**LEARNING OBJECTIVES**

1. Accurately diagnose and assess asthma severity at regular intervals per standardized guidelines.

2. Implement a stepwise approach to asthma treatment that is based on disease severity, sub-type, and phenotype or endotype and addresses underlying comorbidities.

3. Appreciate the role of asthma self-management, including proper inhaler use, with patients at regular intervals to reduce symptom burden.

---

**WHAT IS ASTHMA?**

- A common and complex disease
  - 9.2% incidence in adults in North Carolina
- Chronic inflammation of the airways
- Heterogeneous nature

Characterized by...

- Variable and recurrent symptoms
- Airflow obstruction
- Bronchial hyperresponsiveness
- Underlying inflammation

---

**History of Present Illness**

**Naomi**
30-years-old (Female)

Current Medications
- Fluticasone nasal spray daily PRN
- Fexofenadine 180mg daily PRN

New patient presenting to your practice with a history of seasonal allergic rhinitis.

Every night for the past month she has been experiencing "wheezing attacks" where she starts coughing and feels like her chest is tightening up.

Currently in PhD program in Art history and is under stress.

Denies ever smoking & recreational drug use; social alcohol use; exercises daily.

No food allergies

Father with asthma

---

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Review of Systems

- **HEENT:** worse nasal congestion with heavy pollen
- **Respiratory:** As per HPI
- **Cardiovascular:** Intermittent chest tightness, denies palpitations

Physical Exam

- BMI 21 kg/m²; HR 74 bpm; RR 14; BP 124/64 mmHg
- **HEENT:** Erythematous nasal mucosa; no apparent nasal polyps. Clear oropharynx.
- **Lungs:** clear to auscultation bilaterally. No wheezes or crackles. Deep inspirations elicit coughing.

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**PULMONARY FUNCTION TESTING (PFTs)**

- **Variable expiratory airflow obstruction**
  - Varies over time
  - Improves following bronchodilator
  - Can be induced by provocative stimuli
    - e.g., Methacholine

---

**INTERPRETING PFTs**

Significant bronchodilator response defined as...

**History of Present Illness:**
- History of *exercise induced asthma* and obesity
- Presents with *shortness of breath* × 2 months
- Typically only uses his rescue inhaler before exercise, but recently he has been using it 3 days/week even when not exercising. Has never needed oral steroids.
- No known allergies.
- Actively trying to lose weight, no smoke exposure, works as a pharmacist.

**Physical Exam:**
- BMI 34 kg/m²; HR 83 bpm; RR 17; BP 118/75 mmHg
- HEENT: normal oral and nasal mucosa
- Lungs: *mild end expiratory wheezing*, no accessory muscle use.

**Current Meds:**
- Albuterol inhaler PRN

---

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**RATIONALE**

- Check inhaler technique
- Assess for potential comorbid conditions
- Perform spirometry
- Encourage his continued weight loss efforts
- All of the above

---

**COMMON CAUSES OF UNCONTROLLED ASTHMA THAT IS NOT SEVERE**

- Nonadherence to therapy
- Incorrect inhaler technique
- Comorbidities and psychosocial factors
- Ongoing exposure to asthma triggers

Understanding a patient’s adherence to therapy is always a prerequisite when assessing severe asthma.

---

**SELF MANAGEMENT IMPROVES OUTCOMES**

Self-Management → At Every Point of Contact...

- Assess INHALER TECHNIQUE
- Educate on MEDICATION ADHERENCE
- Develop/confirm ACTION PLAN

---

**ASTHMA ACTION PLANS**

Multiple downloadable sample plans available online...

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**SYLLABI/SLIDES**

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### Classification of Asthma Severity

<table>
<thead>
<tr>
<th>Components of Severity</th>
<th>Intermittent</th>
<th>Persistent</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mild</td>
<td>Moderate</td>
</tr>
<tr>
<td>Impairment</td>
<td>≤ 2 days/week but not daily</td>
<td>12 days/week but not daily</td>
</tr>
<tr>
<td>Nighttime awakenings</td>
<td>&lt; 2/week/month</td>
<td>3-4/week/month</td>
</tr>
<tr>
<td>SABA use for symptom control</td>
<td>≤ 2 days/week but not daily</td>
<td>12 days/week but not daily</td>
</tr>
<tr>
<td>Interference with normal activity</td>
<td>None</td>
<td>Minor limitation</td>
</tr>
</tbody>
</table>

#### Lung function
- Normal FEV1; between exacerbations
- FEV1 > 80% predicted
- FEV1/FVC normal
- FEV1 > 90% but < 80% Predicted
- FEV1/FVC reduced 5%
- FEV1 < 90% but > 80% Predicted
- FEV1/FVC reduced >5%

#### Exacerbations requiring oral corticosteroids
- < 2 exacerbations/year
- 2-4 exacerbations/year
- > 4 exacerbations/year

### Asthma Control

#### Modified Version

<table>
<thead>
<tr>
<th>Well Controlled</th>
<th>Not Well Controlled</th>
<th>Very Poorly Controlled</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 2 days/week</td>
<td>&gt; 2 days/week</td>
<td>Several times a day</td>
</tr>
<tr>
<td>0-2/year</td>
<td>2-4/year</td>
<td>≥ 4/year</td>
</tr>
<tr>
<td>≥ 5/year</td>
<td>&gt; 10/year</td>
<td>≤ 15/year</td>
</tr>
</tbody>
</table>

#### GINA Stepwise Treatment for Asthma 2019

**Step 1:** Daily low dose inhaled corticosteroids (ICS), or as-needed low dose ICS-formoterol.

**Step 2:**
- Low dose ICS-LABA
- Medium dose ICS-LABA

**Step 3:**
- Medium dose ICS-LABA

**Step 4:**
- High dose ICS-LABA

**Step 5:**
- Add low dose OCS but consider side effects

**Other controller options:**
- Leukotriene receptor antagonist (LTRA) or low dose ICS taken whenever SABA taken

**Other reliever options:**
- As-needed low dose ICS-formoterol

### History of Present Illness

- Your patient with a history of asthma and eczema presents with 6 weeks of shortness of breath, nasal and sinus congestion and non-productive cough. Using rescue inhaler daily, wakes up 2-3 times at night. Stopped playing basketball with friends.
- 2 weeks ago he was seen in urgent care and given a 14 days of antibiotics for sinus infection which has not helped.
- Bought his young daughter a pet cat 8 weeks ago
- Former smoker (2 years as a teenager), drinks 4-5 beers on the weekends with friends. Works as an electrician.
- Allergic to shellfish. Mother with eczema.

### Syllabi/slides for this program are a supplement to the live CME session and are not intended for other purposes.
Review of Systems:
- Resp: positive for nasal congestion, intermittent cough
- Constitutional: Denies fevers, body aches
- HEENT: Denies bloody nasal discharge
- CV: Denies chest pain or tightness

Physical Exam:
- BMI 27 kg/m2; RR 14; sO2 97%; BP 124/68 mmHg; Pulse 80 bpm.
- Gen: Overweight male in no acute distress.

GINA Stepwise Treatment for Asthma 2019

For more details about treatment recommendations including in children, supporting evidence, and clinical advice about implementation in different populations, see the full GINA 2019 report (www.ginasthma.org).

History of Present Illness:
- Long history of asthma and hypertension presents with 1 month of chest tightness with wheezing, dry cough and fatigue.
- Using rescue inhaler almost daily.
- Required 2 courses of oral steroids in past year for asthma exacerbations.
- Stopped going to gym.
- No smoke exposure, works as an engineer, stress at work, outdoors daily for work. Drinks 1 glass wine nightly.

Laura
57 years-old (Female)

Current Meds:
- Albuterol inhaler PRN
- Budesonide/Formoterol 160mcg/4.5mcg, 2 puffs twice daily
- Montelukast 10mg nightly
- HCTZ 25mg daily
- Aspirin 81mg daily

Review of Systems:
- Constitutional: no fevers, chills, night sweats
- HEENT: Nasal congestion.
- Respiratory: As per HPI.
- Cardiovascular: Intermittent chest tightness and palpitations.

Physical Exam:
- BP 125/75; RR 20; HR 100; O2 97%; BMI 34kg/m².
- Gen: Appears fatigued, coughing intermittently.
- Lungs: expiratory wheezing; no accessory muscle use.
- Cardiac: tachycardic, no murmurs.

Laura
57 years-old (Female)

Current Meds:
- Albuterol inhaler PRN
- Budesonide/Formoterol 160mcg/4.5mcg, 2 puffs twice daily
- Montelukast 10mg nightly
- HCTZ 25mg daily
- Aspirin 81mg daily

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**ASTHMA PHENOTYPES**

<table>
<thead>
<tr>
<th>Category</th>
<th>Phenotype</th>
</tr>
</thead>
<tbody>
<tr>
<td>Trigger-induced asthma</td>
<td>1. Allergic</td>
</tr>
<tr>
<td></td>
<td>2. Nonallergic</td>
</tr>
<tr>
<td></td>
<td>3. AERD</td>
</tr>
<tr>
<td></td>
<td>4. Infection</td>
</tr>
<tr>
<td></td>
<td>5. Exercise-induced</td>
</tr>
<tr>
<td>Clinical presentation of asthma</td>
<td>6. Preasthma wheezing in infants</td>
</tr>
<tr>
<td></td>
<td>a. Episodic (viral) wheeze</td>
</tr>
<tr>
<td></td>
<td>b. Multi-trigger wheezing</td>
</tr>
<tr>
<td></td>
<td>7. Exacerbation-prone asthma</td>
</tr>
<tr>
<td></td>
<td>8. Asthma associated with apparent irreversible airflow limitation</td>
</tr>
<tr>
<td>Inflammatory markers of asthma</td>
<td>9. Eosinophilic and neutrophilic asthma</td>
</tr>
</tbody>
</table>

AERD, aspirin-exacerbated respiratory disease.

**ASTHMA ENDOTYPES**

**INFAMMATORY MARKERS**

**Type 2 inflammation associated asthma (50-70% of asthma)\(^1,2\)

- Typically includes allergic asthma, exercise-induced asthma, late-onset eosinophilic asthma
- Eosinophilic
- High exhaled nitric oxide (FE\(_{NO}\))
- High IgE
- Mediated by IL-4, IL-5, and IL-13

**Non-type 2 inflammation associated asthma

- Associated with obesity, smoking, older age onset,
- Neutrophilic
- Smooth-muscle mediated
- Mediated by IL-1, IL-6, IL-17, and TNF

IL, interleukin; TNF, tumor necrosis factor.

**SEEKING PERSONALIZED THERAPY**

**TESTS SUGGESTIVE OF TYPE 2 INFLAMMATION PHENOTYPES/ENDOTYPES**

- Blood eosinophils
- FENO
- IgE
- Skin prick testing
- Blood eosinophils

FENO, fractional exhaled nitric oxide.

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**TREATMENT BY ENDOTYPES AND PHENOTYPES**

- Better response to ICS
- Type 2 inflammation associated with:
  - Allergic asthma
  - Eosinophilic asthma
- Better response to leukotriene modifiers
- Aspirin sensitive asthma (aka AERD)
- Respond to (currently available) biologic treatments
- Type 2 inflammation associated asthmatics
  - Severe Allergic asthma
  - Severe Eosinophilic asthma

**ADD-ON BIOLOGIC THERAPIES REDUCE EXACERBATIONS IN ASTHMA ASSOCIATED WITH TYPE 2 INFLAMMATION**

<table>
<thead>
<tr>
<th>Drug</th>
<th>Target</th>
<th>Indication</th>
<th>Suggested patients</th>
<th>Route of Admin.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Omalizumab</td>
<td>Anti-IgE</td>
<td>IgE ≥ 300 IU/ml, positive skin test or elevated specific IgE level in response to aero-allergen, FENO ≥ 200 ppb</td>
<td>≥ 6 yrs old with severe persistent allergic asthma</td>
<td>SC injection</td>
</tr>
<tr>
<td>Mepolizumab</td>
<td>Anti-IL5</td>
<td>≥ 2 exacerbations in past year</td>
<td>≥ 12 yrs old with severe eosinophilic asthma</td>
<td>SC injection</td>
</tr>
<tr>
<td>Reslizumab</td>
<td>Anti-IL5</td>
<td>≥ 1 exacerbation in past year</td>
<td>≥ 18 yrs old with severe eosinophilic asthma</td>
<td>IV infusion</td>
</tr>
<tr>
<td>Benralizumab</td>
<td>Anti-IL5</td>
<td>≥ 2 exacerbations in past year</td>
<td>≥ 12 yrs old with severe eosinophilic asthma</td>
<td>SC injection</td>
</tr>
<tr>
<td>Dupilumab</td>
<td>Anti-IL4</td>
<td>≥ 1 exacerbation in past 1-2 yrs</td>
<td>≥ 12 yrs old with moderate to severe eosinophilic asthma or OCS-dependent asthma</td>
<td>SC injection</td>
</tr>
</tbody>
</table>

**TREATING COMORBIDITIES IMPROVES SYMPTOMS**

*Comorbidities more common in severe asthma*

- Atopic dermatitis
- GERD
- Obesity
- Obstructive sleep apnea
- Rhinosinusitis/nasal polyps
- Vocal cord dysfunction

**LET'S REVIEW...**

- Spirometry should be done in every patient with suspected asthma
- Follow-up care is just as important as initial accurate diagnosis
- Evaluate medication adherence and proper inhaler use at every encounter
- Self management strategies are not optional but rather a key component to standard treatment
- Regular reassessment of pulmonary function tests should be standard of care in asthma patients

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LET’S REVIEW…

► Refer patients to pulmonary specialist when refractory to treatment since they may benefit from phenotype or endotype specific add-on treatments
► Serum eosinophils, skin prick allergen testing, serum or sputum IgE, and fractional exhaled nitric oxide are all tests that can help further subtype difficult to treat asthma
► Always be alert for potential comorbidities that can contribute to asthma symptoms and exacerbation frequency
► Consider stepping down treatment if patient’s symptoms have been improved for at least 3 months

ONLINE RESOURCES

GINA pocket guide for asthma:

GINA pocket guide for difficult-to-treat and severe asthma:

Sample Asthma Action plan printout:
https://www.lung.org/assets/documents/asthma/asthma-action-plan.pdf

Sample Asthma action plan printout from Asthma and Allergy Foundation of America:
https://www.aafa.org/media/1601/asthma-action-plan-aafa.pdf

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