

Asthma Guidelines for Children: A Clinician's Perspective

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Disclosures and Conflicts of Interest



I have no association, financial or otherwise, with any pharmaceutical, laboratory, or medical equipment manufacturer or distributor.

I am a Senior Medical Director for Superior HealthPlan, the sponsor of this educational activity.





- Making the Diagnosis
- Asthma Guidelines



Making the Diagnosis

Diagnosing Asthma in Young Children



Three benefits to making an early and accurate asthma diagnosis:

- 1. To identify the most effective treatment to alleviate symptoms and prevent mortality
- 2. To educate the parent or primary caregiver to manage symptoms and avoid triggers
- 3. To estimate prognosis

Making the Asthma Diagnosis: History of Asthma Triggers



- Precipitating or aggravating factors that are important in children with asthma:
 - Viral upper respiratory infection*
 - Allergen exposure*
 - Exercise and hyperventilation (as part of exercise or for other reasons, such as crying or laughing)
 - Airborne irritants, especially cigarette smoke or other fumes
 - Changes in the weather, including cold air or humidity
 - Gastroesophageal reflux*

Onset of Symptoms in Children with Asthma^{1,2}





McNicol KN, Williams HE. *BMJ.* 1973;4:7-11.
 Wainwright C, Isles AF, Francis PW. *MJA* 1997;167:218-222.

Asthma and Wheezing in the First 6 Years of Life



- There are 2 different wheezing syndromes that coexist in different patients, during the first 3 years of life:
 - <u>Transient</u> wheezing: Smaller airway caliber, no bronchial hyperresponsiveness, and resolution by age 6
 - Of patients who wheezed before age 3, 60% fell into this category
 - <u>Persistent</u> wheezing: These patients are characterized by the presence of atopy, bronchial hyperresponsiveness, and significant deterioration in lung function by age 6
 - Of patients who wheezed before age 3, 40% fell into this category
- It is this *relatively substantial* proportion who have earlyonset asthma and are <u>at risk</u> of progressive asthma throughout childhood and adulthood

Natural History of Childhood Asthma





Wheezing and Asthma



- The most common cause of wheezing in young children is a viral respiratory infection
- However, the strongest predictor for wheezing that continues into asthma is atopy
 - 70%-90% of children with asthma have allergies (documented by allergy testing, such as positive skin tests to inhaled allergens)

American Academy of Allergy Asthma & Immunology. *Pediatric Asthma: Promoting Best Practice, Guide for Managing Asthma in Children*. Available at: http://www.aaaai.org/members/resources/initiatives/pediatricasthma.stm. Accessed October 15, 2007.

Asthma Predictive Index



- To identify high risk children (2 and 3 years of age), they must have*:
 - ≥4 wheezing episodes in the past year (at least one must be MD diagnosed)
- Plus one of the following:
 - One major criterion
 - Parent with asthma
 - Atopic dermatitis
 - Aero-allergen sensitivity
 - Two minor criteria
 - Food sensitivity
 - Peripheral eosinophilia (≥4%)
 - Wheezing not related to infection

*Modified from: Castro-Rodriguez JA, Holberg CJ, Wright AL, et al. A clinical index to define risk of asthma in young children with recurrent wheezing. *Am J Respir Crit Care Med*. 2000;162(4 Pt 1):1403–1406



Asthma Guidelines





 Guidelines for the Diagnosis and Management of Asthma (EPR-3), found here: <u>https://www.nhlbi.nih.gov/health-topics/guidelines-for-</u> <u>diagnosis-management-of-asthma</u>

Evolution of EPR 1-2-3





Global Initiative for Asthma (GINA)



- Revision 2014
- Update 2015
- Update 2016
- Update 2017



Guidelines Implementation Panel (GIP)



- Guidelines Implementation Panel Report for Expert Panel Report 3, found at: <u>http://www.nhlbi.nih.gov/guidelines/asthma/gip_rpt.pdf</u>
 - Recommendations and strategies to implement EPR-3
 - Six key messages



Guidelines Implementation Panel (GIP)



- GIP's 6 Key Messages
 - 1. Inhaled Corticosteroids (Medications)
 - 2. Asthma Action Plan (Education)
 - 3. Asthma Severity
 - 4. Asthma Control
 - 5. Re-assessment/Follow-up
 - 6. Allergen and Irritant Exposure Control

Inhaled Corticosteroids





Inhaled Corticosteroids: Dosing Guide



FIGURE 4: ESTIMATED COMPARATIVE DAILY DOSAGES FOR COMMON INHALED CORTICOSTEROIDS

	Low daily dose		Medium daily dose			High daily dose			
Drug	Child 0-4 years of age	Child 5-11 years of age	≥12 years of age and adults	Child 0-4 years of age	Child 5-11 years of age	≥12 years of age and adults	Child 0-4 years of age	Child 5-11 years of age	≥12 years of age and adults
Beclomethasone HFA 40 or 80 mcg/puff	NA	80-160 mcg	80-240 mcg	NA	>160- 320 mcg	>240- 480 mcg	NA	>320 mcg	>480 mcg
Budesonide inhaled Inhalation suspension for nebulization	0.25- 0.5 mg	0.5 mg	NA	>0.5- 1.0 mg	1.0 mg	NA	>1.0 mg	2.0 mg	NA
Fluticasone HFA/MDI 44, 110, or 220 mcg/puff	176 mcg	88-176 mcg	88-264 mcg	>176-352 mcg	>176-352 mcg	>264-440 mcg	>352 mcg	>352 mcg	>440 mcg

Source: NIH, National Heart, Lung and Blood Institute. Expert Panel Report 3: Guidelines for the Diagnosis and Management of Asthma (EPR-3 2007). http://www.nhlbi.nih.gov/guidelines/asthma/index.htm.

Inhaled Corticosteroids: Dosing Guide



Drug	Low Daily Dose (μg)		Medium Daily Dose (μg)		High Daily Dose (μg)	
	> 5 years	< 5 years	> 5 years	< 5 years	> 5 years	< 5 years
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	N/A	250-500	N/A	500-1000	N/A	>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



Effects of ICS on Inflammation





Before and After 3 Months of Treatment With an ICS

Laitinen LA, Laitinen A, Haahtela T. J Allergy Clin Immunol. 1992;90:32-42.

Inhaled Corticosteroids: Drug v. Device





Inhaled Corticosteroids: Obstacles



- 'The specialist has to prescribe them'
- 'Did you say steroids?'
- 'I've done my research...'
- Expense
- Hassle

Asthma Action Plan



GO	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 & play to	MEDICINE For asthma with exercise, ta	HOW MUCH	HOW OFTEN/WHEN	
CAUTION	Continue with green ze	one medicine and a	dd:	
You have any of these: • First signs of a cold • Exposure to known trigger • Cough • Mild wheeze • Tight chest • Coughing at night	MEDICINE	HOW MUCH	HOW OFTEN/ WHEN	
DANGER	Take these medicines a	and call your docto	r now.	
Your asthma is getting worse fast: Medicine is not helping Peak flow: Prostbing is hard	MEDICINE	HOW MUCH	HOW OFTEN/WHEN	

Breathing is hard
 &fast
 reading
 below
 Can't talk well

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! If you cannot contact your doctor, go directly to the emergency room. DO NOT WAIT. Make an appointment with your primary care provider within two days of an ER visit or hospitalization.



Asthma Severity



Components of Severity		Classification of Asthma Severity (0-4 years of age)					
			Persistent				
		Intermittent	Mild	Moderate	Severe		
	Symptoms	≤2 days/week	>2 days/week but not daily	Daily	Throughout the day		
	Nighttime awakenings		1–2x/month	3-4x/month	>1x/week		
Impairment	Short-acting beta ₂ -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	None	Minor limitation	Some limitation	Extremely limited		
Disk	Exacerbations		 ≥2 exacerbations in 6 months requiring oral systemic corticosteroids, or ≥4 wheezing episodes/1 year lasting >1 day AND risk factors for persistent asthma 				
systemic corticosteroids		Consider severity and interval since last exacerbation.					
		Exacerbations of	any severity may occu	ir in patients in any	severity category.		
Recommended Step for Initiating Therapy		Step 1	Step 2Step 3 and consider short course of oral systemic corticosteroids				
(See fig treatm	ure 4-1a for ent steps.)	In 2–6 weeks, depending on severity, evaluate level of asthma control that is achieved. If no clear benefit is observed in 4–6 weeks, consider adjusting therapy or alternative diagnoses.					

Level of severity is determined by both impairment and risk. Assess impairment by caregivers recall of previous 2-4 weeks.

Asthma Severity



Components of Severity		Classification of Asthma Severity (5–11 years of age)					
				Persistent			
		Intermittent	Mild	Moderate	Severe		
	Symptoms	≤2 days/week	>2 days/week but not daily	Daily	Throughout the day		
	Nighttime awakenings	≤2x/month	3-4x/month	>1x/week but not nightly	Often 7x/week		
Impairment	Short-acting beta ₂ -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	None	Minor limitation	Some limitation	Extremely limited		
	Lung function	 Normal FEV₁ between exacerbations 					
		 FEV₁ >80% predicted 	• FEV ₁ = >80% predicted	• FEV ₁ = 60–80% predicted	• FEV ₁ <60% predicted		
		• FEV₁/FVC >85%	• FEV ₁ /FVC >80%	• FEV ₁ /FVC = 75-80%	• FEV₁/FVC <75%		
	Evenerhetiene	0–1/year (see note) ≥2/year (see note)					
Risk Exacerbations requiring oral systemic corticosteroids		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 Initiating Therapy (See figure 4–1b for treatment steps.)		Step 1	Sten 2	Step 3, medium- dose ICS option	Step 3, medium-dose ICS option, or step 4		
		Step 1	5100 2	and consider short course of oral systemic corticosteroids			
		In 2–6 weeks, evaluate level of asthma control that is achieved, and adjust therapy accordingly.					

Spirometry in the Diagnosis of Asthma in Children



- Spirometry is a simple, powerful, and widely available tool for investigating lung function
- There are published guidelines for making measurements and their interpretation
- There is a variety of published normative data, allowing for interpretation of results based on specific vital statistics
- With proper training and adequate time, sometimes even fairly young children can produce useful results

Spirometry: Sometimes Even on the Very Young



- Only 3 Years Old
- Excellent and quite interpretable flow-volume curve
- Sustained expiratory maneuver
- Forced vital capacity (FVC) of 1.2 L
- FEV₁^a/FVC is >0.85
- Peak expiratory flow (PEF) is >2 L/sec

Office Medic Spirometry System, Version 4.5.3, QRS Diagnostic, LLC						
Pulmo	onary Fu	inction I	Report	t		
Consign Day	e E Time: 7/	23/2007 12.0	17 PM	-		
Name:	101000			Age: 3		
Account Nu	umber:			Height: 3 ft 5 i		
Gender:	Fema	le		Weight: 39 lbs		
Race:	Cauca	asian		Smoking-Pack Years: 0		
FVC pre test res	ults			AND A PROPERTY OF THE ALL ADDRESS OF THE DESCRIPTION OF THE ALL ADDRESS OF THE ADDRESS OF THE ALL ADDRESS OF THE ADDRES		
[
Parameter	Pred.	Result	% Pred.			
Test Sequence		#1				
FVC [I]	50	1.197				
FEVI		1.021				
FEVI/FVC		0.852				
FEVO [1]		0.852				
FEVOS		0.852				
FEV3 [1]		1 195				
FEV3/FVC		0.998				
PEFR [1/s]		2.072				
FEF25% [1/s]		1.972				
FEF50% [1/s]		1.288				
FEF75% [1/s]		0.485	1			
FEF25-75% [l/s]		1.075				
FIVC [l]		1.009				
FIV0.5 [l]		0.240				
FIV1 [1]		0.663				
FIV3 [1]		0.995				
FIV1/FIVC		0.657				
FIV3/FIVC		0.986				
PIFR [I/S]		0.906				
FIF30% [1/s]		0.838				
FIF 2 1 2 [1/s]		0.000				
FVC/FIVC		1 186				
Ext. Vol. [1]		0.042				
Date		7/23/2007				
Time		12:09 PM				
Mouthpiece #		8636-3514		0		
Physician/Tech		mundi				
FVC Interpretation:	Interpretation n	ot available, pat	ient parame	ters fall outside selected predicted range.		
Session Comments:						
Discloimer: All test	results should t	e evaluated by a	qualified p	physician.		
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Asthma Control



Components of Control		Classification of Asthma Control (0–4 years of age)				
		WellNot WellControlledControlled		Very Poorly Controlled		
Symptoms		≤2 days/week	>2 days/week	Throughout the day		
	Nighttime awakenings	$\leq 1x/month$	>1x/month	>1x/week		
Impairment	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		
Diala	Exacerbations requiring oral systemic corticosteroids	0-1/year	2-3/year	> 3/year		
KISK	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.				
Recommended Action for Treatment (See figure 4–1a for treatment steps.)		 Maintain current treatment. Regular followup every 1-6 months. Consider step down if well controlled for at least 3 months. 	 Step up (1 step) and Reevaluate in 2-6 weeks. If no clear benefit in 4-6 weeks, consider alternative diagnoses or adjusting therapy. For side effects, consider alternative treatment options. 	 Consider short course of oral systemic corticosteroids, Step up (1-2 steps), and Reevaluate in 2 weeks. If no clear benefit in 4-6 weeks, consider alternative diagnoses or adjusting therapy. For side effects, consider alternative treatment options. 		

Asthma Control



Components of Control		Classification of Asthma Control (5–11 years of age)					
		Well Controlled	Not Well Controlled	Very Poorly Controlled			
	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	≤1x/month	$\geq 2x/month$	≥2x/week			
	Interference with normal activity	None	Some limitation	Extremely limited			
Impairment	Short-acting beta2-agonist use for symptom control (not prevention of EIB)	≤2 days/week	>2 days/week	Several times per day			
	Lung function						
	• FEV_1 or peak flow	>80% predicted/ personal best	60–80% predicted/ personal best	<60% predicted/ personal best			
	• FEV ₁ /FVC	>80%	75-80%	<75%			
	Exacerbations requiring	0−1/year ≥2/year (see note)					
	oral systemic corticosteroids	Consider severity and interval since last exacerbation					
Risk Reduction in lung growth Treatment-related adverse effects		Evaluation requires long-term followup.					
		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.					
Recommended Action for Treatment (See figure 4–1b for treatment steps.)		 Maintain current step. Regular followup every 1-6 months. Consider step down if 	 Step up at least 1 step and Reevaluate in 2 6 weeks 	 Consider short course of oral systemic corticosteroids, Step up 1-2 steps, and Recevaluate in 2 weeks 			
		well controlled for at least 3 months.	 For side effects: consider alternative treatment options. 	 For side effects, consider alternative treatment options. 			

Asthma Control



Components of Control		Classification of Asthma Control (≥12 years of age)				
		Well Controlled	Not Well Controlled	Very Poorly Controlled		
	Symptoms	≤2 days/week	>2 days/week	Throughout the day		
	Nighttime awakenings	$\leq 2x/month$	1-3x/week	\geq 4x/week		
	Interference with normal activity	None	Some limitation	Extremely limited		
Impairment	Short-acting beta ₂ -agonist use for symptom control (not prevention of EIB)	≤2 days/week	>2 days/week	Several times per day		
Impanment	FEV_1 or peak flow	>80% predicted/ personal best	60–80% predicted/ personal best	<60% predicted/ personal best		
	Validated questionnaires					
	ATAQ ACQ ACT	0 ≤0.75* ≥20	1-2 ≥1.5 16-19	3-4 N/A ≤15		
	Exacerbations requiring oral systemic	0−1/year ≥2/year (see note)				
	corticosteroids	Consider severity and interval since last exacerbation				
Risk	Progressive loss of lung function	Evaluation requires long-term followup care				
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.				
Recommended Action for Treatment (see figure 4–5 for treatment steps)		 Maintain current step. Regular followups every 1–6 months to maintain control. Consider step down if well controlled for at least 3 months. 	 Step up 1 step and Reevaluate in 2–6 weeks. For side effects, consider alternative treatment options. 	 Consider short course of oral systemic corticosteroids, Step up 1-2 steps, and Reevaluate in 2 weeks. For side effects, consider alternative treatment options. 		

Re-assessment/Follow-up





Re-assessment/Follow-up

Asthma Control Test 4-11 Years Old





Allergen and Exposure Control





Asthma Inflammation: Cells and Mediators





Asthma Inflammation: Cells and Mediators





EPR3:



The 4 Components of Asthma Care

- Monitoring and assessment of asthma control and severity with results obtained from:
 - Objective tests
 - Physical examination
 - Patient history
 - Patient report
- Patient education (and their families)
 - "For a partnership in asthma care."
- Control of environmental factors and co-morbid conditions affecting asthma
- Medications
 - Pharmacological therapy

EPR3: Goals of Therapy



- Reducing impairment
 - Prevent chronic and troublesome symptoms (eg, coughing or breathlessness in the daytime, in the night, or after exertion)
 - Require infrequent use (≤ 2 days/week) of inhaled short-acting β_2 -agonist (SABA) for quick relief of symptoms
 - Maintain (near) nórmal lung function
 - Maintain normal activity levels (including exercise and other physical activity and attendance at school or work)
 - Méet patients' and families' expectations of and sátisfaction with asthma care
- Reducing risk
 - Prevent recurrent exacerbations and minimize need for ED visits and hospitalizations
 - Prevent progressive loss of lung function
 - Provide optimal pharmacotherapy with minimal or no adverse effects

In Conclusion: EPR-3 and Pediatric Asthma



- Severity, control, and responsiveness to treatment are key elements of asthma assessment and monitoring
- The goal of asthma therapy is to achieve control by:
 - reducing current impairments
 - future risks of adverse events
- Periodic assessments of asthma control are recommended to determine:
 - whether the goals of therapy are being met
 - if adjustments to treatment are necessary
- A stepwise approach to therapy should be used to achieve and maintain control
- ICSs are *the* preferred controller therapy in patients of any age with persistent asthma

Future Directions... EPR4?



- 1. Asthma phenotype
- 2. Genotype-phenotype correlation
- 3. Imprinting
- 4. Inflammatory markers
- 5. Pharmacogenomics
- 6. Biologics
- 7. Microbiome





- National Asthma Education and Prevention Program
 - <u>http://www.nhlbi.nih.gov/about/naepp/</u>
- American Academy of Allergy, Asthma, and Immunology
 - <u>http://www.aaaai.org</u>
- American College of Chest Physicians
 - <u>http://www.chestnet.org</u>
- American Thoracic Society
 - <u>http://www.thoracic.org</u>
- American College of Allergy, Asthma, and Immunology
 - <u>http://www.acaai.org</u>
- The Centers for Disease Control and Prevention
 - <u>http://www.cdc.gov/asthma</u>



Questions and Answers