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PEDIATRIC ASTHMA

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Disclosures

Dr. Izadi serves on the scientific advisory board and conducts clinical research for Sumitomo Pharma America

These disclosures do not influence today's presentation

Objectives

1) Describe why underdiagnosis of asthma occurs in children and some factors that increase the risk of developing asthma

2) List key elements to obtain from the history to evaluate asthma

3) Discuss importance of starting ICS early for persistent asthma and when PRN ICS/LABA can be considered

4) Contrast technique and age considerations for HFA vs dry powder inhalers

5) Discuss important elements to consider regarding racial and social disparities in asthma

Outline

1) Introduction
2) Differential
3) Diagnosis
4) Evaluation
5) Asthma Guidelines and Steps
6) Asthma Inhaler Types
7) Important Considerations
8) Racial and Social Considerations

Asthma Introduction

- Most prevalent chronic respiratory disease worldwide
- Affects >300 million of all ethnic groups and all ages
- Most common chronic disease in children

- **General Definition**: chronic inflammatory disease of the airways characterized by variable symptoms of wheeze, breathlessness, chest tightness and/or cough associated with expiratory airflow limitation

Asthma Differential

Clinical clue	Possible diagnosis
PERINATAL AND FAMILY HISTORY	
Symptoms present from birth	Chronic lung disease of prematurity, PCD, CF
Family history of unusual chest disease	CF, Neuromuscular disorders, PCD
Severe upper respiratory tract disease	PCD
SYMPTOMS AND SIGNS	
Persistent moist cough	PBB, Bronchiectasis, Recurrent aspiration, PCD, CF
Excessive vomiting	GERD (w/without aspiration)
Dysphagia	Swallowing problems (w/without aspiration)
Breathlessness with light headedness and peripheral tingling	Dysfunctional breathing, Panic attacks
Inspiratory stridor	Tracheal or laryngeal disorder
Abnormal voice or cry	Laryngeal problems
Focal signs in chest	Developmental anomaly, FB, Post-infective syndrome
Persistent wheeze	Extrinsic intra thoracic airway compression, Airway-malacia, Luminal obstruction, CF, FB
Finger clubbing	CF, Bronchiectasis
Failure to thrive	CF, GERD

CF, cystic fibrosis; FB, foreign body; GERD, gastro-esophageal reflux disease; PBB, protracted bacterial bronchitis; PCD, primary ciliary dyskinesia.

Alternative diagnosis	When to suspect
Cystic fibrosis and bronchiectasis	Daily cough productive of sputum, clubbing, malabsorption and failure to thrive, recurrent chest infections, airways bacterial colonization
Immunodeficiency	Recurrent airway infections, Systemic infections (from a few months of age)
Primary ciliary dyskinesia	Neonatal upper airway symptoms, Chronic rhinosinusitis, Recurrent otitis media, Daily wet cough, Laterality defects
Protracted Bacterial Bronchitis	Cronich wet cough, Poor response to Beta-2 agonists, Good response to prolonged course of antibiotics
Airway malacia	Monophonic wheeze when the child is active, High risk setting (i.e., pt operated for tracheo-esophageal fistula or vascular ring), Presence of associated stridor
Airway foreign body	Abrupt onset of symptoms, History of choking, Unilateral monophonic wheeze, Focal hyperinflation of lung
Habit cough	Prolonged dry, honking cough; Absence of cough during sleep; Absence of any physical findings
Vocal cord dysfunction	Absence of structural abnormalities, Sudden worsening of "asthma" symptoms, No response to asthma medications
Bronchiolitis obliterans	History of severe viral respiratory infection in the first 3 years of life

Ullmann, Nicola, et al. *Frontiers in pediatrics* 6 (2018): 276.

Asthma Diagnosis

Underdiagnosis is a problem in pediatrics

- Mainly a clinical diagnosis, asthma can begin at **any age**
- Objective testing (i.e spirometry) **less useful** in children
- Most childhood asthma will improve or remit

Many admissions for asthma in young children could be prevented by <u>earlier diagnosis and/or controller</u>

- Start ICS for any exacerbation requiring systemic steroids or >1 PCP/ER visit that only requires albuterol

Asthma Predictive Index (API)

Major Criteria	Minor Criteria
1. Parental MD asthma	1. MD allergic rhinitis
2. MD eczema	2. Wheezing apart from colds
	3. Eosinophilia (⩾ 4%)

* Loose index for the prediction of asthma: Early wheezer plus at least one of two major criteria or two of three minor criteria. Stringent index for the predication of asthma: Early frequent wheezer plus at least one of two major criteria or two of three minor criteria.

Castro-Rodríguez, José A., et al. AJRCCM 162.4 (2000): 1403-1406.
https://www.mdcalc.com/asthma-predictive-index-api

- For children ≤3 years, predicts future asthma risk
- If positive, consider more empiric asthma treatment

Pediatric Asthma Risk Score (PARS)

Pediatric Asthma Risk Score (PARS) Scoring Sheet			
	Possible Scores		
	No	Yes	Child's Score
1. Parental Asthma	0	2	
2. Eczema before age 3 years	0	2	
3. Wheezing apart from colds	0	3	
4. Wheezing before age 3 years	0	3	
5. African-American Race	0	2	
6. SPT positive to ≥ 2 aero and/or food allergens	0	2	
Child's PARS (add lines 1-6 above):			

Myers et al. JACI 143.5 (2019): 1803-1810.

- Better sensitivity and specificity for mild/moderate asthma
- Calculates asthma risk percentage by age 7 based on score
- **https://pars.research.cchmc.org/**

Evaluation = All About Control

Control = **Risk/Impairment** given treatment they actually take (**Adherence)**

Risk = exacerbations and systemic steroids

- Frequency of hospital/intubations, ER, sys steroids for asthma (inc. PCP Rx)
- Get lifetime estimate and over the last year/date of most recent

Impairment = asthma symptoms

- Frequency of Symptoms/Albuterol required, Nighttime Awakening w/cough
- Exercise symptoms are less important

Treatment = adherence of asthma medications

- Frequency of meds that they **actually take** (not just prescribed)
- Normalize poor adherence before you ask, ask in multiple ways
- **Technique is often poor** and not evaluated
- Albuterol unfortunately initiated late in illness or only if symptoms are *really* bad

Guidelines

- Several guidelines for asthma, recently updated 2020-2021
- - **“SMART”, Single Maintenance and Rescue Therapy** introduced
  - National Heart Lung, and Blood Institute (NHLBI) of US NIH
  - Global Initiative for Asthma (GINA)

- Keys
  - NHLBI: add ICS to PRN albuterol for illness in mild asthma (0-4y)
  - NHLBI: **Uncontrolled** is symptoms twice or more **per week**
  - GINA: for rescue use ICS with every PRN albuterol or PRN ICS/LABA
  - GINA: **Uncontrolled** is symptoms twice or more **per month**

- **Bottom Line**
  - Needing/Taking a lot of PRN albuterol has poor outcomes, **Uncontrolled** is not ok.
    - **Add Daily ICS Early or make them take ICS whenever they take Rescue**
  - Patients prescribed daily ICS have poor adherence
    - So take ICS whenever they take Rescue or take ICS/LABA for rescue so at least get some ICS

NHLBI/GINA Combined Simple Steps

	Intermittent Step 1	Mild Persistent Step 2	Persistent Step 3+
Classification	Symptoms ≤2 week **and** No exacerbations	Symptoms ≥2 week or 1 Exacerb in last year	Symptoms most days or Multiple exacerbations in last year ***Refer to specialist***
All Ages	PRN Albuterol Consider + Daily ICS during illness (0-4y) OR ICS with each PRN Albuterol use (any age)	Daily ICS* Low Dose +PRN Albuterol *Can also consider ICS/LABA	Daily ICS Mid-High Dose + PRN Albuterol OR Daily ICS/LABA Low-Mid† -Dose + PRN Albuterol †Can also consider High-Dose
Alternative Route for ≥12y	PRN ICS/Formoterol	PRN ICS/Formoterol OR Daily ICS* Low Dose + PRN ICS/Formoterol	Daily ICS/LABA Low-Mid† -Dose + PRN ICS/Formoterol

SMART Considerations

- SMART requires **Formoterol** LABA

- SMART is **not always** the "best"
  - Careful changing inhaler process family is used to
  - Formoterol may not give enough relief and at most Q4H
  - Highest dose offered may be more mid-dose (Budesonide/Formoterol 160/4.5)
  - Some patients may respond to Salmeterol better

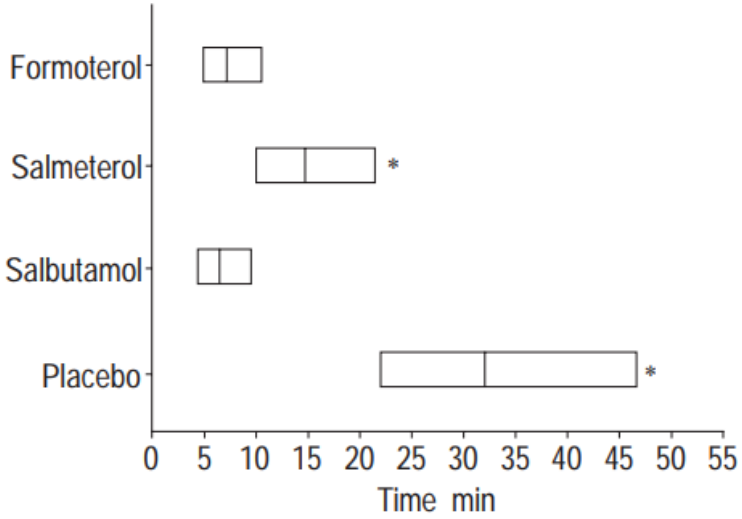

Fig. 1. – Geometric mean value and 95% confidence interval for the time to recovery of forced expiratory volume in one second (FEV_1) to 85% of baseline after a methacholine-induced fall in FEV_1 of ≥30% with formoterol, 12 µg *via* Turbuhaler®; salmeterol, 50 µg *via* Diskhaler®; salbutamol, 50 µg *via* Turbuhaler® and placebo. *: significantly different from formoterol ($p<0.017$).

Children's Hospital Los Angeles

2024 Respiratory Treatments

Allergy & Asthma Network

800.878.4403 • AllergyAsthmaNetwork.org

Allergy & Asthma Network is a national nonprofit organization dedicated to ending needless death and suffering due to asthma, allergies and related conditions through outreach, education, advocacy and research.

American College of Allergy, Asthma & Immunology

VIATRIS · Theravance Biopharma

DSI - DOSE INDICATOR
G - GENERIC AVAILABLE
N - NEBULIZER VIAL
DISEASE STATES:
A - ASTHMA
C - COPD

SHORT-ACTING BETA$_2$-AGONIST (SABA) BRONCHODILATORS
relax tight muscles in airways and offer quick relief of symptoms such as coughing, wheezing and shortness of breath for 3-6 hours

- **Albuterol Sulfate Inhalation Solution** 0.63, 1.25 mg, 2.5mg; 3 mL — G N
- **ProAir RespiClick®** 90 mcg — albuterol sulfate inhalation powder — DSI A
- **Proventil® HFA** 90 mcg — albuterol sulfate — DSI A G
- **Ventolin® HFA** 90 mcg — albuterol sulfate — DSI A G
- **Xopenex®** 0.31, 0.63, 1.25 mg/3 mL — levalbuterol hydrochloride inhalation solution — A G N
- **Xopenex HFA®** 45 mcg — levalbuterol tartrate — A G

SABA and ICS
contains SABA to relax airway muscles and offer quick relief of symptoms, and inhaled corticosteroid (ICS) to reduce inflamed airways

- **AIRSUPRA®** 90/80 mcg — albuterol and budesonide — DSI A

INHALED CORTICOSTEROIDS (ICS)
reduce and prevent swelling of airway tissue; they do not relieve sudden symptoms of coughing, wheezing or shortness of breath

- **Alvesco® HFA** 80, 160 mcg — ciclesonide — DSI A
- **Arnuity® Ellipta®** 50, 100, 200 mcg — fluticasone furoate inhalation powder — DSI A
- **Asmanex® HFA** 50, 100, 200 mcg — mometasone furoate — DSI A
- **Asmanex® Twisthaler®** 110, 220 mcg — mometasone furoate inhalation powder — DSI A
- **Fluticasone Propionate Diskus Inhalation Powder** 50, 100, 250 mcg — authorized generic of Flovent Diskus — DSI A
- **Fluticasone Propionate HFA** 44, 110, 220 mcg — authorized generic of Flovent HFA — DSI A
- **Pulmicort Flexhaler®** 90, 180 mcg — budesonide inhalation powder — DSI A
- **Pulmicort Respules®** 0.25, 0.50, 1.0 mg/2 mL — budesonide inhalation suspension — A G N
- **QVAR Redihaler®** 40, 80 mcg — beclomethasone dipropionate — DSI A

LONG-ACTING BETA$_2$-AGONIST (LABA) BRONCHODILATORS
relax tight muscles in airways and offer lasting relief of symptoms such as coughing, wheezing and shortness of breath for at least 12 hours

- **Brovana®** 15 mcg/2 mL — arformoterol tartrate inhalation solution — C N
- **Perforomist®** 20 mcg/2 mL — formoterol fumarate inhalation solution — C N
- **Serevent® Diskus®** 50 mcg — salmeterol xinafoate inhalation powder — DSI A C
- **Striverdi® Respimat®** 2.5 mcg — olodaterol hydrochloride — DSI C

MUSCARINIC ANTAGONISTS (ANTICHOLINERGICS)
relieve cough, sputum production, wheeze and chest tightness associated with chronic lung diseases

SHORT-ACTING

- **Atrovent® HFA** 17 mcg — ipratropium bromide — DSI C

LONG-ACTING

- **Incruse® Ellipta®** 62.5 mcg — umeclidinium inhalation powder — DSI C
- **Ipratropium Bromide Inhalation Solution** 0.5/3 mg; 3 mL — C G N
- **Spiriva® HandiHaler®** 18 mcg — tiotropium bromide inhalation powder — C
- **Spiriva® Respimat®** 1.25, 2.5 mcg — tiotropium bromide — DSI A C
- **Tudorza® Pressair®** 400 mcg — aclidinium bromide inhalation powder — DSI C
- **Yupelri®** 175 mcg; 3 mL — revefenacin inhalation solution — C N

COMBINATION MEDICATIONS
contain ICS and LABA

- **Advair Diskus®** 100/50, 250/50, 500/50 mcg — fluticasone propionate and salmeterol inhalation powder — DSI A C G
- **Advair® HFA** 45/21, 115/21, 230/21 mcg — fluticasone propionate and salmeterol xinafoate — DSI A G
- **AirDuo® RespiClick®** 55/14, 113/14, 232/14 mcg — fluticasone propionate and salmeterol inhalation powder — DSI A G
- **Breo® Ellipta®** 50/25, 100/25, 200/25 mcg — fluticasone furoate and vilanterol inhalation powder — DSI A C G
- **Breyna®** 80/4.5, 160/4.5 mcg — budesonide and formoterol fumarate dihydrate (approved generic of Symbicort) — DSI A C
- **Dulera®** 50/5, 100/5, 200/5 mcg — mometasone furoate and formoterol fumarate dihydrate — DSI A
- **Symbicort®** 80/4.5, 160/4.5 mcg — budesonide and formoterol fumarate dihydrate — DSI A C G
- **Wixela Inhub®** 100/50, 250/50, 500/50 mcg — fluticasone propionate and salmeterol xinafoate (approved generic of Advair Diskus) — DSI A C

contain LABA and long-acting muscarinic antagonist (LAMA)

- **Anoro® Ellipta®** 62.5/25 mcg — umeclidinium and vilanterol inhalation powder — DSI C
- **Bevespi Aerosphere®** 9/4.8 mcg — glycopyrrolate and formoterol fumarate — DSI C
- **Duaklir® Pressair®** 400/12 mcg — aclidinium bromide and formoterol fumarate — DSI C
- **Stiolto® Respimat®** 2.5/2.5 mcg — tiotropium bromide and olodaterol — DSI C

contain ICS, LABA and LAMA

- **Trelegy® Ellipta®** 200/62.5/25 mcg, 100/62.5/25 mcg — fluticasone furoate, umeclidinium and vilanterol inhalation powder — DSI A C
- **Breztri Aerosphere®** 160/9/4.8 mcg — budesonide, glycopyrrolate and formoterol fumarate — DSI C

contain SABA and short-acting muscarinic antagonist (SAMA)

- **Combivent® Respimat®** 20/100 mcg — ipratropium bromide and albuterol — DSI C
- **Ipratropium Bromide and Albuterol Sulfate Inhalation Solution** 0.5mg/2.5mg; 3ml — C G

BIOLOGICS
target cells and pathways that cause airway inflammation; delivered by injection or IV

- **Cinqair®** 62.5/25 ml — reslizumab — A
- **Dupixent®** 100, 200, 300 mg — dupilumab — A
- **Fasenra®** 30 mg — benralizumab — A
- **Nucala®** 100 mg — mepolizumab — A
- **Tezspire®** 210 mg — tezepelumab-ekko — A
- **Xolair®** 75 to 375 mg — omalizumab — A

PDE4 INHIBITORS
target lung inflammation and reduce exacerbations

- **Daliresp®** 250, 500 mcg — roflumilast — C

LEUKOTRIENE MODIFIERS
block chemicals called leukotrienes that cause airway inflammation; available as tablet or granules

- **Singulair®** 4, 5, 10 mg — montelukast — A
- **Zafirlukast** 10, 20 mg — A
- **Zileuton** 600 mg — A

Reviewed by Dennis Williams, PharmD

Generic versions of some brand name inhalers are not included on this poster. Generic inhalers may be a different color than brand name versions.

Treatments

	Nebulizer 	Propellent Actuated 	Breath Actuated 
Form	"Nebulized" Machine & Mask	"Puffs" HFA **& Spacer** +/- Mask	"Inhalations" Diskus format or Click Devices
Technique	Keep mask on for **10-15 minutes** Requires no coordination	Younger (<8y, *including infants*) -Spacer + Mask: per puff breathe normally in/out 10 times Older (≥8y) -Spacer: per puff **slow** deep breath, hold 10 sec **Almost all are Suspension:** Shake 1st if not used within week, 2 puffs qday > 1 puff bid	Younger (<6y) -**Not recommended** Older (≥6y): -per inhalation load device with click/tab breathe in **fast** and deep, hold 10 sec
Key ICS	Budesonide	Fluticasone Fluticasone/Salmeterol Budesonide/**Formoterol** Mometasone/**Formoterol**	Beclomethasone Fluticasone/Salmeterol Fluticasone furoate/Vilanterol

Treatment Considerations

- Spacer for HFA is important
  - Protective against technique errors and side effects

- ICS/LABA preferred and becoming less difficult
  - Especially consider if high impairment and/or exercise symptoms
  - FDA sometimes an issue, Only *Diskus* form *goes* down to 4y, Inhaler starts at 6y
  - Less insurance prior authorization required

- Montelukast is not for everyone
  - Particularly helpful in isolated exercise-induced asthma (especially older)
  - Interestingly, good evidence (DBPC studies) suggest it can help in pediatric OSA
  - **FDA Black Box:** neuropsychiatric events, concern for increased suicidality (adolescents & adults)
  - also known for vivid dreams/nightmares and rarely behavioral changes

Other Considerations

- Asthma Action Plans
  - Written plan rec for all patients in general practice setting

- Controlling rhinitis is important
  - *Daily proper use* of nasal corticosteroids (Fluticasone) can help asthma

- Environmental allergies can play a major role
  - **Check Environmental IgEs**
  - Do **NOT** check Food IgEs for chronic asthma or rhinitis
    - Be careful, do **NOT** send "Childhood Allergy Panel" or "Childhood Allergy Profile," they contain foods with the environmentals

Racial and Social Disparities

- Significant racial disparities exist
  - For example, Black and Puerto Rican Americans 2 to 3 times more likely to be hospitalized and die from asthma
  - Black Americans are 5 times more likely to visit ER for asthma

- Guidelines generally based on mostly white populations
  - Higher risk groups may need earlier/higher treatments
  - Advocate for inclusion of underrepresented groups in research

Racial and Social Disparities

- Social determinants of health are important
  - Housing, transportation, food insecurity have major impact
  - Consider lack of access to care and barriers to adherence
  - Consider difficult air pollution and indoor allergen circumstances
  - **Exacerbations = Start ICS**, take responsibility even in ED
  - Elicit social worker assistance and services early

- Consider language barrier and education
  - Proper translation and time for education is important

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