Fresh Air: What’s New With Asthma 2019

Asha Anandaiah, MD
Director, Pulmonary Consult Service
Program Director, Harvard PCCM Fellowship
Beth Israel Deaconess Medical Center
Division of Pulmonary, Critical Care & Sleep Medicine
Disclosures

• None
Overview

- Review pathophysiology of asthma
- Describe basic “step up” approach to asthma management
- Introduce asthma phenotypes
- Discuss newer therapies- biologics, BT
What is asthma?

- Examined 21 cases of fatal asthma
- Airway wall thickening
- Submucosal edema
- Smooth muscle hypertrophy
- Eosinophilic infiltration

Huber, Arch Internal Med; 30: 689.
What is asthma?

Case

- 46 F h/o chronic rhinitis presents with several months of cough and episodic chest tightness and wheezing.
- Seen once before for these complaints and prescribed an albuterol MDI, which she has been using with some relief.
- SH: Works as an MA on an inpatient medical floor.
- PE notable for
  - HEENT: pale, swollen nasal turbinates w/clear discharge, posterior pharyngeal cobblestoning
  - Lungs: good air movement, faint end exp wheeze
- Labs: WBC 8, 7% Eos
- CXR: Clear
Diagnosis of Asthma

• Characteristic symptoms
  – Intermittent dyspnea, cough, and wheezing

• Variable expiratory airflow limitation
  – Confirmatory testing is recommended
  – Up to 1/3 of patients with an asthma diagnosis may not have asthma

Aaron, JAMA 2017; 317: 269-279.
Diagnosis of Asthma

- Spirometry with post-bronchodilator testing
  - Criteria: FEV1 or FVC increase of 200ml and 12%

<table>
<thead>
<tr>
<th>Spirometry</th>
<th>Pre Observed</th>
<th>Pre % Predicted</th>
<th>Predicted</th>
<th>Post Observed</th>
<th>Post % Predicted</th>
<th>%Change</th>
</tr>
</thead>
<tbody>
<tr>
<td>FVC (L)</td>
<td>2.89</td>
<td>74</td>
<td>3.91</td>
<td>3.07</td>
<td>78</td>
<td>6</td>
</tr>
<tr>
<td>FEV1 (L)</td>
<td>1.87</td>
<td>56</td>
<td>3.34</td>
<td>2.40</td>
<td>72</td>
<td>29</td>
</tr>
<tr>
<td>FEV1/FVC (%)</td>
<td>65</td>
<td>76</td>
<td>85</td>
<td>78</td>
<td>92</td>
<td>21</td>
</tr>
<tr>
<td>FEFmax (L/sec)</td>
<td>3.50</td>
<td>49</td>
<td>7.11</td>
<td>5.38</td>
<td>76</td>
<td>54</td>
</tr>
<tr>
<td>TET</td>
<td>10.17</td>
<td></td>
<td></td>
<td>8.40</td>
<td></td>
<td>-17</td>
</tr>
<tr>
<td>Drug Name</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Diagnosis of Asthma

- Bronchoprovocation testing (Methacholine Challenge)
  - Criteria: PC20 < 8 mg/mL

<table>
<thead>
<tr>
<th>Baseline Spirometry:</th>
<th>Observed</th>
<th>% Predicted</th>
<th>Predicted</th>
</tr>
</thead>
<tbody>
<tr>
<td>FVC:</td>
<td>3.69</td>
<td>81</td>
<td>4.55</td>
</tr>
<tr>
<td>FEV₁:</td>
<td>3.00</td>
<td>85</td>
<td>3.52</td>
</tr>
<tr>
<td>FEV₁/FVC:</td>
<td>81</td>
<td>108</td>
<td>75</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Concentration (mg/mL):</th>
<th>FEV₁:</th>
<th>% Diluent:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diluent:</td>
<td>2.80</td>
<td>100%</td>
</tr>
<tr>
<td>0.0625 mg/mL</td>
<td>2.79</td>
<td>100%</td>
</tr>
<tr>
<td>0.25 mg/mL</td>
<td>2.91</td>
<td>104%</td>
</tr>
<tr>
<td>1 mg/mL</td>
<td>2.84</td>
<td>101%</td>
</tr>
<tr>
<td>4 mg/mL</td>
<td>2.68</td>
<td>96%</td>
</tr>
<tr>
<td>16 mg/mL</td>
<td>2.65</td>
<td>95%</td>
</tr>
</tbody>
</table>
Excluding other possible causes

• Other airway disorders
  – Upper airway
    • Sinusitis/PND
    • Vocal cord dysfunction
  – Lower airway
    • COPD
    • Bronchiectasis
    • Mechanical obstruction (tumor)
    • Eosinophilic bronchitis
• CHF
• Pulmonary infiltration with eosinophilia
• Aspiration
Asthma-- Approach to treatment

• Identify and ameliorate triggers

• Assess severity and initiate pharmacotherapy
  o Controller medications
  o Rescue medication

• Consider action plan in case of worsening control

Adapted from: NHLBI EPR3 Guidelines on Asthma, 2007
Approach to treatment

• Identify and ameliorate triggers

• Assess severity and initiate pharmacotherapy
  o Controller medications
  o Rescue medication

• Consider action plan in case of worsening control

Adapted from: NHLBI EPR3 Guidelines on Asthma, 2007
Approach to treatment - triggers

• **Inhalant Allergens - year round symptoms**
  - Pets
  - Mold
  - Dust mites
  - Cockroaches

• **Inhalant Allergens - seasonal**
  - Early spring? Trees
  - Late spring? Grasses
  - Late summer/autumn? Weeds
  - Summer and Fall (Alternaria, Cladosporium, mites)
  - Cold months in temperate climates? (animal dander)

• **Tobacco Smoke**
• **Pollutants/Irritants**
  - Wood burning stove/fireplace
  - Perfumes, cleaning agents
  - Paint
• **Workplace exposures**
• **Rhinitis**
• **GERD**
• **Sulfite sensitivity**
• **Medications**
  - Aspirin
  - NSAIDs
  - Beta blockers

Adapted from: NHLBI EPR3 Guidelines on Asthma, 2007
Case

• Triggers: (allergies/nasal congestion, viral infections, strong odors, stress)
  – Aggressive rhinitis management: nasal rinses, fluticasone NS, fexofenadine
  – Allergy referral: + skin testing to dust mites, oak
  – ENT referral: +polyps, underwent sinus surgery

AERD? No h/o asa or NSAID sensitivity
Approach to treatment

• Identify and ameliorate triggers

• Assess severity and initiate pharmacotherapy
  o Controller medications
  o Rescue medication

• Consider action plan in case of worsening control

Adapted from: NHLBI EPR3 Guidelines on Asthma, 2007
# Asthma severity assessment

<table>
<thead>
<tr>
<th>Components of Severity</th>
<th>Classification of Asthma Severity (Youths ≥12 years of age and adults)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Intermittent</td>
</tr>
<tr>
<td><strong>Impairment</strong></td>
<td></td>
</tr>
<tr>
<td>Normal FEV₁/FVC:</td>
<td></td>
</tr>
<tr>
<td>8–19 yr</td>
<td>85%</td>
</tr>
<tr>
<td>20–39 yr</td>
<td>80%</td>
</tr>
<tr>
<td>40–59 yr</td>
<td>75%</td>
</tr>
<tr>
<td>60–80 yr</td>
<td>70%</td>
</tr>
<tr>
<td><strong>Symptoms</strong></td>
<td>≤2 days/week</td>
</tr>
<tr>
<td><strong>Nighttime awakenings</strong></td>
<td>≤2x/month</td>
</tr>
<tr>
<td><strong>Short-acting beta₂-agonist use for symptom control (not prevention of EIB)</strong></td>
<td>≤2 days/week</td>
</tr>
<tr>
<td><strong>Interference with normal activity</strong></td>
<td>None</td>
</tr>
<tr>
<td><strong>Lung function</strong></td>
<td>Normal FEV₁ between exacerbations</td>
</tr>
<tr>
<td></td>
<td>FEV₁ ≥80% predicted</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Lowest level of treatment required to maintain control</th>
<th>Step 1</th>
<th>Step 2</th>
<th>Step 3 or 4</th>
<th>Step 5 or 6</th>
</tr>
</thead>
</table>

NHLBI EPR3 Guidelines on Asthma, 2007
Approach to treatment- drugs

Step 1
Preferred: Low-dose ICS
Alternative: SABA PRN

Step 2
Preferred: Low-dose ICS + LABA
Alternative: Cromolyn, LTRA, Nedocromil, or Theophylline

Step 3
Preferred: Medium-dose ICS + LABA
Alternative: Medium-dose ICS + either LTRA, Theophylline, or Zileuton
Consider Omalizumab for patients who have allergies

Step 4
Preferred: High-dose ICS + LABA
Consider Omalizumab for patients who have allergies

Step 5
Preferred: High-dose ICS + LABA + oral corticosteroid

Step 6
Step up if needed (first, check adherence, environmental control, and comorbid conditions)

Assess control

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

Each step: Patient education, environmental control, and management of comorbidities.
Steps 2-4: Consider subcutaneous allergen immunotherapy for patients who have allergic asthma (see notes).

Quick-Relief Medication for All Patients
- SABA as needed for symptoms. Intensity of treatment depends on severity of symptoms: up to 3 treatments at 20-minute intervals as needed. Short course of oral systemic corticosteroids may be needed.
- Use of SABA >2 days a week for symptom relief (not prevention of EIB) generally indicates inadequate control and the need to step up treatment.

NHLBI EPR3 Guidelines on Asthma, 2007
Approach to treatment- drugs

Figure 1. Stepped-Care Approach to Asthma Treatment.

Fanta, NEJM 2009; 360: 1002.
Is a controller medication always necessary?

- Rescue ICS+ fast-acting LABA compared to maintenance ICS
  - No difference in exacerbation rate
  - Inferior for daily symptom control
  - 75-80% decrease in ICS exposure

- Rescue ICS+fast-acting LABA compared to rescue SABA
  - Superior for exacerbation rate

Bateman, NEJM 2018; 378: 1877
O’Byrne, NEJM 2018; 378: 1865.
What if patients who are taking only rescue albuterol took rescue ICS-formoterol instead?

Controlled Trial of Budesonide–Formoterol as Needed for Mild Asthma

- Prn budesonide-formoterol compared to prn albuterol in patients who had been given the diagnosis of asthma and only an albuterol inhaler for treatment.
- Prn budesonide-formoterol was superior to prn albuterol in preventing exacerbations (0.2 vs 0.4 per year, relative rate 0.5)

Beasley, NEJM 2019; 380: 2020
• Controversial recommendation: No longer recommends SABA alone.
• ICS-formoterol recommended (off label) as rescue inhaler for all patients
# Mild Asthma Treatment

<table>
<thead>
<tr>
<th>Step</th>
<th>Conventional Treatment Controller (prn)</th>
<th>Rescue</th>
<th>GINA 2019 Recommendations Controller</th>
<th>Rescue (prn)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Step 1</td>
<td>SABA</td>
<td></td>
<td>ICS-formoterol</td>
<td></td>
</tr>
<tr>
<td>Step 2</td>
<td>ICS</td>
<td>SABA</td>
<td>Low dose ICS</td>
<td>SABA</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>ICS-formoterol</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>ICS + SABA</td>
<td></td>
</tr>
<tr>
<td>Step 3</td>
<td>ICS-LABA</td>
<td>SABA</td>
<td>ICS-formoterol</td>
<td>ICS-formoterol</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>ICS + LABA</td>
<td>SABA</td>
</tr>
</tbody>
</table>
Case

- Daily ICS/LABA started
- 4 weeks later, pt reports improvement in symptoms, but persistent albuterol use almost daily
- Montelukast added

Fanta, NEJM 2009; 360: 1002.
Leukotriene modifiers

- **LTMs alone:**
  - Improve lung function
  - Decrease symptoms
  - Decrease exacerbations
  - Equivalent to ICS in “real world” settings

- **Compared to LABA:**
  - Lower reduction in exacerbation
  - Lower improvement in lung function
  - Equivalent in “real world” settings?
Approach to treatment

• Identify and ameliorate triggers

• Assess severity and initiate pharmacotherapy
  o Controller medications
  o Rescue medication

• Consider action plan in case of worsening control
# Asthma Action Plan

## ASTHMA ACTION PLAN

**Name:**

**Date:**

**Doctor:**

**Medical Record #:**

**Doctor’s Phone #:**

**Day:**

**Night/Weekend:**

**Emergency Contact:**

**Doctor’s Signature:**

---

**Personal Best Peak Flow:**

**Use these daily controller medicines:**

<table>
<thead>
<tr>
<th>MEDICINE</th>
<th>HOW MUCH</th>
<th>HOW OFTEN/WHEN</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Peak flow:**

**from**

**to**

For asthma with exercise, take:

**Continue with green zone medicine and add:**

<table>
<thead>
<tr>
<th>MEDICINE</th>
<th>HOW MUCH</th>
<th>HOW OFTEN/WHEN</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Peak flow:**

**from**

**to**

**CALL YOUR ASTHMA CARE PROVIDER.**

**DANGER**

Take these medicines and call your doctor now.

<table>
<thead>
<tr>
<th>MEDICINE</th>
<th>HOW MUCH</th>
<th>HOW OFTEN/WHEN</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Peak flow:**

**reading below**

---

**GET HELP FROM A DOCTOR NOW!** Your doctor will want to see you right away. It's important!

- Make an appointment with your asthma care provider within two days of an ER visit or hospitalization.
- If you cannot contact your doctor, go directly to the emergency room, DO NOT WAIT.
Should increasing ICS dose be part of an asthma action plan?

Quadrupling Inhaled Glucocorticoid Dose to Abort Asthma Exacerbations

- Quadrupling ICS at early signs or worsening control led to a reduction in asthma exacerbations
  - 45% vs 52% had exacerbations in one year

McKeever, NEJM 2018; 378: 902.
Case

- 46F with rhinitis/sinusitis, asthma, peripheral eosinophilia with persistent asthma symptoms and exacerbations.
  - Fluticasone/Salmeterol (500/50mcg)
  - Montelukast 10mg qhs
  - Intranasal rinses/steroids, s/p sinus surgery

- What next?

Fanta, NEJM 2009; 360: 1002.
Refractory asthma

- Patient education
  - Adherence
  - Technique
- Asthma mimics/Asthma “plus” disorders
  - Churg Strauss Syndrome (EGPA)
  - Allergic Bronchopulmonary Aspergillosis
  - Aspirin Exacerbated Respiratory Disease
- Additional therapy
Tiotropium

Peters, NEJM 2010; 363: 1715.
Kerstjens, NEJM 2012; 367:1198.
## Asthma phenotypes

<table>
<thead>
<tr>
<th>Cluster 1</th>
<th>Mild Allergic Asthma</th>
<th>Early onset; atopic; normal lung function ≤ 2 controller medications; minimal health care utilization; minimal sputum eosinophilia</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cluster 2</td>
<td>Mild-Moderate Allergic Asthma</td>
<td>Most common cluster; early onset; atopic; borderline FEV1 but reverse to normal; ≤ 2 controller medications; low health care utilization; infrequent need for oral corticosteroids; minimal sputum eosinophilia</td>
</tr>
<tr>
<td>Cluster 3</td>
<td>More Severe Older Onset Asthma</td>
<td>Older; very late onset; higher BMI (obese); less atopic; slightly decreased FEV1 with some reversibility; frequent need for oral corticosteroids despite ≥ 3 controller medications including high doses of inhaled corticosteroids; sputum eosinophilia</td>
</tr>
<tr>
<td>Cluster 4</td>
<td>Severe Variable Allergic Asthma</td>
<td>Early onset; atopic; severely decreased FEV1, but very reversible to near normal; high frequency of symptoms and albuterol use; “variable&quot; with need for frequent oral corticosteroids; high health care utilization; sputum eosinophilia</td>
</tr>
<tr>
<td>Cluster 5</td>
<td>Severe Fixed Airflow Asthma</td>
<td>Older; longest duration; less atopic; severely decreased FEV1 with less reversibility (COPD similarities); high frequency of symptoms and albuterol use despite oral corticosteroids; high health care utilization; co-morbidities Both sputum eosinophilia and neutrophilia</td>
</tr>
</tbody>
</table>

Jarjour, AJRCCM 2012; 185: 356.
# Asthma phenotypes

<table>
<thead>
<tr>
<th>Cluster 1</th>
<th>Mild Allergic Asthma</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Early onset; atopic; normal lung function; ≤2 controller medications; minimal health care utilization; minimal sputum eosinophilia</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Cluster 2</th>
<th>Mild-Moderate Allergic Asthma</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Most common cluster; early onset; atopic; borderline FEV1 but reverse to normal; ≤2 controller medications; low health care utilization; infrequent need for oral corticosteroids; minimal sputum eosinophilia</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Cluster 3</th>
<th>More Severe Older Onset Asthma</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Older; very late onset; higher BMI (obese); less atopic; slightly decreased FEV1 with some reversibility; frequent need for oral corticosteroids despite ≥3 controller medications including high doses of inhaled corticosteroids; sputum eosinophilia</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Cluster 4</th>
<th>Severe Variable Allergic Asthma</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Early onset; atopic; severely decreased FEV1, but very reversible to near normal; high frequency of symptoms and albuterol use; “variable” with need for frequent oral corticosteroids; high health care utilization; sputum eosinophilia</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Cluster 5</th>
<th>Severe Fixed Airflow Asthma</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Older; longest duration; less atopic; severely decreased FEV1 with less reversibility (COPD similarities); high frequency of symptoms and albuterol use despite oral corticosteroids; high health care utilization; co-morbidities; Both sputum eosinophilia and neutrophilia</td>
</tr>
</tbody>
</table>

Jarjour, AJRCCM 2012; 185: 356.
Phenotypes ➔ Endotypes

Bice, Ann Allergy Asthma Immunol 2015; 112: 108.
Phenotypes → Endotypes

Bice, Ann Allergy Asthma Immunol 2015; 112: 108.
Omalizumab: Anti-IgE Monoclonal Antibody

Requirements:

- Sensitization to perennial aeroallergen
- IgE 30-700 IU/mL

Holgate, Nat Rev Imm 2008 (8): 218.
Omalizumab- efficacy

• Cochrane Review (2014):
  – Acute exacerbations: OR 0.55 (26% → 16%)
  – Hospitalizations OR 0.16 (3% → 0.5%)
  – Ability to withdraw ICS OR 2.5
  – No significant change in ability to withdraw oral steroids*
Asthma phenotypes

Cluster 1
Mild Allergic Asthma
- Early onset; atopic; normal lung function
- ≤ 2 controller medications; minimal health care utilization
- Minimal sputum eosinophilia

Cluster 2
Mild-Moderate Allergic Asthma
- Most common cluster; early onset; atopic; borderline FEV1
- But reversible to normal; ≤ 2 controller medications; low health care utilization; infrequent need for oral corticosteroids
- Minimal sputum eosinophilia

Cluster 3
More Severe Older Onset Asthma
- Older; very late onset; higher BMI (obese); less atopic
- Slightly decreased FEV1 with some reversibility;
- Frequent need for oral corticosteroids despite ≥ 3 controller medications including high doses of inhaled corticosteroids
- Sputum eosinophilia

Cluster 4
Severe Variable Allergic Asthma
- Early onset; atopic; severely decreased FEV1, but very reversible to near normal; high frequency of symptoms and albuterol use; “variable” with need for frequent oral corticosteroids; high health care utilization
- Sputum eosinophilia

Cluster 5
Severe Fixed Airflow Asthma
- Older; longest duration; less atopic; severely decreased FEV1 with less reversibility (COPD similarities)
- High frequency of symptoms and albuterol use despite oral corticosteroids; high health care utilization; co-morbidities
- Both sputum eosinophilia and neutrophilia

Jarjour, AJRCCM 2012; 185: 356.
Asthma phenotypes

Cluster 1
Mild Allergic Asthma
Early onset; atopic; normal lung function ≤ 2 controller medications; minimal health care utilization; minimal sputum eosinophilia

Cluster 2
Mild-Moderate Allergic Asthma
Most common cluster; early onset; atopic; borderline FEV1 but reverse to normal; ≤ 2 controller medications; low health care utilization; infrequent need for oral corticosteroids; minimal sputum eosinophilia

Cluster 3
More Severe Older Onset Asthma
Older; very late onset; higher BMI (obese); less atopic; slightly decreased FEV1 with some reversibility; frequent need for oral corticosteroids despite ≥ 3 controller medications including high doses of inhaled corticosteroids; sputum eosinophilia

Cluster 4
Severe Variable Allergic Asthma
Early onset; atopic; severely decreased FEV1, but very reversible to near normal; high frequency of symptoms and albuterol use; “variable” with need for frequent oral corticosteroids; high health care utilization; sputum eosinophilia

Cluster 5
Severe Fixed Airflow Asthma
Older; longest duration; less atopic; severely decreased FEV1 with less reversibility (COPD similarities); high frequency of symptoms and albuterol use despite oral corticosteroids; high health care utilization; co-morbidities; Both sputum eosinophilia and neutrophilia

Jarjour, AJRCCM 2012; 185: 356.
Phenotypes ➔ Endotypes

Bice, Ann Allergy Asthma Immunol 2015; 112: 108.
Anti-IL-5 Monoclonal Antibody

- IL-5 is driver of eosinophilic inflammation
- Mepolizumab FDA approved November 2015
- Reslizumab (IV) FDA approved March 2016
- Benralizumab (anti- IL-5R) FDA approved November 2017
Mepolizumab (anti-IL-5)- Efficacy

- Approximately 50% reduction in exacerbations
- Approximately 50% reduction in steroid dose

Bel, NEJM 2014; 371: 1189.
Benralizumab (anti-IL-5R) - Efficacy

- ~50% reduction in exacerbations
- ~50% reduction in steroid dose

Nair, NEJM 2017; 376:2448.
Phenotypes → Endotypes

Bice, Ann Allergy Asthma Immunol 2015; 112: 108.
Dupilumab (anti-IL-4R)

Rabe, NEJM 2018: 378; 2475.
Phenotypes → Endotypes

Bice, Ann Allergy Asthma Immunol 2015; 112: 108.
Biologics for Asthma

•~4% of asthma patients have severe asthma

•Auto-injectors now available for self-administration
Bronchial Thermoplasty

- 3 separate bronchoscopies
- 3 weeks apart
- Thermal energy applied to all accessible airways beyond mainstem bronchi

- FDA approved 2010 for adults with severe asthma not controlled with ICS/LABA.

Wahidi and Wenzel, AJRCCM 2012; 185: 709.
Bronchial Thermoplasty

- Modest reduction in exacerbations
- No clear change in daily symptoms/QOL
- Largest trials excluded most severe asthmatics


Torrego, Cochrane Database Sys Rev 2014
Asthma Management
Asthma Management

**Conventional management**
- ICS/LABA
- Triggers
- Treat co-existing conditions

Adapted from: Israel, NEJM 2017; 377.965.
Asthma Management

Conventional management
• ICS/LABA
• Triggers
• Treat co-existing conditions

Nonbiologic add-on therapy
• LTM
• Tiotropium
• Oral glucocorticoid

Adapted from: Israel, NEJM 2017; 377.965.
Asthma Management

Conventional management
• ICS/LABA
• Triggers
• Treat co-existing conditions

Nonbiologic add-on therapy
• LTM
• Tiotropium
• Oral glucocorticoid

Persistent T2 inflammation
• Evaluate for: allergens, rhinosinusitis, AERD, ABPA
• Omalizumab (IgE 30-700, +RAST)
• Mepolizumab/Benralizumab (AEC >150-300)
• Dupilumab

Adapted from: Israel, NEJM 2017; 377.965.
Asthma Management

**Conventional management**
- ICS/LABA
- Triggers
- Treat co-existing conditions

**Nonbiologic add-on therapy**
- LTM
- Tiotropium
- [Theophylline]
- Oral glucocorticoid

**Persistent T2 inflammation**
- Evaluate for: allergens, rhinosinusitis, AERD, ABPA
- Omalizumab (IgE 30-700, +RAST)
- Mepolizumab/Benralizumab (AEC >150-300)
- Dupilumab

**NonT2 inflammation (neutrophilic)**
- Consider induced sputum for eos
- Evaluate for: irritants, infections
- Treat infection
- Consider macrolide

Adapted from: Israel, NEJM 2017; 377.965.
Summary

- Address asthma triggers in all patients
- Follow a “Step” approach to drug therapy
- Inhaled steroids remain the mainstay of asthma controller therapy
- Symptom-triggered therapy with ICS-formoterol is effective for patients with mild asthma
- The armamentarium is rapidly expanding for severe asthma
- We have entered an age of asthma biologics targeted to specific phenotypes