจียนหลังกินนม

- คุณแม่เป็นภูมิแพ้ที่จมูก เคยเป็นหอบหืดตอนเป็นเด็ก 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 ≥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 (≥ 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

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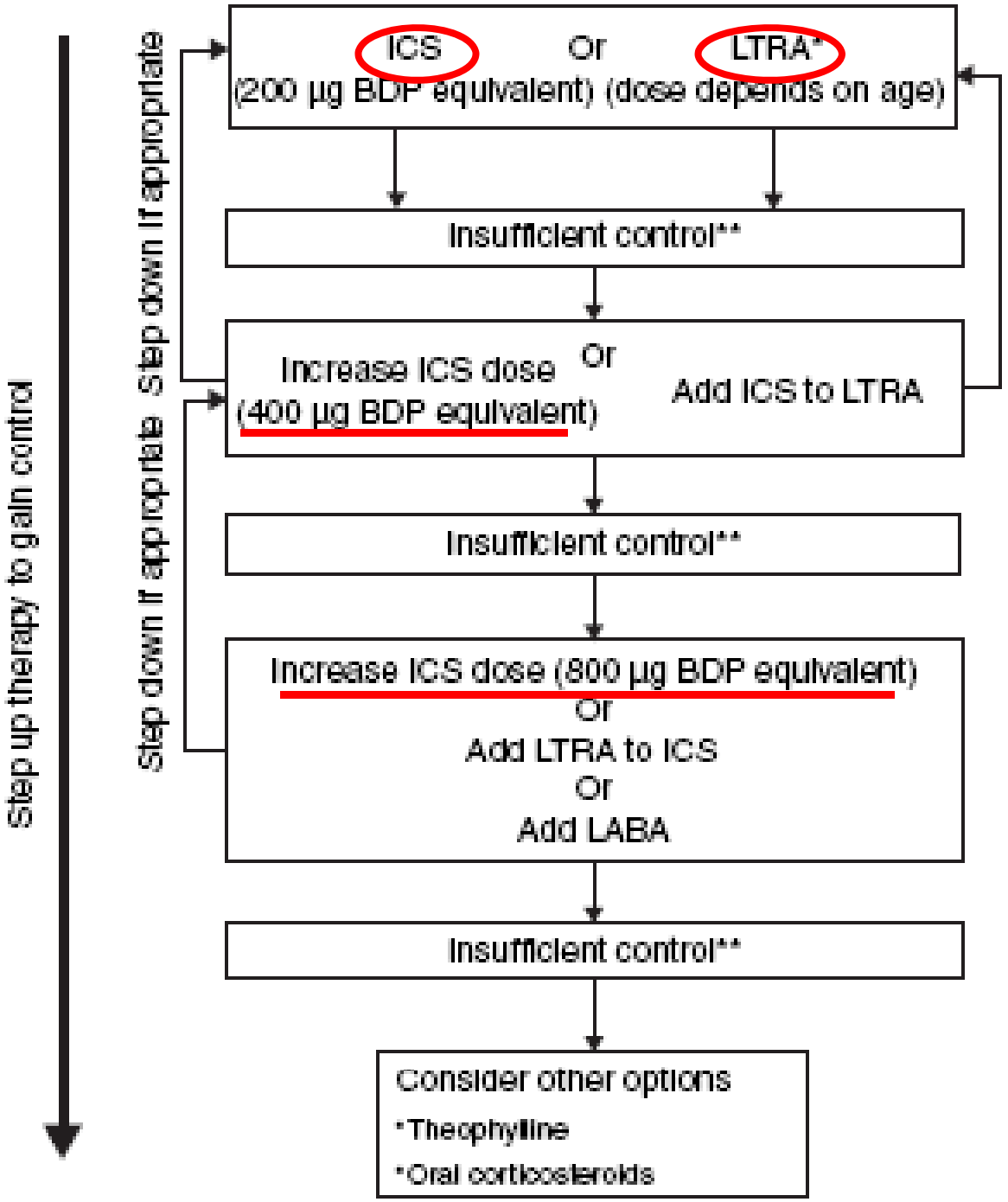
Children ≤ 5 years



How to prevent post-bronchiolitis wheezing or asthma?

- Inhaled/systemic corticosteroid
- Montelukast
- Ribavirin

How to prevent post-bronchiolitis wheezing or asthma?

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How to prevent post-bronchiolitis wheezing or asthma?

Inhaled/systemic corticosteroid

- 2 RCTs
- 1 Cochrane Review

Intermittent inhaled corticosteroids in infants with episodic wheezing

Objective: to assess the efficacy of inhaled budesonide vs placebo after 1st episode of wheezing in reducing subsequent respiratory syptoms during the first 3 years of life

Patients:

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

Bisgaard H, et al. New Engl J Med 2006; 354: 1998-2005

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

Bisgaard H, et al. New Engl J Med 2006; 354: 1998-2005

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

Bisgaard H, et al. New Engl J Med 2006; 354: 1998-2005

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

Blom DJM, et al. Cochrane Database 2007

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

Blom DJM, et al. Cochrane Database 2007

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

Ducharme FM, et al. New Engl J Med 2009; 360;4.

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

Ducharme FM, et al. New Engl J Med 2009; 360;4.

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

Ducharme FM, et al. New Engl J Med 2009; 360;4.

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 symtoms of post-RSV bronchiolitis in children

Patients: RSV-positive 3-24 months admitted for at least 24 hours for a 1st or 2nd 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

Bisgaard H, et al. Am J Respir Crit Care Med 2008; 178:854.

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 ie.corticosteroid, nebulized hypertonic saline, racemic albuterol may be helpful in certain patients (further research studies are required)
- Palivizumab is not effective in acute wheezing

Conclusion (cont')

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