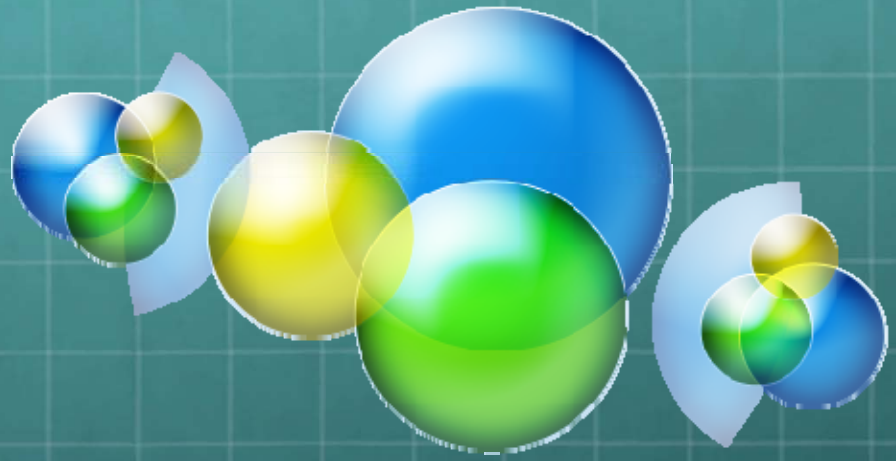

Nuts and Bolts of Childhood Asthma Management
Pediatric Postgraduate Conference 2019

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Discussion goals

- Practitioners understand mechanisms and pathophysiology for asthma
- Practitioners diagnose and classify asthma severity
- Practitioners manage asthma
- Practitioners identify how to help patients and their families achieve best control for the patient

Why is optimal asthma management important?

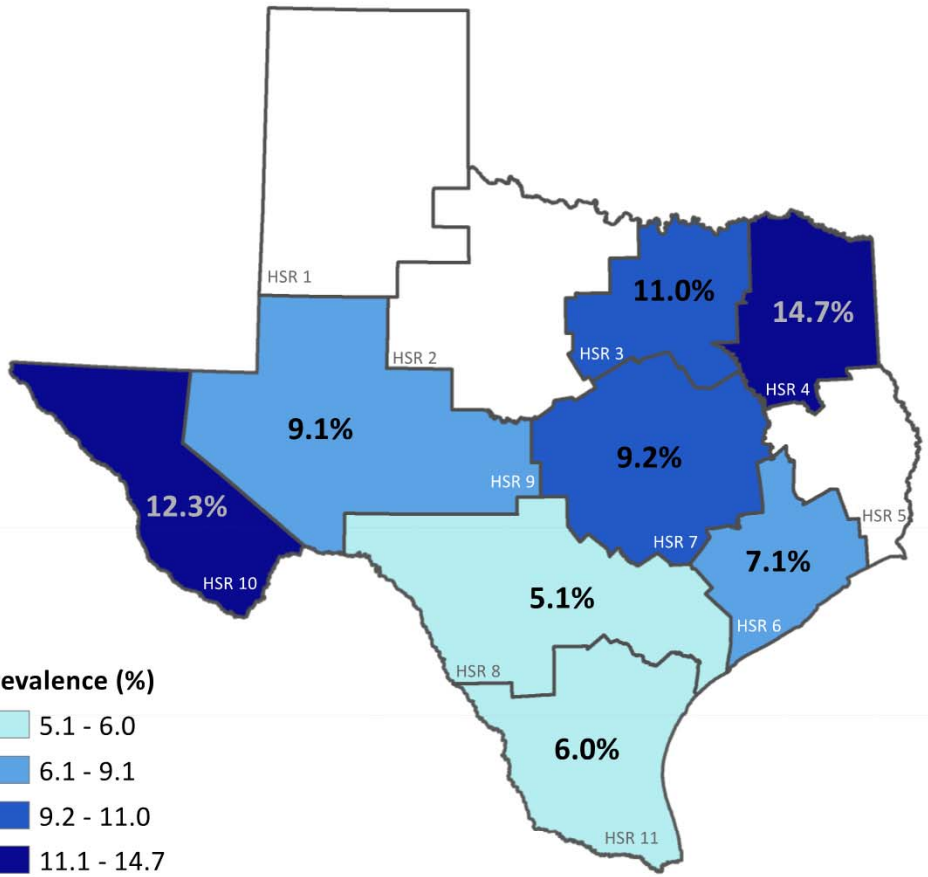
Asthma remains a disease of morbidity and mortality nationally and locally

Asthma Facts

- Asthma is the one of the most common serious chronic diseases of childhood.
- In 2015, childhood asthma prevalence was 8.4% or 1 in 12 children has asthma
- In 2013, asthma was the primary diagnosis for more than 1.5 million emergency department visits. Children with asthma were more likely to use the ED as the usual place for medical care than those without asthma.
- In 2012, asthma was the primary diagnosis for 10.5 million physician office visits.
- In 2013, 13.8 million school days were missed due to asthma
- Black Americans had an asthma death rate of 23.9 per million persons versus 8.4/million persons non Hispanic whites, 7.3/million Hispanics, 10/million other non Hispanics

United States Environmental Protection Agency (EPA-402-F-04-019) May 2017

Child Current Asthma Prevalence by Health Service Region (HSR), Texas, 2013



Texas Current Asthma Prevalence Among Children = 9.1% (95% CI: 7.5-10.6)

Data Classification: Quantiles.
Data Source: 2013 Texas Behavioral Risk Factor Surveillance System (BRFSS),
Center for Health Statistics, Texas Department of State Health Services.
Current asthma among children is defined as "Yes" responses to both of the following questions,
"Has a doctor, nurse, or other health professional ever said that the child has asthma? and
"Does the child still have asthma?".

Created by Erin Wu, 3/4/2015

OSER
Office of Surveillance, Evaluation, and Research

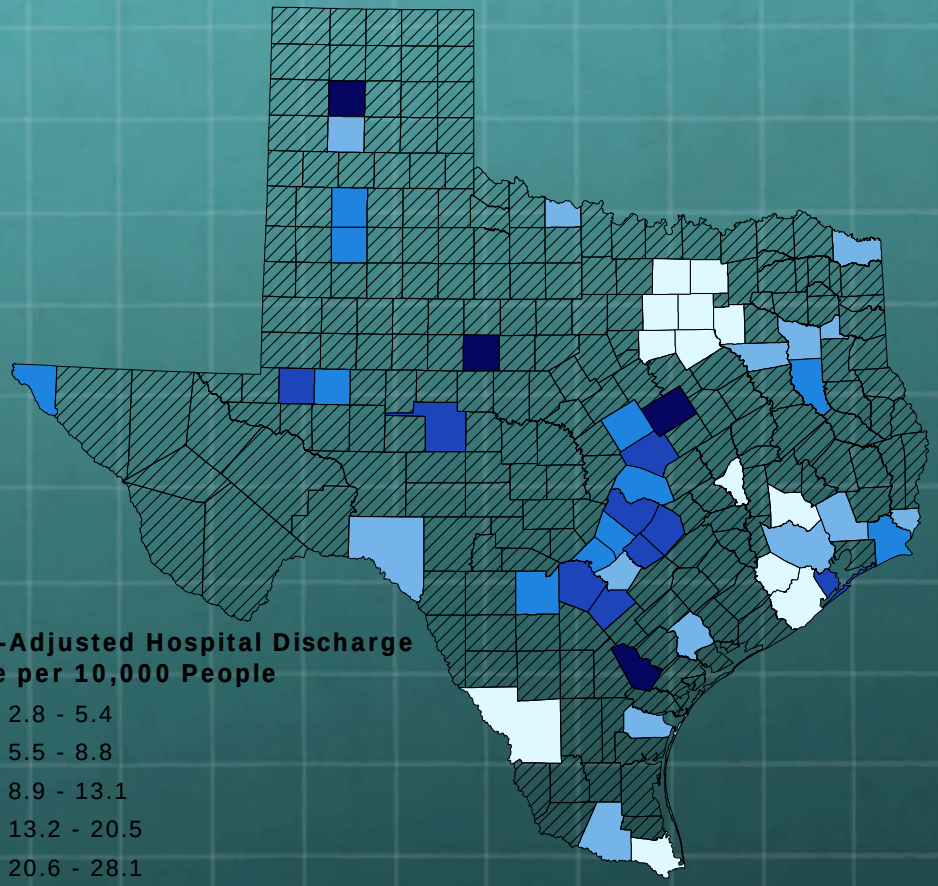
TEXAS Department of State Health Services

Asthma Prevalence: Children 0 to 17 years old

	Health Service Region 1	State of Texas
Total		479,712 or 7%
White	**---**	**188,081 or 9.2%**
Black	**---**	**84,096 or 10.7%**
Hispanic	**----**	**169,417 or 5.1%**
Other	**----**	**----**
Boys		274,235 or 8.1%
Girls		198,108 or 5.9%
0-4 years old	**----- (2009 1.4%)**	80,027 or 5.4%
5-9 years old	**---- (2008 14.8%)**	**119,316 or 7.4%**
10 – 14 years old	**----**	**147,180 or 9.9%**
15-17 years old	**----**	**89,965 or 8.1%**

Reference: Texas Department of State Health Services _ 2016 Child Asthma Fact Sheet. Based on 2013 Texas Population Data and 2014 Texas Behavioral Risk Factor Surveillance System. Based on adult respondent reporting randomly selected child diagnosis and affirmative response about child still having asthma. Asthma prevalence higher in Region 8 (11.8%) and 10 (13.7%) compared to state

Age-Adjusted Childhood Asthma Hospital Discharge Rates, per 10,000 People, by County, Texas, 2016



Age-Adjusted Hospital Discharge Rate per 10,000 People

- 2.8 - 5.4
- 5.5 - 8.8
- 8.9 - 13.1
- 13.2 - 20.5
- 20.6 - 28.1
- Data not available (< 12 discharges)

The overall age-adjusted childhood asthma hospital discharge rate for Texas was 8.6 per 10,000 people.

Data Classification: Quantiles
Data Source: Inpatient Hospital Discharge Public Use Data File, 2016
Center for Health Statistics, Texas Department of State Health Services
An asthma hospitalization is described as a hospital record listing ICD-10 code J45 as the principal diagnosis.

Created by Liping Mou 9/13/2018

TEXAS Health and Human Services | Texas Department of State Health Services

Hospital Rates, Children 0-17 years old
Annual Hospital Discharges per 10,000 children

	Health Service Region 1	State of Texas
Total	320 or 13.9/10,000	7,736 or 10.9/10,000
White		**2,012 or 8.8/10,000**
Black		**2,163 or 27/10,000**
Hispanic		**3,041 or 8.7/10,000**
Other		**483 or 10.1/10,000**
Boy		4,879 or 13.5/10,000
Girl		2,857 or 8.3/10,000
0-4		**3,271 or 16.9/10,000**
5-9		**2,897 or 14.8/10,000**
10 – 14		**1,266 or 6.4/10,000**
15 - 17		**302 or 2.6/10,000**

Reference: Texas Department of State Health Services _ 2016 Child Asthma Fact Sheet
Based on 2013 Texas Hospital Inpatient Discharge Public Use Data File. Based on ICD-9 code for principal diagnosis asthma. Regions 9, 8, 2, 10, 1, & 7 (out of 11) had highest rates and Regions 4 & 6 had lowest rates. But overall, rates decreased from 2012 data file.

Texas Asthma Mortality Rates (per 100 000 persons)

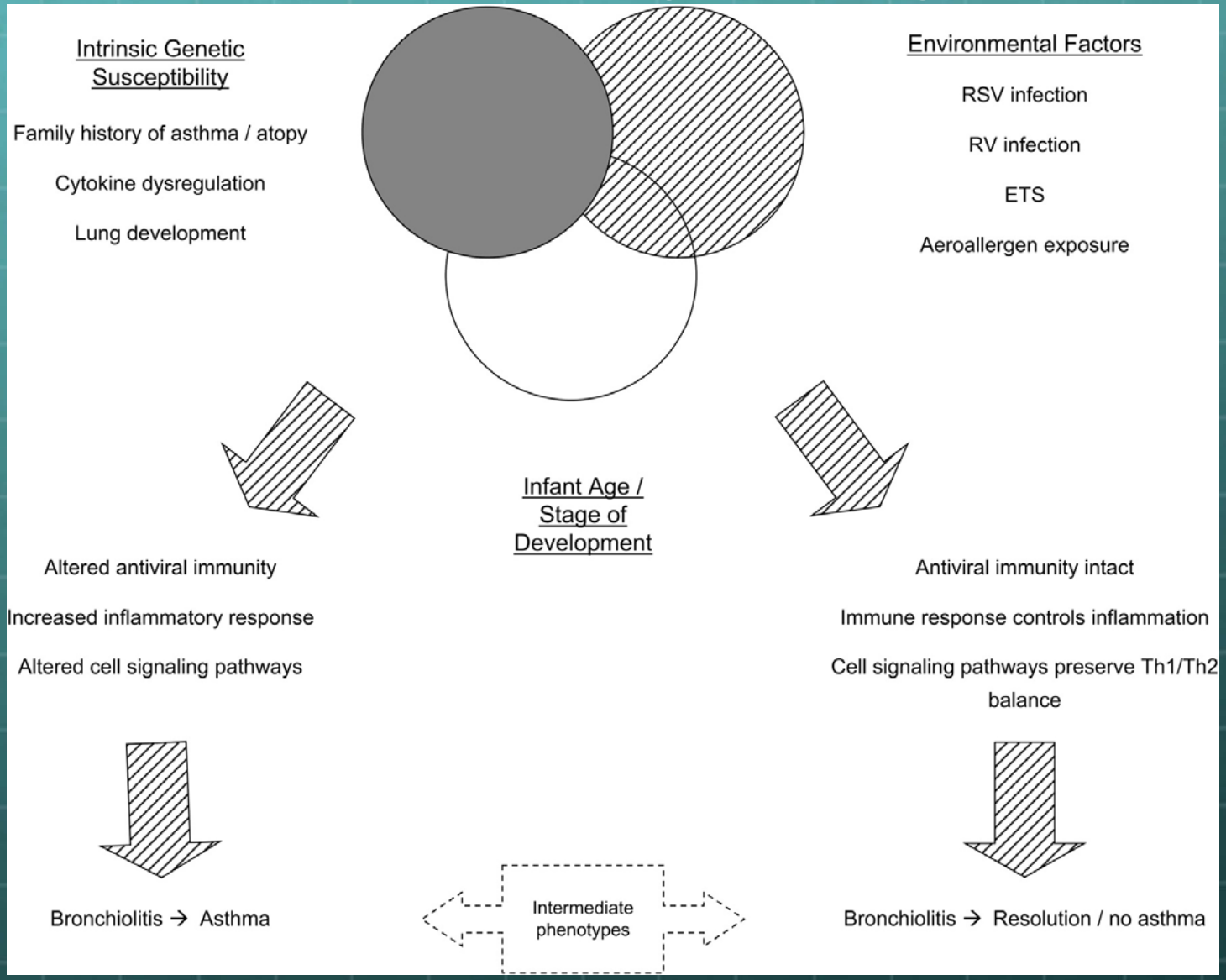
	Region 1	State
Total		9.1
White	**----**	**8.8**
Black	**----**	19.7
Hispanic	**---**	**5.6**
Other	**---**	**11.1**
Male	----	7.1
Female	----	10.6
0-17	**---**	**2.3**
18-44	**---**	**3.5**
45-64	**---**	**11.3**
65+	**---**	**35**

Reference: Texas Department of State Health Services _ 2014 Texas Asthma Burden Report. 2006 – 2012 Vital Statistics Unit, Based on ICD-10 codes J45 and J46 for asthma

About 40% of children during the 1st year of life old have wheezing, of those 1/3 go on to develop asthma.

How can you advise parents of asthma risk in those with wheezing in the 1st 3 years of life?

Possible mechanisms of developing asthma during early childhood



Singh AM et al Am J Resp Crit care med 2007

The influence of RSV on the development of asthma depends upon the age of exposure, genetic background of the host (i.e. inflammatory mediators, lung development , family history of atopy/asthma) and possible interactions with other environmental factors such as tobacco exposure and allergen exposure

Wheezing Phenotypes in Children and Risk of Childhood Asthma

Phenotype	Lung Function Max Expiratory Flow at FRC during 1st year of life and 6 years old	IgE levels Cord blood IgE levels were not significantly different in groups	+Skin test reactivity: atopy
Never wheezing (no LRI with wheeze in 1st 3 years of life and no wheeze by 6 years old)			
Transient wheezing (at least 1 LRI with wheeze in 1st 3 years of life but no wheezing by 6 years old)	Significantly lower at infancy than all other groups At 6 years of age increased from infancy but was significantly lower than never wheezing group	Similar IgE levels at age 6 as the never wheeze group	Similar atopy prevalence at age 6 as never wheeze group
Wheezing of late onset (no LRI with wheezing in 1st 3 years of life but wheezing by 6 years old)	At infancy and 6 years of age not different than never wheezing group		Atopy prevalence at 6 years old significantly higher than never wheeze group
Persistent wheezing (at least 1 LRI with wheeze in 1st 3 years of life and wheezing at 6 years old)	At infancy, not significantly different from never wheezing group. At 6 years of age decreased from infancy and was significantly lower than all other groups	IgE levels at 9 months age higher than never wheeze group IgE levels at 6 years old significantly higher than transient wheeze & never wheeze groups	Atopy prevalence at 6 years old significantly higher than never wheeze group

By age 11, atopy prevalence and IgE levels in late onset and persistent wheezers was higher than never wheezers. By age 16 atopy prevalence was higher in the persistent wheezers vs never wheezers and transient wheezers. By age 11 and 16, atopy prevalence was higher in the late onset wheezers vs. transient wheezers. Max expiratory flows (lung function) got better over time for transient wheezers but at age 11 and 16 remained lower for vs. never wheezers. Max expiratory flows got lower over time for persistent wheezers and at age 11 and 16 remained lower than never wheeze group. Similar findings in other European prospective cohort studies

Asthma and Wheezing in the First Six Years of Life. Martinez, FD, et. al. N Engl J Med 1995: 332:133-138. Outcome of Asthma and Wheezing in the First Six Years of Life, Follow-up through Adolescence. Morgan WJ, et al. Am J Resp Crit Care Med. 2005: 172(10): 1253-1258.
Tucson Children's Respiratory Study – prospective birth cohort study

ASTHMA PREDICTIVE INDEX

A birth cohort study (Tucson Children's Respiratory Study found that persistent wheezers had reduced maximal expiratory flows by 6 years old and abnormal lung function persisted at age 16. This tool developed to capture high risk children

Criteria	Stringent API [5]	Loose API [5]	Modified API [6,7]
Wheezing	Early (≤3 years) frequent wheezing[a]	Early (≤3 years) wheezing	≥4 episodes/year during first 3 years of life
Major criteria			
Parent with asthma	Yes	Yes	Yes
Physician-diagnosed atopic dermatitis	Yes	Yes	Yes
Sensitization to ≥1 aeroallergen	Not included	Not included	Yes
Minor criteria			
Wheezing unrelated to colds	Yes	Yes	Yes
Blood eosinophils ≥4%	Yes	Yes	Yes
Physician-diagnosed allergic rhinitis	Yes	Yes	Not included
Sensitization to foods (milk, egg and peanut)	Not included	Not included	Yes

For a positive API in each version, children must meet the wheezing criterion as well as at least one major criterion or at least two minor criteria.
[a]Score of ≥3 on scale of 1–5 for wheezing (1 = 'very rarely' and 5 = 'most days').
API, Asthma Predictive Index.

FENO (fraction of exhaled NO – eosinophilic inflammation) at 4 years of age is higher in persistent wheezers and associated with asthma at 7 years old

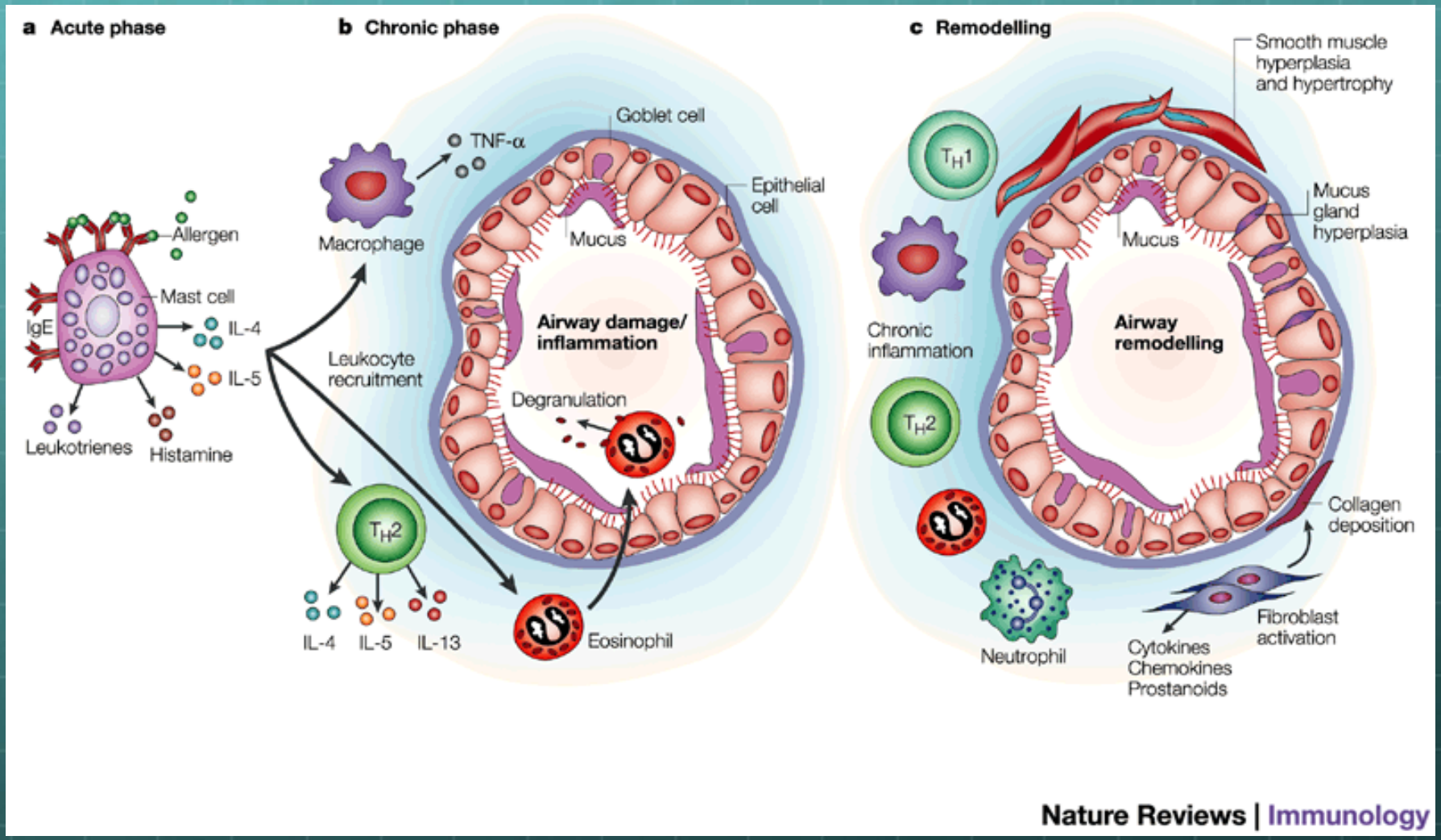
- van der Valk RJ et at. Clin Exp Allergy 2012; 49: 1329-1336 and Moeller A et al. J Allergy Clin Immunol 2008; 121:705-709

Current and future management of the young child with early onset wheezing. Burbank, A; Szefler, S; Current Opinion in Allergy & Clinical Immunology. 17(2):146-152, April 2017.

Developed from the Tucson Children's Respiratory Study (Birth Cohort study) J Allergy Clin Immunol 2003; 111: 661-675 – Taussig, LM, Martinez, FD. Castro-Rodriguez CE, et al, Am J Resp Crit Care Med 2000; 162: 1403-1406. Morgan WJ et al. Am J Resp Crit Care Med 2005; 172: 1253-1258

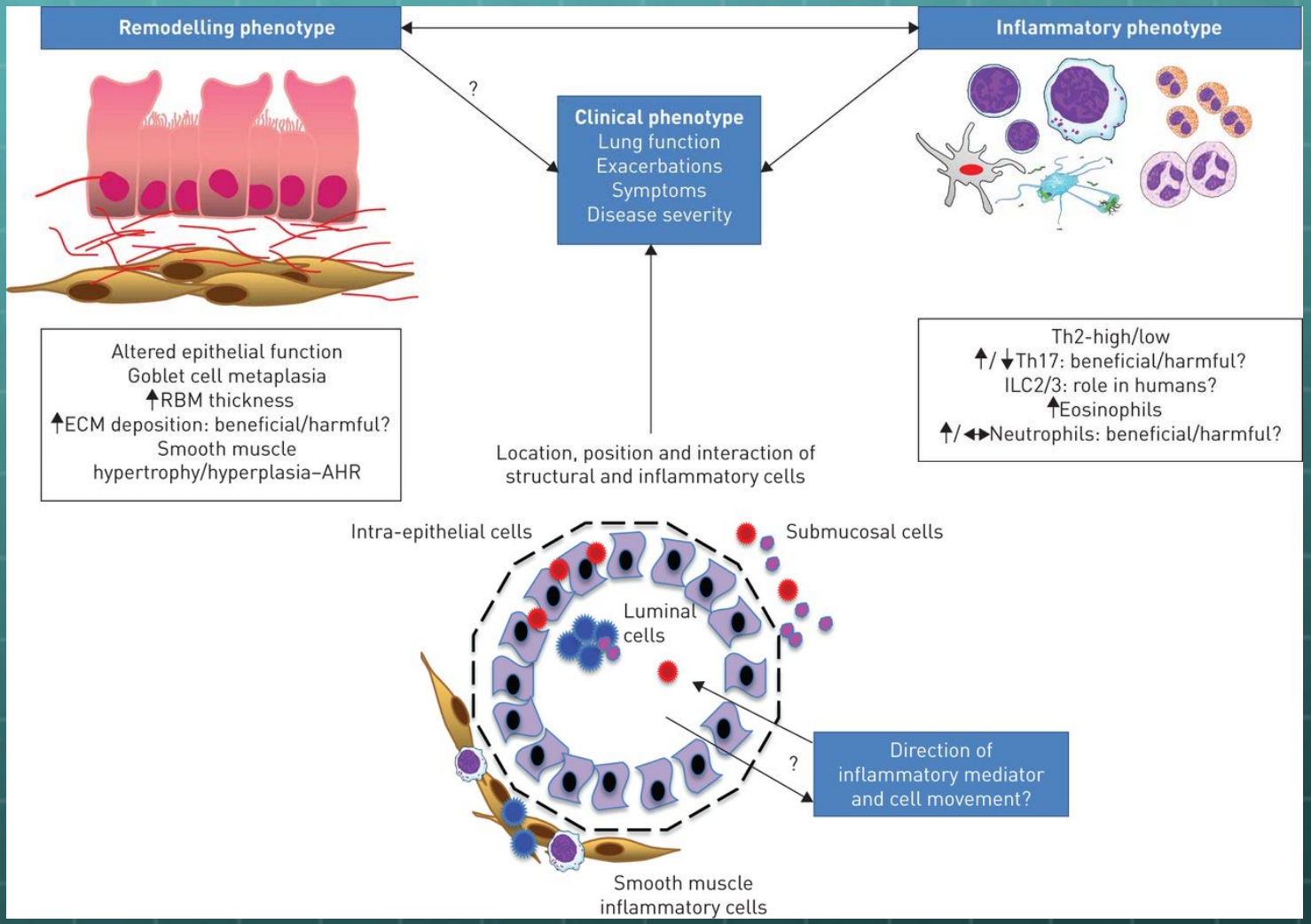
Asthma involves airway inflammation and airway remodeling

Asthma Pathogenesis



Inflammation cell and cytokine activation result in acute bronchoconstriction and airway obstruction,
Activation of T helper (T_H) 2 cells and macrophages and recruitment and degranulation of eosinophils result in airway responsiveness.
Structural airway changes or airway remodeling (mucus gland hyperplasia, smooth muscle hypertrophy, extracellular matrix deposition, reticular basement membrane thickness, angiogenesis) are associated with irreversible loss of lung function.

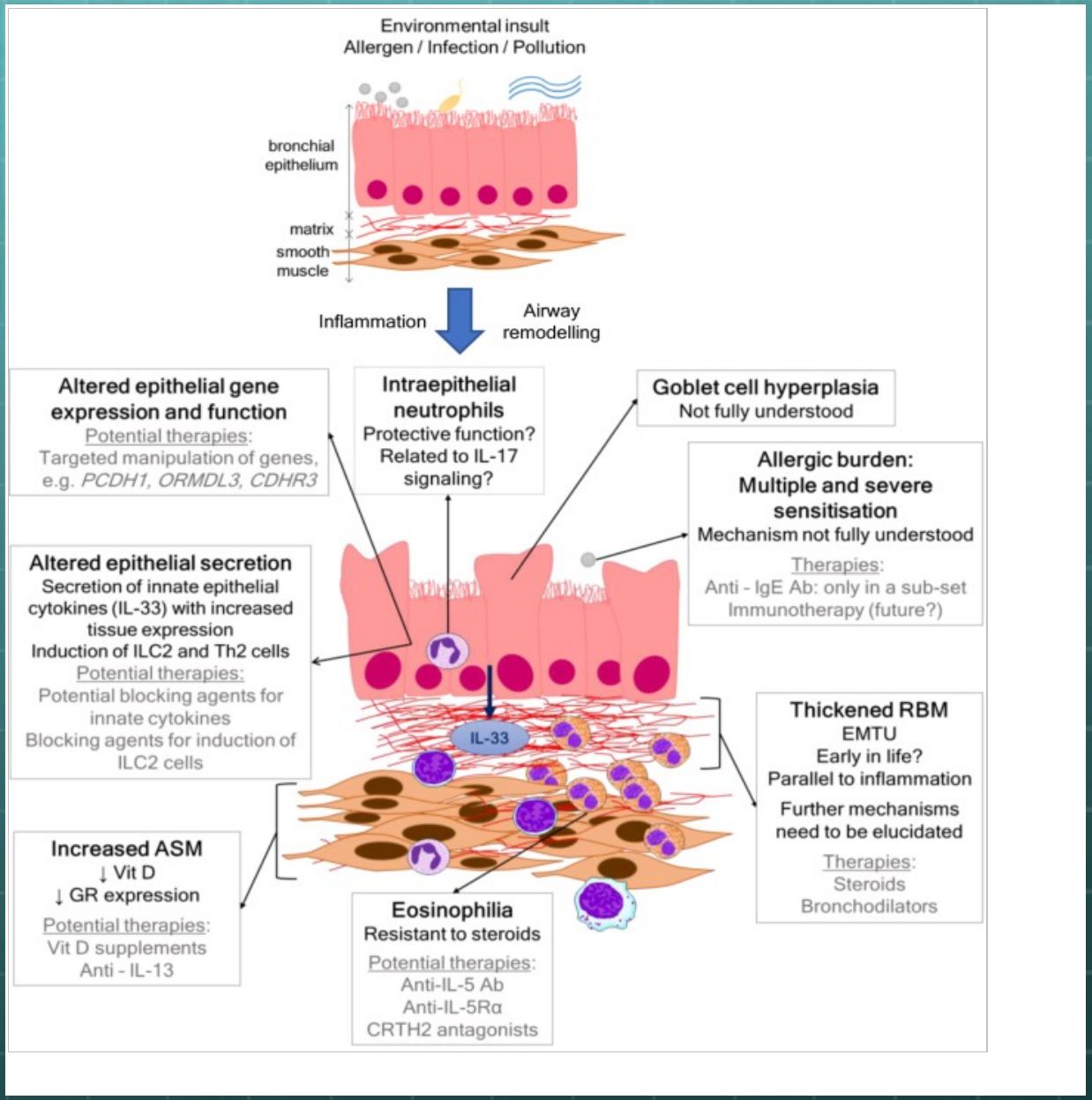
Altered Inflammatory and remodeling profile interaction determine disease manifestation



Predominant inflammatory cells profiles of individuals with asthma can affect clinical disease and response to therapy. Airway remodeling can also play a similar role. Biopsy of children's airways show airway remodeling may not be always be associated with and may occur in parallel to chronic inflammation. ECM-extracellular matrix. RBM-reticular basement membrane. AHR-airways hyper-responsiveness

Sejal Saglani, and Clare M. Lloyd Eur Respir J 2015;46:1796-1804;

Proposed pathways of remodeling may aid in developing therapies for children with severe asthma



Front Pediatr. 2017; 5:154

Asthma is a heterogeneous disease characterized by numerous phenotypes and pathophysiologic pathways (endotypes)

Identifying remodelling, clinical and inflammatory phenotypes and endotypes or pathophysiology pathways may aid in individually targeted therapy

Eosinophilic (biopsy, BAL, sputum, serum, FENO): High Th2 lymphocytic profile.
Early onset allergic childhood asthma (small segment have severe childhood asthma profile – symptomatic despite high dosed ICS or systemic steroids), responsive to inhaled corticosteroids and airway remodeling present. Uncommonly, may have late onset non-allergic eosinophillic asthma which tends to inhaled corticosteroid resistant

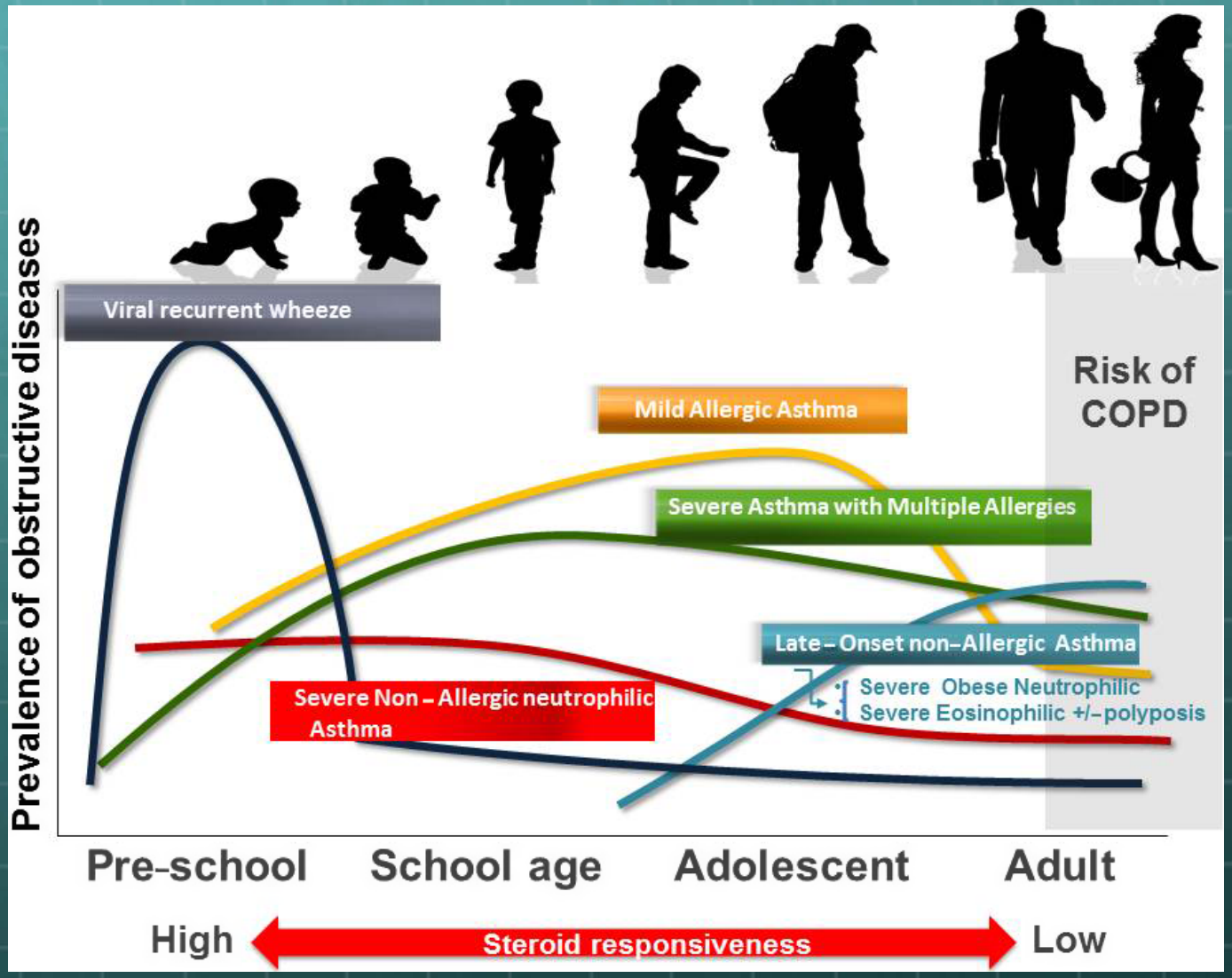
Neutrophilic (sputum): Th1 lymphocytic profile. In childhood, this phenotype is rare.
Older, pubertal girls with high BMI. Those triggered by respiratory illness, GERD, tobacco smoke exposure, and early onset with poor prognosis ; adult phenotype: late onset and inhaled corticosteroid resistant

Paucigranulcytic or paucicellular (low sputum eosinophil and neutrophil): mild disease and viral triggered, early transient wheezers, good prognosis

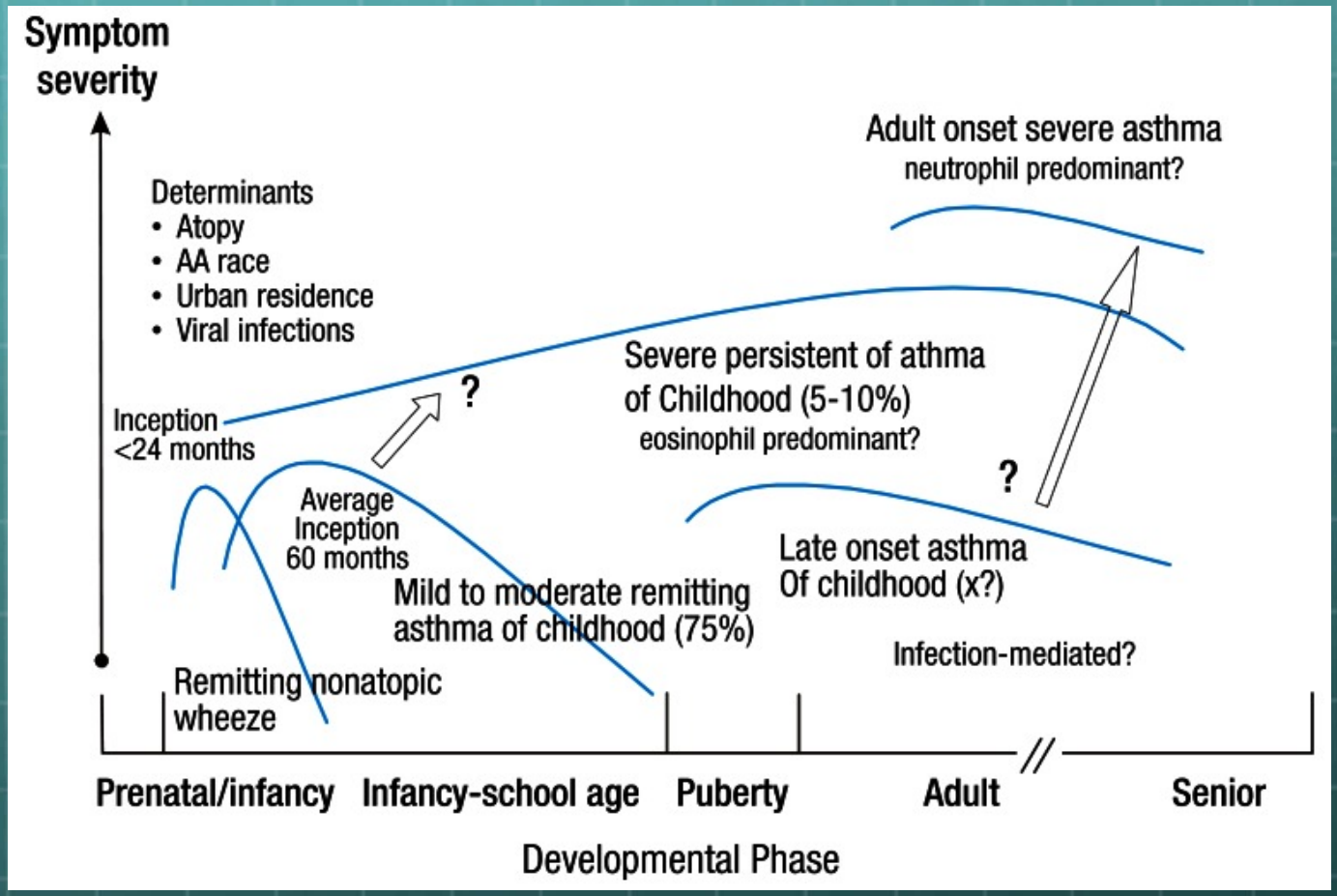
May be stable but 38-40% of patients may change phenotype within 1 year regardless of asthma severity

Clinical phenotypes in asthma during childhood. Just J et al Clin Experim Allergy: 2017; 479(7): 848-855
Phenotypes and Endotypes of Uncontrolled Asthma Severe Asthma: New Treatments. J Investig Allergol Clin Immunol 2013; Vol 23(2):76-88

Recognized Asthma Endotypes & Phenotypes in childhood



Clinical & Experimental Allergy 2017. Volume 47, Issue 7: 848-855
17 MAY 2017 DOI: 10.1111/cea.12939
http://onlinelibrary.wiley.com/doj/10.1111/cea.12939/full#cea12939-fig-0001



Korean J Pediatr. 2013 May; 56(5): 191-195 and Fitzpatrick AM and Teague WG. Pediatr Allergy Immunol Pulmonol 2010; 23: 131-138 – Severe Asthma Research Program

Severe asthma: low prevalence (5-10%) but high healthcare utilization

This definition implies relevant comorbidities, social issues, and medication adherence have been addressed

Major criteria (must have at least 1 to achieve control)

- Treatment with high-dose ICS, treatment with continuous oral corticosteroids at least 50% of the year

Minor criteria (must have at least 2)

- Treatment with additional controller, daily use of short-acting bronchodilator, baseline FEV1 <80%, one or more urgent care visits for asthma in previous year, ≥3 oral steroid in prior year, prompt deterioration of asthma with reduction of ICS or oral steroids, near fatal asthma event requiring intubation - Adopted from the ATS Workshop on Refractory Asthma

- NIH, NHLBI, Severe Asthma Research Program (SARP) compares severe vs. mild-moderate asthma in children from 8 clinical sites (ethnically diverse and gender balanced)
  - Children birth to 5 had symptoms earlier with 1st 24 months of age and higher prevalence of atopy
    Findings in children after 24 months age include eosinophilic profiles w//RBM changes and neutrophilic profiles
  - Children 6 to 11 and 12-17 tended to have be of African American or mixed race, have higher serum IgE, increased FENO, greater healthcare utilization, lower baseline FEV1 (which although improving with bronchodilator remained lower)
  - PFT shows evidence of structural airway changes (remodeling) as young as 6 years old
  - In adults with severe asthma, allergic features were less prevalent

Fitzpatrick AM and Teague WG. Pediatr Allergy Immunol Pulmonol 2010; 23: 131-138

PEDIATRIC ALLERGY, IMMUNOLOGY, AND PULMONOLOGY
Mary Ann Liebert, Inc. publishers
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PMC full text: Pediatr Allergy Immunol Pulmonol. 2010 Jun; 23(2): 131–138.
doi: 10.1089/ped.2010.0021

Table 2.

Thresholds of High-Dose Inhaled Corticosteroids in Adults and Children

	Adults (12 years and older), minimum mcg/day	*Children (<12 years), minimum mcg/day*
Fluticasone	880 mcg (Flovent® HFA)	440 mcg (Flovent® HFA)
Fluticasone/salmeterol	1,000 mcg (Advair® discus)	500 mcg (Advair® discus)
	920 mcg (Advair® HFA)	460 mcg (Advair® HFA)
Budesonide	1,600 mcg (Pulmicort® Turbuhaler)	600 mcg (Pulmicort® Turbuhaler)
	1,440 mcg (Pulmicort® Flexhaler)	450 mcg (Pulmicort® Flexhaler)
		2,000 mcg (Pulmicort® Respules)
Budesonide/formoterol	640 mcg (Symbicort® HFA)	480 mcg (Symbicort® HFA)
Flunisolide	800 mcg (Aerospan®)	1,250 mcg (Aerobid®)
	2,500 mcg (Aerobid®)	
Beclomethasone	640 mcg (Qvar® HFA)	160 mcg (Qvar® HFA)
Triamcinolone	2,500 mcg (Azmacort®)	1,200 mcg (Azmacort®)
Mometasone	880 mcg (Asmanex® Twisthaler)	440 mcg (Asmanex® Twisthaler)

Management Guidelines

- Based on the NIH, National Heart, Lung, and Blood Institute, National Asthma Education and Prevention Program: Expert Panel Report which provides a comprehensive review of pathogenesis and recommendations for management based on peer reviewed medical literature and consensus of experts

- Expert Panel Report 2007 can be found and downloaded for FREE at http://www.nhlbi.nih.gov

- The key components put forth by the guidelines for asthma care:

1) Diagnose and assess the characteristics and severity of asthma

Monitor whether asthma control is achieved and maintained

– via history, physical, lung function and asthma control questionnaires

2) Patient education

3) Control of environmental factors and comorbid conditions that affect asthma

4) Pharmacologic therapy

Recognition of key factors for diagnosing asthma:

1) Wheeze (Lack of wheeze does not exclude asthma), cough especially worse at night, recurrent difficulty breathing or chest tightness

2) Symptoms occurring in the presence of characteristic triggers

3) Reversible airflow obstruction (low FEV1, FEV1/FVC, FEF) demonstrated by:

   Forced expiratory volume in 1 second (FEV1) **volume** increase ≥ 12% or 200 ml from baseline after inhalation of short acting bronchodilator

   May need to look at clinic response to short acting beta agonist, or spirometry improvement following 2 to 3 weeks of steroid treatment and/or consider other bronchoprovocative testing (exercise or methacholine)

   NIH EPR 3 **does not** recommend peak flow for diagnosis – but GINA (Global Initiative for Asthma) guidelines also uses peak flow improvement of 20% post bronchodilator to diagnose asthma

4) Consideration of and/or ruling out alternative diagnoses

Characteristic Asthma Triggers

- **Viral Infection**
- **Environmental**

Tobacco exposure

Allergen:

Food

Animal Dander

Dust mite

Pollen

Cockroach

Mold

- Hormonal
  - Menses
  - Pregnancy
  - Thyroid disease
- Cold air exposure or weather change
- Exercise
- Emotion
  - Laughing hard
  - Crying hard
  - Anxiety

- Irritants:
  - Strong odor
  - Pollutants
  - Occupational chemicals
  - Particulate matter
  - Gas/vapors

Comorbidities which may worsen Asthma

- Atopy (allergies – environmental and food)
- Gastroesophageal reflux
- Rhinitis (esp. allergic related)/Sinusitis
- Obesity
- Allergic bronchopulmonary aspergillosis
- Obstructive sleep apnea

Everything that Wheezes is not Asthma

- **Congenital**

Tracheobronchomalacia

Tracheostenosis

Tracheobroncheal malformations

Vascular compression

Cardiac lesion with chamber or vessel dilation

- **Intrinsic Bronchial Obstruction**

Bronchiolitis

Bronchitis

GERD

Foreign body

- Intrinsic Bronchial Obstruction

Cystic Fibrosis

Bronchiectasis

Bronchiolitis Obliterans

- Extrinsic Bronchial Obstruction

Mediastinal mass

Lymph node enlargement

Edema

Cardiomegaly

- Vocal cord dysfunction

Chronic Cough in Pediatrics

- **Infectious**

Upper respiratory , Sinusitis, Pertussis

Lower respiratory ,

Viral (RSV, parainfluenza, rhinovirus, adenovirus)

Chlamydia, Tuberculosis

- **Congenital**

Cystic fibrosis

Immune deficiency

Ciliary anomaly

Bronchopumonary anomaly

Vascular ring

- Misc

Gastroesophageal reflux
Aspiration
Airway foreign body
Interstitial lung disease
- idiopathic
- sequelae of chronic aspiration
- sequelae of AIDS
- sequelae of collagen vascular disease

Bronchiectasis
Airway compression due to hilar mediastinal adenopathy or cardiomegaly
Cardiac disease
Environmental irritants
Drug (i.e. ACE inhibitors)
Habit cough

Pediatric Chest Pain

- **Other Pulmonary related**

  Bronchitis, pneumonia, pleuritis

  Pleural effusion, pneumothorax

- **Cardiac**

  Congenital heart disease

  Acquired heart disease

  valvular – mitral valve prolapse

  coronary – Kawasaki disease

  myocardial – viral

  pericarditis, pericardial effusion

  Tachyarrhythmia

- GI related
  Gastroesophageal reflux
  Esophagitis
  Pancreatitis (due to CF)

- Misc
  Costochondritis
  Trauma
  Sickle cell disease vaso-occlusive crisis
  Malignancy
  Psychogenic

Dyspnea (Shortness of Breath)

- **Supraglottic**

  Nasopharyngeal obstruction

  Laryngeal obstruction/anomaly

- **Obstructive lung disease**

  Cystic fibrosis, bronchitis

  Bronchiectasis/Bronchiolitis obliterans

- **Restrictive lung disease**

  Interstitial lung or pleural disease

  Kyphoscoliosis, neuromuscular disease

  Pneumonia

- Diagphragmatic dysfunction
  Cervical injury/insult

- Cardiac
  Congenital heart disease
  Acquired heart disease
  valvular
  coronary
  pericarditis
  myocarditis

- Metabolic acidosis

- Psychogenic

Components of Severity		Classification of Asthma Severity (Children 0-4 years of Age)			
		Intermittent	Persistent		
			Mild	Moderate	Severe
Impairment	Symptoms	≤2 days per week	> 2 days per week; not daily	Daily	Throughout the day
	Nighttime awakenings	0	1-2x/month	3-4x/month	>1x/week
	Short acting beta agonists for symptom control (not prevention of EIB)	≤2 days per week	> 2 days per week; not daily	Daily	Several times per day
	Interference with normal activity	None	Minor limitation	Some limitation	Extremely limited
Risk Risk of exacerbation or progressive loss of lung function	Exacerbations requiring oral systemic steroids	0-1/year	≥2 exacerbations in 6 months (oral steroids) or ≥4 wheezing episodes/year lasting > 1 day AND risk factors for persistent asthma		
		Consider severity and interval since last exacerbation. Frequency and severity may fluctuate overtime. Exacerbations of any severity may occur in patients in any severity category			

Classify severity with symptoms off or prior to being on controller therapy

National Heart, Lung, and Blood Institute, National Asthma Education and Prevention Program: Expert Panel Report 3: Guidelines for the Diagnosis and Management of Asthma, Full Report 2007

Components of Severity		Classification of Asthma Severity (Children 5-11 years of Age)			
		Intermittent	Persistent		
			Mild	Moderate	Severe
Impairment	Symptoms	≤2 days per week	>2 days/wk but not daily	Daily	Throughout the day
	Nighttime Awakenings	≤2x/month	3-4x/month	>1x/wk but not nightly	Often 7x/wk
	Short acting beta agonist use for symptom control (not prevention of EIB)	≤2 days per week	>2 days/wk 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% pred FEV1/FVC >85%	FEV1 ≥80% pred FEV1/FVC >80%	FEV1 = 60 - 80%pred FEV1/FVC = 75 - 80%	FEV1 < 60%pred FEV1/FVC < 75%
Risk Risk of exacerbation or progressive loss of lung function	Exacerbations requiring oral systemic steroids	0-1 per year	≥2 in one year		
		Consider severity and interval since last exacerbation. Frequency and severity may fluctuate overtime for any patient in any severity category. Relative annual risk of exacerbation may be related to FEV1.			

Classify severity with symptoms off or prior to being on controller therapy

National Heart, Lung, and Blood Institute, National Asthma Education and Prevention Program: Expert Panel Report 3: Guidelines for the Diagnosis and Management of Asthma, Full Report 2007

Components of Severity		Classification of Asthma Severity (Children ≥12 years of Age)			
		Intermittent	Persistent		
			Mild	Moderate	Severe
Impairment Normal FEV1/FVC: 8-19yo 85% 20-39yo 80% 40-59yo 75% 60-80yo 70%	Symptoms	≤2 days per week	>2 days/wk but not daily	Daily	Throughout the day
	Nighttime Awakenings	≤2x/month	3-4x/month	>1x/wk but not nightly	Often 7x/wk
	Short acting beta agonist use for symptom control (not prevention of EIB)	≤2 days per week	>2 days/wk but not >1x/day	Daily	Several times per day
	Interference with normal activity	None	Minor limitation	Some limitation	Extremely limited
	Lung Function	Normal FEV1 between exacerbations FEV1 >80% pred FEV1/FVC normal	FEV1 ≥80% pred FEV1/FVC normal	FEV1 = >60 but <80% pred FEV1/FVC reduced 5%	FEV1 < 60%pred FEV1/FVC reduced 5%
Risk	Exacerbations requiring oral systemic steroids	0-1 per year	≥2 in one year		
		Consider severity and interval since last exacerbation. Frequency and severity may fluctuate overtime for any patient in any severity category. Relative annual risk of exacerbation may be related to FEV1.			

Classify severity with symptoms off or prior to being on controller therapy

National Heart, Lung, and Blood Institute, National Asthma Education and Prevention Program: Expert Panel Report 3: Guidelines for the Diagnosis and Management of Asthma, Full Report 2007

Classifying severity in patients after asthma becomes controlled

Retrospective assignment based on Lowest level of treatment required to maintain control	Classification of Asthma Severity			
	Intermittent	Persistent		
	Step 1	Mild	Moderate	Severe
		Step 2	Step 3 or 4	Step 5 or 6

For population-based evaluations, clinical research, or characterization of a patient's overall asthma severity after control is achieved. For clinical management , focus is evaluating level of control, not severity, once treatment is established.

National Heart, Lung, and Blood Institute, National Asthma Education and Prevention Program: Expert Panel Report 3: Guidelines for the Diagnosis and Management of Asthma, Full Report 2007


Anne Geddes Galleries

Case # 1

Jessie - 19 months old

- 1st episode viral/RSV bronchiolitis at 5 months old
- Required 2 courses of systemic steroids for wheeze/cough not improving after 24 hours beta agonist therapy at 13 months old and 18 months old
- Jessie has eczema and peanut allergy
- Reports no daytime symptoms between episodes
- Reports 1 night a week of cough that responds to beta agonist
- Jessie is not on controller therapy


Anne Geddes Galleries

Case # 1

Jessie - 19 months old

Based upon impairment and risk assessment, Jessie's asthma severity is:

a. Intermittent Asthma
b. Mild Persistent Asthma
c. Moderate Persistent Asthma
d. Severe Persistent Asthma
e. Insufficient information available


Anne Geddes Galleries

Case # 1

Jessie - 19 months old

Based upon impairment and risk assessment, Jessie's asthma severity is:

a. Intermittent Asthma
b. Mild Persistent Asthma
c. Moderate Persistent Asthma
d. Severe Persistent Asthma
e. Insufficient information available

Components of Severity		Classification of Asthma Severity (Children 0-4 years of Age)			
		Intermittent	Persistent		
			Mild	Moderate	Severe
Impairment	Symptoms	≤2 days per week	>2 days per week; not daily	Daily	Throughout the day
	Nighttime awakenings	0	1-2x/month	3-4x/month	>1x/week
	Short acting beta agonists for symptom control (not prevention of EIB)	≤2 days per week	>2 days per week; not daily	Daily	Several times per day
	Interference with normal activity	None	Minor limitation	Some limitation	Extremely limited
Risk Risk of exacerbation or progressive loss of lung function	Exacerbations requiring oral systemic steroids	0-1/year	≥2 exacerbations in 6 months (oral steroids) or ≥4 wheezing episodes/year lasting > 1 day AND risk factors for persistent asthma		
		Consider severity and interval since last exacerbation. Frequency and severity may fluctuate overtime. Exacerbations of any severity may occur in patients in any severity category			

Classify severity with symptoms off or prior to being on controller therapy

National Heart, Lung, and Blood Institute, National Asthma Education and Prevention Program: Expert Panel Report 3: Guidelines for the Diagnosis and Management of Asthma, Full Report 2007

Case # 2

Tracy – 15 years old

- Not on any controller therapy
- Says things are going alright and doesn't really have problems with wheeze, chest tightness, cough, or difficulty breathing. and chest tightness.
- Tracy has been in basketball:
  - Takes 15 minutes to run one mile.
  - Practices 5 days a week.
  - Takes a break after 20 minutes because of hard breathing then resumes practice.
- Lung function shows forced expiratory volume in 1 sec (FEV1) of 55% predicted this volume increases 19% after short acting beta agonist

Case # 2

Tracy – 15 years old

Based upon impairment and risk assessment, Tracy's asthma severity is:

a. Intermittent Asthma
b. Mild Persistent Asthma
c. Moderate Persistent Asthma
d. Severe Persistent Asthma
e. Insufficient information available

Case # 2

Tracy – 15 years old

Based upon impairment and risk assessment, Tracy's asthma severity is:

a. Intermittent Asthma
b. Mild Persistent Asthma
c. Moderate Persistent Asthma
d. Severe Persistent Asthma
e. Insufficient information available

Components of Severity		Classification of Asthma Severity (Children ≥12 years of Age)			
		Intermittent	Persistent		
			Mild	Moderate	Severe
Impairment Normal FEV1/FVC: 8-19yo 85% 20-39yo 80% 40-59yo 75% 60-80yo 70%	Symptoms	≤2 days per week	>2 days/wk but not daily	Daily	Throughout the day
	Nighttime Awakenings	≤2x/month	3-4x/month	>1x/wk but not nightly	Often 7x/wk
	Short acting beta agonist use for symptom control (not prevention of EIB)	≤2 days per week	>2 days/wk but not >1x/day	Daily	Several times per day
	Interference with normal activity	None	Minor limitation	Some limitation	Extremely limited
	Lung Function	Normal FEV1 between exacerbations FEV1 >80% pred FEV1/FVC normal	FEV1 ≥80% pred FEV1/FVC normal	FEV1 = >60 but <80% pred FEV1/FVC reduced 5%	FEV1 < 60%pred FEV1/FVC reduced 5%
Risk	Exacerbations requiring oral systemic steroids	0-1 per year	≥2 in one year		
		Consider severity and interval since last exacerbation. Frequency and severity may fluctuate overtime for any patient in any severity category. Relative annual risk of exacerbation may be related to FEV1.			

Classify severity with symptoms off or prior to being on controller therapy

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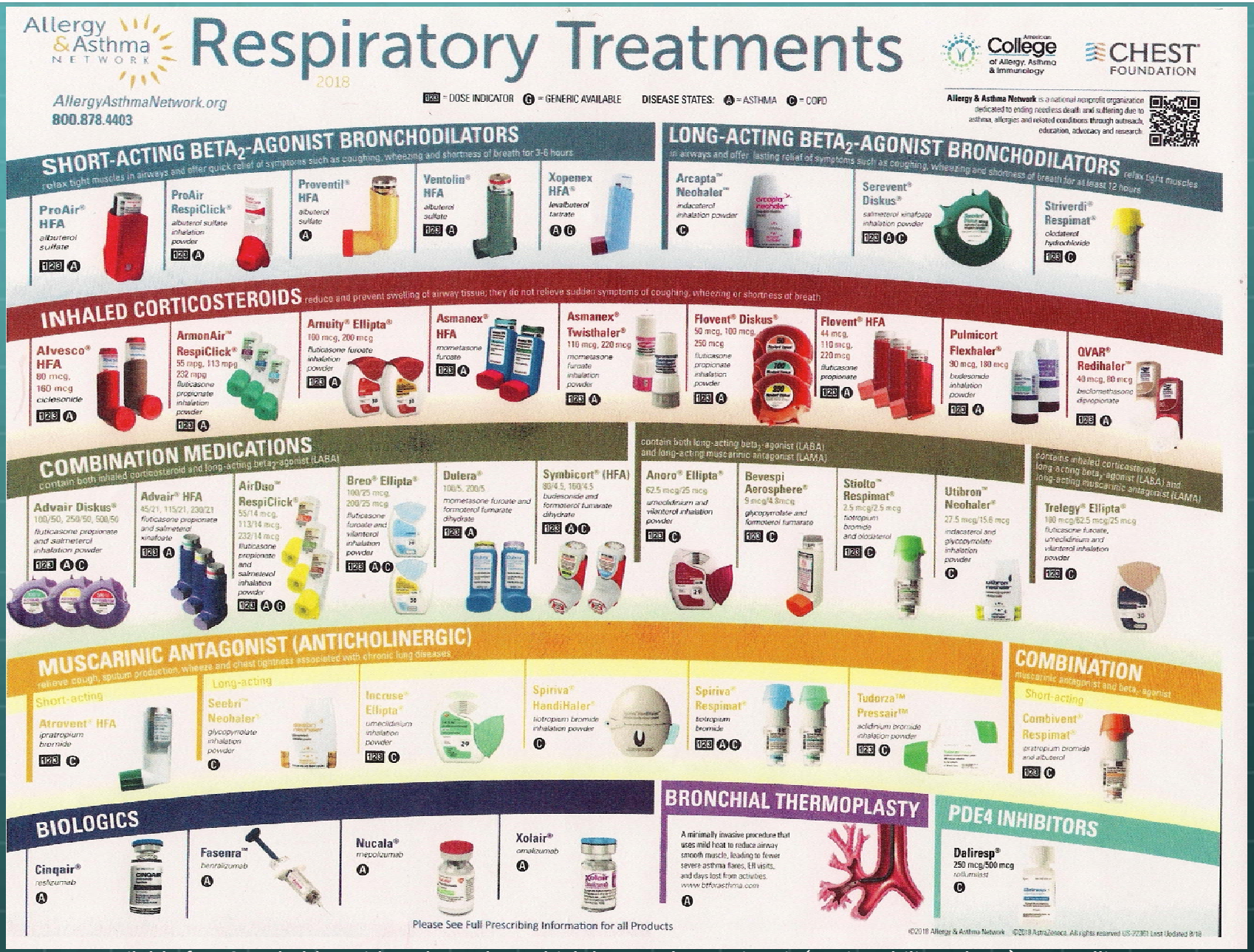


Available for 18 and older with asthma: bronchial thermoplasty, Cinqair (eosinophilic asthma), Breo ellipta
For COPD and NOT asthma: Muscarinic: Incruse Ellipta, Tudorza, Seebri. PDE4 inhibitor: Daliresp.
Combination: Anoro ellipta, Bevespi, Stiolto, Utibron, Trelegy. Long acting beta agonist: Arcapta, Striverdi
Serevent can ONLY be used with inhaled steroid for asthma . Dupixent is a biologic for 12 years and up.

Current Long Term Therapies Address Mechanisms Involved in Asthma

Inhaled glucocorticoid steroids (ICS): glucocorticoid receptor modulates inflammation gene transcription

- beclomethasone, budesonide, ciclesonide, fluticasone furoate, fluticasone propionate, mometasone furoate

Combination ICS – long acting beta agonist (LABA) – LABA inhibit mast cell mediators and potentiate translocation of glucocorticoid receptor

- budesonide/formoterol (ages 6 and up), fluticasone/salmeterol (ages 4 and up Advair powder disc, ages 12 and up Advair/Airduo aerosol inhaler), mometasone/formoterol (ages 12 and up), fluticasone/vilanterol (ages 18 and up)

Leukotriene modifiers: block mediators that promote airway smooth muscle contraction, vascular leakage, inflammatory cell infiltration, mucus secretion, and airway hyper-responsiveness

- montelukast (ages 6 months and older allergic rhinitis, ages 1 yo and up for asthma, 6yo and older for exercise induced bronchospasm), zafirlukast (ages 5 and up – associated with hepatic dysfunction), zileuton (12 and up)

Current Long Term Therapies Address Mechanisms Involved in Asthma

Mast cell stabilizers

- cromolyn (FDA approved for 2 years and up), nedocromil (FDA approved for 3 years and up)

Long acting muscarinic antagonist – anticholinergic

- tiotropium (FDA approved 6 years and up)

Methylxanthine - bronchodilator

- theophylline a phosphodiesterase (PDE) inhibitor (EPR3 recommends start at 5 years & up)

Immunotherapy – alters immune response to allergen from T_H2 (IgE) to T_H1 (IgG)

Immune modulator - Omalizumab Xolair (monoclonal anti IgE – approved 6 year and older)

- Mepolizumab Nucala (IL-5 antagonist – approved 12 yo and up)

- Benralizumab Fasenra (IL-5 receptor antagonist approved 12 yo and older)

- Dupilumab Dupixent (IL 3 & IL 4 antagonist approved 12 yo and older)

- Reslizumab Cinqair (IL 5 antagonist approved for 18 yo and older

Inhaled glucocorticoid steroids (ICS):

Efficacy:

- 400 micrograms daily budesonide improved clinical efficacy (compared to nedocromil and placebo)

Childhood Asthma Management Program (CAMP) Research Group NEJM 2000

(multicenter study in children 5 to 12 years old with mild to moderate persistent asthma – sponsored by NIH, one of the authors on advisory board and consultant for various drug companies i.e. Merck, Glaxo Wellcome, Sepracor

Clinical benefits and airway responsiveness changes in this same group did not persist after therapy discontinued - Strunk et al J Pediatrics 2009

- Systemic review of double blind randomized dose response studies of children treated for at least 4 weeks with fluticasone: Plateau of response between 100 and 200 micrograms. One study showed additional efficacy at 400 micrograms in severe asthmatics. Masoli et al Arch Childhood Dis 2004

Inhaled glucocorticoid steroids (ICS):

Airway remodeling: While inhaled steroids reduce some characteristics of airway remodeling, it does not halt the occurrence

- Trigg CJ et al Am J Respir Crit Care Med; 1994; 150: 17-22. 25 adults treated with beclomethasone 1000 microg/d for 4 months versus placebo showed reduced mast cells and eosinophils as well as reduced basement membrane thickness.

- Obase Y et al. Int Arch Allery Immunol; 2010; 151 (3): 247-54. Children with mild or moderate asthma symptoms were treated with budesonide. Matrix metaloproteinase (MMP-8 plays role in remodeling) and tissue MMP inhibitors (TIMP-1) in sputum and expression in airway inflammatory cells were measured. Budesonide reduced MMP levels and increased TIMP-s levels. TIMP-1 lower and MM8/TIMP-1 higher in asthma vs healthy controls.

- Grzela K et al. Cent Eur J Immunol; 2016; 41 (2): 221-227. Use of teenage patient with asthma exacerbation treated with fluticasone (500-1000 microg/d) and salmeterol for 4 weeks. While levels of exhaled nitric oxide was reduced, levels of exhaled matrix metalloproteinase (MMP-9 – plays role in remodeling) remained at baseline high levels. Compared to matched controls asthma patients had higher exhaled NO and MMP-9 levels

Inhaled glucocorticoid steroids (ICS)

Safety:

Childhood Asthma Management Program (CAMP) multicenter study in children 5 to 12 years old with mild to moderate persistent asthma

- **400 micrograms daily budesonide**

3 yr use – no effects on hypothal-pituitary-adrenal axis - Bacharier et al Pediatrics 2004

4 to 6 year use – mean increase in height in first year 1.1 cm less than placebo with similar rate of growth, projected final height by end of study, and bone density – Childhood Asthma Management Program Research Group NEJM 2000

Systemic review of double blind randomized dose response studies of children treated for at least 4 weeks with fluticasone: Likelihood of adrenal suppression at 400 micrograms versus 200 micrograms. - Masoli et al Arch Childhood Dis 2004

Weigh the benefits and risks of high dose ICS

Rinse mouth after use to reduce likelihood of oral candidiasis

With use of nebulized ICS (budesonide) avoid nebulization into eyes

Combination ICS – long acting beta agonist (LABA)

Clinical studies have shown higher clinical efficacy using combination ICS/LABA versus ICS alone

RCT's children > 2yo and adults with asthma Ni Chroinin et al Cochrane Database Sys Review 2005 (Oct 19;(4): CD005535

Meta analysis of RCT adding LABA to fluticasone versus increasing ICS by at least 2 fold in adults: Masoli et al Thorax 2005

Combination ICS – long acting beta agonist (LABA)

Black box warning study:

SMART (salmeterol multi-center asthma research trial) study.

RCT to study effects of salmeterol on respiratory related death or life threatening episodes. Secondary come asthma related death. Meant to enroll > 60 000 subjects and follow for 28 weeks of therapy

- Study stopped after enrolling over 26 000 subjects.
- There was no difference in primary outcome
- Asthma related deaths: 13 on salmeterol versus 3 on placebo
- African Americans: 8 deaths on salmeterol versus 1 on placebo
- Caucasians: 5 deaths on salmeterol versus 2 on placebo
- Asthma death lower in ICS users versus non-ICS users
- Lower percentage of African Americans were on ICS
- In the population not on ICS, there was greater number of asthma deaths in those on salmeterol versus placebo

Cazzola and Matera Ther Adv Respir Dis 2007; 1(1): 35-46

LABA should not be used as monotherapy for persistent asthma and should be added after the addition of/or adjunctively with ICS

Leukotriene modifiers

Block mediators that promote airway smooth muscle contraction, vascular leakage, inflammatory cell infiltration, mucus secretion, and airway hyperresponsiveness

Budesonide (0.5 mg a day) or monteleukast 4 or 5 mg in children 2 to 8 years old with mild persistent asthma, although both provided good asthma control. Overall ICS favored
- Szefler et al J Allergy Clin Immunol 2007; 120: 1043-1050 (sponsored by AztraZeneca).

Montaleukast (5 mg) comparable with fluticasone (100 mcg bid) in children 6 to 14 years old with mild persistent asthma – Garcia et al Pediatrics 2005 (some authors employed at Merck)

Adults with moderate persistent asthma fluticasone 100 mcg bid decreased airway hyperreactivity and reduced daytime symptoms versus 10 mg monteleukast – Kanniess et al Eur Respir J 2000; 20:853-858 (study sponsored by GlaxoSmithKline – makers of fluticasone)

<u>Although ICS preferred, leukotriene antagonists can be alternative monotherapy for mild persistent asthma</u>

Mast cell stabilizers

- 400 micrograms daily budesonide versus 16 mg neocromil versus placebo

Neither budesonide nor nedocromil is better than placebo in terms of lung function but budesonide improves airway responsiveness and provides better asthma control versus placebo or nedocromil
Childhood Asthma Management Program Research Group NEJM 2000
- Needs to be given up to QID

- Although ICS preferred, mast cell stabilizers can be used as alternative monotherapy in mild persistent asthma.

Methylxanthine

- Thoephylline (Bronchodilator) – oral therapy

Attempt to achieve steady state (48 hours on same dose) serum level for bronchospasm 10 to 20 mcg/dl

Beware of drug interactions:

Decreases theophylline level by increasing metabolism – phenobarbital, phenytoin, carbamazapine, rifampin, smoking

Increases theophylline level by decreasing metabolism – macrolides, quinolones, cimetidine

Beware of exacerbating conditions such as: cardiac dysrhythmias (not including bradyarrhythmia), seizure disorders, GERD

Short Discussion of Quick Relief Medication

Albuterol versus Levalbuterol

1/ Double blinded randomized controlled study in 129 children in ED (US) setting with acute moderate to severe exacerbation showed no difference in change of clinical asthma score or lung function after treatment - Qureshi et al, Ann Emerg Med 2005

2/ Double randomized placebo controlled study of 81 children 6 to 18 with severe exacerbation in inpatient setting of continuous levalbuterol versus racemic albuterol (CHOP) showed no changes in clinical outcome – Andrews et al J Pediatrics 2009

Effect of Ipratropium bromide (IB) on exacerbation

1/ Double blinded randomized placebo controlled study of 434 children 2 to 18 yo in ED setting with moderate to severe exacerbation. Rate of hospitalization lower in those receiving adjunctive IB (in addition to albuterol and systemic steroid) versus adjunctive placebo. This was especially noted in the severe exacerbation – Qureshi NEJM 1998

2/ Double blinded randomized placebo controlled study of 210 hospitalized children 1 to 18 yo utilizing a standard asthma care algorithm. In addition to albuterol, systemic steroid and oxygen used based on algorithm, comparison of adjunctive IB (with albuterol) versus adjunctive placebo did not improve clinical outcomes – Craven et al J Pediatric 2001

Short Discussion on Systemic Steroids for Exacerbation

Oral prednisone or prednisoline or IV methylprednisolone or IV hydrocortisone

A systematic review article looking at randomized controlled studies in hospitalized children 1 to 18 yo with exacerbations (9 studies fulfilled the criteria) Insufficient data to establish dose response relationship and no difference in use of IV methylprednisolone versus oral prednisone – Zhang and Mendoza J Paediatrics and Child Health 2005

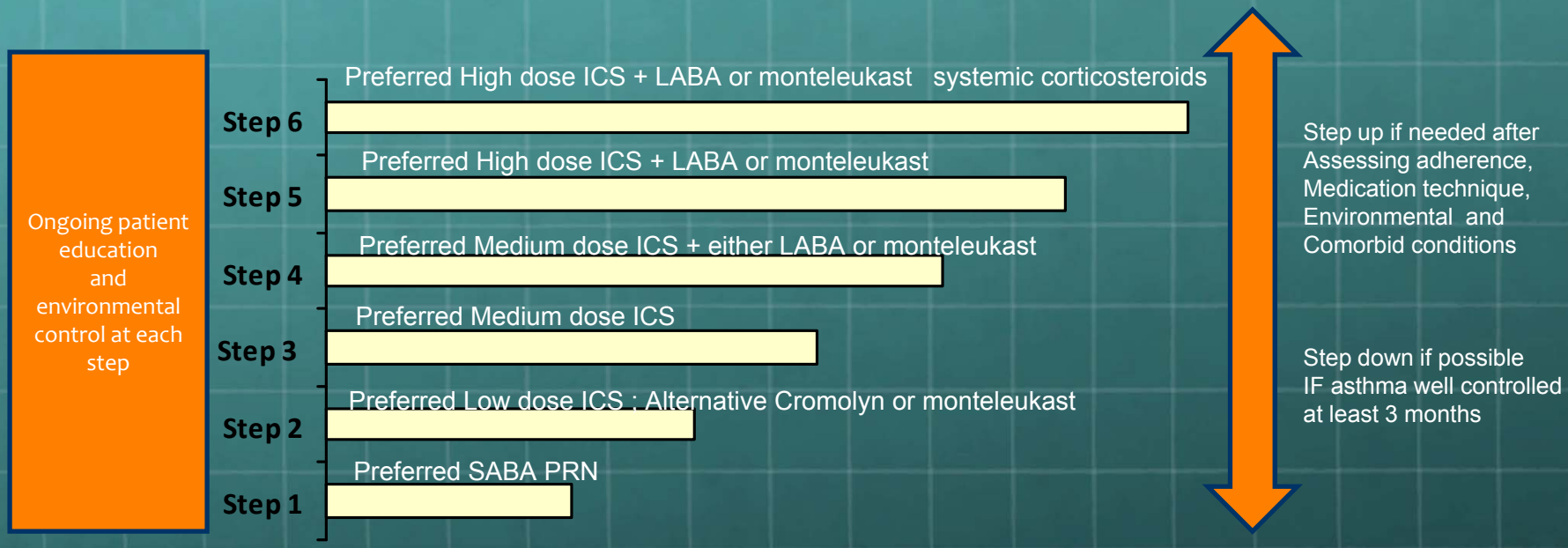
Expert panel 2007 does not recommend superiority of IV or oral sytemic steroid and oral may be used as long as GI tolerated. No advantage for high dose steroids in severe exacerbation (child dose should not exceed 60 mg a day and adult dose should not exceed 80 mg a day). No need to taper if duration up to 10 days

Asthma Treatment for Control

Lowest level of treatment required to maintain control	Classification of Asthma Severity			
	Intermittent	Persistent		
		Mild	Moderate	Severe
	Step 1	Step 2	Step 3 or 4	Step 5 or 6

National Heart, Lung, and Blood Institute, National Asthma Education and Prevention Program: Expert Panel Report 3: Guidelines for the Diagnosis and Management of Asthma, Full Report 2007

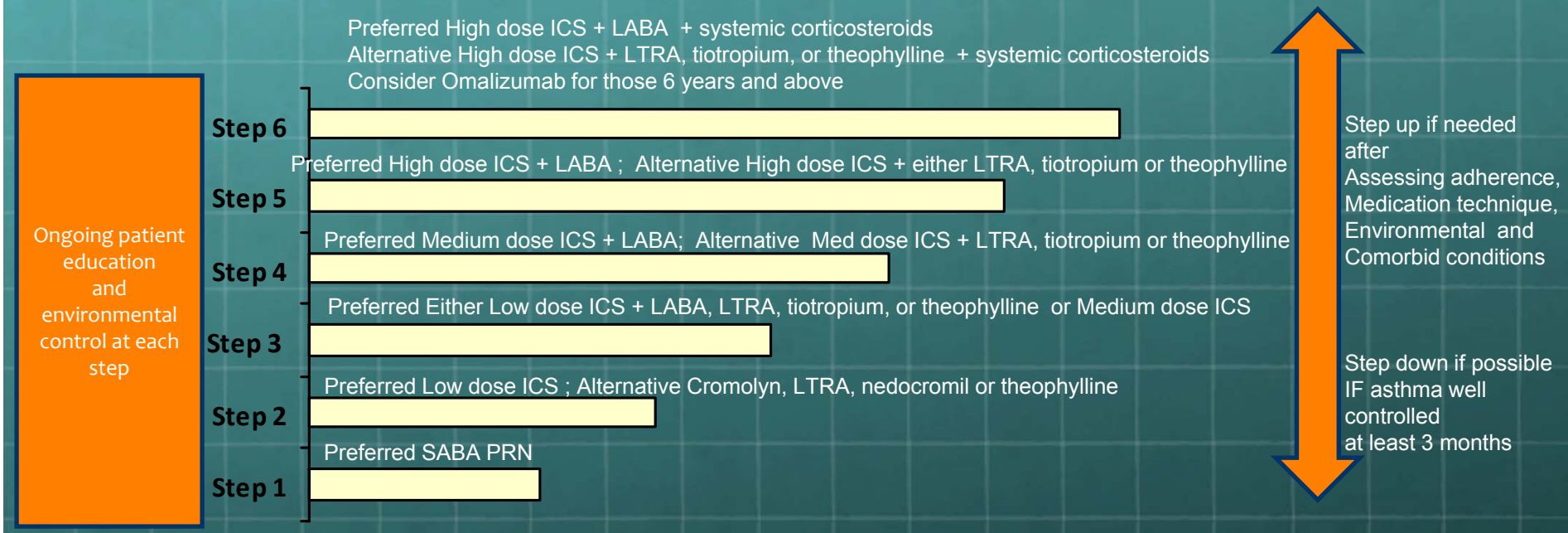
Step wise Approach to Asthma Management Ages 0-4 years old



Step 1 pertains to intermittent asthma
Steps 2 – 6 pertains to persistent asthma when daily therapy is needed

SABA – short acting beta agonist; ICS – inhaled corticosteroid; LABA long acting beta agonist
National Heart, Lung, and Blood Institute, National Asthma Education and Prevention Program: Expert Panel Report 3: Guidelines for the Diagnosis and Management of Asthma, Full Report 2007

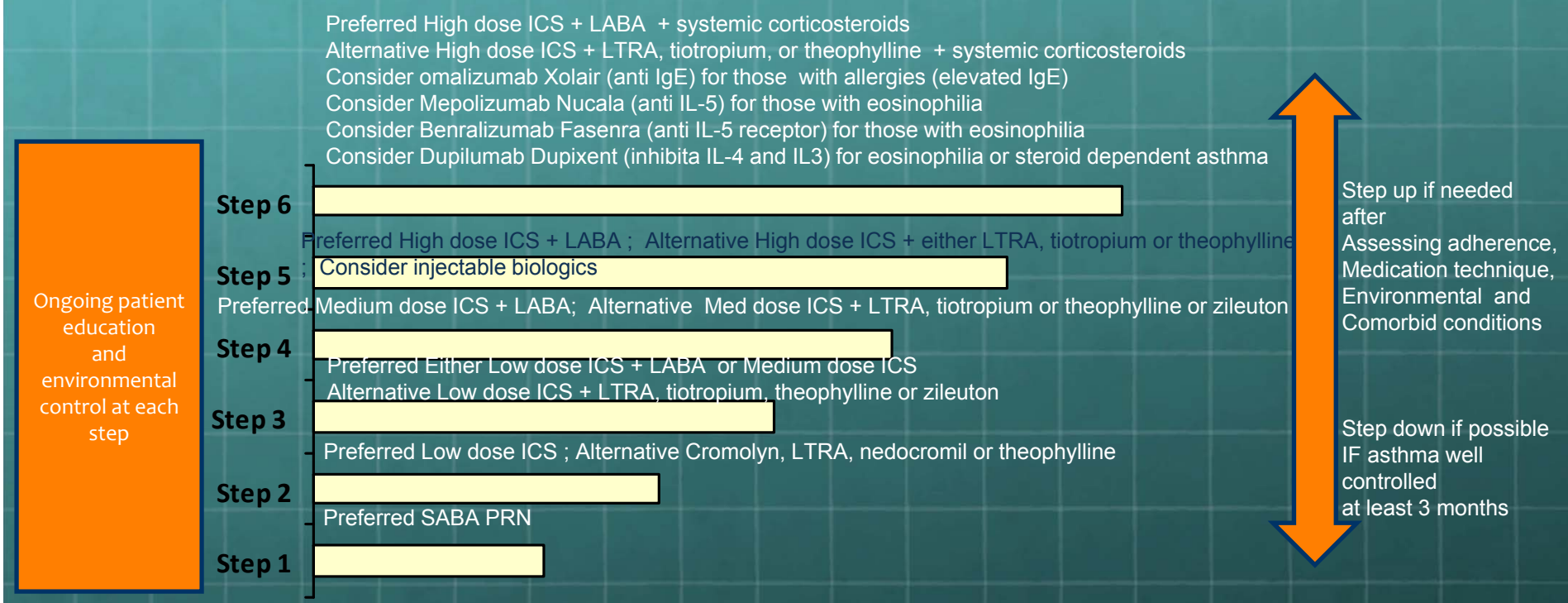
Step wise Approach to Asthma Management Ages 5-11 years old



Step 1 pertains to intermittent asthma
Steps 2 – 6 pertains to persistent asthma when daily therapy is needed

SABA – short acting beta agonist; ICS – inhaled corticosteroid; LABA long acting beta agonist
LTRA – leukotriene receptor antagonist
National Heart, Lung, and Blood Institute, National Asthma Education and Prevention Program: Expert Panel Report 3: Guidelines for the Diagnosis and Management of Asthma, Full Report 2007

Step wise Approach to Asthma Management Ages ≥ 12 years old



Step 1 pertains to intermittent asthma

Steps 2 – 6 pertains to persistent asthma when daily therapy is needed

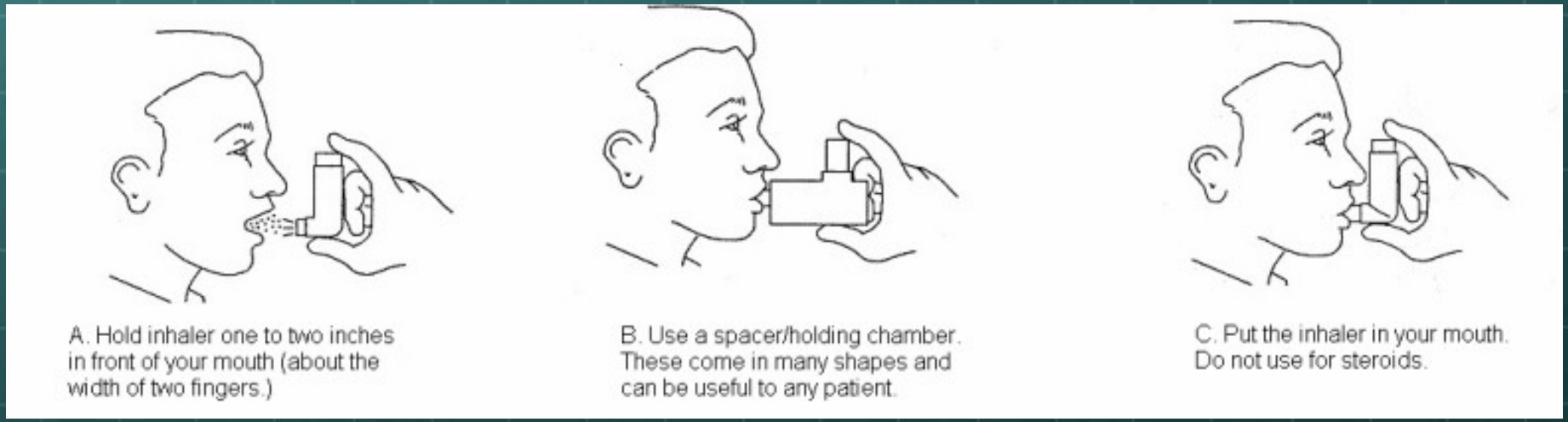
SABA – short acting beta agonist; ICS – inhaled corticosteroid; LABA long acting beta agonist

LTRA – leukotriene receptor antagonist

National Heart, Lung, and Blood Institute, National Asthma Education and Prevention Program: Expert Panel Report 3: Guidelines for the Diagnosis and Management of Asthma, Full Report 2007

1. Remove cap from inhaler
2. Shake inhaler
3. Breathe out
4. Position inhaler/aerochamber as below
5. As one starts inhalation press down on inhaler canister
6. Take slow deep breath in (about 5 to 7 seconds of inhalation)
7. Hold breath for 10 seconds
8. Let breath out
9. Repeat second puff after 60 seconds

If using an aerochamber with mask – step 3 would be skipped and position mask over nose and mouth. After pressing down canister, child would breathe in and out 6 to 8 times and wait one minute before second puff



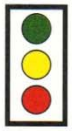
A. Hold inhaler one to two inches in front of your mouth (about the width of two fingers.)

B. Use a spacer/holding chamber. These come in many shapes and can be useful to any patient.

C. Put the inhaler in your mouth. Do not use for steroids.

www.mckinley.illinois.edu

I am not being paid by this company : I just wanted to show different aerochambers



Texas Tech Physicians
Pediatric Clinic Medical Pavilion
Lubbock, TX
(806)743-7337

Patient Name:
MRN:
DOB:

ASTHMA ACTION PLAN

Controller Medicine: _____ Quick Relief Medicine: _____

GREEN ZONE GO!

Breathing is good, no cough or wheeze. Playing without problems.

Peak flow greater than _____

Follow Your Regular Treatment Plan:

Medicine	How Much	How Often /How long

For asthma with exercise, take quick relief medicine 20 minutes before exercise

YELLOW ZONE Caution Yellow

Cough, wheeze, tightness in the chest, waking up at night.

Peak flow from _____ to _____

1. Take 2 puffs of your quick relief medicine or 1 nebulizer treatment with 1 vial of your quick relief medicine. You may repeat this treatment twice if needed. Wait 20 minutes between treatments.

If your symptoms are better after these treatments take medicine listed below:

Medicine	How Much	How Often /How long

If your symptoms are not better or your peak flow is not back in your green zone:
1. Continue quick relief medicine 2 puffs or 1 nebulizer treatment every 3 to 4 hours
2. Call the clinic for an appointment.

RED ZONE DANGER!

Medicine is not helping. Breathing is hard and fast. Nose opens wide when you breathe. Can't talk well. Can't walk. Ribs show when you breathe.

Peak flow less than _____

1. Take 2 puffs of your quick relief medicine or 1 nebulizer treatment with 1 vial of your quick relief medicine. You may repeat this treatment two times if needed. Wait 20 minutes between treatments.

- If your symptoms are better:
1) continue your quick relief medicine every 3-4 hours as needed
2) Call the clinic as soon as possible

- If your symptoms are NOT BETTER go to the emergency room right away.

Go to Emergency Room or call 911 if:
1) your symptoms don't improve after 3 doses of your quick relief medicine.
2) you can't catch your breath or talk because you are short of breath
3) your lip or fingertips are blue or purple
4) you still need your quick relief medicine more often than every 3 to 4 hours

Reviewed with patient/family, verbalized understanding _____.

C:/documents and settings/jrangelh/my documents/asthma/new asthma action plan revised 4/10/08

An asthma action plan is an important component of education & management

Green zone peak flow	**80 – 100% best**
Yellow zone peak flow	**50 – 80% best**
Red zone peak flow	**< 50% best**

CHILDREN & ADOLESCENTS - POLGAR † PEAK EXPIRATORY FLOW RATE [liters/minute]				
HEIGHT		MALE	FEMALE	MALES & FEMALES COMBINED
[inches]	[cm]			
43	109	143	153	147
44	112	157	166	160
45	114	171	178	174
46	117	185	190	187
47	119	199	202	200
48	122	214	215	214
49	125	228	227	227
50	127	242	239	240
51	130	256	252	254
52	132	270	264	267
53	135	285	276	280
54	137	299	289	294
55	140	313	301	307
56	142	327	313	320
57	145	341	326	333
58	147	356	338	347
59	150	370	350	360
60	152	384	363	373
61	155	398	375	387
62	158	412	387	400
63	160	427	400	413
64	163	441	412	427
65	165	455	424	440
66	168	469	437	453
67	170	483	449	467

CHILDREN 3 TO 6 YEARS ZAPLETAL††		
HEIGHT		PEAK EXPIRATORY FLOW RATE [liters/minute]
[inches]	[cm]	
35	89	93
36	91	99
37	94	105
38	97	112
39	99	119
40	102	125
41	104	133
42	106	140
43	109	147
44	112	155
45	114	163
46	117	171
47	119	180
48	122	189
49	125	197
50	127	206
51	130	216

*Hankinson J, Odencrantz J, Fedan K: Spirometrics Reference Values from a Sample of the General U.S. Population (NHANES III). Am J Respir Crit Care Med 1999;159:179-187.

†Polgar G, Promhadt V: Pulmonary function testing in children: Techniques and standards. Philadelphia, W.B. Saunders Company, 1971.

††Zapletal A, Chalupova' J: Forced Expiratory Parameters in Healthy Preschool Children (3 - 6 Years of Age). Pediatric Pulmonology 2003; 35:200-207.

While not useful for assessing asthma severity, A peak flow meter is a useful management tool for establishing control

Recommended Frequency of Office Spirometry

- At the time of initial assessment
-After treatment is initiated and symptoms and peak flows have stabilized, to document attainment of (near) "normal" airway function
- During a period of progressive or prolonged loss of asthma control
- At least every 1–2 years to assess the maintenance of airway function

May be indicated more often than every 1– 2 years, depending on the clinical severity and response to management

Should be followed to detect potential for decline and rate of decline of pulmonary function over time

National Heart, Lung, and Blood Institute, National Asthma Education and Prevention Program: Expert Panel Report 3: Guidelines for the Diagnosis and Management of Asthma, Full Report 2007

Components of Control		Classification of Asthma Control (Children 0-4 years of Age)		
		Well Controlled	Not Well Controlled	Very Poorly Controlled
Impairment	Symptoms	≤ 2 days per week	>2 days per week	Throughout the day
	Nighttime awakenings	≤1/month	>1/month	≥1x/week
	Short acting beta agonists for symptom control (not prevention of EIB)	≤2 days per week	>2 days per week	Several times per day
	Interference with normal activity	None	Some limitation	Extremely limited
Risk Risk of exacerbation or progressive loss of lung function	Exacerbations requiring oral systemic steroids	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.		

National Heart, Lung, and Blood Institute, National Asthma Education and Prevention Program: Expert Panel Report 3: Guidelines for the Diagnosis and Management of Asthma, Full Report 2007

Components of Control		Classification of Asthma Control (Children 5-11 years of Age)		
		Well Controlled	Not Well controlled	Very Poorly Controlled
Impairment	Symptoms	≤2 days/wk but not more than once on each day	>2 days/wk or multiple times on ≤2 days/wk	Throughout the day
	Nighttime Awakenings	≤1x/month	≥2x/month	≥2x/week
	Short acting beta agonist use for symptom control (not prevention of EIB)	≤2 days per week	>2 days per week	Several times per day
	Interference with normal activity	None	Some limitation	Extremely limited
	Lung Function			
	FEV1 or peak flow	>80% pred/personal best	60 – 80% pred/personal best	<60% pred/personal best
	FEV1/FVC	>80%	75-80%	<75%
Risk Risk of exacerbation or progressive loss of lung function	Exacerbations requiring oral systemic steroids	0-1/year	≥2/year	
	Reduction in lung growth	Evaluation of reduction in lung growth 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 the overall assessment of risk.		

National Heart, Lung, and Blood Institute, National Asthma Education and Prevention Program: Expert Panel Report 3: Guidelines for the Diagnosis and Management of Asthma, Full Report 2007

Components of Control		Classification of Asthma Control (Children ≥12 years of Age)		
		Well Controlled	Not Well controlled	Very Poorly Controlled
Impairment	**Symptoms**	**≤2 days/wk**	**>2 days/wk**	**Throughout the day**
	Nighttime Awakenings	**≤2x/month**	**1-3x/wk**	**≥4x/week**
	Short acting beta agonist use for symptom control (not prevention of EIB)	**≤2 days per week**	**>2 days per week**	**Several times per day**
	Interference with normal activity	**None**	**Some limitation**	**Extremely limited**
	Lung Function **FEV1 or peak flow** **Validated Questionnaires**	**>80% pred/personal best**	**60 – 80% pred/personal best**	**<60% pred/personal best**
Risk Risk of exacerbation or progressive loss of lung function	Exacerbations requiring oral systemic steroids	**0-1/year** **Consider severity and interval since last exacerbation**	**≥2/year** **Consider severity and interval since last exacerbation**	
	Progressive loss of lung function Treatment related adverse effects	**Evaluation of progressive loss of lung function requires long term follow up** **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.**		

National Heart, Lung, and Blood Institute, National Asthma Education and Prevention Program: Expert Panel Report 3: Guidelines for the Diagnosis and Management of Asthma, Full Report 2007

Management based on Control

Recommended Action for Treatment	Well controlled	Not well controlled	Poorly controlled
	•Maintain current Treatment •Follow every 1 to 6 months •Consider step down if well controlled at least 3 months	•Step up 1 step •Reassess in 2 to 6 weeks •If no clear benefit in 4 to 6 wks, consider alternative diagnosis or adjusting therapy •For side effects consider alternative treatment options	•Consider short course of oral systemic steroids •Step up 1-2 steps •Reevaluate in 2 weeks •If no clear benefit in 4 to 6 wks, consider alternative diagnosis or adjusting therapy •For side effects consider alternative treatment options
	Before Step up in therapy: **Review adherence to medication, inhaler technique, and environmental Control. If alternative treatment was used, discontinue it and use preferred treatment for that step.**		

Consult asthma specialist if step 4 care (step 3 if 0 - 4 years old) or higher required. Consider consultation at step 3 (step 2 if 0 - 4 years old)

National Heart, Lung, and Blood Institute, National Asthma Education and Prevention Program: Expert Panel Report 3: Guidelines for the Diagnosis and Management of Asthma, Full Report 2007

Role of Nitric Oxide in Asthma

- FENO (fraction of exhaled NO) elevated in asthmatics versus healthy controls (Persson et al Lancet 1994)
- FENO can be a biomarker of eosinophilic airway inflammation in asthma patient -- correlation between FENO and eosinophillic inflammation in airway biopsies and sputum eosinophil levels of children with asthma (Payne et al Am J Resp Crit Care Med 2001, Piacentini et al Eur Respir J 1999)
- ICS decreases FENO significantly in a dose dependent manner in patients with asthma (Bodini A et al Mediators of Inflammation Vol 2006, Kharitonov SA Am J Respir Crit Care Med 1996)
- FENO measurements are easy to obtain and a sensitive marker of eosinophillic airway inflammation and steroid responsiveness which can aid with asthma diagnosis management (American Thoracic Society Recs)

Jordan – 8 years old

- Presents with 3 days a weeks of wheeze and chest tightness with no night symptoms and lung function shows forced expiratory volume in 1 second (FEV1) 96% predicted
  Jordan is on no controller therapy

- What is her asthma severity?
  a. Intermittent Asthma
  b. Mild Persistent Asthma
  c. Moderate Persistent Asthma
  d. Severe Persistent Asthma
  e. Insufficient information available

Jordan – 8 years old

- Appropriately classified as (b) mild persistent asthma and started on low dose inhaled corticosteroid (this is preferred and leukotriene antagonists, mast cell stabilizers and methylxanthines are alternative therapies)

Components of Severity		Classification of Asthma Severity (Children 5-11 years of Age)			
		Intermittent	Persistent		
			Mild	Moderate	Severe
Impairment	Symptoms	≤2 days per week	>2 days/wk but not daily	Daily	Throughout the day
	Nighttime Awakenings	≤2x/month	3-4x/month	>1x/wk but not nightly	Often 7x/wk
	Short acting beta agonist use for symptom control (not prevention of EIB)	≤2 days per week	>2 days/wk 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% pred FEV1/FVC >85%	FEV1 ≥80% pred FEV1/FVC >80%	FEV1 = 60 - 80%pred FEV1/FVC = 75 - 80%	FEV1 < 60%pred FEV1/FVC < 75%
Risk Risk of exacerbation or progressive loss of lung function	Exacerbations requiring oral systemic steroids	0-1 per year	≥2 in one year		
		Consider severity and interval since last exacerbation. Frequency and severity may fluctuate overtime for any patient in any severity category. Relative annual risk of exacerbation may be related to FEV1.			

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Jordan – 8 years old

- Returns 4 weeks later on controller therapy. Jordan's mother is pleased the child has no symptoms
- Mother says the child coughed 3 nights (but not > 1 night/wk) but feels it is due to nasal drip
- Jordan's Peak flow meter reading is 70% of best (yellow zone)

Jordan – 8 years old

Based on this information, what is Jordan's asthma control

a. Well controlled
b. Not Well controlled
c. Poorly controlled
d. Unsure with information given

Jordan – 8 years old

Based on this information, what is Jordan's asthma control

a. Well controlled

b. Not Well controlled

c. Poorly controlled

d. Unsure with information given

Components of Control		Classification of Asthma Control (Children 5-11 years of Age)		
		Well Controlled	Not Well controlled	Very Poorly Controlled
Impairment	Symptoms	≤2 days/wk but not more than once on each day	>2 days/wk or multiple times on ≤2 days/wk	Throughout the day
	Nighttime Awakenings	≤1x/month	≥2x/month	≥2x/week
	Short acting beta agonist use for symptom control (not prevention of EIB)	≤2 days per week	>2 days per week	Several times per day
	Interference with normal activity	None	Some limitation	Extremely limited
	Lung Function			
	FEV1 or peak flow	>80% pred/personal best	60 – 80% pred/personal best	<60% pred/personal best
	FEV1/FVC	>80%	75-80%	<75%
Risk Risk of exacerbation or progressive loss of lung function	Exacerbations requiring oral systemic steroids	0-1/year	≥2/year	
	Reduction in lung growth	Evaluation of reduction in lung growth 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 the overall assessment of risk.		

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Jordan – 8 years old

Based on this information, what would you do with Jordan's therapy?

a. Recommend short acting beta agonist prior to bedtime
b. Therapy at step 1 care
c. Therapy at step 2 care
d. Therapy at step 3 care
e. Therapy at step 3 or 4 care

Jordan – 8 years old

Based on this information, what would you do with Jordan's therapy?

a. Recommend short acting beta agonist prior to bedtime
b. Therapy at step 1 care
c. Therapy at step 2 care
d. Therapy at step 3 care
e. Therapy at step 3 or 4 care

Management based on Control

Recommended Action for Treatment	Well controlled	Not well controlled	Poorly controlled
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	Before Step up in therapy: Review adherence to medication, inhaler technique, and environmental Control. If alternative treatment was used, discontinue it and use preferred treatment for that step.		

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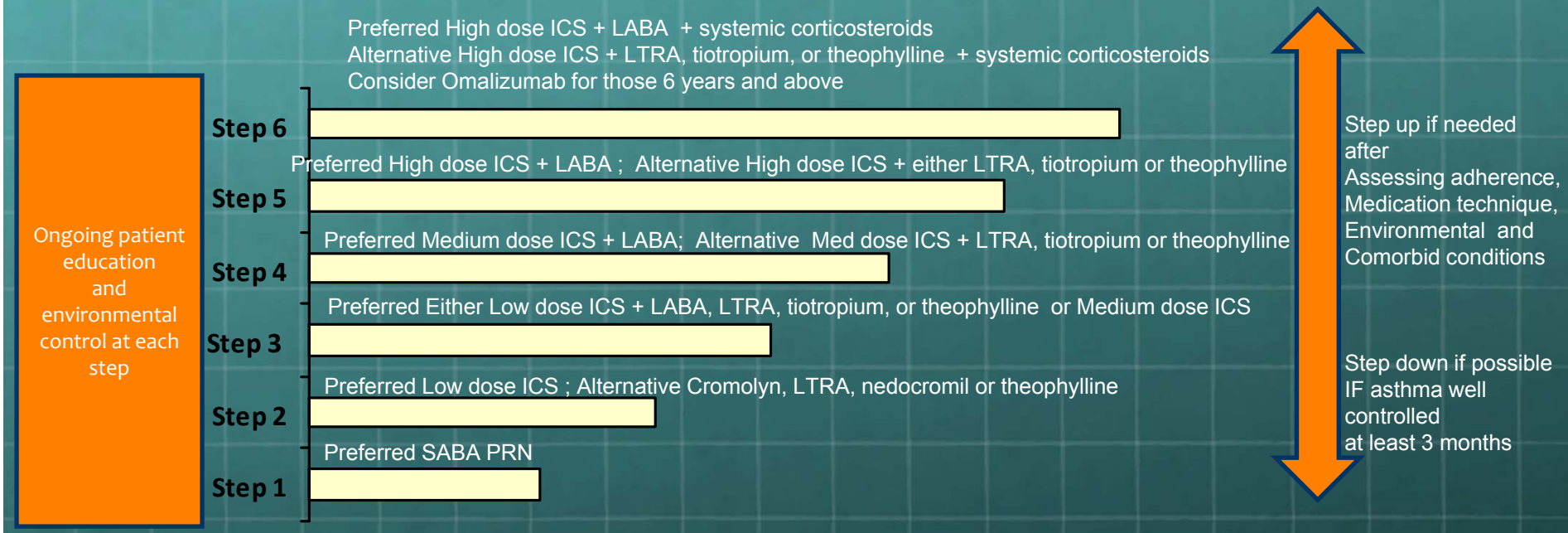
Step wise Approach to Asthma Management Ages 5-11 years old



Step 1 pertains to intermittent asthma
Steps 2 – 6 pertains to persistent asthma when daily therapy is needed

SABA – short acting beta agonist; ICS – inhaled corticosteroid; LABA long acting beta agonist
LTRA – leukotriene receptor antagonist
National Heart, Lung, and Blood Institute, National Asthma Education and Prevention Program: Expert Panel Report 3: Guidelines for the Diagnosis and Management of Asthma, Full Report 2007

Jordan – 8 years old

What therapy is appropriate for Jordan?

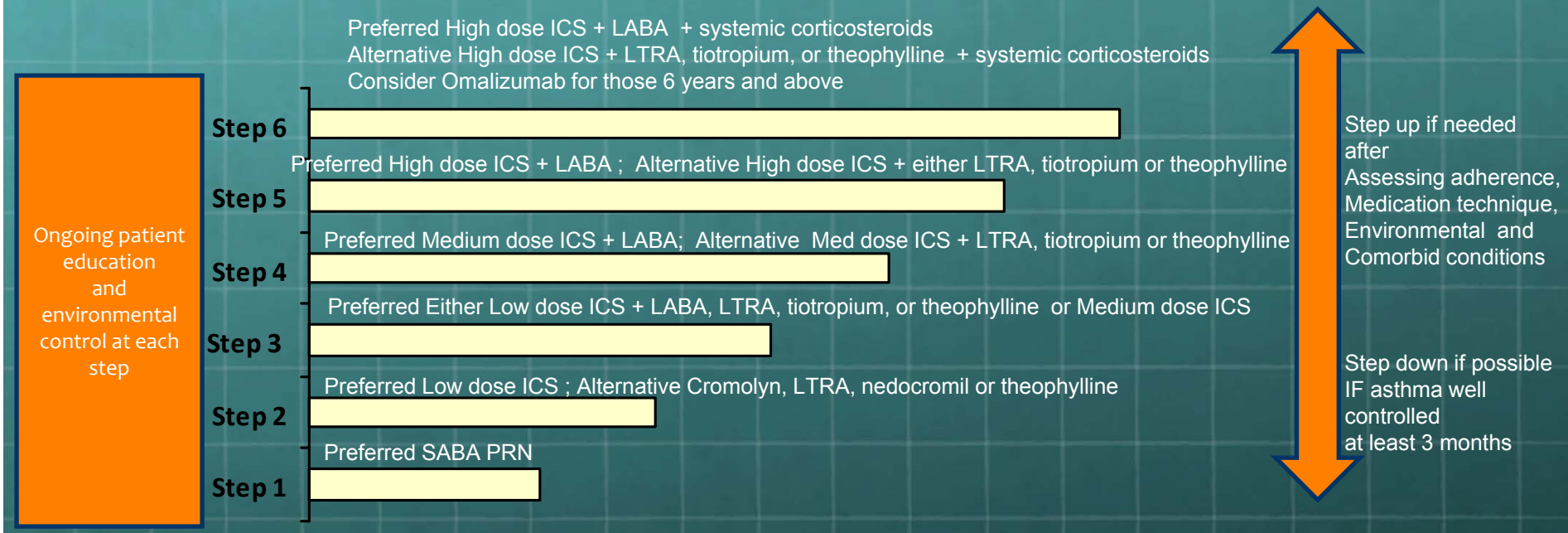
a. Cromolyn alone
b. Low dose inhaled corticosteroid in addition to leukotriene antagonist
c. Medium dose inhaled corticosteroid
d. Theophylline alone
e. b or c would be appropriate

Jordan – 8 years old

What therapy is appropriate for Jordan?

a. Cromolyn, alone
b. Addition of leukotriene antagonist to low dose inhaled corticosteroid
c. Medium dose inhaled corticosteroid
d. Theophylline, alone
e. b or c would be appropriate

Step wise Approach to Asthma Management Ages 5-11 years old



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Jordan – 8 years old

Before adjusting Jordan's therapy, what information would you want to know?

Jordan – 8 years old

Before adjusting Jordan's therapy, what information would you want to know?

Medication compliance and technique (is controller therapy taken daily?)
Environmental issues: Tobacco smoke, allergens (new pets, dust mite), particulate matter/noxious matter (paint, perfume, parental occupational matter)
Comorbidities (i.e. reflux, sinisitis, atopy)

Conclusion

- Asthma still results in considerable morbidity and mortality in the pediatric population
- Identifying asthma phenotypes and endotypes can aid in predicting natural history of asthma and individualizing care
- Proper diagnosis of asthma and appropriately assigning asthma severity is important to management – consider alternative diagnosis
- Follow up for assessment of control and lung function (if child able) is important
- Patient education regarding review of adherence to medication/technique, environmental control and comorbid conditions should be ongoing

Resource

- National Heart, Lung, and Blood Institute, National Asthma Education and Prevention Program: Expert Panel Report 3: Guidelines for the Diagnosis and Management of Asthma, Full Report 2007

Novel concepts in airway inflammation and remodeling in asthma. Eur Resp J 2015; 46:1796-1804

Mechanisms mediating pediatric severe asthma and potential novel therapies. Fron Pediatr. July 2017; 5(154): 1- 13

Clinical phenotypes in asthma during childhood. Clin & Experimental Allergy. July 2017: 47 (7): 848-855