

# New Asthma Guidelines and Difficult to Control Asthma: Current Concepts

Pramod Kelkar, MD  
Founder, National Cough Clinic  
Past-Chair, Metro Asthma Coalition

Allergy & Asthma Care, PA  
(Treating children and adults)  
Offices in Maple Grove, Maplewood, Woodbury  
763-420-1010, 651-501-7872, 651-241-3000  
[www.nationalcoughclinic.com](http://www.nationalcoughclinic.com)

# Learning Objectives

- Understand why the guidelines are important
- Describe the changes in the new asthma guidelines
- Understand the implications for the everyday clinical practice
- Describe the pitfalls in management

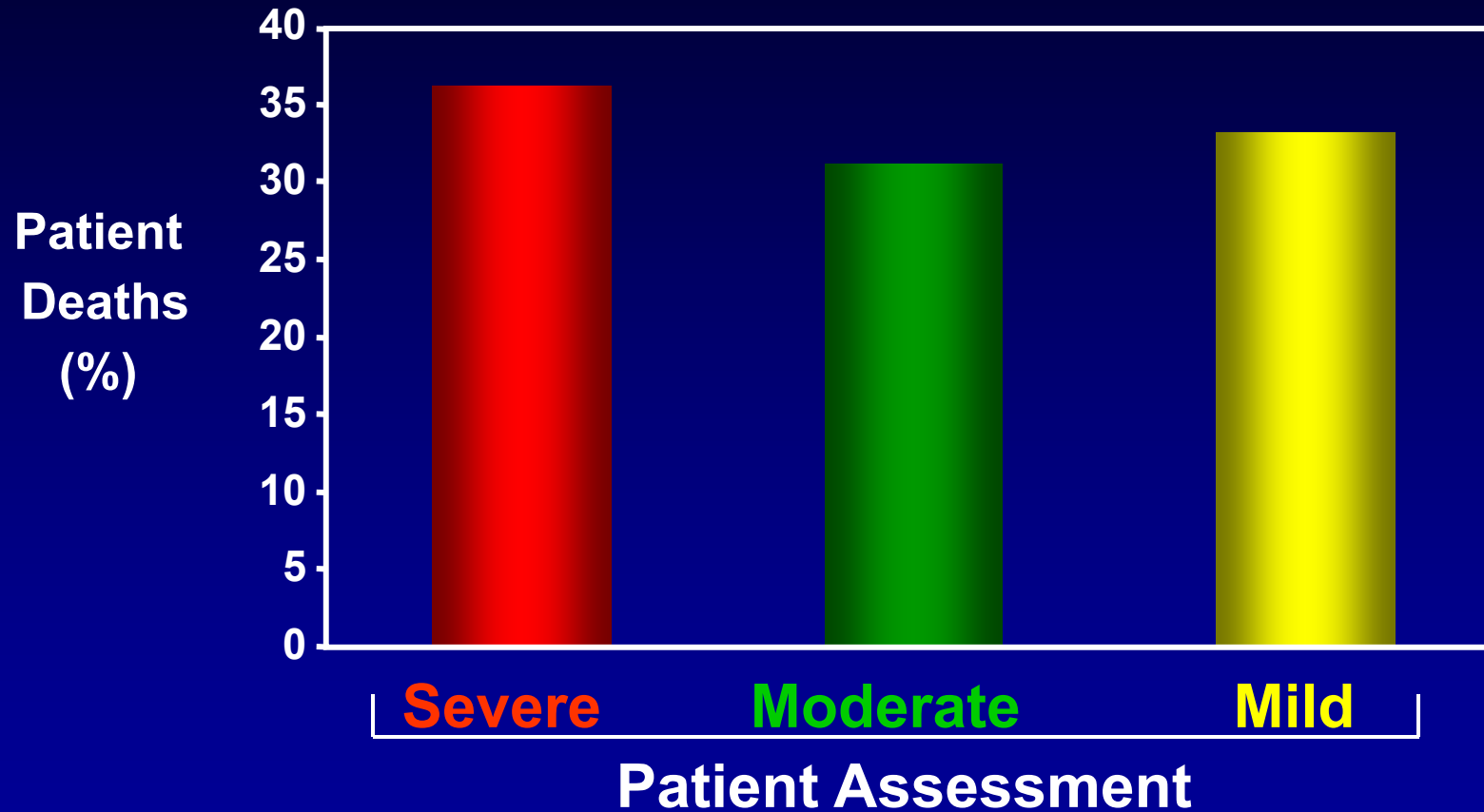
# Disclosures

- Speakers' Bureau/Consultant/Ad Board  
Greer Labs, TEVA, Respiratory Research,  
CoCo Pharma, Merck, MEDA

## Why care about asthma and the new 2007 National Asthma Guidelines

- Asthma is very common (up to 8-10% of the population)
- Increasing incidence
- High burden on the healthcare system (ER visits, hospitalizations)
- *Pay For Performance*

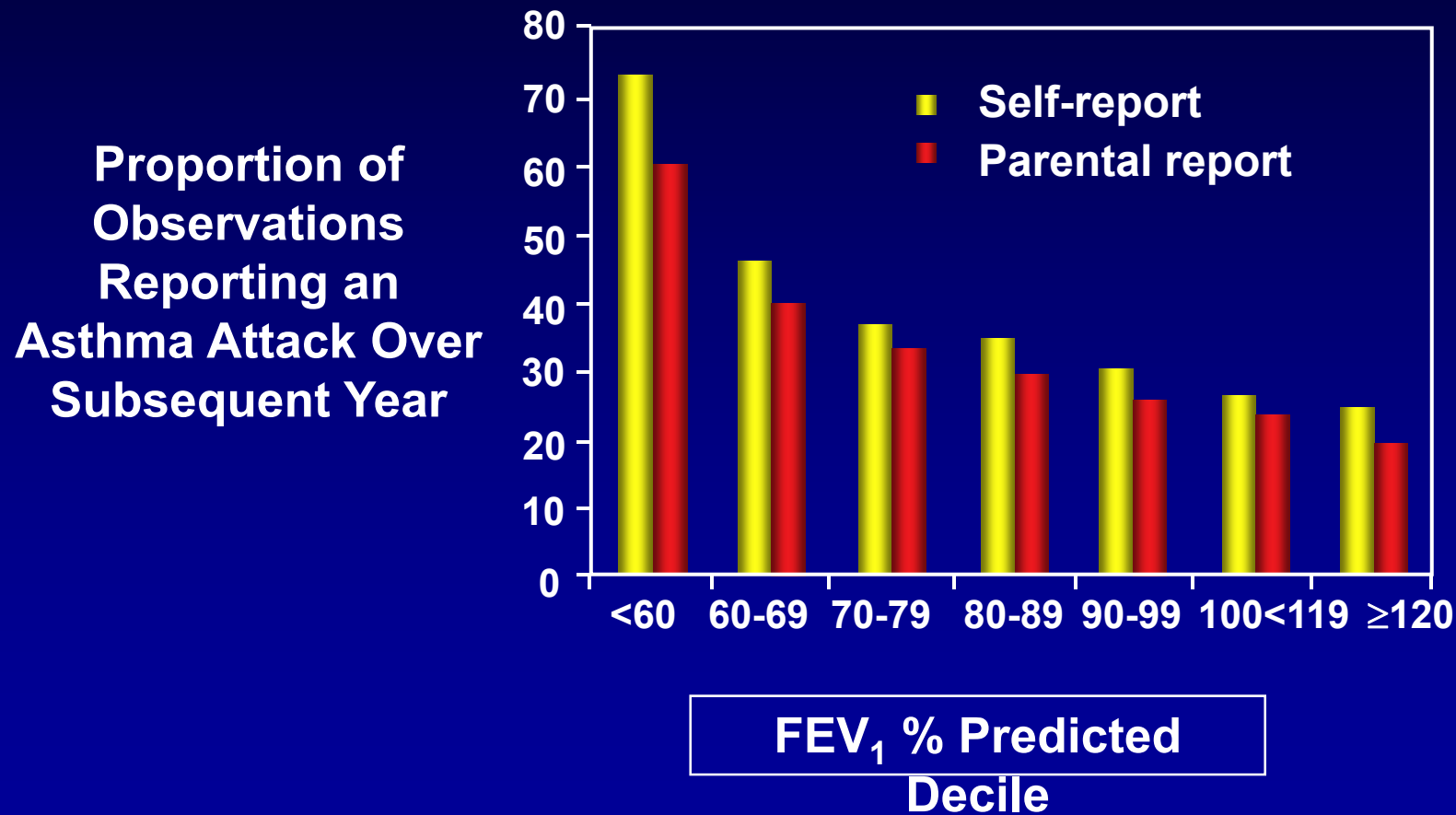
# Pediatric Asthma Deaths: Patients With Mild Asthma Are Also at Risk



Findings from a cohort study reviewing all pediatric asthma-related deaths (n=51) in the Australian state of Victoria from 1986 to 1989.

Robertson et al. *Pediatr Pulmonol.* 1992;13:95-100.

# FEV<sub>1</sub> Is Associated With Risk of Asthma Attacks



Fuhlbrigge et al. J Allergy Clin Immunol. 2001;107:61-67.

# Key New Concepts of Asthma Management

- Elements of assessment and monitoring
  - Severity
  - Control
  - Responsiveness to treatment
- Severity emphasized for initiating therapy
- Control emphasized for monitoring and adjusting therapy
- Severity and control defined in terms of 2 domains
  - Impairment
  - Risk

# Asthma Severity and Control: Impairment Domain

**Impairment = Current Frequency and Intensity of Symptoms and Functional Limitations**

## Symptoms

- Nighttime awakenings
- Need for short-acting  $\beta_2$ -agonists (SABAs) for quick relief of symptoms
- School days missed
- Exercise tolerance


## Lung Function

- Spirometry
- Peak flow

# Asthma Severity and Control: Risk Domain

- Future likelihood of asthma exacerbations, progressive decline in lung function over time, or risk of adverse effects from medications
- Assessment
  - Frequency and severity of exacerbations
  - Prednisone use
  - ER visits
  - Lung function
  - Minimally invasive biomarkers may play an increased role in the future (NO)

# Asthma Severity in Children Aged 0 to 4 Years

Components of Severity		Classification of Asthma Severity			
		Intermittent	Persistent		
			Mild	Moderate	Severe
<b>Impairment</b>	Symptoms	≤2 days/week	>2 days/week but not daily	Daily	Throughout the day
	Nighttime awakenings	<b>0</b>	1-2/month	3-4/month	>1/week
	Short-acting β <sub>2</sub> -agonist use for symptom control (not prevention of EIB)	≤2 days/week	>2 days/week but not daily	Daily	Several times per day
	Interference with normal activity	<b>None</b>	Minor limitation	Some limitation	Extremely limited
<b>Risk</b>	Exacerbations (consider frequency and severity)	0-1/year	≥2 exacerbations in 6 months requiring oral steroids, or ≥4 wheezing episodes/year lasting >1 day AND risk factors for persistent asthma  Frequency and severity may fluctuate over time Exacerbations of any severity may occur in patients in any severity category		

\*Currently not taking controller medication.

EIB = exercise-induced bronchospasm.

Adapted from <http://www.nhlbi.nih.gov/guidelines/asthma/epr3/resource.pdf>. Accessed February 5, 2007.



# Key Changes in Classifying Asthma Severity in Children

- Severity now classified in terms of the new domains of current impairment and future risk
- New measures of impairment
  - Lung function ( $FEV_1/FVC$ )
- New measures of risk
  - Frequent wheezing episodes and risk factors for persistent asthma
  - Frequency and severity of exacerbations
- “Intermittent” category has replaced “mild intermittent” to emphasize that exacerbations can be mild or severe

# Assessing Asthma Control in Children Aged 0 to 4 Years

Components of Control		Classification of Asthma Control		
		Well Controlled	Not Well Controlled	Very Poorly Controlled
Impairment	Symptoms	≤2 days/week	>2 days/week	Throughout the day
	Nighttime awakenings	1/month	>1/month	>1/week
	Interference with normal activity	None	Some limitation	Extremely limited
	Short-acting $\beta_2$ -agonist use for symptom control (not prevention of EIB)	≤2 days/week	>2 days/week	Several times per day
Risk	Exacerbations	0-1/year	2-3/year	>3/year
	Treatment-related adverse effects	Medication side effects can vary in intensity from none to very troublesome and worrisome. The level of intensity does not correlate to specific levels of control but should be considered in the overall assessment of risk.		

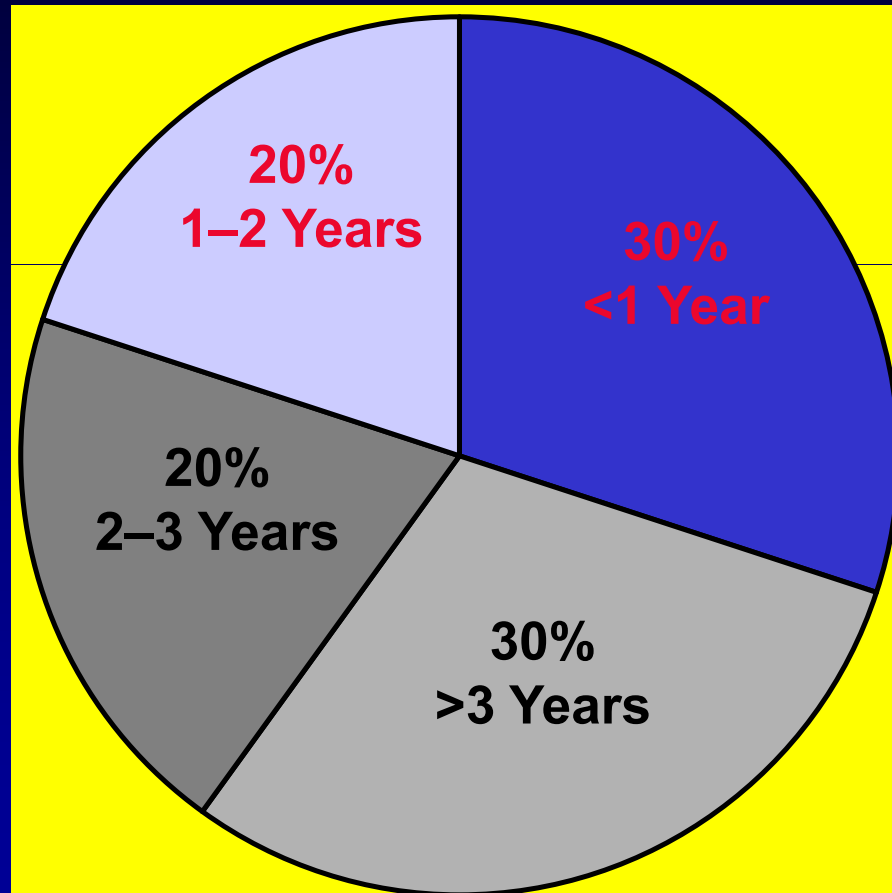
# Asthma Control: 5 to 11 Years and Adults

Components of Control		Classification of Asthma Control		
		Well Controlled	Not Well Controlled	Very Poorly Controlled
Impairment	Symptoms	≤2 days/week but not more than once on each day	>2 days/week or multiple times on ≤2 days/week	Throughout the day
	Nighttime awakenings	≤1/month	≥2/month	≥2/week
	Interference with normal activity	None	Some limitation	Extremely limited
	Short-acting β <sub>2</sub> -agonist use for symptom control (not prevention of EIB)	≤2 days/week	>2 days/week	Several times per day
	Lung function • FEV <sub>1</sub> or peak flow FEV <sub>1</sub> /FVC	>80% predicted/personal best >80% predicted	60%-80% predicted/personal best 75%-80% predicted	<60% predicted/personal best <75% predicted
Risk	Exacerbations	0-1/year	2-3/year	>3/year
	Reduction in lung growth	Evaluation requires long-term follow-up		
	Treatment-related adverse effects	Medication side effects can vary in intensity from none to very troublesome and worrisome. The level of intensity does not correlate to specific levels of control but should be considered in overall assessment.		

# Key Changes in Assessing Asthma Control

- Once treatment is established, emphasis should be on assessment of asthma control rather than on severity
- New measures of impairment
  - Lung function over time ( $FEV_1/FVC$ )
- New measures of risk
  - Frequency of exacerbations
  - Treatment-related side effects

# Onset of Symptoms in Children With Asthma<sup>1,2</sup>



1. Wainwright C et al. *Med J Aust.* 1997;167:218-223.  
2. Dodge R et al. *J Allergy Clin Immunol.* 1996;98:48-54.

# The Risk of Asthma in Wheezing Children: Modified Asthma Predictive Index<sup>1,2</sup>

In the past 12 months, >3 exacerbations of wheezing with at least 1 physician-diagnosed exacerbation **PLUS**

## 1 Major Criterion

- Parental history of asthma
- Physician-diagnosed atopic dermatitis
- Allergic sensitization to  $\geq 1$  aeroallergen\*

**OR**

## 2 Minor Criteria

- Wheezing unrelated to colds
- Blood eosinophils  $\geq 4\%$
- Allergic sensitization to milk, eggs, or peanuts

\*House dust mite, cockroach, dog, cat, mold, grass, tree, and weed.

1. Castro-Rodríguez JA et al. *Am J Respir Crit Care Med.* 2000;162:1403-1406.

2. Guilbert TW et al. *J Allergy Clin Immunol.* 2004;114:1282-1287.

# The Rule of “2”

Daytime asthma symptoms	>2 days per week
Nighttime asthma symptoms	>2 days per month
Rescue $\beta_2$ -agonist canisters	>2 per year
Rescue $\beta_2$ -agonist use	>2 times per week

1. United States Environmental Protection Agency. Asthma facts. Available at: [http://www.epa.gov/asthma/pdfs/asthma\\_fact\\_sheet\\_en.pdf](http://www.epa.gov/asthma/pdfs/asthma_fact_sheet_en.pdf). Accessed February 6, 2007. 2. Children and asthma in America. Asthma in America Web site. Available at: <http://www.asthmainamerica.com/acute.html>. Accessed January 22, 2007. 3. United States Department of Health and Human Services. National Center for Health Statistics Web site. Available at: <http://www.cdc.gov/nchs/hus.htm>. Accessed March 5, 2007. 4. Carlton BG, Lucas DO, Ellis EF, et al. The status of asthma control and asthma prescribing practices in the United States: results of a large prospective asthma control survey of primary care practices. *J Asthma*. 2005;42:529-535. 5. National Institutes of Health. National Asthma Education and Prevention Program Expert Panel Report: Guidelines for the Diagnosis and Management of Asthma—Update on Selected Topics 2002. Available at: <http://www.nhlbi.nih.gov/guidelines/asthma/asthsumm.htm>. Accessed February 6, 2007.

# Asthma Control Test™ (ACT)

1. In the past **4 weeks**, how much of the time did your **asthma** keep you from getting as much done at work, school or at home?

Score

All of the time **1**      Most of the time **2**      Some of the time **3**      A little of the time **4**      None of the time **5**

2. During the past **4 weeks**, how often have you had shortness of breath?

More than once a day **1**      Once a day **2**      3 to 6 times a week **3**      Once or twice a week **4**      Not at all **5**

3. During the past **4 weeks**, how often did your **asthma** symptoms (wheezing, coughing, shortness of breath, chest tightness or pain) wake you up at night, or earlier than usual in the morning?

4 or more nights a week **1**      2 or 3 nights a week **2**      Once a week **3**      Once or twice **4**      Not at all **5**

4. During the past **4 weeks**, how often have you used your rescue inhaler or nebulizer medication (such as albuterol)?

3 or more times per day **1**      1 or 2 times per day **2**      2 or 3 times per week **3**      Once a week or less **4**      Not at all **5**

5. How would you rate your **asthma** control during the past **4 weeks**?

Not controlled at all **1**      Poorly controlled **2**      Somewhat controlled **3**      Well controlled **4**      Completely controlled **5**

Copyright 2002, by QualityMetric Incorporated.

Patient Total Score

# Exploring Reasons for Failure of Asthma Control<sup>1,2</sup>

- “Under or Mis” diagnosis of asthma
- Inadequate therapy for disease severity
- Not addressing environmental allergies
- Poor compliance
- Repeated respiratory infection (daycare)
- Comorbid conditions: Sinus, GERD

1. Joint Task Force on Practice Parameters. *J Allergy Clin Immunol.* 2005;116:S3-S11.

2. National Asthma Education and Prevention Program. *Expert Panel Report 2: Guidelines for the Diagnosis and Management of Asthma.* National Heart, Lung, and Blood Institute, National Institutes of Health; July 1997. NIH publication 97-4051.

# Written Asthma Action Plan

**IMPACT DC** Asthma Action Plan until \_\_\_\_\_

Name: \_\_\_\_\_ Date: \_\_\_\_\_

Primary Care Provider Name: \_\_\_\_\_

Daytime Phone Number: \_\_\_\_\_

Night/Weekend Phone Number: \_\_\_\_\_

Pharmacy Name: \_\_\_\_\_

Pharmacy Phone Number: \_\_\_\_\_

The colors of a traffic light will help you use your asthma medicines.

**Green means Go Zone!**  
Use preventive medicine.

**Yellow means Caution Zone!**  
Add quick-relief medicine.

**Red means Stop Zone!**  
Get help from a doctor.

Personal Best Peak Flow: \_\_\_\_\_

**GO** ACTION: Use these daily preventive anti-inflammatory medicines:

You have *all* of these:

- Breathing is good
- No cough or wheeze
- Sleep through the night
- Can work and play

Peak flow from \_\_\_\_\_ to \_\_\_\_\_

Medicine	How Much	How Often

For asthma with exercise, take:

Medicine	How Much	How Often

**CAUTION** ACTION: Continue with your medicine, as above, and ADD:

You have *any* of these:

- First signs of a cold
- Cough
- Mild wheeze
- Tight chest

Peak flow from \_\_\_\_\_ to \_\_\_\_\_

Medicine	How Much	How Often

Call your primary care provider

**DANGER** ACTION: Take these medicines until you talk to your doctor:

Get help from a doctor now! Do not be afraid of causing a fuss.  
Your doctor will want to see you right away. It's important!

Your asthma is getting worse fast:

- Medicine is not helping
- Breathing is hard and fast
- Nose opens wide
- Ribs show
- Can't talk well

Peak flow below \_\_\_\_\_

Medicine	How Much	How Often

If you cannot contact your doctor, go directly to the emergency room. **DO NOT WAIT.**  
Call an ambulance (911) if necessary.

Make an appointment with your primary care provider within two days of an ER visit or hospitalization.

Adapted from the NH-81



# Clinical Control of Asthma

---

- No (or minimal)\* daytime symptoms
- No limitations of activity
- No nocturnal symptoms
- No (or minimal) need for rescue medication
- Normal lung function
- No exacerbations

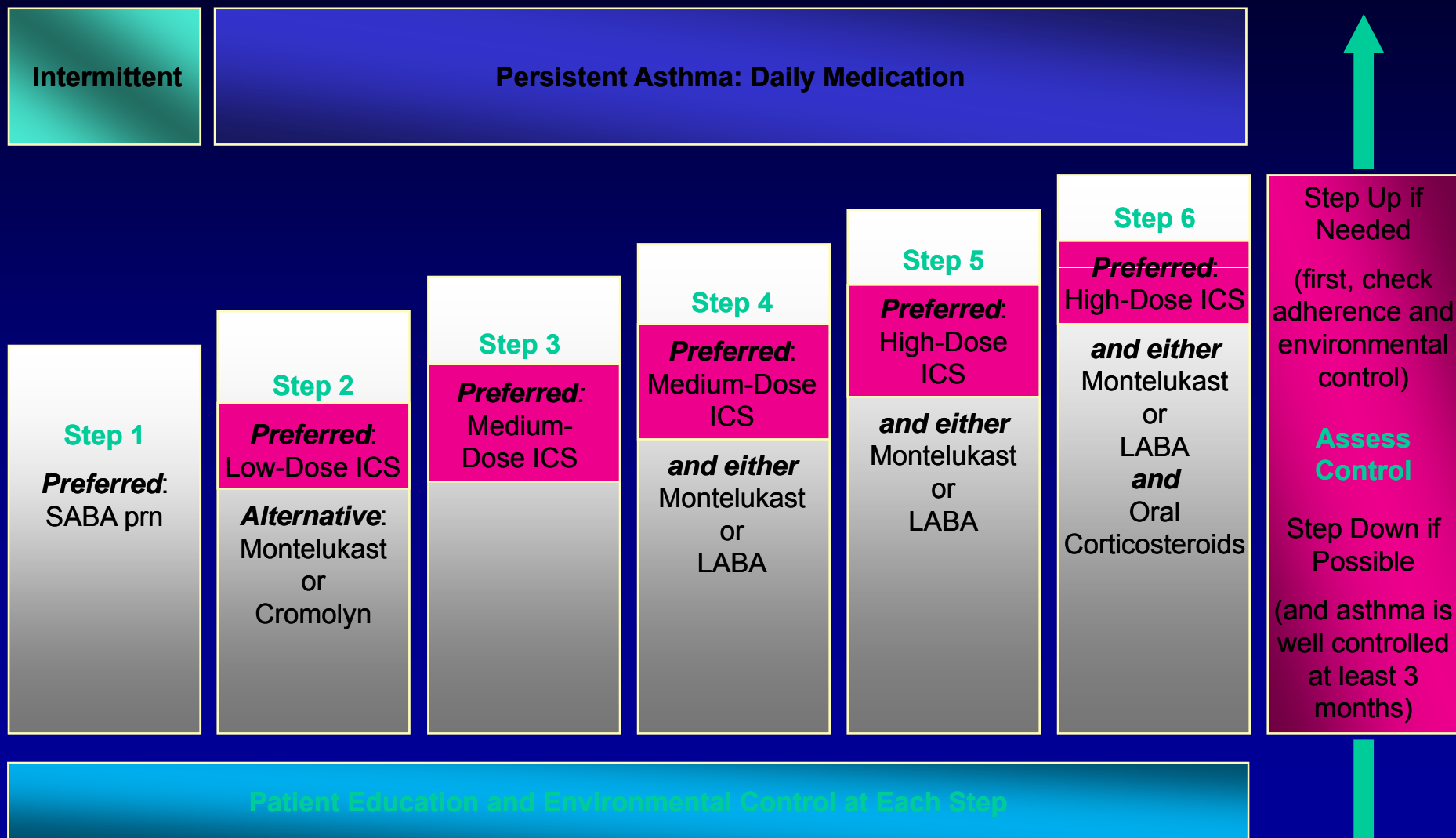
---

\* *Minimal = twice or less per week*

# Key Questions

- Are Peak Flow Meters useful?
- When to give Asthma Action Plans?
- When and why to do allergy testing?
- Can starting early on inhaled steroids prevent airway remodeling?
- What is the role of allergy shots?
- Can allergy shots prevent asthma?

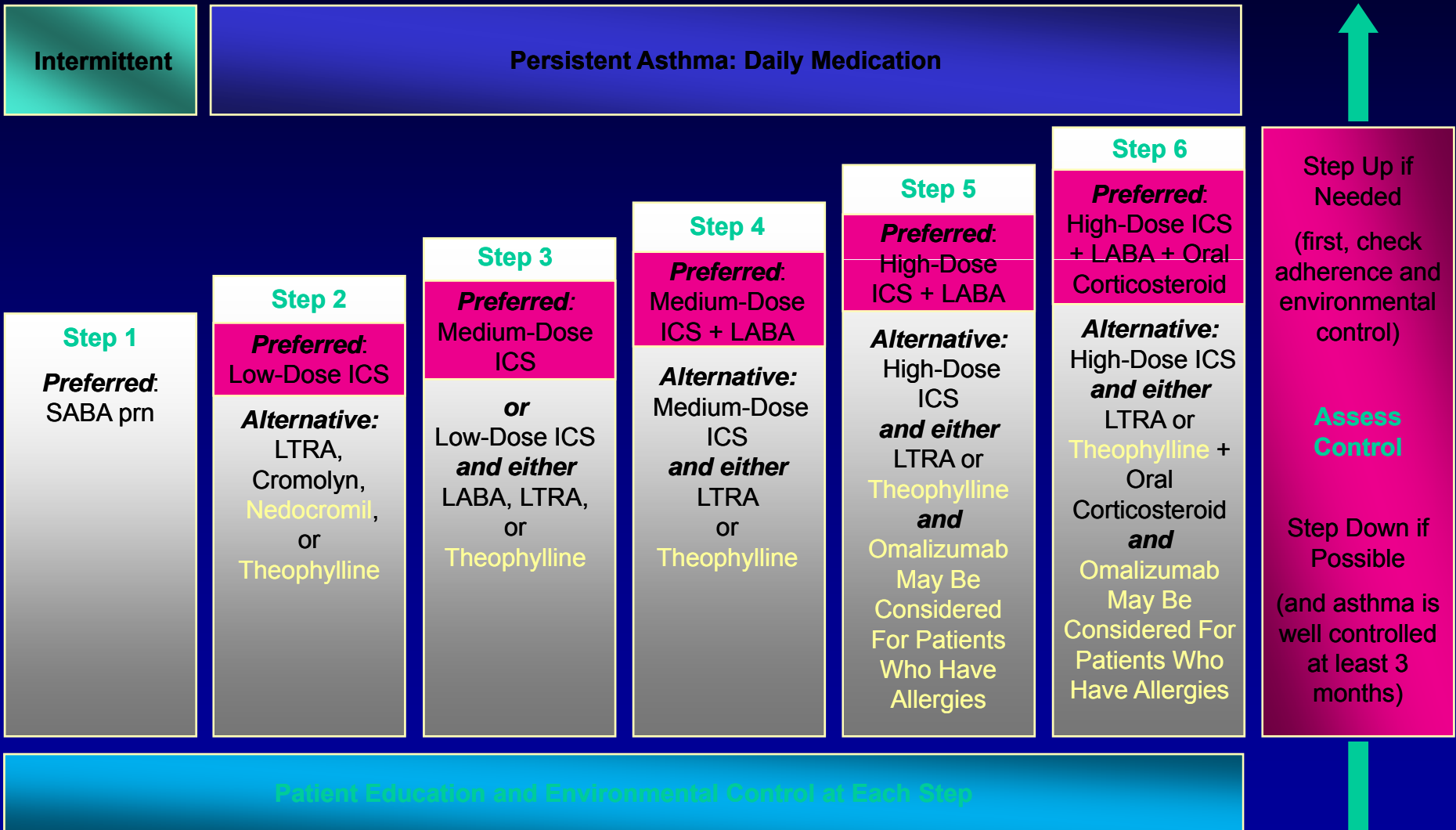
# Stepwise Approach for Managing Asthma in Children Aged 0 to 4 Years



ICS = inhaled corticosteroid; LABA = long-acting  $\beta_2$ -agonist; SABA = short-acting  $\beta_2$ -agonist.

Adapted from <http://www.nhlbi.nih.gov/guidelines/asthma/epr3/resource.pdf>. Accessed February 5, 2007.

# Stepwise Approach for Managing Asthma in Children Aged 5 to 11 Years & Adults



LTRA = leukotriene receptor antagonist.

Adapted from <http://www.nhlbi.nih.gov/guidelines/asthma/epr3/resource.pdf>. Accessed February 5, 2007.

**Intermittent Asthma**

**Persistent Asthma: Daily Medication**  
 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, Nedocromil, LTRA, or Theophylline

**Step 3**  
**Preferred:**  
 Medium-dose ICS  
 OR  
 Low-dose ICS + LABA  
**Alternative:**  
 Low-dose ICS + either LTRA, Theophylline, or Zileuton

**Step 4**  
**Preferred:**  
 Medium-dose ICS + LABA  
**Alternative:**  
 Medium-dose ICS + either LTRA, Theophylline, or Zileuton

**Step 5**  
**Preferred:**  
 High-dose ICS + LABA  
 AND  
 Consider Omalizumab for patients who have allergies

**Step 6**  
**Preferred:**  
 High-dose ICS + LABA + oral corticosteroid  
 AND  
 Consider Omalizumab for patients who have allergies

Step up if needed  
 (first, check adherence, environmental control, and comorbid conditions)

Assess control

Step down if possible  
 (and asthma is well controlled at least 3 months)

**Patient Education and Environmental Control at Each Step**

- Quick-Relief Medication 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.
  - Use of beta<sub>2</sub>-agonist >2 days a week for symptom control (not prevention of EIB) indicates inadequate control and the need to step up treatment.

# Key Recommendations

## Managing asthma in children 0-4 years

- Diagnosis is often difficult.
- Treatment has not been adequately studied.
- Criteria for initiation of long-term-control therapy:
  - 3 wheezing episodes in past year and positive asthma risk profile.
  - those who require symptomatic treatment > 2 days per week
  - two or more severe exacerbations within 6 months



# Estimate Comparative Daily Dosages for Inhaled Glucocorticosteroids by Age

Drug	Low Daily Dose ( $\mu\text{g}$ )		Medium Daily Dose ( $\mu\text{g}$ )		High Daily Dose ( $\mu\text{g}$ )	
	> 5 y	Age $\leq$ 5 y	> 5 y	Age $\leq$ 5 y	> 5 y	Age $\leq$ 5 y
Beclomethasone	200-500	100-200	>500-1000	>200-400	>1000	>400
Budesonide	200-600	100-200	600-1000	>200-400	>1000	>400
Budesonide-Neb Inhalation Suspension		250-500		>500-1000		>1000
Ciclesonide	80 – 160	80-160	>160-320	>160-320	>320-1280	>320
Flunisolide	500-1000	500-750	>1000-2000	>750-1250	>2000	>1250
Fluticasone	100-250	100-200	>250-500	>200-500	>500	>500
Mometasone furoate	200-400	100-200	> 400-800	>200-400	>800-1200	>400
Triamcinolone acetonide	400-1000	400-800	>1000-2000	>800-1200	>2000	>1200

# Follow-Up

- Visits every 2-6 weeks until control achieved
- When control achieved, contact every 3-6 months
- Step-down in therapy
  - Consider with well-controlled asthma for at least 3 months
  - Decrease inhaled steroids by 25-50 % every 3 months to lowest effective dose
  - Patients may relapse with total discontinuation of inhaled corticosteroids

## Peak Flow Meter is optional!

- Maximum expiratory flow rate
- Helps in monitoring (Not diagnosis)
- Very effort dependent
- Poor at detecting early/ mild obstruction
- Can not distinguish between obstruction and restriction

*De-emphasize!*

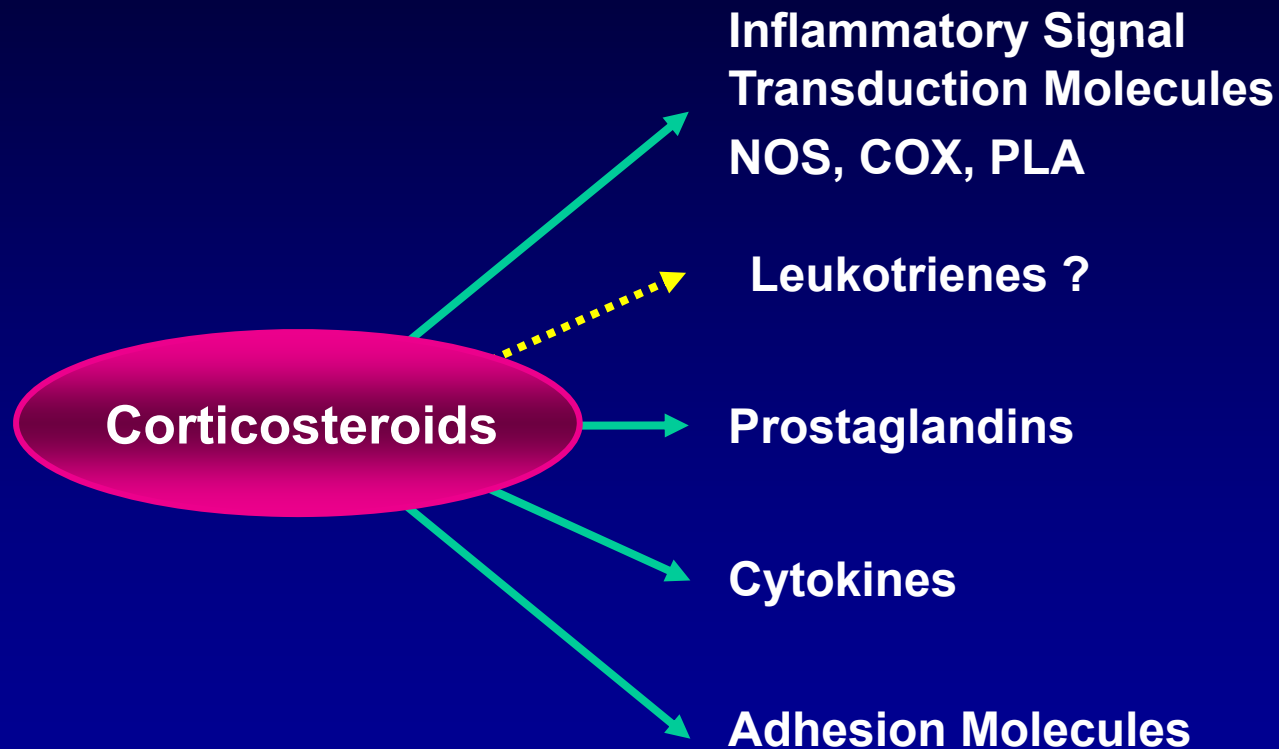
## What can lead to “difficult-to-control” asthma?

- Wrong diagnosis (VCD, FB, CF, others)
- Missed/untreated co-morbidities (Allergies)
- Heterogeneity of asthma
- Wrong medicine:
  - Technique
  - Choice
  - Dose
- Patient factors: compliance, anxiety, obesity

# Pharmacotherapy for Asthma

- Short-acting beta agonists: Proair, Proventil, Ventolin, Maxair autohaler, Xopenex
- Long-acting beta agonists (LABA): Serevent, Foradil
- Inhaled steroids: fluticasone (Flovent), budesonide (Pulmicort), Asmanex (mometasone), Q-Var, Azmacort, Ciclesonide
- Inhaled steroid/LABA combination: Advair, Symbicort
- Leukotriene modifiers: Singulair, Accolate
- Leukotriene inhibitor: Zileuton (zyflo)
- Anti-IgE: Xolair
- Miscellaneous: Theophylline, lidocaine via nebulizer
- Oral steroids: prednisone
- Allergy Immunotherapy/Injections

# Inhaled Steroids Target Multiple Inflammatory Mediators<sup>1-3</sup>



COX = cyclooxygenase; NOS = nitric oxide synthase; PLA = phospholipase A.

1. Barnes PJ. *Eur J Pharmacol.* 2006;533:2-14.

2. Barnes PJ et al. *Am J Respir Crit Care Med.* 1998;157:S1-S53.

3. O'Shaughnessy KM et al. *Am Rev Respir Dis.* 1993;147:1472-1476.

# Can diet affect respiratory system???

- Fruit-based (apples, pears, etc.) dietary fiber intake reduced cough with phlegm (?)
- Omega-3 fatty acid play a role in leukotrienes and inflammation (?)
- Vitamin C for exercise-induced asthma (?)
- Whole grains and fish lower asthma risk (?)
- Vitamin D deficiency in pregnancy-

*Butler LM, et al. Am J Respir and Crit Care Med 2004;170: 279-287*

*Cohen HA, et al. Blocking effect of vitamin C in exercise-induced asthma. Arch Pediatr Adolesc. Med 1997;151:367-70*

*Tabak C, et al. Diet and asthma in Dutch school children. Thorax. 2006;61:1048-1053*

# Thank you!

Pramod Kelkar, MD  
Founder, National Cough Clinic  
Past-Chair, Metro Asthma Coalition

Allergy & Asthma Care, PA  
(Treating children and adults)  
Offices across the Twin Cities  
[www.allergy-care.net](http://www.allergy-care.net)  
[www.nationalcoughclinic.com](http://www.nationalcoughclinic.com)