



# GINA: Global Initiative for Asthma 2006 Report

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June 2007





# Outline

- ◆ GINA
- ◆ Diagnosis/ monitoring: PEF
- ◆ Classification of asthma
- ◆ Goals of treatment
- ◆ Medications
- ◆ Five components for managing asthma
- ◆ Summary



GLOBAL STRATEGY FOR  
ASTHMA MANAGEMENT AND PREVENTION

REVISED 2006



# GINA:

## Global Initiative for Asthma

- ◆ Formed in 1993 in collaboration with the National Heart, Lung, and Blood Institute (NHLBI), National Institutes of Health (NIH) USA, and the World Health Organization (WHO)
- ◆ In January 2004, the GINA Executive Committee recommended that the revision of *Global Strategy for Asthma Management and Prevention*
  - emphasize asthma management based on clinical control, rather than classification by severity
  - the role of the health care professional is to establish patients' current level of treatment and control, then adjust treatment to gain and maintain control

# Peak expiratory flow (PEF): for diagnosis and monitoring

- ◆ Peak flow meter: ideal for patients to use in home settings for day-to-day objective measurement of airflow limitation
- ◆ PEF measurements should preferably be compared to the patient's own previous best measurements using his/her own peak flow meter
  - previous best measurement is usually obtained when the patient is asymptomatic or on full treatment and serves as a reference value
  - PEF is measured in the morning before treatment is taken, when values are often close to their lowest



# Previous classification of asthma



<b>Intermittent</b>
Symptoms less than once a week Brief exacerbations Nocturnal symptoms not more than twice a month <ul style="list-style-type: none"><li>• FEV<sub>1</sub> or PEF <math>\geq</math> 80% predicted</li><li>• PEF or FEV<sub>1</sub> variability <math>&lt;</math> 20%</li></ul>
<b>Mild Persistent</b>
Symptoms more than once a week but less than once a day Exacerbations may affect activity and sleep Nocturnal symptoms more than twice a month <ul style="list-style-type: none"><li>• FEV<sub>1</sub> or PEF <math>\geq</math> 80% predicted</li><li>• PEF or FEV<sub>1</sub> variability <math>&lt;</math> 20 – 30%</li></ul>
<b>Moderate Persistent</b>
Symptoms daily Exacerbations may affect activity and sleep Nocturnal symptoms more than once a week Daily use of inhaled short-acting $\beta_2$ -agonist <ul style="list-style-type: none"><li>• FEV<sub>1</sub> or PEF 60-80% predicted</li><li>• PEF or FEV<sub>1</sub> variability <math>&gt;</math> 30%</li></ul>
<b>Severe Persistent</b>
Symptoms daily Frequent exacerbations Frequent nocturnal asthma symptoms Limitation of physical activities <ul style="list-style-type: none"><li>• FEV<sub>1</sub> or PEF <math>\leq</math> 60% predicted</li><li>• PEF or FEV<sub>1</sub> variability <math>&gt;</math> 30%</li></ul>



# Classification of asthma by level of control



Characteristic	Controlled <u>(All of the following)</u>	Partly Controlled <u>(Any measure present in any week)</u>	Uncontrolled
Daytime symptoms	None (twice or less/week)	More than twice/week	<u>Three or more features of partly controlled asthma present in any week</u>
Limitations of activities	None	Any	
Nocturnal symptoms/awakening	None	Any	
Need for reliever/ rescue treatment	None (twice or less/week)	More than twice/week	
Lung function (PEF or FEV <sub>1</sub> ) <sup>‡</sup>	Normal	< 80% predicted or personal best (if known)	
Exacerbations	None	One or more/year*	

\* Any exacerbation should prompt review of maintenance treatment to ensure that it is adequate.

† By definition, an exacerbation in any week makes that an uncontrolled asthma week.

‡ Lung function is not a reliable test for children 5 years and younger.



# Goals of treatment

- ◆ The goals for successful management of asthma are to:
  - Achieve and maintain control of symptoms
  - Maintain normal activity levels, including exercise
  - Maintain pulmonary function as close to normal as possible
  - Prevent asthma exacerbations
  - Avoid adverse effects from asthma medications
  - Prevent asthma mortality

# Medications

- ◆ Controller medications
  - inhaled glucocorticosteroids
  - leukotriene modifiers
  - long-acting inhaled  $\beta$  2-agonists
  
- ◆ Reliever medications
  - rapid-acting inhaled  $\beta$  2-agonists







# Controller medications: inhaled glucocorticosteroids

- ◆ The most effective anti-inflammatory medications
- ◆ Reduce asthma symptoms, improve lung function, decrease airway hyperresponsiveness, reduce frequency and severity of exacerbations, and reduce mortality
- ◆ Most of the benefit from inhaled steroids is achieved at relatively low doses, equivalent to budesonide 400 mcg/day
- ◆ Smoking reduces the responsiveness to inhaled steroids → higher doses may be required



# Controller medications: inhaled glucocorticosteroids

- ◆ Add-on therapy with another class of controller is preferred over increasing the dose of inhaled steroids
- ◆ Oropharyngeal candidiasis:
  - prevalence may be reduced by using certain spacer devices for pressurized MDIs
  - mouth washing (rinsing with water, gargling, and spitting out)
  - use of prodrugs that are activated in the lungs but not in the pharynx (e.g., ciclesonide) may minimize such effects without the need for a spacer or mouth washing

# Estimated equivalent doses of inhaled glucocorticosteroids



Drug	Low Daily Dose ( $\mu\text{g}$ )	Medium Daily Dose ( $\mu\text{g}$ )	High Daily Dose ( $\mu\text{g}$ ) <sup>‡</sup>
Beclomethasone dipropionate	200 - 500	>500 - 1000	>1000 - 2000
Budesonide* ←	200 - 400	>400 - 800	>800 - 1600
Ciclesonide* ←	80 - 160	>160 - 320	>320 - 1280
Flunisolide	500 - 1000	>1000 - 2000	>2000
Fluticasone	100 - 250	>250 - 500	>500 - 1000
Mometasone furoate* ←	200 - 400	>400 - 800	>800 - 1200
Triamcinolone acetonide	400 - 1000	>1000 - 2000	>2000

† Comparisons based upon efficacy data.

‡ Patients considered for high daily doses except for short periods should be referred to a specialist for assessment to consider alternative combinations of controllers. Maximum recommended doses are arbitrary but with prolonged use are associated with increased risk of systemic side effects.

\* Approved for once-daily dosing in mild patients.

## Notes

- The most important determinant of appropriate dosing is the clinician's judgment of the patient's response to therapy. The clinician must monitor the patient's response in terms of clinical control and adjust the dose accordingly. Once control of asthma is achieved, the dose of medication should be carefully titrated to the **minimum** dose required to maintain control, thus reducing the potential for adverse effects.
- Designation of low, medium, and high doses is provided from manufacturers' recommendations where possible. Clear demonstration of dose-response relationships is seldom provided or available. The principle is therefore to establish the minimum effective controlling dose in each patient, as higher doses may not be more effective and are likely to be associated with greater potential for adverse effects.
- As CFC preparations are taken from the market, medication inserts for HFA preparations should be carefully reviewed by the clinician for the equivalent correct dosage.

# Controller medications:

## long-acting inhaled $\beta_2$ -agonists

- ◆ Not as monotherapy: do not influence the airway inflammation in asthma
- ◆ Most effective when combined with inhaled steroids: preferred when a medium dose of inhaled steroid alone fails to achieve control of asthma
- ◆ Improve symptoms and lung function, reduce the number of exacerbations, and achieve clinical control more rapidly, and at a lower dose of inhaled steroids than inhaled steroids given alone






# Controller medications: long-acting inhaled $\beta$ 2-agonists

- ◆ Combination of formoterol and budesonide for both rescue and maintenance:
  - in patients receiving combination therapy for maintenance
  - given as needed for enhanced protection from severe exacerbations and provide improvements in asthma control at relatively low doses of treatment
- ◆ Formoterol has a more rapid onset of action than salmeterol, which may make it suitable for symptom relief as well as symptom prevention





# Controller medications: leukotriene modifiers

- ◆ Small and variable bronchodilator effect, reduce symptoms, improve lung function, and reduce airway inflammation and asthma exacerbations
- ◆ Effect of being used alone as controller: less than that of low doses of inhaled steroids
- ◆ Add-on therapy: reduce the dose of inhaled steroids, and improve asthma control in patients not controlled with low or high doses of inhaled steroids
- ◆ Less effective than long-acting inhaled  $\beta$  2-agonists as add-on therapy



# Controller medications: others

## ◆ Theophylline

- bronchodilator with modest anti-inflammatory properties at lower dose
- add-on therapy: patients who do not achieve control on inhaled steroids alone, but less effective than long-acting inhaled  $\beta$  2-agonists

## ◆ Long acting oral $\beta$ 2-agonists

- slow release formulations of salbutamol and terbutaline: only on rare occasions when additional bronchodilation is needed



# Reliever medications: rapid-acting inhaled $\beta$ 2-agonists

- ◆ Salbutamol and terbutaline: medications of choice during acute exacerbations and for pretreatment of exercise-induced bronchoconstriction
- ◆ Formoterol: only in patients on regular controller therapy with inhaled steroids
- ◆ Only on as-needed basis at the lowest dose and frequency
- ◆ Increased use, especially daily prn use → deterioration of control → reassess treatment
- ◆ Failure to achieve quick and sustained response → short-term treatment with oral steroids



# Five components to achieve and maintain control of asthma

1. Develop patient-doctor partnership
2. Identify and reduce exposure to risk factors
3. Assess, treat and monitor asthma
4. Manage asthma exacerbations
5. Special considerations (pregnancy, surgery, rhinitis, sinusitis, nasal polyps, occupational asthma, respiratory infections, etc)

# Component 1: Develop patient-doctor partnership

- ◆ Guided self-management: enable patients to gain the knowledge, confidence, and skills to assume a major role in the management of asthma

## Figure 4.1-1. Essential Features of the Doctor-Patient Partnership to Achieve Guided Self-Management in Asthma

- Education
- Joint setting of goals
- Self-monitoring. The person with asthma is taught to combine assessment of asthma control with educated interpretation of key symptoms
- Regular review of asthma control, treatment, and skills by a health care professional
- Written action plan. The person with asthma is taught which medications to use regularly and which to use as needed, and how to adjust treatment in response to worsening asthma control
- Self-monitoring is integrated with written guidelines for both the long-term treatment of asthma and the treatment of asthma exacerbations.



# Component 1: Develop patient-doctor partnership

## ◆ Action plan:

- Regular treatment
- Assess asthma control
- Step-up treatment
- Emergency

### Your Regular Treatment:

1. Each day take \_\_\_\_\_
2. Before exercise, take \_\_\_\_\_

### WHEN TO INCREASE TREATMENT

#### Assess your level of Asthma Control

In the past week have you had:

Daytime asthma symptoms more than 2 times ?	No	Yes
Activity or exercise limited by asthma?	No	Yes
Waking at night because of asthma?	No	Yes
The need to use your [rescue medication] more than 2 times? If you are monitoring peak flow, peak flow less than _____?	No	Yes

*If you answered YES to three or more of these questions, your asthma is uncontrolled and you may need to step up your treatment.*

### HOW TO INCREASE TREATMENT

STEP-UP your treatment as follows and assess improvement every day:

\_\_\_\_\_ [Write in next treatment step here]

Maintain this treatment for \_\_\_\_\_ days [specify number]

### WHEN TO CALL THE DOCTOR/CLINIC.

Call your doctor/clinic: \_\_\_\_\_ [provide phone numbers]

If you don't respond in \_\_\_\_\_ days [specify number]

\_\_\_\_\_ [optional lines for additional instruction]

### EMERGENCY/SEVERE LOSS OF CONTROL

✓ If you have severe shortness of breath, and can only speak in short sentences,

✓ If you are having a severe attack of asthma and are frightened,

✓ If you need your reliever medication more than every 4 hours and are not improving.


1. Take 2 to 4 puffs \_\_\_\_\_ [reliever medication]

2. Take \_\_\_\_\_ mg of \_\_\_\_\_ [oral glucocorticosteroid]

3. Seek medical help: Go to \_\_\_\_\_; Address \_\_\_\_\_

Phone: \_\_\_\_\_

4. Continue to use your \_\_\_\_\_ [reliever medication] until you are able to get medical help.



## Component 2: Identify and reduce exposure to risk factors

- ◆ Possible cause of asthma exacerbations: allergens, viral infections, pollutants, and drugs
- ◆ Reducing exposure to some of these categories of risk factors (e.g. smoking cessation, reducing exposure to secondhand smoke, reducing or eliminating exposure to occupational agents or foods/additives/drugs known to cause symptoms)
- ◆ As many asthma patients react to multiple factors, medications to maintain asthma control have an important role because patients are often less sensitive to these risk factors when their asthma is under good control

# Component 3: Assess, treat and monitor asthma

- ◆ Patients' current level of control and treatment determine the selection of medications

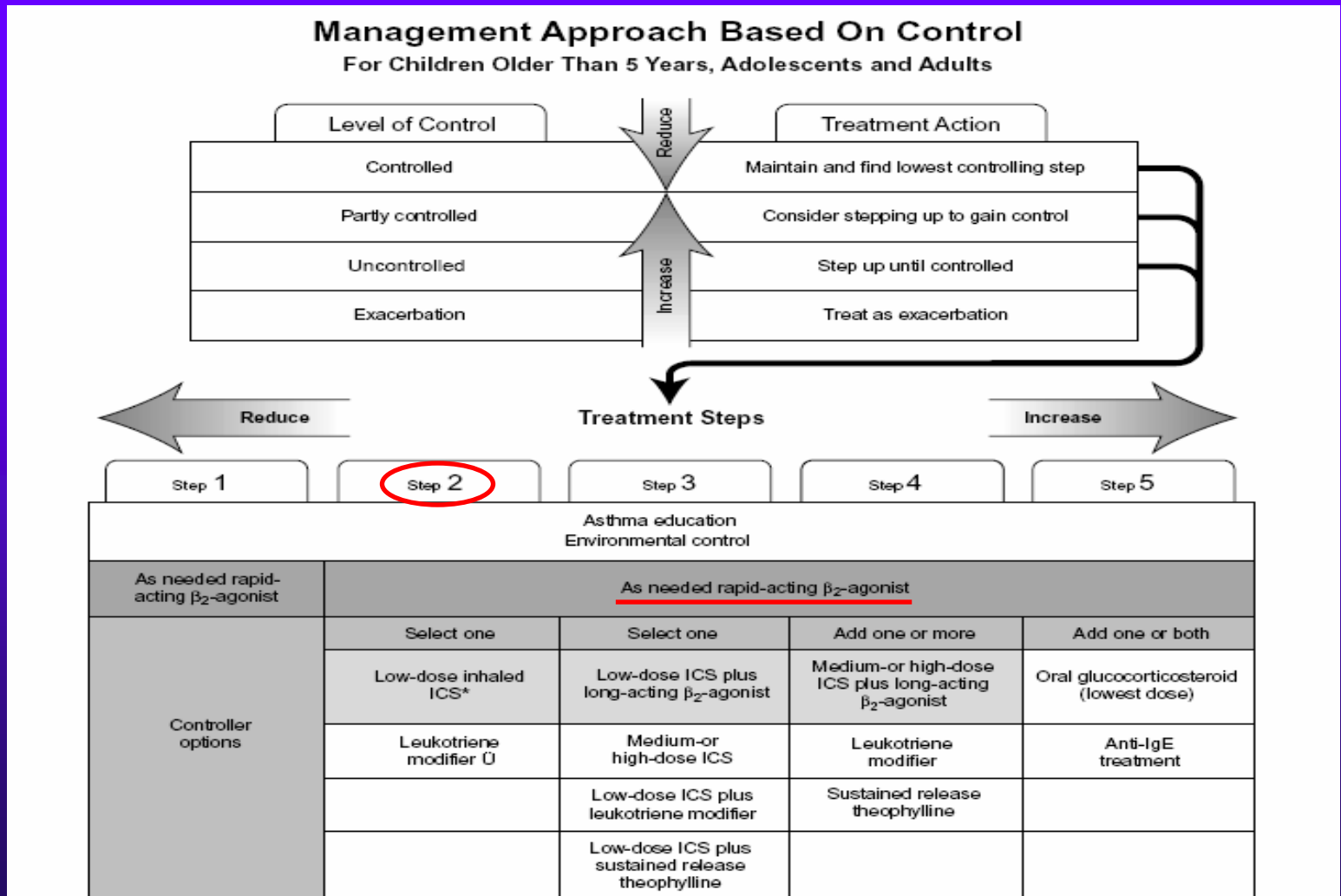
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Exacerbations	None	One or more/year*	One in any week <sup>†</sup>

\* Any exacerbation should prompt review of maintenance treatment to ensure that it is adequate.

† By definition, an exacerbation in any week makes that an uncontrolled asthma week.

‡ Lung function is not a reliable test for children 5 years and younger.

# Component 3: Assess, treat and monitor asthma



\* ICS=inhaled glucocorticosteroids  
 $\bar{O}$ =Receptor antagonist or synthesis inhibitors

# Stepping down



- ◆ Controller medications: improvement begins within days of initiating treatment, but the full benefit after 3 or 4 months
- ◆ Inhaled steroids alone:
  - Medium- to high-doses: a 50% reduction in dose should be attempted at 3 month intervals
  - Low-dose: switched to once-daily dosing







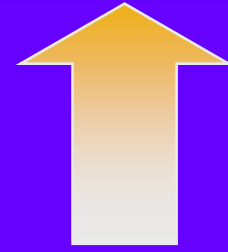
# Stepping down



- ◆ Combination of inhaled steroid and long-acting  $\beta$  2-agonist:
  - reduce the dose of inhaled steroid by 50% while continuing the long-acting  $\beta$  2-agonist until a low-dose is reached, when the long acting  $\beta$  2-agonist may be stopped
  - switch the combination treatment to once-daily dosing
  - substitute with inhaled steroid monotherapy at the same dose contained in the combination inhaler
- ◆ Combination with other controllers:
  - reduce the dose of inhaled steroid by 50% until a low-dose is reached, then the combination treatment stopped
  - stop controller treatment if controlled by the lowest dose and no recurrence of symptoms for one year



# Stepping up



- ◆ Repeated dosing with rapid-onset  $\beta$  2-agonist bronchodilators provides temporary relief
- ◆ Repeated doses over more than one or two days → review and possible increase of controller therapy
- ◆ A four-fold or greater increase in the dose of inhaled steroids for 7-14 days = a short course of oral steroids during acute deterioration
- ◆ Combination of long-acting  $\beta$  2-agonist and an inhaled steroid in a single inhaler both as a controller and reliever: maintains a high level of asthma control and reduces exacerbations requiring systemic steroids and hospitalization



# Component 4: Manage asthma exacerbations

- ◆ Exacerbations: progressive increase in shortness of breath, cough, wheezing, or chest tightness, or respiratory distress
- ◆ Decreases in PEF or FEV1
- ◆ Treatment depending on severity: rapid-acting inhaled bronchodilators, systemic steroids, and oxygen supplementation
- ◆ Aims of treatment: relieve airflow obstruction and hypoxemia, and to plan the prevention of relapses
- ◆ Treatment should continue until measurements of lung function (PEF or FEV1) return to their previous best (ideally) or plateau

# Severity of asthma exacerbations

	Mild	Moderate	Severe	Respiratory arrest imminent										
Breathless	Walking  Can lie down	Talking Infant—softer shorter cry; difficulty feeding  Prefers sitting	At rest Infant stops feeding  Hunched forward											
Talks in	Sentences	Phrases	Words											
Alertness	May be agitated	Usually agitated	Usually agitated	Drowsy or confused										
Respiratory rate	Increased	Increased	Often > 30/min											
	Normal rates of breathing in awake children: <table style="margin-left: auto; margin-right: auto;"> <tr> <td style="text-align: center;">Age</td> <td style="text-align: center;">Normal rate</td> </tr> <tr> <td style="text-align: center;">&lt; 2 months</td> <td style="text-align: center;">&lt; 60/min</td> </tr> <tr> <td style="text-align: center;">2-12 months</td> <td style="text-align: center;">&lt; 50/min</td> </tr> <tr> <td style="text-align: center;">1-5 years</td> <td style="text-align: center;">&lt; 40/min</td> </tr> <tr> <td style="text-align: center;">6-8 years</td> <td style="text-align: center;">&lt; 30/min</td> </tr> </table>			Age	Normal rate	< 2 months	< 60/min	2-12 months	< 50/min	1-5 years	< 40/min	6-8 years	< 30/min	
Age	Normal rate													
< 2 months	< 60/min													
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1-5 years	< 40/min													
6-8 years	< 30/min													
Accessory muscles and suprasternal retractions	Usually not	Usually	Usually	Paradoxical thoraco-abdominal movement										
Wheeze	Moderate, often only end expiratory	Loud	Usually loud	Absence of wheeze										
Pulse/min.	< 100	100-120	>120	Bradycardia										
	Guide to limits of normal pulse rate in children: <table style="margin-left: auto; margin-right: auto;"> <tr> <td style="text-align: center;">Infants</td> <td style="text-align: center;">2-12 months—Normal Rate</td> <td style="text-align: center;">&lt; 160/min</td> </tr> <tr> <td style="text-align: center;">Preschool</td> <td style="text-align: center;">1-2 years</td> <td style="text-align: center;">&lt; 120/min</td> </tr> <tr> <td style="text-align: center;">School age</td> <td style="text-align: center;">2-8 years</td> <td style="text-align: center;">&lt; 110/min</td> </tr> </table>			Infants	2-12 months—Normal Rate	< 160/min	Preschool	1-2 years	< 120/min	School age	2-8 years	< 110/min		
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Pulsus paradoxus	Absent < 10 mm Hg	May be present 10-25 mm Hg	Often present > 25 mm Hg (adult) 20-40 mm Hg (child)	Absence suggests respiratory muscle fatigue										
PEF after initial bronchodilator % predicted or % personal best	Over 80%	Approx. 60-80%	< 60% predicted or personal best (< 100 L/min adults) or response lasts < 2hrs											
PaO <sub>2</sub> (on air) <sup>†</sup>  and/or PaCO <sub>2</sub> <sup>†</sup>	Normal Test not usually necessary  < 45 mm Hg	> 60 mm Hg  < 45 mm Hg	< 60 mm Hg  Possible cyanosis  > 45 mm Hg; Possible respiratory failure (see text)											
SaO <sub>2</sub> % (on air) <sup>†</sup>	> 95%	91-95%	< 90%											
	Hypercapnea (hypoventilation) develops more readily in young children than in adults and adolescents.													

\*Note: The presence of several parameters, but not necessarily all, indicates the general classification of the exacerbation.


†Note: Kilopascals are also used internationally; conversion would be appropriate in this regard.



# Management of exacerbation at community setting

- ◆ Milder exacerbations (less than 20% reduction in peak flow, nocturnal awakening, and increased use of short acting  $\beta 2$ -agonists):
  - Repeated administration of rapid-acting inhaled  $\beta 2$ -agonists (2 to 4 puffs every 20 minutes for the first hour)
  - After the first hour, the dose will depend on the severity of the exacerbation. Mild exacerbations respond to 2 to 4 puffs every 3 to 4 hours; moderate exacerbations will require 6 to 10 puffs every 1 or 2 hours
  - Oral steroids (0.5 to 1 mg of prednisolone/kg or equivalent during a 24-hour period), especially if exacerbations develop after instituting the other short-term treatment options recommended for loss of control

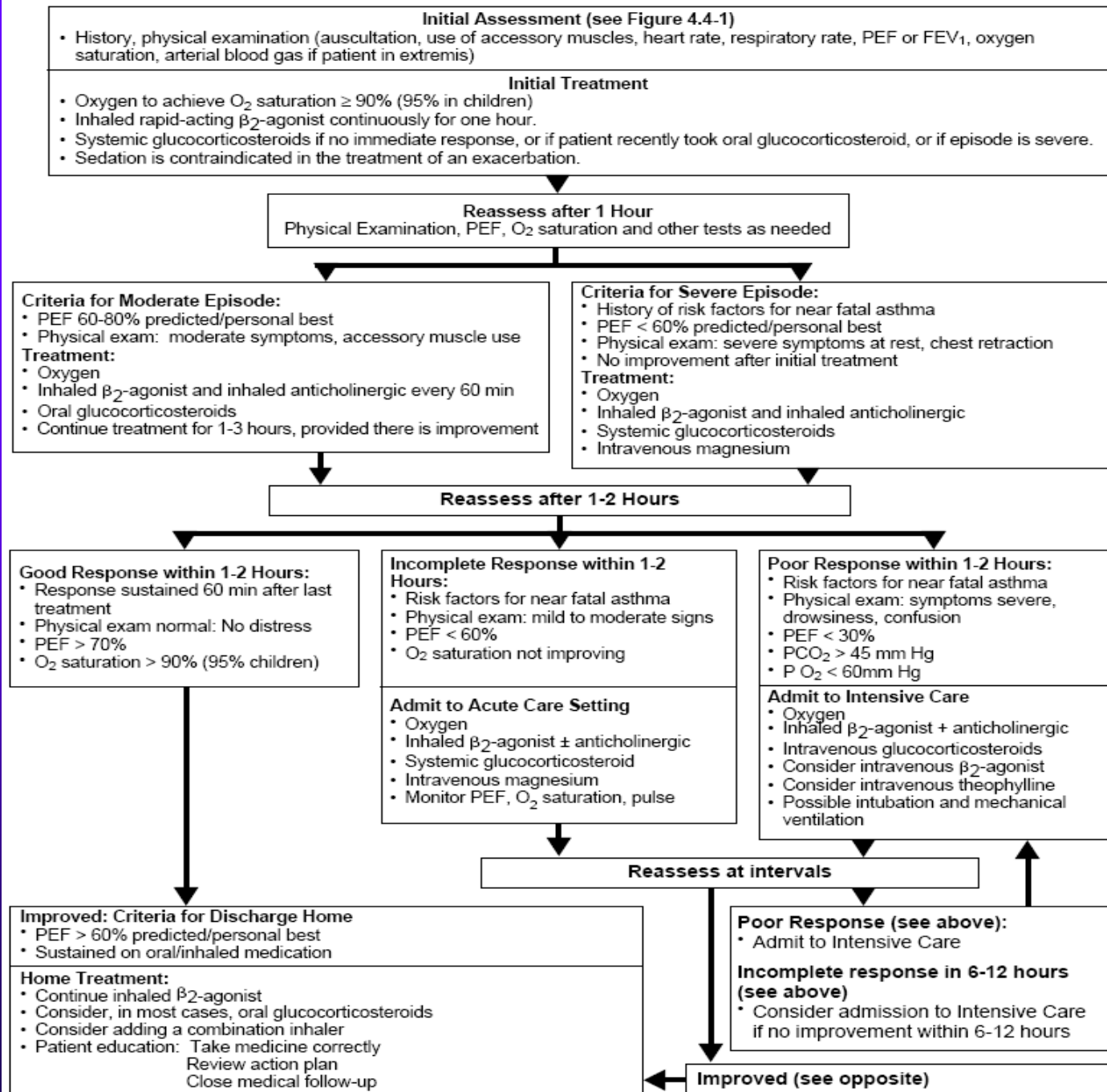




# Management of exacerbation at acute care setting

- ◆ Assessment: brief history + physical examination + prompt initiation of therapy:
  - History: severity and duration of symptoms, all current medications, the patient's response to this therapy; time of onset and cause of the present exacerbation; and risk factors for asthma-related death
  - Physical examination: patient's ability to complete a sentence, pulse rate, respiratory rate, use of accessory muscles, etc.
  - Functional assessments: PEF or FEV1 and arterial oxygen saturation measurements treatment is. Oxygen saturation in children should normally be greater than 95%, and oxygen saturation less than 92% is a good predictor of the need for hospitalization.

**Figure 4.4-2: Management of Asthma Exacerbations in Acute Care Setting**





# Management of exacerbation at acute care setting

- ◆ To achieve arterial oxygen saturation of  $\geq 90\%$  ( $\geq 95\%$  in children), oxygen should be administered
- ◆ Rapid-acting inhaled  $\beta_2$ -agonists should be administered at regular intervals
- ◆ Adrenaline SC or IM may be indicated for acute treatment of anaphylaxis and angioedema, but is not routinely indicated during asthma exacerbations
- ◆  $\beta_2$ -agonist + anticholinergic: better bronchodilation than either drug alone and should be administered before methylxanthines are considered



# Management of exacerbation at acute care setting

- ◆ Oral steroids should be used to treat all but the mildest exacerbations, especially if:
  - The initial rapid-acting inhaled  $\beta$  2-agonist therapy fails to achieve lasting improvement
  - The exacerbation develops even though the patient was already taking oral steroids
  - Previous exacerbations required oral steroids



# Management of exacerbation at acute care setting

- ◆ Oral steroids:
  - as effective as IV steroids
  - require at least 4 hours to produce clinical improvement
- ◆ Daily doses:
  - equivalent to 60-80 mg methylprednisolone as a single dose
  - 300-400 mg hydrocortisone in divided doses
- ◆ Inhaled steroids are effective as part of therapy for asthma exacerbations
- ◆ IV MgSO<sub>4</sub> (single 2 g infusion over 20 minutes):
  - adults with FEV<sub>1</sub> 25-30% predicted at presentation
  - those who fail to respond to initial treatment





# Management of exacerbation at acute care setting

- ◆ For patients discharged from the emergency department:
  - A 7-day course of oral steroids for adults or 3-5 days for children + bronchodilator therapy (used on an as-needed basis until the patient returns to preexacerbation use of bronchodilators)
  - Ipratropium bromide may be quickly discontinued
  - Initiate or continue inhaled steroids
  - Review patients' inhaler technique and use of peak flow meter, provide an action plan
  - Identify and avoid factors that precipitated the exacerbation
  - Review use of controller therapy
  - Follow-up appointment



# Component 5: Special considerations

## ◆ Pregnancy

- Overall perinatal prognosis for children born to women with asthma that is well-managed during pregnancy is comparable to that for children born to women without asthma
- For most medications used to treat asthma there is little evidence to suggest an increased risk to the fetus. Inhaled steroids have been shown to prevent exacerbations of asthma during pregnancy.
- Acute exacerbations should be treated aggressively in order to avoid fetal hypoxia: nebulized rapid-acting  $\beta$  2-agonists and oxygen and systemic steroids when necessary



# Summary

- ◆ Managing asthma: based on clinical control
  - role of the health care professional: establish patients' current level of treatment and control, and adjust treatment to gain and maintain control
- ◆ 5 components to achieve and maintain control of asthma:
  1. Develop patient-doctor partnership
  2. Identify and reduce exposure to risk factors
  3. Assess, treat and monitor asthma
  4. Manage asthma exacerbations
  5. Special considerations e.g. pregnancy



# The End Q&A

Thank you very much!