ASTHMA-COPD OVERLAP SYNDROME 2018:
What’s All the Fuss?

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Speaker: AAN, Integrity CME, National Jewish Health, AstraZeneca,
Sunovion, Teva

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HEROES: Are WE Listening As They Did?
Diagnosis and initial treatment of asthma, COPD and asthma-COPD overlap (ACO)

A joint project of GINA and GOLD

GINA Global Strategy for Asthma Management and Prevention

GOLD Global Strategy for Diagnosis, Management and Prevention of COPD
Background

- For patients with respiratory symptoms, infectious diseases and non-pulmonary conditions need to be distinguished from chronic airways disease.
- In patients with chronic airways disease, the differential diagnosis differs by age:
  - Children and young adults: most likely to be asthma
  - Adults >40 years: COPD becomes more common, and distinguishing asthma from COPD becomes more difficult.
- Many patients with symptoms of chronic airways disease have features of both asthma and COPD:
  - This has been called asthma-COPD overlap (ACO).
- Asthma-COPD overlap is not a single disease:
  - It is likely that a range of different underlying mechanisms and origins will be identified.
Patients with features of both asthma and COPD have worse outcomes than those with asthma or COPD alone

- Frequent exacerbations
- Poor quality of life
- More rapid decline in lung function
- Higher mortality
- Greater health care utilization

Reported prevalence of overlap varies by definitions used

- Concurrent doctor-diagnosed asthma and COPD are found in 15–20% of patients with chronic airways disease
- Reported rates of overlap are between 15–55% of patients with chronic airways disease, depending on the definitions used for ‘asthma’ and ‘COPD’, and the population studied
- Prevalence varies by age and gender
Asthma-COPD overlap

- “Asthma-COPD overlap” does not mean a single disease entity
  - It includes patients with several different forms of airways disease (phenotypes) caused by a range of different underlying mechanisms

- Persistent airflow limitation may be found in:
  - Some children with asthma (McGeachie NEJM 2016)
  - Many adults with a history of asthma (Lange NEJM 2015)
  - Smokers and ex-smokers, especially with earlier start of smoking (Lange NEJM 2015)
  - Patients with low lung function in early adulthood with normal decline over time (Lange NEJM 2015)
  - Patients with normal lung function in early adulthood but rapid decline over time (Lange NEJM 2015)

- Some patients with COPD have increased sputum/blood eosinophils
  - This may be associated with higher risk of exacerbations and greater response to corticosteroids
Distinguishing asthma from COPD can be problematic
- Particularly in smokers and older adults
- Some patients may have clinical features of both asthma and COPD

Most clinical trials and guidelines are about asthma or COPD alone

“Asthma-COPD overlap” is not a single disease entity
- As for asthma and COPD, it includes patients with several different forms of airways disease (phenotypes)
- These features are caused by a range of different underlying mechanisms

The descriptive term asthma-COPD overlap (ACO) is useful
- It maintains awareness by clinicians, researchers and regulators of the needs of these patients

To avoid the impression that this is a single disease, the previous term Asthma COPD Overlap Syndrome (ACOS) is no longer advised.

What's new in GINA 2018?

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Objectives of the asthma-COPD overlap chapter

- To provide interim advice to assist clinicians (especially in primary care and non-pulmonary specialties):
  - To identify patients with a disease of chronic airflow limitation
  - To distinguish asthma from COPD and identify patients who have features of both
  - To decide on safe initial treatment and/or need for referral

- To stimulate research into airways disease, by promoting:
  - Study of characteristics and outcomes in broad populations of patients with chronic airflow limitation
  - Research into underlying mechanisms that might allow development of specific interventions for prevention and management in this population
Asthma

Asthma is a heterogeneous disease, usually characterized by chronic airway inflammation. It is defined by the history of respiratory symptoms such as wheeze, shortness of breath, chest tightness and cough that vary over time and in intensity, together with variable expiratory airflow limitation. [GINA 2018]
## Definitions

### Asthma

Asthma is a heterogeneous disease, usually characterized by chronic airway inflammation. It is defined by the history of respiratory symptoms such as wheeze, shortness of breath, chest tightness and cough that vary over time and in intensity, together with variable expiratory airflow limitation. [GINA 2018]

### COPD

Chronic obstructive pulmonary disease (COPD) is a common, preventable and treatable disease that is characterized by persistent respiratory symptoms and airflow limitation that is due to airway and/or alveolar abnormalities usually caused by significant exposure to noxious particles or gases. [GOLD 2018]
## Definitions

### Asthma

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### COPD

Chronic obstructive pulmonary disease (COPD) is a common, preventable and treatable disease that is characterized by persistent respiratory symptoms and airflow limitation that is due to airway and/or alveolar abnormalities usually caused by significant exposure to noxious particles or gases. [GOLD 2018]

### Asthma-COPD overlap [not a definition, but a description for clinical use]

Asthma-COPD overlap (ACO) is characterized by persistent airflow limitation with several features usually associated with asthma and several features usually associated with COPD. Asthma-COPD overlap is therefore identified in clinical practice by the features that it shares with both asthma and COPD. This is not a definition, but a description for clinical use, as asthma-COPD overlap includes several different clinical phenotypes and there are likely to be several different underlying mechanisms.
Stepwise approach to diagnosis and initial treatment

For an adult who presents with respiratory symptoms:

1. Does the patient have chronic airways disease?
2. Syndromic diagnosis of asthma, COPD and overlap
3. Spirometry
4. Commence initial therapy
5. Referral for specialized investigations (if necessary)
Step 1 – Does the patient have chronic airways disease?

**STEP 1**

DIAGNOSE CHRONIC AIRWAYS DISEASE
Do symptoms suggest chronic airways disease?

- **Yes**
- **No**

Consider other diseases first
Step 1 – Does the patient have chronic airways disease?

- Clinical history: consider chronic airways disease if
  - Chronic or recurrent cough, sputum, dyspnea or wheezing, or repeated acute lower respiratory tract infections
  - Previous doctor diagnosis of asthma and/or COPD
  - Previous treatment with inhaled medications
  - History of smoking tobacco and/or other substances
  - Exposure to environmental hazards, e.g. airborne pollutants

- Physical examination
  - May be normal
  - Evidence of hyperinflation or respiratory insufficiency
  - Wheeze and/or crackles
Step 1 – Does the patient have chronic airways disease?

- **Radiology** (CXR or CT scan performed for other reasons)
  - May be normal, especially in early stages
  - Hyperinflation, airway wall thickening, hyperlucency, bullae
  - May identify or suggest an alternative or additional diagnosis, e.g. bronchiectasis, tuberculosis, interstitial lung disease, cardiac failure

- **Screening questionnaires**
  - Designed to assist in identification of patients at risk of chronic airways disease
  - May not be generalizable to all countries, practice settings or patients
  - See GINA and GOLD reports for examples
Step 2 – Syndromic diagnosis of asthma, COPD and asthma-COPD overlap

- Assemble the features that, **when present**, most favor a diagnosis of typical asthma or typical COPD

- Compare the number of features on each side
  - If the patient has ≥3 features of either asthma or COPD, there is a strong likelihood that this is the correct diagnosis

- Consider the level of certainty around the diagnosis
  - Diagnoses are made on the weight of evidence
  - The absence of any of these features does not rule out either diagnosis, e.g. absence of atopy does not rule out asthma
  - When a patient has a similar number of features of both asthma and COPD, consider the diagnosis of asthma-COPD overlap
**STEP 2**  
SYNDROMIC DIAGNOSIS IN ADULTS  
(i) Assemble the features for asthma and for COPD that best describe the patient.  
(ii) Compare number of features in favour of each diagnosis and select a diagnosis

<table>
<thead>
<tr>
<th>Features: if present suggest -</th>
<th>ASTHMA</th>
<th>COPD</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age of onset</strong></td>
<td>Before age 20 years</td>
<td>After age 40 years</td>
</tr>
<tr>
<td><strong>Pattern of symptoms</strong></td>
<td>Variation over minutes, hours or days</td>
<td>Persistent despite treatment</td>
</tr>
<tr>
<td></td>
<td>Worse during the night or early morning</td>
<td>Good and bad days but always daily symptoms and exertional dyspnea</td>
</tr>
<tr>
<td></td>
<td>Triggered by exercise, emotions including laughter, dust or exposure to allergens</td>
<td>Chronic cough &amp; sputum preceded onset of dyspnea, unrelated to triggers</td>
</tr>
<tr>
<td><strong>Lung function</strong></td>
<td>Record of variable airflow limitation (spirometry or peak flow)</td>
<td>Record of persistent airflow limitation (FEV₁/FVC &lt; 0.7 post-BD)</td>
</tr>
<tr>
<td><strong>Lung function between symptoms</strong></td>
<td>Normal</td>
<td>Abnormal</td>
</tr>
<tr>
<td><strong>Past history or family history</strong></td>
<td>Previous doctor diagnosis of asthma</td>
<td>Previous doctor diagnosis of COPD, chronic bronchitis or emphysema</td>
</tr>
<tr>
<td></td>
<td>Family history of asthma, and other allergic conditions (allergic rhinitis or eczema)</td>
<td>Heavy exposure to risk factor: tobacco smoke, biomass fuels</td>
</tr>
<tr>
<td><strong>Time course</strong></td>
<td>No worsening of symptoms over time. Variation in symptoms either seasonally, or from year to year</td>
<td>Symptoms slowly worsening over time (progressive course over years)</td>
</tr>
<tr>
<td></td>
<td>May improve spontaneously or have an immediate response to bronchodilators or to ICS over weeks</td>
<td>Rapid-acting bronchodilator treatment provides only limited relief</td>
</tr>
<tr>
<td><strong>Chest X-ray</strong></td>
<td>Normal</td>
<td>Severe hyperinflation</td>
</tr>
</tbody>
</table>

**NOTE:** • These features best distinguish between asthma and COPD. • Several positive features (3 or more) for either asthma or COPD suggest that diagnosis. • If there are a similar number for both asthma and COPD, consider diagnosis of ACO

<table>
<thead>
<tr>
<th>DIAGNOSIS</th>
<th>Asthma</th>
<th>Some features of asthma</th>
<th>Features of both</th>
<th>Some features of COPD</th>
<th>COPD</th>
</tr>
</thead>
<tbody>
<tr>
<td>CONFIDENCE IN DIAGNOSIS</td>
<td>Asthma</td>
<td>Asthma</td>
<td>Could be ACO</td>
<td>Possibly COPD</td>
<td>COPD</td>
</tr>
</tbody>
</table>
STEP 3
PERFORM SPIROMETRY

Marked reversible airflow limitation (pre-post bronchodilator) or other proof of variable airflow limitation

FEV₁/FVC < 0.7 post-BD
Step 3 - Spirometry

- Essential if chronic airways disease is suspected
  - Confirms chronic airflow limitation
  - More limited value in distinguishing between asthma with fixed airflow limitation, COPD and asthma-COPD overlap

- Measure at the initial visit or subsequent visit
  - If possible measure before and after a trial of treatment
  - Medications taken before testing may influence results

- Peak expiratory flow (PEF)
  - Not a substitute for spirometry
  - Normal PEF does not rule out asthma or COPD
  - Repeated measurement may confirm excessive variability, found in asthma or in some patients with asthma-COPD overlap
## Step 3 - Spirometry

<table>
<thead>
<tr>
<th>Spirometric variable</th>
<th>Asthma</th>
<th>COPD</th>
<th>Overlap</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal FEV&lt;sub&gt;1&lt;/sub&gt;/FVC pre- or post-BD</td>
<td>Compatible with asthma</td>
<td>Not compatible with diagnosis (GOLD)</td>
<td>Not compatible with diagnosis</td>
</tr>
<tr>
<td>Post-BD FEV&lt;sub&gt;1&lt;/sub&gt;/FVC &lt;0.7</td>
<td>Indicates airflow limitation; may improve</td>
<td>Required for diagnosis by GOLD criteria</td>
<td>Usual in asthma-COPD overlap (ACO)</td>
</tr>
<tr>
<td>FEV&lt;sub&gt;1&lt;/sub&gt; ≥80% predicted</td>
<td>Compatible with asthma (good control, or interval between symptoms)</td>
<td>Compatible with GOLD category A or B if post-BD FEV&lt;sub&gt;1&lt;/sub&gt;/FVC &lt;0.7</td>
<td>Compatible with mild ACO</td>
</tr>
<tr>
<td>FEV&lt;sub&gt;1&lt;/sub&gt; &lt;80% predicted</td>
<td>Compatible with asthma. A risk factor for exacerbations</td>
<td>Indicates severity of airflow limitation and risk of exacerbations and mortality</td>
<td>Indicates severity of airflow limitation and risk of exacerbations and mortality</td>
</tr>
<tr>
<td>Post-BD increase in FEV&lt;sub&gt;1&lt;/sub&gt; &gt;12% and 200mL from baseline (reversible airflow limitation)</td>
<td>Usual at some time in course of asthma; not always present</td>
<td>Common in COPD and more likely when FEV&lt;sub&gt;1&lt;/sub&gt; is low</td>
<td>Common in ACO, and more likely when FEV&lt;sub&gt;1&lt;/sub&gt; is low</td>
</tr>
<tr>
<td>Post-BD increase in FEV&lt;sub&gt;1&lt;/sub&gt; &gt;12% and 400mL from baseline</td>
<td>High probability of asthma</td>
<td>Unusual in COPD. Consider ACO</td>
<td>Compatible with diagnosis of ACO</td>
</tr>
</tbody>
</table>
A New Approach to CAPTURE™ COPD®
An NHLBI-funded study

Chronic obstructive pulmonary disease (COPD) by the numbers

3rd leading cause of death in the U.S.

15+ million Americans have been diagnosed with COPD
12 million Americans are thought to have undiagnosed COPD

Earlier detection of COPD might help primary care physicians offer treatment to improve patient condition.

COPD
Assessment in Primary Care To Identify Undiagnosed Respiratory Disease and Exacerbation Risk

Peak Expiratory Flow (PEF) Test Help Identify COPD Risk

5 questions that can help primary care physicians identify patients at risk for COPD:

1. Have you ever lived or worked in a place with dirty or polluted air, smoke, second-hand smoke or dust?
2. Does your breathing change with seasons, weather, or air quality?
3. Does your breathing make it difficult to do things such as carry heavy loads, shovel dirt or snow, jog, play tennis, or swim?
4. Compared to others your age, do you tire easily?
5. In the past 12 months, how many times did you miss work, school, or other activities due to a cold, bronchitis, or pneumonia?

Score and Next Steps
A patient's answers indicate level of risk for COPD and recommended next steps.

<table>
<thead>
<tr>
<th>Score</th>
<th>Next Step</th>
</tr>
</thead>
<tbody>
<tr>
<td>5-6: HIGH RISK</td>
<td>Refer for diagnostic testing.</td>
</tr>
<tr>
<td>2-4: MODERATE RISK</td>
<td>Include a PEF test with a referral threshold (males &lt;300 L/min; females &lt;250 L/min) during patient visit.</td>
</tr>
<tr>
<td>0-1: MINIMAL RISK</td>
<td>No immediate further testing.</td>
</tr>
</tbody>
</table>

Questions 1-4:  
Yes = 1, No = 0  
Question 5:  
0 = 0, 1, 2 or more = 2 (3-point scale)

Visit nhlbi.nih.gov for more information about COPD.
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**COPD**
**A**ssessment in **P**rimary Care **T**o Identify **U**ndiagnosed **R**espiratory Disease and **E**xacerbation Risk

Peak Expiratory Flow (PEF) Test

Help Identify COPD Risk
5 questions that can help primary care physicians identify patients at risk for COPD:

1. Have you ever lived or worked in a place with dirty or polluted air, smoke, second-hand smoke or dust?
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Score and Next Steps

A patient’s answers indicate level of risk for COPD and recommended next steps.

| Questions 1–4: | Yes = 1, No = 0 |
| Question 5: | 0 = 0, 1 = 1, 2 or more = 2 (3-point scale) |

- **5–6: HIGH RISK**
  - Refer for diagnostic testing.

- **2–4: MODERATE RISK**
  - Include a PEF test with a referral threshold (males <350 L/min; females <250 L/min) during patient visit.

- **0–1: MINIMAL RISK**
  - No immediate further testing.

Visit nhlbi.nih.gov for more information about COPD.

* Questionnaire has not yet been approved for clinical use.
** Estimated
† A peak flow meter can measure air flow rate quickly and inexpensively.
### STEP 4
#### INITIAL TREATMENT*

<table>
<thead>
<tr>
<th>Asthma drugs</th>
<th>Asthma drugs</th>
<th>ICS and consider LABA +/- or LAMA</th>
<th>COPD drugs</th>
<th>COPD drugs</th>
</tr>
</thead>
<tbody>
<tr>
<td>No LABA monotherapy</td>
<td>No LABA monotherapy</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*Consult GINA and GOLD documents for recommended treatments.*
Step 4 – Commence initial therapy

- Initial pharmacotherapy choices are based on both efficacy and safety
- If syndromic assessment suggests asthma as single diagnosis
  - Start with low-dose ICS, add LABA and/or LAMA if needed for poor control despite good adherence and correct technique
  - Do not give LABA alone without ICS
- If syndromic assessment suggests COPD as single diagnosis
  - Start with bronchodilators or combination therapy
  - Do not give ICS alone without LABA and/or LAMA
- If differential diagnosis is equally balanced between asthma and COPD
  - Few studies – overlap patients are excluded from most RCTs
  - For safety, start treatment as for asthma, with low or moderate dose ICS, pending further investigations
  - Usually also add LABA and/or LAMA, or continue if already prescribed
- The interim safety recommendation for ICS to be included in treatment for patients with COPD who have a history of asthma is supported by a well-designed case-control study \((Gershon \ JAMA \ 2014)\)
Step 4 – Commence initial therapy

- For all patients with chronic airflow limitation:
  - Treat modifiable risk factors including advice about smoking cessation
  - Treat comorbidities
  - Advise about non-pharmacological strategies including physical activity, and, for COPD or asthma-COPD overlap, pulmonary rehabilitation and vaccinations
  - Provide appropriate self-management strategies
  - Arrange regular follow-up

- See GINA and GOLD reports for details
STEP 5 SPECIALISED INVESTIGATIONS or REFER IF:

- Persistent symptoms and/or exacerbations despite treatment.
- Diagnostic uncertainty (e.g. suspected pulmonary hypertension, cardiovascular diseases and other causes of respiratory symptoms).
- Suspected asthma or COPD with atypical or additional symptoms or signs (e.g. haemoptysis, weight loss, night sweats, fever, signs of bronchiectasis or other structural lung disease).
- Few features of either asthma or COPD.
- Comorbidities present.
- Reasons for referral for either diagnosis as outlined in the GINA and GOLD strategy reports.
Step 5 – Refer for specialized investigations if needed

- Refer for expert advice and extra investigations if patient has:
  - Persistent symptoms and/or exacerbations despite treatment
  - Diagnostic uncertainty, especially if alternative diagnosis (e.g. TB, cardiovascular disease) needs to be excluded
  - Suspected airways disease with atypical or additional symptoms or signs (e.g. hemoptysis, weight loss, night sweats, fever, chronic purulent sputum). Do not wait for a treatment trial before referring
  - Suspected chronic airways disease but few features of asthma, COPD or asthma-COPD overlap
  - Comorbidities that may interfere with their management
  - Issues arising during on-going management of asthma, COPD or asthma-COPD overlap
## Step 5 – Refer for specialized investigations if needed

<table>
<thead>
<tr>
<th>Investigation</th>
<th>Asthma</th>
<th>COPD</th>
</tr>
</thead>
<tbody>
<tr>
<td>DLCO</td>
<td>Normal or slightly elevated</td>
<td>Often reduced</td>
</tr>
<tr>
<td>Arterial blood gases</td>
<td>Normal between exacerbations</td>
<td>In severe COPD, may be abnormal between exacerbations</td>
</tr>
<tr>
<td>Airway hyper-responsiveness</td>
<td>Not useful on its own in distinguishing asthma and COPD. Higher levels favor asthma</td>
<td></td>
</tr>
<tr>
<td>High resolution CT scan</td>
<td>Usually normal; may show air trapping and increased airway wall thickness</td>
<td>Air trapping or emphysema; may show bronchial wall thickening and features of pulmonary hypertension</td>
</tr>
<tr>
<td>Tests for atopy (sIgE and/or skin prick tests)</td>
<td>Not essential for diagnosis; increases probability of asthma</td>
<td>Conforms to background prevalence; does not rule out COPD</td>
</tr>
<tr>
<td>FENO</td>
<td>FENO &gt;50ppb is associated with eosinophilic airway inflammation</td>
<td>Usually normal. Low in current smokers</td>
</tr>
<tr>
<td>Blood eosinophilia</td>
<td>Supports diagnosis of eosinophilic airway inflammation</td>
<td>May be present in COPD including during exacerbations</td>
</tr>
<tr>
<td>Sputum inflammatory cells</td>
<td>Role in differential diagnosis not established in large populations</td>
<td></td>
</tr>
</tbody>
</table>

*GINA 2018, Box 5-5*
THANK YOU

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