Asthma Update 2015: Has Anything Changed?

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Conflict of Interest/Disclosure

Sheri Stensland declares no conflicts of interest, real or apparent, and no financial interests in any company, product, or service mentioned in this program, including grants, employment, gifts, stock holdings, and honoraria.

Pharmacist Objectives

- Discuss the pathophysiology, symptoms and goals of asthma treatment
- Compare the NHLBI and GINA asthma guidelines
- Demonstrate the use of the soft-mist inhaler
- Explain the asthma-COPD overlap syndrome (ACOS)

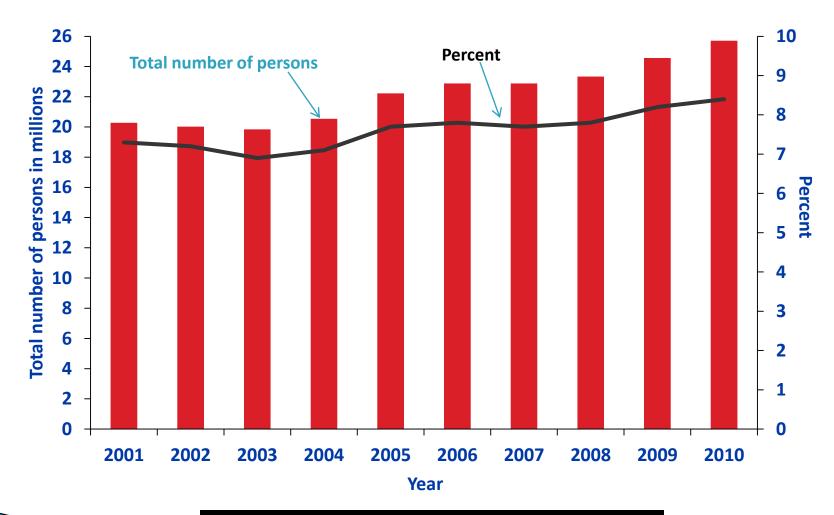
Pharmacy Technician Objectives

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Asthma Definition

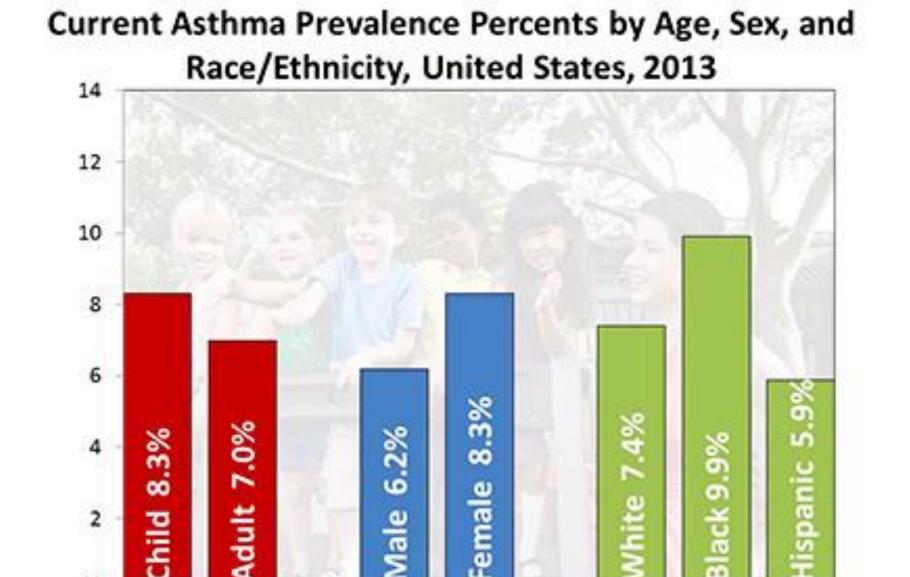
- Chronic inflammatory disorder of the lungs that is <u>reversible</u>
- Associated with symptoms of
 - Wheezing
 - Coughing
 - Chest tightness
 - Shortness of breath
- Nighttime/early morning awakenings often occur with the above symptoms

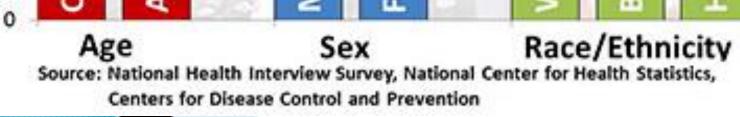
Current Asthma Prevalence: United States, 2001-2010



One in 12 people (about 26 million, or 8% of the U.S. population) had asthma in 2010, compared with 1 in 14 (about 20 million, or 7%) in 2001.

http://www.cdc.gov/nchs, http://series/sr_03/sr03_035.pdf





Female

Male 6.2%

/hite 7.4%

lack 9.9%

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http://www.cdc.gov/asthma/asthmadata.htm

Adult 7.0%

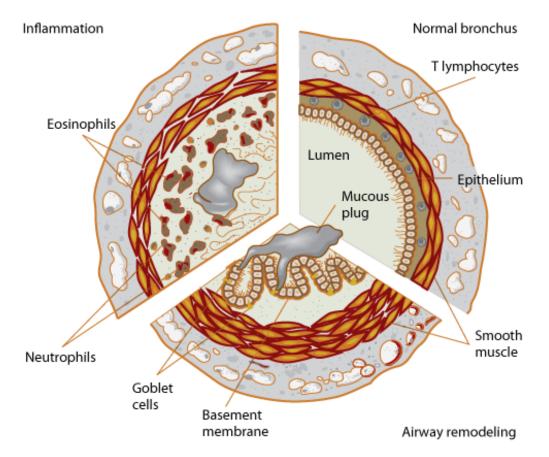
8.3%

child

4

2

Pathophysiology



Source: DiPiro JT, Talbert RL, Yee GC, Matzke GR, Wells BG, Posey LM: Pharmacotherapy: A Pathophysiologic Approach, 8th Edition: www.accesspharmacy.com

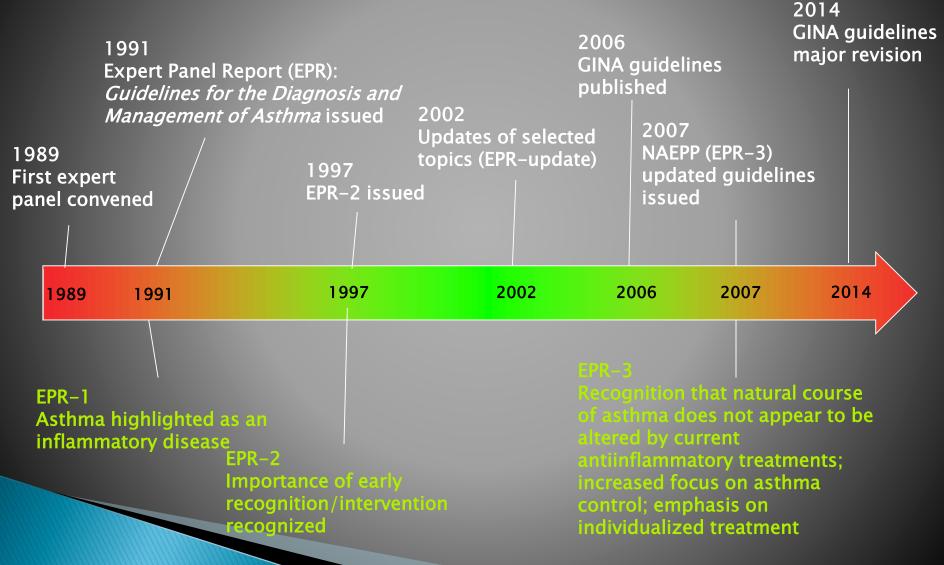
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NHLBI Guidelines Expert Panel Report - 3

Goals of Treatment

- No missed days from school or work
- No sleep disruption
- Maintain normal activities
- No (or minimal) need for ER visits or hospitalizations (decrease healthcare utilization)
- Normal or near-normal lung function

Timelime of the EPR Guidelines



NAEPP, NHLBI, NIH. Expert Panel Report 3: Guidelines for the Diagnosis and Management of Asthma. August 2007.

Treatment Pathways

Goals of asthma therapy

- Reduce Impairment
 - Prevent chronic and troublesome symptoms
 - Maintain "normal" pulmonary function and activity levels
 - Meet patients' and families' expectations and satisfaction with asthma care
- Reduce Risk
 - Prevent recurrent exacerbations and minimize the need for ER visits or hospitalizations
 - Provide optimal pharmacotherapy with minimal adverse effects
 - Minimize ER visits and hospitalizations



Pharmacotherapy - Step 1

CLASSIFYING ASTHMA SEVERITY AND INITIATING THREATMENT IN YOUTHS

≥ 12 YEARS OF AGE AND ADULTS

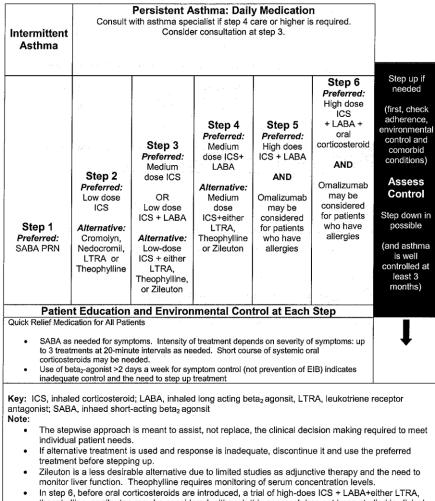
- Utilize chart to determine classification
 - If any discrepancy occurs between parameters ALWAYS go to the higher level
- Chart indicates step of therapy to initiate

ity Symptoms Nighttime awakenings hort-acting beta ₂ - agonist use for symptom control hot prevention of EIB) Interference with normal activity Lung Function	Intermittent None *Normal FEV1 betweet evacerbations	Mild >2 days/week But not daily 3-4x/month >2 days/week but not >1x daily Minor limitation	Persistent Moderate Daily >1x/weekly but not nightly Daily Some limitation	Severe Throughout the day Often 7x/week Several times per day Extremely limited		
Nighttime awakenings hort-acting beta ₂ - agonist use for symptom control not prevention of EIB) nterference with normal activity	<pre><2_days/week </pre> <2x/month <2 days/week None *Normal FEV1 between	>2 days/week But not daily 3-4x/month >2 days/week but not >1x daily	Daily >1x/weekly but not nightly Daily	Throughout the day Often 7x/week Several times per day		
Nighttime awakenings hort-acting beta ₂ - agonist use for symptom control not prevention of EIB) nterference with normal activity	<2x/month <2 days/week None *Normal FEV1 between	But not daily 3-4x/month >2 days/week but not >1x daily	>1x/weekly but not nightly Daily	Often 7x/week Several times per day		
awakenings hort-acting beta ₂ - agonist use for symptom control not prevention of EIB) nterference with normal activity	<2 days/week None *Normal FEV1 between	>2 days/week but not >1x daily	not nightly Daily	Several times per day		
agonist use for symptom control not prevention of EIB) nterference with normal activity	None *Normal FEV1 between	not >1x daily		day		
normal activity	*Normal FEV ₁ between	Minor limitation	Some limitation	Extremely limited		
Lung Function	between					
	*FEV ₁ >80% predicted *FEV ₁ /FVC normal	*FEV ₁ = >80% predicted * FEV ₁ /FVC > 80%	*FEV ₁ =60- but < 80% predicted *FEV ₁ /FVC reduced 5%	*FEV ₁ <60% predicted *FEV ₁ /FVC reduced 5%		
Exacerbations	0-2/year	>2/year	1000			
Rísk (consider frequency and severity)		Frequency and severity may fluctuate over time for				
a alla tra im haran	Relative	annual risk of exacer	bations may be relate			
Recommended Step for Initiating Therapy (See figure 4-5 for treatment steps)		0	Step 3	Step 4 or 5,		
		Step 2	And consider short course of systemic oral corticosteroids			
		In 2-6 weeks, evaluate level of asthma control that is achieved, and adjust therapy accordingly.				
ds. erity is determined vious 2-4 weeks an n is defined as an a acerbations/year ind	by both impairment a d spirometry. Assign acute episode of signa dicate persistent asth	nd risk. Assess impa severity to the most s and symptoms requi ma. There are no dat	irment domain by pa severe category in wi ring oral systemic co a to correspond frequ	tient's/caregiver's hich any feature rrticosteroids. More uencies of		
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Pharmacotherapy - Step 2

- Create Medication
 Plan
 - Remember to take any patient specific issues into account (e.g. pregnancy)

STEPWISE APPROACH FOR MANAGING ASTHMA IN YOUTHS ≥ 12 YEARS OF AGE AND ADULTS



theophylline, or zileuton may be considered, although this approach has not been studied in clinical trials.

Pharmacotherapy – Step 3

Determine current level of control

- This step is for "returning patients"
- Utilizes either the ATAQ or ACT
- Place information into chart to help determine level of control and changes in therapy

ASTHMA THERAPY ASSESSMENT QUESTIONNAIRE (ATAQ)

- 1. In the past 4 weeks did you miss any work, school, or normal daily activities because of your asthma? (1 point for Yes)
- 2. In the past 4 weeks did you wake up at night because of your asthma? (1 point for yes)
- 3. Do you believe your asthma was well-controlled in the past 4 weeks? (1 point for No)
- Do you use an inhaler for <u>quick relief</u> from asthma symptoms? If yes, what is the <u>highest number of puffs in</u> <u>one day</u> you took of this inhaler? (1 point for more than 12)

Total points = 0-4, with more points indicating more control problems.

Assessing Level of Control and Change in Therapy

		Classification of Asthma Control (>12 years)			
Components of Control		Well Controlled	Not Well Controlled	Very Poorly Controlled	
	Symptoms	<2 days/week	>2 days/week	Throughout the da	
	Nighttime awakenings	_≤2x/month	1-3 /month	<u>>4x</u> /week	
Impairment Short-acting use for sympt preventi FEV ₁ or Validated q AT	Interference with normal activity	None	Some limitation	Extremely limited	
	Short-acting beta ₂ –agonist use for symptom control (not prevention of EIB)	<2 days/week	>2 days/week	Several times per o	
	FEV ₁ or peak flow	>80% predicted/ Personal best	60-80% predicted/ Personal best	<60% predicted Personal best	
	Validated questionnaires ATAQ ACQ ACT	0 _<0.75 _≥20	1-2 ≥1.5 16-19	3-4 N/A 15	
Risk	Exacerbations	0-1 per year	2-3 per year	>3 per year	
	Progressive loss of lung function	Evaluation requires long term follow up.			
Non	Treatment-related adverse effects	Medication side effects can vary in intensity from none to very troublesome and worrisome. The level of intensity does not correla to specific levels of control but should be considered in the overall assessment of risk.			
Recommended Action For Treatment (See figure 4-5 for treatment steps.)		*Maintain current step * Consider step down if well controlled for at least 3 months.	*Step up at least 1 step and *Reevaluate in 2-6 weeks. *For side effects, consider alternative treatment options.	* Consider short cou of systemic oral corticosteroids * Step up (1-2 steps and *Reevaluate in 2 wee *For side effects, consider alternativ	

The level of control is based on the most severe impairment or risk category. Assess impairment domain by
caregiver's recall of previous 2-4 weeks and by spirometry/or peak flow measures. Symptom assessment for
longer periods should reflect a global assessment such as inquiring whether the patient's asthma is better or worse
since the last visit.

Exacerbation is defined as an acute episode of signs and symptoms requiring oral systemic corticosteroids.

Before step up in therapy:

Assess adherence to medications and environmental control.

- If alternative treatment option was used in a step, discontinue it and use preferred treatment for that step.

GINA Guidelines

Global

Initiative for

Asthma

 Collaboration with NHLBI, National Institutes of Health and WHO

GINA Global Strategy for Asthma Management and Prevention

- > 2014 major revision
- Not a guideline a way to manage asthma
- Moved from practice-focused to patientcentered approach

"New" Asthma Definition

"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."

Global Strategy for Asthma Management and Prevention

CONTROL = Symptom control + risk factors for

adverse outcomes

NHLBI vs. GINA

NHLBI

Reduce Impairment

- Symptoms
- Maintain normal activities
- Meet expectations

Reduce Risk

- Prevent exacerbations
- Optimal pharmacotherapy
- Reduce hospitalizations

- Symptom control
 - How often
 - When

GINA

- Effects on activities
- Risk control
 - Potential for flare-ups
 - Airflow limitations
 - Medication side effects

Global Strategy for Asthma Management and Prevention

- Management of asthma
 - Treat asthma to control symptoms and minimize risk
 - Cycle of Care Assess, adjust, and review
 - Check technique and adherence
 - Review non-pharmacologic, modify risk factors and comorbidities

NHLBI vs. GINA

NHLBI

- Assess level of control
 - Impairment
 - Symptom
 - Lung function
 - Risk
 - Side effects
 - Adherence
- What's missing?

Inhaler Technique Assessement!

GINA

- Assess
 - Diagnosis
 - Symptoms
 - Risk factors (lung function)
 - Inhaler technique
 - Adherence
 - Patient preference
- Adjust
- Review

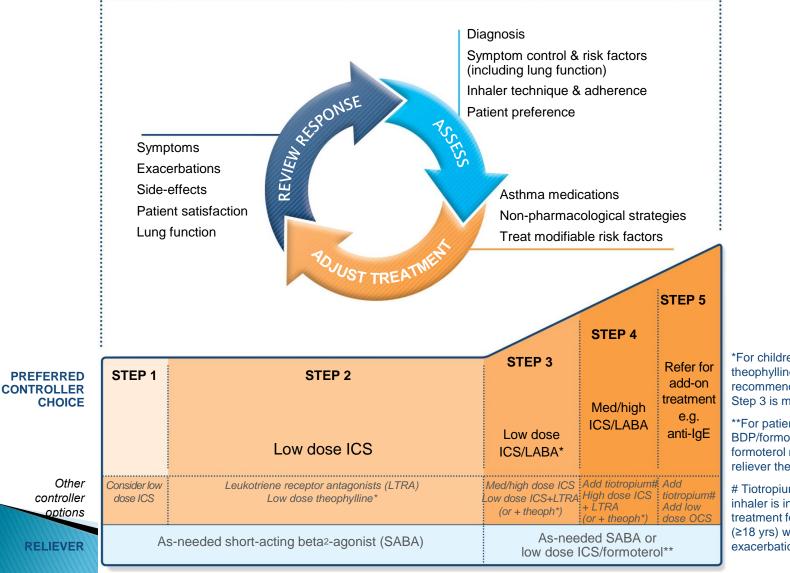
NHLBI Pharmacotherapy

STEPWISE APPROACH FOR MANAGING ASTHMA IN YOUTHS > 12 YEARS OF AGE AND ADULTS

Intermittent Asthma	Persistent Asthma: Daily Medication Consult with asthma specialist if step 4 care or higher is required. Consider consultation at step 3.					
	a an tag					
Step 1 Preferred: SABA PRN	Step 2 Preferred: Low dose ICS Alternative: Cromolyn, Nedocromil, LTRA or Theophylline	Step 3 Preferred: Medium dose ICS OR Low dose ICS + LABA Alternative: Low-dose ICS + either LTRA, Theophylline, or Zileuton	Step 4 Preferred: Medium dose ICS+ LABA Alternative: Medium dose ICS+either LTRA, Theophylline or Zileuton	Step 5 Preferred: High does ICS + LABA AND Omalizumab may be considered for patients who have allergies	Step 6 Preferred: High dose ICS + LABA + oral corticosteroid AND Omalizumab may be considered for patients who have allergies	Step up if needed (first, check adherence, environmental control and comorbid conditions) Assess Control Step down in possible (and asthma is well controlled at least 3 months)
Quick Relief Medi SABA as to 3 treat corticoste Use of be inadequa Key: ICS, inhale antagonist; SAB. Note: The step	cation for All Pati needed for symp ments at 20-minu eroids may be ne eta ₂ -agonist >2 d te control and the ed corticosteroi A, inhaed short	otoms. Intensity o tte intervals as ne eded. ays a week for syn a need to step up d; LABA, inhaled -acting beta ₂ ago is meant to ass	of treatment depended. Short court mptom control (not treatment d long acting be onsit	nds on severity o rse of systemic of ot prevention of E eta ₂ agonsit, LTF	f symptoms: up ral IB) indicates	·

- Zileuton is a less desirable alternative due to limited studies as adjunctive therapy and the need to monitor liver function. Theophylline requires monitoring of serum concentration levels.
- In step 6, before oral corticosteroids are introduced, a trial of high-does ICS + LABA+either LTRA, theophylline, or zileuton may be considered, although this approach has not been studied in clinical trials.

GINA pharmacotherapy



*For children 6-11 years, theophylline is not recommended, and preferred Step 3 is medium dose ICS

**For patients prescribed BDP/formoterol or BUD/ formoterol maintenance and reliever therapy

Tiotropium by soft-mist inhaler is indicated as add-on treatment for adults (≥18 yrs) with a history of exacerbations

Global Strategy for Asthma Management and Prevention – 2015 Update

Add-on tiotropium by soft-mist inhaler as an "other controller"

Steps 4 and 5 (GINA)

- Management of asthma in pregnancy
- DPI's can be used to deliver SABA's in mildmoderate asthma exacerbations
- Assessment of risk factors
 - Over-use of SABA is a risk factor for exacerbations
 - Very high use is a risk factor for asthma-related death

Tiotropium (Spiriva) – Respimat

- Long-acting muscarinic antagonist (LAMA)
- Approved in U.S. in 2004 first line agent in COPD – Handihaler
- > 24 hour antimuscarinic activity
- Muscarinic receptor stimulation = bronchoconstriction and mucous production

Tiotropium - Add-on maintenance treatment for asthma

- Based on two Phase III clinical trials
- Patients not controlled on ICS or ICS/LABA treatment
- Results:
 - Improved lung function
 - Increased time to first exacerbation
- GINA approved as "other" controller for Step 4 or 5 (severe asthma)
- Not currently FDA approved in U.S. (under review)

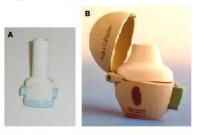
Inhalation Delivery Devices

Metered dose inhaler (MDI)



Dry powder inhaler (DPI)

Single-dose devices



Multiple-dose devices



Inhalation Delivery Devices

Breath–activated inhaler

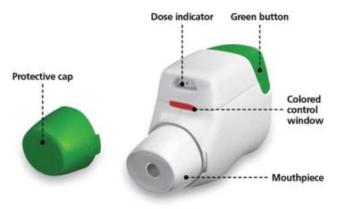




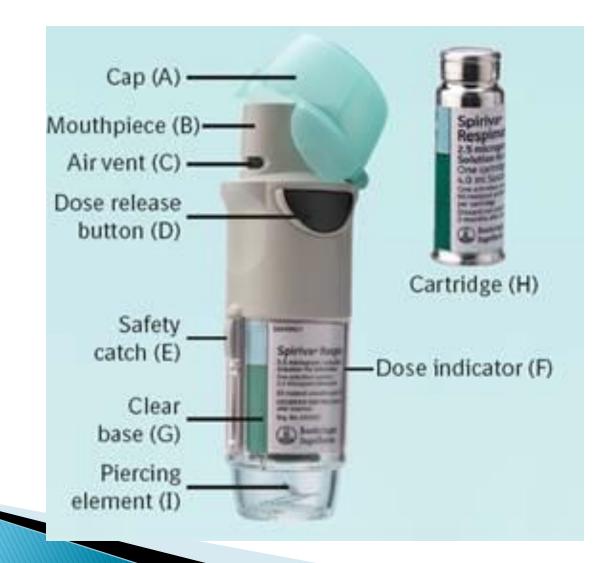
Figure A

Soft-mist inhaler



Respimat Soft-Mist Inhaler Device

Respimat Device



How to Use the Respimat (TOP)



TURN



OPEN



PRESS

Respimat Use

- Must be primed upon first use
- No need to shake with each use (no propellant)
- Turn base to load dose
- Open cap after turning base
- Press the button to release the dose
- Use a slow deep breath

ACOS Asthma-COPD Overlap Syndrome

Asthma-COPD Overlap Syndrome (ACOS)

Children and young adults = asthma Adults >40yo = COPD more common

However, many patients may have features of both asthma and COPD

Distinguishing between asthma and COPD may be difficult

ACOS

- Patients with both features may have worse outcomes:
 - Frequent exacerbations
 - Poor quality of life
 - Higher mortality
 - Greater healthcare utilization
- Rates of ACOS 15–55% of patients with chronic airway disease

Definitions

- Asthma Defined earlier in this presentation
- COPD persistent airflow limitation that is usually progressive and associated with enhanced chronic inflammatory responses in the airways
- ACOS persistent airflow limitation with several features usually associated with asthma and several features usually associated with COPD.

Feature	Asthma	COPD	ACOS
Age of onset	Usually childhood onset but can commence at any age.	Usually > 40 years of age	Usually age ≥40 years, but may have had symptoms in childhood or early adulthood
Pattern of respiratory symptoms	Symptoms may vary over time (day to day, or over longer periods), often limiting activity. Often triggered by exercise, emotions including laughter, dust or exposure to allergens	Chronic usually continuous symptoms, particularly during exercise, with 'better' and 'worse' days	Respiratory symptoms including exertional dyspnea are persistent but variability may be prominent
Lung function	Current and/or historical variable airflow limitation, e.g. BD reversibility, AHR	FEV, may be improved by therapy, but post-BD FEV/FVC < 0.7 persists	Airflow limitation not fully reversible, but often with current or historical variability
Lung function between symptoms	May be normal between symptoms	Persistent airflow limitation	Persistent airflow limitation
Past history or family history	Many patients have allergies and a personal history of asthma in childhood, and/or family history of asthma	History of exposure to noxious particles and gases (mainly tobacco smoking and biomass fuels)	Frequently a history of doctor-diagnosed asthma (current or previous), allergies and a family history of asthma, and/or a history of noxious exposures
Time course	Often improves spontaneously or with treatment, but may result in fixed airflow limitation	Generally, slowly progressive over years despite treatment	Symptoms are partly but significantly reduced by treatment. Progression is usual and treatment needs are high
Chest X-ray	Usually normal	Severe hyperinflation & other changes of COPD	Similar to COPD
Exacerbations	Exacerbations occur, but the risk of exacerbations can be considerably reduced by treatment	Exacerbations can be reduced by treatment. If present, comorbidities contribute to impairment	Exacerbations may be more common than in COPD but are reduced by treatment. Comorbidities can contribute to impairment
Typical airway inflammation	Eosinophils and/or neutrophils	Neutrophils in sputum, lymphocytes in airways, may have systemic inflammation	Eosinophils and/or neutrophils in sputum.

Initial Treatment

- Asthma (single disease)
 - ICS
 - Add-on LABA and/or LAMA (if needed)
- COPD (single disease)
 - LABA and/or LAMA
 - Add-on ICS (not monotherapy)
- ACOS
 - ICS + LABA and/or LAMA

Case: Asthma, COPD, or ACOS?

- AP is a 78yo female who presents to the pharmacy today (it is early Spring) with a prescription for an Advair Diskus 500/50 inhaler. She is complaining of increased SOB that wakes her up at night at least 2 nights a week, and wheezing. She complains of productive cough that can lead to SOB. Over the years she has had increased symptoms during the Spring due to allergies, but states lately she has had daily symptoms especially after her daily walk and has needed her short-acting inhaler. After using her inhaler she gets relief but only for short periods of time.
- > PMH: asthma (since she was a child)
- Hyperlipidemia (2002)

FEV1: 70%

- SH: denies alcohol/elicit drug use
- Smoker ½ ppd x 5 years (stopped around 1980), her husband smokes 1ppd

Case (Cont'd)

- Meds:
- Advair 250/50 Diskus 1 puff bid
- Albuterol MDI 2 puffs prn
- Albuterol 0.083% neb bid prn
- Amox-Clav 875mg1 bid (has had 5 courses of abx over past 9 months)
- Atorvastatin 10mg 1 hs
- Budesonide 0.5mg/2ml neb bid
- Prednisone 10mg burst therapy (has had 7 courses over past 9 months)
- OTC's:
- Zyrtec 10mg1 qd
- Sudafed 30mg
 1 prn
- Allbee w/C 1 qd

Favors Asthma	Favors COPD	
Onset before age 20 years	Onset after age 40 years	
 Variation in symptoms over minutes, hours or days Symptoms worse during the night or early morning Symptoms triggered by exercise, emotions including laughter, dust or exposure to allergens 	 Persistence of symptoms despite treatment Good and bad days but always daily symptoms and exertional dyspnea Chronic cough and sputum preceded onset of dyspnea, unrelated to triggers 	
 Record of variable airflow limitation (spirometry, peak flow) 	 Record of persistent airflow limitation (post-bronchodilator FEV1/FVC < 0.7) 	
 Lung function normal between symptoms Previous doctor diagnosis of asthma Family history of asthma, and other allergic conditio 	 Lung function abnormal between symptoms Previous doctor diagnosis of COPD, chronic bronchitis or emphysema Heavy exposure to a risk factor: tobacco smoke, biomass fuels 	For a patient, count the number of checked boxes in each column. If 3 or more are checked for either asthma or COPD, that
 No worsening of symptoms over time. Symptoms vary either seasonally, or from year to year May improve spontaneously or have an immediate response to BD or to ICS over weeks 	 Symptoms slowly worsening over time (progressive course over years) Rapid-acting bronchodilator treatment provides only limited relief. 	diagnosis is suggested. But if there are similar numbers of checked boxes in each column, ACOS should be
a Normal	Severe hyperinflation	considered.

Case (cont'd)

Does our patient have asthma, COPD, or ACOS?
ACOS

What should we start our patient on for initial treatment?

 $ICS \,+\, LABA \ and/or \ LAMA$

Future

- ACOS is very new
- Additional studies need to be done in order to better assess diagnosis, classification, treatment

In Summary

- Review of NHLBI Guidelines
 - Assessment of risk and impairment to guide treatment
- GINA Global Strategy for Asthma Management and Prevention
 - Cycle of care assess, adjust and review
- Tiotropium Add-on treatment in severe asthma
- ACOS New way to assess chronic airway disease

Questions?