Asthma in children – what’s new?

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DISCLOSURES:

♦ Advisory Boards
  - Astra Zeneca
  - MSD
  - Novartis
  - Pharmaplan

♦ Speakers Bureau
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  - MSD

♦ Editorial Board
  - Current Allergy & Clinical Immunology
  - Medical Chronicle
  - WAO Website
Childhood asthma – new developments

- epidemiology
- diagnosis
- new classification
- chronic treatment
- treatment of acute asthma
Prevalence of Clinical Asthma

- Red: >10.1%
- Orange: 7.6 – 10.0%
- Yellow: 5.1 – 7.5%
- Green: 2.5 – 5.0%
- Blue: 0 – 2.5%
- White: No standardized data available
<table>
<thead>
<tr>
<th>Study</th>
<th>Population</th>
<th>Outcome</th>
<th>Prevalence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Keeley 1991</td>
<td>7-9yr Zimbabwe</td>
<td>15% PF exercise</td>
<td>0.1 rural</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>5.8 urban rich/ 3.1 poor</td>
</tr>
<tr>
<td>Nganga 1992</td>
<td>9-12 yr Kenya</td>
<td>15% FEV1 exercise</td>
<td>10.5 urban</td>
</tr>
<tr>
<td>Addo Yobo 1997</td>
<td>9-16 yr Ghana</td>
<td>12.5% PF, exercise</td>
<td>2.7 rural</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>4.7 urban rich/ 2.2 poor</td>
</tr>
<tr>
<td>Nganga 1998</td>
<td>8-12 yr Kenya</td>
<td>15% FEV1 exercise</td>
<td>3.2 rural peasant/12.9 plant</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>10.3 urban rich/ 9.1 poor</td>
</tr>
<tr>
<td>Perzanowski 2001</td>
<td>8-12 yr Kenya</td>
<td>15% FEV1 exercise</td>
<td>9.8 rural plantation</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>12.4 urban</td>
</tr>
</tbody>
</table>
## BHR – South African children

<table>
<thead>
<tr>
<th>Study</th>
<th>Population</th>
<th>Outcome</th>
<th>Prevalence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Van Niekerk 1979</td>
<td>6-9yr Transkei, CT</td>
<td>15% FEV1/ PF exercise</td>
<td>0.14 rural, 3.17 urban</td>
</tr>
<tr>
<td>Vermeulen 1990</td>
<td>8-16 yr Transkei</td>
<td>20% FEV1 histamine</td>
<td>14.2</td>
</tr>
<tr>
<td>Terblanche 1990</td>
<td>6-19 yr, CT</td>
<td>10% FEV1, exerc</td>
<td>5.1</td>
</tr>
<tr>
<td>Calvert 2000</td>
<td>8-13yr Transkei, CT</td>
<td>15% FEV1 or 26% FEF exercise</td>
<td>8.7 rural, 14.9 urban</td>
</tr>
<tr>
<td>Steinman 2002</td>
<td>10-14yr, Transkei, CT</td>
<td>20% FEV1 histamine</td>
<td>17 rural, 34.4 urban</td>
</tr>
</tbody>
</table>
Asthma 12 month prevalence 1995-2002 in South Africa – video questionnaire

<table>
<thead>
<tr>
<th>Symptom</th>
<th>ISAAC 3 2002</th>
<th>ISAAC 1 1995</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Wheeze</td>
<td>8.2%</td>
<td>6.4%</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Exercise induced wheeze</td>
<td>12.8%</td>
<td>11.5%</td>
<td>0.048</td>
</tr>
<tr>
<td>Severe wheeze</td>
<td>6.0%</td>
<td>5.1%</td>
<td>0.032</td>
</tr>
</tbody>
</table>

Zar et al, 2005
Prevalence childhood asthma in Africa

- Increasing in urban and rural populations
  - Decline in urban-rural gradient
- Changes in prevalence – lifestyle
  - Hygiene hypothesis - less infectious diseases – Th2 response, increased allergic disease
  - Diet - reduced anti-oxidants, increase in obesity
  - Environment – house dust mite exposure, smoke exposure, passive smoke, pollution
Diagnosing asthma in children

- Clinical definition
  - recurrent cough / wheeze
  - responsive to bronchodilator

- Other features
  - family history
  - atopy
  - night, exercise-induced symptoms
## Predictive index for asthma in children

<table>
<thead>
<tr>
<th>Major criteria</th>
<th>Minor criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>Parent asthma</td>
<td>Allergic rhinitis</td>
</tr>
<tr>
<td>Eczema</td>
<td>Wheezing apart from colds</td>
</tr>
<tr>
<td></td>
<td>Eosinophilis $&gt;4%$</td>
</tr>
</tbody>
</table>

F. Martinez, USA
Exhaled nitric oxide (FeNO)

- NO is produced in epithelial cells of the bronchial wall part of the inflammatory process
- NO production increases with eosinophilic airway inflammation
Exhaled nitric oxide (FeNO)

- measure of airway inflammation
- derived from airway epithelial cells
- relatively easily measured (hand held device) – 4 years and older
- reproducible, measurement takes secs
  - normal 5-15ppb in children
  - asthmatics – 2-4x increase
Predicted FENO (solid blue line) as function of height and 95% prediction intervals (dashed green and red lines). Adapted from Malmberg et al, Exhaled Nitric Oxide in Healthy Nonatopic School-Age Children: Determinants and Height-Adjusted Reference Values; Pediatric Pulmonology 41:635-642 (2006)
Exhaled air of asthmatic subjects shows between double and four times the normal NO level.

With symptoms and other techniques such as spirometry, FeNO can be used to help diagnose eosinophilic inflammation in asthma.
Factors increasing FeNO

- Airway viral infection (100%)
- Allergic rhinitis (50%)
- Nitrate rich diet (50%)
- Bronchiectasis
- Pneumonia
- Chronic bronchitis
- Chronic lung disease
Factors decreasing FeNO

- Cystic fibrosis (60%)
- Ciliary dyskinesia (45%)
- Exercise (5-25%)
- Bronchoconstriction (25%)
- Pulmonary hypertension
- Heart failure
- HIV
Former classification of asthma

- Intermittent
- Persistent
  - mild
  - moderate
  - severe
## Classify Severity at Presentation

<table>
<thead>
<tr>
<th>Category</th>
<th>Intermittent</th>
<th>Persistent</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mild</td>
<td>Moderate</td>
</tr>
<tr>
<td>Daytime symptoms</td>
<td>≤ 2 / week</td>
<td>2 - 4 / week</td>
</tr>
<tr>
<td>Night-time symptoms</td>
<td>≤ 1 / month</td>
<td>2 - 4 / month</td>
</tr>
<tr>
<td>PEF (predicted)</td>
<td>≥ 80%</td>
<td>≥ 80%</td>
</tr>
</tbody>
</table>

Start treatment at any step depending on the level of severity.

### All Categories
- Short-acting β₂ agonist as needed (reliever)
- Environmental control
- Education / self management

### Step 1: Intermittent
- No daily preventer or controller medication needed.
Asthma control

- Increasing recognition of importance of asthma control in management
- Increasing recognition that control achievable in majority of patients
- Major revision of Global Initiative for Asthma (GINA) guidelines 2006
New Asthma classification

- **CONTROL** key
  - Classification by level of control
    - Controlled
    - Partly Controlled
    - Uncontrolled

2006 www.ginasthma.org
What is CONTROLLED ASTHMA?

- No (*twice or less/ week*) daytime symptoms
- No limitations of activity
- No nocturnal symptoms
- No (*twice or less/ week*) use rescue medication
- Normal or near normal lung function
- No exacerbations

2006 www.ginasthma.org
# Levels of Asthma Control

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Controlled</th>
<th>Partly controlled (Any present in any week)</th>
<th>Uncontrolled</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Daytime symptoms</strong></td>
<td>None (2 or less / week)</td>
<td>More than twice / week</td>
<td>3 or more features of partly controlled asthma present in any week</td>
</tr>
<tr>
<td><strong>Limitations of activities</strong></td>
<td>None</td>
<td>Any</td>
<td></td>
</tr>
<tr>
<td><strong>Nocturnal symptoms / awakening</strong></td>
<td>None</td>
<td>Any</td>
<td></td>
</tr>
<tr>
<td><strong>Need for rescue / “reliever” treatment</strong></td>
<td>None (2 or less / week)</td>
<td>More than twice / week</td>
<td></td>
</tr>
<tr>
<td><strong>Lung function (PEF or FEV&lt;sub&gt;1&lt;/sub&gt;)</strong></td>
<td>Normal</td>
<td>&lt;80% predicted or personal best (if known) on any day</td>
<td></td>
</tr>
<tr>
<td><strong>Exacerbation</strong></td>
<td>None</td>
<td>One or more / year</td>
<td>1 in any week</td>
</tr>
</tbody>
</table>

2006 [www.ginasthma.org](http://www.ginasthma.org)
Control graded

- Night symptoms
- Exercise symptoms
- FEV1/PEF
- Reduction in rescue medication
- Bronchial hyperresponsiveness

DAYS

YEARS
LEVEL OF CONTROL

- Controlled
- Partly controlled
- Uncontrolled
- Exacerbation

TREATMENT OF ACTION

- Maintain and find lowest controlling step
- Consider stepping up to gain control
- Step up until controlled
- Treat as exacerbation

TREATMENT STEPS

REDUCE

- Step 1
- Step 2
- Step 3

INCREASE

- Step 4
- Step 5
How to Assess control?

Composite measures:

- Symptoms - constellation
- PFT, BHR
- Measures of airway inflammation
  - Sputum – eosinophils, cytokines
  - BAL, bronchial biopsy
  - Blood – eosinophils, ECP
  - Exhaled breath condensate
  - FeNO
Paediatric Asthma control test

- validated questionnaire on asthma control in children
- 7 questions
  - 4 completed by child, 3 by parent
- numerical score of 27
  - higher, better control
  - < 19 poor control
- available in SA
  - Eng, Afr, Xhosa, Zulu, Sesotho
Have your child answer these questions.

1. How is your asthma today?
   - 0 Very bad
   - 1 Bad
   - 2 Good
   - 3 Very good

2. How much does your asthma bother you when you run, exercise or play sports?
   - 0 It bothers me a lot. I can't do what I want to do.
   - 1 It bothers me and I don't like it.
   - 2 It bothers me a little but it's okay.
   - 3 It doesn't bother me.

3. Do you cough because of your asthma?
   - 0 Yes, always.
   - 1 Yes, most of the time.
   - 2 Yes, sometimes.
   - 3 No, never.

4. Do you wake up during the night because of your asthma?
   - 0 Yes, always.
   - 1 Yes, most of the time.
   - 2 Yes, sometimes.
   - 3 No, never.

Please answer the following questions on your own.

5. During the last 4 weeks, how many days did your child have any daytime asthma symptoms?
   - 5 None
   - 4 1-3 days
   - 3 4-10 days
   - 2 11-18 days
   - 1 19-24 days
   - 0 Every day

6. During the last 4 weeks, how many days did your child wheeze during the day because of asthma?
   - 5 None
   - 4 1-3 days
   - 3 4-10 days
   - 2 11-18 days
   - 1 19-24 days
   - 0 Every day

7. During the last 4 weeks, how many days did your child wake up during the night because of asthma?
   - 5 None
   - 4 1-3 days
   - 3 4-10 days
   - 2 11-18 days
   - 1 19-24 days
   - 0 Every day

TOTAL
Know your asthma score – ACT now

Score: 25 – Congratulations!
You have TOTAL CONTROL of your asthma. You have no symptoms and no asthma-related limitations. See your doctor or nurse if this changes.

Score: 20 to 24 – On Target
Your asthma may be WELL CONTROLLED but not TOTALLY CONTROLLED. Your doctor or nurse may be able to help you aim for TOTAL CONTROL.

Score: less than 20 – Off Target
Your asthma may NOT BE CONTROLLED. Your doctor or nurse can recommend an asthma action plan to help improve your asthma control.

Note:

Asthma Control Test™ is a trademark of QualityMetric Incorporated ©2002 [insert link to local website]
Alternatives

- Bronchial alveolar lavage (BAL) eosinophils, inflammatory cytokines
- Induced sputum
- Urine
- Blood: eosinophils, ECP
- Breath condensate
- Exhaled air - FeNO
Clinical applications of FeNO

- confirmation of diagnosis of asthma
- response to inhaled steroids
- titrating steroids
- diagnosing relapse or loss of control
- assessing adherence
Figure 5. Different markers of airway inflammation and asthma respond at different rates. $FEV_1 =$ forced expiratory volume in 1 second. Courtesy of Professor de Longste.
What’s new? - pharmacotherapy

- ICS
- LTRA
- LA $\beta_2$ bronchodilators
- Combination therapy
Inhaled corticosteroids in children

- most effective preventative therapy for asthma
- dose-response trials
  - marked, rapid clinical improvement in symptoms at low daily doses
  - similar response except for EIA
- most children well controlled on doses ≤ 400ug/day ICS (BDP)
- safe at these doses
Dose-response curves for the therapeutic effect and systemic activity of increasing doses of inhaled corticosteroid.
FeNO and response to ICS

Silkoff, 2001
Giving inhaled steroids

- MDI-spacer optimal delivery system – ease, cost, efficacy, safety
- Use MDI with spacer
  - Reduced oropharyngeal deposition
  - Reduced side effects
  - Increased delivery medication to lungs
Commercially available spacers
500ml Plastic bottle spacer
Choice of spacer devices:

- < 3 years  MDI + spacer with mask
- > 3 years  MDI + spacer with mouthpiece or DPI
What’s new? - ICS
CFC free inhaled corticosteroids

- Switch to **HFA preparations**
- **HFA-BDP vs CFC-BDP**
  - smaller particles
  - slower velocity
  - increased lung deposition
  - increased penetration small airways
- same effect at half dose
Add-on therapy

- Long acting $\beta_2$ agonists
- Leukotriene antagonists
Long acting $\beta_2$ agonists, single-dose

- salmeterol, formoterol
- formoterol rapid onset action
- bronchodilation for up to 12 hrs
- protection against EIA up to 12 hrs
- heterogeneity in response - drug delivery, disease, $\beta_2$ receptors
Safety - LA $\beta_2$

- increased asthma deaths in salmeterol multicentre (SMART) study, *Chest 2006*
- 28 week study – salmeterol vs placebo

<table>
<thead>
<tr>
<th></th>
<th>salmet</th>
<th>placebo</th>
<th>RR</th>
</tr>
</thead>
<tbody>
<tr>
<td>n</td>
<td>13176</td>
<td>13179</td>
<td></td>
</tr>
<tr>
<td>All</td>
<td>13 (0.1%)</td>
<td>3 (0.02%)</td>
<td>4.37 (1.2-15.3)</td>
</tr>
<tr>
<td>Afr/Amer</td>
<td>7 (0.3%)</td>
<td>1 (0.04%)</td>
<td>7.26 (8-46)</td>
</tr>
</tbody>
</table>

*But – pts poorly controlled at baseline, under-use ICS*
LA $\beta_2$ versus increasing dose ICS

- **Adult studies** – reduced exacerbations, better control, improved PFTs when add-on LA $\beta_2$ rather than increasing dose steroid

- **Paediatric studies** - DIFFERENT
  - significant small improvement FEV1, PF
  - impact on asthma control, exacerbation rate variable and inconsistent – *Greenstone et al, Cochrane review 2006*

- ? clinical importance

- individual benefit
## Combination therapy

<table>
<thead>
<tr>
<th>Combination Device</th>
<th>Dose (ug)</th>
</tr>
</thead>
<tbody>
<tr>
<td>salmeterol/ fluticasone (Seretide)</td>
<td>50/100</td>
</tr>
<tr>
<td>DPI (Accuhaler)</td>
<td>50/250</td>
</tr>
<tr>
<td></td>
<td>50/500</td>
</tr>
<tr>
<td>MDI CFC free</td>
<td>25/50, 25/125, 25/250</td>
</tr>
<tr>
<td>formoterol/ budesonide (Symbicort)</td>
<td>4.5/80</td>
</tr>
<tr>
<td>DPI (Turbuhaler)</td>
<td>4.5/160</td>
</tr>
<tr>
<td></td>
<td>9/320</td>
</tr>
</tbody>
</table>
Combination therapy

- Little data in children, especially preschool
- Approved for use in children older than 4 years
- Preferable rather than 2 separate inhalers
- LA $\beta_2$ should NOT be used as monotherapy
Current recommendation:
LA $\beta_2$ in childhood asthma

- Add-on therapy if poorly controlled on 400ug/ day inhaled budesonide
- EIB as needed
- Fixed combination products promising for maintenance and relief – only formoterol
Use of leukotriene antagonists

- add-on therapy in mild / moderate asthma with ICS
- children with mild persistent (monotherapy)
- children with viral induced exacerbations
- inability / refusal to take inhaled therapy
- individual variability in response to LTRA

*Meyer JACI 2003*
Montelukast add-on - 6-14 year olds

<table>
<thead>
<tr>
<th>Trial</th>
<th>Number patients</th>
<th>Duration of study</th>
<th>Study design</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Simon</td>
<td>279 persistent asthma</td>
<td>12 weeks</td>
<td>montelukast 5mg + budesonide 200 ug per day</td>
<td>FEV1 improved (p=0.06) less B2 use fewer exacerbations</td>
</tr>
<tr>
<td><em>J Pediatr, 2001</em></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Knorr</td>
<td>336 with asthma 35% on ICS</td>
<td>8 weeks</td>
<td>montelukast 5mg with/out ICS</td>
<td>improved morning FEV1 less B2 use</td>
</tr>
<tr>
<td><em>JAMA, 1998</em></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
LTRA - add-on therapy in children

- improvement in lung function
- decrease in bronchodilator use
- decrease exacerbations

Simons, Allergy, 2000,
Knorr et al. JAMA 1998
# Montelukast monotherapy 2-5 year olds

<table>
<thead>
<tr>
<th>Trial</th>
<th>No. of patients</th>
<th>Duration</th>
<th>Study design</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Knorr</strong></td>
<td>689 children 2-5 yrs with asthma</td>
<td>12 weeks</td>
<td>Montelukast 4mg vs placebo</td>
<td>well tolerated, safe improvement in asthma control</td>
</tr>
<tr>
<td><em>Pediatr 2001</em></td>
<td></td>
<td></td>
<td>Primary endpoint - safety</td>
<td></td>
</tr>
<tr>
<td>Bisgaard H</td>
<td>130 infants 3-36 mnths post RSV bronchiolitis</td>
<td>28 days</td>
<td>Montelukast 5mg vs placebo within 7 days of symptoms</td>
<td>Reduced symptoms</td>
</tr>
<tr>
<td><em>AJRCCM 2003</em></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PREVIA</td>
<td>768 children with intermittent asthma</td>
<td>12 month</td>
<td>montelukast 4/5 mg vs placebo</td>
<td>asthma exacerbations decreased 32% prolonged time to exacerbations</td>
</tr>
<tr>
<td>Bisgaard H</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><em>AJRCCM 2005</em></td>
<td></td>
<td></td>
<td></td>
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</tr>
</tbody>
</table>
# Montelukast monotherapy 6-14 years

<table>
<thead>
<tr>
<th>Trial</th>
<th>Number patients</th>
<th>Duration study</th>
<th>Study design</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Knorr</strong> JAMA 1998</td>
<td>336 asthmatics (FEV1 50-85%)</td>
<td>8 weeks</td>
<td>montelukast 5mg vs placebo</td>
<td>improved morning FEV1 less B2 use</td>
</tr>
<tr>
<td><strong>Szefer SJ JACI 2005</strong></td>
<td>45 mild persistent asthma</td>
<td>18 week</td>
<td>Fluticasone 100 bd vs montelukast</td>
<td>improved FEV1 89% fluticasone vs 49% montelukast</td>
</tr>
<tr>
<td><strong>MOSAIC Garcia ERS 2004</strong></td>
<td>996 mild persistent</td>
<td>12 months</td>
<td>montelukast 5mg vs fluticasone 100 bd for rescue free days</td>
<td>comparable rescue free days and no.attacks</td>
</tr>
</tbody>
</table>
LTRA vs ICS as monotherapy

- CLIC study – montelukast vs fluticasone (100 bd) in 144 children 6-17yr with mild/moderate
- crossover design 8 weeks each therapy
- more responded to fluticasone, but some responded to montelukast only

Szefer et al JACI 2005
LTRA vs ICS as monotherapy

- 17% responded to both, 23% to fluticasone alone, 5% to montelukast alone, 55% no response as defined by change in FEV1

- Clinical vs PFT response

<table>
<thead>
<tr>
<th></th>
<th>FEV1</th>
<th>asthma free days</th>
</tr>
</thead>
<tbody>
<tr>
<td>Both</td>
<td>17%</td>
<td>52%</td>
</tr>
<tr>
<td>FP alone</td>
<td>23%</td>
<td>17%</td>
</tr>
<tr>
<td>Monteluk alone</td>
<td>5%</td>
<td>4%</td>
</tr>
<tr>
<td>Neither</td>
<td>55%</td>
<td>36%</td>
</tr>
</tbody>
</table>

*Szefler et al JACI 2005*
Difference in FEV1 response between fluticasone and montelukast

Szefer et al JACI 2005
LTRA vs ICS as monotherapy

- response to fluticasone assoc with more airway inflammation – higher FeNO, IgE, BHR, lower FEV1
- response to montelukast associated with young age, short duration symptoms

*Szefler et al JACI 2005*
New paediatric asthma guidelines

- Previous asthma management guidelines for children deficient
  - 2007: The Practall Guidelines
Table 2c. Stepwise Approach for Managing Asthma in Children Aged 5–11 Years

**Intermittent Asthma**
Consult with asthma specialist if step-4 care or higher is required.
Consider consultation at step 3.

**Step 1**
Preferred: SABA prn

**Step 2**
Preferred: low-dose ICS
Alternative: cromolyn, LTRA, nedocromil, or theophylline

**Step 3**
Preferred: EITHER low-dose ICS + LABA, LTRA, OR theophylline or medium-dose ICS
Alternative: medium-dose ICS + either LTRA or theophylline

**Step 4**
Preferred: high-dose ICS + LABA
Alternative: high-dose ICS + either LTRA or theophylline

**Step 5**
Preferred: high-dose ICS + LABA + oral systemic corticosteroid
Alternative: high-dose ICS + either LTRA or theophylline + oral corticosteroid

**Step 6**
Preferred: high-dose ICS + LABA + oral systemic corticosteroid
Alternative: high-dose ICS + either LTRA or theophylline + oral corticosteroid

**Step up if needed**
(first, check adherence, environmental control, and comorbid conditions).
Assess Control
Step down if possible
(and asthma is well controlled for at least 3 months).

Each step:
Steps 2–4: Patient education, environmental control, and management of comorbidities
Consider subcutaneous allergen immunotherapy for patients who have allergic asthma.

Quick-Relief Medications for All Patients:
- SABA as needed for symptoms. Intensity of treatment depends on severity of symptoms:
  up to 3 treatments at 20-minute intervals as needed. Short course of systemic oral corticosteroids may be needed.
- Caution: Increasing use of SABA or use more than 2 days a week for symptom relief (not prevention of EIB) generally indicates inadequate control and the need to step up treatment.
Table 1c. Stepwise Approach for Managing Asthma in Children Aged ≤4 Years

<table>
<thead>
<tr>
<th>Step 1</th>
<th>Step 2</th>
<th>Step 3</th>
<th>Step 4</th>
<th>Step 5</th>
<th>Step 6</th>
</tr>
</thead>
<tbody>
<tr>
<td>Preferred: SABA prn</td>
<td>Preferred: medium-dose ICS Alternatives: cromolyn or SINGULAIR*</td>
<td>Preferred: medium-dose ICS + either LABA or SINGULAIR*</td>
<td>Preferred: high-dose ICS + either LABA or SINGULAIR*</td>
<td>Preferred: High-dose ICS + either LABA or SINGULAIR* Oral systemic corticosteroids</td>
<td>Step up if needed (first, check adherence, inhaler technique, and environmental control). Assess Control Step down if possible (and asthma is well controlled for at least 3 months).</td>
</tr>
</tbody>
</table>

### Patient Education and Environmental Control at Each Step

- Quick-Relief Medications for All Patients:  
  - SABA as needed for symptoms. Intensity of treatment depends on severity of symptoms.  
  - With viral respiratory infection: SABA every 4 to 6 hours for up to 24 hours (longer with physician consult). Consider short course of oral systemic corticosteroids if exacerbation is severe or patient has history of previous severe exacerbations.  
  - Caution: Frequent use of SABA may indicate the need to step up treatment. See text for recommendations on initiating daily long-term control therapy.
Algorithm of preventive pharmacologic treatment for asthma in children >2 yrs of age (The Practall Guidelines-2007)

**ICS (200 µg BDP equivalent)**
- Step up therapy to gain control
- Step down if appropriate

**LTRA (Dose depends on age)**
- Step down if appropriate

**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
  - Anti IgE
Asthma treatment in children aged 0-2yrs (The Practall Guidelines-2007)

- Consider a diagnosis of asthma if >3 episodes of bronchial obstruction within 6 months
- Intermittent β2 agonists are first choice
- LTRA daily controller therapy for viral wheezing
- Nebulized or inhaled corticosteroids as daily controller therapy for persistent asthma
- Evidence of atopy/allergy lowers the threshold for use of ICS
- Use oral corticosteroids (e.g. 1-2 mg/kg prednisone)
What’s new? - acute asthma

- Inhaled $\beta_2$ mainstay
  - MDI-spacer vs nebulised
  - Higher doses MDI-spacer
- Oral corticosteroids
- Inhaled anti-cholinergic – reduction in hospitalisation
- Increased dose ICS – 4x
- $\text{MgSO}_4$ – inhaled, iv
Treatment of Asthma Exacerbations

Magnesium Sulfate

**Controversial:**
- Inconsistent data
- Used in very severe asthma in emergency settings:
  - FEV1 < 25% predicted
  - Other signs of severe disease
- Dosage: 1.2 - 2 gm IV over 10 - 20 min in 50 ml saline
- Minor side effects
IV Magnesium in acute asthma

- Not to be used routinely
- Selected cases:
  - adults with $\text{FEV}_1 \ 25\text{-}30\%$
  - adults and children who fail to respond to initial treatment
  - children: $\text{FEV}_1$ fails to improve above 60% after 1 hr of care $^{1,2}$ (Evidence B)
- Single 2g infusion/20 mins
- No side-effects reported

Refs: 1. Rowe et al Cochrane database syst rev 2000
  2. Fitzgerald West J Med 2000
Conclusions

- diagnosis – clinical, but FeNO promising
- inhaled therapy optimal – MDI/spacer
- ICS most effective, safe controller therapy
- add-on therapy– LTRA, LABA (combination products preferable)
- MgSO₄ for treatment of acute severe asthma?
THANK YOU