Asthma Update: Biologic Therapy in Asthma

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Asthma in the United States


Asthma is a chronic inflammatory disease of both the large and small airways. It is expensive and there is no cure.2

Asthma costs the United States $56 billion each year.1

In 2008, asthma caused
• 10.5 million missed school days
• 14.2 million missed work days

In 2010, 18.7 million adults (equal to 1 in 12 adults) and 7 million children (equal to 1 in 11 children) had asthma.1

Asthma in Wisconsin

- In 2005, there were more than 22,000 hospital emergency department visits for asthma costing more than $17 billion.
- In 2005, there were more than 5,500 hospitalizations for asthma, costing an average of $8,251 per hospitalization.
- Children, particularly those under the age of four, have the highest rates of asthma emergency department visits and hospitalizations.
- Asthma hospitalization rates are nearly six times higher in African Americans than whites.
- Between 2000 and 2005 asthma was the underlying cause of death in an average of 74 deaths per year.

- Adapted from American Lung Association, Asthma 101

Asthma Pathophysiology

- Genetic predisposition
- Innate vulnerability
- Atopy/allergy
- Environmental triggers
- Inflammation underlies disease processes
- Phenotype varies by individual and over time
- Clinical symptoms also vary by individual and over time

AIRWAY INFLAMMATION

AHR=airway hyperresponsiveness

Impact

Symptoms

Airway Obstruction
AHR/Bronchospasm
Airway Remodeling

Locations

Bronch
ducts

Mainstem bronchus

Small airway

Normal*
Asthma*
Fatal asthma*

Small airway in control subject
Small airway in subject with fatal asthma

*Images reproduced with permission from Dr. Francis Green, Department of Pathology and Lab Medicine, University of Calgary.

Asthma Is a Chronic Inflammatory Disease of Both the Large and Small Airways

Asthma diagnosis

- History
  - Symptoms
  - Frequency
  - Impairment

- Physical

- Spirometry
- Fractional exhaled nitric oxide (FENO)

Symptoms

- Wheeze
- Cough
- Short of breath
- Chest tightness/chest pain

Asthma Triggers

- Infections
  - Common cold
  - Sinusitis

- Allergies
  - Seasonal and perennial

- Irritants
  - Smoke, pollution, dust

AIM Survey: Majority of Patients Have “Not Well Controlled” or “Very Poorly Controlled” Asthma

- 71% of asthma patients in the AIM survey met NAEPP criteria for “Not Well Controlled” or “Very Poorly Controlled” asthma

Control Classification Based on NAEPP EPR-3 (N = 2590)

Asthma Medications

- Controller medications
  - Prevent asthma exacerbations
  - Reduce need for reliever medications
  - Generally taken daily (with exceptions)

- Relievers
  - Fast acting
  - Relieve symptoms of asthma exacerbation
  - Taken on as-needed basis

AIM = Asthma Insight and Management Survey

**Step Therapy: Modifying Therapy As Needed For Severity and Control**

- **Evaluate asthma control in 2–6 weeks.** Step up if not well controlled
- **Before stepping up, review:**
  - Adherence
  - Inhaler technique
  - Environmental control measures
  - Comorbid conditions
- **Consider a step down once asthma is well controlled for ≥3 months**
- **LABAs should be used for shortest duration of time required to achieve control, then discontinued**
- **A step down is necessary to identify the minimum therapy required to maintain good control**
- **SABA as needed for symptoms**

**Summary of Asthma Controller medications**

- **Leukotriene modifiers**
- **Inhaled steroids**
- **Long acting beta agonist**
- **Long acting anti muscarinic**
- **Theophylline**
- **Biologics: monoclonal antibodies**
  - Omalizumab
  - Mepolizumab
  - Benralizumab
  - Dupilimab

**CHOICE Survey: Controller Therapy Remains Underused**

- 49% of patients with asthma used no controller medication
  - Among patients not using controller medication, 79% had persistent asthma
  - Among patients using controller medication, 86% reported “not well controlled” or “very poorly controlled” asthma
  - Patients often self-reported their disease as well controlled even though it was not well controlled

**Monoclonal antibodies**

- **Immunoglobulins (antibodies)**
  - Multifunctional component of immune system
- **Polyclonal vs monoclonal**
  - Polyclonal antibodies produced by a number of different B cells
  - Monoclonal antibodies produced by single B cell
- **Monoclonal antibodies may be developed to target**
  - Immunologic diseases
  - Reversal of drugs
  - Cancer
Asthma as an inflammatory disorder

- Asthma inflammation
  - Th1 v Th2
  - Components of inflammatory cascade in asthma/allergies
    - IgE
    - IL2, IL4, IL5, IL13
    - cytokine thymic stromal lymphopoietin (TSLP)

Omalizumab (Xolair)

- Anti-IgE
- IgE
  - Produced by B cells
  - Influenced by IL-4 and IL-13
  - Found on mast cells, basophils
    - Mast cells/basophils release inflammatory mediators
      - Histamine, tryptases, chymases, cysteinyl leukotrienes, prostaglandins
  - IgE is necessary for allergic reaction, most asthmatics are allergic

Omalizumab

- Indication
  - Age 6 and older
  - Moderate to severe asthma
  - IgE between 30-700 IU/mL
  - Positive skin test or specific IgE to perennial allergen
- Dosing
  - 150 to 375mg every two to four weeks
- Efficacy
  - Reduced risk of exacerbation from 26% to 16%
  - Reduced hospitalization from 3% to 0.5%; Reduced inhaled steroid dose; Has not resulted in discontinuation of oral steroids
- Cost
  - $15,619 to $84,603.35 per year (depending on dose)

Mepolizumab (Nucala)

- IL-5 antagonist (anti-IL-5)
- IL-5 is largely responsible for growth, maturation and recruitment of eosinophils
- Eosinophil
  - WBC, granulocyte lineage (also with neutrophils and basophils)
  - Involved in response to infection, tissue remodeling, tumor surveillance
  - Key component of allergic response
  - Usually tissue dwelling

Mepolizumab (Nucala)

- Indication
  - Severe asthma
  - Age 12 and older
  - Eosinophilic phenotype (150 eosinophils/microL)
- Dosing
  - 100mg subQ every 4 weeks
- Efficacy
  - Reduced exacerbations (-47% in MENSA trial), improved FEV1 (in some studies)
- Cost
  - $41,308/year

Reslizumab (Cinqair)

- IL-5 antagonist (anti-IL-5)
- IL-5 is largely responsible for growth, maturation and recruitment of eosinophils
- Eosinophil
  - WBC, granulocyte lineage (also with neutrophils and basophils)
  - Involved in response to infection, tissue remodeling, tumor surveillance
  - Key component of allergic response
  - Usually tissue dwelling
Reslizumab (Cinqair)

- **Indication**
  - Severe asthma
  - Age 18 and older
  - Blood eosinophil count 400/microL

- **Dosing**
  - 3 mg/kg by intravenous infusion over 20 to 50 minutes, every 4 weeks
  - Anaphylaxis risk

- **Efficacy**
  - Reduced asthma exacerbations by 50% (Lancet Respir Med. 2015 May;3(5):355-66)

- **Cost**
  - $22,757.76 for 60kg individual (100mg/10ml), $105.36/ml

Benralizumab (Fasenra)

- **Indication**
  - Severe asthma with eosinophilic phenotype
  - Age 12 and older
  - Eosinophilic phenotype (300 eosinophils/microL)

- **Dosing**
  - 30mg subQ every 4 weeks for the first 3 doses, then once every 8 weeks

- **Efficacy**
  - Improved exacerbations, prebronchodilator FEV₁ and symptoms scores
  - Those with <300 eos/microL effect on exacerbations was borderline
  - Reduced oral steroid dose

- **Cost**
  - $34,212/year on maintenance. Year one: $39,914.53