การประชุมใหญ่ประจำปี ครั้งที่ 10
Easy Asthma & COPD Clinic Network
10-11 มีนาคม 2557
How to Achieve Pediatric Asthma Admission Rate Near ‘Zero’?

Jamaree Teeratakulpisarn
Department of Pediatrics
Khon Kaen University
10 March 2014
Quality Improvement Process

**Input**
- Leader
- Personnel
- Data
  - Prevalence, exacerbation rate, etc
  - Cost

**Process**
- Management guideline
  - Adapt guideline to fit your own situation
  - Pitfall
  - Team work
  - Skill

**Output/Outcome**
- Asthma control (Zero exacerbation)
- Improve quality of life
- Reduce the whole cost
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**Output/Outcome**
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- Improve quality of life
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Problems in pediatric asthma

Doctor & health care team
- Misdiagnosis & Under diagnosis
- Under & inappropriate treatment
- Appropriate inhalation technique
- Associated disease: AR, sinusitis
- Fear of steroid side effect

Care givers & children
- Compliance & inhalation technique
- Fear of steroid side effect
Problems in pediatric asthma

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Misdiagnosis & Under Dx

Presentation: fever, cough, dyspnea

PE: crepitation, rhonchi, wheezing

• Acute lower respiratory tract infection
  – pneumonia
  – bronchitis
  – bronchiolitis
  – viral-induced wheezing (wheezing associated respiratory infection, WARI)

• Asthma – may have no abnormal signs
Pneumonia

Criteria for diagnosis

• Clinical – fever, cough, dyspnea (including fast breathing)

• CXR – infiltration on CXR
Pneumonia
Recurrent Pneumonia

Definition

defined as more than 1 episode per year or more than 3 episodes in a lifetime

These children require

- more extensive workup to find out underlying condition or
- find out another diagnosis

Nicholas John Bennett, et al. eMedicine
Acute bronchitis

- Recurrent episodes of acute or chronic infectious bronchitis are unusual in children and should alert the clinician to the likelihood of asthma.
Acute bronchiolitis

- Present with cough and dyspnea (wheezing or rhonchi, may have crepitation) after common cold (viral URI)

- First episode in children under 2 years old
Viral-induced wheezing

Wheezing associated respiratory infection

- Wheezing follow common cold or viral URI (like acute bronchiolitis)
- Usually used in recurrent episodes in children < 5 years old
- Have to differentiate with ASTHMA
How to differentiate between viral-induced wheezing vs asthma?
Viral-induced wheezing & asthma

- Asthma predictive index (API)
- Therapeutic diagnosis
Viral-induced wheezing & asthma

- Asthma predictive index (API)
- Therapeutic diagnosis
Asthma Predictive Index (API)

Major criteria
1. Parental asthma (MD diagnosis)
2. MD diagnosed atopic eczema (child)

Minor criteria
1. MD diagnosed allergic rhinitis (child)
2. Wheezing apart from cold
3. Eosinophilia (≥ 4%)

Recurrent wheezing in ≤5 yrs

Asthma Predictive Index

- **NO**
  - Viral-induced wheezing
    - Recurrent > 3 episodes
      - ICS + $\beta_2$ agonist 3 mo
        - Not improve: Other diagnosis
        - Improve: OFF treatment FU
  - Change diagnosis

- **YES**
  - Asthma
    - Recurrent wheeze
Recurrent wheezing in ≤5 yrs

Asthma Predictive Index

- NO
  - Viral-induced wheezing
    - Recurrent > 3 episodes
      - ICS + β₂ agonist 3 mo
        - Not improve: Other diagnosis
        - Improve: OFF treatment FU
  - Other diagnosis

- YES
  - Asthma
    - Change diagnosis

Recurrent wheeze
Misdiagnosis & Under Dx

Presentation: fever, cough, dyspnea
PE: crepitation, rhonchi, wheezing

• Acute lower respiratory tr infection
  – pneumonia: recurrent – unusual
  – bronchitis: recurrent – unusual
  – bronchiolitis: 1st episode in <2 years
  – viral-induced wheezing (wheezing associated respiratory infection, WARI): recurrent episodes, no API

• Asthma: recurrent episodes with Asthma Predictive Index (API)
Problems in pediatric asthma

Doctor & health care team
- Misdiagnosis & Under diagnosis
- Under & inappropriate treatment
- Appropriate inhalation technique
- Associated disease: AR, sinusitis
- Fear of steroid side effect

Care givers & children
- Compliance & inhalation technique
- Fear of steroid side effect
Under & inappropriate treatment

- Delay start controller
- Inappropriate step up
- Inadequate treatment of acute exacerbation at ER - lead to admission
### Levels of Asthma Control

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Controlled</th>
<th>Partly controlled</th>
<th>Uncontrolled</th>
</tr>
</thead>
<tbody>
<tr>
<td>Daytime symptoms: wheezing, cough, difficult breathing</td>
<td>None (less than twice/week, typically for short periods of the order of minutes and rapidly relieved by use of a rapid-acting bronchodilator)</td>
<td>≥Twice a week (typically for short periods of the order of minutes and rapidly relieved by use of a rapid-acting bronchodilator)</td>
<td>&gt;Twice a week (typically last minutes or hours or recur, but partially or fully relieved by a rapid-acting bronchodilator)</td>
</tr>
<tr>
<td>Limitations of activities</td>
<td>None (child is fully active, plays and runs without limitation or symptoms)</td>
<td>Any (cough, wheeze or difficulty breathing, during exercise, play or laughing)</td>
<td>Any (cough, wheeze or difficulty breathing, during exercise, play or laughing)</td>
</tr>
<tr>
<td>Nocturnal symptoms or awakening</td>
<td>None (including no nocturnal coughing during sleep)</td>
<td>Any (coughs during sleep or wakes with cough, wheezing, and/or difficult breathing)</td>
<td>Any (coughs during sleep or wakes with cough, wheezing, and/or difficult breathing)</td>
</tr>
<tr>
<td>Need for reliever/rescue</td>
<td>≤ 2 days/week</td>
<td>&gt; 2 days/week</td>
<td>&gt; 2 days/week</td>
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</table>

Any exacerbation should prompt review of maintenance treatment.
# Treatment Steps

<table>
<thead>
<tr>
<th><strong>Reduce</strong></th>
<th><strong>Increase</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Step 1</strong></td>
<td><strong>Step 5</strong></td>
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<tr>
<td><strong>Step 2</strong></td>
<td></td>
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<tr>
<td><strong>Step 3</strong></td>
<td></td>
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<tr>
<td><strong>Step 4</strong></td>
<td></td>
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</table>

## Asthma Education

### Environmental Control

<table>
<thead>
<tr>
<th>Controller Options</th>
<th>Step 1</th>
<th>Step 2</th>
<th>Step 3</th>
<th>Step 4</th>
<th>Step 5</th>
</tr>
</thead>
<tbody>
<tr>
<td>Leukotriene Modifier**</td>
<td>as needed rapid-acting ( \beta_2 )-agonist</td>
<td>as needed rapid-acting ( \beta_2 )-agonist</td>
<td>medium- or high-dose ICS plus long-acting ( \beta_2 )-agonist</td>
<td>oral glucocorticosteroid (lowest dose)</td>
<td></td>
</tr>
<tr>
<td>Low-dose ICS*</td>
<td>low-dose ICS plus long-acting ( \beta_2 )-agonist</td>
<td>medium- or high-dose ICS plus long-acting ( \beta_2 )-agonist</td>
<td>leukotriene modifier</td>
<td>anti-IgE treatment</td>
<td></td>
</tr>
<tr>
<td>Low-dose ICS plus Leukotriene Modifier**</td>
<td>low-dose ICS plus leukotriene modifier</td>
<td>sustained-release theophylline</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Low-dose ICS plus Sustained-release Theophylline</td>
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*inhaled glucocorticosteroids

**receptor antagonist or synthesis inhibitors
<table>
<thead>
<tr>
<th>Step</th>
<th>Treatment Steps</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td><strong>reduce</strong></td>
</tr>
<tr>
<td>2</td>
<td><strong>reduce</strong></td>
</tr>
<tr>
<td>3</td>
<td><strong>reduce</strong></td>
</tr>
<tr>
<td>4</td>
<td><strong>increase</strong></td>
</tr>
<tr>
<td>5</td>
<td><strong>increase</strong></td>
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</table>

**For children < 5 years**

**Controller Options**

<table>
<thead>
<tr>
<th>Controller Options</th>
<th>Select One</th>
<th>Add One or More</th>
<th>Add One or Both</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>low-dose ICS*</td>
<td>medium- or high-dose ICS</td>
<td>oral glucocorticosteroid (lowest dose)</td>
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<tr>
<td></td>
<td>low-dose ICS plus long-acting β2-agonist</td>
<td>medium- or high-dose ICS plus long-acting β2-agonist</td>
<td>leukotriene modifier</td>
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<td>leukotriene modifier**</td>
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<td>low-dose ICS plus leukotriene modifier</td>
<td></td>
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<td>low-dose ICS plus sustained-release theophylline</td>
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<table>
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<tr>
<th>REDUCE</th>
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<tr>
<td>STEP 1</td>
<td>STEP 2</td>
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<tr>
<td><strong>TREATMENT STEPS</strong></td>
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<tr>
<td></td>
<td>asthma education</td>
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<tr>
<td>SELECT ONE</td>
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<td><strong>CONTROLLER OPTIONS</strong></td>
<td><strong>as needed rapid-acting β₂-agonist</strong></td>
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<td></td>
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<tr>
<td>low-dose sustained release theophylline</td>
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<td><strong>Preferred option for adult and older children</strong></td>
<td></td>
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*inhaled glucocorticosteroids
** receptor antagonist or synthesis inhibitors
How to start & step up

• Initial
  – ICS: Budesonide 100-200 ug bid
    Fluticasone 125-250 ug bid
  Via spacer
For 2 – 3 months
How to start & step up

• Initial
  – ICS: Budesonide 100-200 ug bid
    Fluticasone 125-250 ug bid
    Via spacer
  For 2 - 3 months: if not improve
• Ask for compliance
• Assess proper inhalation technique
• Assess associated disease – allergic rhinitis, sinusitis
How to start & step up

• Initial
  – ICS: Budesonide 100-200 ug
  – Fluticasone 125-250 ug bid
  Via spacer
  For 2 – 3 months if not improve
• Ask for compliance: good
• Assess proper inhalation technique: OK
• Assess associated disease – allergic rhinitis, sinusitis: OK
## Treatment Steps

### Step 1 - Reduce

- **Step 1:** Asthma education

### Step 2 - Environmental Control

- **Step 2:** As needed rapid-acting β₂-agonist

### Step 3 - Select One

- **Select One:** Low-dose ICS

### Step 4 - Add One or More

- **Add One or More:** Medium- or high-dose ICS plus long-acting β₂-agonist

### Step 5 - Add One or Both

- **Add One or Both:** Oral glucocorticosteroid (lowest dose) + anti-IgE treatment

### Controller Options

- **Leukotriene modifier**
- **Medium- or high-dose ICS**
- **Low-dose ICS plus sustained-release theophylline**

---

*Inhaled glucocorticosteroids
**Receptor antagonist or synthesis inhibitors*
BADGER Study
(Best ADd-on therapy Giving Effective Response)

Background

- For children who have uncontrolled asthma despite the use of low-dose inhaled corticosteroids (ICS), evidence to guide step-up therapy is lacking.
Results

• 165 patients completed the study period
• A differential response occurred in 161/165 (98%)
Pairwise Comparison of Three Step-up Therapies and the Overall Probability of Best Response

A Pairwise Comparisons

<table>
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<th>Therapy Comparison</th>
<th>LABA better</th>
<th>Neutral</th>
<th>ICS better</th>
</tr>
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<tbody>
<tr>
<td>LABA vs. ICS</td>
<td>54%</td>
<td>32%</td>
<td>14%</td>
</tr>
<tr>
<td>p value</td>
<td>p 0.004</td>
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<tr>
<td>LABA vs. LTRA</td>
<td>52%</td>
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Pairwise Comparison of Three Step-up Therapies and the Overall Probability of Best Response

B  Probability of Best Response

LABA

ICS

LTRA

Probability of Best Response

0.0  0.1  0.2  0.3  0.4  0.5  0.6
BADGER Conclusion

• Nearly all the children had a differential response to each step-up therapy

• LABA step-up was significantly more likely to provide the best response than either ICS or LTRA step-up

• However, many children had a best response to ICS or LTRA step-up therapy, highlighting the need to regularly monitor and appropriately adjust each child's asthma therapy
Common pitfall

• Inadequate dose of ICS
• Inappropriate use of combination Px
  - Too low ICS
  - Too high ICS
• Inadequate assessment before step up
Long term prophylaxis

Consideration

- Increase in dose of ICS is not accompanied by proportional increase in effects but increases systemic bioavailability
National Asthma Council Australia
Problems in pediatric asthma

Doctor & health care team
- Misdiagnosis & Under diagnosis
- Under & inappropriate treatment
- Appropriate inhalation technique
- Associated disease: AR, sinusitis
- Fear of steroid side effect

Care givers & children
- Compliance & inhalation technique
- Fear of steroid side effect
Using an MDI

Need a proper hand-lung synchronism
Incorrect Use of pMDI

MDIs must be used with spacer in children
Problems in pediatric asthma

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Under & inappropriate treatment

- Delay start controller
- Inappropriate step up
- Inadequate treatment of acute exacerbation at home and ER
  - lead to admission
Common pitfall

• Inadequate dose of $\beta_2$ agonist
  - MDI
  - Nebulization

• Delay systemic corticosteroid
Typical inhalation and exhalation airflow traces from an adult, a child and an infant.
Both pMDI & Nebulization

- Low lung deposition
- Loss drug in device

Depend on
- Gas flow
- Different device used
- Volume of drug solution
Common pitfall

• Inadequate dose of $\beta_2$ agonist: initial
  - MDI initial ~ 2 – 4 puffs q 15–20 min
  - Nebulization 2.5 – 4 mL

• Delayed systemic corticosteroid
  - Start prednisolone 1-2 mg/kg/day or
  - Hydrocortisone 5 mg/kg/dose IV q 6 hr
Problems in pediatric asthma

Doctor & health care team
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- Under & inappropriate treatment
- Appropriate inhalation technique
- Associated disease: AR, sinusitis
- Fear of side effect: steroid

Care givers & children
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- Fear of steroid side effect
Safety profile of ICS

Growth

• No significant effects on growth of low dose ICS (100-200 ug/day)
• Reduction on growth rate ~ delay in skeleton maturation
• Attain normal adult height (predict from family members) but at a later age
• Uncontrolled or severe asthma adversely affects growth and final adult height
Clinical Safety of Inhaled Corticosteroids for Asthma in Children
An Update of Long-Term Trials

Søren Pedersen
Department of Paediatrics, University of Southern Denmark, Kolding Hospital, Kolding, Denmark

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<td>Merkus et al. [13]</td>
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<td>Allen et al. [15]</td>
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<td>Bisgaard et al. [17]</td>
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<td>Jonasson et al. [18]</td>
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<td>Childhood Asthma Management Program Research Group [19]</td>
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<td>Verbene et al. [20]</td>
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<td>Tinkelman et al. [21]</td>
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<td>de Benedictis et al. [25]</td>
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<td>Rao et al. [26]</td>
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To assess the safety of long-term use of inhaled corticosteroids in children with asthma, a systematic review of the literature was performed focusing on randomised, controlled studies of ≥12 months’ duration, to obtain data with maximum relevance to clinical practice. Specific searches were conducted to identify studies examining each of the following three areas: growth, bone mineral density and cortisol levels.

In conclusion, this literature review supports the theory that recommended doses of inhaled corticosteroids can be administered to children for the long-term management of asthma with minimal risk of clinically relevant adverse effects on growth, bone density or cortisol levels.
Safety profile of ICS

Oral candidiasis, hoarseness, teeth

• Relate to concomitant use of antibiotics and high daily dose
• Reduction by spacer, mouth rinsing
• Increase dental erosion due to oral pH reduction result from $\beta_2$ agonist inhalation
Safety profile of ICS

Lower respiratory tract infection (pneumonia and TB)

• Long-term use of ICS is NOT associated with an increase incidence of LRI and TB
Summary

• Recurrent wheezing ≥ 3 times – ICS as therapeutic treatment
• Appropriate dose of ICS
• Before step up – look for
  – Inhalation technique
  – Compliance
  – Environmental avoidance
  – Co-morbidity esp. AR, sinusitis, OSA
Asthma control can be achieved in pediatric patients?

- Early diagnosis and treatment
- All ICSs are essential medications and supported by Government
- Cost-effectiveness
  - Improve quality of life
  - Cheap price of ICS
  - Few side effects of ICS either growth, superimpose infection
‘Zero’ admission!
Make it real
We all can do
THANK YOU
10th EACC Annual Meeting
TEAMWORK • SHARE • ACHIEVE

การประชุมใหญ่ประจำปี ครั้งที่ 10
Easy Asthma & COPD Clinic Network
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