Asthma Management Across the Lifespan: Age-specific Considerations for Diagnosis and Treatment

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Disclosures

- Speaker for Aerocrine, Genentech, Meda, and Merck.
- I have no conflicts of interest relative to today’s presentation.
Learning Objectives

- Upon completion of this session, participants should be able to identify age specific considerations of asthma as it relates to childhood, adolescence, pregnancy, and older adults.

- Upon completion of this session, participants should be able to identify asthma treatment options for children and adults.
Asthma is a:

- A. Greek word meaning “panting”
- B. Latin word meaning “wheezing”
- C. Egyptian word meaning “lungs”
- D. Hebrew word meaning “chest congestion”
Asthma is a:

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- B. Latin word meaning “wheezing”
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- D. Hebrew word meaning “chest congestion”
Annual Burden of Asthma

- 6.8 million (9.3%) children diagnosed
- 6.8 million (8.7%) adults diagnosed
- 1.8 million emergency department visits
- 14 million missed school days annually
- 14.2 million medical office visits

#1 Pediatric Chronic Illness

CDC, 2014
Definition of Asthma

A chronic inflammatory disease of the airways with the following clinical features:

- Episodic and/or chronic symptoms of airway obstruction
- Bronchial hyperresponsiveness to triggers
- Evidence of at least partial reversibility of the airway obstruction
- Alternative diagnoses are excluded
Childhood Asthma
Wheezing - Asthma?

Wheezing with upper respiratory infections is very common in small children, but:

- Many of these children will not develop asthma.
- Asthma medications may benefit patients who wheeze whether or not they have asthma.

All that wheezes is not asthma.
Phenotypic Expressions of Childhood Wheezing Disorders

1. Viral induced wheezing
2. Severe intermittent wheezing
3. Exercise bronchospasm/asthma
4. Persistent asthma
5. Severe asthma
Rhinovirus (RV)

- RV infections can produce more than upper airway illnesses during infancy.
- Children who develop asthma by 6 years of age have a significantly increased burden of viral wheezing illnesses in early life.
- Pulmonary function abnormalities at 6 years of age are most significantly associated with early childhood wheezing illnesses due to RV (not RSV).
- Of all outpatient wheezing viral illnesses in early life, those due to RV are most significant.
RV vs. RSV
Wheezing in First 3 Years of Life and Asthma at 6 Years of Age

Oral Prednisolone for Preschool Children with Acute Virus-induced Wheezing

Randomized, double-blind, placebo-controlled trial comparing a 5-day course of oral prednisolone (10 mg daily for children 10-24 months and 20 mg daily for older children) versus placebo in 700 children between the ages of 10 and 60 months.

No difference in 7-day symptom scores, albuterol use, or readmission

Primarily non-atopic and 60% first time wheezers

Episodic Use of an ICS or LTRA in Preschool Children with Moderate-to-Severe Intermittent Wheezing

Acute Intermittent Management Strategies (AIMS)

Study Overview

- Randomized, multicenter, double-blind, placebo-controlled 1 year trial
- 238 children, 12-59 months, with recurrent episodes of intermittent wheezing
  - 2 episodes in the previous year
  - 2 urgent care visits, 2 oral steroid courses, or 1 of each
- Primary outcome = episode free days
- Secondary outcomes = symptoms scores during illnesses and oral corticosteroids (OCS) use

Primary Outcome AIMS:
Mean Proportion of Episode Free Days

![Chart showing Mean Proportion of Episode Free Days for Montelukast, Budesonide, and Conventional Therapy. The values are 0.73, 0.76, and 0.74 respectively.](image)
Results

- In preschool children with moderate-to-severe intermittent wheezing, episodic use of either budesonide or montelukast early in RTIs, when added to albuterol, did not increase the proportion of EFDs or decrease oral corticosteroid use over a 12-month period.

- However, indicators of severity of acute illnesses were reduced, particularly in children with positive asthma predictive indices.
## Asthma Predictive Index

<table>
<thead>
<tr>
<th>Major Criteria</th>
<th>Minor Criteria</th>
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</thead>
<tbody>
<tr>
<td>1. Parental MD asthma †</td>
<td>1. MD allergic rhinitis §</td>
</tr>
<tr>
<td>2. MD eczema ‡</td>
<td>2. Wheezing apart from colds</td>
</tr>
<tr>
<td></td>
<td>3. Eosinophilia (≥4%)</td>
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</tbody>
</table>

*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 prediction of asthma: early frequent wheezer plus at least one of the two major criteria or two of three minor criteria.

†History of a physician diagnosis of asthma. ‡Physician diagnosis of atopic dermatitis at age 2 or 3. §Physician diagnosis of allergic rhinitis at age 2 or 3.
Cough - Asthma?

Consider asthma in children with:

- Recurrent episodes of cough with or without wheezing
- Nocturnal awakening because of cough
- Cough that is associated with exercise/play
- Cough without wheeze is often not asthma

Cough may be the only symptom present in some patients with asthma.
A Longitudinal, Population-based, Cohort Study of Childhood Asthma Followed to Adulthood

Figure 2. Mean (± SE) FEV₁:FVC Ratios Measured at 9, 11, 13, 15, 18, 21, and 26 Years in Male (Panel A) and Female (Panel B) Study Members, According to the Pattern of Wheezing.

Results

- In an unselected birth cohort, more than one in four children had wheezing that persisted from childhood to adulthood or that relapsed after remission. The factors predicting persistence or relapse were sensitization to house dust mites, airway hyperresponsiveness, female sex, smoking, and early age at onset.

- These findings, together with persistently low lung function, suggest that outcomes in adult asthma may be determined primarily in early childhood.
Results

- The 2 treatment groups were similar at baseline for sex, race, age, weight, and height. At the end of double-blind treatment, mean growth velocity was $6.01 \pm 1.84$ cm/52 weeks for flunisolide HFA ($n = 106$) and $6.19 \pm 1.30$ cm/52 weeks for placebo ($n = 112$) ($P = .425$). Mean advancement in bone age during the 1-year study was similar for the 2 groups: $0.93 \pm 0.46$ years for flunisolide HFA ($n = 70$) and $1.01 \pm 0.41$ years for placebo ($n = 75$) ($P = .128$).

- Flunisolide HFA did not suppress growth or bone maturation at the highest approved dose for children with persistent asthma.

Long-Term Inhaled Corticosteroids in Preschool Children at High Risk for Asthma

Change in height from baseline represented by the panel on the left. The difference between groups with associated p-values represented on the right. At the end of 24 months the fluticasone group averaged 1.1 cm less than the placebo group. At the end of the observation period (months) the difference between groups was 0.7 cm.

Results

Clinical improvement was observed while the children were treated with the inhaled corticosteroid but disappeared after treatment had been discontinued.

The natural course of asthma in young children at high risk for subsequent asthma is not modified by two years of treatment with inhaled corticosteroids. The treatment, however, did reduce the burden of illness. Inhaled corticosteroids can be used to control active disease but should not be used to prevent asthma in high-risk preschool children.

Early Intervention with Budesonide in Mild Persistent Asthma

Early Intervention with Budesonide in Mild Persistent Asthma

- Budesonide therapy reduces the risk of a severe asthma exacerbation by 44% in patients with mild persistent asthma.
- Daily treatment with low dose budesonide decreases the need for oral corticosteroids in mild persistent asthma.
- Budesonide daily improves asthma control
  - More symptom free days
  - Less additional asthma medication

Spacers and Valved Holding Chambers

- Metered-dose inhalers with valved holding chambers (VHCs) have been shown to be equivalent to small-volume nebulizers (SVNs) for the delivery of bronchodilators in children.

- Advantages
  1) aerodynamic filtration: the chamber’s dimensions allow the larger particles to decelerate and deposit in the device instead of in the mouth or throat, thus reducing impaction of particles in the upper airway.
  2) provision of a reservoir of aerosol from which the infant or child can breathe tidally, thus ensuring aerosol delivery on inspiration without the need to coordinate precisely the aerosol discharge and inhalation.
Pediatric Asthma Management

- Environmental Control
- Proper Pharmacologic Treatment
- Allergen Immunotherapy
Stepwise Approach for Managing Asthma in Children Aged ≤4 Years

<table>
<thead>
<tr>
<th>Classification of Asthma Severity</th>
<th>Intermittent</th>
<th>Persistent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mild</td>
<td>Step 1</td>
<td>Step 2</td>
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<tr>
<td>Moderate</td>
<td>Step 3</td>
<td>Step 3</td>
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<tr>
<td>Severe</td>
<td>Step 3</td>
<td>Step 3</td>
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</table>

**Step 1: Intermittent Asthma**
- **Preferred:** SABA prn
- **Alternative:** cromolyn or montelukast

**Step 2: Persistent Asthma: Daily Medication**
- Consult with asthma specialist if step-3 care or higher is required. Consider consultation at step 2.

**Step 3: Step up if needed**
(first, check adherence, inhaler technique, and environmental control)

**Step 4: Assess control**

**Step 5: Step down, if possible**
(and asthma is well controlled for at least 3 months)

**Step 6: Patient Education and Environmental Control at Each Step**

**Quick-Relief Medication for All Patients**

Montelukast is indicated for prophylaxis and chronic treatment of asthma only in patients aged 12 months and older. Safety and effectiveness of montelukast in patients younger than 12 months have not been established.

Asthma in Adolescence
Teens don’t want to be “different”

- Teens underreport symptoms.
- Many teens stop taking their controller meds and rely only upon their rescue medications.
- Very common for teens to be in denial about having asthma.
- Increased risk with substance abuse.
- Uncontrolled asthma can lead to depression and low self-esteem.
Who’s Using?

- Adolescents with asthma use recreational drugs as much, if not more, than adolescents without asthma, and even more so, if they also suffer from both asthma and depression.

Bender, B. G. (2007). Depression symptoms and substance abuse in adolescents with asthma. *Annals of Allergy, Asthma & Immunology: Official Publication of the American College of Allergy, Asthma, & Immunology, 99*(4), 319-324.
Asthma and Substance Abuse

- Poor clinical status as an outcome of substance use is well documented.
- Asthma is impacted by substance use, both by harm to the underlying disease process and its impact on medical therapy.
- Individuals with substance use disorders and asthma are 1) less likely to seek out routine care, 2) experience frequent and severe health complications, 3) have increased risk for hospitalization and require longer stays.
Exercise Induced Bronchospasm (EIB)

- EIA may reflect sub optimally controlled asthma, which may require adjustment of overall therapy of asthma.
- Goal: Facilitate normal activity levels, including competitive sports.
- Individualize therapy.
Diagnosis of EIB

- Normal PFT at rest
- No other stimulus for bronchospasm
- Most common in allergic rhinitis patients
- Dx: 10% decrease FEV$_1$ after 8 minutes of exercise at 90% maximum predicted heart rate
- Rx: B-agonist before exercise, LTRA daily
Asthma and obesity tend to increase in parallel which suggests a potential link between these two conditions.

Of the 10 selected studies, eight showed positive associations between overweight/obesity and asthma. Although the role of sex is not clear, obesity precedes, and is associated with, the persistence and intensity of symptoms of asthma.

What Can Teens Do

- Avoid triggers
- Not allowing friends to smoke around them
- Hanging up wet towels and clothes and cleaning up spills before mold can grow
- Washing clothes and bedding regularly
- Clean their inhalers regularly and remember that, because the devices are pressurized, they should never leave them in a hot car or close to sources of heat.
### Stepwise Approach for Managing Asthma in Children Aged 5 to 11 Years

<table>
<thead>
<tr>
<th>Recommened Step for Initiating Treatment</th>
<th>Classification of Asthma Severity</th>
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<tbody>
<tr>
<td></td>
<td>Intermittent</td>
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<td>Mild</td>
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<td>Step 1</td>
<td>Step 2</td>
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#### Intermittent Asthma

<table>
<thead>
<tr>
<th>Step 1</th>
<th>Step 2</th>
<th>Step 3</th>
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<tbody>
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<td><strong>Preferred:</strong></td>
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<tr>
<td>SABA prn</td>
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<td><strong>Alternative:</strong></td>
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<td>cromolyn, LTRA, nedocromil, or theophylline</td>
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</tbody>
</table>

#### Persistent Asthma: Daily Medication

Consult with asthma specialist if step 4 care or higher is required. Consider consultation at step 3.

<table>
<thead>
<tr>
<th>Step 1</th>
<th>Step 2</th>
<th>Step 3</th>
<th>Step 4</th>
<th>Step 5</th>
<th>Step 6</th>
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<tbody>
<tr>
<td><strong>Preferred:</strong></td>
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<tr>
<td>low-dose ICS</td>
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<td><strong>Alternative:</strong></td>
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<tr>
<td>low-dose ICS + LABA, LTRA, or theophylline</td>
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<td>OR</td>
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<tr>
<td>medium-dose ICS</td>
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</tbody>
</table>

**Assess control**

Step down, if possible

(and asthma is well controlled for at least 3 months)

**Step up if needed**

(first, check adherence, environmental control, and comorbid conditions)

**Patient Education and Environmental Control at Each Step**

Steps 2–4: Consider subcutaneous allergen immunotherapy for patients who have allergic asthma.

**Quick-Relief Medication for All Patients**

# Stepwise Approach for Managing Asthma in Youths Aged ≥12 Years and in Adults

## Classification of Asthma Severity

<table>
<thead>
<tr>
<th>Intermittent</th>
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<tbody>
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<td>Moderate</td>
</tr>
<tr>
<td>Step 1</td>
<td>Step 2</td>
</tr>
</tbody>
</table>

### Intermittent Asthma

**Preferred:** low-dose ICS + LABA
**Alternative:** medium-dose ICS

**Preferred:** low-dose ICS + LTRA, theophylline, or zileuton

### Persistent Asthma: Daily Medication

Consult with asthma specialist if step-4 care or higher is required. Consider consultation at step 3.

**Step 5**

**Preferred:** high-dose ICS + LABA + oral corticosteroid
AND consider omalizumab for patients who have allergies

**Step 6**

**Preferred:** high-dose ICS + LABA + oral corticosteroid
AND consider omalizumab for patients who have allergies

### Patient Education and Environmental Control at Each Step

Steps 2–4: Consider subcutaneous allergen immunotherapy for patients who have allergic asthma.

### Quick-Relief Medication for All Patients

- **Preferred:** SABA pm
- **Alternative:** cromolyn, LTRA, nedocromil, or theophylline

**Step up if needed**
(first, check adherence, environmental control, and comorbid conditions)

**Assess control**

**Step down, if possible**
(and asthma is well controlled for at least 3 months)

Asthma in Pregnancy
Asthma Complicates 3-8% of Pregnancies

- Studies show that pregnant women with asthma have an increased number of asthma exacerbations and poorer asthma outcomes than non-pregnant asthma patients.

- Pregnant patients with asthma have an increased risk of lower birth weight infants than pregnant patients without asthma.


Enriquez, R., Griffin, M., Carroll, K., Wu, P., Cooper, W., Gebretsadik, T., et al. (2007). Effect of maternal asthma and asthma control on pregnancy and perinatal outcomes. *Journal of Allergy, Asthma & Immunology*, 120(3), 625-630.
Rule of 1/3’s

- 1/3 get better
- 1/3 get worse
- 1/3 stay same

Studies show that asthma often gets worse in the late 2^{nd} and 3^{rd} trimesters for pregnant patients and then tends to improve the 9^{th} month of pregnancy.
Changing physiology

- Pregnancy dyspnea
  - Increased tidal volume
  - Decreased ERV and RV and FRC
  - Intact FEV1
  - Less than normal PCO2
  - Above normal PO2
Associated Risks

Poor controlled asthma has been associated with 15% to 20 % increase in

- Preterm delivery
- Preeclampsia
- Growth retardation
- Need for C/S
- Maternal morbidity
- Maternal mortality

In patients with severe asthma, the risks increase to 30% to 100%.

Managing Asthma Exacerbations During Pregnancy

FENO guided treatment reduces exacerbations 50%

Tobacco use impacts the child in three ways: in utero exposure, after birth through environmental tobacco smoke (ETS), and through active smoking in adolescence.

The risk of developing asthma during the first 7 years was 25% higher in children whose mother smoked less than 10 cigarettes per day during pregnancy and 36% higher in children whose mothers smoked more than 10 cigarettes per day.

Allergy Shots and Pregnancy

- Allergen immunotherapy can be continued during pregnancy
- But, should **not** be started for the 1\textsuperscript{st} time in a pregnant woman
A: Well-controlled studies have failed to demonstrate a risk to the fetus.

B: Animal reproduction studies demonstrate an adverse effect on the fetus. There are no well-controlled studies in pregnant women. The potential benefits of this drug may outweigh the potential risks.

C: There is positive evidence of human fetal risk based on adverse reaction data from research or clinical experience. The potential benefits of this drug may outweigh the potential risks.

D: Studies in humans and animals have demonstrated fetal abnormalities. There is positive evidence of human fetal risk. The risks of this drug outweighs any benefit to its use.
<table>
<thead>
<tr>
<th>Drug Category</th>
<th>FDA Category</th>
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<tbody>
<tr>
<td><strong>Short-Acting Bronchodilators</strong></td>
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<tr>
<td>Albuterol HFA (ProAir, Proventil, Ventolin)</td>
<td>C</td>
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<tr>
<td>Albuterol Nebulized Solution</td>
<td>C</td>
</tr>
<tr>
<td>Levalbuterol HFA (Xopenex)</td>
<td>C</td>
</tr>
<tr>
<td>Levalbuterol Nebulized Solution</td>
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</tr>
<tr>
<td>Pirbuterol (Maxair)</td>
<td>C</td>
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<tr>
<td>Terbutaline (oral)</td>
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<td><strong>Long-Acting Bronchodilators (LABA)</strong></td>
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<td>Salmeterol Diskus (Serevent)</td>
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<tr>
<td>Formoterol (Foradil Aerolizer)</td>
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<tr>
<td><strong>Inhaled Corticosteroids (ICS)</strong></td>
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<tr>
<td>Budesonide Nebulized/DPI (Pulmicort)</td>
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<tr>
<td>Beclomethasone HFA (Qvar)</td>
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<td>Ciclesonide HFA (Alvesco)</td>
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<tr>
<td>Fluticasone HFA/Diskus (Flovent)</td>
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<td>Mometasone DPI (Asmanex Twisthaler)</td>
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<td><strong>Systemic Corticosteroids</strong></td>
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<td>Prednisone</td>
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<td>Methyl prednisone</td>
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<td><strong>Combination of ICS and LABA</strong></td>
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<tr>
<td>Budesonide/Fomoterol HFA (Symbicort)</td>
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<td><strong>Leukotriene Agents</strong></td>
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<td>Zafirlukast (Accolate)</td>
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<td>Montelukast Tablets (Singulair)</td>
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<tr>
<td>Zileuton Tablets (Zyflo CR)</td>
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<td><strong>Anticholinergic</strong></td>
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<tr>
<td>Ipratropium HFA/Nebulized Solution (Atrovent)</td>
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<tr>
<td><strong>Anti IgE</strong></td>
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<tr>
<td>Omalizumab Injectable (Xolair)</td>
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HFA = Hydrofluoroalkane Inhaler  
DPI = Dry Powder Inhaler
Asthma in Older Adults
Clinical Phenotypes That Don’t Fit

- Obesity…. 50%
- Smoking….30%
- Asthma-COPD Overlap
- Asthma in the elderly
- Severe Asthma…10%
The Landscape

- Older adults with asthma report increased and prolonged diurnal and nocturnal symptoms and have more frequent and extended asthma-related hospitalizations than younger patients.

- The greatest increase in asthma mortality rate between 1979 and 1996 occurred primarily among adults over 65 years, with older black women being the most significantly affected.

- Asthma appreciably decreases the quality of life among older adults and this age group experiences more asthma related deaths than any other age group.

Booming Population

- Older adults, defined as those 65 years and older, comprise 13% of the U.S. population.
- It is estimated by 2050 that the older adult population segment will grow to 25%.
- The largest population growth is anticipated to be in those 85 years and older.

Gibson PG, McDonald VM, Marks GM. Lancet 2010; 376:803
Asthma has been shown to be at least as common in the elderly as in younger age groups.

In one study of 2000 patients over 75, 28% had experienced wheeze in the last 12 months and 60% had had at least one respiratory symptom.

It is common for older adults with asthma to demonstrate limited or partial airway reversibility (less than 12% decrease in FEV₁) on spirometry.

This partial reversibility may be due to airway remodeling, presence of emphysema or COPD, damage to the alveoli, or bronchiectasis.
Consideration of Age in Lung Function

- Age related physiological changes in the lung
- Increased duration of exposure to “lung insults”
- Higher consequence on morbidity and mortality
- Ageing may influence response to, and treatment, of asthma
The Decline

Figure 1  Model for growth and decline of FEV<sub>1</sub>. The upper curve represents normal predicted lung function changes with age. The lower two curves represent subjects who did not achieve their maximum expected FEV<sub>1</sub>. In one case the FEV<sub>1</sub> declines at its predicted rate after the plateau phase, and in the second case (a smoker) lung function declines at an accelerated rate. Adapted from Rijken et al. (1991) Am Rev Respir Dis; 143: 1456–1457.
Lung Physiology: Intrinsic Ageing

Reduced
- Lung elasticity
- Respiratory muscle strength
- Chest wall compliance
- FEV1 (declines before FVC)
- Bronchial hyper-responsiveness
- Perception of bronchoconstriction
- Diffusion capacity
- Arterial oxygen pressure and saturation
- Ventilatory response to hypoxia and (more worryingly) hypercapnia

Increased
- Residual volume
- Lung compliance
- Oxygen uptake on exercise

Unchanged
- Total lung capacity
- Airways resistance
- Pulmonary arterial resistance
- Arterial CO2 levels
Lung Physiology: Extrinsic Ageing

- Tobacco smoking
- Occupational exposure
- Asthma
- Atopy
- Obesity
- Excessive alcohol consumption
- Respiratory infection in early life
- Nutritional status at birth
- Maternal or passive smoking
Asthma Phenotypes in Older Adults

- those with a longstanding history of moderate to severe asthma that is only partially reversible
- those diagnosed with asthma as an adult.

Current asthma guidelines do not differentiate asthma management between these two phenotypes in older adults.
Asthma Treatment in Older Adults

- Studies show that age alone does not influence response to treatment
- Factors which can influence treatment include
  - Cognition
  - Side effects (esp steroids)
  - Compliance
  - Manual dexterity
Response to Albuterol

- Older age does not alter the acute response to inhaled bronchodilator drugs.
- The average time to peak effect of albuterol is 5 to 10 minutes in both young and older patients with asthma.
- For diagnostic testing, the use of a combination of albuterol and ipratropium bromide versus the traditional use of albuterol, may produce more effective bronchodilation in older adults if there is coexisting COPD.
- The peak effect of albuterol/ipratropium bromide is 30 minutes and the results that albuterol/ipratropium produce are less specific for asthma than albuterol alone.

Concerns for Bone Density Loss

- Patients taking a prolonged course of oral corticosteroids (≥ 5 mg daily for ≥ 3 months) have demonstrated associated low-bone mass or bone loss.

- The National Osteoporosis Foundation recommends bone density testing for all women 65 years or older and all men 70 years or older.

- If there is a concern about osteoporosis, bone density testing is recommended for postmenopausal women younger than 65 years and men 50 to 69 years.

Flu and Pneumonia Vaccine

- Recommend influenza vaccine annually.
- Recommend patients 19-64 years with asthma and all adults 65 years and older be vaccinated with the pneumococcal polysaccharide vaccine ($\text{PPSV}_{23}$).
- Usually only one dose of PPSV is needed, but a second dose is recommended for people 65 years and older who got their first dose when they were younger than age 65 and it has been 5 or more years since the first dose.
- The Advisory Council on Immunization Practices (ACIP) identifies asthma as an independent risk factor for invasive pneumococcal disease and includes it in the group of chronic pulmonary diseases that are indicated for PPSV.
Thank You!
ksrance@allergypartners.com