10-8-2014

Updates in Asthma Management

Jed Grant
University of the Pacific, jgrant@pacific.edu

Asthma in Primary Care

Jed Grant, PA-C
Program Director, SJVC PA Program
Staff PA, AMCH Emergency Department

Objectives

- Apply the NAEPP guideline measures of severity and control including current impairment and future risk to determine initial and appropriate therapy.
- Identify the six steps of managing asthma for each of the 3 pediatric age groups of the NAEPP guidelines.
- Know how to assess asthma control through measurable lung function.
- Identify potential adverse side-effects and indicators of inadequate treatment of ICS and alternative medication options to personalize asthma treatment at the time of initiating long-term control therapy

Epidemiology

- 7-10% of population
- 500,000 admissions, 4500 deaths
- More common in male children and female adults
- Genetic predisposition
- Increased incidence of hospitalization in blacks and children or young adults
  - Death rates highest in blacks age 15-24
- Increasing prevalence over last 20 years

CMD&T 2014

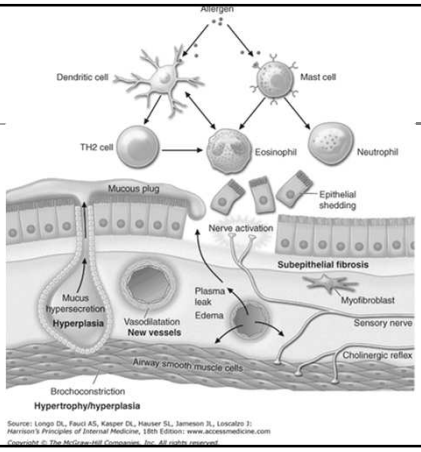
Definition

- A disease of diffuse airway inflammation caused by a variety of triggering stimuli resulting in partially or completely reversible bronchoconstriction.

Merck Manual, 19th ed

Pathophysiology

- Inflammatory cellular infiltrates
  - PMN, Eosinophils, Lymphocytes (esp T)
- Goblet cell hyperplasia
  - Sometimes with plugging of airways with thick mucus
- Collagen deposition beneath basement membrane
- Smooth muscle hypertrophy
- Airway edema
- Mast cell activation
- Denuding of airway epithelium



Predisposing factors

- Atopy
- Obesity
- Allergens/Airway irritants
  - Dust mites
  - Cockroaches
  - Cat dander
  - Seasonal pollens

Triggers and Types

- URI
- Aspiration
- GERD
- Weather/Seasonal changes
- Stress
- Tobacco smoke
- Ozone, particulates
- ASA in some patients
- Environmental
- Occupational
  - May have delayed onset
- Catamenial (menstrual)
- Exercise induced
- Cardiac

Exercise Induced Bronchoconstriction

- Begins during exercise or within 3 minutes of terminating exertion
- Peak sx within 10-15 min of onset
- Resolves within 60 min
- Related to airway attempt to humidify air during exercise

Cardiac Asthma

- Wheezing precipitated by decompensated CHF
- Result of pulmonary edema rather than reactive airways

Symptoms

- Episodic
- Dyspnea
- Wheezing
  - With normal respiration
  - May be absent in severe obstruction
- Breathlessness
- Chest tightness
- Cough
- Prolonged expiratory phase
- Use of accessory muscles

Symptoms

- Highly variable
- May be spontaneous or triggered
- Generally worse at night
  - Circadian variation in bronchomotor tone
- NOT wheezing on forced expiration
  - "Zombie breathing"

Diagnosis

- Obstruction easy to find but difficult to quantify
- Pre/Post Spirometry
  - Reduced FEV1/FVC ratio Pre
  - Post bronchodilator
    - Increase in FEV1 of 12% and 200ml
    - Increase in FVC 15% and 200ml

FEV1: Forced Expiratory Volume in 1 second. FVC: Forced Vital Capacity

Diagnosis

- Bronchial provocation testing (Methylcholine) when spirometry non-diagnostic
  - Not when FEV1 <65% of predicted
  - >20% fall in FEV1 positive
  - Neg predictive value 95%
- Exercise challenge testing may be helpful
- CXR is NOT helpful unless complication suspected.

Peak Expiratory Flow (PEF)

- Patient baseline and trend more helpful than absolute numbers
  - PEF varies with height, weight, and gender. Poorly standardized
- Diurnal variation
  - Lowest on awakening, highest midpoint of awake hours
- >20% change day to day or morning to afternoon suggests poorly controlled asthma
- <200L/min is poorly controlled asthma

Diagnosis and workup

- PEF is the most useful clinical tool to determine severity.
- Venous blood gases are useful in the acute phase
  - hypercapnia and acidosis occur at PEF <25%
- ABGs are really only appropriate in the clinical setting of respiratory failure
  - Initially normal or respiratory alkalosis
  - During more severe exacerbation pCO_2 returns to normal and hypoxemia develops
  - Increased pCO_2 and respiratory acidosis indicates impending failure and need for mechanical ventilation

CXR

- Generally not helpful
  - Hyperinflation is usual finding
- May be indicated to rule out pneumonia in exacerbation
- Useful to diagnose cardiac asthma (CHF)

Differential Diagnosis

- All that wheezes is not Asthma!
- Upper airway disorders
  - FB, vocal cord lesions, tracheomalacia
- Lower airway disorders
  - COPD, Bronchiectasis, bronchitis, RSV
- Systemic vasculitidies
- Psychiatric causes (functional asthma)

Complications

- Exhaustion
- Dehydration
- Infection
- Tussive syncope
- Pneumothorax (rare)
- Respiratory failure
- Death

Treatment Guidelines

- National Asthma Education and Prevention Program (NAEPP)
  - Global Initiative for Asthma (GINA)
  - National Institute of Health (NIH)
  - National Heart Lung and Blood Institute (NHLBI)
  - World Health Organization (WHO)
  - Third expert panel (EP3) in 2007

NAEPP-EP3 Guidelines

- Four main components of Asthma diagnosis and management
  - Assess and monitor severity and control
  - Patient education designed to foster a partnership for care
  - Control of environmental factors and comorbid conditions that effect asthma
  - Pharmacologic agents

Assessing and monitoring severity and control

- Severity is intrinsic intensity of the disease process
- Control is the degree to which symptoms and limitations on activity are minimized by therapy.
  - Expressed in terms of impairment and risk
    - Impairment: frequency and intensity of sx
    - Risk: likelyhood of acute exacerbation or chronic decline in lung function
- Responsiveness is the ease with which control is achieved.

Severity of Asthma

- Determined by severity and or frequency of symptoms
  - Night-time awakenings
  - Use of SABA
  - PEF or FEV1
- Intermittent or persistent
- Logs are very helpful

SABA: Short Acting Beta Agonist

Initiating Treatment

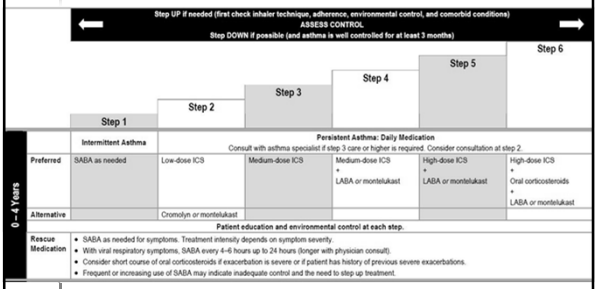
- Asses the severity and impairment of the patient based on historical symptoms and/or PEF.
- Go to the area on the chart that corresponds to the patients symptoms and start at that level.
- Helpful to know normal FEV1/FVC
  - Around 80% for most adults, normal decline with age.

Severity of Asthma

Components of SEVERITY		Age (Years)	Classification of Asthma SEVERITY (Intermittent vs. Persistent)			
			Intermittent	Persistent: Mild	Persistent: Moderate	Persistent: Severe
Impairment	Symptoms	All	≤ 2 days/week	> 2 days/week but not daily	Daily	Throughout the day
	Nighttime awakenings	0 – 4	0	1–2x/month	3–4x/month	> 1x/week
		≥ 5	≤ 2x/month	3–4x/month	> 1x/week but not nightly	Often 7x/week
	SABA use for symptom control	All	≤ 2 days/week	> 2 days/week but not daily	Daily	Several times a day
	Interference with normal activity	All	None	Minor limitation	Some limitation	Extremely limited
	Lung function:					
	FEV_1 (predicted) or PEF (personal best)	≥ 5	Normal FEV_1 between exacerbations > 80%	> 80%	60–80%	< 60%
	FEV_1/FVC	5 – 11	> 85%	> 80%	75–80%	< 60%
		≥ 12	Normal	Normal	Reduced 5%	Reduced > 5%
Risk	Exacerbations requiring oral corticosteroids	0 – 4	≤ 1x/year	≥ 2x in 6 months or ≥ 4 wheezing episodes/year lasting > 1 day AND risk factors for persistent asthma		
		5 – 11		≥ 2x/year		
		≥ 12		Consider severity and interval since last exacerbation. Frequency and severity may fluctuate over time for patients in any severity category. Relative annual risk of exacerbations may be related to FEV_1.		
Recommended step for starting treatment		0 – 4	Step 1	Step 2	Step 3	Step 3
		5 – 11				Step 3 or 4
		≥ 12				Step 4 or 5
		All	Consider short course of oral corticosteroids			
		All	In 2–6 weeks, evaluate level of asthma control that is achieve and adjust therapy accordingly. For children 0–4 years old, if no clear benefit is observed in 4–6 weeks, stop treatment and consider alternative diagnosis or adjusting therapy.			

FEV_1, forced expiratory volume in 1 second; FVC, forced vital capacity; PEF, peak expiratory flow; SABA, short-acting beta-agonist

Initiating Treatment



ICS: Inhaled corticosteroid. LABA: Long Acting Beta Agonist.

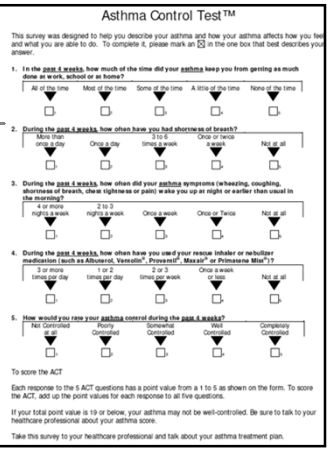
Assessing Control

Components of CONTROL		Age (Years)	Level of Asthma CONTROL		
			Well Controlled	Not Well Controlled	Very Poorly Controlled
Impairment	Symptoms	0 – 4	≤ 2 days/week but ≤ 1x/day	> 2 days/week or multiple times on ≤ 2 days/week	Throughout the day
		5 – 11	≤ 2 days/week	> 2 days/week	
		≥ 12			
	Nighttime awakenings	0 – 4	≤ 1x/month	> 1x/month	> 1x/week
		5 – 11		≥ 2x/month	≥ 2x/week
		≥ 12	≤ 2x/month	1–3x/week	≥ 4x/week
	Interference with normal activity	All	None	Some limitation	Extremely limited
	SABA use for symptoms	All	≤ 2 days/week	> 2 days/week	Several times per day
	Lung function				
	FEV_1 (predicted) or PEF (personal best)	≥ 5	> 80%	60-80%	< 60%
	FEV_1/FVC	5 – 11	> 80%	75-80%	< 75%
	Validated questionnaires				
	ATAQ	≥ 12	0	1–2	3–4
	ACQ	≥ 12	≤ 0.75	≥ 1.5	n/a
	ACT	≥ 12	≥ 20	16–19	≤ 15
Risk	Exacerbations requiring oral corticosteroids	0 – 4	≤ 1x/year	2-3x/year	> 3x/year
		5 – 11		≥ 2x/year	
		≥ 12		Consider severity and interval since last exacerbation	
	Reduction in lung growth	5 – 11	Evaluation requires long-term follow-up care		
	Loss of lung function	≥ 12	Evaluation requires long-term follow-up care		
	Treatment-related adverse effects	All	Medication side effects can vary in intensity from none to very troublesome and worrisome.		
Recommended treatment actions		All	Maintain current step; regular follow-up at every 1–6 months; consider stepping down if well controlled for ≥ 3 months	Step up 1 step	Step up 1–2 steps and consider short course of oral corticosteroids
				Before stepping up, review adherence to medication, inhaler technique, environmental control, and comorbid conditions. If an alternative treatment option was used in a step, discontinue and use the preferred treatment for that step.	
				Reevaluate the level of asthma control in 2–6 weeks and adjust therapy accordingly.	
				For side effects, consider alternative treatment options.	

ACQ, Asthma Control Questionnaire; ACT, Asthma Control Test; ATAQ, Asthma Therapy Assessment Questionnaire; FEV_1, forced expiratory volume in 1 second; FVC, forced vital capacity; PEF, peak expiratory flow; SABA, short-acting beta-agonist

Asthma Control Test

- There are different types of tests to help the patient quantify symptoms.
- Objective measure of control.



Asthma Control Test™

This survey was designed to help you describe your asthma and how your asthma affects how you feel and what you are able to do. To complete it, please mark an ☒ in the one box that best describes your answer.

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?**
   All of the time | Most of the time | Some of the time | A little of the time | None of the time
2. **During the past 4 weeks, how often have you had shortness of breath?**
   More than once a day | Once a day | 3 to 6 times a week | Once or twice a week | Not at all
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 | 2 to 3 nights a week | Once a week | Once or Twice | Not at all
4. **During the past 4 weeks, how often have you used your rescue inhaler or nebulizer medication (such as Albuterol, Ventolin®, Proventil®, Maxair® or Primatene Mist®)?**
   3 or more times per day | 1 or 2 times per day | 2 or 3 times per week | Once a week or less | Not at all
5. **How would you rate your asthma control during the past 4 weeks?**
   Not Controlled at all | Poorly Controlled | Somewhat Controlled | Well Controlled | Completely Controlled

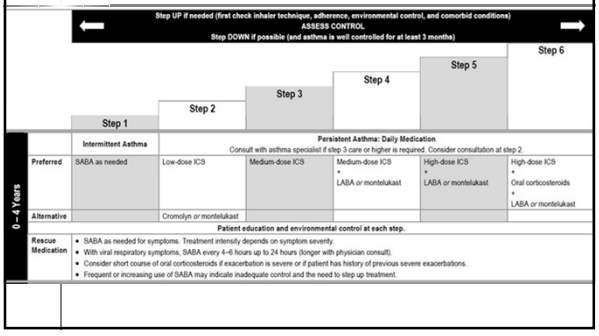
To score the ACT

Each response to the 5 ACT questions has a point value from a 1 to 5 as shown on the form. To score the ACT, add up the point values for each response to all five questions.

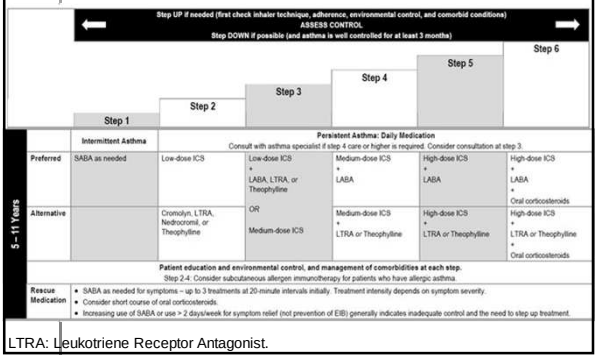
If your total point value is 19 or below, your asthma may not be well-controlled. Be sure to talk to your healthcare professional about your asthma score.

Take this survey to your healthcare professional and talk about your asthma treatment plan.

Age 0-4

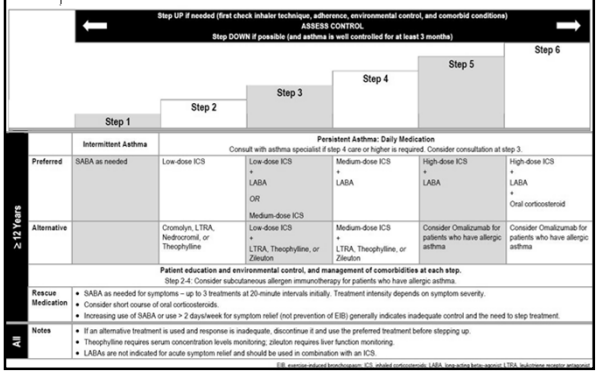


Age 5-11



LTRA: Leukotriene Receptor Antagonist.

Age >12



Acute Treatment

- Short acting Beta-adrenergic agonists
  - Albuterol
  - Levalbuterol
  - Bitolterol
  - Pirbuterol
  - Terbutaline
  - 6-12 puffs/hr = one HHN
- Anticholinergics
  - Ipratropium bromide
  - One HHN/0.5mg in acute exacerbation
- No response; send to ER

Emergency Treatment

- Check theophylline level if they are taking it, but no other role in acute exacerbation
- Corticosteroids
  - Methylprednisolone
  - Prednisone
- Consider CXR, ABX if fever or purulent sputum

Emergency Treatment

- Oxygen to maintain SaO2 of >90%
- MgSO4: 2g IV over 20 min
- Mechanical ventilation/admission
  - Ketamine for induction
- Heliox?
  - Not used if hypoxic
- Inhaled general anesthetic?
- NO mucolytics, anxiolytics, hypnotics

Control of mild/moderate exacerbations

- USE CHARTS
- Mild exacerbation
  - Beta agonist at increased doses
  - Add inhaled corticosteroid, or short course of PO steroid if already on inhaled steroids
    - Doubling dose of ICS is not effective and is no longer recommended

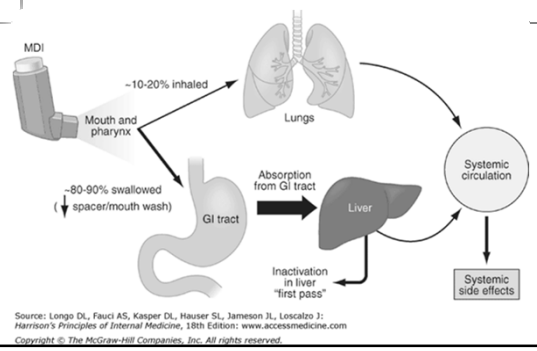
Control of mild/moderate exacerbations

- Moderate exacerbation
  - 3 HHN of beta agonist in 1 hour
  - Systemic corticosteroids
    - PO or IV
  - Observe
  - IF better after 3 HHN home on PO steroids
  - If not better send to ER

Long Term Treatment

- Anti-inflammatory agents
  - ICS (preferred first line agents)
  - May have additive effect with B agonists
  - Maximal effect takes months
  - Use of spacer and mouth wash after dose very important to limit side effects and systemic absorption
  - Systemic corticosteroids
    - Taper not needed under 10 days

Pharmacodymics of ICS



Source: Longo DL, Fauci AS, Kasper DL, Hauser SL, Jameson JL, Loscalzo J: *Harrison's Principles of Internal Medicine*, 18th Edition: www.accessmedicine.com

Inhaled Corticosteroids

Drug	Low Dose (24hrs)	High Dose (24 hrs)
Beclomethasone HFA 40 or 80 mcg	80-240mcg	>480mcg
Budesonide DPI 90, 180, or 200 mcg	180-600mcg	>1200mcg
Flunisolide 250mcg	500-1000mcg	>2000mcg
Flunisolide HFA 80mcg	320mcg	>640mcg
Fluticasone HFA 44,110,220 mcg DPI 50,100,250mcg	88-264mcg 100-300mcg	>440mcg >500mcg
Mometasone DPI 200mcg	200mcg	>400mcg
Triamcinolone acetonide 75mcg	300-750 mcg	>1500mcg

Long term treatment

- Long acting bronchodilators
  - Mast cell stabilizers
    - Cromolyn, nedocromil
    - Response less predictable than ICS/CS
    - May take 4-6 weeks to see maximal response
  - Long acting Beta adrenergic agonists (LABA)
    - Salmeterol, formoterol
    - Dry powder delivery
    - Available combined with steroids in one MDI
    - NOT for acute or mono-therapy use
  - Phosphodiesterase inhibitors
    - Theophylline
      - Narrow therapeutic window

Long Term Treatment

- Anticholinergic
  - Tiotropium
    - Long acting
    - Add on therapy when low dose ICS is not adequate
- Leukotriene modifiers
  - Leukotrienes are biochemical mediators which increase inflammation, vascular permeability, mucus secretion and smooth muscle contraction
  - Alternative to low dose ICS or add on equivalent to LABA
  - Montelukast, zafirlukast are LTRAs.
  - Zileuton has different MOA and can cause elevated ALT levels

Long Term Treatment

- Desensitization
  - Best for known trigger
- Immunotherapy
  - Omalizumab- recominant Ab that binds IgE without activating mast cells
- Vaccination
  - Pneumovax and flu

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