Diagnosis and Management of Pediatric Asthma

Faculty/Presenter Disclosure

- Faculty: Alan Kaplan MD CCFP(EM) FCFP
- Chair Family Physician Airways Group of Canada
- Chair of Special Interest Focused Practice, College of Family Physicians in Respiratory Medicine.

- Relationships with commercial interests:
  - Grants/Research Support: none
  - Speakers Bureau/Honoraria: Astra Zeneca, Boehringer Ingelheim, Griffols, Pfizer, Purdue, Merck Frost, Novartis, Sanofi, Takeda.
  - Consulting Fees: Aerocrine, Novartis, Takeda, Purdue, Pfizer
  - Other: Member of Health Canada Section on Allergy and Respiratory Therapeutics.
    Member of Public Health Agency of Canada section on Respiratory Surveillance
    Member of Metropolitan TB subcommittee of the CTS
    Editorial board of the Primary Care Respiratory Journal

- Faculty: John Li MD MCFP
- Executive Family Physician Airways Group of Canada
- Executive of Special Interest Focused Practice, College of Family Physicians in Respiratory Medicine.

- Relationships with commercial interests:
  - Grants/Research Support: none
  - Speakers Bureau/Honoraria: Astra Zeneca, Purdue
  - Consulting Fees: Boehringer Ingelheim, Pfizer, Novartis, Takeda, Purdue, Pfizer, Merck Frost, Novartis, Sanofi
  - Other: n/a

Disclosure of Commercial Support

- This program has received no financial support.
- This program has received no in-kind support.

- Potential for conflict(s) of interest:
  - A) there are no organizations supporting this program
  - B) The following companies make respiratory products that I may mention in this talk including: Aerocrine, Astra Zeneca, Boehringer Ingelheim, Griffols, GSK, Merck Frost, Pfizer, Purdue, Novartis, Sanofi, Takeda.
  - There are no organizations supporting a product that will be discussed in this program.

Mitigating Potential Bias

- We will mitigate any bias by discussing appropriately all treatment and diagnostic options for respiratory care in my talk today

This is where we were!
ICS not being used
High dose beta agonists being used then in Australia
We have done better, using ICS appropriately, but...
There is still ++ morbidity from this disease
This talk is to highlight how we can separate those that need persistent therapy from those who do not, and how to do so
Objectives

- Diagnose true pre-school asthma as distinguished from "viral wheezing"
- Effectively treat the pediatric asthma patient
- Formulate a systematic follow up plan for pediatric asthma patients

Pediatric Asthma: Prevalence and Impact

- Most common chronic disease among children – 10-15% affected
- Major cause of pediatric hospital admissions and ED visits
- 26-45% of children with asthma still have inadequate control

Presentations of Wheezing

- The most common cause of wheezing in young children is viral respiratory infection
  BUT
- The strongest predictor for wheezing that develops into asthma is ATOPY
  - About 70–90% of children with asthma are atopic (i.e., positive skin tests)

Categories of Wheezing

1. Transient early wheezing
2. Persistent early-onset wheezing
3. Late-onset wheezing

Transient Early Wheezing

- Starts before age 3 and often outgrown by 3 years
- Later asthma is rare
- Often associated with
  | Prematurity
  | Parental smoking
- Symptoms are intermittent/ seasonal
- Include wheeze and shortness of breath
PHENOTYPES OF ASTHMA

Persistent Early-Onset Wheezing
- Starts before age 3, may develop into asthma
- Recurrent episodes associated with acute viral respiratory infections
- No evidence of atopy
- No family history of atopy
- Usually caused respiratory syncytial virus (RSV) in children under 2
- Symptoms persist through school age to age 12

Late-Onset Wheezing
- Begins after age 3
- Patient commonly atopic
- Associated with eczema
- Airway pathology characteristic of asthma
- Wheeze persists after 6 years with other symptoms of asthma

Billy: Presentation
- 2-ya-o, presents with 4th episode of wheezing in past 18 months
- Medical history
  - At 6 months old: Admitted with bronchiolitis caused by respiratory syncytial virus
  - At 9 months old: Seen in ED with cold complicated by wheezing and severe cough
  - Rx: short-acting β₂ adrenergic receptor agonist (MDI with chamber) + antibiotic x 7 days
  - At 11 months old: Another ED visit, similar episode as 9 months
  - Rx: an ICS b.i.d. x 2 wks for upper RTIs

Pediatric Asthma: Diagnosis and Patterns
- In patients <6 y, in whom conventional pulmonary function testing is not feasible, asthma diagnosis based on:
  - Typical symptom pattern
  - Wheezing cough or dyspnea of varying severity
  - Therapy response – acutely to bronchodilators or over several weeks to anti-inflammatories
  - Absence of “warning signs” for alternative diagnoses

Billy: Presentation (cont.)
- Medical history (cont.)
  - 4 more colds complicated by wheezing, cough, and dyspnea since last ED visit
    - During 2 episodes, “bronchitis” diagnosed, given azithromycin
    - Wheezing typically improves for 2 h after receiving short-acting β₂ adrenergic receptor agonist
    - Asymptomatic between colds
- Other/family history
  - No other medical problems, growth normal
  - Born at term, but small for gestational age (Mother smoked 10 cigarettes/day through pregnancy)
  - What diagnoses would you consider at this point?
Pediatric Asthma: Alternative Diagnoses

<table>
<thead>
<tr>
<th>Clinical finding</th>
<th>Potential diagnosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Failure to thrive, steatorrhea</td>
<td>Cystic fibrosis</td>
</tr>
<tr>
<td>Frequent, persistent, or unusual infections</td>
<td>Immunodeficiency</td>
</tr>
<tr>
<td>Chronic rhinitis and severe recurrent otitis media, s/o alar inwards</td>
<td>Primary ciliary dyskinesia</td>
</tr>
<tr>
<td>Severe regurgitation or vomiting</td>
<td>Gastroesophageal reflux</td>
</tr>
<tr>
<td>Persistent wheezing</td>
<td>Fixed obstructive lesion of the airway (e.g., hilar adenopathy, vascular ring, aspirated foreign body)</td>
</tr>
<tr>
<td>Heart murmur or known congenital heart disease</td>
<td>Wheezing caused by congestive heart failure</td>
</tr>
<tr>
<td>Nasal breathing caused by retained upper airway secretions, aspiration</td>
<td>Swallowing disorder (particularly if an underlying neurologic disorder or developmental delay)</td>
</tr>
</tbody>
</table>

Kovesi et al. CMAJ 2009

Pediatric Asthma: Determining Risk for Persistent Asthma

**Modified Asthma Predictive Index**

- Wheezing on ≥4 occasions during first 3 years of life, ≥1 episode observed by physician
- Combined with ≥1 major risk factor(s):
  - Parental history of asthma
  - Physician-diagnosed atopic dermatitis
  - Allergic sensitization to ≥1 aeroallergen (e.g.: house dust mite, cockroach, dog, cat, mold, grass, tree)
- OR combined with ≥2 minor risk factors:
  - Wheezing unrelated to colds
  - Allergic sensitization to milk, eggs, or peanuts
  - Blood eosinophils >4%

* A positive result indicates a child who is at the highest risk of persistent asthma

Kovesi et al. CMAJ 2009

New simpler predictive index

**Three things:**

1) Atopic dermatitis (1)
2) Familial asthma (1)
3) IGE polysenstization (2)

**Score / 4**

Dupuy A et al, A simple tool to identify mild to severe childhood asthma. Journal of Asthma, 2011
**Pediatric Asthma: Management of Intermittent Asthma**

- Intermittent ICS use **NOT** recommended
  - Ineffective for treatment of intermittent wheezing
- Regular ICS therapy should be used for children:
  - With severe or prolonged symptoms
  - Who have visited ED or been admitted
- Although ICS can be used to control symptoms, does not prevent progression to persistent asthma
- LTRAs can be used continuously during viral season, or at onset of viral infection
  - Reduce symptoms and visits to health care providers

ICS: inhaled corticosteroid; LTRA: leukotriene receptor antagonist

---

**Billy: Diagnosis and Management**

- Diagnosis of severe intermittent asthma
- Modified Asthma Predictive Index result negative
- Family told he has “2/3 chance of eventually "outgrowing" asthma, probably by school age
- Prescribed regular treatment with and ICS b.i.d. by valved holding chamber and short-acting β2-adrenergic receptor agonist p.r.n.
- 5 months later:
  - 5 colds over this period
  - No asthma-related symptoms; ICS dose halved
- 9 months later:
  - No difficulties with colds after first 5 months; ICS discontinued

---

**Choosing an Inhaler Device for Children with Asthma**

<table>
<thead>
<tr>
<th>Device Type</th>
<th>Age Group</th>
</tr>
</thead>
<tbody>
<tr>
<td>MDI plus a Valved Holding chamber with mask</td>
<td>Infants</td>
</tr>
<tr>
<td>MDI plus a Valved Holding chamber with mask</td>
<td>(2-5 yrs)</td>
</tr>
<tr>
<td>MDI plus a Valved Holding chamber with mouthpiece</td>
<td>5+ yrs</td>
</tr>
<tr>
<td>Dry powder inhalers</td>
<td>6+ yrs</td>
</tr>
</tbody>
</table>

---

**Chantal: Presentation**

- 4 y-o, with 1 year history of asthma
- Medical history:
  - Wheezing in association with colds beginning at 11 months
  - At 3 years of age
    - Nighttime cough even between colds
    - Sustained activity led to wheezing and dyspnea
    - Asthma diagnosed
    - Prescribed an ICS b.i.d. by spacer + short-acting β2-adrenergic receptor agonist p.r.n.
    - Parents worried about adverse effects and gave meds only when child was especially unwell
    - Over past year:
      - 2 ED visits, received oral corticosteroid
      - Never admitted
      - Eczema
- Family history:
  - Both parents have allergic rhinitis
- How would you optimize management of Chantal’s asthma?

---

**NON-PHARMACOLOGICAL MANAGEMENT OF ASTHMA**

- Trigger avoidance
- Stop adult smoking in the family
- Exercise
- Education
- Self-management
**Pediatric Asthma: Management of Persistent Asthma**

- ICS first choice for persistent asthma
  - Administer daily (including between exacerbations) for minimum of one season at a time

**ICS**: inhaled corticosteroid; **LABA**: long-acting β-agonist; **LTRA**: leukotriene receptor antagonist

**Effects of Inhaled Corticosteroids on Inflammation**

E = Epithelium

BM = Basement Membrane

Pre- and post-3 month treatment with budesonide (BUD) 600 mcg BID


**Pediatric Daily ICS Dose (mcg)**

(Age 6-11 years)

<table>
<thead>
<tr>
<th>Product – (Trade Name)</th>
<th>Low</th>
<th>Medium</th>
<th>High</th>
</tr>
</thead>
<tbody>
<tr>
<td>Beclomethasone dipropionate HFA (QVAR®)</td>
<td>≤ 200</td>
<td>201-400</td>
<td>&gt;400</td>
</tr>
<tr>
<td>Budesonide (Pulmicort® Turbuhaler®)</td>
<td>≤ 400</td>
<td>401-800</td>
<td>&gt;800</td>
</tr>
<tr>
<td>Ciclesonide (Alvesco®)</td>
<td>≤ 200</td>
<td>201-400</td>
<td>&gt;400</td>
</tr>
<tr>
<td>Fluticasone (Flovent® MDI and spacer; Flovent® Diskus®)</td>
<td>≤ 200</td>
<td>201-500</td>
<td>&gt;500</td>
</tr>
</tbody>
</table>

**Low to Moderate Dose ICS is Safe and Effective in Young Children with Asthma**

**Decreases**
- Asthma symptoms
- Rescue medication use
- Exacerbations
- Prednisone use
- Emergency health service use
- Hospitalizations
- Inflammatory markers
- Bronchial Hyperreactivity

**Increases**
- Quality of Life
- Pulmonary Function

**Low to Moderate Dose ICS Side Effects:**

**ICS growth effect**
- Limited, small, apparently transient reduction in growth velocity
- Projected final height by bone age similar to placebo

**Other safety issues**
- No adverse effect on bone density
- No association with cataracts
- No adverse effect on sexual maturation
- No adverse effect on psychological growth
- Decreased thrush with mouth rinsing and use of aerochamber
- Adrenal suppression

**Effectiveness of Intermittent ICS Therapy in Preschoolers**

Percentage of Symptom-free days during the Two-Week Treatment Periods for All 294 Children Who Received at Least One Study Treatment


Copyright © 2006 Massachusetts Medical Society.
**Pediatric Asthma: Management of Persistent Asthma**

- ICS first choice for persistent asthma
  - Administer daily (including between exacerbations) for minimum of one season at a time
- ICS very effective when used optimally; therefore, if unsuccessful:
  - Question asthma diagnosis
  - Consider possible comorbid conditions
  - Review technique of drug delivery
- If asthma control remains inadequate with moderate ICS dose:
  - Increase dose or add LTRA
- Role of adding LABA to ICS:
  - Evidence to support use in adolescents
  - Minimal evidence for preschool and school-aged children
- Referral to pediatric asthma specialist should be considered for patients requiring add-on therapy

**Chantal: Management and Follow-up**

- Parents agree to continue the ICS b.i.d. long-term
- Then, family begins to care for sick grandmother’s dog & insist they can’t give the dog up
  - Previous skin prick tests indicated Chantal allergic to cats and dogs
- Chantal begins awakening with night-time cough
  - 3 nights/wk
- Dyspnea on exertion - stops preschool gymnastics program
- How could you improve her asthma control?

**Chantal: Further Management**

- Chantal has poor control and is at risk for a severe exacerbation
- Assess medication adherence, inhaler technique
- Consider:
  - Increasing ICS dose 50-100%
  - Adding an LTRA
  - Reduces symptoms, risk of an exacerbation
  - Evidence for adjunctive LABA is meager in children
  - Efficacy of LABA in adolescents is probably similar to that in adults

**Chantal: Long-Term Management**

- 6 months later
  - The family dog is run over by a garbage truck, and Chantal’s asthma seems to settle down
  - Following your advice, the family does not replace the dog. They steam-clean the carpets & upholstery, and clean their heating ducts
- A year later
  - The plant where Chantal’s father works closes. He finds a job at a fast-food restaurant, but no longer has health benefits
  - He can’t afford Chantal’s inhalers, and asks whether you can cut back on her therapy
- How would you assess whether you can taper her therapy? If it’s feasible, how would you do it?

**Asthma continuum 2012**

2012 Asthma Management Continuum: Distinctively yours and mine and we.

**Chantal: Assessing and Tapering Therapy**

- Assess asthma control using guidelines criteria:
  - Day and night symptoms, physical activity, bronchodilator use, number of exacerbations, spirometry if ≥ 6 yrs

ICS: inhaled corticosteroid; LABA: long-acting β-agonist; LTRA: leukotriene receptor antagonist

Kovesi et al. 2009

Chantal:

CMAJ

Riethmiller, C; Lemiere, P; Ducharme, et al. Canadian Pediatric Society Asthma Clinical Assembly. Canadian Thoracic Society


ICS: inhaled corticosteroid; LTRA: leukotriene receptor antagonist

Kovesi et al. 2009
Minimum Criteria for Acceptable Control of Asthma in Preschoolers

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Frequency or Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Daytime Symptoms</td>
<td>&lt; 4 days per week</td>
</tr>
<tr>
<td>Nighttime Symptoms</td>
<td>&lt; 1 night/week</td>
</tr>
<tr>
<td>Physical Activity</td>
<td>Normal</td>
</tr>
<tr>
<td>Use of rapid-acting bronchodilator</td>
<td>&lt; 4 times per week (unless before exercise only)</td>
</tr>
<tr>
<td>Exacerbations</td>
<td>Mild, infrequent (no more than once a year)</td>
</tr>
<tr>
<td>School, preschool or child care</td>
<td>None missed</td>
</tr>
</tbody>
</table>

Pediatric Asthma Action Plan Sample

Chantal: Assessing and Tapering Therapy

- Assess asthma control using guidelines criteria:
  - Day and night symptoms, physical activity, bronchodilator use, number of exacerbations, spirometry if ≥ 6 yrs
- If good control, try stopping LTRA (to save money) & re-assess in ~2 months
  - If control worsens: re-start LTRA
  - If control maintained: try decreasing ICS dose every 2-3 months by 30-50%; resume prior dose if control worsens

Inhaled Corticosteroids: Side Effects

- Growth:
  - 1 cm less growth during 1st year only
  - Subsequent growth velocity on therapy and final adult height usually normal
  - Long-term ICS: monitor with stadiometer, growth chart
- Adrenal Axis:
  - Suppression uncommon; less suppression than 4 courses/year prednisone
  - Very high doses (fluticasone) can cause symptomatic adrenal suppression, hypoglycemia
  - High ICS doses: avoid or have expert prescribe

Developmental Issues in Pediatric Asthma

- A clinical diagnosis in a preschooler should be reevaluated as the child reaches school age
- Triggers need to be reevaluated as the child grows
- Growth should be measured and plotted at follow-up visits
- Inhalation device choice needs to be developmentally appropriate and will change as the child grows
- Family and child need asthma education and responsibility for care needs to shift to child as they approach adolescence
Key Differences between Pediatric and Adult Asthma Management

Medication Differences:
- Most children will achieve control on a low-dose ICS.
- If a low-dose ICS is not adequate to maintain asthma control:
  - in children 6 to 11 years: increase ICS to a moderate dose or add LTRA
  - in patients 12 years and over: add a LABA to the low dose ICS, ideally in the form of a combination inhaler.
- High doses of ICS may be associated with significant side effects in children and should only be used by asthma specialists.
- Most children 6 years and over should be able to use a holding chamber with a mouthpiece or a dry powder inhaler.

Key Messages: Diagnosis and Management of Pediatric Asthma

- Pattern of asthma
  - Determine if transient or persistent
  - Most children with transient pattern (e.g. intermittent asthma) will “outgrow” their asthma
- Management of intermittent asthma
  - Intermittent ICS not recommended
  - Regular ICS for children with severe or prolonged symptoms and those who have ED visits or hospital admissions
  - LTRA can be used continuously during the viral season, or at the onset of viral infections

Key Messages: Management of Pediatric Asthma

- Management of persistent asthma
  - Daily ICS preferred therapy
  - Treat for at least a season at a time
  - If ICS unsuccessful consider:
    - Question diagnosis of asthma
    - Comorbid conditions
  - If asthma uncontrolled with moderate dose ICS
    - Increase ICS dose or add LTRA
    - Minimal evidence for LABA in preschool and school-aged children
  - Refer patients requiring add-on therapy
- Assess asthma control (guidelines criteria) every visit
  - Monitor growth with growth chart if on ICS at each visit

ICS: inhaled corticosteroid; LTRA: leukotriene receptor antagonist
LABA: long-acting β-agonist; MDI: metered-dose inhaler

We have come a long way!!