Asthma/COPD 2021: Meeting the Challenge to Provide Optimal Management

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Disclosures

- Speaker Bureau: Sanofi-Pasteur, Merck, Pfizer, AbbVie, Biohaven
- Consultant: Sanofi-Pasteur, Pfizer, Merck, GlaxoSmithKline

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Objectives

Upon completion, the participant will be able to:

1. Identify statistics regarding asthma and COPD
2. Discuss the signs and symptoms of asthma and COPD
3. Discuss treatment options for asthma and COPD

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Asthma

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Asthma is...

- Derived from the Greek word for panting or breathlessness
- Recurrent airflow obstruction caused by chronic airway inflammation with a superimposed bronchospasm
- Leads to… wheezing, breathlessness and a cough

Guidelines for the Diagnosis and Management of Asthma—Update on Selected Topics 2002. NIH, NHLBI. June 2002. NIH publication no. 02-5075.

Prevalence of Asthma

- Impacts approximately 19 million individuals in the United States (18 and older)
- Most common chronic disease of childhood affecting 5.5 million children
- Increasing incidence of this disease
  - 76% increase in the prevalence of asthma within the past decade

https://www.cdc.gov/nchs/fastats/asthma.htm accessed 04-01-2021

Impact of Asthma

- 9.8 million visits to providers office annually
- 1.6 million ED visits annually
  - 189,000 hospitalizations
- 3524 deaths annually (2019)
  - Highest rates: adults (5x more likely than children to die)
- Children: boys > girls
- Adults: women > men

https://www.cdc.gov/nchs/fastats/asthma.htm accessed 04-01-2021

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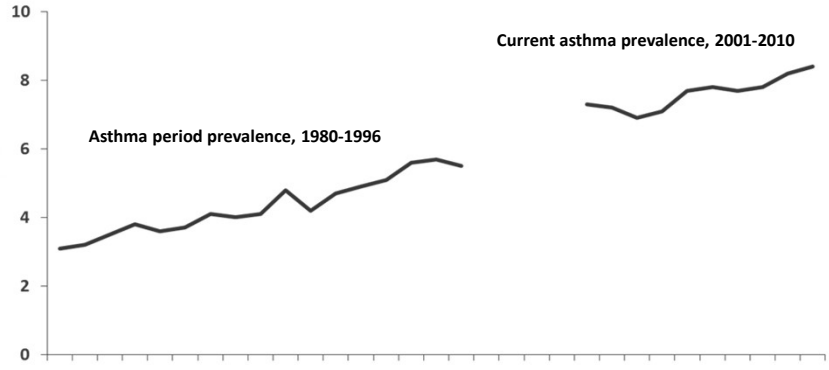
Asthma Period Prevalence and Current Asthma Prevalence: United States, 1980-2010



The percentage of the U.S. population with asthma increased from 3.1% in 1980 to 5.5% in 1996 and 7.3% in 2001 to 8.4% in 2010.

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Pathophysiology of Asthma

- Likely genetic predisposition with environmental triggers
- Genetic predisposition
  - Chromosome: 5Q31-Q33
- Results from repeated exposure to allergens in the individual already equipped with the genetic predisposition
- Upon exposure to an allergen, there is a release of IgE antibodies
- IgE antibody binds with the antigen

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Pathophysiology of Asthma

- IgE/allergen complex - then attaches itself to the mast cells on the nasal and bronchial mucosa
- Release of numerous chemical mediators

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Histamine

- Histamine is stored mainly in the mast cell
  - Circulated in the blood via the basophil
- Causes an increase in blood flow to the affected area.
  - Responsible for the increased nasal discharge, edematous mucous membranes, sneezing, itchy nose and eyes, and hives
  - Also associated with airway inflammation and bronchoconstriction

Adapted from Creticos. *Adv Stud Med*. 2002;2(14):499-503.

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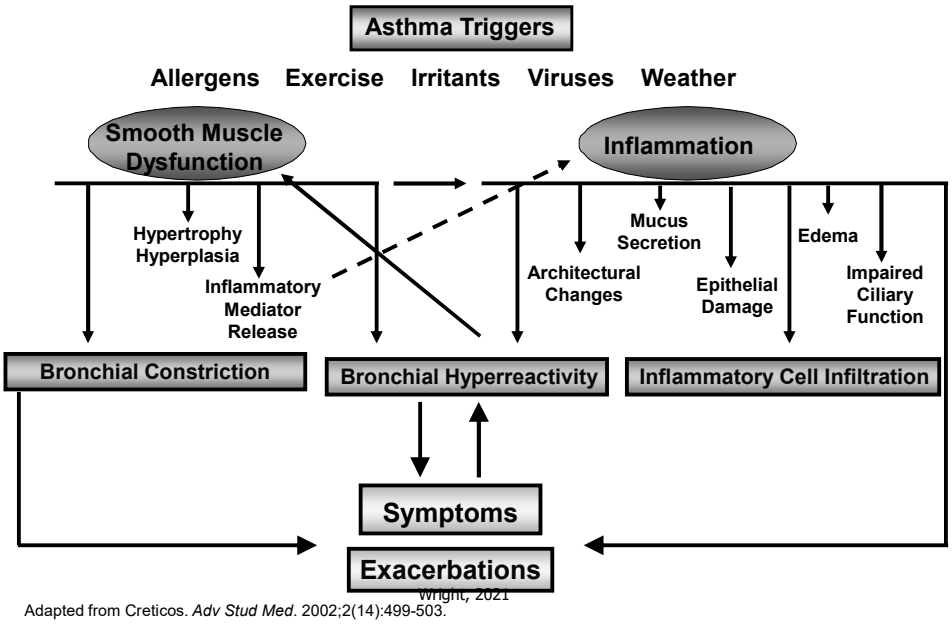
Components of Asthma



Adapted from Creticos. *Adv Stud Med*. 2002;2(14):499-503.

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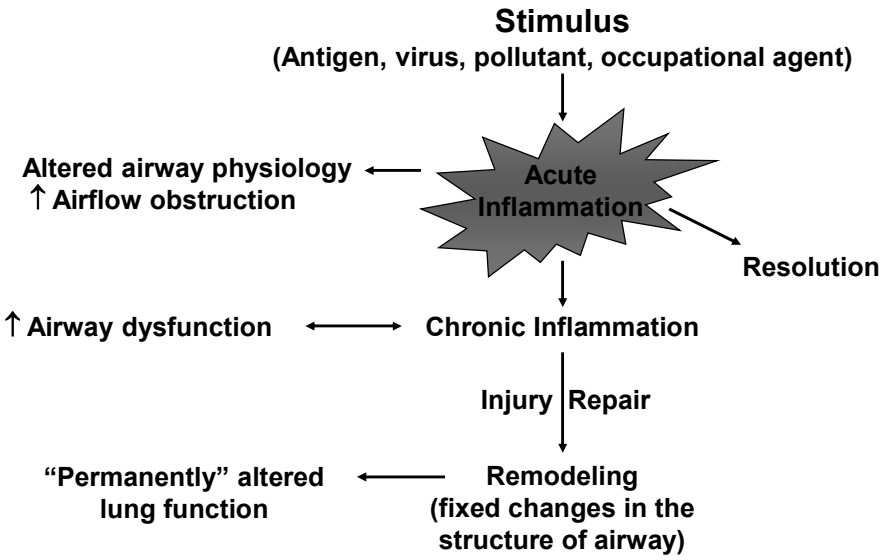
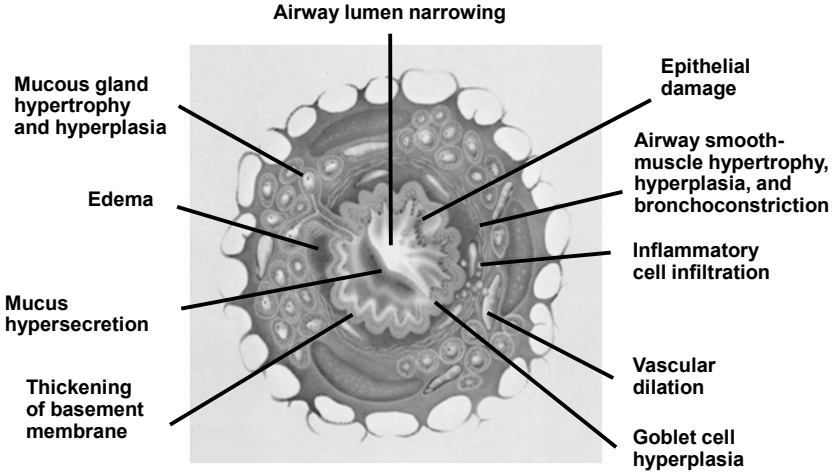
Consequences of Inflammation in Asthma



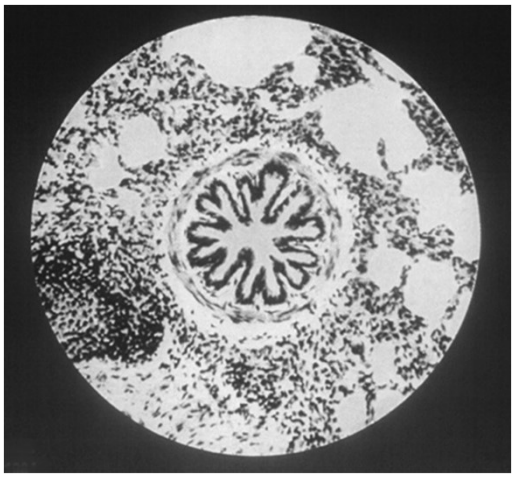
Adapted from Creticos. *Adv Stud Med*. 2002;2(14):499-503.

Asthma: Pathophysiologic Features and Changes in Airway Morphology



Adapted from *Expert Panel Report. Guidelines for the Diagnosis and Management of Asthma.* NIH, NHLBI. 1991. NIH publication 91-3042.

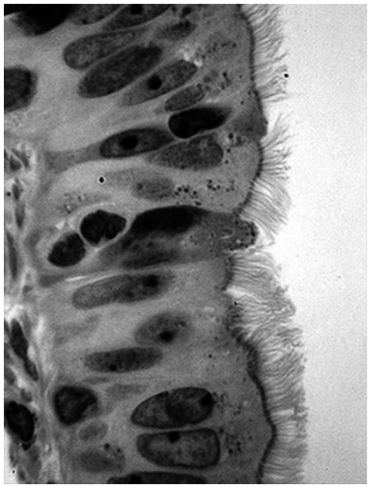
Cross Section of Bronchiole Showing Bronchospasm



Color Atlas of Respiratory Disease. Volume 2, 1995.

15

Epithelial Damage in Asthma



Normal

Asthmatic

Jeffery P. In: Asthma, Academic Press 1998.

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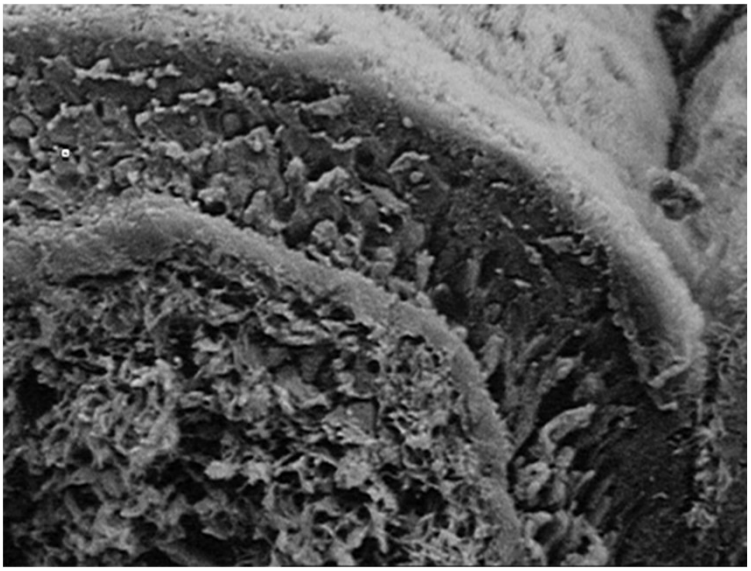
Basement Membrane Thickening



Jeffery P. In: Asthma, Academic Press 1998

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Asthma is...

- A disease of:
  - Inflammation
    - Primary Process
  - Hyperresponsiveness
  - Airway bronchoconstriction
  - Excessive mucous production

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Diagnosis of Asthma

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M.E.

- 21-year-old female
  - C/o shortness of breath with running; present x months. Accompanied by coughing
  - Denies CP, audible wheezing, runny nose, dizziness
  - Has not been previously evaluated
  - Nonsmoker
  - Bronchiolitis: infancy

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Diagnosis of Asthma

- History and Physical Examination
- Spirometry is needed to make diagnosis
- Monitoring:
  - Peak Flow Meters

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Important:

2% of individuals who present with asthma symptoms have a significant cardiorespiratory condition (other than asthma)

https://www.aafp.org/afp/2020/0615/p762.html accessed 04-01-2021

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Symptoms and Signs of Asthma in Children and Adults

- Coughing, particularly at night or after exercise
- Wheezing
- Chest tightness
- SOB
- Cold that lingers x months

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Methods for Measuring Airway Caliber

Maximum PEFR airflow achieved	FVC, FEV_1 $FEF_{25\%-75\%}$	Airway Resistance
Home	Office/Clinic	Clinic/Laboratory

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M.E. (continued)

- VSS
- Lungs clear
- Heart: S1, S2, RRR; no S3 or S4; no murmurs
- Spirometry (Quality A)
  - FEV1: 72% predicted
  - FEV1/FVC ratio: 94% predicted

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Diagnosis

- Diagnosis:
  - Improvement of 12% or more in FEV1 and 200 mL from baseline after bronchodilator OR
  - 20% improvement in PEFR post bronchodilator

https://www.aafp.org/afp/2020/0615/p762.html accessed 04-01-2021

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M.E. (continued)

- Baseline spirometry (Quality A)
  - FEV1: 72% predicted
  - FEV1/FVC ratio: 94% predicted
- Post-bronchodilator
  - FEV1: 90% (up 18%)
  - FEV1/FVC ratio: 95%

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Classification of Asthma Severity (Youths≥12 Years of Age and Adults)

Initial Diagnosis: Determine Severity and Treatment Needed

Components of Severity		Intermittent	Mild	Persistent Moderate	Severe
Impairment	**Symptoms**	≤2 days/week	>2 days/week but not daily	Daily	Throughout the day
	Nighttime awakenings	≤2x/month	3-4x/month	>1x/week but not nightly	Often 7x/week
	Short-acting $beta_2$-agonist use for symptom control (not prevention of EIB)	≤2 days/week	>2 days/week but not >1x/day	Daily	Several times per day
Normal FEV_1/FVC: 8-19 y 85% 20-39 y 80% 40-59 y 75% 60-80 y 70%	Interference with normal activity	None	Minor limitation	Some limitation	Extreme limitation
		Normal FEV_1 between exacerbations			
	Lung function	FEV_1 >80% predicted	FEV_1 >80% predicted	FEV_1 >60% but <80% predicted	FEV_1 <60% predicted
		FEV_1/FVC normal	FEV_1/FVC normal	FEV_1/FVC reduced 5%	FEV_1/FVC reduced >5%
Risk	Exacerbations requiring oral systemic corticosteroids	0-1/year (see note)		≥2/year (see note)	
		Consider severity and interval since last exacerbation. Frequency and severity may fluctuate over time for patients in any severity category.			
		Relative annual risk of exacerbations may be related to FEV_1			
Recommended Step for initiating Treatment		Step 1	Step 2	Step 3 and consider short course of oral systemic corticosteroids	Step 4
		In 2 to 6 weeks, evaluate level of asthma control that is achieved and adjust therapy accordingly.			

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M.E. (continued)

- Diagnosis:
  - Moderate Persistent Asthma
- Plan: Step 3 Care

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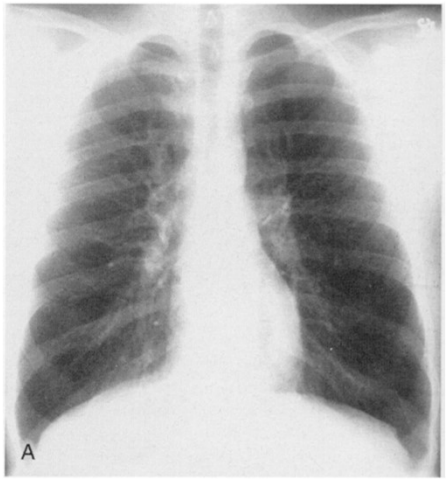
Asthma

- Hyperinflation
- Diaphragm is down to the 11th ribs
- Most patients with asthma have normal x-rays



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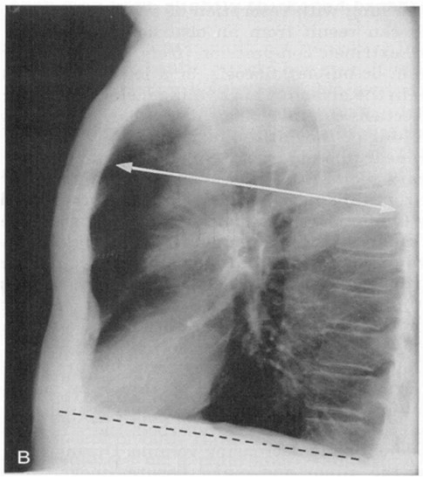
Chronic Asthma Changes

- Increased AP Lateral diameter
- The way you know that AP/Lat diameter is increased by this clear space between the sternum and the ascending aorta
- Flat diaphragms



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Treatment of Asthma

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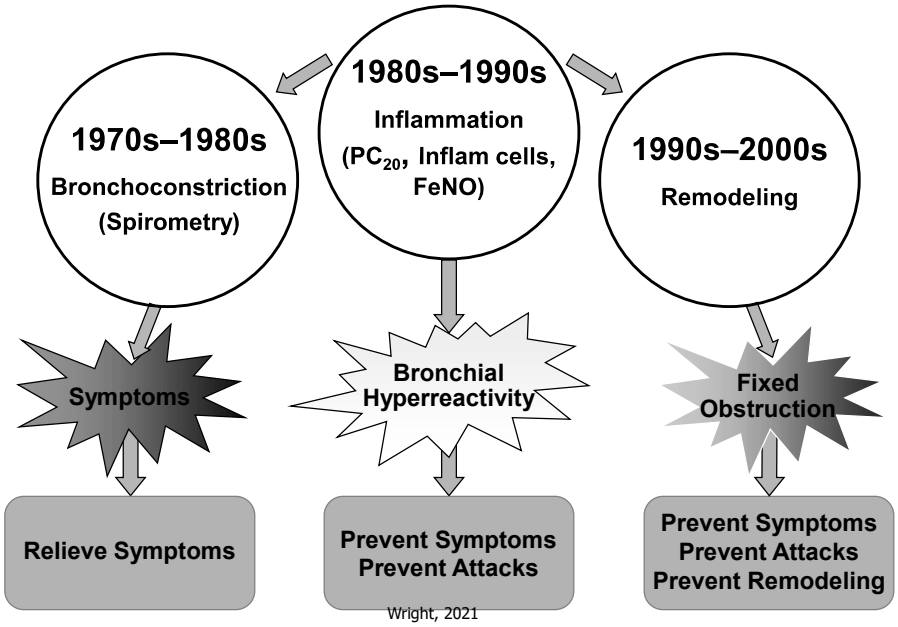
Evolution of Asthma Paradigms



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Childhood Asthma Control Can Predict Adult Lung Status

- Study of 119 asthmatic children during 1966 and 1969
- Ages: 5-14 were evaluated using FEV1
- Follow-up performed 17-18 years later and 27-28 years later
- Children who were well controlled during childhood had the smallest decline in total lung volume during adulthood

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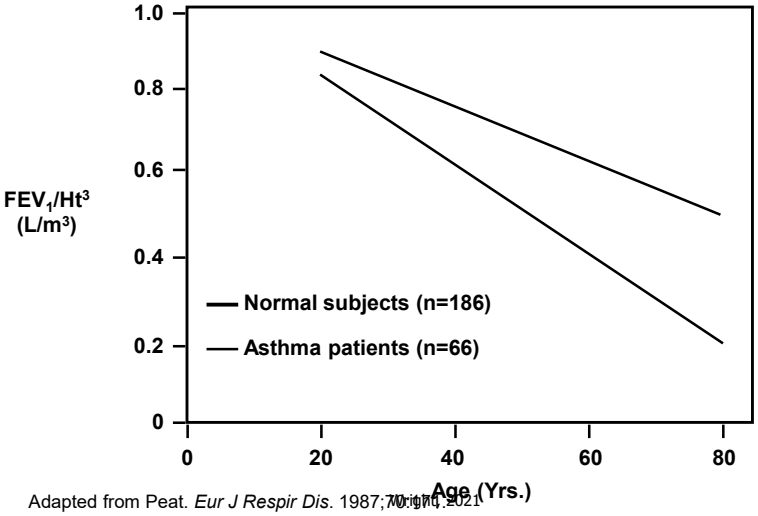
Rate of Decline in FEV_1



Adapted from Peat. *Eur J Respir Dis*. 1987;70:171.

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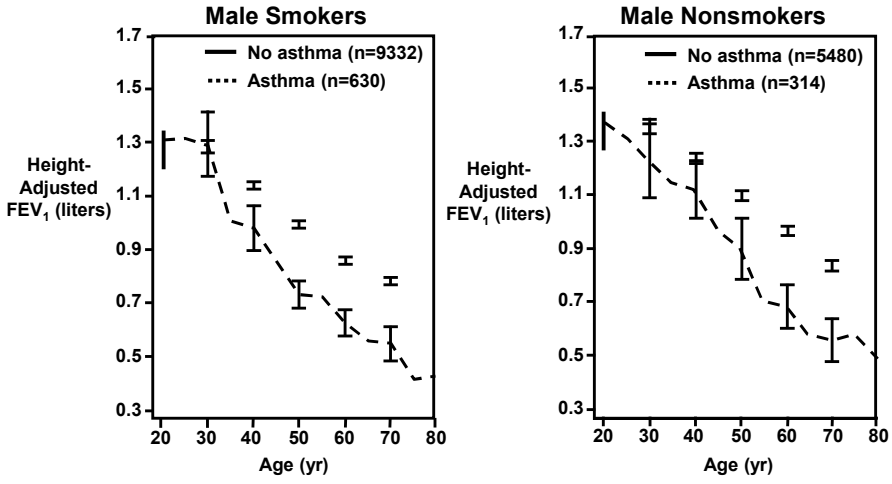
Changes With Age in FEV_1 According to Smoking and Asthma Status



Lange et al. *N Engl J Med*. 1998;339:1194-1200.

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Table 10-14: Classification of Asthma Severity (Youths≥12 Years of Age and Adults)

Initial Diagnosis: Determine Severity and Treatment Needed

Components of Severity		Persistent			
		Intermittent	**Mild**	**Moderate**	**Severe**
Impairment **Normal FEV_1/FVC:** **8-19 y 85%** **20-39 y 80%** **40-59 y 75%** **60-80 y 70%**	**Symptoms**	≤2 days/week	>2 days/week but not daily	Daily	Throughout the day
	Nighttime awakenings	≤2x/month	3-4x/month	>1x/week but not nightly	Often 7x/week
	Short-acting $beta_2$-agonist use for symptom control (not prevention of EIB)	≤2 days/week	>2 days/week but not >1x/day	Daily	Several times per day
	Interference with normal activity	None	Minor limitation	Some limitation	Extreme limitation
		Normal FEV_1 between exacerbations			
	Lung function	FEV_1 >80% predicted	FEV_1 >80% predicted	FEV_1 >60% but <80% predicted	FEV_1 <60% predicted
		FEV_1/FVC normal	FEV_1/FVC normal	FEV_1/FVC reduced 5%	FEV_1/FVC reduced >5%
Risk	Exacerbations requiring oral systemic corticosteroids	0-1/year (see note)		≥2/year (see note)	
		Consider severity and interval since last exacerbation. Frequency and severity may fluctuate over time for patients in any severity category.			
		Relative annual risk of exacerbations may be related to FEV_1			
Recommended Step for initiating Treatment		Step 1	Step 2	Step 3	Step 4
		In 2 to 6 weeks, evaluate level of asthma control that is achieved and adjust therapy accordingly.		and consider short course of oral systemic corticosteroids	

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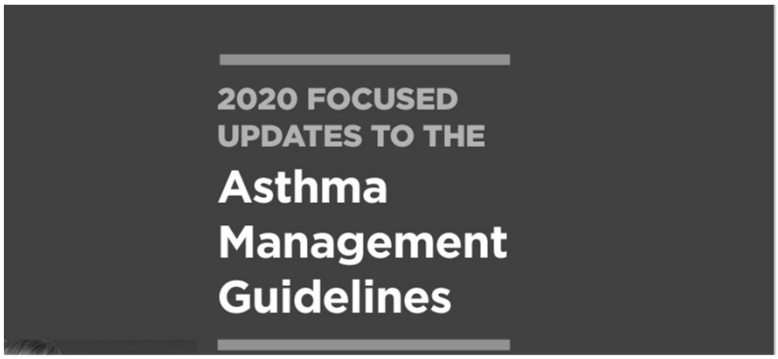

https://www.nhlbi.nih.gov/health-topics/all-publications-and-resources/2020-focused-updates-asthma-management-guidelines

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Indoor Allergen Mitigation

- Can be very helpful for individuals with allergic component
- Recommend air purifiers, mattress and pillow covers, HEPA filters

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Stepwise Approach Ages 0 – 4 Years

Figure I.b: Stepwise Approach for Management of Asthma in Individuals Ages 0–4 Years

	Intermittent Asthma	Management of Persistent Asthma in Individuals Ages 0–4 Years				
Treatment	STEP 1	STEP 2	STEP 3	STEP 4	STEP 5	STEP 6
Preferred	PRN SABA and At the start of RTI: Add short course daily ICS▲	Daily low-dose ICS and PRN SABA	Daily medium-dose ICS and PRN SABA	Daily medium-dose ICS-LABA and PRN SABA	Daily high-dose ICS-LABA and PRN SABA	Daily high-dose ICS-LABA + oral systemic corticosteroid and PRN SABA
Alternative		Daily montelukast* or Cromolyn,* and PRN SABA		Daily medium-dose ICS + montelukast* and PRN SABA	Daily high-dose ICS + montelukast* and PRN SABA	Daily high-dose ICS + montelukast*+ oral systemic corticosteroid and PRN SABA
			For children age 4 years only, see Step 3 and Step 4 on Management of Persistent Asthma in Individuals Ages 5–11 Years diagram.			

Assess Control

- First check adherence, inhaler technique, environmental factors,▲ and comorbid conditions.
- **Step up** if needed; reassess in 4–6 weeks
- **Step down** if possible (if asthma is well controlled for at least 3 consecutive months)

Consult with asthma specialist if Step 3 or higher is required. Consider consultation at Step 2.

Control assessment is a key element of asthma care. This involves both impairment and risk. Use of objective measures, self-reported control, and health care utilization are complementary and should be employed on an ongoing basis, depending on the individual's clinical situation.

Abbreviations: ICS, inhaled corticosteroid; LABA, long-acting beta$_2$-agonist; SABA, inhaled short-acting beta$_2$-agonist; RTI, respiratory tract infection; PRN, as needed

▲ Updated based on the 2020 guidelines.

* Cromolyn and montelukast were not considered for this update and/or have limited availability for use in the United States. The FDA issued a Boxed Warning for montelukast in March 2020.

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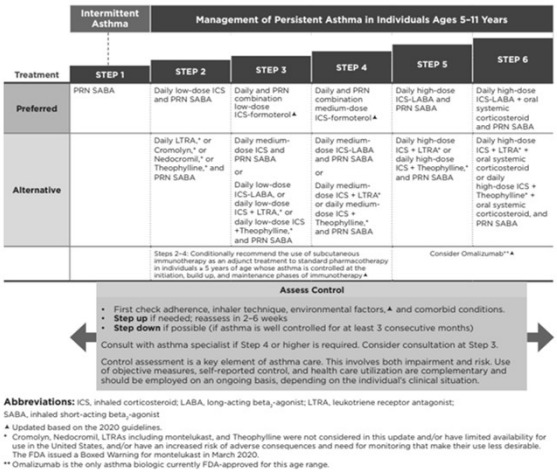
Stepwise Approach
Ages 5 – 11 Years

Figure I.c: Stepwise Approach for Management of Asthma in Individuals Ages 5–11 Years



Abbreviations: ICS, inhaled corticosteroid; LABA, long-acting beta$_2$-agonist; LTRA, leukotriene receptor antagonist; SABA, inhaled short-acting beta$_2$-agonist

▲ Updated based on the 2020 guidelines.

* Cromolyn, Nedocromil, LTRAs including montelukast, and Theophylline were not considered in this update and/or have limited availability for use in the United States, and/or have an increased risk of adverse consequences and need for monitoring that make their use less desirable. The FDA issued a Boxed Warning for montelukast in March 2020.

** Omalizumab is the only asthma biologic currently FDA-approved for this age range.

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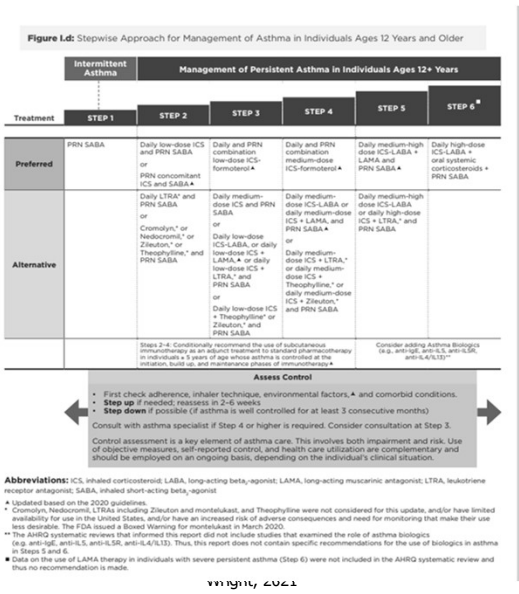
Stepwise Approach
Ages 12 Years and Older

Figure I.d: Stepwise Approach for Management of Asthma in Individuals Ages 12 Years and Older



Abbreviations: ICS, inhaled corticosteroid; LABA, long-acting beta$_2$-agonist; LAMA, long-acting muscarinic antagonist; LTRA, leukotriene receptor antagonist; SABA, inhaled short-acting beta$_2$-agonist

▲ Updated based on the 2020 guidelines.

* Cromolyn, Nedocromil, LTRAs including Zileuton and montelukast, and Theophylline were not considered for this update, and/or have limited availability for use in the United States, and/or have an increased risk of adverse consequences and need for monitoring that make their use less desirable. The FDA issued a Boxed Warning for montelukast in March 2020.

** The AHRQ systematic reviews that informed this report did not include studies that examined the role of asthma biologics (e.g. anti-IgE, anti-IL5, anti-IL5R, anti-IL4/IL13). Thus, this report does not contain specific recommendations for the use of biologics in asthma in Steps 5 and 6.

■ Data on the use of LAMA therapy in individuals with severe persistent asthma (Step 6) were not included in the AHRQ systematic review and thus no recommendation is made.

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M.E. (continued)

- Where do we go with her?
- Plan:
  - ICS with LABA (formoterol)
  - Return for f/u in 4 - 6 weeks
    - If well-controlled, continue x 3 months
    - If not well-controlled, step up care

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Major Focus in EPR-3

- Controlling asthma is a major focus of the EPR-3 and EPR-4 guidelines

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Assessing Asthma Control (Youths ≥12 Years of Age and Adults)

Follow-up Visits: Determine Level of Control and Treatment Needed

Components of Control		Well-controlled	Not Well-controlled	Very Poorly Controlled
Impairment	Symptoms	≤2 days/week	>2 days/week	Throughout the day
	Nighttime awakenings	≤2 x/month	1-3x/week	≥4x/week
	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 day
	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
	Exacerbations	0-1/year	≥2/year (see note)	
	Progressive loss of lung function	Consider severity and interval since last exacerbation		
Risk	Treatment-related adverse effects	Evaluation requires long-term follow-up care		
		Medication side effects can vary in intensity from none to very troublesome and worrisome. The level of intensity does not correlate to specific levels of control but should be considered in the overall assessment of risk.		

*ACQ values of 0.76-1.4 are indeterminate regarding well-controlled asthma.
Key: EIB, exercise-induced bronchospasm; FEV_1, forced expiratory volume in 1 second. See figure 3-8 for full name and source of ATAQ, ACQ, ACT.

Monitoring Control in Clinical Practice: Asthma Control Test™ for Patients Aged ≥12 Years[1]

1. In the past **4 weeks**, how much of the time did your **asthma** keep you from getting as much done at work, school or at home?
   All of the time ○ Most of the time ○ Some of the time ○ A little of the time ○ None of the time ○ ☐
2. During the past **4 weeks**, how often have you had shortness of breath?
   More than once a day ○ Once a day ○ 3 to 6 times a week ○ Once or twice a week ○ Not at all ○ ☐
3. During the past **4 weeks**, how often did your **asthma** symptoms (wheezing, coughing, shortness of breath, chest tightness or pain) wake you up at night or earlier than usual in the morning?
   4 or more nights a weeky ○ 2 or 3 nights a week ○ Once a week ○ Once or twice ○ Not at all ○ ☐
4. During the past **4 weeks**, how often have you used your rescue inhaler or nebulizer medication (such as albuterol)?
   3 or more times per day ○ 1 or 2 times per day ○ 2 or 3 times per week ○ Once a week or less ○ Not at all ○ ☐
5. How would you rate your **asthma** control during the **past 4 weeks**?
   Not controlled at all ○ Poorly controlled ○ Somewhat controlled ○ Well controlled ○ Completely controlled ○ ☐

Level of Control Based on Composite Score[2]

≥20 = Controlled

16-19 = Not Well Controlled

≤15 = Very Poorly Controlled

Regardless of patient's self assessment of control in Question 5

1. Asthma Control Test™ copyright, QualityMetric Incorporated 2002, 2004. All rights reserved.
2. Available at: http://www.nhlbi.nih.gov/guidelines/asthma/epr3/resource.pdf. Accessed February 5, 2007.

Short -Acting Beta-2 Agonists

- Albuterol (Proventil HFA, Ventolin HFA, ProAir HFA, Xopenex HFA)
  - 90mcg/puff, 200 puffs
  - 1 - 2 puffs every 4-6 hours or 2 puffs 15 minutes before exercise
  - Onset: 5 minutes
- Generic albuterol HFA is now available

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Short-Acting Beta-2 Agonists

- Usage of these medications more than 2 times/week is indicative of poor control
- 1 inhaler = 200 inhalations

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Controller Medications

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Inhaled Corticosteroids

- Most potent and effective anti-inflammatory medication currently available

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Inhaled Corticosteroids

- Examples
  - Beclomethasone (QVAR)
  - Budesonide (Pulmicort)
  - Fluticasone (Flovent, ArmonAir, Arnuity Ellipta)
  - Mometasone (Asmanex)
  - Ciclesonide (Alvesco)

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Comparative Daily Doses: ICS

ESTIMATED COMPARATIVE DAILY DOSAGES: INHALED CORTICOSTEROIDS FOR LONG-TERM ASTHMA CONTROL

	0–4 years of age			5–11 years of age			≥12 years of age		
Daily Dose	**Low**	**Medium***	**High***	**Low**	**Medium***	**High***	**Low**	**Medium***	**High***
MEDICATION									
Beclomethasone MDI†	N/A	N/A	N/A	80–160 mcg	>160–320 mcg	>320 mcg	80–240 mcg	>240–480 mcg	>480 mcg
40 mcg/puff				1–2 puffs 2x/day	3–4 puffs 2x/day		1–3 puffs 2x/day	4–6 puffs 2x/day	
80 mcg/puff				1 puff 2x/day	2 puffs 2x/day	≥3 puffs 2x/day	1 puff am, 2 puffs pm	2–3 puffs 2x/day	≥4 puffs 2x/day
Budesonide DPI†	N/A	N/A	N/A	180–360 mcg	>360–720 mcg	>720 mcg	180–540 mcg	>540–1,080 mcg	>1,080 mcg
90 mcg/inhalation				1–2 inhs† 2x/day	3–4 inhs† 2x/day		1–3 inhs† 2x/day		
180 mcg/ inhalation					2 inhs† 2x/day	≥3 inhs† 2x/day	1 inh† am, 2 inhs† pm	2–3 inhs† 2x/day	≥4 inhs† 2x/day
Budesonide Nebules	0.25–0.5 mg	>0.5–1.0 mg	>1.0 mg	0.5 mg	1.0 mg	2.0 mg	N/A	N/A	N/A
0.25 mg	1–2 nebs†/day			1 neb† 2x/day					
0.5 mg	1 neb†/day	2 nebs†/day	3 nebs†/day	1 neb†/day	1 neb† 2x/day				
1.0 mg		1 neb†/day	2 nebs†/day		1 neb†/day	1 neb† 2x/day			
Ciclesonide MDI†	N/A	N/A	N/A	80–160 mcg	>160–320 mcg	>320 mcg	160–320 mcg	>320–640 mcg	>640 mcg
80 mcg/puff				1–2 puffs/day	1 puff am, 2 puffs pm–2 puffs 2x/day	≥3 puffs 2x/day	1–2 puffs 2x/day	3–4 puffs 2x/day	
160 mcg/puff				1 puff/day	1 puff 2x/day	≥2 puffs 2x/day		2 puffs 2x/day	≥3 puffs 2x/day
Flunisolide MDI†	N/A	N/A	N/A	160 mcg	320–480 mcg	≥480 mcg	320 mcg	>320–640 mcg	>640 mcg
80 mcg/puff				1 puff 2x/day	2–3 puffs 2x/day	≥4 puffs 2x/day	2 puffs 2x/day	3–4 puffs 2x/day	≥5 puffs 2x/day

* It is preferable to use a higher mcg/puff or mg/inhalation formulation to achieve as low a number of puffs or inhalations as possible.
† Abbreviations: DPI, dry powder inhaler (requires deep, fast inhalation); inh, inhalation; MDI, metered-dose inhaler (releases a puff of medication); neb, nebule.

https://www.nhlbi.nih.gov/files/docs/guidelines/asthma_qrg.pdf

52

To Reduce Side Effects of Inhaled Corticosteroids

- Administer with spacers or holding chambers
- Rinse mouth after inhalation
- Use lowest possible dose to maintain control
- Children - monitor growth

53

Schenkel, E. et. al

- 98 patients randomized to either placebo or mometasone furoate aqueous nasal spray
- Ages: 3 - 9 years
- After 1 year, there was no suppression of height in the children using the nasal corticosteroid when compared with the child using placebo

Pediatrics Vol 105 No. 2 February 2000, p. 22

54

Remember...

- Poorly controlled asthma often delays growth
- In general, children with asthma tend to have longer periods of reduced growth rates prior to puberty

55

Leukotriene Receptor Antagonists

- Cysteinyl leukotriene production in the body has been associated with airway edema, smooth muscle constriction and the inflammatory process
- These medications block the leukotriene receptors which in turn is able to prevent inflammation and bronchoconstriction

56

Montelukast (Singulair)

- (Montelukast) Singulair
  - 4 mg Granules once daily: 12 – 23 months
  - 4 mg tablet for children 2 - 5 years of age
  - 5mg qhs for ages 6-14
  - 10mg qhs for ages 15 and older

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Montelukast (Singulair)

- Drug Interactions
  - Metabolized through CYP2A6 (minor pathway)
  - Phenobarbital: decreases montelukast but no dosage adjustment is required
- Side effects: headache, fatigue, dizziness, Churg-Strauss
- Precautions
  - Not for an acute exacerbation
- Category: B

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Updates

- Montelukast (Singulair)
  - FDA strengthened warnings re: serious behavior changes and mood changes

59

Methylxanthines

- Theophylline
  - Theo-24, Theo-Dur, Uni-Dur, Slo-Bid
  - Bronchodilatation and increases the force with which the diaphragm contracts
  - 6 years and older
  - Difficult to manage and as a result has not really gained wide spread acceptance
  - Indicated for individuals with moderate to severe asthma
  - Numerous drug interactions

60

Theophylline

- Numerous medications, foods and chemicals interact with theophylline
  - All of the following decrease theophylline levels
    - Smoking (cigarettes and marijuana)
    - High protein/low carbohydrate diet
    - Phenytoin
    - Phenobarbital
    - Carbamazepine
    - Ketoconazole
    - Diuretics

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Theophylline

- Theophylline levels (normal 6-15mcg/dL)
  - 15-25: GI upset, N/V, diarrhea, abdominal pain
  - 25-35: Tachycardia, occasional PVC's
  - >35: Ventricular tachycardia, seizures
- Category: C

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Long-Acting Beta-2 Agonists

- Salmeterol (Serevent)
  - Diskus
    - ≥4 years of age-1 puff po q 12 hours
  - No role for acute exacerbations
  - Seems to help children affected by the nocturnal cough and wheezing
  - Good for prevention of exercise induced asthma

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Long-Acting Beta-2 Agonists

- Formoterol (Foradil, Perforomist)
  - ≥ 5 years of age: 1 inhalation every 12 hours
  - May be used for prevention of EIB
- Olodaterol (Striverdi Respimat)
  - Indicated for COPD only
- Indacaterol (Arcapta Neohaler)
  - Indicated for COPD only

64

LABA

- REMOVED: FDA warning regarding increased deaths in patients treated with LABA
- Should be used only with inhaled corticosteroid in the patient with asthma

www.fda.gov/CDER/Drug/infopage/LABA/default.htm accessed 07-20-2010

65

Combination Products

- Fluticasone/salmeterol (Advair, AirDuo, Wixela Inhub)
- Budesonide/formoterol (Symbicort)
- Mometasone/formoterol (Dulera)
- Fluticasone/vilanterol (Breo Ellipta)

66

Monoclonal Antibodies

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Omalizumab (Xolair)

- Indicated for adults and adolescents (6 and older) with moderate to severe persistent asthma who have a positive skin test or *in vitro* reactivity to a perennial aeroallergen
- And…whose symptoms are inadequately controlled with inhaled corticosteroids
- SC injection (weight and IGE based)
- Every 2 – 4 weeks
- Warning: anaphylaxis

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Omalizumab (Xolair)

- Recombinant DNA-derived humanized IgG1 monoclonal antibody that selectively binds to human immunoglobulin E (IgE).
- Inhibits the binding of IgE to the high-affinity IgE receptor on the surface of mast cells and basophils
- Limits the degree of release of mediators of the allergic response.

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Eosinophilic phenotypes

- Interleukin-4/13 antagonist
  - Dupilumab (Dupixent)
- Interleukin-5 antagonists
  - Mepolizumab (Nucala)
  - Reslizumab (Cinqair)
  - Benralizumab (Fasenra)

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LAMA

- LAMA
  - Long acting bronchodilator
  - Increasing/emerging role in the management of asthma
  - Controller medication
  - LAMA are only added to patient with poorly controlled asthma after LABA/ICS is in place

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LAMA

- Caution: urinary retention and glaucoma
- Approved LAMA
  - Tiotroprium bromide: approved 6 years of age and older - asthma

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Triple Drug Therapy

- Fluticasone, umeclidinium, and vilanterol (Trelegy Ellipta)
  - 1 inhalation daily
- LAMA only to be used when patient is on an ICS/LABA combination and is not well-controlled

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Fractional Exhaled Nitric Oxide

- Nitric oxide can be measured in exhaled breath
- Measure of airway inflammation
- Used:
  - When diagnosis is uncertain
  - In children 4 years of age and younger with recurrent wheezing

https://www.nhlbi.nih.gov/health-topics/all-publications-and-resources/2020-focused-updates-asthma-management-guidelines

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Fractional Exhaled Nitric Oxide

- FeNO > 50 ppb (or > 35 ppb in children ages 5 – 12 years) are consistent with elevated T2 (Type 2) inflammation and support diagnosis of asthma
- Allergic rhinitis can increase FeNO levels as well; interpret cautiously

https://www.nhlbi.nih.gov/health-topics/all-publications-and-resources/2020-focused-updates-asthma-management-guidelines

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FeNO Testing

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Acute Asthma Exacerbation Management

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Severity of Acute Exacerbations

FIGURE 5–1. CLASSIFYING SEVERITY OF ASTHMA EXACERBATIONS IN THE URGENT OR EMERGENCY CARE SETTING

Note: Patients are instructed to use quick-relief medications if symptoms occur or if PEF drops below 80 percent predicted or personal best. If PEF is 50–79 percent, the patient should monitor response to quick-relief medication carefully and consider contacting a clinician. If PEF is below 50 percent, immediate medical care is usually required. In the urgent or emergency care setting, the following parameters describe the severity and likely clinical course of an exacerbation.

	Symptoms and Signs	Initial PEF (or FEV_1)	Clinical Course
Mild	Dyspnea only with activity (assess tachypnea in young children)	PEF ≥70 percent predicted or personal best	▪ Usually cared for at home ▪ Prompt relief with inhaled SABA ▪ Possible short course of oral systemic corticosteroids
Moderate	Dyspnea interferes with or limits usual activity	PEF 40–69 percent predicted or personal best	▪ Usually requires office or ED visit ▪ Relief from frequent inhaled SABA ▪ Oral systemic corticosteroids; some symptoms last for 1–2 days after treatment is begun
Severe	Dyspnea at rest; interferes with conversation	PEF <40 percent predicted or personal best	▪ Usually requires ED visit and likely hospitalization ▪ Partial relief from frequent inhaled SABA ▪ Oral systemic corticosteroids; some symptoms last for >3 days after treatment is begun ▪ Adjunctive therapies are helpful
***Subset:* Life threatening**	Too dyspneic to speak; perspiring	PEF <25 percent predicted or personal best	▪ Requires ED/hospitalization; possible ICU ▪ Minimal or no relief from frequent inhaled SABA ▪ Intravenous corticosteroids ▪ Adjunctive therapies are helpful

Key: ED, emergency department; FEV_1, forced expiratory volume in 1 second; ICU, intensive care unit; PEF, peak expiratory flow; SABA, short-acting $beta_2$-agonist

http://www.nhlbi.nih.gov/guidelines/asthma/asthsumm.pdf accessed 06-15-2019

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Acute Asthma Exacerbation

- Measure FEV1
- Inhaled short acting beta 2 agonist: Up to three treatments of 2-4 puffs by MDI at 20 minute intervals OR a single nebulizer
- Can repeat x 1 – 2 provided patient tolerates
- Prednisone
  - What dose and schedule??

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COPD

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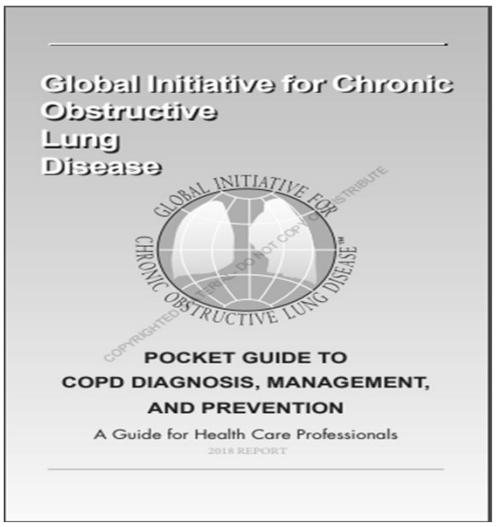
Global Initiative for Chronic Obstructive Lung Disease, 2018



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Case Study

- 55 year old male
- Presents with 3 year history of worsening sob on exertion
  - Denies chest pain, diaphoresis, palpitations, lightheadedness
- Smoker x 35 years; 1 ppd

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Case Study

- PMH
  - Asthma in childhood
- ROS
  - Wheezing with exercise and URI's
  - Sputum production every morning

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Case Study

- Physical examination
  - VS: 128/78, Pulse: 88, RR: 20, Temp: 97.2
  - HEENT: normal
  - Heart: S1, S2, RRR; no S3, S4, murmurs
  - Lungs: clear, but diminished
  - O2 sat – 97% on RA

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COPD Definition

- 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.

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Definition and Overview

OVERALL KEY POINTS:

- The most common respiratory symptoms include dyspnea, cough and/or sputum production.
- The main risk factor for COPD is tobacco smoking but other environmental exposures such as biomass fuel exposure and air pollution may contribute.

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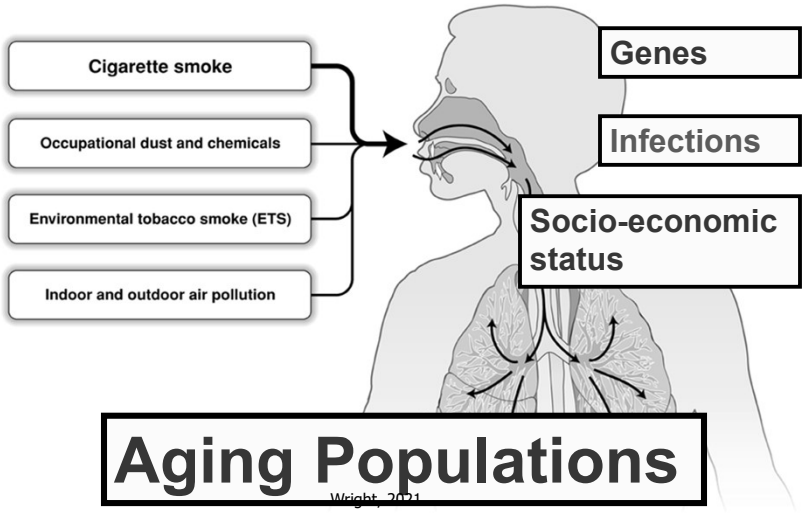
Chronic Obstructive Pulmonary Disease (COPD)

- COPD is currently the fourth leading cause of death in the world.[1]
- COPD is projected to be the 3rd leading cause of death by 2020.[2]
- More than 3 million people died of COPD in 2012 accounting for 6% of all deaths globally.
- Globally, the COPD burden is projected to increase in coming decades because of continued exposure to COPD risk factors and aging of the population.

1. Lozano R, Naghavi M, Foreman K, et al. Global and regional mortality from 235 causes of death for 20 age groups in 1990 and 2010: a systematic analysis for the Global Burden of Disease Study 2010. *Lancet* 2012; 380(9859): 2095-128.
2. Mathers CD, Loncar D. Projections of global mortality and burden of disease from 2002 to 2030. *PLoS Med* 2006; **3**(11): e442.

Global Strategy for Diagnosis, Management and Prevention of COPD

Risk Factors for COPD



Wright, 2021

Alpha-1 antitrypsin deficiency (AATD)

- Alpha-1 antitrypsin deficiency (AATD) screening
  - Screen all individuals with COPD, particularly those who live in areas of high prevalence
  - Levels < 20% may suggest familial homozygous deficiency and family members should be screened

https://goldcopd.org/wp-content/uploads/2018/02/WMS-GOLD-2018-Feb-Final-to-print-v2.pdf

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Diagnosis and Initial Assessment

OVERALL KEY POINTS:

- COPD should be considered in any patient who has dyspnea, chronic cough or sputum production, and/or a history of exposure to risk factors for the disease.
- Spirometry is required to make the diagnosis; the presence of a post-bronchodilator FEV1/FVC < 0.70 confirms the presence of persistent airflow limitation.
- The goals of COPD assessment are to determine the level of airflow limitation, the impact of disease on the patient's health status, and the risk of future events (such as exacerbations, hospital admissions, or death), in order to guide therapy.

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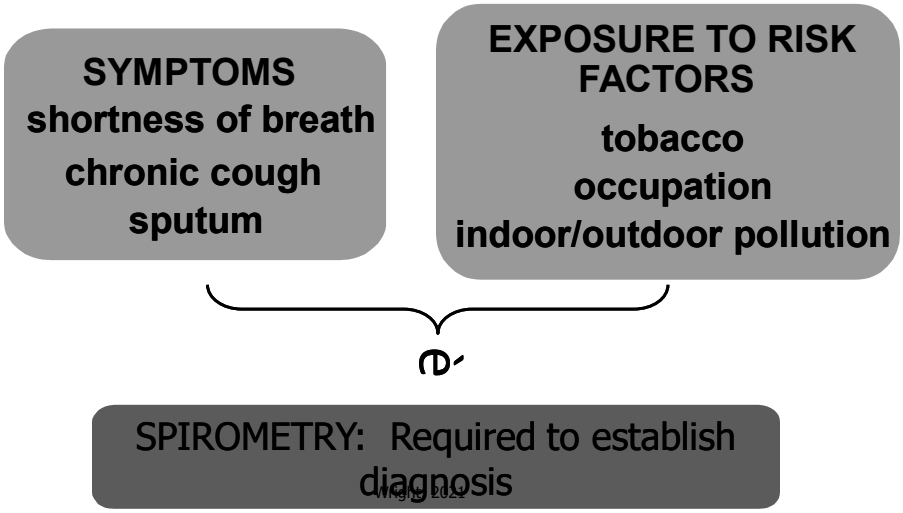
Global Strategy for Diagnosis, Management and Prevention of COPD

Diagnosis of COPD



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Global Strategy for Diagnosis, Management and Prevention of COPD

Assessment of Airflow Limitation: Spirometry

- Spirometry should be performed after the administration of an adequate dose of a short-acting inhaled bronchodilator to minimize variability.
- A post-bronchodilator $FEV_1/FVC < 0.70$ confirms the presence of airflow limitation.
- Where possible, values should be compared to age-related normal values to avoid overdiagnosis of COPD in the elderly.

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Spirometry Testing

- CPT codes
  - 94010: $32.84 (FEV1/FVC)
  - 94060: $56.65 (spirometry before and after bronchodilator)
  - 94375: $36.81 (flow loop)
  - 94620: $64.59 (pulmonary stress test)

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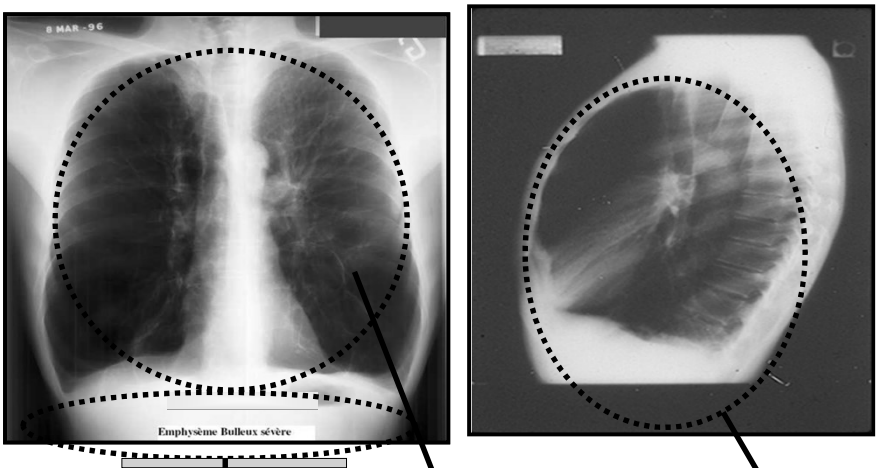
Utilized with permission from Fitzgerald Health Education Associates, 2007



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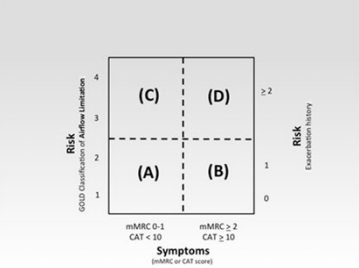

Global Strategy for Diagnosis, Management and Prevention of COPD

Combined Assessment of COPD

*When assessing risk, choose the **highest** risk according to GOLD grade or exacerbation history*

Patient	Characteristic	Spirometric Classification	Exacerbations per year	mMRC	CAT
A	Low Risk Less Symptoms	GOLD 1-2	≤ 1	0-1	< 10
B	Low Risk More Symptoms	GOLD 1-2	≤ 1	≥ 2	≥ 10
C	High Risk Less Symptoms	GOLD 3-4	≥ 2	0-1	< 10
D	High Risk More Symptoms	GOLD 3-4	≥ 2	≥ 2	≥ 10

Wright, 2021

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Global Strategy for Diagnosis, Management and Prevention of COPD

Assessment of COPD

- Assess symptoms

Use the COPD Assessment Test(CAT)

or

mMRC Breathlessness scale

Wright, 2021

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Global Strategy for Diagnosis, Management and Prevention of COPD

Assessment of Symptoms

COPD Assessment Test (CAT): An 8-item measure of health status impairment in COPD (http://catestonline.org).

Breathlessness Measurement using the Modified British Medical Research Council (mMRC) Questionnaire: relates well to other measures of health status and predicts future mortality risk.

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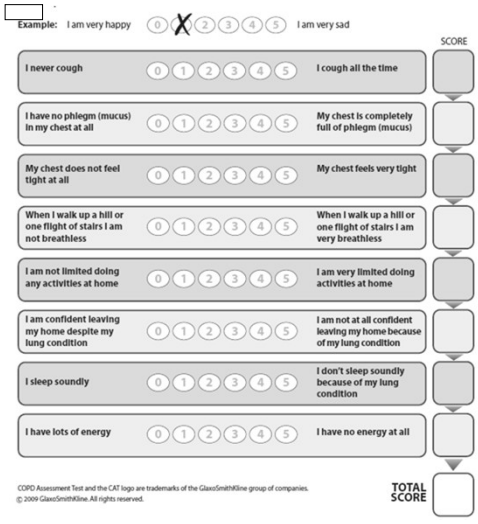
CAT: What are the questions?



Reproduced from: COPD Assessment Test Healthcare Professional User Guide

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Global Strategy for Diagnosis, Management and Prevention of COPD

Classification of Severity of Airflow Limitation in COPD*

In patients with $FEV_1/FVC < 0.70$:

GOLD 1: Mild	$FEV_1 \geq 80\%$ predicted
GOLD 2: Moderate	$50\% \leq FEV_1 < 80\%$ predicted
GOLD 3: Severe	$30\% \leq FEV_1 < 50\%$ predicted
GOLD 4: Very Severe	$FEV_1 < 30\%$ predicted

**Based on Post-Bronchodilator FEV_1*

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Case Study

- Spirometry Test Results
  - FEV1
    - Pre-bronchodilator: 2.22 L (69%)
    - Postbronchodilator: 243 L (76%)
    - Change: 9%
  - FVC
    - Pre: 4.22 L (107%)
    - Post: 4.45 L (113%)
    - Change: 5%

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Case Study

- Spirometry Test Results
  - FEV1/FVC
    - Pre: 53%
    - Post: 55%
  - CAT test: 12

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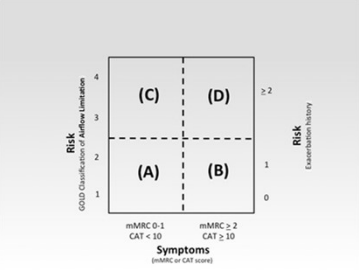

Global Strategy for Diagnosis, Management and Prevention of COPD

Combined Assessment of COPD

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C	High Risk Less Symptoms	GOLD 3-4	≥ 2	0-1	< 10
D	High Risk More Symptoms	GOLD 3-4	≥ 2	≥ 2	≥ 10

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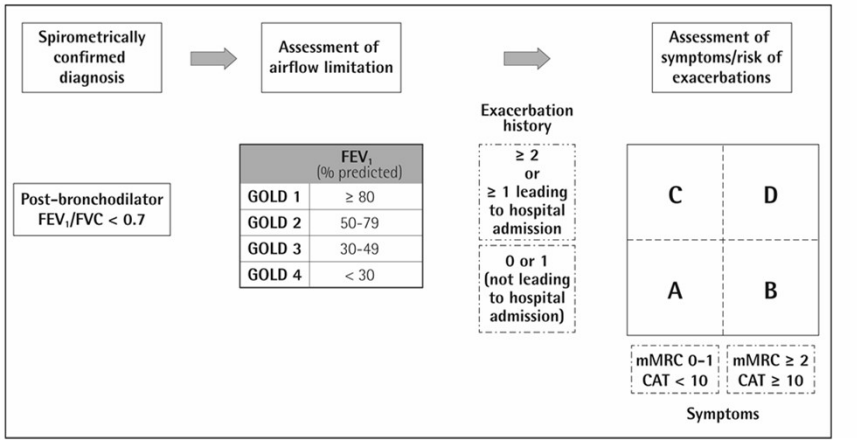
ABCD Assessment Tool

Figure 2.4. The refined ABCD assessment tool



What Patient Type is Our Patient?

- A
- B
- C
- D

What Would You Initiate?

- What would you do?
- Which medication would you choose??

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Evidence Supporting Prevention & Maintenance Therapy

OVERALL KEY POINTS (1 of 3):

- Smoking cessation is key. Pharmacotherapy and nicotine replacement reliably increase long-term smoking abstinence rates.
  - The effectiveness and safety of e-cigarettes as a smoking cessation aid is uncertain at present.
- Pharmacologic therapy can reduce COPD symptoms, reduce the frequency and severity of exacerbations, and improve health status and exercise tolerance.
- Inhaler technique needs to be assessed regularly.

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Evidence Supporting Prevention & Maintenance Therapy

OVERALL KEY POINTS (2 of 3):

- Influenza vaccination decreases the incidence of lower respiratory tract infections.
- Pneumococcal vaccination decreases lower respiratory tract infections.
- Pulmonary rehabilitation improves symptoms, quality of life, and physical and emotional participation in everyday activities.
- In patients with severe resting chronic hypoxemia, long-term oxygen therapy improves survival.

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Global Strategy for Diagnosis, Management and Prevention of COPD

Therapeutic Options: COPD Medications

Beta$_2$-agonists
Short-acting beta$_2$-agonists
Long-acting beta$_2$-agonists
Anticholinergics
Short-acting anticholinergics
Long-acting anticholinergics
Combination short-acting beta$_2$-agonists + anticholinergic in one inhaler
Methylxanthines
Inhaled corticosteroids
Combination long-acting beta$_2$-agonists + corticosteroids in one inhaler
Systemic corticosteroids
Phosphodiesterase-4 inhibitors

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Global Strategy for Diagnosis, Management and Prevention of COPD

Manage Stable COPD: Non-pharmacologic

Patient Group	Essential	Recommended	Depending on local guidelines
A	Smoking cessation (can include pharmacologic treatment)	Physical activity	Influenza vaccination Pneumococcal vaccination
B, C, D	Smoking cessation (can include pharmacologic treatment) Pulmonary rehabilitation	Physical activity	Influenza vaccination Pneumococcal vaccination

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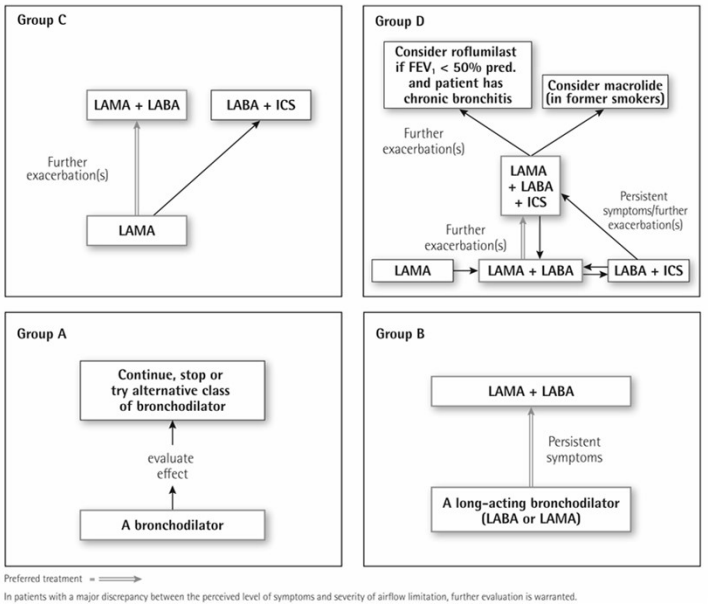
Figure 4.1. Pharmacologic treatment algorithms by GOLD Grade [highlighted boxes and arrows indicate preferred treatment pathways]



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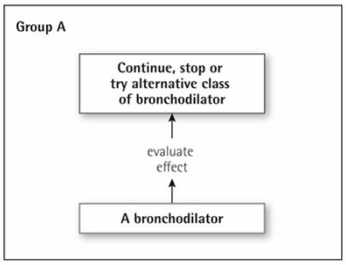
Pharmacologic treatment algorithms

Group A

- All Group A patients should be offered bronchodilator treatment based on its effect on breathlessness. This can be either a short- or a long-acting bronchodilator.
- This should be continued if symptomatic benefit is documented.

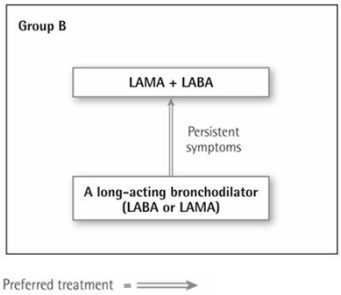


 Wright, 2021

Pharmacologic treatment algorithms

Group B

- Initial therapy should consist of a long acting bronchodilator. Long-acting inhaled bronchodilators are superior to short-acting bronchodilators taken as needed i.e., *pro re nata* (prn) and are therefore recommended.
- There is no evidence to recommend one class of long-acting bronchodilators over another for initial relief of symptoms in this group of patients. In the individual patient, the choice should depend on the patient's perception of symptom relief.
- For patients with persistent breathlessness on monotherapy the use of two bronchodilators is recommended.

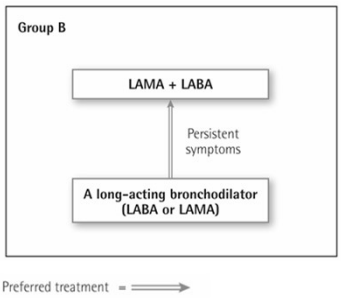


 Wright, 2021

Pharmacologic treatment algorithms

Group B (continued)

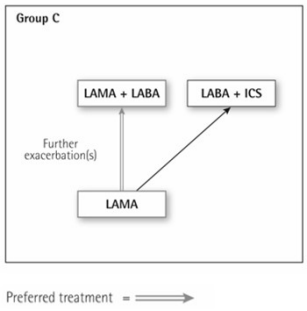
- For patients with severe breathlessness initial therapy with two bronchodilators may be considered.
- If the addition of a second bronchodilator does not improve symptoms, we suggest the treatment could be stepped down again to a single bronchodilator.
- Group B patients are likely to have comorbidities that may add to their symptomatology and impact their prognosis, and these possibilities should be investigated.



Pharmacologic treatment algorithms

Group C

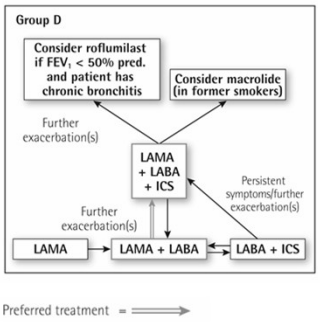
- Initial therapy should consist of a single long acting bronchodilator. In two head-to head comparisons the tested LAMA was superior to the LABA regarding exacerbation prevention, therefore we recommend starting therapy with a LAMA in this group.
- Patients with persistent exacerbations may benefit from adding a second long acting bronchodilator (LABA/LAMA) or using a combination of a long acting beta$_2$-agonist and an inhaled corticosteroid (LABA/ICS). As ICS increases the risk for developing pneumonia in some patients, our primary choice is LABA/LAMA.



Pharmacologic treatment algorithms

Group D

- We recommend starting therapy with a LABA/LAMA combination because:
  - In studies with patient reported outcomes as the primary endpoint LABA/LAMA combinations showed superior results compared to the single substances. If a single bronchodilator is chosen as initial treatment, a LAMA is preferred for exacerbation prevention based on comparison to LABAs (for details see GOLD 2017 Chapter 3).
  - A LABA/LAMA combination was superior to a LABA/ICS combination in preventing exacerbations and other patient reported outcomes in Group D patients (for details see GOLD 2017 Chapter 3).
  - Group D patients are at higher risk of developing pneumonia when receiving treatment with ICS.



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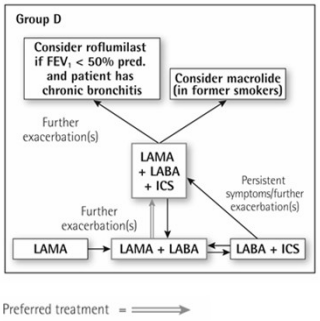
Pharmacologic treatment algorithms

Group D (continued)

- In some patients initial therapy with LABA/ICS may be the first choice. These patients may have a history and/or findings suggestive of asthma-COPD overlap. High blood eosinophil counts may also be considered as a parameter to support the use of ICS, although this is still under debate
- In patients who develop further exacerbations on LABA/LAMA therapy we suggest two alternative pathways:
  - Escalation to LABA/LAMA/ICS. Studies are underway comparing the effects of LABA/LAMA vs. LABA/LAMA/ICS for exacerbation prevention.
  - Switch to LABA/ICS. However, there is no evidence that switching from LABA/LAMA to LABA/ICS results in better exacerbation prevention. If LABA/ICS therapy does not positively impact exacerbations/symptoms, a LAMA can be added.



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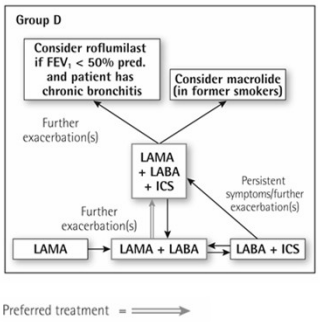
Pharmacologic treatment algorithms

Group D (continued)

If patients treated with LABA/LAMA/ICS still have exacerbations the following options may be considered:

- Add roflumilast. This may be considered in patients with an FEV1 < 50% predicted and chronic bronchitis,particularly if they have experienced at least one hospitalization for an exacerbation in the previous year.
- Add a macrolide. The best available evidence exists for the use of azithromycin. Consideration to the development of resistant organisms should be factored into decision making.
- Stopping ICS. A reported lack of efficacy, an elevated risk of adverse effects (including pneumonia) and evidence showing no significant harm from withdrawal supports this recommendation



Bronchodilators

- Important pharmacological treatment
  - Short (albuterol) and long acting (formoterol, salmeterol, aformoterol)
  - Improve emptying of lungs, exercise tolerance and reduce hyperinflation

Short Acting Anticholinergics

- SAMA
  - Ipratroprium bromide (inhaled and nebulized)
- SAMA/SABA
  - Ipratroprium bromide/albuterol (inhaled or nebulized)

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All Stages…

- SABA or SAMA should be available to individuals with all stages of COPD
- May be used as needed and with exacerbations

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Long Acting Muscarinic Antagonists

- LAMAs
  - Umeclidinium inhaled (Incruse Ellipta)
  - Tiotroprium inhaled (Spiriva Respimat or Handihaler)
  - Glycopyrrolate inhaled (Lonhala Magnair, Seebri Neohaler)
  - Aclidinium bromide inhaled (Tudorza Pressair)
  - Revefenacin inhaled (Yupelri nebulizer)

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Long Acting Beta-2 Agonists

- LABAs
  - Salmeterol (Serevent)
  - Arformoterol inhaled (Brovana, Perforomist)
  - Indacaterol inhaled (Arcapta Neohaler)
  - Olodaterol inhaled (Striverdi Respimat)
  - Formoterol (Foradil Aerolizer)

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Long Acting Muscarinic Antagonists/Long-Acting Beta-2 Agonists

- LAMA/LABA combination
  - Umeclidinium/vilanterol (Anoro Ellipta)
  - Glycopyrrolate/formoterol (Bevespi Aerosphere)
  - Tiotropium/olodaterol inhaled (Stiolto Respimat)
  - Indacaterol/glycopyrrolate inhaled (Utibron Neohaler)

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Inhaled Corticosteroids

- ICSs
  - Beclomethasone (QVAR and QVAR Redihaler)
  - Budesonide (Pulmicort Flexhaler and Respules)
  - Flunisolide (AeroBid, Aerospan)
  - Fluticasone (Flovent, Arnuity Ellipta, ArmonAir)
  - Mometasone (Asmanex HFA and Twisthaler)
  - Ciclesonide (Alvesco)

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Triple Drug Inhaler

- Fluticasone furoate/umeclidinium/ vilanterol inhaled (Trelegy Ellipta)

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Methylxanthines

- Theophylline
  - Theo-24, Theo-Dur, Uni-Dur, Slo-Bid
  - Bronchodilatation and increases the force with which the diaphragm contracts
  - 6 years and older
  - Difficult to manage and as a result has not really gained wide spread acceptance
  - Indicated for individuals with moderate to severe asthma
  - Numerous drug interactions

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Phosphodiesterase-4 Inhibitors

- PDE-4s
  - Roflumilast (Daliresp)
    - 250 mcg once daily x 4 weeks then…
    - 500 mcg po once daily
    - Caution: liver disease, mood changes
    - Decreases acute exacerbations by approximately 20% - 25%

Antimicrobials

- Macrolide antimicrobial
  - Nonsmokers
  - Best evidence exists with azithromycin 250 mg daily
  - Macrolides have anti-inflammatory and immunoregulatory effects
  - Potential QT prolongation and temporary and permanent hearing deficits

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4203601/accessed 02-24-2019

Long-term oxygen therapy

- Goal
  - To ensure adequate oxygen delivery to the vital organs by increasing the baseline PaO_2 at rest to => 60 mm Hg at sea level and/ or producing a SaO_2=> 90%.

Utilized with permission from Fitzgerald Health Education Associates, 2008

Long-term oxygen therapy

- Indications to initiate long-term (> 15 hours/day) oxygen therapy
  - PaO2 < 55 mmHg or SaO2 < 88%
  - OR… PaO2 > 55 but < 60 mmHg with right heart failure or erythrocytosis
  - Goal: SaO2 $\geq$ 90%
    - Source- www.goldcopd.org

Pulmonary Rehab

- Exercise training
- Nutrition counseling
- Education
- Conducted over 6 weeks
- Improves exercise performance and reduces dyspnea (no improvement on FEV1)

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Surgery

- Bullectomy
- Lung Volume Reduction Surgery
- Lung transplant surgery

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Global Strategy for Diagnosis, Management and Prevention of COPD

Manage Exacerbations

An exacerbation of COPD is:

"*an acute event characterized by a worsening of the patient's respiratory symptoms that is beyond normal day-to-day variations and leads to a change in medication.*"

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Management of Exacerbations

OVERALL KEY POINTS (1 of 3):

- An exacerbation of COPD is defined as an acute worsening of respiratory symptoms that results in additional therapy.
- Exacerbations of COPD can be precipitated by several factors. The most common causes are respiratory tract infections.
- The goal for treatment of COPD exacerbations is to minimize the negative impact of the current exacerbation and to prevent subsequent events.
- Short-acting inhaled beta$_2$-agonists, with or without short-acting anticholinergics, are recommended as the initial bronchodilators to treat an acute exacerbation.

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Management of Exacerbations

OVERALL KEY POINTS (2 of 3):

- Maintenance therapy with long-acting bronchodilators should be initiated as soon as possible before hospital discharge.
- Systemic corticosteroids can improve lung function (FEV_1), oxygenation and shorten recovery time and hospitalization duration. Duration of therapy should not be more than 5-7 days.
- Antibiotics, when indicated, can shorten recovery time, reduce the risk of early relapse, treatment failure, and hospitalization duration. Duration of therapy should be 5-7 days.
- Methylxanthines are not recommended due to increased side effect profiles.

 Wright, 2021 135

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Management of Exacerbations

COPD exacerbations are defined as an acute worsening of respiratory symptoms that result in additional therapy.

- They are classified as:
  - Mild (treated with short acting bronchodilators only, SABDs)
  - Moderate (treated with SABDs plus antibiotics and/or oral corticosteroids) or
  - Severe (patient requires hospitalization or visits the emergency room). Severe exacerbations may also be associated with acute respiratory failure.

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Global Strategy for Diagnosis, Management and Prevention of COPD

Manage Exacerbations: Key Points

- The most common causes of COPD exacerbations are viral upper respiratory tract infections and infection of the tracheobronchial tree.
- Diagnosis relies exclusively on the clinical presentation of the patient complaining of an acute change of symptoms that is beyond normal day-to-day variation.
- The goal of treatment is to minimize the impact of the current exacerbation and to prevent the development of subsequent exacerbations.

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Global Strategy for Diagnosis, Management and Prevention of COPD

Manage Exacerbations: Key Points

- Short-acting inhaled beta$_2$-agonists with or without short-acting anticholinergics are usually the preferred bronchodilators for treatment of an exacerbation.
- COPD exacerbations can often be prevented.

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Global Strategy for Diagnosis, Management and Prevention of COPD

Manage Exacerbations: Treatment Options

Oxygen: titrate to improve the patient's hypoxemia with a target saturation of 88-92%.

Systemic Corticosteroids: Shorten recovery time, improve lung function (FEV_1) and arterial hypoxemia (PaO_2), and reduce the risk of early relapse, treatment failure, and length of hospital stay. A dose of 30-40 mg prednisolone per day for 5 – 7 days is recommended.

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New Information Emerging…

- 40 mg daily x 5 days may be all that is necessary for exacerbation of COPD
- Equal outcomes

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Global Strategy for Diagnosis, Management and Prevention of COPD

Manage Exacerbations: Treatment Options

Antibiotics should be considered and/or prescribed with moderate – severe exacerbations:

- Three cardinal symptoms: increased dyspnea, increased sputum volume, and increased sputum purulence.
- Who require mechanical ventilation or hospitalization.

Antimicrobial Therapy

Mild to Moderate Exacerbations Antimicrobial therapy may not be indicated. If prescribed, consider spectrum of antimicrobial activity and side effects)	**If prescribed, use one of the following:** **1. Amoxicillin 875 mg 1 pill bid x 5 – 7 days** **2. TMP-SMX DS 1 pill bid x 5 – 7 days** **3. Doxycycline 100 mg 1 pill bid x 5 - 7 days** **4. Cephalosporin (cefdinir, cefpodoxime, cefuroxime)**
More Moderate - Severe Exacerbations **Severe: hospital admission**	Use one of the following: 1. Amoxicillin-clavulanate 875 mg 1 pill bid x 5 – 7 days 2. Cephalosporin: 2nd – 3rd generation 3. Azithromycin or clarithromycin 4. Respiratory fluoroquinolone (moxifloxacin or levofloxacin)

Source: Gilbert, D., Chambers, H., Saag, M, Pavia, A. (2017) The Sanford Guide to Antimicrobial Therapy (47th ed.). Sperryville, VA: Antimicrobial Therapy, Inc.

FDA Warning

- Fluoroquinolones:
  - Spontaneous tendon rupture
  - Tendonitis
  - Peripheral neuropathy
  - Aortic dissection
  - Significant hypoglycemia

https://www.forbes.com/sites/brucelee/2018/12/21/fda-warns-about-what-fluoroquinolone-antibiotics-may-do-to-your-aorta/#121315605e7e

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Global Strategy for Diagnosis, Management and Prevention of COPD

Manage Exacerbations: Indications for Hospital Admission

- Marked increase in intensity of symptoms
- Severe underlying COPD
- Onset of new physical signs
- Failure of an exacerbation to respond to initial medical management
- Presence of serious comorbidities
- Frequent exacerbations
- Older age
- Insufficient home support

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